

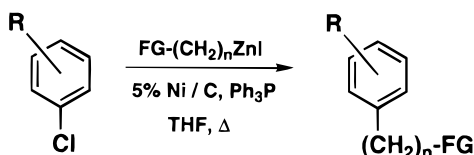
Nickel on Charcoal (“Ni/C”): An Expedient and Inexpensive Heterogeneous Catalyst for Cross-Couplings between Aryl Chlorides and Organometallics. I. Functionalized Organozinc Reagents

Bruce H. Lipshutz* and Peter A. Blomgren

Department of Chemistry
University of California
Santa Barbara, California 93106

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Although organopalladium chemistry continues to offer a wealth of impressive opportunities for the elaboration of molecular architecture,¹ as with any metal, there are limitations. Within the group 10 triad, processes mediated by organonickel complexes have begun to claim an increasing share of the carbon–carbon bond-forming spotlight normally reserved for its southern neighbor.² Such inveterate “name” reactions as Negishi,^{3a} Suzuki,^{3b} and Stille^{3c} couplings, among others,^{3d} which historically are Pd(0)-driven, are now being scanned with varying levels of success under Ni(0) catalysis.⁴ Aside from the many virtues of nickel (e.g., its low cost, usually greater reactivity, etc.), essentially all of its known C–C bond forming chemistry takes place in solution.⁵ In this report, we disclose the first successful, seemingly general, use of in situ generated nickel(0) on charcoal (“Ni/C”) as an efficient *heterogeneous* catalyst for mediating carbon–carbon bond constructions involving chloroarenes and functionalized organozinc reagents.



Nickel(II) is best impregnated on carbon using Ni(NO₃)₂⁶ together with a commercial source of charcoal that is of high surface area.⁷ Admixture of the charcoal, e.g., together with 5 mol % by weight of an aqueous solution of this nickel salt,

* Corresponding author. Telephone: 805-893-2521. Fax: 805-893-8265. E-mail: lipshutz@chem.ucsb.edu.

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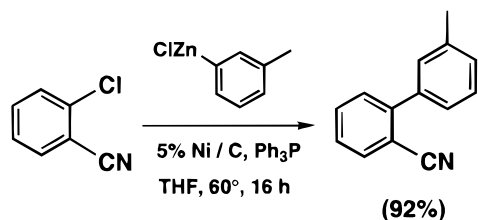
Table 1. Reactions of Aryl Chlorides with Functionalized Zinc Reagents Catalyzed by Ni/C

Aryl chloride	Product ^a	Yield(%) ^b
		80
		69
		62
		85
		66 ^c
		71
		84
		72
		91
		82

^a Fully characterized by IR, NMR, MS, and HRMS data. ^b Isolated, chromatographically purified materials. ^c EtOAc was used as the solvent due to the poor solubility of the zinc reagent in THF.

followed by evaporation of the water, washing with water and THF, and then drying under vacuum at room temperature, affords Ni(II)/C.⁸ Although this black powdery material was originally shown to be reduced to Ni(0) by heating to 400 °C, more recently it has been found that such treatment adversely alters the texture

(8) Procedure for preparing Ni(II)/C: Darco activated carbon [KB 100 mesh, lot No. 05031AR, surface area 1500 m²/g, pore volume 1.5 cm³/g, <30% H₂O] (5.00 g) was dried under vacuum (100 °C, 0.5 mmHg) for 12 h to yield 3.75 g of dried material (for weight purposes only). H₂O (75 mL) was deoxygenated by vigorously bubbling argon through the liquid for 2 h and was added to a 100-mL round-bottom flask containing the dried carbon and an efficient magnetic stir bar. Ni(NO₃)₂·6H₂O (545 mg, 1.87 mmol) dissolved in H₂O (5 mL, deoxygenated) was then added to the stirring suspension and the mixture heated in a sand bath equilibrated at 170 °C. The water was allowed to distill under an atmosphere of argon until the mixture was dry. The sand bath was then cooled, *undistilled*, degassed THF (50 mL) was introduced, and the mixture was placed in a sand bath equilibrated to 100 °C, and the liquid was distilled under Ar. The black solid was then washed with degassed H₂O (3 × 100 mL) and distilled THF (2 × 100 mL) and then dried under vacuum (0.5 mmHg) at 100 °C with stirring for 12 h. Evaporation of the filtrates led to recovery of 113 mg (0.39 mmol) of Ni(II). Thus, 0.27 g (1.48 mmol) Ni(II) was adsorbed onto 3.75 g of charcoal, leading to 1.48 mmol/4.02 g (total weight) or 0.37 mmol Ni(II)/g C.

