

Copper + Nickel-in-Charcoal (Cu–Ni/C): A Bimetallic, Heterogeneous Catalyst for Cross-Couplings

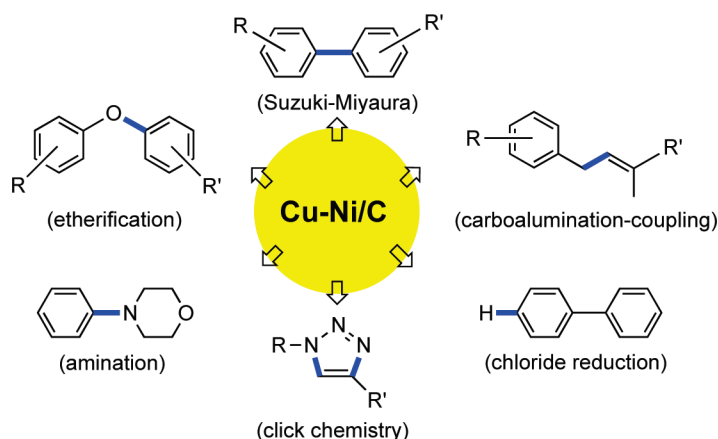
Bruce H. Lipshutz,* Danielle M. Nihan, Ekaterina Vinogradova, Benjamin R. Taft,
and Žarko V. Bošković

Department of Chemistry & Biochemistry, University of California,
Santa Barbara, California 93106

lipshutz@chem.ucsb.edu

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ABSTRACT



A new heterogeneous catalyst composed of copper and nickel oxide particles supported within charcoal has been developed. It catalyzes cross-couplings that traditionally use palladium, nickel, or copper, including Suzuki–Miyaura reactions, Buchwald–Hartwig aminations, vinylallene alkylations, etherifications of aryl halides, aryl halide reductions, asymmetric conjugate reductions of activated olefins, and azide–alkyne “click” reactions.

Transition-metal-based heterogeneous catalysis offers attractive opportunities in “green” chemistry. Aside from features commonly highlighted in this regard, including simplicity of workup, recyclability, and minimization of metallic waste,¹ solid supports have the potential to house more than one

metal and, hence, catalyze multiple types of bond constructions. Such “multifunctional” catalysts (Figure 1) are very few in number, as Felpin and Fouquet have discussed in their timely review on this subject.² Our contributions in heterogeneous catalysis have focused on the use of carbon as the matrix into which metals are readily impregnated. Both activated charcoal and less costly graphite can be used en route to nickel-in-charcoal (Ni/C),^{3a} nickel-on-graphite (Ni/C_g),^{3b} and copper-in-charcoal (Cu/C).^{3c} Base metals such as copper and nickel, in the form of their nitrate salts, are readily adsorbed; the resulting catalysts mediate a variety of “name” reactions typically associated with group 10 and 11 transition metals.

(1) Sheldon, R. A.; Arends, I.; Hanefeld, U. *Green Chemistry and Catalysis*; Wiley-VCH: Weinheim, 2007.

(2) Felpin, F.-X.; Fouquet, E. *ChemSusChem.*, DOI: 10.1002/cssc.200800110.

(3) (a) Lipshutz, B. H.; Blomgren, P. A. *J. Am. Chem. Soc.* **1999**, *121*, 5819–5820. (b) Lipshutz, B. H.; Frieman, B. A.; Butler, T.; Kogan, V. *Angew. Chem., Int. Ed.* **2006**, *45*, 800–803. (c) Lipshutz, B. H.; Frieman, B. A.; Tomaso, A. E. *Angew. Chem., Int. Ed.* **2006**, *45*, 1259–1264. (R)-DTBM-SEGPHOS = (R)-(-)-5,5'-bis[di(3,5-di-*tert*-butyl-4-methoxyphosphino)]-4,4'-bi-1,3-benzodioxole. CAS registry no. 566940-03-2.

