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Ferrocenylmethylphosphines as ligands for room temperature Ni(0)-catalyzed Suzuki–Miyaura cross-coupling reactions of aryl arenesulfonates and aryl chlorides

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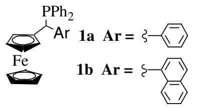
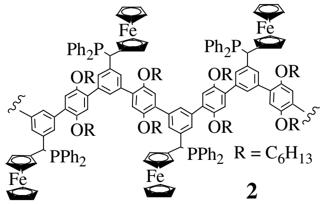
Abstract—Readily available ferrocenylmethylphosphine was found as an efficient ligand for room temperature Ni(0)-catalyzed Suzuki–Miyaura cross-couplings of aryl arenesulfonates. Ferrocenylmethylphosphine and its polymeric form were also found as useful ligands for Ni(0)-catalyzed Suzuki–Miyaura couplings of deactivated aryl chlorides.

Aryl arenesulfonates represent a large family of synthetic materials that are readily accessible from phenols and inexpensive arenesulfonyl chlorides.[1] Although remarkable progress has been made in employing aryl halides/triflates as coupling partners in Suzuki–Miyaura coupling reactions including conducting the reactions at room temperature during the past years,[2–4] limited success has been realized for widely available aryl arenesulfonates, especially under mild reaction conditions. To date, only a few reports have appeared and the reported systems have required either the use of lithium arylborates[5] or elevated reaction temperature (80 or 130 °C).[1a,6–10] Recently, we have documented $Ni(COD)_2$/PCy_3 as the first general catalyst system for room temperature cross-coupling reactions of aryl arenesulfonates with arylboronic acids.[11] Despite the high catalytic activity of $Ni(COD)_2/PCy_3$, both $Ni(COD)_2$ and PCy_3 are air sensitive. In our effort to develop less air-sensitive catalyst systems, for example, catalyst systems derived from less air-sensitive ligands, we found that readily available ferrocenylmethylphosphine **1a**[12] was an efficient ligand for the room temperature Suzuki–Miyaura cross-coupling reactions of aryl arenesulfonates. We also found that **1a** as well as ferrocenylmethylphosphine polymer **2**[4e] was an efficient ligand for the room temperature Suzuki–Miyaura cross-coupling reactions of aryl chlorides. Herein our results are reported.





2

We have previously evaluated a number of commercially available monophosphines PR_3 (R = Ph, *o*-tolyl, *n*-Bu, *i*-Bu, *t*-Bu, Buchwald's dicyclohexylbiphenylphosphine, and di-*t*-butylbiphenylphosphine) for $Ni(COD)_2$-catalyzed cross-coupling of *p*-tolyl tosylate with phenylboronic acid and low to moderate conversions were observed (0–56%).[11] To establish the catalytic property of ferrocenylmethylphosphines **1**, the same cross-coupling reaction was thus used as the model reaction. We found that although **1b** was not a good ligand, **1a** was quite an efficient one for this coupling (Table 1). The fact that **1a** is a more efficient ligand than monophosphines PR_3 (R = Ph, *o*-toly, *n*-Bu, *i*-Bu, *t*-Bu, Buchwald's dicyclohexyl biphenylphosphine, and di-*t*-butylbiphenylphosphine), in which some of them such as n-Bu_3P, i-Bu_3P, and t-Bu_3P are more electron-rich than **1a** and some of them are bulkier than **1a**, suggested that both the electron-richness and the size of the monophosphine ligand play important roles in the Ni(0) catalyst system.

