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A novel *P*,*S*-heterodonor ligand and palladium(0) complex catalyzed Suzuki cross-coupling reaction

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Abstract—Axially dissymmetric *P*,*S*-heterodonor ligand **L3** synthesized from BINOL is an effective promoter in the palladium(0)-catalyzed Suzuki cross-coupling reaction of phenylboronic acid with aryl bromides and iodide at 60–80 °C. On the basis of ^{13}C and ^{31}P NMR spectroscopic investigation and X-ray diffraction, it was revealed that *N*,*N*-dimethylthiocarbamate–phosphine ligand **L3** might be a *P*,*S*-heterodonor bidentate ligand to palladium(0) center.

Palladium-catalyzed Suzuki cross-coupling reaction of aryl halides with arylboronic acids is a powerful method for accessing structurally diversified biaryls.[1,2] Cross-coupling between aryl bromides,[3] chlorides,[4] fluorides,[5] tosylates,[6,7] and boronic acids is possible by using palladium complexes with sterically hindered and electron-rich phosphines ligands[8,9] or *N*-heterocyclic carbene (NHC) ligand such as those developed by Buchwald and co-workers[4b,10] Fu,[4a,11] and Herrmann,[12] respectively. The formation of asymmetric, multidentate ligands, focusing on the aspects of hemilability,[13] has been of great interest. In particular, the improved catalytic activity of transition metal complexes with hemilabile ligands has been received considerable attention in recent years.[14] The hemilabile P/S$^-$,[15] P/S,[16] P/O,[17] and N/O$^-$,[18] ligand systems to rhodium, palladium, nickel, or other transition metals are well known. Those P/S ligands have been successfully used in asymmetric allylic substitution reactions[19] and Heck reaction.[20] However, only one example of *P*/*S* ferrocenediyl ligands used in Suzuki cross-coupling reaction was reported.[21] Recently, we are interested in the axially chiral *P*,*S*-heterodonor ligands derived from (*R*)-BINOL [(*R*)-(+)-1,1′-bi-2-naphthol] in asymmetric catalysis and found that they are effective chiral ligands in asymmetric palladium-catalyzed allylic substitution of 1,3-diphenyl-2-propenyl acetate by dimethyl malonate in the presence of organic base.[22] Herein we report the Suzuki cross-coupling reaction of various aryl bromides and iodide with phenylboronic acid catalyzed by a Pd(0) complex derived from *P*,*S*-heterodonor ligand and Pd(dba)$_2$.

Heterodonor ligands **L1**–**L3** shown in Figure 1 were prepared from BINOL according to the previous

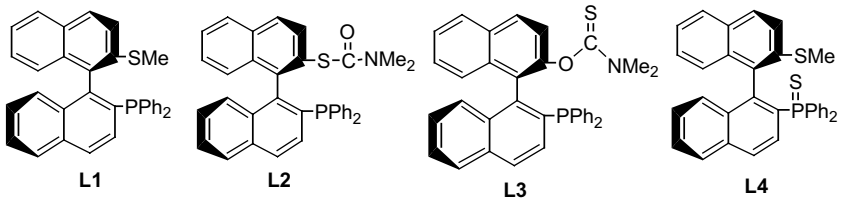

Figure 1.

Keywords: Cross-coupling reaction; Aryl bromides; Phenylboronic acid; *N*,*N*-Dimethylthiocarbamate–phosphine ligand; *P*,*S*-Heterodonor bidentate ligand.
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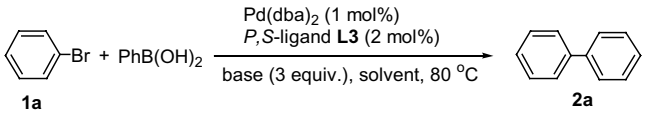
Table 1. Screening of solvents and bases for Suzuki cross-coupling of bromobenzene with phenylboronic acid using *P*,*S*-heterodonor ligand **L3**[a]