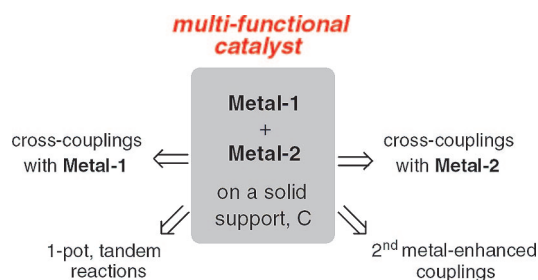
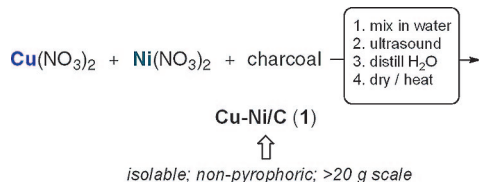


Figure 1. Prospects for heterogeneous multifunctional metal catalysts.

Heterogeneous bimetallic catalysts, on the other hand, may exploit three additional elements of practicality: (1) reduction of the mass of solid support otherwise involved for each metal if used individually; (2) application to reactions that either require, or are aided by, a second metal (e.g., Sonogashira or Stille couplings, respectively); and (3) utility in tandem processes that enlist each metal independently in a one-pot sequence. While reports on Pd–Co/Si,^{4a} Pd–Os/LDH,^{4b} and Rh–Pd/Gel^{4c} have appeared, to the best of our knowledge, no examples of multimetals on carbon are known, nor are there any catalysts of this type offering the chemistry of either copper or nickel (let alone both in one reagent). In this paper, we describe the preparation as well as several applications of the new catalyst copper + nickel-in-charcoal (Cu–Ni/C).

Scheme 1. Preparation of Cu–Ni/C



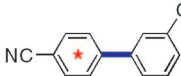
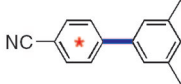
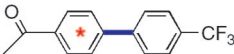
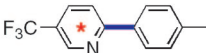
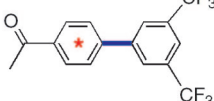
Preparation of Cu–Ni/C (1) (Scheme 1). Initially, the catalyst was prepared using a 1:1 ratio of aqua-colored $\text{Cu}(\text{NO}_3)_2$ to green $\text{Ni}(\text{NO}_3)_2$, each being loaded in a sequential fashion. The resulting species containing an arbitrarily chosen 5 wt % of Cu and 5 wt % of Ni, while active for several types of copper-catalyzed reactions, was relatively inactive insofar as nickel catalysis was concerned (relative to Ni/C).

A second-generation catalyst was then prepared using a 1:4 ratio of $\text{Cu}(\text{NO}_3)_2$ to $\text{Ni}(\text{NO}_3)_2$ (2 wt % of Cu, 8 wt % of

Ni), again loading the metals in a sequential fashion. In this case, both copper- and nickel-catalyzed reactions could be performed with rates comparable to those observed with Cu/C and Ni/C used independently. Finally, a third-generation catalyst was prepared, further streamlining the procedure by *simultaneously* loading both copper and nickel on the charcoal support, again in a 1:4 ratio. That is, by simply combining 2% $\text{Cu}(\text{NO}_3)_2$, 8% $\text{Ni}(\text{NO}_3)_2$, activated charcoal, and water in one pot followed by brief ultrasonication (so as to distribute and impregnate these salts into the charcoal matrix), subsequent distillation of the water and drying under vacuum provides active 2Cu–8Ni/C.

Cross-Couplings Catalyzed by 2Cu–8Ni/C. Cu–Ni/C catalyzes Suzuki–Miyaura couplings of aryl bromides and chlorides with aryl boronic acids in good yields (Table 1).

