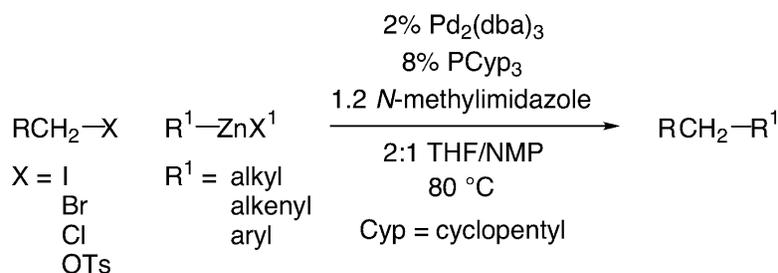## Article

Palladium-Catalyzed Negishi Cross-Coupling Reactions of Unactivated Alkyl Iodides, Bromides, Chlorides, and Tosylates

Jianrong Zhou, and Gregory C. Fu

$$RCH_2{-}X \quad R^1{-}ZnX^1 \xrightarrow[\substack{2:1\ \text{THF/NMP} \\ 80\ °C}]{\substack{2\%\ Pd_2(dba)_3 \\ 8\%\ PCyp_3 \\ 1.2\ N\text{-methylimidazole}}} RCH_2{-}R^1$$

$$X = I,\ Br,\ Cl,\ OTs$$

$$R^1 = \text{alkyl, alkenyl, aryl}$$

Cyp = cyclopentyl

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Palladium-Catalyzed Negishi Cross-Coupling Reactions of Unactivated Alkyl Iodides, Bromides, Chlorides, and Tosylates

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Abstract: A single method (2% Pd$_2$(dba)$_3$/8% PCyp$_3$/NMI in THF/NMP at 80 °C; Cyp = cyclopentyl) achieves the cross-coupling of a range of β-hydrogen-containing primary alkyl iodides, bromides, chlorides, and tosylates with an array of alkyl-, alkenyl-, and arylzinc halides. The process is compatible with a variety of functional groups, including esters, amides, imides, nitriles, and heterocycles.

Introduction

Palladium- and nickel-catalyzed cross-coupling reactions are among the most useful methods for generating carbon–carbon bonds, and their importance has been demonstrated in fields ranging from natural-products synthesis to materials science.[1] To date, nearly all investigations have focused on reactions of *aryl* or *alkenyl* electrophiles (e.g., halides and sulfonates). In contrast, reports of couplings of *alkyl* electrophiles are relatively rare, except for activated compounds that lack β hydrogens (e.g., benzyl halides).[2] It is generally believed that efficient cross-coupling of simple alkyl halides/sulfonates is impeded by slow oxidative addition and by rapid β-hydride elimination (Figure 1). Clearly, the ability to couple unactivated alkyl electrophiles would dramatically expand the scope of cross-coupling processes.

During the past decade, some useful progress toward addressing this challenge has been achieved. In 1992, Suzuki published a pioneering study of Pd(PPh$_3$)$_4$-catalyzed cross-couplings of primary alkyl iodides with 9-BBN derivatives.[3] We subsequently determined that Pd/PR$_3$ (PR$_3$ = PCy$_3$ or P(t-Bu)$_2$Me) can serve as an effective catalyst for Suzuki reactions of primary alkyl bromides, chlorides, and tosylates with trialkylboranes.[4] Furthermore, we established that, in the case of bromides, boronic acids are also suitable coupling partners.[5]
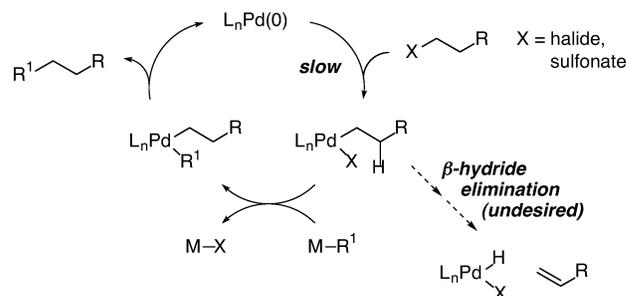

Figure 1. Outline of a pathway for palladium-catalyzed cross-coupling of alkyl electrophiles.

