# Nickel-Catalyzed Reductive Cross-Coupling of Unactivated Alkyl Halides
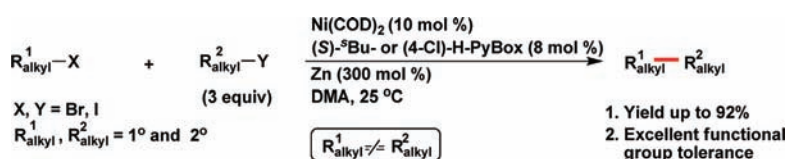
Xiaolong Yu, Tao Yang, Shulin Wang, Hailiang Xu, and Hegui Gong*

*Department of Chemistry, Shanghai University, 99 Shang-Da Road, Shanghai 200444, China*

*hegui_gong@shu.edu.cn*

ABSTRACT



A Ni-catalyzed reductive approach to the cross-coupling of two unactivated alkyl halides has been successfully developed. The reaction works efficiently for primary and secondary halides, with at least one being bromide. The mild reaction conditions allow for excellent functional group tolerance and provide the $C(sp^3)-C(sp^3)$ coupling products in moderate to excellent yields.

The transition-metal-catalyzed cross-coupling reactions of alkyl halides and organometallic reagents developed by Fu and many others represent elegant advances toward C−C bond formation on $sp^3$ carbons.[1−3] On the other hand, the development of catalytic reductive coupling approaches directly between two organohalides has emerged to be a powerful strategy to C−C bond formation,[4−6] which has led to an efficient synthesis of aryl−alkyl cross-coupling[5] and alkyl−alkyl homocoupling products.[6] To the best of our knowledge, a direct catalytic cross-coupling of two unactivated alkyl halides to form $C(sp^3)-C(sp^3)$ bonds has yet to be explored.

In contrast to the conventional coupling approaches utilizing alkyl metallic nucleophiles to generate alkyl−alkyl bonds, the development of a catalytic reductive coupling method between two alkyl halides is advantageous, considering that alkyl halides are generally more accessible and easier to handle than alkyl nucleophiles. However, the challenges are noticeable. First, alkyl halides are in general considered as poor coupling partners in the transition metal-catalyzed coupling reactions.[1b] Second, it is of great difficulty to identify a catalytic system that can effectively disfavor the highly competitive homocoupling side reactions for the two alkyl halide partners with similar structures. Herein, we report an unprecedented mild Ni-catalyzed reductive cross-coupling reaction of two unactivated alkyl halides that provides efficient synthesis of alkyl−alkyl C−C bonds.

To begin with, we chose the coupling of 4-bromo-1-tosylpiperidine **1** with $n\text{-}C_3H_7I$ and $n\text{-}C_4H_7Br$ as the model reactions (Table 1). After considerable effort, we determined

(1) For selected reviews, see: (a) Rudolph, A.; Lautens, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2656–2670. (b) Frisch, A. C.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 674–688.

(2) For recent examples on Ni-Catalyzed asymmetrical cross-couplings of alkyl halides, see: (a) Lou, S.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 1264–1266. (b) Lou, S.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 5010–5011. (c) Owston, N. A.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 11908–11909.

(3) For recent examples of Pd-, Cu-, and Fe-catalyzed cross-couplings on alkyl electrophiles, see: (a) He, A.; Falck, J. R. *J. Am. Chem. Soc.* **2010**, *132*, 2524–2525. (b) Terao, J.; Todo, H.; Begum, S. A.; Kuniyasu, H.; Kambe, N. *Angew. Chem., Int. Ed.* **2007**, *46*, 2086–2089. (c) Hatakeyama, T.; Hashimoto, T.; Kondo, Y.; Fujiwara, Y.; Seike, H.; Takaya, H.; Tamada, Y.; Ono, T.; Nakamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 10674–10676. (d) Fürstner, A.; Martin, R.; Krause, H.; Seidel, G.; Goddard, R.; Lehmann, C. W. *J. Am. Chem. Soc.* **2008**, *130*, 8773–8787.

