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Nickel-Catalyzed Stille Cross Coupling of C−O Electrophiles

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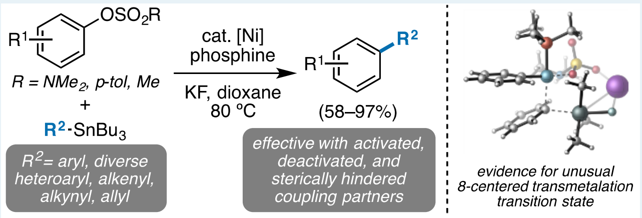
Supporting Information

ABSTRACT: Aryl sulfamates, tosylates, and mesylates undergo efficient Ni-catalyzed cross coupling with diverse organostannanes in the presence of relatively unhindered alkylphosphine ligands and KF. The coupling is valuable for difficult bond constructions, such as aryl—heteroaryl, aryl—alkenyl, and aryl—alkynyl, using nontriflate phenol derivatives. A combination of experimental and computational studies implicates an unusual mechanism for transmetalation involving an 8-centered cyclic transition state. This reaction is inhibited by chloride sources due to slow transmetalation of organostannanes at a Ni(II)—chloride intermediate. These studies help to explain why prior efforts to achieve Ni-catalyzed Stille coupling of phenol derivatives were unsuccessful.



KEYWORDS: *cross-coupling, DFT, nickel, phenol derivatives, transmetalation*

Phenol-derived electrophiles have numerous advantages over aryl halides as cross-coupling partners including synthetic utility as directing groups as well as the low cost and high availability of phenols.[1] Highly activated phenol derivatives like aryl triflates are difficult to carry through multiple synthetic steps because of their tendency toward hydrolysis. However, recent developments in nickel catalysis have enabled less labile phenol derivatives such as sulfonates, sulfamates, carbamates, and esters to be used in Suzuki−Miyaura,[2] Negishi,[3] Kumada,[3a,4] and other cross couplings.[1] Despite these advances, the Ni-catalyzed Stille coupling of phenol derivatives has remained elusive since Percec's early report that homocoupling dominates in the reaction of aryl mesylates with PhSnBu$_3$ using NiCl$_2$(PPh$_3$)$_2$ as a precatalyst (Scheme 1a).[3a,5] The poor efficiency of cross coupling was attributed to slow transmetalation from tin to nickel.

The palladium-catalyzed Stille coupling of aryl halides and triflates is a powerful C−C bond-forming strategy.[6] Although other methods—especially Suzuki−Miyaura couplings—are often preferred because of tin's toxicity, the Stille coupling remains important due to the stability and high functional group tolerance of organostannanes.[7,8] Nevertheless, when using more inert phenol-derived electrophiles, the Pd-catalyzed Stille reaction is limited to unhindered electron-deficient or -neutral aryl sulfonates and a small scope of organostannanes.[9] Because Ni is more reactive than Pd with C−O bonds,[1] we reasoned that Ni catalysis should enable more efficient and general Stille coupling of nontriflate phenol derivatives if the problem of slow transmetalation can be overcome. Here we report that Ni(0) catalyzes the cross coupling of diverse aryl sulfamates and sulfonates with aryl-, heteroaryl-, alkenyl-, alkynyl-, and allylstannanes (Scheme 1b). Moreover, we provide evidence for a novel transmetalation mechanism and an explanation for an inhibitory effect of chloride in this system.

We first examined the reaction between **1** and PhSnBu$_3$ in the presence of Ni(cod)$_2$, PCy$_3$, and KF in 1,4-dioxane (Table 1). Aryl sulfamates are synthetically valuable C−O electrophiles because they are also effective directing groups for ortho metalation.[10] The ligand PCy$_3$ was chosen on the basis of its efficacy in Ni-catalyzed Suzuki−Miyaura couplings of aryl sulfamates.[11] KF was added because fluoride is known to accelerate Pd-catalyzed Stille couplings.[6,12,13] A poor yield of **2** was observed after 18 h at 60 °C (entry 1), but increasing the reaction temperature to 80 °C improves the yield of **2** to 60% (entry 2). None of the homocoupled product **3** was detected. Interestingly, the addition of LiCl shuts down reactivity (entry 3) even though chloride salts are commonly included in Pd-catalyzed Stille couplings of aryl triflates.[6,14] Gratifyingly, nearly quantitative conversion to **2** was achieved with several

Scheme 1. Ni-Catalyzed Stille Coupling of Phenol-Derived Electrophiles

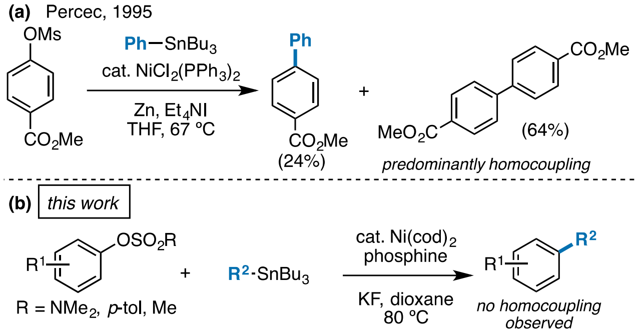


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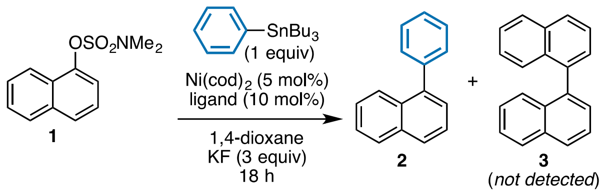
Table 1. Optimization of the Ni-Catalyzed Stille Coupling



entry	ligand	temp. (°C)	additive	**2** (%)[a]
1	PCy_3	60		27
2	PCy_3	80		60
3	PCy_3	80	LiCl (3 equiv)	n.d.
4	PBu_3	80		88
5	$PPhEt_2$	80		≥99
6	$PPhMe_2$	80		96
7	PPh_2Me	80		≥99
8	PPh_3	80		52
9[b]	$PPhEt_2$	80		n.d.