In addition to the Suzuki reaction, notable advances in cross-coupling alkyl electrophiles have also been described for the Kumada reaction. In 2002, Kambe reported that a nickel complex can catalyze the coupling of unfunctionalized Grignard reagents with primary alkyl bromides and tosylates, as well as one chloride.[6] Later that year, Beller extended the use of Pd/PCy$_3$ to cross-couplings of primary alkyl chlorides with aryl Grignards.[7] Most recently, Kambe developed a nickel- and a copper-catalyzed method for coupling primary alkyl fluorides with Grignard reagents.[8]

Some preliminary success has also been reported for Stille and Hiyama reactions of alkyl electrophiles; thus, earlier this year we described the utility of Pd/P(t-Bu)$_2$Me for coupling alkenylstannanes with primary alkyl bromides[9] and arylsilanes with primary bromides and iodides.[10] Finally, in a series of groundbreaking studies beginning in 1995, Knochel demon-

(1) For reviews of metal-catalyzed cross-coupling reactions, see: (a) *Metal-Catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998. (b) *Cross-Coupling Reactions: A Practical Guide*; Miyaura, N., Ed.; Topics in Current Chemistry Series 219; Springer-Verlag: New York, 2002. (c) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-i., Ed.; Wiley-Interscience: New York, 2002.

(2) For an overview of the difficulty of achieving coupling reactions of alkyl electrophiles, see: Cárdenas, D. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 384–387; Cárdenas, D. J. *Angew. Chem., Int. Ed.* **1999**, *38*, 3018–3020. See also: Luh, T.-Y.; Leung, M.-k.; Wong, K.-T. *Chem. Rev.* **2000**, *100*, 3187–3204.

(3) Ishiyama, T.; Abe, S.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1992**, 691–694.

(4) (a) Bromides: Netherton, M. R.; Dai. C.; Neuschütz, K.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 10099–10100. (b) Chlorides: Kirchhoff, J. H.; Dai, C.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 1945–1947. (c) Tosylates: Netherton, M. R.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3910–3912.

(5) Kirchhoff, J. H.; Netherton, M. R.; Hills, I. D.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 13662–13663.

(6) Terao, J.; Watanabe, H.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2002**, *124*, 4222–4223. Kambe's proposed mechanism for this transformation differs from the "standard" cross-coupling pathway illustrated in Figure 1.

(7) Frisch, A. C.; Shaikh, N.; Zapf, A.; Beller, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 4056–4059.
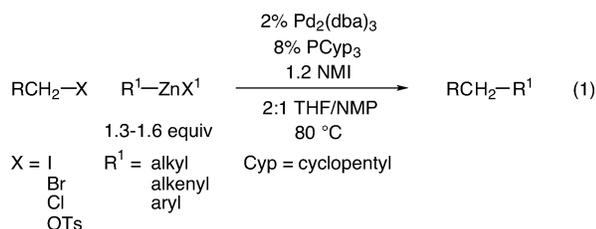
(8) Terao, J.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2003**, *125*, 5646–5647.

(9) Menzel, K.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 3718–3719.

(10) Lee, J.-Y.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 5616–5617.

strated that nickel complexes can catalyze Negishi reactions of primary alkyl bromides and iodides with a range of organozinc reagents.[11,12]

