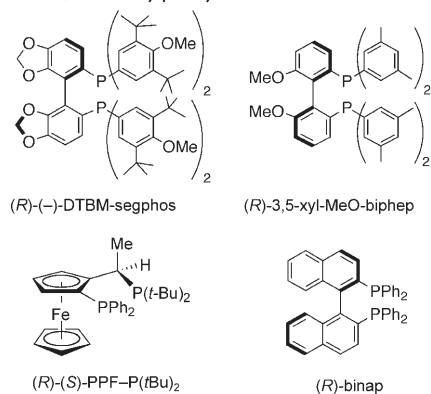


Table 1: Effect of ligand on asymmetric hydrosilylations catalyzed by CuH-in-charcoal.

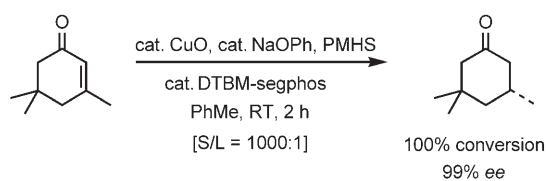


Ligand (L*)	Conversion	ee [%]
DTBM-segphos	complete in 10 h	88
PPF-P(<i>t</i> Bu) ₂	incomplete after 24 h	12
MeO-biphep	complete in 8 h	80
binap	complete in 18 h	41

Ar = 3,5-dimethylphenyl.



[L*CuO]/C is reduced by the silane presumably via transient species [L*Cu(OR)₂] or [L*CuLR] to [L*CuH]/C, after which the intended hydrosilylation takes place smoothly.^[7] Indicative that CuO and/or Cu₂O may well be the precursor(s) to active CuH under these conditions, the corresponding homogeneous catalyst was prepared using especially inexpensive, black CuO (2.5 mol %). Upon addition of NaOPh, along with PMHS, this new combination leads to an active catalyst that reacts using the homogeneous analogue (Scheme 2).



Scheme 2. Reaction of the homogeneous catalyst system.

Several ligands L* were screened to determine whether this parameter impacts the chemistry of [L*CuH] under these heterogeneous conditions (Table 1). Those studied included nonracemic DTBM-segphos,^[19] josiphos,^[20] MeO-biphep,^[21] and binap,^[22] using an iminophosphorane **1** as the substrate. The data pointed to *R*-(-)-DTBM-segphos as the bisphosphine ligand of choice.

Representative examples of functionalities responsive to this new technology at a substrate-to-ligand (S/L) ratio of 1000:1 are illustrated in Table 2, which includes comparison data, where available, for the corresponding reactions carried

out previously under homogeneous conditions. Hydrosilylation of acetophenone occurred readily with [(DTBM-segphos)CuH]/C in toluene, even at -50 °C, with 93% *ee* (entry 1). Likewise, heteroaromatic 2-acetylfuran reacts under these mild conditions (entry 2).^[14c] The keto ester precursor to the antidepressant prozac (entry 3) is reduced at cold temperatures as well and in high yield with high *ee*. Aryl imines (entries 4 and 5) were found to be the most sluggish of the substrates examined as they required 10 h under ultrasonication conditions and 6% ligand to reach completion. Curiously, the *ee* values observed were noticeably lower than those routinely realized using this catalyst under homogeneous conditions,^[14c] even when the sonication-bath temperature was held at 32 °C (or ca. 10 °C below the maximum temperature the bath would normally reach), thus foreshadowing distinctions between [L*CuH] in solution and heterogeneous [L*CuH]/C (see below).





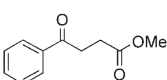
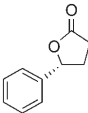
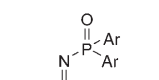
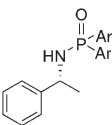
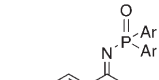
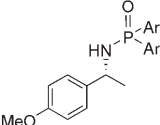


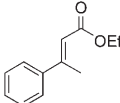
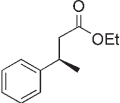


Several 1,4-reductions were also investigated: For example, the reaction with isophorone proceeds in toluene at room temperature within 1 h to afford the desired *R* product in high yield and with > 98% *ee* (entry 6). Repeating this experiment at a S/L ratio of 10000:1 afforded identical results (Scheme 3). A cinnamyl enoate (entry 7) was slow to be reduced with Cu/C at ambient temperature using conventional stirring (incomplete after 48 h); with ultrasonication, however, complete conversion took place within 1 h. An unsaturated lactone (entry 8) was reduced without resorting to ultrasonication.