(4) For recent examples of catalytic coupling of Ar−Ar halides, see: (a) Lee, K.; Lee, P. H. *Tetrahedron Lett.* **2008**, *49*, 4302–4305. (b) Wang, L.; Zhang, Y.; Liu, L.; Wang, Y. *J. Org. Chem.* **2006**, *71*, 1284–1287. (c) Gosmini, C.; Bassene-Ernst, C.; Durandetti, M. *Tetrahedron* **2009**, *65*, 6141–6146. (d) Wang, L.; Lu, W. *Org. Lett.* **2009**, *11*, 1079–1082. (e) Amatore, M.; Gosmini, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 2089–2092.

(5) For the coupling of alkyl with aryl or alkenyl halides, see: (a) Czaplik, W. M.; Mayer, M.; Grupe, S.; von Wangelin, A. J. *Pure Appl. Chem.* **2010**, *82*, 1545–1553. (b) Everson, D. A.; Shrestha, R.; Weix, D. J. *J. Am. Chem. Soc.* **2010**, *132*, 920–921. (c) Krasovskiy, A.; Duplais, C.; Lipshutz, B. H. *J. Am. Chem. Soc.* **2009**, *131*, 15592–15593. (d) Czaplik, W. M.; Mayer, M.; von Wangelin, A. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 607–610. (e) Krasovskiy, A.; Duplais, C.; Lipshutz, B. H. *Org. Lett.* **2010**, *12*, 4742–4744.

(6) For catalytic homocoupling of two alkyl electrophiles, see: (a) Prinsell, M. R.; Everson, D. A.; Weix, D. J. *Chem. Commun.* **2010**, 5743–5745. and references cited therein (b) Goldup, S. M.; Leigh, D. A.; McBurney, R. T.; McGonigal, P. R.; Plant, A. *Chem Sci* **2010**, *1*, 383–386.

that Ni(COD)$_2$ (10 mol %), (S)-$^s$Bu-Pybox **3a** (8 mol %),[7,8] and Zn (300 mol %) in DMA (N,N-dimethylacetamide)[9] at 25 °C were optimal for n-propyl iodide (300 mol %), providing the coupling product **2a** in a 67% yield (entry 1) after 12 h (Tables S1−S7, Supporting Information).[10] The side reactions arising from **1** consisted of homocoupling (∼26%), hydro-dehalogenation of the C−Br bond (<5%), and β-H elimination (trace).[11] Interestingly, use of 2 equiv of n-C$_3$H$_7$I provided **2a** in a 59% yield as opposed to 49% employing 5 equiv of n-C$_3$H$_7$I, indicating that the cross-coupling should not be simply attributed to a statistically controlled process (Table S6, Supporting Information).[10] Other Ni sources (Table S3, Supporting Information), ligands including **3b**−**3j**, $^t$Bu-Terpy, and bathophenanthroline (entries 2−12), solvents (Table S4, Supporting Information), reductants (Table S5, Supporting Information) and temperatures (Table S1, Supporting Information) were either ineffective or less effective.[10] Notably, excess (S)-$^s$Bu-Pybox **3a** (>10%) led to a decrease in yield (Table S2, Supporting Information). For n-BuBr (entries 1−4, 10−17), the optimal ligand was identified as (4-Cl)-H-Pybox **3n** (entry 16); (4-Me)- **3k** and (4-Ph)-H-Pybox **3l** were comparable (entries 13 and 14). The profile of the byproducts derived from **1** after 16 h was similar to that with n-PrI. In comparison, under the optimized conditions, 4-iodo-1-tosylpiperidine was much less effective due to homocoupling, generating **2a** in 37% with n-C$_3$H$_7$I and a trace amount of **2b** with n-C$_4$H$_9$Br, respectively. It should be noted when the less effective Pybox ligands were employed in Table 1, **1** was consumed and majorly converted to the homocoupling byproduct. Therefore, tuning the structures of Pybox ligands appeared to be crucial to suppress the homocoupling side reactions whiling promote the cross-coupling efficiency.

