

Room-Temperature Ni(0)-Catalyzed Cross-Coupling Reactions of Aryl Arenesulfonates with Arylboronic Acids

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



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The Suzuki–Miyaura coupling reactions of aryl halides/triflates with arylboronic acids are among the most powerful transformations in organic synthesis.¹ Although remarkable progress has been made in employing very inert, widely available aryl chlorides as coupling partners in Suzuki–Miyaura coupling reactions including conducting the reactions at room temperature during the past years,^{2,3} very limited success has been realized for widely available aryl arenesulfonates,^{4–9} a large family of synthetic materials that are readily accessible from phenols and cheap arenesulfonyl chlorides. To date, only few reports have appeared, and the reported systems have required either the use of lithium arylborates⁴ or elevated reaction temperature (80 or 130 °C).^{5–7} To our knowledge, aryl arenesulfonates have not been established as synthetically useful substrates for the Suzuki–Miyaura couplings under mild conditions. In view of their easier preparation, increased stability, and less expense relative to aryl triflates, it is of great interest to develop general protocols to employ aryl arenesulfonates as coupling partners for Pd(0)- and Ni(0)-catalyzed Suzuki–Miyaura cross-coupling reactions under mild reaction conditions. Herein, we disclose the room-temperature Ni(0)-catalyzed cross-coupling reactions of aryl arenesulfonates with arylboronic acids.

At the outset of our research, we recognized that aryl arenesulfonates are structurally different from aryl halides: they contain C–O bonds that undergo oxidative addition as compared to C–Cl bonds for aryl chlorides. This structural difference implies that catalyst systems that work well for the room-temperature cross-couplings of aryl chlorides may not work for the room-temperature Suzuki–Miyaura couplings of aryl arenesulfonates. Our initial experiments unsurprisingly showed that catalysts derived from Pd(0) and monophosphines including Buchwald's arylphosphines¹⁰ were ineffective for the coupling of *p*-tolyl tosylate with phenylboronic acid at room temperature (Table 1, entries 1–3). It has been established that the Ni(0) species, in situ generated from Ni(PCy₃)₂Cl₂, underwent oxidative addition with aryl tosylates at 130 °C.⁵ Our study on the room-temperature cross-coupling of *p*-tolyl tosylate with phenylboronic acid suggested that Ni(PCy₃)₂Cl₂ and Ni(PCy₃)₂Cl₂/Zn were inefficient catalysts likely because of their ineffectiveness to generate catalytically active Ni(0) species under the reaction conditions (Table 1, entries 4, 5). We have thus focused on using Ni(COD)₂ as catalyst precursor for the development of general catalysts that can effect the room-temperature Suzuki–Miyaura couplings of aryl arenesulfonates. A number of phosphines have been screened, and the results are summarized in Table 1. As shown in Table 1, less electron-rich triarylphosphines (PPh₃, P(*o*-tolyl)₃) and bidentate DPPF and DPPE were poor ligands, and low conversions of *p*-tolyl tosylate were observed (<20%). Electron-rich tri-*tert*-butylphosphine and Buchwald's arylphosphines were also ineffective ligands. Electron-rich but less sterically hindered tri-*n*-butylphosphine and tri-*i*-butylphosphine were more efficient ligands, and moderate conversions were observed. Tricyclohexylphosphine was found to be an excellent

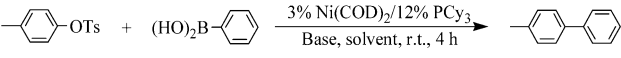
Table 1. Room-Temperature Pd(0) and Ni(0)-Catalyzed Cross-Couplings of *p*-Tolyl Tosylate with Phenylboronic Acid^a