Observations regarding a β,β-disubstituted *Z*-enone **3** (Table 3) were most unexpected, as the Cu/C reagent formed in the presence of a josiphos analogue (namely, [(PPF-P(*t*Bu)₂)CuH]/C; PPF-P(*t*Bu)₂ = (*R*)-(-)-1-[(*S*)-(diphenylphosphino)ferrocenyl]ethyl-di-*tert*-butylphosphine) led to the formation of keto product **4** in only 17% *ee*. Earlier studies on enones in solution with this identical catalyst at low temperatures,^[23] and even at 60 °C,^[24] had given products such as *ent*-**4** in > 90% *ee*. Switching to the segphos system, substantially increased the *ee* value to 64%. Curiously, however, with *tert*-butanol in the reaction mixture, used routinely to enhance reaction rates (by quenching the intermediate copper enolate),^[14d,25] the *ee* value was dramatically decreased. Clearly, the solid support can have a significant influence on the selectivity of these hydrosilylations.

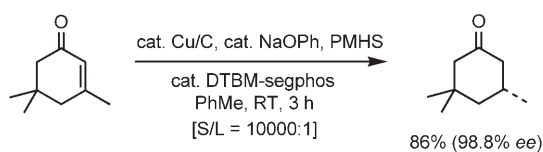
The prospects for recycling Cu/C were investigated, notwithstanding its virtually cost-free nature. Collection by filtration from a reaction mixture followed by drying and reuse led to identical results (Scheme 3). Particularly intriguing is the finding that after filtration, direct reuse (no isolation or drying) of the catalyst, and without the addition of more DTBM-segphos or NaOPh, product **5** was afforded in the same yield and with no erosion in reaction rate or enantioselectivity (Scheme 4). Apparently, the phosphine ligand is sequestered and maintained at the copper center.^[26]

Quantitative inductively coupled plasma atomic emission spectrometry (ICP-AES)^[27] was employed to determine the loading of copper within the charcoal, as well as the extent of copper bleed into solution during reactions performed with 0.022 mmol copper at room temperature and under ultrasonication. The loading of Cu/C was found to be 0.344 mmol Cu/g catalyst. Asymmetric conjugate reductions of isophor-

Table 2: Asymmetric hydrosilylations catalyzed by [(*R*)-(-)-DTBM-segphos]CuH]-in-charcoal.

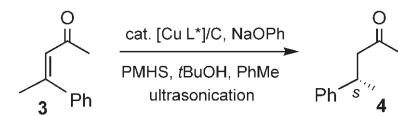
Entry	Substrate	Product	Yield [%] ^[a]	<i>t</i> [h]	[L*CuH]/C		<i>ee</i> [%]	[L*CuH] (solution)	
					<i>T</i> [°C]	<i>ee</i> [%]		<i>t</i> [h]	<i>T</i> [°C]
1			95	8	-50	93	5	-50	93 ^[14a]
2			91	8	-50	86	12 ^[b]	-50	92 ^[14e]
3			89	8	-45	94	- ^[c]	- ^[c]	- ^[c]
4			92	10	- ^[d]	88	17	RT	99 ^[14c]
5			90	10	- ^[d]	84	17	RT	98 ^[14c]
6			70 ^[e]	3	RT	99	8	0	92 ^[14b]
7			99	1	- ^[d]	99	2 ^[f]	RT	98 ^[14d]
8			83	7	RT	98	3	0	99 ^[14d,24]

[a] Isolated, chromatographically purified materials. [b] Using 0.5 mol % catalyst. [c] Not determined. [d] Using ultrasonication. [e] Product is volatile; some was lost during purification. [f] Using 1 mol % catalyst. Ar = 3,5-dimethylphenyl.


Scheme 3. 1,4-Reduction with isophorone at S/L = 10000:1.