A variety of aryl arenesulfonates and arylboronic acids have been examined for the room temperature

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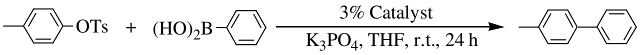
Table 1. Ni(0)-Catalyzed Suzuki cross-couplings of *p*-tolyl tosylate[a]



Entry	Catalyst	Conversion (%)
1	$Ni(COD)_2$	0
2	$Ni(COD)_2$ + 1–4 PR_3 (R = Ph, *o*-tolyl, *n*-Bu, *i*-Bu, *t*-Bu)	0–56[b]
3	$Ni(COD)_2$ + 1 **1a**	31
4	$Ni(COD)_2$ + 2 **1a**	37
5	$Ni(COD)_2$ + 3 **1a**	72
6	$Ni(COD)_2$ + 4 **1a**	64
7	$Ni(COD)_2$ + 3 **1b**	10

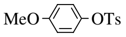
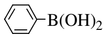
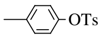
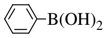
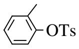
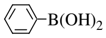
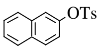
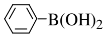
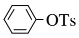
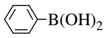
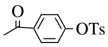
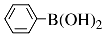
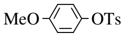
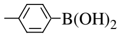
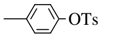
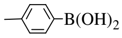
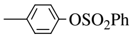
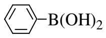
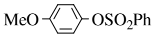
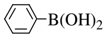
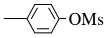
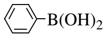
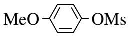
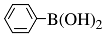
[a] Reaction conditions: tolyl tosylate (1.0 equiv), phenylboronic acid (1.5 equiv), K_3PO_4 (3 equiv), THF (2 ml).

[b] Ref. 11.

Ni(0)/**1a**-catalyzed cross-coupling reactions, and the results are summarized in Table 2. As shown in Table 2, the Ni(0)/**1a** proved to be an useful catalyst for both activated and deactivated aryl tosylates, including those with *ortho*- and *para*-substituents. Aryl benzenesulfonates were found to be less reactive than aryl tosylates (Table 2, entries 9 and 10). We also tested aryl mesylates and found that they were much less reactive than their corresponding tosylates. In fact, reactions involving mesylates as substrates did not go to completion under our condition (Table 2, entries 11 and 12).

Table 2. Room temperature Ni(0)-catalyzed cross-couplings of aryl arenesulfonates with arylboronic acids[a]

$$\text{Ar-OSO}_2\text{R} + (\text{HO})_2\text{B}-\text{Ar}' \xrightarrow[\text{K}_3\text{PO}_4\text{, THF, r.t., 48 h}]{4\%\text{Ni(COD)}_2/12\%\ \mathbf{1a}} \text{Ar -Ar}'$$

Entry	Ar–OSO_2R	Ar′–$B(OH)_2$	Yield[b] (%)
1			87
2			86
3			77[c]
4			94
5			96
6			94
7			94
8			99
9			82
10			54[d]
11			69[e]
12			54[f]

[a] Reaction conditions: aryl sulfonates (1.0 equiv), arylboronic acid (1.5 equiv), K_3PO_4 (3 equiv), THF (2 ml), room temperature.

[b] Isolated yields (average of two runs).

[c] 80% Conversion was observed.

[d] 54% Conversion was observed.

[e] 74% Conversion was observed.

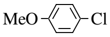
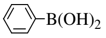
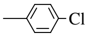
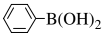
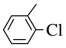
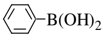
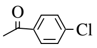
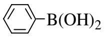
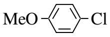
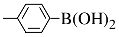
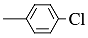
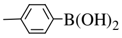
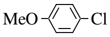
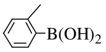
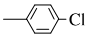
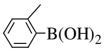
[f] 59% Conversion was observed.

Our success in employing ferrocenylmethylphosphine **1a** as ligand for room temperature Ni(0)-catalyzed Suzuki–Miyaura cross-couplings of aryl sulfonates prompted us to investigate its application as a ligand for room temperature Ni(0)-catalyzed cross-coupling reactions of deactivated aryl chlorides with arylboronic acids, a notable advance in organometallic chemistry.[3] Reported Pd(0) or Ni(0) catalyst systems for this transformation required the use of bulky, electron-rich monodentate ligands such as *t*-Bu_3P, dialkylarylphosphines, and *N*-heterocyclic carbenes.[4,13] Compared to these ligands, the less bulky and less electron-rich ferrocenylmethylphosphine **1a** is more air stable and/or more readily available. Our study showed that by using THF as solvent, K_3PO_4 as the base, ferrocenylmethylphosphine **1a** was an excellent ligand for the cross-coupling reactions of aryl chlorides including the electron-rich ones with arylboronic acids. Good to excellent isolated yields were obtained (Table 3).