Using the optimized procedure, cross-coupling of a range of alkyl halides with **1** was examined, furnishing the coupling products **2c**−**p** (Table 2). The elongated n-heptyl chain slightly diminished the yields (entries 1 and 2). The byproducts derived from n-heptyl iodide and bromide comprised the homocoupling (∼70% based on n-C$_7$H$_{15}$X) (Table S9, Supporting Information),[10] the hydro-dehalogenation of the C−I bond (10%) or C−Br bond (<5%), and the β-H elimination (trace). A small quantity (<5%) of n-heptyl bromide was also recovered after the reaction was run for 16

(7) The Ni(COD)$_2$/(S)-$^s$Bu-Pybox **3a** catalytic system has proven to be highly efficient for the Negishi coupling of unactivated alkyl halides with primary alkylzincs: Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 14726−14727.

(8) For other selected examples of Ni/Pybox-catalyzed Negishi couplings, see: (a) Lundin, P. M.; Esquivias, J.; Fu, G. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 154−156. (b) Gong, H.; Sinisi, R.; Gagné, M. R. *J. Am. Chem. Soc.* **2007**, *129*, 1908−1909.

(9) DMA of extra dry (Acros), extra pure (99.5%, Acros), and AR grade (Aladdin Co., China, $8/1 L) qualities gave similar yields. The details of the effects of water and acids are provided in Table S7 (Supporting Information).

(10) See the Supporting Information for details.

(11) In addition to refs 2a−2c, other non-Pybox ligands have also been used in the Ni-catalyzed cross-coupling of alkyl halides to avoid β-H elimination: (a) Breitenfeld, J.; Vechorkin, O.; Corminboeuf, C.; Scopelliti, R.; Hu, X. *Organometallics* **2010**, *29*, 3686−3689. (b) Smith, S. W.; Fu, G. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 9334−9336. (c) Gong, H.; Gagné, M. R. *J. Am. Chem. Soc.* **2008**, *130*, 12177−12183. (d) Powell, D. A.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 7788−7789.

**Table 1.** Optimization for the Coupling of **1** and n-C$_n$H$_{2n+1}$-X$^a$



| entry | ligand | yield$^b$ (%) | |
| | | n = 3, X = I | n = 4, X = Br |
|---|---|---|---|
| 1 | **(S)-$^s$Bu-Pybox (3a)** | **67** | 47 |
| 2 | (S)-Me-Pybox (**3b**) | 64 | 35 |
| 3 | (S)-$^i$Pr-Pybox (**3c**) | 35 | 24 |
| 4 | (S)-Ph-Pybox (**3d**) | 56 | 36 |
| 5 | (S)-$^t$Bu-Pybox (**3e**) | <5 | NA$^c$ |
| 6 | (4-Me)-(S)-$^s$Bu-Pybox (**3f**) | 60 | NA |
| 7 | (4-Ph)-(S)-$^s$Bu-Pybox (**3g**) | 40 | NA |
| 8 | (4-MeO)-(S)-$^s$Bu-Pybox (**3h**) | 52 | NA |
| 9 | (4-Cl)-(S)-$^s$Bu-Pybox (**3i**) | 50 | NA |
| 10 | $^t$Bu-Terpy | 18 | 25 |
| 11 | bathophenanthroline | <5 | 15 |
| 12 | (4-H)-H-Pybox (**3j**) | 43 | 51 |
| 13 | (4-Me)-H-Pybox (**3k**) | NA | 65 |
| 14 | (4-Ph)-H-Pybox (**3l**) | NA | 65 |
| 15 | (4-MeO)-H-Pybox (**3m**) | NA | 40 |
| 16 | **(4-Cl)-H-Pybox (3n)** | NA | **67** |
| 17 | (4-(4-F-Ph))-H-Pybox (**3o**) | NA | 55 |
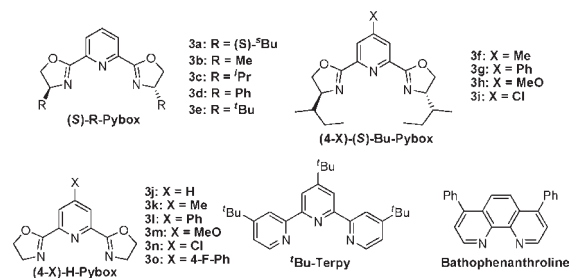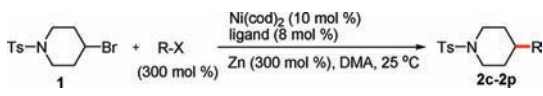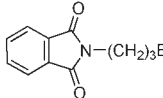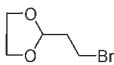