Entry	Base	Solvent	Time (h)	Yield (%)[b]
				2a
1	^{t}BuOK	PhMe	9	64
2	^{t}BuOK	DMF	10	69
3	^{t}BuOK	1,4-Dixane	10	22
4	^{t}BuOK	DMSO	4	94
5	^{t}BuOK	^{i}PrOH	10	16
6	Cs_2CO_3	DMSO	38	10
7	Na_2CO_3	DMSO	38	9
8	KOH	DMSO	13	16
9	$K_3PO_4{\cdot}3H_2O$	DMSO	10	82
10[c]	^{t}BuOK	DMSO	4	15
11[d]	^{t}BuOK	DMSO	4	90
12[e]	^{t}BuOK	DMSO	6	58

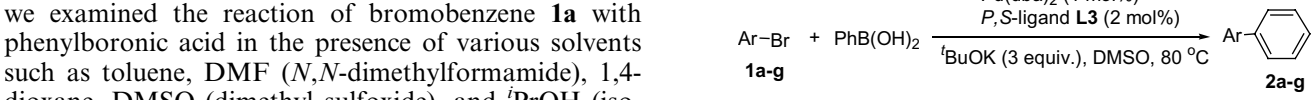
[a] Reactions were carried out with 1.0 equiv of bromobenzene, 1.5 equiv of phenylboronic acid, and 3.0 equiv of base in 3 mL of solvent, 1 mol% of $Pd(dba)_2$ used as the catalyst precursor with 2 mol% of *P*,*S*-ligand **L3**.
[b] Isolated yield.
[c] 1.5 equiv of base was used.
[d] 1 mol% of *P*,*S*-ligand **L3** was used.
[e] No ligand was used.

literature.[23] Ligand **L4** was prepared upon heating ligand **L1** with sulfur in toluene at 120 °C for 10 h. These heterodonor ligands **L1**–**L4** were examined in the Suzuki cross-coupling reaction catalyzed by $Pd(dba)_2$. On a preliminary survey, we found that the palladium(0) complex derived from *P*,*S*-heterodonor ligand **L3** with $Pd(dba)_2$ was the best catalyst in this reaction.[24] The corresponding Suzuki cross-coupling products could be obtained in higher yields in the presence of ligand **L3**. In our next search for optimal reaction conditions, we examined the reaction of bromobenzene **1a** with phenylboronic acid in the presence of various solvents such as toluene, DMF (*N*,*N*-dimethylformamide), 1,4-dioxane, DMSO (dimethyl sulfoxide), and ^{i}PrOH (isopropanol) with base ^{t}BuOK. The results are summarized in Table 1. The best yield of **2a** (94%) was obtained when DMSO was used as solvent for 4 h (Table 1, entries 1–5). Since a base is required in this cross-coupling reaction, we also examined different bases such as ^{t}BuOK, Cs_2CO_3, Na_2CO_3, KOH, and $K_3PO_4{\cdot}3H_2O$ in this reaction. We found that ^{t}BuOK is a better base for the coupling reaction of **1a** with phenylboronic acid compared with others under the identical conditions (Table 1, entries 4, and 6–9). We also found that 3.0 equiv of base was necessary because using 1.5 equiv of ^{t}BuOK as a base, the cross-coupling product **2a** was isolated in low yield (15%) (Table 1, entry 10). In the presence of 1.0 mol% of ligand **L3**, the yield was slightly decreased to 90% (Table 1, entry 11). Although many palladium catalysts themselves were proved to be excellent catalysts for biaryl coupling even in the absence of phosphine ligands,[25,26] we found that $Pd(dba)_2$ was less effective (58% isolated yield) in DMSO compared with those in the presence of ligand **L3** (Table 1, entry 12). Therefore, the combination of **L3** with $Pd(dba)_2$ is required to get **2a** in higher yield.

A wide range of electronically and structurally diverse aryl bromides with phenylboronic acid can be cross-coupled efficiently under these optimized conditions. The results are summarized in Table 2. As can be seen from Table 2, with respect to the electron-rich, electron-neutral, and electron-poor aryl bromides, they reacted with phenylboronic acid smoothly to provide the corresponding biaryl products in good to high yields in most cases (Table 2, entries 1–5). Using sterically hindered aryl bromide **1f** as substrate, the corresponding cross-coupling product was also obtained in high yield (99%) (Table 2, entry 6). In addition, the cross-coupling reaction of iodobenzene with phenylboronic acid can be carried out at lower temperature (60 °C) under the similar conditions to give **2a** in high yield (91%) (Table 2, entry 7).