Scheme 1. Ni/C-Catalyzed Coupling of an Aryl Chloride to Form a Biaryl

of the catalyst support and its reactivity.⁷ In our hands we find it experimentally easier to add PPh₃ (3–4 equiv, 15–20 mol % vs ArCl), stir for 15–30 min, and then add 10 mol % of either *n*-BuLi or MeMgBr, thereby generating catalytically active Ni(0)/C.

Our initial study has focused on couplings with organozinc reagents⁹ as nucleophiles. Rather than relying on more reactive aryl bromides, iodides, or pseudohalides usually required for the oxidative addition step in Pd(0)-catalyzed couplings,¹⁰ we anticipated insertion of Ni(0) into aryl chlorides should follow from early observations in this field by Kumada and Tamao.¹¹ As documented in Table 1, a variety of substituted zinc halides and aryl chlorides, most notably with each partner bearing electrophilic functionality (i.e., ketones, esters, nitriles, aldehydes, etc.), readily and efficiently couple in refluxing THF under these heterogeneous conditions. Particularly noteworthy is the example involving a sulfur(II)-containing educt (entry 8). In addition, Ni/C can effect biaryl couplings, such as that illustrated in Scheme 1. The selection of *o*-chlorobenzonitrile reflects the considerable scrutiny that this substrate's coupling (as a representative, inexpensive aryl chloride) with tolylboronic acid has been receiving of late, albeit still under the influence of catalytic Pd(0).¹²

To assess the critical question of catalyst bleed from the charcoal surface, analyses by ICP-AES (inductively coupled plasma-atomic emission spectroscopy)¹³ were conducted.¹⁴ Thus, upon completion of a reaction, the mixture was filtered through Celite, the filter cake was washed with THF and the solvent

removed in vacuo. Digestion of the residue with aqua regia then provided a sample appropriate for an ICP study, where only trace amounts (0.0015% vs ArCl) of nickel could be detected. Additional evidence could be garnered from control experiments, where (1) use of this amount of nickel as a homogeneous catalyst in a coupling reaction under our standard conditions afforded essentially none of the expected product; (2) interruption of an ongoing coupling by removal of the Ni/C via filtration followed by reexposure of the now clear reaction solution to the original conditions did not lead to additional cross-coupling to any significant degree.¹⁵

In summary, nickel on charcoal has been developed as an inexpensive, heterogeneous, and highly effective catalyst for mediating Negishi couplings between functionalized zinc reagents and substituted aryl chlorides. As with heterogeneous reactions in general, the simplicity in workup is especially attractive.¹⁶ Importantly, retention of nickel on the solid support offers control over such critical parameters as waste disposal and toxicity. While at present there remain interesting questions surrounding the surface chemistry of this active catalyst, it is nonetheless apparent that several other useful carbon–carbon and carbon–heteroatom couplings, in particular involving organometallics of Mg, Sn, Zr, Cu, and B, are likely to proceed via such Ni/C catalysis. Indeed, several of these have already shown promise, the details of which will be reported in due course.

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Supporting Information Available: Full spectral, chromatographic, and mass spectrometry data, along with ¹H and ¹³C NMR spectra for all new compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(16) General procedure for the Ni(0)/C coupling of aryl chlorides and alkylzinc iodides. To a flame-dried 25-mL round-bottom flask was added Ni-(II)/C (136 mg, 0.05 mmol, 0.369 mmol/g) and triphenylphosphine (53 mg, 0.20 mmol) under argon at room temperature. Dry THF (1.8 mL) was added and the slurry allowed to stir for 20 min. *n*-Butyllithium (38 μ L, 2.6 M in hexanes, 0.10 mmol) was added dropwise with swirling. After 5 min, the aryl chloride (1.0 mmol) was added. Upon the mixture being cooled to –78 °C, the iodozinc reagent (prepared from 1.5 to 2.0 mmol of the precursor iodide, 1.0–2.0 M in THF)⁹ containing lithium chloride (85 mg, 2.0 mmol) was then slowly added via cannula. The mixture was warmed to room temperature over 0.5 h, and finally heated to reflux for 12–24 h. The crude reaction mixture was then filtered through a pad of Celite and the filter cake further washed with THF (30 mL). Solvents were then removed on a rotary evaporator, and the resulting oily residue was chromatographed on silica gel.

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