

## Macromolecular Effect: Synthesis of a Ferrocenylmethylphosphine-Containing Polymer as Highly Efficient Ligands for Room-Temperature Palladium(0)-Catalyzed Suzuki Cross-Coupling Reactions of Aryl Chlorides

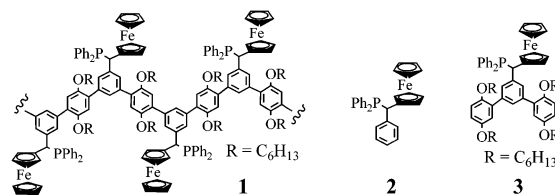
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Palladium-catalyzed carbon-carbon and carbon-heteroatom bond formations are among the most powerful transformations in organic synthesis.<sup>1,2</sup> Coordinatively unsaturated palladium complexes such as 14-electron  $(R_3P)_2Pd(0)$ , formed through either ligand dissociation or displacement, are generally accepted as the catalytically active species in most palladium(0)-catalyzed reactions. As compared to the extensively studied 14-electron  $(R_3P)_2Pd(0)$  complexes, coordinatively unsaturated  $(R_3P)Pd(0)$  complexes which are believed to be more active remain "elusive". Recently, insight into the importance of  $(R_3P)Pd(0)$  complexes as catalytically active species has been gained.<sup>3-6</sup> For example, through the kinetic study, Hartwig demonstrated that the monocoordinated (*o*-tolyl<sub>3</sub>P)Pd complex acts as a catalytically active intermediate for various coupling reactions.<sup>3</sup> Fu proposed that Pd(0)/P(*t*-Bu)<sub>3</sub>-catalyzed Suzuki coupling reactions of aryl chlorides with arylboronic acids involve (*t*-Bu<sub>3</sub>P)Pd(0) species as the catalytically active species, although an isolated complex has not been obtained.<sup>4</sup> Coordinatively unsaturated (monophosphine)-Pd(0) complexes remain largely unexplored because of the lack of a general method to access them,<sup>6</sup> mainly due to the tendency of monophosphines, even very bulky ones, to form  $(R_3P)_2Pd(0)$  complexes. It is therefore fundamentally interesting and synthetically useful to develop general approaches to coordinatively unsaturated (monophosphine)-Pd(0) complexes.

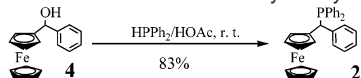
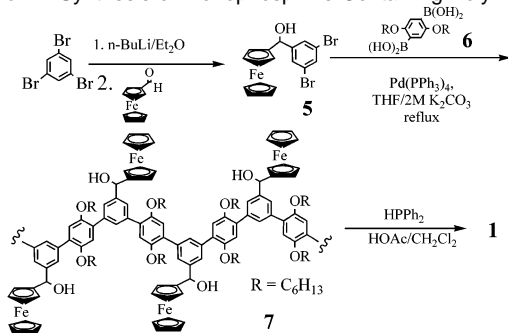
Mechanistically, means that can prevent two monophosphines from coordinating to one Pd(0) center should favor the formation of coordinatively unsaturated  $(R_3P)Pd(0)$  complexes.<sup>1</sup> We envision that using rigid and sterically regular monophosphine-containing polymers as ligands could be a general approach to  $(R_3P)Pd(0)$  complexes which are difficult or impossible to be accessed by using monomeric monophosphines or flexible, sterically irregular monophosphine-containing polymers.<sup>7</sup> We reason that the rigidity and stereoregularity of rigid and sterically regular polymers with suitable monophosphine installation could make the second monophosphine ligand unavailable for coordination, and thus only one, rather than two, monophosphine moiety will coordinate to one palladium(0) center when they are used as ligands. This macromolecular approach may allow for the use of relatively small monophosphine moieties as ligands for reactions that typically require the use of bulky, electron-rich phosphines. On the basis of this hypothesis, we designed and synthesized monophosphine-containing polymer **1** based on the rather small ferrocenylmethylphosphine **2** and employed **1** as ligands for room-temperature palladium(0)-catalyzed Suzuki cross-coupling reactions of aryl chlorides,<sup>4,5,8,9</sup> for which monophosphines **2** and **3** are ineffective ligands. Our study showed that using sterically regular monophosphine-containing polymer as ligands is a feasible approach to access highly active transition metal catalysts. Herein our results are reported.



The synthesis of polymer **1** is based on our recent finding of the one-step, high yield conversion of ferrocenylmethyl alcohol **4** to ferrocenylmethylphosphine **2** (Schemes 1 and 2).<sup>10</sup> As shown in Scheme 2, reaction of 1,3,5-tribromobenzene with *n*-BuLi (1 equiv) followed by treatment with ferrocenecarboxaldehyde generated ferrocenylmethyl alcohol **5** in 80% yield.<sup>11</sup> Polymerization of **5** with diboronic acid **6**<sup>12</sup> was carried out by using the Suzuki coupling polymerization condition (Pd(PPh<sub>3</sub>)<sub>4</sub>, THF/2 M K<sub>2</sub>CO<sub>3</sub>).<sup>12</sup> Treatment of the generated polymer **7** with excess HPPH<sub>2</sub> in HOAc/CH<sub>2</sub>Cl<sub>2</sub> at room temperature afforded polymer **1** in 86% yield. The <sup>1</sup>H NMR spectrum of **1** showed complete conversion of -OH to -PPh<sub>2</sub> as evidenced by the disappearance of peaks of the methylene group that connects to the OH group at 5.50–5.57 ppm and the OH peaks at 2.4 ppm. <sup>31</sup>P NMR of **1** in CDCl<sub>3</sub> (H<sub>3</sub>PO<sub>4</sub> as standard) shows one major peak at 1.78 ppm along with a minor peak at 2.50 ppm, corresponding to the phosphine moieties at the end of the polymer chain. **1** is an air-stable solid and soluble in common organic solvents such as CH<sub>2</sub>Cl<sub>2</sub>, THF, and toluene. Gel permeation chromatography shows that the molecular weight of **1** is *M*<sub>w</sub> = 7700, *M*<sub>n</sub> = 3100 (PDI = 2.49) (THF, polystyrene standards).