Since the Pd complex derived from *N*,*N*-dimethylthiocarbamate–phosphine ligand **L3** and $Pd(dba)_2$ in situ is the active catalyst for Suzuki cross-coupling reaction of aryl halides with phenylboronic acid, we next investigated the NMR spectroscopic behavior of this complex in solution to gain more information of the coordination style of ligand **L3** to palladium(0) center. As it is well known that phosphine and sulfur atom can both coordinate to palladium(II) center,[19,21] we believe that ligand **L3** is a *P*,*S*-bidentate ligand to Pd(0) center. The evidence was obtained from ^{13}C and ^{31}P NMR measurements of **L3** in the absence or presence of $Pd(dba)_2$ in DMSO-d_6. We found that the thiocarbamate signal (C=S) of **L3** in ^{13}C NMR spectrum was downfield shifted from 185.19 to 188.47 ppm. Simi-

Table 2. Palladium-catalyzed Suzuki cross-coupling of aryl bromides and isobenzene with phenylboronic acid using *P*,*S*-heterodonor ligand **L3**[a]



Entry	ArX	Time (h)	Yield (%)[b]
			2
1	**1a**: Bromobenzene	4	**2a**, 94
2	**1b**: 2-Bromotoluene	4	**2b**, 99
3	**1c**: 4-Bromobiphenyl	4	**2c**, 81
4[c]	**1d**: 4-Bromochlorobenzene	15	**2d**, 93
5[d]	**1e**: 4-Bromoanisole	9.5	**2e**, 52
6	**1f**: 1-Bromo-3-5-dimethylbenzene	4	**2f**, 99
7[e]	**1g**: Iodobenzene	6	**2g**, 91

[a] Reactions were carried out with 1.0 equiv of aryl bromides, 1.5 equiv of phenylboronic acid, and 3.0 equiv of ^{t}BuOK in 3 mL of DMSO, 1% of $Pd(dba)_2$ used as the catalyst precursor with 2 mol% of *P*,*S*-ligand **L3**.
[b] Isolated yield.
[c] DMF was used as the solvent.
[d] $K_3PO_4{\cdot}3H_2O$ was used as the base and the reaction was carried out at 120 °C.
[e] The reaction was carried out at 60 °C.

larly, the ^{31}P NMR spectrum of **L3** was also changed from −14.71 to +20.62 ppm after heating at 80 °C for 1 h with $Pd(dba)_2$, unless two signals appeared at −14.71 and +20.62 ppm.[27] These ^{13}C and ^{31}P NMR spectroscopic data suggest that the sulfur atom and the phosphorus atom in ligand **L3** do indeed coordinate to the Pd(0) center and the sulfur atom in thiocarbonyl group of **L3** can more easily coordinate to Pd(0) center than the phosphorus atom of triarylphosphine group. In order to get more straightforward evidence of the coordination pattern of **L3** to Pd center, we decided to prepare a Pd(II) complex from **L3** with bis(benzonitrile)palladium dichloride $[Pd(PhCN)_2Cl_2]$ because it is known that sulfur and phosphorus atoms can coordinate to Pd(II) center to give a stable Pd(II) complex, which can be subjected to the X-ray diffraction.[19] The Pd(II) complex **3**, prepared from the reaction of **L3** with $Pd(MeCN)_2Cl_2$, was obtained as an orange powder. The single crystals for X-ray diffraction were obtained by recrystallization from dichloromethane and toluene (1:4). The ORTEP draw is shown in Figure 2 in which **L3** acts as a bidentate ligand to Pd(II) center providing a nine-membered chelate ring with an irregular, partially boat-like conformation.[28] The bond distances of Pd–S and Pd–P are 2.3012 and 2.2585 Å, respectively, which are in the normal region.[19] Overall, these results indicate that *N*,*N*-dimethylthiocarbamate ligand **L3** might be a *P*,*S*-bidentate heterodonor ligand to Pd(0) center under reaction conditions, although the detailed mechanism awaits further investigation.