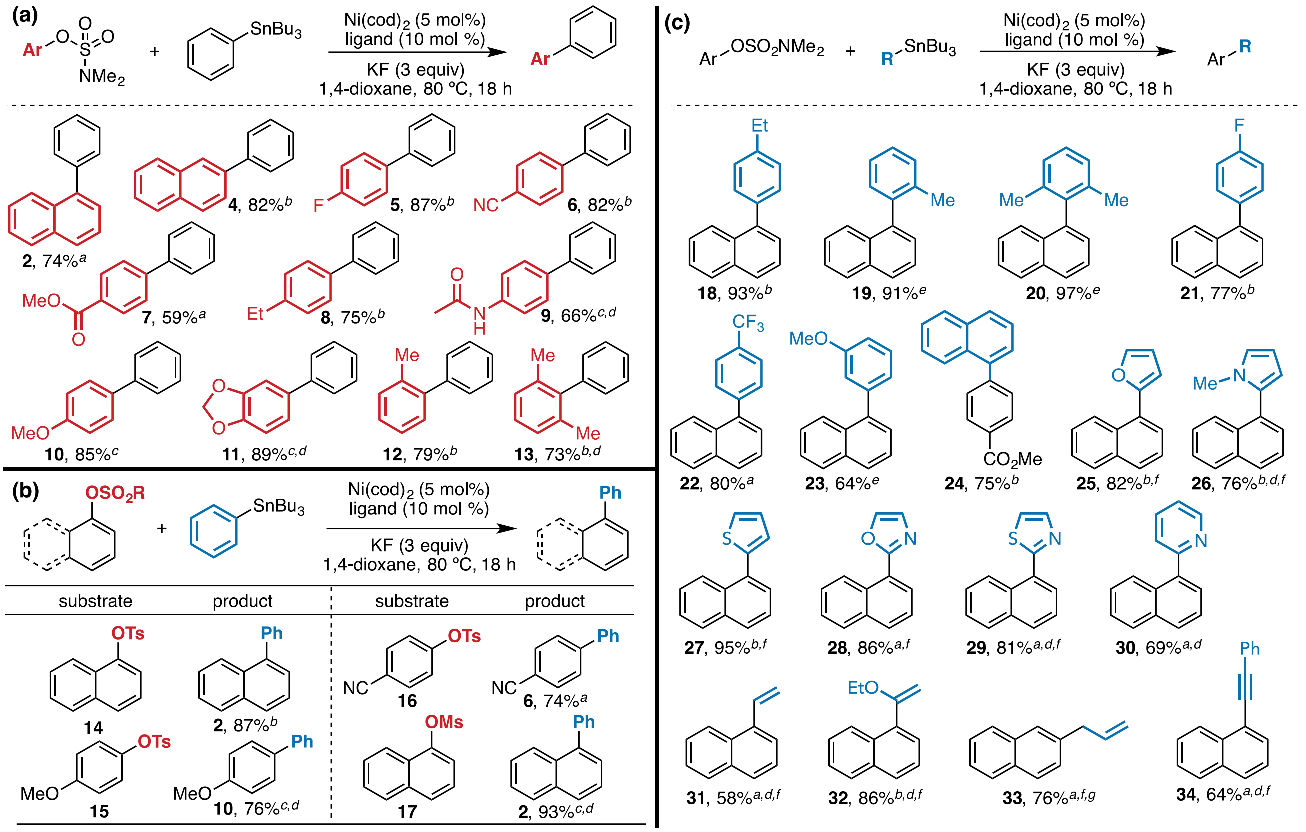
[a] GC yield calibrated against undecane as an internal standard. n.d. = not detected. Average of two runs. [b] Without KF.

less sterically hindered mono-, di-, and trialkylphosphines (entries 4–7). At least one alkyl substituent on the phosphine is needed for high conversion: the use of PPh_3 gives only a moderate yield (entry 8). No reaction is observed in the absence of KF (entry 9).

With several optimal ligands in hand (PBu_3, $PPhEt_2$, $PPhMe_2$, PPh_2Me), the scope of aryl sulfamates was examined (Scheme 2a). Activated (**2** and **4–7**) and deactivated (**8–13**) aryl sulfamates undergo efficient cross coupling. Steric hindrance on the electrophile is well tolerated (**12** and **13**), as are fluorides,[15] nitriles,[16] esters,[1,2d,e] amides,[17] and acetals[18]—functional groups that are also known to undergo activation by Ni(0) (**5–7**, **9**, and **11**). In addition to aryl sulfamates, both activated (**14** and **16**) and deactivated (**15**) aryl tosylates, as well as naphthyl mesylate **17**, readily undergo the Ni-catalyzed Stille coupling (Scheme 2b).

Diverse organostannanes are effective coupling partners, including aryl tributylstannanes bearing electron-donating (**18–20**) and -withdrawing (**21–23**) substituents or containing fused aromatic rings (**24**) (Scheme 2c). This reaction is effective for constructing diverse C–C bonds that are largely inaccessible from nontriflate phenol derivatives by other cross-coupling methods. For example, 2-(tributylstannyl) oxygen-, nitrogen-, and sulfur-containing five- and six-membered heteroaryl nucleophiles undergo efficient cross coupling (**25–30**). In contrast, the analogous Suzuki–Miyaura coupling of nontriflate phenol derivatives has not been demonstrated with most of the corresponding organoboron reagents.[19] Alkenyl stannanes (**31** and **32**) are readily coupled to afford products complementary to the Ni-catalyzed Heck reaction of nontriflate phenolic electrophiles,[20] a reaction that is limited to alkyl- or aryl-substituted alkenes and does not include enol ethers. The use of allyl- and alkynyltributyl stannanes permits allylation and alkynylation of phenol-derived electrophiles (**33** and **34**).[21,22]

Scheme 2. Scope of (a) Aryl Sulfamates, (b) Other Phenol Derivatives, and (c) Organostannanes



[a] Ligand = $PPhMe_2$. [b] Ligand = $PPhEt_2$ [c] Ligand = PBu_3. [d] With 10 mol % $Ni(cod)_2$ and 20 mol % ligand. [e] Ligand = PPh_2Me. [f] BHT added during isolation. [g] Product comprises ~9:1 ratio of **33** to the isomerized alkene 2-(1-propen-1-yl)naphthalene.

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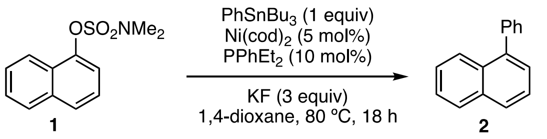
As described above, during reaction optimization we found that 3 equiv of LiCl completely inhibits this Ni-catalyzed reaction (see Table 1 entry 3). Further exploration revealed that even a substoichiometric quantity of LiCl severely impairs catalysis (Table 2, compare entries 1 and 2). The inhibitory effect of LiCl is observed even when Li^+ is sequestered by a crown ether (entry 3), suggesting that inhibition is due to chloride rather than Li^+. The crown ether itself does not inhibit catalysis (entry 4). To further explore this phenomenon, additional chloride salts were evaluated as additives. Indeed, NBu_4Cl, KCl, and $ZnCl_2$ were all found to impair catalysis even at low loadings (10 mol %, entries 5−7).