The room-temperature Pd(0)-catalyzed Suzuki cross-coupling reaction of aryl chlorides with arylboronic acids has only been realized recently and represents a notable advance in Pd(0)-catalyzed coupling reactions.<sup>4,5,9</sup> Among a few phosphine systems developed for this objective, only Buchwald's dialkylphosphines are effective for couplings of both activated and unactivated aryl chlorides.<sup>5</sup> We have employed **1** as ligands for this transformation. We found that **1**/Pd(0) complexes can achieve this objective. As shown in Table 1, both activated and unactivated aryl chlorides can be coupled with arylboronic acids in the presence of 5% **1**/Pd(OAc)<sub>2</sub> (1:1) complexes. In contrast, no reaction was observed when monophosphine **2**/Pd(OAc)<sub>2</sub> or **3**/Pd(OAc)<sub>2</sub> complexes (2:1 or 1:1) were used for the reaction.

The ability of **1**/Pd(0) complexes to effect the room-temperature Suzuki cross-coupling of unactivated aryl chlorides indicates that the catalytically active species in **1**/Pd(0) complexes are highly active and are different from those in **2**/Pd(0) or **3**/Pd(0) systems. We have excluded the possibility of Pd(0) itself as the catalytically active species because no reaction was observed when the cross-coupling reaction of *p*-chloroanisole with phenyl boronic acids was carried out without a phosphine ligand.<sup>9b</sup> Previous catalyst systems

**Scheme 1.** Direct Conversion of Ferrocenylmethyl Alcohol **4** to **2****Scheme 2.** Synthesis of Monophosphine-Containing Polymer **1****Table 1.** Room-Temperature Palladium(0)-Catalyzed Cross-Couplings of Aryl Chlorides with Arylboronic Acids<sup>a</sup>

Entry	Ar-X	(HO) <sub>2</sub> B-Ar'	Yield(%)
1			75
2			50
3			42
4			78
5			52
6			38
7			50

<sup>a</sup> Reaction conditions (not optimized): aryl chlorides (1.0 mmol), arylboronic acids (1.5 equiv), KF (3 equiv), ligand (5%), THF (2 mL), room temperature.

that involve the use of bulky, electron-rich phosphines as ligands showed that (R<sub>3</sub>P)Pd(0) complexes, rather than (R<sub>3</sub>P)<sub>2</sub>Pd(0) complexes, are catalytically active species for the Suzuki cross-couplings of aryl chlorides.<sup>4a</sup> It is thus reasonable to assume that the catalytically active species in 1/Pd(0) complexes are most likely the (R<sub>3</sub>P)Pd(0) complexes.

We have tried to study the <sup>31</sup>P NMR of 1/Pd(0) complexes, formed by mixing 1/Pd<sub>2</sub>(dba)<sub>3</sub> (2:1) or 1/Pd(OAc)<sub>2</sub> (1:1) in the presence of PhB(OH)<sub>2</sub> (2 equiv)/KF (3 equiv) in THF-*d*<sub>8</sub>. However, 1/Pd(0) complexes are insoluble in THF-*d*<sub>8</sub>. The formation of insoluble 1/Pd(0) complexes may indicate that interchain coordination occurred between palladium(0) and monophosphine moieties. Because ferrocenylmethylphosphine moieties are regularly attached to the polymer chain, some of the monophosphine moieties are expected to remain as noninterchain cross-linking sites. Coordination of these monophosphine moieties to palladium(0) should afford a certain amount of (R<sub>3</sub>P)Pd(0) complexes, which are most likely the active catalysts for the reaction of aryl chlorides with arylboronic acids. On the other hand, the formation of insoluble 1/Pd(0) complexes may also account for the relatively high loading of catalysts because it will limit the formation of (R<sub>3</sub>P)Pd(0) complexes and make it more difficult to access these catalytically active sites.

In summary, we have designed and synthesized a ferrocenylmethylphosphine-containing polymer from readily available starting materials. We have demonstrated that relatively small, not so electron-rich RPPH<sub>2</sub> moieties, after being appropriately incorporated into a rigid and sterically regular polymer system, can be efficient

ligands for room-temperature cross-couplings of aryl chlorides with arylboronic acids, for which corresponding monomeric monophosphines are totally inactive. Our work not only showed that using rigid and sterically regular monophosphine-containing polymers as ligands is a feasible approach to access highly active palladium catalysts, but it also holds future promise for the development of unprecedented highly efficient palladium catalyst systems, as many options to improve the efficiency of **1** may be envisioned. The macromolecular approach described here may open a new avenue to other coordinatively unsaturated mono(ligand)-transition metal complexes. The synthesis of monophosphine-containing polymers that can avoid the interchain cross-linking and related polymers including optically active ones, and their application as ligands for transition metal catalysis, are currently under active investigation, and the results will be reported in due course.

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**Supporting Information Available:** Synthesis and characterization of **1**, **2**, **3**, **5**, and **7**, and the general procedure for 1/Pd(0)-catalyzed cross-coupling of aryl chlorides (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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