In this communication, we disclosed an efficient catalytic system for Suzuki cross-coupling reaction of aryl halides with phenylboronic acid catalyzed by $Pd(dba)_2$ and an easily available and novel *N*,*N*-dimethylthiocarbamate ligand **L3**. These reactions could take place at 60–80 °C and complete within 4–6 h. We confirmed that this *N*,*N*-dimethylthiocarbamate ligand is a novel type of a *P*,*S*-bidentate ligand to Pd(0) center under reaction conditions on the basis of ^{13}C NMR and ^{31}P NMR spectroscopic investigation and X-ray diffraction. Efforts are underway to elucidate the mechanistic details of this catalytic system and to extend the scope of this novel *P*,*S*-bidentate ligand in other C–C bond forming transformations.

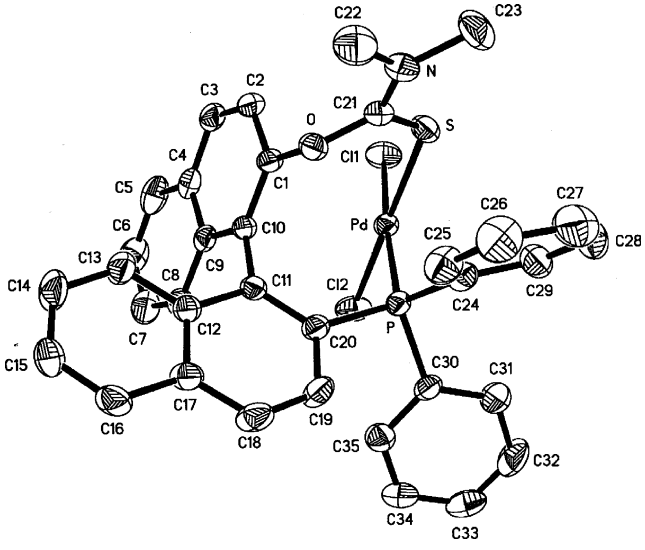


Figure 2. The ORTEP draw of complex **3**.

Acknowledgements

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24. Ligands **L1** and **L2** produced the Suzuki cross-coupling products in 6% and 21% yields, respectively, in general Suzuki cross-coupling experimental procedure [$Pd(dba)_2$ (1.0 mol%), ligand (2.0 mol%), ^{t}BuOK (3.0 equiv), bromobenzene (1.0 equiv), and phenylboronic acid (1.5 equiv) in DMSO at 80 °C]. Ligand **L4** gave no product under the same conditions.
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27. The ^{31}P NMR spectrum showed one signal at −14.71 ppm at the moment after addition of $Pd(dba)_2$ at room temperature. Upon heating at 80 °C for 0.5 h, a new signal at +20.62 ppm appeared along with the signal at −14.71 ppm and continuously upon heating at 80 °C for 1 h, the signal at −14.71 ppm disappeared and the signal at +20.62 ppm left.
28. The X-ray crystal data of Pd complex **3**: $C_{43}H_{38}NOPCl_4PdS$, formula weight: 895.97, temperature: 293(2) K, crystal system, space group: orthorhombic, $P2(1)2(1)2(1)$, unit cell dimensions: $a = 11.7766(6)$ Å, $b = 13.7252(7)$ Å, $c = 25.4436(13)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $V = 4112.6(4)$ Å^3, $Z_{value} = 4$, $D_{calc} = 1.447$ g/cm^3, $F_{000} = 1824$, Crystal size: $0.560 \times 0.255 \times 0.136$ mm, Data/restraints/parameters = 9413/6/437, Final R indices [$I > 2\sigma(I)$]: $R1 = 0.0442$, $wR2 = 0.1082$, R indices (all data): $R1 = 0.0528$; $wR2 = 0.1121$. Its crystal structure has been deposited at the Cambridge Crystallographic Data Centre and has been allocated the deposition numbers: CCDC 213072.