

C–C Bond Formation Catalyzed Heterogeneously by Nickel-on-Graphite (Ni/C_g)

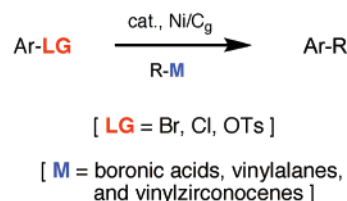
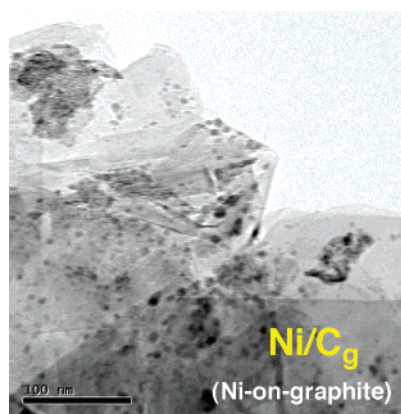
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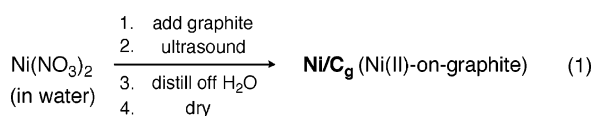
ABSTRACT



Inexpensive nickel(II) mounted on graphite (Ni/C_g) can be easily activated and used to heterogeneously catalyze cross-couplings involving aryl halides/tosylates with boronic acids, vinylalanes, and vinylzirconocenes. Comparisons are made with the charcoal analogue, Ni/C, and some unusual chemoselectivities between these catalysts have been uncovered.

Graphite: an especially stable allotropic form of carbon characterized by unsaturated sheets separated by 3.35 Å. As a solid support harboring metal atoms capable of catalyzing carbon–carbon bond formations, it offers very attractive economics (being less expensive than charcoal), a freely flowing nature (that makes handling quite convenient), and unlike charcoal, a well-ordered array (that could translate into chemoselectivity differences between metal-impregnated derivatives). Mounting Ni(II) between layers of graphite (Ni/C_g; eq 1) leads to an effective catalyst containing nanometer blobs of metal distributed randomly throughout

the layers (Figure 1).¹ Upon conversion to active nickel(0) using *n*-BuLi in THF (15 min, rt), aromatic tosylates and mesylates can be reduced with excellent functional group tolerance using in situ formed K⁺ or Cs⁺ salts of commercially available Me₂NH•BH₃ as a mild source of hydride.² The ability of Ni/C_g to insert into aryl C–OTs/C–OMs bonds,¹ rather than relying on more activated and costly triflates,³ suggested that cross-couplings with various organometallics should take place to afford valued carbon–carbon bonds under heterogeneous conditions. In this letter we describe the first Ni/C_g-catalyzed C–C bond-forming



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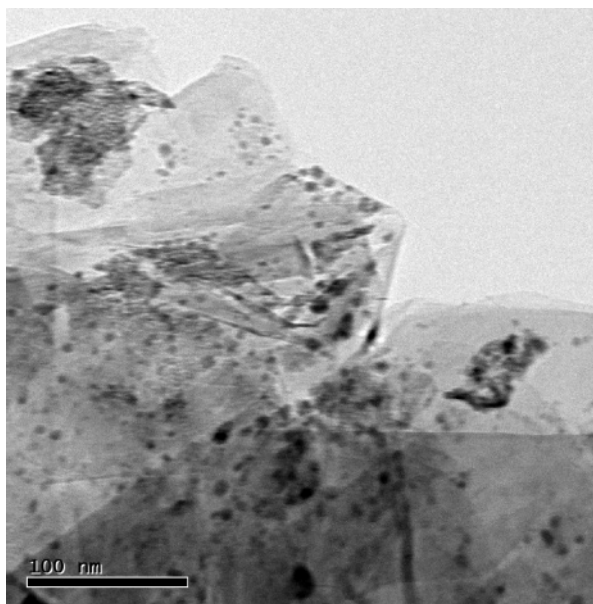
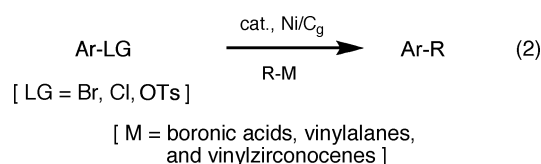


Figure 1. TEM of Ni/C_g showing graphite sheets and dark blobs of nickel.

reactions, using boronic acids, vinylzirconocenes, and vinylalanes as coupling partners (eq 2).



