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Pyridyl-Supported Pyrazolyl−*N*-Heterocyclic Carbene Ligands and the Catalytic Activity of Their Palladium Complexes in Suzuki−Miyaura Reactions

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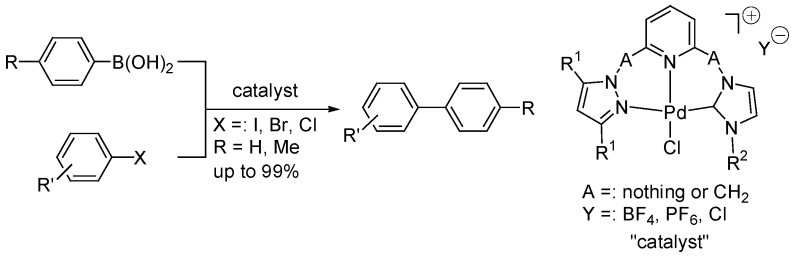

Palladium complexes of two new types of unsymmetrical pyridyl-supported pyrazolyl−*N*-heterocyclic carbene ligands were synthesized and structurally characterized. A strategy to release the steric strain of the ligand was realized by the introduction of methylene linkers to the ligand molecule. All the palladium complexes exhibited good to excellent catalytic activity in Suzuki−Miyaura reactions of phenyl or *p*-tolylboronic acid with aryl halides including iodobenzene, aryl bromides, and activated aryl chlorides under mild conditions, revealing that the new ligands are promising for the construction of highly active transition-metal catalysts.

Introduction

Development of new ligands bearing donor atoms other than phosphorus has been arousing more and more interest in the fields of coordination chemistry, homogeneous catalysis, and organic synthesis. Mixed-donor ligands have been widely used as a result of the versatility arising from the different stereoelectronic properties of the multiple coordination sites, providing unique reactivity of their metal complexes.[1] Ligand lability is an important feature of many efficient catalysts involving ligand dissociation during the catalytic cycle. But this lability may also lead to catalyst decomposition. Thus, a strong coordination site is required for a ligand to be used for the preparation of a transition-metal catalyst, especially when other labile ligands are present. In general, a balance between the stability of the organometallic catalysts and the need to incorporate dissociable ligands is desirable for highly efficient catalysts relying on ligand dissociation in the catalytic reaction. Bidentate pyridyl-containing ligands are common in coordination chemistry and homogeneous catalysis, while recently well-documented pyridyl-backboned ligands have been confined to symmetrical tridentate planar N_3 ligands of type **A** such as 2,2′:6′,2″-terpyridines,[2] 2,6-bis(imino)pyridines,[3] and 2,6-bis(oxazolinyl)pyridines[4] (Scheme 1). Very recently, our group and Karam et al. reported a new class of pseudo N_3 ligands of type **B**, that is, 2,6-bis(pyrazol-1-yl)pyridines, which have been successfully used to construct transition-metal catalysts.[5] A few tridentate *N*-heterocyclic "pincer" biscarbene ligands (CNC) of types **C**[6] and **D**,[7] and their transition-metal complexes have also recently been reported.

N-Heterocyclic carbenes (NHCs)[8] have emerged as a very useful class of ligands for coordination chemistry and transition-

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(3) Tellmann, K. P.; Gibson, V. C.; White, A. J. P.; Williams, D. J. *Organometallics* **2005**, *24*, 280 and references therein.

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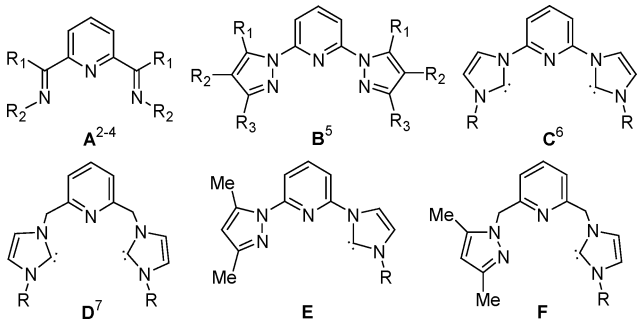
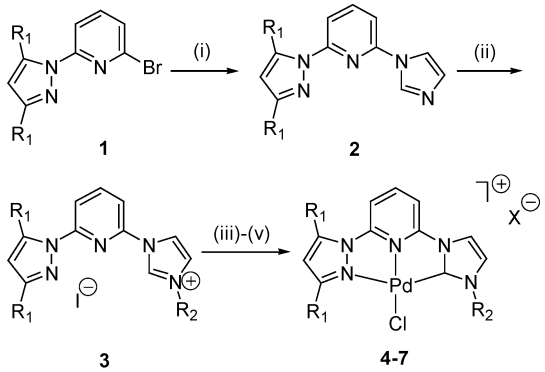
SCHEME 1. N_3, Pseudo N_3, CNC, and NNC Ligands