Table 1. Cu–Ni/C Catalyzed Suzuki–Miyaura Reactions^{a,b}

$\text{Ar}^*\text{-X} + \text{Ar}'\text{-B(OH)}_2 \xrightarrow[\text{KF (3 equiv.), LiOH (5 equiv.) dioxane, } \mu\text{W}}]{2\text{Cu-8Ni/C (2.5 mol \% Ni) PPh}_3 \text{ (15 mol \%)}} \text{Ar-Ar}'$					
entry	product	X	time (min)	temp (°C)	yield
1		Cl	66	200	82
2		Cl	60	180	92
3		Cl	66	200	84
4		Cl	60	180	90
5		Br	75	180	78

^a The red asterisk indicates a halide coupling partner. ^b All yields are for isolated material.

Reactions take place in dioxane at 180–200 °C over ca. 1 h under microwave irradiation. The presence of copper in Cu–Ni/C in excess of 2.5 wt % has an unfavorable effect on the reaction, lowering the extent of conversion. A 6- to 10-fold excess of Ph_3P to nickel was used in the presence of potassium fluoride and lithium hydroxide as a base. Under the investigated conditions, electron-rich aryl halides could not be successfully coupled. The results are comparable to those obtained using monometallic catalyst Ni/C.⁵

Anilines and diarylamines can be formed from aryl halides and primary or secondary alkyl- or arylamines using 2Cu–8Ni/C ligated with DPPF (diphenylphosphinoferrocene; 1–2 equiv relative to Ni). Lithium *tert*-butoxide, a base previously identified as crucial for the success of aminations with Ni/C,⁵ effected the same transformation with this bimetallic catalyst as well (Figure 2). Most of the reactions

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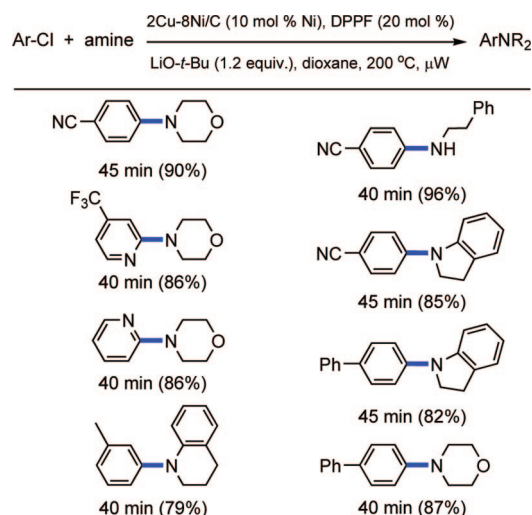


Figure 2. Cu–Ni/C-catalyzed aryl chloride aminations.

investigated were efficient, giving good isolated yields, and proceeded within 1 h in a microwave reactor at 200 °C.

Heterogeneous reductions (dehalogenation) of aromatic chlorides can be smoothly accomplished with Cu–Ni/C ligated with PPh₃, along with commercially available Me₂NH·BH₃ as a stoichiometric and mild hydride source (Figure 3).⁶ The choice of hydride is crucial in that it impacts

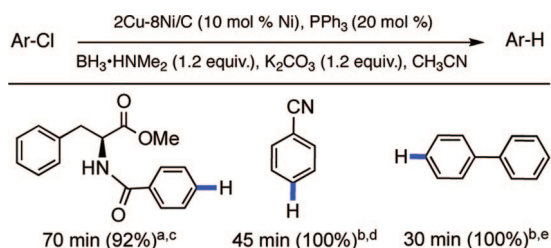


Figure 3. Products of Cu–Ni/C-catalyzed reductions of aryl chlorides. Key: (a) isolated, chromatographically pure material; (b) GC conversion; (c) run at 120 °C; (d) run at 130 °C; (e) run at 180 °C.

the extent of metal bleed into solution (which is significant, e.g., with Et₃SiH).⁶ A microwave reactor provides for short reaction times (0.5 h), and simple filtration of the catalyst and standard workup gives products in high yields. Unlike Ni/C, Cu–Ni/C cannot be used for dehalogenation of substrates that contain ketone functional groups, as significant amounts of the corresponding alcohol were observed, indicating that isolated carbonyl groups are competitively reduced, perhaps by electron-transfer processes or trace amounts of generated heterogeneous copper hydride.