Suzuki Couplings. Ni/C_g-catalyzed Suzuki couplings were studied extensively with the intent to make comparisons with the corresponding reactions using Ni/C (nickel-in-charcoal)⁴ and to examine both aryl halides and tosylates as educts (Tables 1, 2, respectively). In general, Ni/C_g proved to be as effective, within experimental error, or better as a catalyst than Ni/C. That is, couplings were faster (extent of conversion was greater for a given time), yields were higher (by isolation), and the overall quality of the reactions appeared to be cleaner (by TLC). Aryl chlorides (entries A–D) and bromides (entries E, F) coupled with boronic acids either under conditions of conventional heating in refluxing dioxane, or with microwave assistance.⁵

The observation that, while the deactivated and somewhat sterically hindered case of *o*-chloroanisole was unresponsive to Ni/C, the graphite-supported catalyst (Ni/C_g) was very

Table 1. Comparison of Ni/C vs Ni/C_g in Suzuki Couplings

$\text{R}-\text{C}_6\text{H}_4-\text{X} \xrightarrow[\text{Ar-B(OH)}_2, \text{LiBr, dioxane, } \Delta]{\text{Ni cat., PPh}_3, \text{K}_3\text{PO}_4} \text{R}-\text{C}_6\text{H}_4-\text{Ar}$					
entry	substrate	boronic acid	catalyst	time (h)	yield (%) ^a
A			Ni/C	>12	40
B			Ni/C	14	90
			Ni/C _g	10	92
C			Ni/C	>12 ^b	0
			Ni/C _g	12	89
			Ni/C _g	0.7 ^c	87
D			Ni/C _g	0.7 ^c	87
E			Ni/C _g	9	87
F			Ni/C _g	7	86

^a Isolated, chromatographically purified material. ^b Reaction was allowed to stir overnight at reflux. ^c Under microwave conditions at 180 °C.

effective at mediating the desired biaryl bond formation was unexpected (entry C). This was the first of such chemoselectivity differences between catalysts to be noted (vide infra).

Cases of aryl tosylates that, as anticipated (vide supra), likewise afforded biaryl products in good isolated yields are less common (Table 2). Examples of both activated and deactivated partners suggest a reasonably broad scope associated with this process. With a temperature increase from 180 °C to 200 °C, expected shorter reaction times were observed without erosion in yields (entries 2, 4 vs 3, 5, 6). Here again, Ph₃P was the ligand of choice;⁴ attempts to use, for example, S-Phos,⁶ led to no conversion under otherwise identical conditions (as in entry 3). Particularly noteworthy is the observation that little-to-no homocoupling of either the aryl tosylate or boronic acid was seen in these reactions. Surprisingly, neither aryl nor alkyl trifluoroborates⁷ coupled with aryl tosylates, even under microwave conditions (200 °C) involving an activated substrate (Scheme 1).

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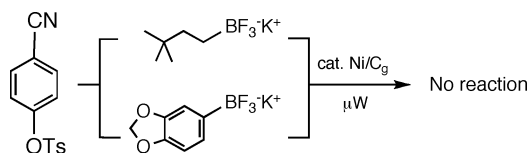
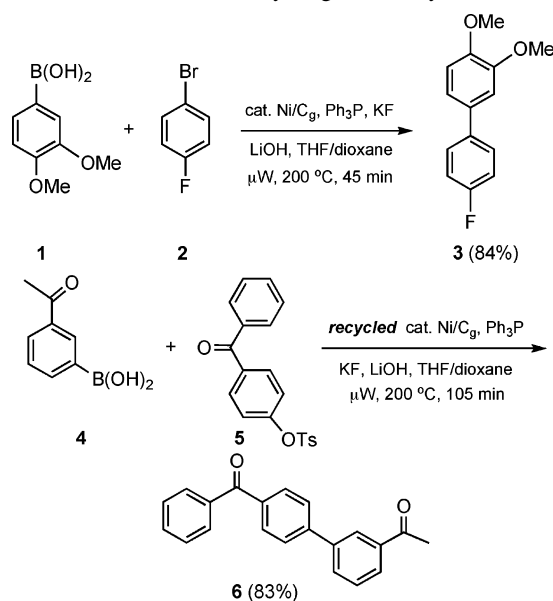
Table 2. Suzuki Couplings with Aryl Tosylates

$\text{R}-\text{C}_6\text{H}_4-\text{OTs} \xrightarrow[\text{Ar-B(OH)}_2, \text{KF, THF/dioxane, } \mu\text{W}]{\text{Ni/C}_g, \text{PPh}_3, \text{LiOH}} \text{R}-\text{C}_6\text{H}_4-\text{Ar}$				
entry	substrate	boronic acid	time (h)	yield (%) ^a
1			2 ^b	100 ^c
2			4.5 ^d	81
3			1.5 ^b	83
4			4.5 ^d	80
5			1.5 ^b	80
6			1.5 ^b	91

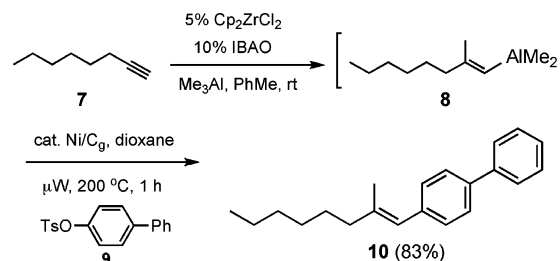
^a Isolated, chromatographically purified material. ^b At 200 °C. ^c GC conversion, to known biaryl (see SI). ^d At 180 °C.