$^a$ Reaction conditions: **1** (100 mol %, 0.16 M in DMA), n-C$_n$H$_{2n+1}$-X (300 mol %), Ni(COD)$_2$ (10 mol %), ligand (8 mol %), Zn (300 mol %), 25 °C, 12 h for X = I, 16 h for X = Br. $^b$ Isolated yields. $^c$ Not available.

h. In both cases, the major side reactions for **1** were homocoupling. For benzyloxy- and phenyl-tethered alkyl halides, the bromides appeared to be more efficient than the iodide analogues (entries 3−7). The length of the alkyl chain in benzyloxylated bromides did not seem to affect the reactivity (entries 3 and 4). Other functionalities compatible with the reaction conditions included imide, ester, alkene, acetal, and even alcohol (entries 8−14). The secondary bromides also provided **2m**−**p** in moderate to fairly good yields, except for a poor result for cyclopropyl bromide (entries 15−19).

In order to gain insight into this coupling method, we carefully monitored the reaction progress using the examples illustrated in Table 2. Interestingly, examination of n-C$_7$H$_{15}$I (entry 1) and benzoyloxypentyl iodide (entry 12) demonstrated that higher cross-coupling yields were obtained when slower rates of homocoupling of the primary alkyl iodides took place. n-Heptyl and benzoyloxypentyl iodides were consumed within 2 and 1 h, respectively, by majorly

**Table 2.** Coupling of **1** (Limiting Reagent) with Various Alkyl Halides[a]



| entry | R-X | | ligand | product | yield (%)[b] |
|---|---|---|---|---|---|
| 1 | n-C₇H₁₅X | X = I | **3a** | **2c** | 60 |
| 2 | | X = Br | **3n** | **2c** | 63 |
| 3 | BnO⁀X | n = 3, X = Br | **3n** | **2d** | 48 |
| 4 | | n = 1, X = Br | **3n** | **2e** | 50 |
| 5 | | n =1, X = I | **3a** | **2e** | 37 |
| 6 | Ph⁀X | X = Br | **3n** | **2f** | 67[c] |
| 7 | | X = I | **3a** | **2f** | 48[c] |
| 8 | phthalimidyl–(CH₂)₃Br | | **3n** | **2g** | 65[c] |
| 9 | HO⁀X | X = Br | **3n** | **2h** | 60 |
| 10 | | X = I | **3a** | **2h** | 17 |
| 11 | BzO⁀X | X = Br | **3n** | **2i** | 65 |
| 12 | | X = I | **3a** | **2i** | 30 |
| 13 | ⁀Br | | **3n** | **2j** | 83 |
| 14 | dioxolane⁀Br | | **3n** | **2k** | 71 |
| 15 | cyclopropyl(CH₂)ₙBr | n = 1 | **3n** | **2l** | trace |
| 16 | | n = 3 | **3n** | **2m** | 65 |
| 17 | | n = 4 | **3n** | **2n** | 40 |
| 18 | R⁀Br | R = H | **3n** | **2o** | 72 |
| 19 | | R = Me | **3n** | **2p** | 57 |