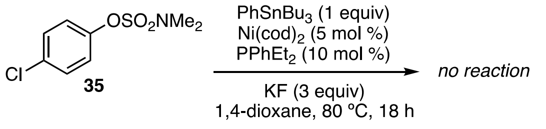
Table 2. Inhibition of Catalysis by Chloride Sources



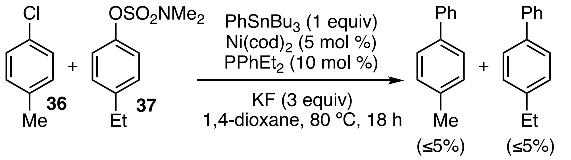
entry	additive(s)	**2** (%)[a]
1	none	≥99[b]
2	LiCl (10 mol %)	13[b]
3	LiCl (10 mol %) + 12-crown-4 (20 mol %)	13[b]
4	12-crown-4 (20 mol %)	≥99[b]
5	NBu_4Cl (10 mol %)	10[b]
6	KCl (10 mol %)	42[b]
7	$ZnCl_2$ (10 mol %)	n.d.

[a] GC yield calibrated against undecane as an internal standard. n.d. = not detected. [b] Average of two runs.

Consistent with catalyst inhibition by chloride sources, no reaction is observed using a chloro-substituted aryl sulfamate **35** (eq 1). An exogeneous aryl chloride **36** also inhibits the Ni-catalyzed Stille coupling of aryl sulfamate **37** (eq 2). Interestingly, cross coupling of the aryl chloride does not take place either, even though aryl chlorides are excellent coupling partners in other types of Ni-catalyzed cross couplings.[23] We hypothesize that the Ni(II)−chloride species formed upon oxidative addition of an aryl chloride[24] or by anion exchange between a Ni(II)−sulfamate and exogeneous Cl^- is relatively inert toward transmetalation with $PhSnBu_3$.[25] Consequently, the catalyst is deactivated by aryl chlorides or chloride salts. This hypothesis could also help to explain why the use of $NiCl_2(PPh_3)$ leads to slow transmetalation with organostannanes, as described by Percec and co-workers.[3a]



(*1*)



(*2*)

To explore this hypothesis, DFT calculations were performed to compare possible mechanisms for transmetalation from tin to nickel using PMe_3 and $PhSnMe_3$ as computationally convenient models (Figure 1a).[26,27] We focused on transmetalation at Ni(II) because recent studies on related Suzuki−Miyaura couplings of aryl sulfamates support a Ni(0)/(II) catalytic cycle in which any Ni(I) species exist as unproductive off-cycle intermediates.[19a,28,29] Complex **38** represents the species resulting from oxidative addition of an aryl sulfamate at Ni(0).[30] In Mechanism A, **38** reacts directly with $PhSnMe_3$ and transmetalation proceeds through a 6-centered cyclic transition state (**TSA**). In Mechanism B, **38** is intercepted by a pentavalent tin fluoride species formed from the reaction of $PhSnMe_3$ with KF.[12b,h,i] Transmetalation takes place through a novel 8-centered transition state with K^+ acting as a bridge between fluoride and oxygen (**TSB**). Mechanism C represents a possible path in the presence of chloride salts: this mechanism proceeds through formation of Ni(II)−chloride complex **39C** followed by transmetalation through a 4-centered cyclic transition state **TSC**. Finally, Mechanism D proceeds through formation of a Ni(II)−fluoride complex **39D** (by anion exchange using KF) and involves F···Sn bond formation in the 4-centered transition state **TSD**.[31,32]

The calculations suggest that, in the absence of chloride, transmetalation proceeds through Mechanism B or D. Both mechanisms justify the requirement for KF in the catalytic conditions and are characterized by relatively low free energies of activation (15.0 kcal/mol for **TSB** measured from **38**; 20.4 kcal/mol for **TSD** measured from **39D**). In contrast, Mechanism A's barrier is much higher (27.8 kcal/mol for **TSA**). The relevance of Mechanism D depends on whether a Ni(II)−fluoride species (**39D**) forms rapidly under the reaction conditions. To explore this possibility, we turned to stoichiometric oxidative addition studies. Aryl sulfamate **42** reacts with $Ni(cod)_2$ and $PPhEt_2$ in 1,4-dioxane to give complex **43** (Figure 1B).[27b] When **43** is heated with KF in 1,4-dioxane for 1 h, no significant changes are observed by ^{31}P, ^{19}F, ^{1}H, or ^{13}C NMR, suggesting that sulfamate-for-fluoride anion exchange does not take place under these conditions.[33] As such, Mechanism D appears improbable, and Mechanism B is more likely to operate under the catalytic conditions.

Further support for the relevance of Mechanism B, involving a bridging K^+ during transmetalation, is provided by experimental evaluation of different counterions for fluoride (Table 3). Whereas **1** undergoes cross coupling in quantitative yield when KF is the fluoride source, LiF and NaF are completely ineffective for this transformation. The poor results with Li^+ and Na^+ counterions could also relate to worse solubility of these salts. However, even the highly soluble salt CsF gives considerably lower yields than KF, suggesting that Cs^+ may not be as effective as K^+ at forming a bridge during transmetalation.

DFT predicts that transmetalation at a Ni(II)−chloride (Mechanism C) is considerably slower than transmetalation through either Mechanism B or Mechanism D ($\Delta G^‡$ for **TSC** = 24.3 kcal/mol measured from **39C**). Accordingly, these calculations are consistent with inhibition by LiCl if a Ni(II)−chloride species forms rapidly under the reaction conditions. This possibility was also investigated through stoichiometric studies. In contrast to the observed lack of reactivity between **43** and KF, **43** is almost completely transformed into a new complex upon heating with LiCl in 1,4-dioxane for 1 h. The new complex is spectroscopically identical to the product formed upon reaction of aryl chloride **45** with $Ni(cod)_2$/$PPhEt_2$, corresponding to trans Ni(II)−chloride complex **44**. When complex **44** is heated with $PhSnBu_3$ and KF in 1,4-