Motivated by our early success in applying Pd/PR$_3$-based catalysts (PR$_3$ = a bulky, electron-rich trialkylphosphine) to Suzuki reactions of alkyl electrophiles, we decided to initiate an investigation of the utility of these catalysts in the Negishi cross-coupling, a process of particular interest due to its high functional-group tolerance and the ready availability of organozinc reagents.[13] We set as our objective the development of a method that is effective for a wide range of unactivated alkyl electrophiles (iodides, bromides, chlorides, and tosylates). In this article, we describe our progress toward achieving that goal, specifically, a single catalyst system that can cross-couple a spectrum of substrates (eq 1).[14]

$$\text{RCH}_2\text{—X} \quad \text{R}^1\text{—ZnX}^1 \xrightarrow[\substack{\text{2:1 THF/NMP} \\ 80\ °\text{C}}]{\substack{2\%\ \text{Pd}_2(\text{dba})_3 \\ 8\%\ \text{PCyp}_3 \\ 1.2\ \text{NMI}}} \text{RCH}_2\text{—R}^1 \qquad (1)$$

1.3-1.6 equiv

X = I   R^1 = alkyl   Cyp = cyclopentyl
Br   alkenyl
Cl   aryl
OTs

Results and Discussion

For our initial studies, we chose to explore couplings of alkylzinc halides, due to their availability from commercial suppliers and from the reaction of zinc with alkyl halides.[15] Knochel has noted that, with his catalyst system, alkylzinc halides are significantly less reactive than diorganozinc reagents, therefore requiring the presence of Bu$_4$NI (3 equiv) in order to achieve efficient cross-coupling.[11] With regard to the alkyl electrophile, we decided to focus on alkyl bromides.

After exploring a variety of reaction parameters, we determined that 2% Pd$_2$(dba)$_3$/8% PCyp$_3$/NMI in THF/NMP at 80 °C can effect the cross-coupling of an alkyl bromide with an organozinc halide in fairly good yield (70%; Table 1, entry 1; dba = dibenzylideneacetone, Cyp = cyclopentyl, NMI = *N*-methylimidazole). An illustrative sampling of the impact of various parameters on the course of the reaction is provided in Table 1.

In the absence of Pd$_2$(dba)$_3$ or PCyp$_3$, none of the desired product is generated (Table 1, entries 2 and 3, respectively). The presence of NMI leads to a somewhat improved yield (entry 1 vs entry 4), perhaps through activation of the organozinc halide

(11) (a) Devasagayaraj, A.; Stüdemann, T.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2723−2725. (b) Giovannini, R.; Stüdemann, T.; Dussin, G.; Knochel, P. *Angew. Chem., Int. Ed.* **1998**, *37*, 2387−2390. (c) Giovannini, R.; Knochel, P. *J. Am. Chem. Soc.* **1998**, *120*, 11186−11187. (d) Giovannini, R.; Stüdemann, T.; Devasagayaraj, A.; Dussin, G.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 3544−3553. (e) Piber, M.; Jensen, A. E.; Rottländer, M.; Knochel, P. *Org. Lett.* **1999**, *1*, 1323−1326. (f) Jensen, A. E.; Knochel, P. *J. Org. Chem.* **2002**, *67*, 79−85.
(12) For reviews of Negishi cross-couplings of organozinc reagents, see ref 1.
(13) For reviews and leading references, see: (a) *Organozinc Reagents, A Practical Approach*; Knochel, P., Jones, P., Eds.; Oxford: New York, 1999. (b) Erdik, E. *Organozinc Reagents in Organic Synthesis*; CRC Press: Boston, 1996. (c) Boudier, A.; Bromm, L. O.; Lotz, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 4414−4435.
(14) As our study was nearing completion, Beller parenthetically described a Pd/PCy$_3$-catalyzed Negishi cross-coupling of 1-chlorohexane with PhZnBr that proceeds in 41% yield: Reference 7.
(15) (a) For reviews and leading references, see: Rieke, R. D.; Hanson, M. V. In *Organozinc Reagents, A Practical Approach*; Knochel, P., Jones, P., Eds.; Oxford: New York, 1999; pp 23−36. Rieke, R. D.; Hanson, M. V. *Tetrahedron* **1997**, *53*, 1925−1956. (b) For a recent report, see: Hou, S. *Org. Lett.* **2003**, *5*, 423−425.