[a] As in Table 1, footnote [a]. [b] Isolated yields. [c] The yield was estimated by NMR analysis of an inseparable mixture (see the Supporting Information).

converting to the homocoupling byproducts, suggesting that the terminal substituents on the primary alkyl iodides play important roles in affecting the rates of homocoupling. The corresponding yields of the desired products were 60% and 30%, respectively (Tables S8 and S9, Supporting Information).[10] Meanwhile, substantial quantities of **1** were recovered in both cases, indicating that the primary alkyl iodides were more reactive than **1**. For phthalimidyl propyl (entry 8), n-heptyl (entry 2), and benzoyloxypentyl (entry 11) bromides, complete consumption of **1** occurred within 4 h. In the case of 1-butenyl bromide (entry 13), it took approximately 4.5 h to digest **1**. A possible Ni–alkene coordination may be responsible for the high yield for **2j** (entry 13).[12] In all these cases, homocoupling accounted for the major side reactions for both coupling partners, though hydro-dehalogenation ( < 5%) and β-hydride elimination (trace) were also observed. Interestingly, substantial amounts of the starting primary alkyl bromides (~30%, i.e. ~1 equiv of alkyl bromides) were recovered, suggesting that the amount of excess alkyl bromides may be reduced to 2 equiv. In fact, use of 2 equiv of n-C₄H₉Br led to a 63% yield. Re-examination of the examples in Table 2 using 2 equiv of primary alkyl bromides generally only caused ~5% loss of yields as compared to those using 3 equiv. Finally, an equimolar mixture of **1** and

(12) Jensen, A. E.; Knochel, P. *J. Org. Chem*. **2002**, *67*, 79–85.

5-bromopentyl benzoate under the optimized reaction conditions gave recovered primary alkyl bromide ( > 60%), **2i** (~30%) and homocoupling of **1** ( > 60%) after 4 h, suggesting that **1** possesses higher reactivity than the primary bromide. This may explain why excess primary alkyl bromides are required to achieve good cross-coupling yields, probably due to enhanced chance for the catalyst or catalytic intermediate to find the less reactive primary bromides. Use of 5 equiv of 5-bromopentyl benzoate, however, did not yield better results than that with 3 equiv.

The scope of primary and secondary bromides as the limiting reagents is illustrated in Table 3. The coupling of cyclic secondary alkyl bromides with primary alkyl halides provided the products **4b**−**13b** in moderate to good yields (entries 1−11). The poor solubility of dodecyl bromide in DMA had little effect on the coupling efficiency (entry 3). No Barbier alkylation of ketone was observed when bromocyclohexanone was used (entries 6−7). The 2-bromo-2,3-dihydro-1*H*-indene bearing active benzylic protons also provided **11b** with a moderate result (entry 9). Notably, substrates containing the β-hydroxyl group also afforded the coupling products **12b**−**13b** in good yields (entries 10 and 11). No enantioselectivities were observed for **12b** and **13b** when (*S*)-ˢBu-Pybox **3a** was used. Moreover, the open chain secondary and primary bromides underwent efficient coupling with ⁱPr-Br, n-C₄H₉X (X = I, Br) and 1-butenyl bromide, affording **14b**−**18b** in moderate to excellent yields (entries 12−18).