Carboaluminations of terminal alkynes lead to (*E*)-vinylalanes that can be coupled to benzylic halides using Ni(0) catalysis.⁷ As illustrated below (Figure 4), the nickel present in heterogeneous 2Cu–8Ni/C smoothly assembles the expected allylated aromatics in good isolated yields.

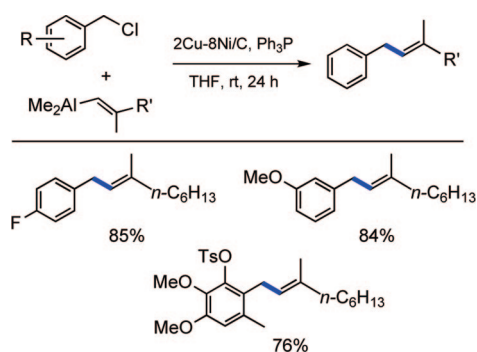


Figure 4. Cu–Ni/C-catalyzed carboaluminations/couplings.

Previously successful catalysis by Cu/C of alkyne–azide reactions⁸ prompted us to investigate catalyst **1** for these cycloadditions. Not unexpectedly, Cu–Ni/C along with 1 equivalent of triethylamine led to cycloadditions between several organic azides and acetylenes at 60 °C within a few

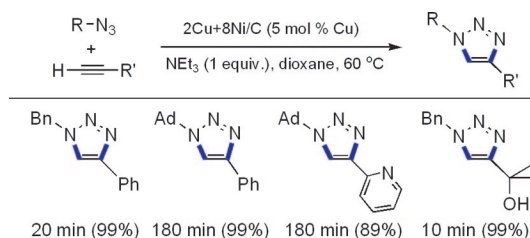


Figure 5. Cu–Ni/C-catalyzed “click” reactions.

hours (Figure 5). Isolated yields were quantitative, and the expected 1,4-regioselectivity was uniformly observed.

Copper-catalyzed conjugate reduction can be effected with this mixed metal heterogeneous reagent enantioselectively, using nonracemic (*R*)-DTBM-SEGPHOS^{3c} or with the achiral ligand bisdiphenylphosphinobenzene (BDP;⁹ Figure 6). Challenging β,β-disubstituted alkenes were reduced without difficulties. Reactions could be performed at rt or at 60 °C in the microwave reactor or in an ultrasonication bath.

Etherification of both activated and deactivated aryl bromides can be achieved using Cu–Ni/C, in this case best achieved with a loading of 5% of each metal (Figure 7). 1,10-Phenanthroline was used as a ligand for copper and

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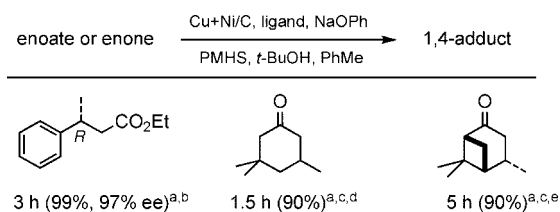


Figure 6. Cu–Ni/C-catalyzed conjugate reductions with CuH. Key: (a) isolated, purified material; (b) (R)-DTBM-SEGPHOS; (c) using cat. (BDP)CuH; (d) microwave heating at 60 °C; (e) run at rt.

Cs_2CO_3 as base.¹¹ Reactions were heated to 200 °C with microwave irradiation.