metal catalysis. NHC ligands have higher donor capability and basicity than phosphine and nitrogen donor ligands, forming strong metal carbene bonds, and they demonstrate less labile properties than phosphine and N-donor ligands, exhibiting a slow dissociation rate.[9,10] Other advantages of NHC ligands are their low prices and easy manipulations compared with tertiary phosphines, and usually no excess of the ligands is necessary during the catalytic reactions. A rich chemistry of pyrazolato ligands has been established over the last two decades,[11] but a few pyrazolyl-based ligands have been reported to construct transition-metal catalysts as a result of their labile coordination ability to late transition metals.[5,12] In our hands, the ruthenium-(II) complex of 2,6-bis(3,5-dimethylpyrazol-1-yl)pyridine (a ligand of type **B**) exhibited very high catalytic activity in transfer hydrogenation of ketones,[5a] suggesting that pyrazolyl can also be a useful ligand to construct transition-metal catalysts in some cases. Keeping in mind the unique properties of NHC ligands, we expect to develop new classes of non-phosphorus mixed-donor ligands of types **E** and **F** that feature a pyridyl backbone, a strong carbene carbon, and a relatively labile pyrazolyl nitrogen donor atom (Scheme 1). Herein, we report the synthesis of pyridyl-supported pyrazolyl−NHC ligands and the catalytic activity of their palladium complexes in Suzuki−Miyaura reactions.

SCHEME 2. Synthesis of Complexes 4−7[a]



	R_1	R_2	X	yield (%)
4a	Me	^{n}Bu	BF_4	65
4b	Me	$^n C_7H_{15}$	BF_4	74
5a	Me	^{n}Bu	PF_6	49
5b	Me	$^n C_7H_{15}$	PF_6	80
6a	H	^{n}Bu	BF_4	47
6b	H	$^n C_7H_{15}$	BF_4	43
7a	H	^{n}Bu	PF_6	44
7b	H	$^n C_7H_{15}$	PF_6	48

[a] Conditions: (i) imidazolatopotassium, diglyme, 130 °C, 4 days. (ii) RI, EtOAc, 90 °C, 4 days. (iii) Ag_2O, CH_2Cl_2, 25 °C, 5 h. (iv) $PdCl_2$, DMF, 90 °C, or $PdCl_2(MeCN)_2$, MeCN, 82 °C, 16 h. (v) $AgBF_4$ or $AgPF_6$, 25 °C, 5 h.

Results and Discussion

Synthesis of the Ligand Precursors and Complexes 4−7 and 10. The synthetic routes of complexes **4**−**7** and **10** are demonstrated in Schemes 2 and 3, respectively. Heteroarylation of imidazole with the known 2-bromo-6-(pyrazol-1-yl)pyridine **1**[13a] afforded 2-(imidazol-1-yl)-6-(pyrazol-1-yl)pyridine **2**, which was then efficiently transformed to the NHC precursors, that is, imidazolium iodides **3** (Scheme 2). Treatment of **3** with Ag_2O generated Ag−NHC complexes that were transmetalated with $PdCl_2$ or $PdCl_2(MeCN)_2$, and subsequently, anion exchange with $AgBF_4$ or $AgPF_6$ afforded Pd−NHC complexes **4**−**7** in 43−80% yields. A reaction of the known **8**[13b] with 1-mesitylimidazole quantitatively formed imidazolium chloride **9**, which was treated with Ag_2O and then transmetalated with $PdCl_2$ to afford complex **10** in 82% yield (Scheme 3). All the new compounds were fully characterized. Complexes **4**−**7** and **10** and their ligand precursors are air- and moisture-stable. When R_2 in **4**−**7** is methyl, ethyl, or propyl, the newly formed complexes are bestowed with very poor solubility. The introduction of *n*-butyl or *n*-heptyl to the imidazolyl ring remarkably increases the solubility of **3** and **4**−**7** in organic solvents. Long alkyl groups

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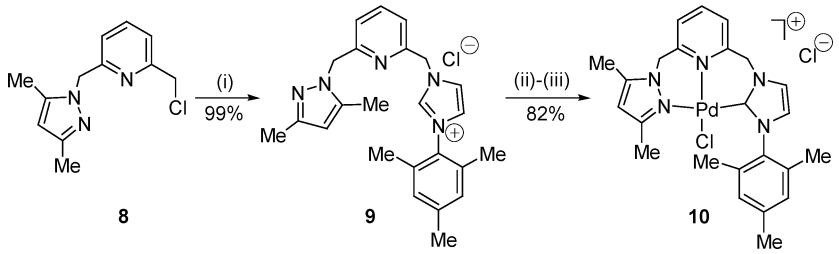
SCHEME 3. Synthesis of Complex 10[a]



[a] Conditions: (i) 1-mesitylimidazole, *i*-PrOH, 82 °C, 5 days. (ii) Ag_2O, CH_2Cl_2, 25 °C, 5 h. (iii) $PdCl_2$, DMF, 90 °C, 16 h.