Since this method displays extraordinary similarity to Fu's Ni/Pybox catalytic Negishi system, it is therefore important to understand whether an in situ organozinc/Negishi process is involved.[7,8] When **1**, (bromomethyl)cyclopropane, and 5-bromopentyl benzoate (up to 1 M in DMA) were independently treated with Zn (up to 3 equiv), no or trace quantities of organozincs formed in the presence or absence of I₂ (up to 10%),[13] (4-Cl)-H-Pybox **3n** (8%), or Ni(COD)₂ (10%) after 16 h at 25 °C, respectively. Next, treatment of 5-iodopentyl benzoate (up to 1 M in DMA) with Zn (1.5 equiv) produced trace amounts of benzoyloxypentylzinc iodide after 16 h at 25 °C. With the addition of 10% Ni(COD)₂, 45% of the starting 5-iodopentyl benzoate (0.47 M in DMA) was converted to organozinc iodide after 1 h,[14] implying possible organozinc/Negishi pathways for alkyl iodides. However, a mixture of **1**, 5-iodopentyl benzoate, and its organozinc reagent in a ratio of 1:1:1.5 in the presence of Ni(COD)₂/**3a** delivered large amount of unreacted **1** (95%) and 5-iodopentyl benzoate (44%) after 1 h. This suggests that a non-Negishi process may be operative and kinetically favored considering 5-iodopentyl benzoate was consumed under our coupling conditions (Table S12, Supporting Information).[10] Moreover, the coupling of **1** with 3-iodo- and -bromopropanol (entries 9 and 10, Table 2) provided the desired products in 17% and 60% yields, respectively. In both cases, homocoupling of **1** and 3-halopropanol was the major side reaction. Formation of

(13) Huo, S. *Org. Lett*. **2003**, *5*, 423–425.
(14) With the use of 5% and 10% I₂ or 8% **3a** as activation reagents, the percent conversion of the starting 5-iodopentyl benzoate (0.47 M in DMA) to the organozinc reagent was 0.22, 68, and 45 after 3 h, respectively.

**Table 3.** Scope of Alkyl Bromides (As the Limiting Reagents)[a]



| entry | X | product (R¹–R²) | yield (%)[b] |
|---|---|---|---|
| 1 | I | | 4b, R = H, n = 1: 72 |
| 2 | Br | | 5b, R = H, n = 2: 72 |
| 3 | I | | 6b, R = H, n = 10: 60 |
| 4 | Br | | 7b, R = CN, n = 2: 55 |
| 5 | I | | 8b, R = Cl, n = 2: 60 |
| 6 | I | | 9b: 65 |
| 7 | Br | | 57 |
| 8[c] | Br | | 10b: 50 |
| 9 | Br | | 11b: 45[d] |
| 10[e,f] | Br | | 12b: 65 |
| 11[f,g] | Br | | 13b: 60 |
| 12 | Br | | 14b: 55 |
| 13 | I | | 15b, R = n-Bu: 50 |
| 14 | Br | | 46 |
| 15 | Br | | 16b, R = 1-butenyl: 65 |
| 16 | I | | 17b, R = n-Bu: 65 |
| 17 | Br | | 72 |
| 18 | Br | | 18b, R = 1-butenyl: 92 |

[a] As in Table 1, footnote [a]. [b] Isolated yields. [c] > 20:1 diastereoselectivity (dr). [d] The yield was estimated by NMR analysis of an inseparable mixture (see the Supporting Information). [e] 4:1 dr. [f] No enantioselectivity using (S)-*s*Bu-Pybox **3a**. [g] 6:1 dr.

3-hydroxypropylzinc halides can be excluded because of intramolecular proton quenching.[15a] Since **1** did not convert to the organozinc reagent even with 10% Ni(COD)₂ (vide supra), an in situ organozinc/Negishi mechanism would be highly implausible in both cases. Additionally, the coupling of **1** with *n*-C₃H₇I in the presence of more acidic 4-bromophenol (3 equiv) gave **2a** in a 48% yield. A Negishi mechanism should not be operative due to instant hydrolysis of organozinc.[15] The collective studies support that the organozinc/Negishi pathways are not

necessary for this cross-coupling event, although the participation of such a process cannot be unambiguously excluded for primary alkyl iodides.