Recycling of Cu–Ni/C. Catalyst **1** was tested for recyclability in two different sequences: (1) where the copper

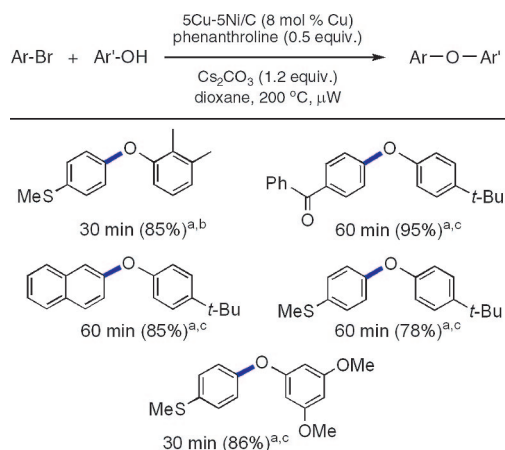


Figure 7. Cu–Ni/C-catalyzed etherifications. Key: (a) isolated, chromatographically purified material; (b) phenol as limiting reagent; (c) aryl bromide as limiting reagent.

content was utilized twice in asymmetric hydrosilylations of enoate **2** (Scheme 2, [A]) and (2) where the Ni in Cu–Ni/C catalyzed a Suzuki–Miyaura coupling followed by the Cu component effecting a click [3 + 2] cycloaddition (Scheme 2, [B]). In both series, catalyst **1** gave results indicative of good recyclability.

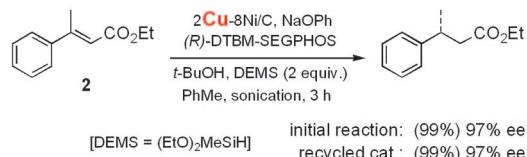
Lastly, a tandem process that illustrates another potential major benefit of having both metals present in the multi-functional catalyst **1**. An initial click reaction between bromoacetylene **3** and *n*-octyl azide followed by amination (without workup) afforded triazole amine **4** in 54% isolated yield. Although the initial Huisgen cycloaddition product could be obtained in 95% yield, the heteroaromatic triazole initially formed is unfortunately prone toward ligation of

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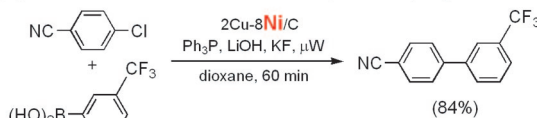
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Scheme 2. Recycling Experiments with Cu–Ni/C

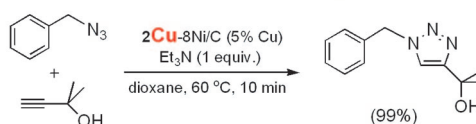
[A] catalyst recycle: asymmetric hydrosilylations with CuH



[B] 1st reaction of Cu–Ni/C: Suzuki–Miyaura coupling

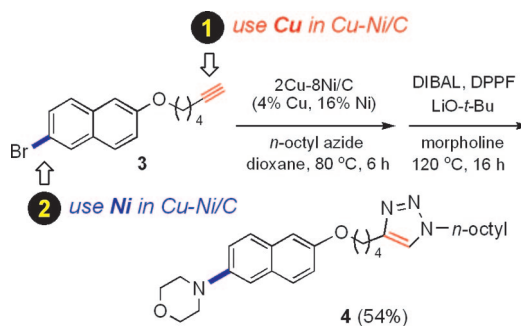


2nd reaction of recovered Cu–Ni/C: click cycloaddition



nickel and subsequent decomposition. Hence, losses due to complexation and/or decomposition on the charcoal of the morpholino product **4** accounted for the lower than expected overall yield.

Scheme 3. One-Pot Tandem Process Using Cu then Ni



In summary, the first example of a mixed-metal, recyclable catalyst composed of Cu and Ni is reported that is capable of mediating both group 10 and group 11 cross-couplings. Other valued combinations of (base and precious) metals-in-carbon are under study.

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Supporting Information Available: Detailed experimental procedures and spectral data for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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