Entry	Catalyst	Conversion (%)
1	Pd ₂ (dba) ₃ + n PR ₃ (R = Cy, <i>t</i> -Bu) (n = 2–4)	0
2	Pd ₂ (dba) ₃ + 2 	0
3	Pd ₂ (dba) ₃ + 2 	0
4	Ni(PCy ₃) ₂ Cl ₂ + 2 PCy ₃	12
5	Ni(PCy ₃) ₂ Cl ₂ /Zn + 2 PCy ₃	11
6	Ni(COD) ₂	0
7	Ni(COD) ₂ + n PPh ₃ (n = 1–4)	13–17
8	Ni(COD) ₂ + n P(<i>o</i> -tolyl) ₃ (n = 1–2)	11–15
9	Ni(COD) ₂ + n DPPE or DPPF (n = 1–2)	0
10	Ni(COD) ₂ + 2 	0
11	Ni(COD) ₂ + 2 	15
12	Ni(COD) ₂ + n <i>t</i> -Bu ₃ P (n = 1–4)	0
13	Ni(COD) ₂ + n <i>n</i> -Bu ₃ P (n = 1–4)	0–56
14	Ni(COD) ₂ + n <i>i</i> -Bu ₃ P (n = 1–4)	23–37
15	Ni(COD) ₂ + PCy ₃	90
16	Ni(COD) ₂ + 2 PCy ₃	99, 90 ^b
17	Ni(COD) ₂ + 3–4 PCy ₃	99 ^b

^a Reaction conditions: tolyl tosylate (1.0 equiv), phenylboronic acid (1.5 equiv), K₃PO₄ (3 equiv), THF (2 mL). ^b Reaction time: 6 h.

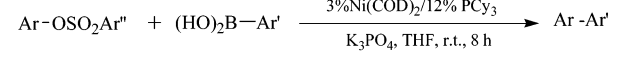
ligand for this coupling, suggesting that both the electron-richness and the size of the phosphine ligand play important roles in the catalyst system. Further study established that catalysts generated from a 1:3 to 1:4 ratio of Ni(COD)₂ and PCy₃ were the most efficient, and the reaction went to completion in 6 h. Among the solvents and bases screened, THF was the best solvent, and K₃PO₄ and K₂CO₃ were the best choice of bases (Table 2).

A variety of aryl arenesulfonates and arylboronic acids have thus been examined for the room-temperature Ni(0)-catalyzed cross-coupling reactions using the optimized catalyst system, and the results are summarized in Table 3. As shown in Table 3, the Ni(0)/PCy₃ system proved to be a general catalyst for both activated and deactivated aryl arenesulfonates, including those with *ortho*-, *meta*-, and *para*-substituents. Complete conversion and excellent isolated yields were observed for all aryl arenesulfonates employed. *p*-Methoxyphenyl benzenesulfonate was slightly less reactive than aryl tosylates, and reactions involving it as coupling partner required 12 h to go to completion (Table 3, entries 14, 16).

Table 2. Solvent and Base Effects in Room-Temperature Ni(0)-Catalyzed Suzuki–Miyaura Cross-Couplings of *p*-Tolyl Tosylate^a


entry	solvent	base	conv (%)	entry	solvent	base	conv (%)
1	benzene- <i>d</i> ₆	K ₃ PO ₄	46	6	THF	K ₂ CO ₃	61
2	dioxane	K ₃ PO ₄	30	7	THF	Na ₂ CO ₃	27
3	toluene	K ₃ PO ₄	32	8	THF	KOH	0
4	THF	K ₃ PO ₄	72	9	THF	Cs ₂ CO ₃	9
5	THF	KF	54				

^a Reaction conditions: tolyl tosylate (1.0 equiv), phenylboronic acid (1.5 equiv), base (3 equiv), solvent (2 mL), room temperature.