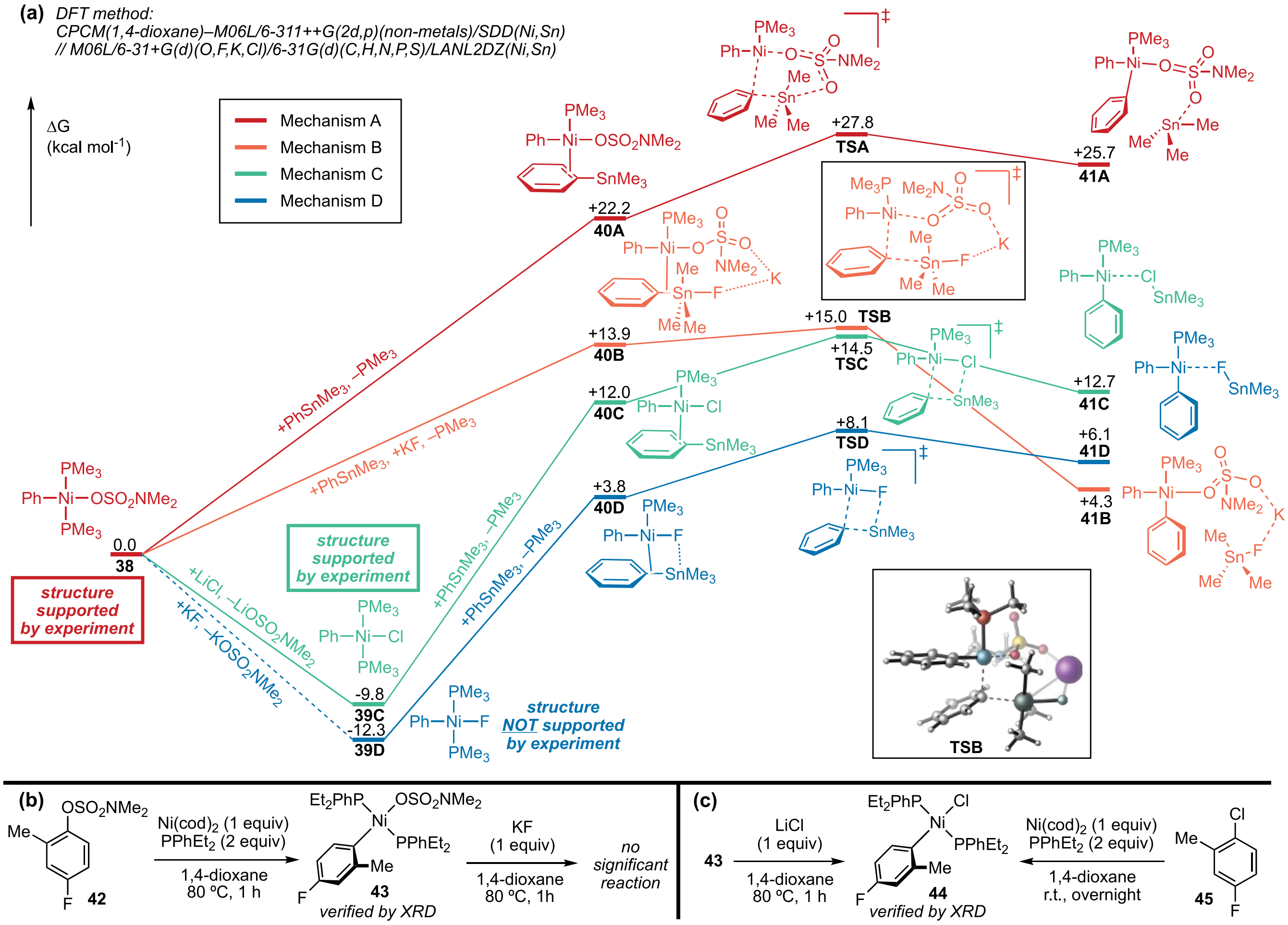
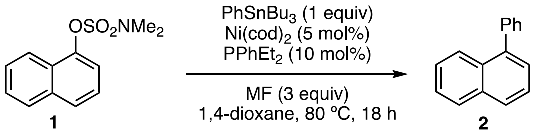


Figure 1. (a) Computational analysis of mechanistic possibilities for transmetalation. (b) Stoichiometric oxidative addition gives **43**, which does not react with KF. (c) Complex **43** reacts with LiCl.

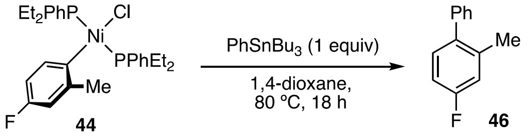
Table 3. Effect of Fluoride Source on Cross Coupling



entry	M$^+$	**2** (%)[a]
1	K$^+$	≥99[b]
2	Li$^+$	n.d.
3	Na$^+$	n.d.
4	Cs$^+$	54[b]

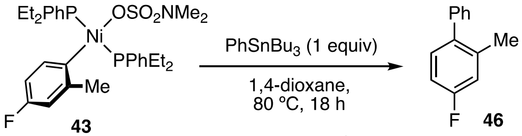
[a] GC yield calibrated against undecane as an internal standard. n.d. = not detected. [b] Average of two runs.

dioxane, only a trace yield of the cross-coupled product **46** is observed (eq 3). In contrast, Ni(II)−sulfamate complex **43** provides a ∼42% yield of **46** under the same conditions using KF (eq 4). Notably, no cross-coupling product is observed with either complex in the absence of KF. Taken together, these DFT and stoichiometric experimental studies support the hypothesis that the Ni-catalyzed Stille coupling is inhibited by chloride sources due to formation of a Ni(II)−chloride intermediate that is slow to undergo transmetalation with organostannanes.



(3)

without KF: n.d.
KF (3 equiv): ≤5%



(4)

without KF: n.d.
KF (3 equiv): 42%

In summary, this paper describes the first efficient Ni-catalyzed Stille cross-coupling of phenol-derived electrophiles. Avoidance of chloride sources and use of KF and mono-, di-, or trialkylphosphines with moderate to low steric bulk are critical to achieving a high yield of cross-coupled products. The cross coupling is characterized by a significantly expanded scope when compared to the Pd-catalyzed Stille coupling of aryl mesylates and tosylates.[9] This methodology is valuable for difficult bond constructions, such as aryl—heteroaryl, aryl—alkenyl, and aryl—alkynyl, using relatively inert phenol derivatives. Computational and experimental mechanistic studies suggest a novel 8-centered cyclic transmetalation transition state. In contrast to some Pd-catalyzed Stille

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couplings of aryl triflates, chloride sources have an inhibitory effect in this system due to the formation of Ni(II)−chloride intermediates that are slow to participate in transmetalation.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.9b00744.

Experimental procedures, characterization data, NMR spectra, crystallographic data, computational details, energies and Cartesian coordinates of minimum energy calculated structures (PDF)
NMR spectra (PDF)
X-ray crystallographic data for **43** (CIF)
X-ray crystallographic data for **44** (CIF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For selected reviews on C—O electrophiles, see: (a) Yu, D. G.; Li, B. J.; Shi, Z. J. Exploration of New C—O Electrophiles in Cross-Coupling Reactions. *Acc. Chem. Res.* **2010**, *43*, 1486. (b) Li, B. J.; Yu, D. G.; Sun, C. L.; Shi, Z. J. Activation of "Inert" Alkenyl/Aryl C—O Bond and Its Application in Cross-Coupling Reactions. *Chem. - Eur. J.* **2011**, *17*, 1728. (c) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A. M.; Garg, N. K.; Percec, V. Nickel-Catalyzed Cross-Couplings Involving Carbon-Oxygen Bonds. *Chem. Rev.* **2011**, *111*, 1346. (d) Mesganaw, T.; Garg, N. K. Ni- and Fe-Catalyzed Cross-Coupling Reactions of Phenol Derivatives. *Org. Process Res. Dev.* **2013**, *17*, 29. (e) Yamaguchi, J.; Muto, K.; Itami, K. Recent Progress in Nickel-Catalyzed Biaryl Coupling. *Eur. J. Org. Chem.* **2013**, *2013*, 19. (f) Tobisu, M.; Chatani, N. Catalytic Transformations Involving the Activation of sp^2 Carbon-Oxygen Bonds. *Top. Organomet. Chem.* **2012**, *44*, 35. (g) Cornella, J.; Zarate, C.; Martin, R. Metal-catalyzed activation of ethers via C—O bond cleavage: a new strategy for molecular diversity. *Chem. Soc. Rev.* **2014**, *43*, 8081. (h) Tobisu, M.; Chatani, N. Cross-Couplings Using Aryl Ethers via C—O Bond Activation Enabled by Nickel Catalysts. *Acc. Chem. Res.* **2015**, *48*, 1717. (i) Tobisu, M.; Chatani, N. Nickel-Catalyzed Cross-Coupling Reactions of Unreactive Phenolic Electrophiles via C—O Bond Activation. *Top. Curr. Chem.* **2016**, *374*, 41.