We have also examined polymer **2** as ligand for the cross-coupling reactions. We found that only moderate conversions were observed for the Suzuki–Miyaura cross-couplings of both *p*-methoxylphenyl tosylate and aryl chlorides at room temperature (Table 4, entries 1–4), which were in sharp contrast to the complete conversion observed for reactions catalyzed by Ni(0)/**1a**. The observed lower conversions might result from: (a) the difficulty to attain optimal number of ligands (3–4) for every Ni(0) due to the polymeric network, and (b) the intermolecular coordination of monophosphine moieties, which makes polymer **2** function as bidentate ligands. Although **2** was not a good ligand for room temperature cross-coupling reactions of aryl tosylates, we found **2** was an efficient ligand for the cross-coupling of aryl chlorides with arylboronic acids

Table 3. Room temperature Ni(0)-catalyzed cross-couplings of aryl chlorides with arylboronic acids[a]

$$\text{Ar-Cl} + (\text{HO})_2\text{B}-\text{Ar}' \xrightarrow[\text{K}_3\text{PO}_4\text{, THF, r.t., 48 h}]{4\%\text{Ni(COD)}_2/12\%\ \mathbf{1a}} \text{Ar -Ar}'$$

Entry	Ar–Cl	Ar′–$B(OH)_2$	Yield[b] (%)
1			89
2			99
3			84
4			98
5			91
6			98
7			73[c]
8			73[c]

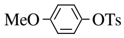
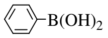
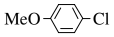
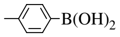
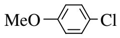
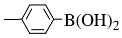
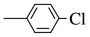
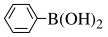
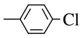
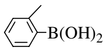
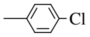
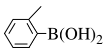
[a] Reaction conditions: aryl chloride (1.0 equiv), arylboronic acids (1.5 equiv), K_3PO_4 (3 equiv), THF (2 ml), room temperature.

[b] Isolated yields (average of two runs).

[c] 88% Conversion was observed.

Table 4. Ni(0)/**2**-Catalyzed Suzuki–Miyaura cross-couplings[a]

$$\text{Ar–X} + (\text{HO})_2\text{B–Ar}' \xrightarrow[\text{K}_3\text{PO}_4\text{, THF, r.t., 48 h}]{4\%\text{Ni(COD)}_2/12\%\ \mathbf{2}} \text{Ar -Ar}'$$

Entry	Ar–X	Ar′–B(OH)$_2$	Yield[b] (%)
1			39
2			24
3			23[c]
4			32
5			69.5[d]
6			66[c,d]

[a] Reaction conditions: aryl sulfonates (1.0 equiv), arylboronic acids (1.5 equiv), K_3PO_4 (3 equiv), THF (2 ml), room temperature.

[b] Isolated yields (average of two runs).

[c] Recovered **2** was used.

[d] Reaction temperature: 60 °C.

at 60 °C, and **2** was recoverable and reusable (Table 4, entries 5 and 6).

In summary, we have demonstrated that readily available ferrocenylmethylphosphine can be employed as an efficient ligand for room temperature Ni(0)-catalyzed Suzuki–Miyaura cross-couplings of aryl arenesulfonates. The catalyst system was also found to catalyze the Suzuki–Miyaura couplings of deactivated aryl chlorides at room temperature. The polymeric ferrocenylmethylphosphine was found to be an efficient ligand for the Ni(0)-catalyzed cross-coupling of aryl chlorides with arylboronic acids, and recoverable and reusable.

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Supplementary data

Experiment procedures and characterization of the cross-coupling products. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.01.145.

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