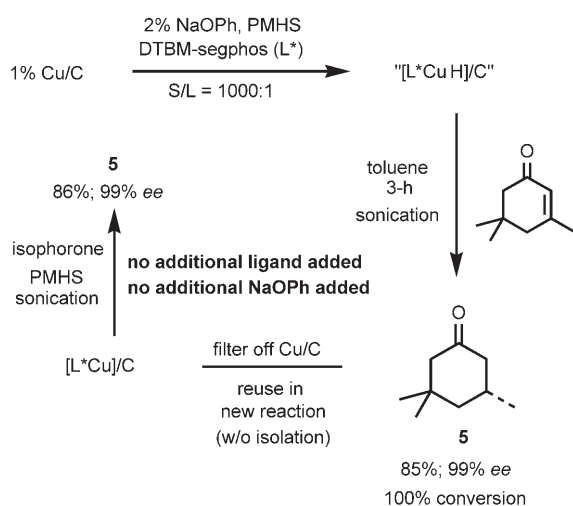
one (1.00-mmol scale) were performed at room temperature using both conventional stirring and ultrasonication conditions (bath temperature = \approx 42°C). ICP-AES analyses showed (as an average of two runs) that 2.5% of the copper used in the reaction had been leached from the support. This value corresponds to 37.0 μ g of copper in solution or a substrate/copper ratio of 1667:1. When the control experiment was performed under conventional conditions without substrate, 0.9% of the copper used was found to have leached from the support (13.9 μ g). For the reactions performed using

Table 3: Asymmetric hydrosilylations on a representative enone with Cu/C.



Ligand (L*)	<i>ee</i> [%]
(<i>R</i>)-(-)-DTBM-segphos	64
(<i>R</i>)-(-)-DTBM-segphos + <i>t</i> BuOH	19
(<i>R</i>)-(<i>S</i>)-PPF-P(<i>t</i> Bu) ₂	17
(<i>R</i>)-(<i>S</i>)-PPF-P(<i>t</i> Bu) ₂ + <i>t</i> BuOH	3

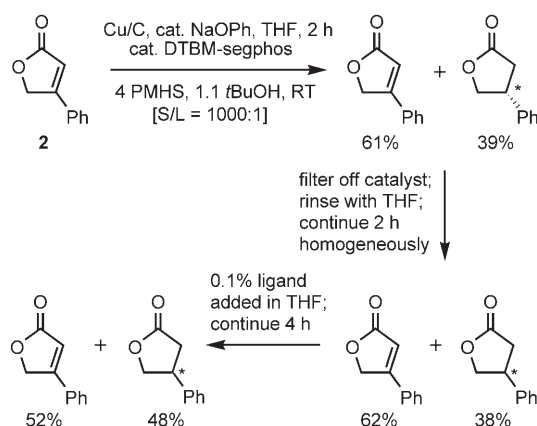
sonication, 3.0% of the 2.2 wt. % copper had bled from the support (44.4 μ g), which corresponds to a substrate/copper ratio of 1389:1. By comparison, using sonication in the absence of substrate decreased the extent of leaching by half (1.5% of the 2.2 wt. % copper, or 22.2 μ g). Reactions



Scheme 4. Recycling of Cu/C as illustrated by the reduction of isophorone.

conducted at subambient temperatures are likely to afford lower levels of copper in solution.

Additional experiments were carried out to lend further support to the claim that hydrosilylations catalyzed by Cu/C are heterogeneous in nature. Thus, unsaturated lactone **2** was treated with in situ generated catalytic [(DTBM-segphos)-CuH]/C for 2 h at ambient temperature (Scheme 5). An



Scheme 5. Homo- versus heterogeneous catalysis by CuH.

aliquot indicated that the ratio of educt to product was 61:39. The incomplete heterogeneous reaction mixture was filtered free of catalyst and the filtrate, which was shown by TLC to contain no DTBM-segphos, was allowed to stand for an additional 2 h. Analysis showed the ratio was essentially unchanged (62:38). Introduction of additional DTBM-segphos (0.1 mol%) followed by another 4-h reaction period led to some additional product (52:48). These observations support the ICP data that are indicative of a finite amount of copper bleeding into the macroscopic medium, as well as point to the essential role played by the ligand for catalysis to occur in solution. That no additional reaction takes place under homogeneous conditions, notwithstanding the confirmed presence of copper, indicates that reduction occurs

within the charcoal matrix where both metal and ligand are present. When considered together with the observed variations in reaction rates and differences in the *ee* values obtained between homogeneous and heterogeneous versions of these hydrosilylations (see Table 2), heterogeneous catalysis is implicated.^[28]