(2) Selected seminal examples: (a) Percec, V.; Bae, J. Y.; Hill, D. H. Aryl Mesylates in Metal-Catalyzed Homocoupling and Cross-Coupling Reactions. 2. Suzuki-Type Nickel-Catalyzed Cross-Coupling of Aryl Arenesulfonates and Aryl Mesylates with Arylboronic Acids. *J. Org. Chem.* **1995**, *60*, 1060. (b) Zim, D.; Lando, V. R.; Dupont, J.; Monteiro, A. L. NiCl$_2$(PCy$_3$)$_2$: A simple and efficient catalyst precursor for the Suzuki cross-coupling of aryl tosylates and arylboronic acids. *Org. Lett.* **2001**, *3*, 3049. (c) Tang, Z. Y.; Hu, Q. S. Room-temperature Ni(0)-catalyzed cross-coupling reactions of aryl arenesulfonates with arylboronic acids. *J. Am. Chem. Soc.* **2004**, *126*, 3058. (d) Guan, B. T.; Wang, Y.; Li, B. J.; Yu, D. G.; Shi, Z. J. Biaryl Construction via Ni-Catalyzed C—O Activation of Phenolic Carboxylates. *J. Am. Chem. Soc.* **2008**, *130*, 14468. (e) Quasdorf, K. W.; Tian, X.; Garg, N. K. Cross-Coupling Reactions of Aryl Pivalates with Boronic Acids. *J. Am. Chem. Soc.* **2008**, *130*, 14422. (f) Tobisu, M.; Shimasaki, T.; Chatani, N. Nickel-catalyzed cross-coupling of aryl methyl ethers with aryl boronic esters. *Angew. Chem., Int. Ed.* **2008**, *47*, 4866.

(3) Selected examples: (a) Percec, V.; Bae, J. Y.; Hill, D. H. Aryl Mesylates in Metal-Catalyzed Homo-Coupling and Cross-Coupling Reactions. 4. Scope and Limitations of Aryl Mesylates in Nickel-Catalyzed Cross-Coupling Reactions. *J. Org. Chem.* **1995**, *60*, 6895. (b) Li, B. J.; Li, Y. Z.; Lu, X. Y.; Liu, J.; Guan, B. T.; Shi, Z. J. Cross-Coupling of Aryl/Alkenyl Pivalates with Organozinc Reagents through Nickel-Catalyzed C—O Bond Activation under Mild Reaction Conditions. *Angew. Chem., Int. Ed.* **2008**, *47*, 10124. (c) Wang, C.; Ozaki, T.; Takita, R.; Uchiyama, M. Aryl Ether as a Negishi Coupling Partner: An Approach for Constructing C—C Bonds under Mild Conditions. *Chem. - Eur. J.* **2012**, *18*, 3482. (d) Tao, J. L.; Wang, Z. X. Pincer-Nickel-Catalyzed Cross-Coupling of Aryl Sulfamates with Arylzinc Chlorides. *Eur. J. Org. Chem.* **2015**, *2015*, 6534.

(4) Selected examples: (a) Wenkert, E.; Michelotti, E. L.; Swindell, C. S. Nickel-Induced Conversion of Carbon-Oxygen into Carbon-Carbon Bonds - One-Step Transformations of Enol Ethers into Olefins and Aryl Ethers into Biaryls. *J. Am. Chem. Soc.* **1979**, *101*, 2246. (b) Hayashi, T.; Katsuro, Y.; Okamoto, Y.; Kumada, M. Nickel-Catalyzed Cross-Coupling of Aryl Phosphates with Grignard and Organo-Aluminum Reagents - Synthesis of Alkylbenzenes, Alkenylbenzenes and Arylbenzenes from Phenols. *Tetrahedron Lett.* **1981**, *22*, 4449. (c) Sengupta, S.; Leite, M.; Raslan, D. S.; Quesnelle, C.; Snieckus, V. Ni(0)-Catalyzed Cross Coupling of Aryl *O*-Carbamates and Aryl Triflates with Grignard Reagents - Directed Orthometalation-Aligned Synthetic Methods for Polysubstituted Aromatics Via a 1,2-Dipole Equivalent. *J. Org. Chem.* **1992**, *57*, 4066. (d) Dankwardt, J. W. Nickel-catalyzed cross-coupling of aryl Grignard reagents with aromatic alkyl ethers: An efficient synthesis of unsymmetrical biaryls. *Angew. Chem., Int. Ed.* **2004**, *43*, 2428. (e) Yu, D. G.; Li, B. J.; Zheng, S. F.; Guan, B. T.; Wang, B. Q.; Shi, Z. J. Direct Application of Phenolic Salts to Nickel-Catalyzed Cross-Coupling Reactions with Aryl Grignard Reagents. *Angew. Chem., Int. Ed.* **2010**, *49*, 4566.

(5) An isolated example of Ni-catalyzed cross coupling of a pseudosaccharyl ether of naphthol with SnMe$_4$ has been reported: Brigas, A. F.; Johnstone, R. A. W. Heteroaromatic ethers of phenols in nickel-catalysed *ipso*-replacement reactions with magnesium, zinc and tin organometallic compounds. *J. Chem. Soc., Perk. Trans. 1* **2000**, 1735.

(6) Selected reviews: (a) Stille, J. K. The Palladium-Catalyzed Cross-Coupling Reactions of Organotin Reagents with Organic Electrophiles. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (b) Espinet, P.; Echavarren, A. M. The mechanisms of the Stille reaction. *Angew. Chem., Int. Ed.* **2004**, *43*, 4704. (c) Carsten, B.; He, F.; Son, H. J.; Xu, T.; Yu, L. P. Stille Polycondensation for Synthesis of Functional Materials. *Chem. Rev.* **2011**, *111*, 1493. (d) Heravi, M. M.; Hashemi, E.; Azimian, F. Recent developments of the Stille reaction as a revolutionized method in total synthesis. *Tetrahedron* **2014**, *70*, 7.