Table 1. Effect of Various Reaction Parameters on the Efficiency of a Negishi Cross-Coupling

$$\text{BnO}\diagup\diagdown\diagup\text{Br} \quad n\text{-Bu—ZnBr} \xrightarrow[\substack{\text{2:1 THF/NMP} \\ 80\ °\text{C},\ 14\ \text{h} \\ \text{"standard" conditions}}]{\substack{2\%\ \text{Pd}_2(\text{dba})_3 \\ 8\%\ \text{PCyp}_3 \\ 1.2\ \text{NMI}}} \text{BnO}\diagup\diagdown\diagup n\text{-Bu}$$

1.3 equiv

entry	change from the standard conditions	yield (%)[a]
1	none	70
2	without 2% Pd$_2$(dba)$_3$	0
3	without 8% PCyp$_3$	0
4	without NMI	54
5	without NMP	48
6	at 30 °C	43
7	with 4% PCyp$_3$	55
8	with 1% Pd$_2$(dba)$_3$, 4% PCyp$_3$	65

[a] Yield according to GC, versus a calibrated internal standard.

Table 2. Effect of the Ligand on the Efficiency of a Negishi Cross-Coupling

$$\text{BnO}\diagup\diagdown\diagup\text{Br} \quad n\text{-Bu—ZnBr} \xrightarrow[\substack{\text{2:1 THF/NMP} \\ 80\ °\text{C},\ 14\ \text{h}}]{\substack{2\%\ \text{Pd}_2(\text{dba})_3 \\ 8\%\ \text{ligand} \\ 1.2\ \text{NMI}}} \text{BnO}\diagup\diagdown\diagup n\text{-Bu}$$

1.3 equiv

entry	ligand	yield (%)[a]
1	PCyp$_3$	70
2	PCy$_3$	65
3	P(*i*-Pr)$_3$	59
4	P(*t*-Bu)$_2$Me	55
5	P(*t*-Bu)$_3$	3
6	P(*n*-Bu)$_3$	9
7	PPh$_3$	5
8	P(*o*-tol)$_3$	1
9	P(2,4,6-trimethoxyphenyl)$_3$	0
10	P(2-furyl)$_3$	2
11	Cy$_2$P(CH$_2$)$_2$PCy$_2$	0[b]
12	1,3-bis(mesityl)-4,5-dihydroimidazolium tetrafluoroborate	4
13	P(OPh)$_3$	0

[a] Yield according to GC, versus a calibrated internal standard. [b] Ligand loading: 4%.

toward transmetalation.[16,17] From an extensive survey of solvents, a 2:1 mixture of THF and NMP emerged as the best; for example, the cross-coupling is significantly less efficient in THF alone (entry 1 vs entry 5). The Negishi reaction does proceed at lower temperature, albeit in lower yield (entry 1 vs entry 6). A decrease in the phosphine:Pd ratio (2:1 in entry 1 vs 1:1 in entry 7) also results in a decreased yield of the desired compound (70% vs 55%). Finally, a reduced catalyst loading (2% palladium) can be employed, at the cost of just a small loss in cross-coupling efficiency (entry 1 vs entry 8).

Not surprisingly, the choice of ligand has a substantial impact on the course of the reaction (Table 2). As we have observed for other cross-couplings of alkyl electrophiles,[4,5,9,10] among the ligands that we have investigated, only trialkylphosphines of the appropriate size furnish active catalysts for this Negishi coupling. PCyp$_3$, which is commercially available, provides the

(16) For a report of enhanced reactivity of an alkylzinc reagent in the presence of NMI, see: Inoue, S.; Yokoo, Y. *J. Organomet. Chem.* **1972**, *39*, 11−16.
(17) The addition of a styrene derivative (3-trifluoromethylstyrene) or *n*-Bu$_4$-NI, which can be critical for efficient coupling with Knochel's nickel-based catalyst (ref 11), has no effect on the Pd$_2$(dba)$_3$/PCyp$_3$-based catalyst.