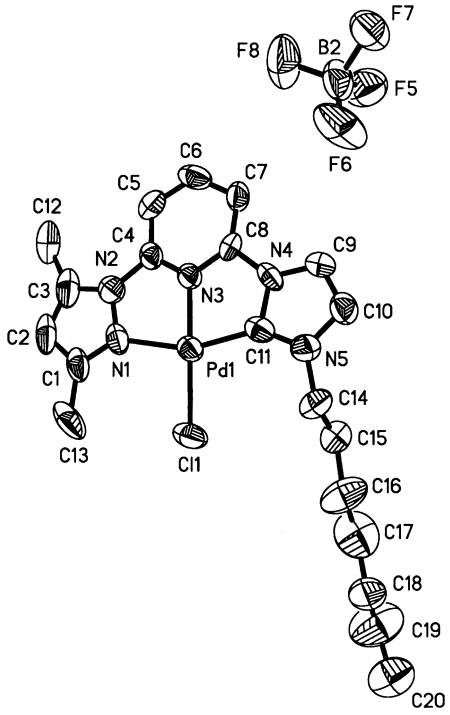


FIGURE 1. Perspective view of **4b**. Selected bond lengths (angstroms) and angles (deg): Pd(1)−C(11) 1.949(13), Pd(1)−N(1) 2.128(10), Pd(1)−N(3) 1.955(9), Pd(1)−Cl(1) 2.285(3), N(1)−Pd(1)−C(11) 158.0(5), N(3)−Pd(1)−Cl(1) 179.6(3).

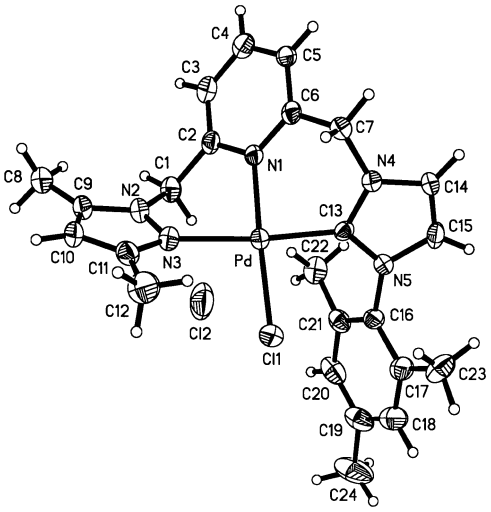


FIGURE 2. Perspective view of **10**. Selected bond lengths (angstroms) and angles (deg): Pd−C(13) 1.975(6), Pd−N(3) 2.078(5), Pd−N(1) 2.029(5), Pd−Cl(1) 2.2818(18), N(3)−Pd−C(13) 174.3(2), N(1)−Pd−Cl(1) 177.86(14).

as substituents are known to improve the solubility of NHC-containing compounds.[14] When R_2 is *n*-heptyl, compounds **3** and **4**−**7** are soluble in organic solvents, independent of the anions (Cl^-, BF_4^-, or PF_6^-). However, when R_2 is *n*-butyl and the anion is chloride, the complex is hardly soluble even in DMF, therefore, anion exchange must be carried out with $AgBF_4$ or $AgPF_6$ for the newly formed complex to gain a better solubility.

X-ray Crystal Structures of the Complexes. The solid-state molecular structures of the ligand precursors **3a** (R_1 = Me, R_2 = *n*-Bu) and **9** and complexes **4b** and **10** were confirmed by an X-ray crystallographic study.[15] The single-crystal structures of **4b** and **10** feature a cationic palladium center that coordinates with a NHC carbene carbon and pyridyl and pyrazolyl nitrogen atoms. The average bond lengths of the Pd−NHC carbene carbon, Pd-pyridyl nitrogen, Pd-pyrazolyl nitrogen, and Pd−Cl in **4b** are 1.959(11), 1.958(8), 2.094(9), and 2.275(3) Å, respectively, revealing two strong and one relatively labile coordination bonds in **4b** (Figure 1). The pyridyl nitrogen−Pd−Cl bond angle is close to 180° (average 179.3(5)°), and the average pyrazolyl N−Pd−NHC carbene carbon bond angle is 158.4(5)°. In complex **10**, the Pd−NHC carbene carbon and Pd−Cl bond lengths are 1.975(6) and 2.2818(18) Å, and the bond lengths of pyridyl nitrogen−Pd and pyrazolyl nitrogen−Pd are 2.029(5) and 2.078(5) Å, respectively (Figure 2), demonstrating that the Pd−C and pyridyl N−Pd bonds are lengthened and the pyrazolyl N−Pd bond is shortened as compared with those in **4b**. The pyridyl N−Pd−Cl bond angle in **10** is 177.86(14)°, and the pyrazolyl N−Pd−NHC carbene carbon bond angle is 174.3(2)°, which is much bigger than its analogue in **4b**, suggesting that introduction of two methylene linkers to the ligand molecule decreases the steric strain of the ligand and thus stabilizes the newly formed complexes. It usually occurs that transition-metal atoms cannot be incorporated into a pyridyl-functionalized N_3 and pseudo N_3 ligand as a result of the specific strain from the ligand. Recent reports on NHCs and their complexes have demonstrated that P, O, or N donor-containing chelating coordination groups can be attached to the