(e) Cordovilla, C.; Bartolome, C.; Martinez-Ilarduya, J. M.; Espinet, P. The Stille Reaction, 38 Years Later. *ACS Catal.* **2015**, *5*, 3040.

(7) Examples discussing the instability of some boronic acids: (a) Tyrrell, E.; Brookes, P. The synthesis and applications of heterocyclic boronic acids. *Synthesis* **2003**, *2003*, 469. (b) Ge, S. Z.; Hartwig, J. F. Highly Reactive, Single-Component Nickel Catalyst Precursor for Suzuki-Miyuara Cross-Coupling of Heteroaryl Boronic Acids with Heteroaryl Halides. *Angew. Chem., Int. Ed.* **2012**, *51*, 12837. (c) Cox, P. A.; Leach, A. G.; Campbell, A. D.; Lloyd-Jones, G. C. Protodeboronation of Heteroaromatic, Vinyl, and Cyclopropyl Boronic Acids: pH-Rate Profiles, Autocatalysis, and Disproportionation. *J. Am. Chem. Soc.* **2016**, *138*, 9145. (d) Sawatzky, R. S.; Stradiotto, M. (DPEPhos)Ni(mesityl)Br: An Air-Stable Pre-Catalyst for Challenging Suzuki-Miyaura Cross-Couplings Leading to Unsymmetrical Biheteroaryls. *Synlett* **2018**, *29*, 799.

(8) Examples of alternative solutions to the instability of some boronic acids: (a) Molander, G. A.; Ellis, N. Organotrifluoroborates: Protected boronic acids that expand the versatility of the Suzuki coupling reaction. *Acc. Chem. Res.* **2007**, *40*, 275. (b) Darses, S.; Genet, J. P. Potassium organotrifluoroborates: New perspectives in organic synthesis. *Chem. Rev.* **2008**, *108*, 288. (c) Dick, G. R.; Woerly, E. M.; Burke, M. D. A General Solution for the 2-Pyridyl Problem. *Angew. Chem., Int. Ed.* **2012**, *51*, 2667. (d) Knapp, D. M.; Gillis, E. P.; Burke, M. D. A General Solution for Unstable Boronic Acids: Slow-Release Cross-Coupling from Air-Stable MIDA Boronates. *J. Am. Chem. Soc.* **2009**, *131*, 6961. (e) Malapit, C. A.; Bour, J. R.; Brigham, C. E.; Sanford, M. S. Base-free nickel-catalysed decarbonylative Suzuki-Miyaura coupling of acid fluorides. *Nature* **2018**, *563*, 100.

(9) (a) Badone, D.; Cecchi, R.; Guzzi, U. Palladium-Catalyzed Coupling of Aryl Arenesulfonates with Organostannanes. *J. Org. Chem.* **1992**, *57*, 6321. (b) Buchwald, S. L.; Naber, J. R.; Fors, B. P.; Wu, X. X.; Gunn, J. T. Stille Cross-Coupling Reactions of Aryl Mesylates and Tosylates Using a Biarylphosphine Based Catalyst System. *Heterocycles* **2010**, *80*, 1215.

(10) (a) Macklin, T. K.; Snieckus, V. Directed *ortho* metalation methodology. The N,N-dialkyl aryl *O*-sulfamate as a new directed metalation group and cross-coupling partner for Grignard reagents. *Org. Lett.* **2005**, *7*, 2519. (b) Board, J.; Cosman, J. L.; Rantanen, T.; Singh, S. P.; Snieckus, V. The Directed *ortho* Metallation-Cross-Coupling Fusion: Development and Application in Synthesis. *Platinum Met. Rev.* **2013**, *57*, 234.

(11) Examples: (a) Quasdorf, K. W.; Riener, M.; Petrova, K. V.; Garg, N. K. Suzuki-Miyaura Coupling of Aryl Carbamates, Carbonates, and Sulfamates. *J. Am. Chem. Soc.* **2009**, *131*, 17748. (b) Quasdorf, K. W.; Antoft-Finch, A.; Liu, P.; Silberstein, A. L.; Komaromi, A.; Blackburn, T.; Ramgren, S. D.; Houk, K. N.; Snieckus, V.; Garg, N. K. Suzuki-Miyaura Cross-Coupling of Aryl Carbamates and Sulfamates: Experimental and Computational Studies. *J. Am. Chem. Soc.* **2011**, *133*, 6352. (c) Leowanawat, P.; Zhang, N.; Resmerita, A. M.; Rosen, B. M.; Percec, V. Ni(COD)$_2$/PCy$_3$ Catalyzed Cross-Coupling of Aryl and Heteroaryl Neopentylglycolboronates with Aryl and Heteroaryl Mesylates and Sulfamates in THF at Room Temperature. *J. Org. Chem.* **2011**, *76*, 9946. (d) Baghbanzadeh, M.; Pilger, C.; Kappe, C. O. Rapid Nickel-Catalyzed Suzuki-Miyaura Cross-Couplings of Aryl Carbamates and Sulfamates Utilizing Microwave Heating. *J. Org. Chem.* **2011**, *76*, 1507. (e) Leowanawat, P.; Zhang, N.; Safi, M.; Hoffman, D. J.; Fryberger, M. C.; George, A.; Percec, V. *trans*-Chloro(1-Naphthyl)bis-(triphenylphosphine)-nickel(II)/PCy$_3$ Catalyzed Cross-Coupling of Aryl and Heteroaryl Neopentylglycolboronates with Aryl and Heteroaryl Mesylates and Sulfamates at Room Temperature. *J. Org. Chem.* **2012**, *77*, 2885. (f) Ramgren, S. D.; Hie, L.; Ye, Y. X.; Garg, N. K. Nickel-Catalyzed Suzuki-Miyaura Couplings in Green Solvents. *Org. Lett.* **2013**, *15*, 3950. (g) Jezorek, R. L.; Zhang, N.; Leowanawat, P.; Bunner, M. H.; Gutsche, N.; Pesti, A. K. R.; Olsen, J. T.; Percec, V. Air-Stable Nickel Precatalysts for Fast and Quantitative Cross-Coupling of Aryl Sulfamates with Aryl Neopentylglycolboronates at Room Temperature. *Org. Lett.* **2014**, *16*, 6326.