Finally, the coupling of alkyl bromide bearing pendant olefin **19a** with (bromomethyl)cyclopropane gave a cyclization/cross-coupling sequence along with ring-opening of cyclopropane product **19b** (eq 1), wherein excellent diastereoselectivity (> 20:1 endo/exo) was observed; this indicates that the two alkyl halides went through radical intermediates during the course of coupling.[16a] Therefore, oxidative addition of low-valent Ni-intermediates to both R¹-X and R²-X involving formation of alkyl radicals appears to be plausible in the catalytic process.[16] Moreover, this coupling event may involve a key R¹-Ni(III)-R² intermediate through oxidative addition of a R¹-Ni(I) species to R²-X prior to the product formation. Though not directly relevant, a similar hypothesis has been suggested in the coupling of aryl–aryl[17] and aryl–alkyl halides,[5b] dimerization of alkyl halides,[6b] as well as Negishi reactions.[18]
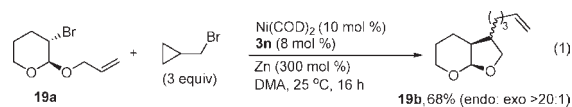


In conclusion, we have established the first effective cross-coupling of two alkyl halides via a Ni-catalyzed reductive process. The mild, easy-to-handle method allows excellent functional group tolerance and provides alkyl–alkyl coupling products in moderate to excellent yields. The catalyst also displays intriguing features in differentiating the alkyl coupling partners, and inhibiting the homocoupling side reactions that may be further improved by tuning the ligand structures. Whereas alkyl bromides are unlikely to involve an in situ organozinc/Negishi process, such pathways cannot be unambiguously ruled out for primary alkyl iodides, although a non-Negishi process appears to be kinetically more favored. Further improvement of the coupling efficiency as well as understanding the reaction mechanism will be the focus of our future investigations.

**Supporting Information Available.** Spectral data of new compounds and experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

(15) (a) Knochel has demonstrated that 73% of OctZnBr·LiCl is protonated after 5 min with 1 equiv of *i*Pr-OH, and using phenol as the proton source led to an instant complete hydrolysis of octylzinc bromide after 30 s: Manolikakes, G.; Hernandez, C. M.; Matthias, A.; Schade, M. A.; Metzger, A.; Knochel, P. *J. Org. Chem.* **2008**, *73*, 8422–8436. (b) Under Ni-catalyzed Negishi conditions, a 1:3:3 mixture of **1**, benzoyloxypentyl zinc bromide, and 4-Br-phenol only gave recovered **1**.

(16) (a) González-Bobes, F.; Fu, G. C. *J. Am. Chem. Soc.* **2006**, *128*, 5360–5361. (b) Gong, H.; Andrews, R. S.; Zuccarello, J. L.; Lee, S. J.; Gagné, M. R. *Org. Lett.* **2009**, *11*, 879–882.

(17) For mechanistic discussions on the Ni-catalyzed reductive coupling of aryl–aryl halides involving Ni^I and Ni^III intermediates, see: (a) Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 7547–7560. (b) Colon, I.; Kelsey, D. R. *J. Org. Chem.* **1986**, *51*, 2627–2637. (c) Amatore, C.; Jutand, A. *Organometallics* **1988**, *7*, 2203–2214. (d) Klein, A.; Budnikova, Y. H.; Sinyashin, O. G. *J. Organomet. Chem.* **2007**, *692*, 3156–3166.

(18) For mechanistic studies that implicate Ni^I and Ni^III intermediates in Ni-catalyzed Negishi reactions, see: (a) Lin, X.; Phillips, D. L. *J. Org. Chem.* **2008**, *73*, 3680–3688. (b) Phapale, V. B.; Buñuel, E.; García-Iglesias, M.; Cárdenas, D. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 8790–8795. (c) Jones, G. D.; Martin, J. L.; McFarland, C.; Allen, O. R.; Hall, R. E.; Haley, A. D.; Brandon, R. J.; Konovalova, T.; Desrochers, P. J.; Pulay, P.; Vicic, D. A. *J. Am. Chem. Soc.* **2006**, *128*, 13175–13813.