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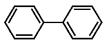
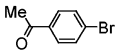
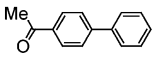
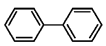
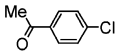
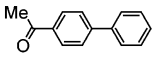
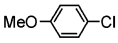
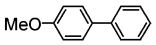
(15) Crystal data for **4b**: $C_{20}H_{27}BClF_4N_5Pd$, triclinic, $P\bar{1}$, a = 13.5919(14) Å, b = 19.444(2) Å, c = 20.692(2) Å, V = 4803.6(9) Å^3, Z = 8, T = 293(2) K, R(F) = 7.00% for 17 605 reflections ($3.14 \le 2\theta \le 51.0°$). Crystal data for **10**: $C_{24}H_{27}Cl_2N_5Pd$, orthorhombic, Pbcn, a = 22.812(3) Å, b = 15.838(2) Å, c = 14.956(2) Å, V = 5403.8(13) Å^3, Z = 8, T = 293(2) K, R(F) = 6.03% for 5888 observed reflections ($4.14 \le 2\theta \le 54.00°$). The crystallographic data for the ligand precursors **3a** and **9** are presented in the Supporting Information.

TABLE 1. Suzuki−Miyaura Reactions of $PhB(OH)_2$ with Aryl Halides Catalyzed by 4a, 4b, 5b, and 10

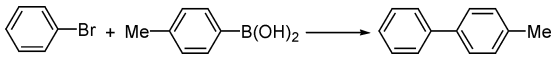
aryl halide[a]	catalyst (mol%)	time (h)	product	yield[b] (%)
 (**11a**)	**4a** (0.5)	2	 (**12a**)	97
 (**11b**)	**4a** (1.0)	5	**12a**	96
11b	**4b** (1.0)	5	**12a**	97
11b	**5b** (1.0)	5	**12a**	96
11b	**10** (1.0)	5	**12a**	97
 (**11c**)	**4a** (0.5)	3	 (**12b**)	99
 (**11d**)	**4a** (5.0)	24[c]		52
11d	**4b** (5.0)	24[c]	**12a**	52
11d	**5b** (5.0)	24[c]	**12a**	42
11d	**10** (5.0)	24[c]	**12a**	48
 (**11e**)	**4a** (5.0)	24[c]		86
11e	**4b** (5.0)	24[c]	**12b**	87
11e	**5b** (5.0)	24[c]	**12b**	80
11e	**10** (5.0)	24[c]	**12b**	86
 (**11f**)	**4a** (5.0)	24[c]	 (**12c**)	30
11f	**4b** (5.0)	24[c]	**12c**	30
11f	**5b** (5.0)	24[c]	**12c**	22
11f	**10** (5.0)	24[c]	**12c**	27

[a] Conditions: aryl halide, 2.0 mmol; $PhB(OH)_2$, 2.5 mmol; K_2CO_3, 4 mmol; solvent (DMF/H_2O, v/v = 20:1), 8 mL; 80 °C; 0.1 MPa. [b] Isolated yields. [c] 120 °C.

carbene as hemilabile arms to stabilize the NHC transition-metal complexes.[9,10] Thus, the structural modification of a ligand, as exemplified by the synthesis of **10** (Scheme 3), is necessary to increase the specific bond angle between the relatively labile coordinative site, metal center, and the strong donor atom, which might help a metal to be complexed with the ligand.

Suzuki−Miyaura Reactions of $PhB(OH)_2$ with Aryl Halides Catalyzed by 4a, 4b, 5b, and 10 under Unoptimized Reaction Conditions. NHC transition-metal catalysts have been successfully employed in Suzuki−Miyaura reactions.[16] Recently, a few pyridyl-functionalized mono-NHC ligands have also been

TABLE 2. Optimization of Suzuki−Miyaura Reaction Conditions[a]



entry	base	solvent	time (h)	yield[b] (%)
1	K_2CO_3	DMF	10	74
2	K_2CO_3	dioxane	10	50
3	K_2CO_3	CH_3CN	10	26
4	K_2CO_3	THF	10	19
5	K_2CO_3	EtOH	10	83
6	K_2CO_3	$EtOH/H_2O$ (v/v = 10:1)	1.5	95
7	K_2CO_3	DMF/H_2O (v/v = 20:1)	1.5	97
8	K_2CO_3	DMF/H_2O (v/v = 10:1)	1.5	98
9	K_2CO_3	DMF/H_2O (v/v = 5:1)	1.5	90
10	K_3PO_4	DMF/H_2O (v/v = 10:1)	0.5	99
11	Cs_2CO_3	DMF/H_2O (v/v = 10:1)	<0.5	100
12	LiOH	DMF/H_2O (v/v = 10:1)	1.5	91
13	KOH	DMF/H_2O (v/v = 10:1)	1.5	49

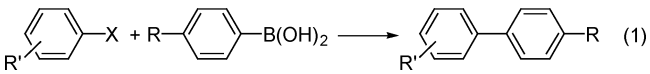
[a] Conditions: bromobenzene, 1.0 mmol; *p*-tolylboronic acid, 1.5 mmol; base, 2.0 mmol; solvent, 5 mL; 80 °C; catalyst **6a**, 2.0 mol%. [b] GC yields (average of two runs using biphenyl ether as the internal standard).