Table 3. Negishi Cross-Couplings of Alkyl Bromides with Alkylzinc Reagents

$$R{-}Br + R^1{-}ZnBr \xrightarrow[\substack{\text{2:1 THF/NMP} \\ 80\,°C,\ 14\ h}]{\substack{\text{2\% Pd}_2\text{(dba)}_3 \\ \text{8\% PCyp}_3 \\ \text{1.2 NMI}}} R{-}R^1$$

(1.3 equiv)

entry	R—Br	R¹—ZnBr	yield (%)[a]
1	n-Dec—Br	n-Bu—ZnBr	90
2	n-Dec—Br	Bu(Et)CH—CH₂—ZnBr	89
3	cyclohexyl-CH₂CH₂—Br	Bu(Et)CH—CH₂—ZnBr	76
4	Ph—CH₂CH₂CH₂—Br	cyclohexyl-CH₂—ZnBr	83
5	n-Dec—Br	CH₂=CH—CH₂CH₂—ZnBr	52
6	BnO—CH₂CH₂CH₂—Br	NC(Me)₂C—CH₂CH₂CH₂—ZnBr	68
7	TBSO—CH₂CH₂CH₂—Br	NC(Me)₂C—CH₂CH₂CH₂—ZnBr	67
8	NC—(CH₂)₅—Br	EtO₂C—(CH₂)₄—ZnBr	65

[a] Isolated yield (average of two runs).

highest yield (entry 1). Whereas PCy₃, P(i-Pr)₃, and P(t-Bu)₂Me are reasonably effective (entries 2−4), more (e.g., P(t-Bu)₃; entry 5) and less (e.g., P(n-Bu)₃; entry 6) bulky trialkylphosphines are not useful under these conditions. Similarly, triarylphosphines (entries 7−10), a chelating electron-rich phosphine (entry 11), an N-heterocyclic carbene (entry 12), and a phosphite (entry 13) afford essentially none of the desired product.[18]

Our optimized conditions (Pd₂(dba)₃/PCyp₃/NMI) are suitable for Negishi cross-couplings of a range of primary alkyl bromides with alkylzinc reagents (Table 3). The catalyst system tolerates functional groups such as olefins, ethers, nitriles, and esters (entries 5−8).[19]

In addition to bromides, other families of alkyl electrophiles can be cross-coupled under our standard conditions (Table 4). Thus, an array of primary alkyl iodides (entries 1 and 2), tosylates (entries 3 and 4), and chlorides (entries 5−7) couple with alkylzinc reagents to provide the desired products.[20] As for alkyl bromides (Table 3), these reactions can be ac-

(18) For the less-effective ligands, the major identifiable side products are the alkyl chloride (organozinc reagents from Aldrich can contain 2−3 wt % chloride) and/or the alkane (from reduction of the alkyl bromide).

(19) Notes: (a) Under the standard conditions, reaction of 1-bromodecane with Et₂Zn (0.65 or 1.3 equiv) furnishes an ∼68% yield (by GC versus an internal standard) of the desired cross-coupling product. (b) When a secondary alkylzinc reagent is employed as the coupling partner, isomerization is observed (e.g., for the reaction of 1-bromononane with i-PrZnBr, we obtain an ∼60% yield of n-dodecane). Isomerization is common for Negishi cross-couplings of aryl halides with branched alkylzinc reagents, when catalyzed by Pd/(monodentate phosphine) complexes. For example, see: Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158−163.

(20) Notes: (a) Negishi cross-couplings of secondary alkyl halides/tosylates are inefficient under these conditions. (b) Because organozinc reagents (e.g., n-BuZnBr) from Aldrich can contain 2−3 wt % chloride, some trans-halogenation (RBr → RCl) occurs under the cross-coupling conditions. As a consequence, selective mono-functionalization of 1-bromo-6-chlorohexane (Table 4, entry 7) cannot be achieved with these reagents.