(12) (a) Littke, A. F.; Fu, G. C. The first general method for Stille cross-couplings of aryl chlorides. *Angew. Chem., Int. Ed.* **1999**, *38*, 2411. (b) Grasa, G. A.; Nolan, S. P. Palladium/imidazolium salt catalyzed coupling of aryl halides with hypervalent organostannates. *Org. Lett.* **2001**, *3*, 119. (c) García Martinez, A.; Osío Barcina, J.; Colorado Heras, M. D. R.; de Fresno Cerezo, A. Reactions of vinyl and aryl triflates with hypervalent tin reagents. *Organometallics* **2001**, *20*, 1020. (d) Littke, A. F.; Schwarz, L.; Fu, G. C. Pd/P(t-Bu)$_3$: A mild and general catalyst for Stille reactions of aryl chlorides and aryl bromides. *J. Am. Chem. Soc.* **2002**, *124*, 6343. (e) Su, W. P.; Urgaonkar, S.; McLaughlin, P. A.; Verkade, J. G. Highly active palladium catalysts supported by bulky proazaphosphatrane ligands for Stille cross-coupling: Coupling of aryl and vinyl chlorides, room temperature coupling of aryl bromides, coupling of aryl triflates, and synthesis of sterically hindered biaryls. *J. Am. Chem. Soc.* **2004**, *126*, 16433. (f) Echavarren, A. M. Couplings with monoorganotin compounds: A "radical" twist from the original Stille reaction. *Angew. Chem., Int. Ed.* **2005**, *44*, 3962. (g) Naber, J. R.; Buchwald, S. L. Palladium-catalyzed Stille cross-coupling reaction of aryl chlorides using a pre-milled palladium acetate and XPhos catalyst system. *Adv. Synth. Catal.* **2008**, *350*, 957. (h) Ariafard, A.; Yates, B. F. Subtle Balance of Ligand Steric Effects in Stille Transmetalation. *J. Am. Chem. Soc.* **2009**, *131*, 13981. (i) Herve, M.; Lefevre, G.; Mitchell, E. A.; Maes, B. U. W.; Jutand, A. On the Triple Role of Fluoride Ions in Palladium-Catalyzed Stille Reactions. *Chem. - Eur. J.* **2015**, *21*, 18401.

(13) For use of fluoride in a Ni-catalyzed Stille coupling of Ar—NMe$_3^+$ electrophiles see: Wang, D. Y.; Kawahata, M.; Yang, Z. K.; Miyamoto, K.; Komagawa, S.; Yamaguchi, K.; Wang, C.; Uchiyama, M. Stille coupling via C—N bond cleavage. *Nat. Commun.* **2016**, *7*, 12937.

(14) (a) Farina, V.; Krishnan, B.; Marshall, D. R.; Roth, G. P. Palladium-Catalyzed Coupling of Arylstannanes with Organic Sulfonates - a Comprehensive Study. *J. Org. Chem.* **1993**, *58*, 5434. (b) Casado, A. L.; Espinet, P.; Gallego, A. M. Mechanism of the Stille reaction. 2. Couplings of aryl triflates with vinyltributyltin. Observation of intermediates. A more comprehensive scheme. *J. Am. Chem. Soc.* **2000**, *122*, 11771. (c) Verbeeck, S.; Meyers, C.; Franck, P.; Jutand, A.; Maes, B. U. W. Dual Effect of Halides in the Stille Reaction: In Situ Halide Metathesis and Catalyst Stabilization. *Chem. - Eur. J.* **2010**, *16*, 12831.

(15) (a) Amii, H.; Uneyama, K. C—F Bond Activation in Organic Synthesis. *Chem. Rev.* **2009**, *109*, 2119. (b) Tobisu, M.; Xu, T.; Shimasaki, T.; Chatani, N. Nickel-Catalyzed Suzuki-Miyaura Reaction of Aryl Fluorides. *J. Am. Chem. Soc.* **2011**, *133*, 19505.

(16) (a) Bonesi, S. M.; Fagnoni, M. The Aromatic Carbon-Carbon ipso-Substitution Reaction. *Chem. - Eur. J.* **2010**, *16*, 13572. (b) Garcia, J. J.; Brunkan, N. M.; Jones, W. D. Cleavage of carbon-carbon bonds in aromatic nitriles using nickel(0). *J. Am. Chem. Soc.* **2002**, *124*, 9547.

(17) For reviews see: (a) Meng, G. R.; Shi, S. C.; Szostak, M. Cross-Coupling of Amides by N—C Bond Activation. *Synlett* **2016**, *27*, 2530. (b) Takise, R.; Muto, K.; Yamaguchi, J. Cross-coupling of aromatic esters and amides. *Chem. Soc. Rev.* **2017**, *46*, 5864. (c) Gao, Y.; Ji, C. L.; Hong, X. Ni-mediated C—N activation of amides and derived catalytic transformations. *Sci. China: Chem.* **2017**, *60*, 1413. (d) Liu, C. W.; Szostak, M. Twisted Amides: From Obscurity to Broadly Useful Transition-Metal-Catalyzed Reactions by N—C Amide Bond Activation. *Chem. - Eur. J.* **2017**, *23*, 7157. (e) Dander, J. E.; Garg, N. K. Breaking Amides using Nickel Catalysis. *ACS Catal.* **2017**, *7*, 1413.

(18) Graham, T. J. A.; Doyle, A. G. Nickel-Catalyzed Cross-Coupling of Chromene Acetals and Boronic Acids. *Org. Lett.* **2012**, *14*, 1616.

(19) Suzuki—Miyaura cross coupling of inert phenol derivatives with 2-furyl and 2-thiophenyl boron reagents has been shown, see refs 11b 11c, 11e, and (a) Mohadjer Beromi, M.; Nova, A.; Balcells, D.; Brasacchio, A. M.; Brudvig, G. W.; Guard, L. M.; Hazari, N.; Vinyard, D. J. Mechanistic Study of an Improved Ni Precatalyst for Suzuki-Miyaura Reactions of Aryl Sulfamates: Understanding the Role of

Ni(I) Species. *J. Am. Chem. Soc.* **2017**, *139*, 922. (b) Xing, T.; Zhang, Z.; Da, Y. X.; Quan, Z. J.; Wang, X. C. Ni-catalyzed Suzuki-Miyaura coupling reactions of pyrimidin-2-yl phosphates, tosylates and pivalates with arylboronic acids. *Tetrahedron Lett.* **2015**, *56*, 6495. (c) Molander, G. A.; Beaumard, F. Nickel-Catalyzed C—O Activation of Phenol Derivatives with Potassium Heteroaryltrifluoroborates. *Org. Lett.* **2010**, *12*, 4022. (d) Kobayashi, Y.; Mizojiri, R. Nickel-catalyzed coupling reaction of lithium organoborates and aryl mesylates possessing an electron withdrawing group. *Tetrahedron Lett.* **1996**, *37*, 8531.