TABLE 3. Screening of the Catalysts for the Suzuki−Miyaura Reaction[a]

entry	1	2	3	4	5	6	7	8	9
catalyst	**4a**	**4b**	**5a**	**5b**	**6a**	**6b**	**7a**	**7b**	**10**
yield[b,c] (%)	91(99)	89(95)	85(97)	79(95)	99	97	98	96	60(86)[d]

[a] Conditions: bromobenzene, 1.0 mmol; *p*-tolylboronic acid, 1.5 mmol; Cs_2CO_3, 2.0 mmol; solvent, DMF/H_2O (v/v = 10:1), 5.0 mL; catalyst, 2.0 mol%; 80 °C; 15 min. [b] GC yield (average of two runs using biphenyl ether as the internal standard). [c] yields at 30 min in parentheses. [d] 110 °C.

shown their promising properties for constructing efficient catalysts.[17] Combining the lability of pyrazolyl as a ligand and the strong σ-donor property of the pyridyl-functionalized NHC moiety, it is reasonable to expect that the present complexes **4**−**7** and **10** are potential efficient catalysts for Suzuki−Miyaura reactions (eq 1). Under unoptimized reaction conditions, as



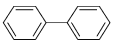
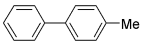
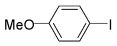
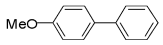
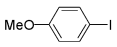
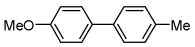
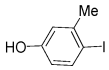
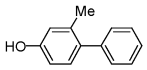
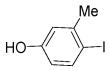
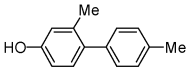
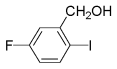
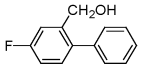
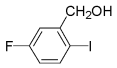
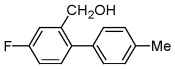
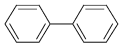
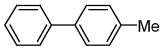
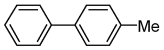
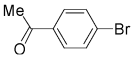
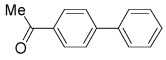
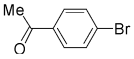
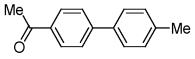
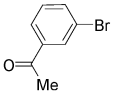
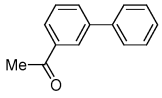
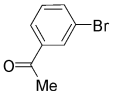
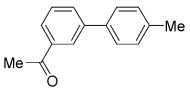
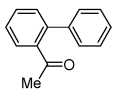
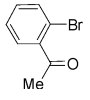
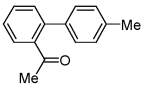
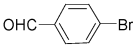
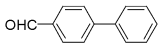
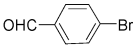
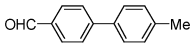
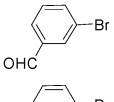
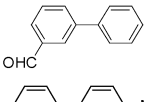
(1)

shown in Table 1, the coupling reactions of selected aryl halides with $PhB(OH)_2$ were carried out in a mixture of solvents (DMF/H_2O, v/v = 20:1) at 80 °C using K_2CO_3 as the base. The catalyst, with a loading of 0.5−5.0 mol%, was employed without an additional ligand. Complexes **4a**, **4b**, **5b**, and **10** exhibited excellent catalytic activity in the Suzuki−Miyaura reactions of $PhB(OH)_2$ with iodobenzene, aryl bromides, and activated chloride, that is, 4′-chloroacetophenone **11e** (Table 1). The reactions of iodobenzene **11a**, bromobenzene **11b**, and 4′-bromoacetophenone **11c** gave the coupling products in >96% isolated yields. At a higher temperature, that is, 120 °C, reactions of the activated aryl chloride **11e** afforded the product in 80−87% yields. Unreactive chlorobenzene **11d** and 4-methoxychlorobenzene **11f** gave biphenyl derivatives in moderate (42−52%) to low (22−30%) yields, respectively. The alkyl or aryl substituent on the imidazolylidene moiety did not obviously affect the catalytic activity of the complexes. The order of the anions on the catalytic activity of the complexes is BF_4^- > Cl^-

(16) (a) Marion, N.; Navarro, O.; Mei, J. G.; Stevens, E. D.; Scott, N. M.; Nolan, S. P. *J. Am. Chem. Soc.* **2006**, *128*, 4101. (b) Phan, N. T. S.; Sluys, M. V. D.; Jones, C. W. *Adv. Synth. Catal.* **2006**, *348*, 609. (c) Kim, J.-H.; Kim, J.-W.; Shokouhimehr, M.; Lee, Y.-S. *J. Org. Chem.* **2005**, *70*, 6714. (d) Hadei, N.; Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G. *Org. Lett.* **2005**, *7*, 1991. (e) Miura M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2201. (f) Navarro, O.; Kelly, R. A., III; Nolan, S. P. *J. Am. Chem. Soc.* **2003**, *125*, 16194. (g) Herrmann, W. A.; Öfele, K.; Preysing, D. V.; Schneider, S. K. *J. Organomet. Chem.* **2003**, *687*, 229.