Table 4. Negishi Cross-Couplings of Alkyl Iodides, Tosylates, and Chlorides with Alkylzinc Reagents

$$R{-}X + R^1{-}ZnBr \xrightarrow[\substack{\text{2:1 THF/NMP} \\ 80\,°C,\ 14\ h}]{\substack{\text{2\% Pd}_2\text{(dba)}_3 \\ \text{8\% PCyp}_3 \\ \text{1.2 NMI}}} R{-}R^1$$

(1.3 equiv)

entry	R—X	R¹—ZnBr	yield (%)[a]
1	n-Dec—I	n-Bu—ZnBr	87
2	phthalimido—CH₂CH₂CH₂—I	n-Bu—ZnBr	48
3	n-Dodec—OTs	n-Bu—ZnBr	86
4	NC—(CH₂)₄—OTs	NC(Me)₂C—CH₂CH₂CH₂—ZnBr	64
5	n-Dec—Cl	n-Bu—ZnBr	97
6	(pyridin-2-yl)—(CH₂)₆—Cl	n-Bu—ZnBr	77
7	Br—(CH₂)₆—Cl	n-Bu—ZnBr	70[b]

[a] Isolated yield (average of two runs). [b] Alkyl halide:organozinc = 1:2.6. Product: double Negishi cross-coupling.

complished in the presence of a variety of functional groups (Table 4). *In terms of versatility, this Pd₂(dba)₃/PCyp₃-based catalyst for Negishi cross-couplings is unique among all of the methods that have been described for coupling alkyl electrophiles—the same catalyst is effective for chlorides, bromides, iodides, and tosylates.*

The range of cross-coupling partners is not limited to alkylzinc reagents. Thus, Pd₂(dba)₃/PCyp₃ couples alkyl bromides (Table 5, entries 1−5), iodides (entries 6−8), tosylates (entry 9), and chlorides (entry 10) even with hindered alkenylzincs (geminally and cis-substituted). In addition, arylzinc compounds are suitable substrates (entries 11 and 12). The examples illustrated in Table 5 demonstrate that the catalyst tolerates the presence of a variety of functional groups (e.g., esters, acetals, ethers, amides, and imides).

Like many other trialkylphosphines, PCyp₃ undergoes oxidation upon exposure to air. We have determined that the corresponding air-stable phosphonium salt, [HPCyp₃]BF₄, can serve as a substitute for PCyp₃ in our Negishi cross-couplings.[21] Under the reaction conditions, the excess zinc reagent (1.6 equiv) deprotonates the phosphonium salt, liberating PCyp₃, which binds to palladium to generate the active catalyst. As illustrated in Table 5, the phosphonium salt and the phosphine typically furnish comparable yields.

We have also applied Pd/PCyp₃ to Negishi reactions of alkenylzinc reagents generated in situ through titanium-catalyzed syn hydrometalation of alkynes[22] (Table 6). Our ability to achieve this multicomponent coupling provides further evidence for the robustness of the method.

Summary

In conclusion, we have developed a catalyst system that is effective for Negishi reactions of a broad spectrum of unacti-

(21) For previous applications of this general strategy, see: (a) Netherton, M. R.; Fu, G. C. *Org. Lett.* **2001**, *3*, 4295−4298. (b) References 9 and 10.

(22) Gao, Y.; Harada, K.; Hata, T.; Urabe, H.; Sato, F. *J. Org. Chem.* **1995**, *60*, 290−291.