(20) (a) Ehle, A. R.; Zhou, Q.; Watson, M. P. Nickel(0)-Catalyzed Heck Cross-Coupling via Activation of Aryl C—OPiv Bonds. *Org. Lett.* **2012**, *14*, 1202. (b) Tasker, S. Z.; Gutierrez, A. C.; Jamison, T. F. Nickel-Catalyzed Mizoroki-Heck Reaction of Aryl Sulfonates and Chlorides with Electronically Unbiased Terminal Olefins: High Selectivity for Branched Products. *Angew. Chem., Int. Ed.* **2014**, *53*, 1858. (c) Li, Y. X.; Wang, K.; Ping, Y. Y.; Wang, Y. F.; Kong, W. Q. Nickel-Catalyzed Domino Heck Cyclization/Suzuki Coupling for the Synthesis of 3,3-Disubstituted Oxindoles. *Org. Lett.* **2018**, *20*, 921.

(21) Ni-catalyzed allylation of inert phenol derivatives (aryl phosphate) has been shown using allylmagnesium bromide:Sibi, M. P.; Sermadurai, S.; Zimmermann, N.; Serum, E.; MA, G.; Moorthy, R.; Kalliokoski, K. Novel Monomers from Biomass. International Patent WO 2016/022943 A2, Feb 11, 2016.

(22) Ni-catalyzed alkynylation of inert phenol derivatives (methyl ethers) has been shown using an alkynylmagnesium bromide reagent: Tobisu, M.; Takahira, T.; Ohtsuki, A.; Chatani, N. Nickel-Catalyzed Alkynylation of Anisoles via C—O Bond Cleavage. *Org. Lett.* **2015**, *17*, 680.

(23) For selected examples of Ni-catalyzed Suzuki−Miyaura cross coupling of aryl chlorides see refs 7b, 11f, and (a) Saito, S.; Ohtani, S.; Miyaura, N. Synthesis of biaryls via a nickel(0)-catalyzed cross-coupling reaction of chloroarenes with arylboronic acids. *J. Org. Chem.* **1997**, *62*, 8024. (b) Percec, V.; Golding, G. M.; Smidrkal, J.; Weichold, O. $NiCl_2$(dppe)-catalyzed cross-coupling of aryl mesylates, arenesulfonates, and halides with arylboronic acids. *J. Org. Chem.* **2004**, *69*, 3447. (c) Tang, Z. Y.; Hu, Q. S. Triphenylphosphine as a ligand for room-temperature Ni(0)-catalyzed cross-coupling reactions of aryl chlorides with arylboronic acids. *J. Org. Chem.* **2006**, *71*, 2167.

(24) The oxidative addition of aryl chlorides at Ni(0) is generally faster or competitive with oxidative addition of C—O electrophiles: see refs 2b, 2d, 11d, and (a) Li, X. J.; Zhang, J. L.; Geng, Y.; Jin, Z. Nickel-Catalyzed Suzuki-Miyaura Coupling of Heteroaryl Ethers with Arylboronic Acids. *J. Org. Chem.* **2013**, *78*, 5078. (b) Chen, L. S.; Lang, H. Y.; Fang, L.; Yu, J. J.; Wang, L. M. Nickel-Catalyzed Desulfitative Suzuki-Miyaura Cross-Coupling of *N*,*N*-Disulfonylmethylamines and Arylboronic Acids. *Eur. J. Org. Chem.* **2014**, *2014*, 6385. (c) LaBerge, N. A.; Love, J. A. Nickel-Catalyzed Decarbonylative Coupling of Aryl Esters and Arylboronic Acids. *Eur. J. Org. Chem.* **2015**, *2015*, 5546. (d) Hanley, P. S.; Ober, M. S.; Krasovskiy, A. L.; Whiteker, G. T.; Kruper, W. J. Nickel- and Palladium-Catalyzed Coupling of Aryl Fluorosulfonates with Aryl Boronic Acids Enabled by Sulfuryl Fluoride. *ACS Catal.* **2015**, *5*, 5041.

(25) To our knowledge, the Ni-catalyzed coupling of aryl chlorides with arylstannanes has not been described, although Ni-catalyzed coupling of ArCl with vinyl, alkynyl, and allyl stannanes has some limited precedent: (a) Shirakawa, E.; Yamasaki, K.; Hiyama, T. Nickel-catalysed cross-coupling reactions of aryl halides with organostannanes. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2449. (b) Shirakawa, E.; Yamasaki, K.; Hiyama, T. Cross-coupling reaction of organostannanes with aryl halides catalyzed by nickel-triphenylphosphine or nickel-lithium halide complex. *Synthesis* **1998**, *1998*, 1544.

(26) Calculations were performed at the CPCM(1,4-dioxane)-M06L/BS2//M06L/BS1 level, where BS1 = 6-31+G(d) for O, F, K, Cl, 6-31G(d) for C, H, N, P, S, and LANL2DZ for Ni, Sn, and BS2 = SDD for Ni, Sn, and 6-311++G(2d,p) for all other elements. Calculations performed using Gaussian09: (a) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A. J.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, Revision C.1; Gaussian, Inc.: Wallingford, CT, 2009. Images of optimized structures were generated with CYLview: (b) *CYLview*, 1.0b; Université de Sherbrooke: Legault, CY, 2009; http://www.cylview.org (accessed on Mar 1, 2019).

(27) (a) The use of PMe_3 provides ∼25% yield of **46** in the catalytic cross-coupling of substrate **42** with $PhSnBu_3$ (see SI). (b) Substrate **42** undergoes catalytic cross coupling with $PhSnBu_3$ in the presence of $Ni(cod)_2$, $PPhEt_2$, and KF to provide **46** in quantitative yield (see SI).

(28) However, the involvement of odd-electron Ni species cannot be ruled out without a more in-depth mechanistic study.

(29) Catalysis by Ni(I) was tentatively ruled out in a Ni-catalyzed Stille coupling of $Ar—NMe_3^+$ electrophiles (see ref 13).

(30) Sulfamate can bind in a κ^1 or κ^2 fashion; based on experimental evidence its hapticity in an oxidative addition complex seems to depend on the size of the phosphine ligand. Compare complex **43** (κ^1 sulfamate with two $PPhEt_2$ ligands) to $ArNi(PCy_3)(\kappa^2\text{-}OSO_2NMe_2)$ in: Hooker, L. V.; Neufeldt, S. R. Ligation state of nickel during C—O bond activation with monodentate phosphines. *Tetrahedron* **2018**, *74*, 6717.

(31) A 4-centered cyclic transition state involving Ni−fluoride has been proposed for the Ni-catalyzed Stille coupling of $Ar—NMe_3^+$ electrophiles (see ref 13).

(32) "Open" (noncyclic) transmetalation transition states could not be located computationally. With palladium, these are considered most relevant in highly polar solvents in the absence of strongly coordinating anions, a scenario unlike the system currently under study.

(33) Similarly, when **42** is stirred with $Ni(cod)_2$, $PPhEt_2$, and KF in 1,4-dioxane overnight, the only product observed by NMR is the nickel sulfamate complex **43** (there is no evidence for formation of a nickel fluoride species, see SI).