(17) Selected recent reports, see: (a) Chiu, P. L.; Lai, C.-L.; Chang, C.-F.; Hu, C.-H.; Lee, H. M. *Organometallics* **2005**, *24*, 6169. (b) Frey, G. D.; Schütz, J.; Herdtweck, E.; Herrmann, W. A. *Organometallics* **2005**, *24*, 4416 and references therein.

TABLE 4. Suzuki−Miyaura Reactions Catalyzed by Complex 6a[a]

entry	ArX	R in 4-R-$C_6H_4(OH)_2$	catalyst (mol%)	time (h)	product	yield[b] (%)
1		H	0.5	0.2		97
2		Me	0.5	0.2		97
3		H	1.0	0.2		98
4		Me	1.0	0.2		98
5		H	2.0	0.5		99
6		Me	2.0	0.5		99
7		H	1.0	1.0		99
8		Me	1.0	1.0		97
9		H	1.0	1.0		99[c]
10		Me	1.0	10		97[c]
11		Me	2.0	0.5		99[c]
12		H	1.0	0.5		98
13		Me	1.0	0.5		98
14		H	1.0	0.5		99
15		Me	1.0	0.5		98
16		H	1.0	1.0		97
17		Me	2.0	1.0		97
18		H	1.0	0.5		99
19		Me	1.0	0.5		98
20		H	1.0	0.5		98
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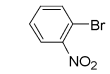
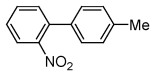
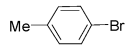
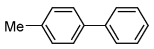
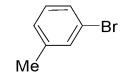
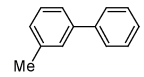
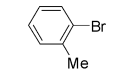
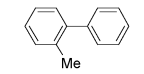
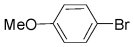
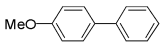
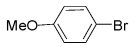
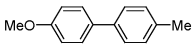
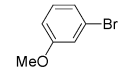
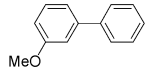
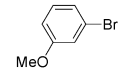
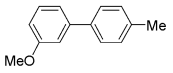
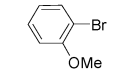
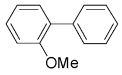
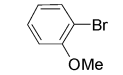
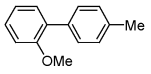
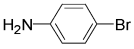
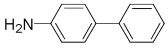
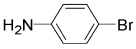
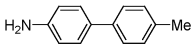
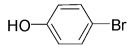
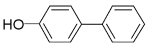
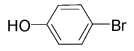
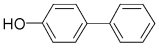
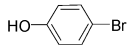
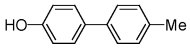
25		Me	1.0	0.5		98
26		H	3.0	2.0		98[c]
27		H	3.0	2.0		98[c]
28		H	3.0	24		97[c]
29		H	3.0	2.0		95
30		Me	3.0	2.0		94
31		H	3.0	2.0		95
32		Me	3.0	2.0		95
34		H	3.0	5.0		90
35		Me	3.0	5.0		89
36		H	3.0	5.0		79
37		Me	3.0	5.0		80
38		H	3.0	5.0		55
39		H	3.0	5.0[d]		90
40		Me	3.0	5.0[d]		87

[a] Conditions: ArX, 1.0 mmol; arylboronic acid, 1.5 mmol; Cs_2CO_3, 2.0 mmol; DMF/H_2O (v/v = 10:1), 5 mL; 80 °C. [b] Isolated yields. [c] About 10% of the self-coupling product of arylboronic acid was detected. [d] 120 °C.

> PF_6^-. The complexes with tetrafluoroborate as the anion, that is, **4a** and **4b**, exhibited the highest catalytic activity, while the PF_6^- complex, that is, **5b**, demonstrated the lowest catalytic activity. With chloride as the anion, complex **10** showed a catalytic activity between those of **4a**, **4b**, and **5b**.

Optimization of Suzuki−Miyaura Reaction Conditions and Screening of the Catalysts. When complex **6a** was used as the catalyst, the coupling reaction of bromobenzene with *p*-tolylboronic acid was carried out under different conditions to optimize the reaction conditions (Table 2). It was found that a mixture of DMF/H_2O (v/v = 10:1) and Cs_2CO_3 are the suitable solvent and base for the reaction at 80 °C, respectively. Under the stated conditions, only Cs_2CO_3 prompted the aryl halide to reach complete conversion. Presence of water remarkably accelerated the reaction (Table 1, entries 1, 5−7). The reaction proceeded slowly at temperatures below 80 °C. Under the optimized conditions, the reaction of bromobenzene with *p*-tolylboronic acid reached completion to selectively form the desired coupling product within half an hour (Table 2, entry 11).