Table 5. Negishi Cross-Couplings of Alkyl Electrophiles with Alkenyl- and Arylzinc Reagents

$$R-X \quad R^1-ZnX^1 \xrightarrow[\substack{1.6 \text{ equiv}}]{\substack{2\% \text{ Pd}_2(dba)_3 \\ 8\% \text{ PCyp}_3 \text{ or } [HPCyp_3]BF_4 \\ 1.2 \text{ NMI} \\ \hline 2{:}1 \text{ THF/NMP} \\ 80 \text{ °C, 12 h}}} R-R^1$$

entry	R—X	R^1—ZnX^1	isolated yield (%)	
			PCyp$_3$	[HPCyp$_3$]BF$_4$
1	n-Dec—Br	Ph, ZnX^1	93	93
2	t-Bu-O-C(O)-(CH$_2$)$_4$-Br	Me, ZnX^1	68	71
3	THPO-(CH$_2$)$_3$-Br	Me, ZnX^1	76	77
4	BnO-(CH$_2$)$_3$-Br	Me, Me, ZnX^1	83	75
5	Et$_2$N-C(O)-(CH$_2$)$_4$-Br	Me, Me, ZnX^1	81	72
6	n-Dec—I	Me, ZnX^1	98	93
7	n-Dec—I	Ph, ZnX^1	93	93
8	phthalimido-(CH$_2$)$_3$-I	Ph, ZnX^1	74	76
9	cyclohexenyl-CH$_2$-OTs	Ph, ZnX^1	58	53
10	(EtO)$_2$CH-(CH$_2$)$_2$-Cl	Ph, ZnX^1	73	78
11	EtO-C(O)-(CH$_2$)$_4$-Br	MeO-C$_6$H$_4$-ZnX^1	74	69
12	n-Dec—I	Ph—ZnX^1	65	62

Table 6. One-Pot Hydrozincation/Negishi Cross-Coupling of Alkyl Electrophiles

$$\text{ZnBr}_2 + \text{LiH} \rightarrow \text{"H—ZnBr"} \xrightarrow[\substack{\text{Cp}_2\text{TiCl}_2 \\ \text{catalyst}}]{\text{Me}{-}{\equiv}{-}R^1} \underset{H}{\overset{Me}{\diagdown}}{=}\underset{ZnBr}{\overset{R^1}{\diagup}} \xrightarrow[\text{Pd/PCyp}_3]{R-X} \underset{H}{\overset{Me}{\diagdown}}{=}\underset{R}{\overset{R^1}{\diagup}}$$

entry	Me—≡—R^1	R—X	yield (%)	
			PCyp$_3$	[HPCyp$_3$]BF$_4$
1	Me—≡—Me	Ph-(CH$_2$)$_3$-Br	63	48
2	Me—≡—Me	PhO-(CH$_2$)$_3$-Br	53	51
3[a]	Me—≡—Ph	cyclohexyl-(CH$_2$)$_2$-Br	61	63
4	Me—≡—Me	phthalimido-(CH$_2$)$_3$-I	69	72
5[a]	Me—≡—Ph	CH$_2$=CH-(CH$_2$)$_8$-OTs	59	62

[a] The product is an ∼95:5 mixture of regioisomers.

vated alkyl electrophiles; indeed, to the best of our knowledge this is the first nickel- or palladium-catalyzed method for cross-coupling alkyl electrophiles that can be applied to iodides, bromides, chlorides, and tosylates. A range of organozinc (alkyl, alkenyl, and aryl) reagents may be employed, and the functional-group compatibility of the catalyst is good.[23]

On the basis of the observations reported in this and earlier studies from our laboratory, we believe that Pd/trialkylphosphine-based catalysts hold unusual promise for addressing the challenge of achieving a wide array of cross-coupling reactions of unactivated alkyl electrophiles. Efforts to substantiate this hypothesis, as well as to understand the origin of this intriguing reactivity, are underway.

Supporting Information Available: Experimental procedures and compound characterization data (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

(23) We have also determined that under these conditions Pd/PCyp$_3$ is effective for coupling reactions of *aryl* bromides (PhBr + BuZnBr: 85% yield; PhBr + PhZnBr: 70% yield), iodides (PhI + BuZnBr: 87% yield; PhI + PhZnBr: 72% yield), and triflates (PhOTf + BuZnBr: 88% yield; PhOTf + PhZnBr: 76% yield). Aryl chlorides react very slowly.