Table 3. Room-Temperature Ni(0)-Catalyzed Cross-Couplings of Aryl Arenesulfonates with Arylboronic Acids^a


Entry	Ar-OSO ₂ Ar''	Ar'-B(OH) ₂	Yield(%) ^b
1	MeO-C ₆ H ₄ -OTs	Ph-B(OH) ₂	86
2	p-Cl-C ₆ H ₄ -OTs	Ph-B(OH) ₂	93
3	m-Cl-C ₆ H ₄ -OTs	Ph-B(OH) ₂	93 ^c
4	1-naphthyl-OTs	Ph-B(OH) ₂	99
5	2-naphthyl-OTs	Ph-B(OH) ₂	90
6	4-methoxy-2-tolyl-OTs	Ph-B(OH) ₂	89
7	4-(trifluoromethyl)-phenyl-OTs	Ph-B(OH) ₂	94
8	MeO-C ₆ H ₄ -OTs	m-Cl-C ₆ H ₄ -B(OH) ₂	93
9	p-Cl-C ₆ H ₄ -OTs	m-Cl-C ₆ H ₄ -B(OH) ₂	95
10	MeO-C ₆ H ₄ -OTs	p-Cl-C ₆ H ₄ -B(OH) ₂	95
11	p-Cl-C ₆ H ₄ -OTs	m-Cl-C ₆ H ₄ -B(OH) ₂	95
12	Ph-OTs	MeO-C ₆ H ₄ -B(OH) ₂	94
13	1-naphthyl-OTs	MeO-C ₆ H ₄ -B(OH) ₂	99
14	MeO-C ₆ H ₄ -OSO ₂ Ph	Ph-B(OH) ₂	92 ^d
15	p-Cl-C ₆ H ₄ -OSO ₂ Ph	m-Cl-C ₆ H ₄ -B(OH) ₂	95
16	MeO-C ₆ H ₄ -OSO ₂ Ph	m-Cl-C ₆ H ₄ -B(OH) ₂	95 ^d

^a Reaction conditions: aryl sulfonates (1.0 equiv), arylboronic acids (1.5 equiv), K₃PO₄ (3 equiv), THF (2 mL), room temperature. ^b Isolated yields (average of two runs). ^c Reaction time: 10 h. ^d Reaction time: 12 h.

The mild reaction condition permitted us to use NMR spectroscopy to study the Suzuki–Miyaura couplings of aryl arenesulfonates, specifically, the coupling of *p*-methoxyphenyl tosylate (*p*-MeOPhOTs) with phenylboronic acid (PhB(OH)₂). ¹H NMR showed that mixing *p*-MeOPhOTs with Ni(COD)₂ (1 equiv) and PCy₃ (4 equiv) in THF-*d*₈ at room temperature generated the oxidative addition intermediate with 67% conversion of the tosylate within 15 min and 94% conversion in 4 h. The oxidative addition intermediate completely converted to the cross-coupling product in 1 h when mixed with PhB(OH)₂ and K₃PO₄. Interestingly, when *p*-MeOPhOTs, Ni(COD)₂ (1 equiv), PCy₃ (4 equiv), PhB(OH)₂ (1.5 equiv), and K₃PO₄ (3 equiv) were mixed in THF-*d*₈ at room temperature, ¹H NMR showed that 100% conversion was observed for *p*-MeOPhOTs within 10 min with the oxidative addition complex as the intermediate. The observation of the oxidative addition inter-

mediate suggested that the oxidative addition should not be slower than the transmetalation/reductive elimination steps. Why the oxidative addition occurred faster in the presence of PhB(OH)₂ and base remains unclear at present¹¹ and is worthy of further investigation.

In summary, we have demonstrated for the first time that readily available aryl arenesulfonates can be employed as coupling partners for room-temperature Suzuki–Miyaura cross-couplings in general. The catalyst system, derived from Ni(COD)₂ and PCy₃, represents the first general palladium or nickel catalyst system that can catalyze the Suzuki–Miyaura couplings of aryl arenesulfonates at room temperature. Because several other cross-coupling reactions such as the Kumada coupling and the Negishi coupling are believed to furnish the products via the same oxidative addition intermediate as the Suzuki–Miyaura couplings,¹² aryl arenesulfonates may also be suitable coupling partners for these cross-couplings at room temperature. Efforts toward this direction are underway.

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Supporting Information Available: Experimental procedure and data for Ni(COD)₂/PCy₃-catalyzed cross-coupling of aryl arenesulfonates (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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