When the same reaction conditions were used, the catalytic activity of complexes **4**−**7** and **10** were tested, as shown in Table 3. While complexes **6a**,**b** and **7a**,**b** exhibited high catalytic activities, **6a** showed the highest catalytic activity (Table 3, entries 5−8). However, the corresponding complexes with substituents on the pyrazolyl ring, that is, **4a**,**b** and **5a**,**b**, demonstrated lower catalytic activity, exhibiting comparable catalytic efficiency only with a longer period (Table 3, entries 1−4). These results reveal that alkyl substituents on the pyrazolyl ring obviously decrease the catalytic activity of the complexes, presumably as a result of steric and electronic effects. Complexes with BF_4 as the anion are bestowed with higher catalytic activity than their corresponding PF_6 analogues. Under the same conditions, complex **10** showed the lowest catalytic activity. Complex **10** is rather stable at 80 °C. It may generate catalytically active Pd(0) species very slowly, resulting in the slow initiation of the reaction and the relatively low conversion of the aryl halide even at 110 °C within the test period (Table 3, entry 9).

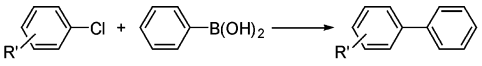
Suzuki−Miyaura Reactions of Aryl Iodides and Bromides Catalyzed by 6a. Using complex **6a** as the catalyst and Cs_2CO_3 as the base, coupling reactions of aryl iodides and bromides with phenyl or *p*-tolylboronic acid were carried out in DMF in the presence of a small amount of water at 80 °C. With 0.5−2.0 mol% of the catalyst, aryl iodides easily underwent the reaction to give the desired products in ≥97% yields (Table 4,

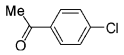
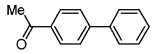
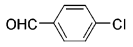
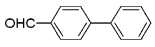
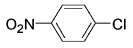
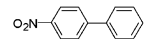
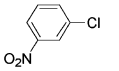
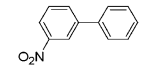
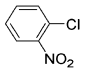
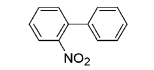
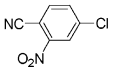
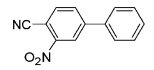
entries 1−8). The reactions of iodobenzene and 4-methoxyiodobenzene were completed within 12 min. In a similar fashion, the reactions of aryl bromides were also efficiently carried out with 1.0−3.0 mol% of the catalyst. Loading of the catalyst obviously influenced the reaction rate. With 2.0 mol% of the catalyst, the coupling of bromobenzene with *p*-tolylboronic acid reached completion within half an hour (entry 11). However, with 1.0 mol% of the catalyst, the same reaction could only achieve comparable results within 10 h (entry 10). It is noteworthy that the reaction usually went fast during the first 2 h and then became very slow. The coupling reactions of activated bromides such as 3- and 4-acetylbromobenzene, 3- and 4-bromobenzaldehydes, or 2- and 4-nitrobromobenzenes were efficiently achieved to afford the desired products in ≥97% isolated yields with a 1.0 mol% loading of the catalyst within half an hour (entries 12−15 and 18−25). Presumably as a result of steric hindrance, the reactions of 2-acetylbromobenzene proceeded relatively slower than those of 3- and 4-acetylbromobenzenes, and the reactions approached completion over a period of 1 h (entries 16 and 17). Reactions of relatively unreactive bromides bearing an alkyl or alkoxy as the substituent achieved with a loading of 3.0 mol% catalyst afforded the coupling products in 89−98% yields over a period of 2−5 h (entries 26, 27, and 29−35). The relatively hindered substrate, that is, 2-methylbromobenzene, only demonstrated poor reactivity within 24 h (entry 28). Reactions of unreactive aryl bromides bearing a functional group such as an amino or hydroxyl group afforded the coupling products in moderate to good yields (55−90% yields) though with a longer period. The reactions were more efficiently achieved at a higher temperature, for example, 120 °C (entries 36−40). In most cases, no obvious reactivity difference was found between phenylboronic acid and *p*-tolylboronic acid, except the cases of entries 9 and 10 (Table 4).

All the complex catalysts are stable at temperatures below 80 °C under the reaction conditions, and no palladium black formation was observed during the reaction at these temperatures. When the coupling reactions were fast, for example, reaching a complete conversion for the aryl halide within half an hour, no palladium black was generated during the reaction. In some cases, when the reaction was slow at 80 °C or the reaction was carried out at a temperature above 80 °C, a small amount of palladium black could be formed as the reaction proceeded.

Suzuki−Miyaura Reactions of Aryl Chlorides Catalyzed by 6a. The reactions of activated aryl chlorides with phenylboronic acid were carried out with 5.0 mol% of catalyst **6a** at 120 °C, and the desired coupling products were obtained in isolated yields up to 98% (Table 5). Somehow, the reaction of *m*-nitrochlorobenzene only afforded the coupling product in 30% isolated yield, although a complete conversion of *m*-nitrochlorobenzene was reached (Table 5, entry 4). The chloride substrates exhibited much lower reactivity than their iodide and bromide analogues. Unreactive aryl chlorides such as chlorobenzene and 4-methylchlorobenzene underwent the coupling reactions very slowly under the stated conditions.