Catalyst recycling was demonstrated by the successive cross-couplings illustrated in Scheme 2. Thus, following the Ni/C_g-catalyzed coupling of boronic acid **1** (1.5 equiv) with bromide **2** to biaryl **3**, filtration returned Ni/C_g that was used directly upon reactivation with *n*-BuLi, along with introduction of fresh reagents. Cross-coupling between deactivated boronic acid **4** and tosylate **5** gave diaryl ketone **6** in good yield.

Carboalumination/Cross-Coupling. One representative example of a Ni/C_g-catalyzed cross-coupling between an in situ formed vinylalane and an aryl tosylate was investigated

Scheme 1. Attempted Couplings with Trifluoroborate Salts**Scheme 2.** Recycling the Catalyst

(Scheme 3). Such a coupling between these two types of partners appears to be unprecedented. Octyne (**7**) was treated under newly developed conditions leading to full control of regiochemistry in Negishi carboalumination to **8**,⁸ using a pre-equilibrated reagent derived from Me₃Al (1.5 equiv), catalytic Cp₂ZrCl₂ (5 mol %), and isobutylaluminumoxane (IBAO; 10 mol %) in toluene at room temperature. Subsequent coupling with aryl tosylate **9** gave the corresponding styrene derivative **10** in good isolated yield.

Scheme 3. Carboalumination/Cross-coupling: Vinylalane + Aryl Tosylate

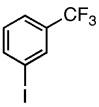
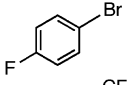

Hydrozirconation/Cross-Coupling. Prior studies using Ni/C have shown that this catalyst can assist in couplings between in situ formed vinylzirconocenes and aryl halides.⁹ Likewise, Ni/C_g can be used for this purpose, where iodides, bromides, and chlorides undergo cross-couplings to *E*-substituted styrenes (Table 3). Both rates and efficiencies were found to be as good or better with Ni/C_g. Unfortunately, neither type of Negishi reaction with vinylzirconocenes¹⁰ or

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Table 3. Ni/C_g-Catalyzed Cross-Couplings with Vinyl-zirconocenes

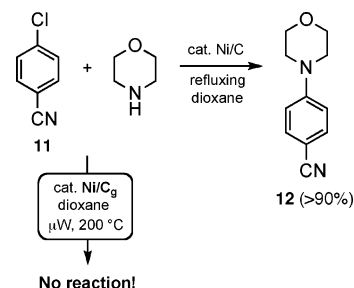
1-octyne		$\xrightarrow[\text{THF, rt}]{\text{Cp}_2\text{Zr(H)Cl}}$	$\xrightarrow[\text{Ar-X, THF, } \mu\text{W}^a]{\text{Ni/C}_g, \text{PPh}_3}$	$\text{Ar}-\text{CH}=\text{CH}-\text{C}_6\text{H}_{13-n}$	
entry	alkyne	Ar-X	time (min)	yield (%) ^b	
1	$\equiv\text{C}_6\text{H}_{13-n}$		10	85	
2	$\equiv\text{C}_6\text{H}_{13-n}$		15	83	
3	$\equiv\text{C}_6\text{H}_{13-n}$		40	90	

^a At 200 °C. ^b Isolated.

their derived zinc halide derivatives¹¹ led to C–C bond formation with aryl tosylates at temperatures up to 200 °C.

Chemoselectivity in Aminations: Ni/C vs Ni/C_g. Attempts to utilize Ni/C_g to catalyze aminations of aryl chlorides were surprisingly unsuccessful, notwithstanding prior observations where Ni/C has been shown to effect aryl C–N bond constructions readily, even under conditions of conventional heating in refluxing dioxane (Scheme 4).¹² Thus, it was quite unexpected that none of the aminated

Scheme 4. Chemoselectivity between Catalysts in Aminations



product **12** was detected by GC from the combination of morpholine and activated chloride **11**. While potentially synthetically valuable, an explanation for this chemoselectivity is not apparent.

In summary, nickel-on-graphite (Ni/C_g), a safe and especially inexpensive material, can be used to catalyze cross-couplings with various organometallic reagents (boronic acids, and vinylic zirconocenes and alanes) and aryl halides as well as, in some cases, aryl tosylates. This catalyst tends to afford cleaner reactions relative to its charcoal predecessor. Unexpected chemoselectivities between nickel-on-graphite, or nickel-in-charcoal (Ni/C), have been discovered and may provide rare opportunities in heterogeneous catalysis.

Acknowledgment. Financial support provided by the NIH (GM 40287) is warmly acknowledged. We are indebted to Dr. Louise Weaver (University of New Brunswick) for TEM data.

Supporting Information Available: Procedures and full characterization of new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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