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

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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, carboaluminations, 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 groups 10 and 11 transition metals.

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

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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>.

metal (e.g., Sonogashira or Stille couplings, respectively), and (3) utility in tandem processes that enlist each metal independently in a 1-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 multi-metals 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 *Letter* we describe the preparation as well as several applications of the new catalyst copper + nickel-in-charcoal (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 % Cu and 5 wt % 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 % Cu, 8 wt % 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). 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. Six to ten-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. 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 investigated were efficient, giving good isolated yields, and proceeded within an hour in a microwave reactor at 200 °C.

Heterogeneous reductions (dehalogenation) of aromatic chlorides can be smoothly accomplished with Cu-Ni/C ligated with PPh_3 , along with commercially available $\text{Me}_2\text{NH}\cdot\text{BH}_3$ as a stoichiometric and mild hydride source (Figure 3).⁶ The choice of hydride is crucial in that it impacts the extent of metal bleed into solution (which is significant, e.g., with Et_3SiH).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.

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 an equivalent of triethylamine led to cycloadditions between several organic azides and acetylenes at 60 °C within a few 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*)-DTBMSEGP₃^{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,¹⁰ 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 (Table 7). 1,10-Phenanthroline was used as a ligand for copper, and Cs₂CO₃ 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 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 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.

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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
Prospects for heterogeneous multi-functional metal catalysts

Figure 2.
Cu-Ni/C Catalyzed Aryl Chloride Aminations

Figure 3.

Products of Cu-Ni/C Catalyzed Reductions of Aryl Chlorides

^aIsolated, chromatographically pure material. ^bGC conversion. ^cRun at 120 °C. ^dRun at 130 °C. ^eRun at 180 °C.

Figure 4.
Cu-Ni/C Catalyzed Carboaluminations/couplings

Figure 5.
Cu-Ni/C Catalyzed "Click" Reactions

Figure 6.

Cu-Ni/C Catalyzed Conjugate Reductions with CuH

^aIsolated, purified material. ^b(*R*)-DTBM-SEGPHOS. ^cUsing cat. (BDP)CuH. ^dMicrowave heating at 60 °C. ^eRun at rt.

Figure 7.

Cu-Ni/C Catalyzed Etherifications

^aIsolated, chromatographically purified material. ^bPhenol as limiting reagent. ^cAryl bromide as limiting reagent.

Scheme 1.
Preparation of Cu-Ni/C

[A] catalyst recycle: asymmetric hydrosilylations with CuH [DEMS = (EtO)₂MeSiH]

initial reaction: (99%) 97% ee

recycled cat.: (99%) 97% ee

[B] 1st reaction of Cu-Ni/C: Suzuki-Miyaura coupling **2nd reaction of recovered Cu-Ni/C: click cycloaddition**

Scheme 2.
Recycling Experiments with Cu-Ni/C

Table 1

Cu-Ni/C Catalyzed Suzuki-Miyaura Reactions^{a,b}

$\text{Ar}^*-X + \text{Ar}'-\text{B}(\text{OH})_2 \xrightarrow[\text{KF (3 equiv), LiOH (5 equiv), dioxane, } \mu\text{W}}]{2\text{Cu-Ni/C (2.5 mol \% Ni), PPh}_3 \text{ (15 mol \%)}} \text{Ar}-\text{Ar}'$		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

^aIndicates halide coupling partner.^bAll yields are for isolated material.