TABLE 5. Suzuki−Miyaura Coupling of Activated Aryl Chlorides[a]



entry	ArCl	time (h)	product	yield[b,c] (%)
1		5.0		68 (85)
2		5.0		80 (94)
3		2.0		95 (97)
4		5.0		30 (100)
5		5.0		84 (85)
6		1.0		98 (100)

[a] Conditions: aryl chloride, 1.0 mmol; phenylboronic acid, 1.5 mmol; Cs_2CO_3, 2.0 mmol; solvent, DMF/H_2O (v/v = 10:1), 5 mL; 120 °C; catalyst **6a**, 5.0 mol%. [b] Isolated yields. [c] GC conversions in parentheses.

Conclusion

In summary, two new types of unsymmetrical pyridyl-supported pyrazolyl−NHC ligands have been developed to construct transition-metal catalysts. Structural modification by introducing methylene linkers to the ligand molecule was realized to release the specific steric strain of the ligand. That all the palladium complexes of the present NNC ligands exhibited good to excellent catalytic activity in Suzuki−Miyaura reactions of aryl halides has been implied that the new ligands are very promising for the construction of highly active transition-metal catalysts.

Experimental Section

Synthesis of 2-(Imidazol-1-yl)-6-(3,5-dimenthylpyrazol-1-yl)-pyridine (2a). A mixture of potassium (0.63 g, 16.0 mmol), imidazole (1.09 g, 16.0 mmol), and dry diglyme (50 mL) was vigorously stirred at 70 °C. Until beads of the molten potassium were not evident, 2-bromo-6-(3,5-dimenthylpyrazol-1-yl)pyridine (4.00 g, 16.0 mmol) was added. The reaction mixture was heated at 130 °C for 96 h and then quenched by methanol (1.0 mL). After being cooled to ambient temperature, the mixture was filtered through Celite, and all the volatiles were removed under reduced pressure. Isolation by silica gel column chromatography with ethyl acetate as the eluent afforded **2a** as a white solid (3.50 g, 92%).

Synthesis of 2-(3-*n*-Heptylimidazol-3-ium-1-yl)-6-(3,5-dimethylpyrazol-1-yl)pyridine Iodide (3b). A mixture of **2a** (1.64 g, 6.85 mmol) and iodoheptane (3.10 g, 13.70 mmol) in ethyl acetate (50 mL) was stirred at 90 °C for 4 days to give a white precipitate. The crude product was isolated by filtration, washed with diethyl ether (3 × 10 mL), and dried in vacuo to afford **3b** as a white solid (3.11 g, 97%).

Synthesis of [PdCl(NNC^{NHC}-*n*-C_7H_{15})]BF_4 (4b). To a solution of the imidazolium salt **3b** (1.00 g, 2.15 mmol) in CH_2Cl_2 (50 mL), was added Ag_2O (0.25 g, 1.08 mmol). The mixture was stirred in the dark at ambient temperature for 5 h. After all the volatiles were removed under reduced pressure, $PdCl_2(CH_3CN)_2$ (0.56 g, 2.15 mmol) and CH_3CN (50 mL) were added and stirred at 82 °C for 16 h. After the mixture was cooled to ambient temperature, $AgBF_4$ (0.42 g, 2.15 mmol) was added and further stirred for 5 h. The mixture was filtered through Celite, and all the volatiles were removed under reduced pressure to afford a pale yellow residue. Recrystallization from a solution of CH_2Cl_2 at −20 °C afforded the product **4b** as a pale yellow solid (0.90 g, 74%). Yellow crystals suitable for X-ray crystallographic analysis were grown by diffusion

of diethyl ether vapor into a saturated solution of **4b** in acetonitrile at room temperature.

Typical Procedure for the Suzuki−Miyaura Reactions. In a typical run, a mixture of aryl halide (1.0 mmol), phenylboronic acid (1.5 mmol), Cs_2CO_3 (2.0 mmol), and a catalyst in 5 mL of solvent (DMF/H_2O, v/v = 10:1) was stirred under the stated conditions. After the reaction mixture was cooled to ambient temperature, 15 mL of diethyl ether and 15 mL of water were added. The organic layer was separated, and the aqueous phase was extracted with 10 mL of diethyl ether. The combined organic phase was dried over anhydrous $MgSO_4$ and then filtered. All the volatiles were removed under reduced pressure to give a crude product that was subject to purification by silica gel column chromatography to afford the pure product. The products were identified by comparison with the authentic samples and/or by ^1H and $^{13}C\{^1H\}$ NMR measurements. The isolated yields are based on the average results for two runs.

Acknowledgment. We are grateful to the "Hundred Talented Program" Funding of Chinese Academy of Sciences for support of this research.

Supporting Information Available: Experimental details, copies of NMR spectra for new compounds, and X-ray crystallographic files for **3a**, **4b**, **9**, and **10** (files in CIF, 95 pages). This material is available free of charge via the Internet at http://pubs.acs.org.

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