Micrographs using transmission electron microscopy (TEM) were recorded from a sample of Cu/C mounted on a grid, which displays 2D images.^[29] The brighter grayish portions correspond to charcoal, whereas darker regions correspond to areas with higher copper concentrations. Figure 1a suggests a relatively even distribution of copper

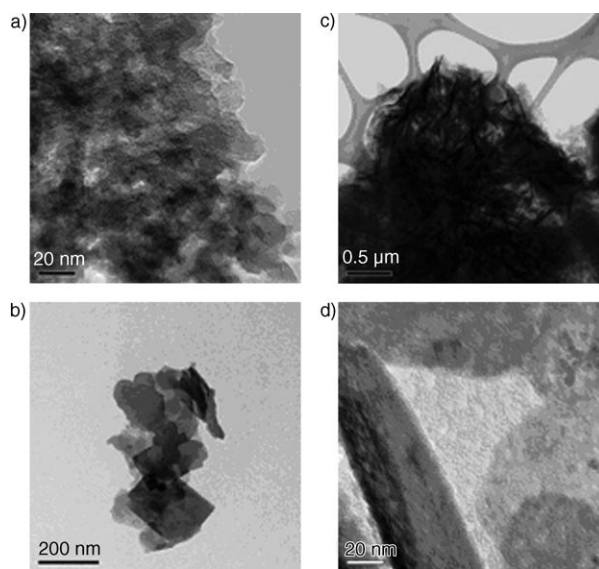


Figure 1. TEM images of Cu^{II}/C: a) bright field image showing dispersion of copper atoms; b) clusters of copper atoms; c) needles of copper atoms in a cluster; d) higher magnification of a copper cluster.

within the charcoal matrix, thought to derive from pretreatment of the catalyst with ultrasound. Figure 1b displays a magnified region of one of these darker regions and shows overlapping copper crystals. Figure 1c shows another perspective of copper conglomerates in the shape of needles on and within the charcoal matrix. Figure 1d illustrates a magnified cross section of a copper conglomerate. Taken together, these initial TEM images indicate a distribution of copper conglomerates on and within the charcoal pores throughout the catalyst. As was the case with Ni/C,^[5] in situ reduction from Cu^{II} to reactive Cu^IH/C by a silane at ambient temperatures is unlikely to alter this array.

In summary, copper(II) has been impregnated within a charcoal matrix using ultrasonication under mild conditions to lead to a heterogeneous reagent, copper-in-charcoal (Cu/C). Once ligated by catalytic amounts of a nonracemic bisphosphine and NaOPh in the presence of a silane, a chiral copper(I) hydride reagent is generated. This species is very effective in asymmetric hydrosilylation reactions of a variety of functional groups, thus affording products in high yields and with excellent *ee* values.^[30] ICP and TEM analyses, along with comparison data for the corresponding reactions in

solution, suggest that the chemistry observed is occurring in a heterogeneous fashion.

Experimental Section

Preparation of Cu^{II}/C: Darco KB (5.00 g, 100 mesh) activated carbon (25% H₂O content) was added to a 100-mL round-bottom flask containing a stirring bar. A solution of Cu(NO₃)₂·3H₂O (Acros Organics, Cu content by ICP determination: 127%; 555.7 mg, 2.92 mmol) in deionized H₂O (35 mL) was added to activated carbon, and deionized H₂O (40 mL) was added to wash down the sides of the flask. The flask was purged under argon and stirred vigorously for 1 min. The flask was submerged in an ultrasonic bath under a positive argon flow for 30 min. The flask was attached to an argon-purged distillation setup and placed in a preheated 175–180°C sand bath with stirring plate. As the distillation ended, the flask temperature rises automatically but should be held below 210°C for an additional 15 min. Upon cooling to room temperature, toluene (25 mL) was added to wash down the sides of the flask. The flask was again placed into the hot sand bath until the toluene/H₂O azeotrope had distilled. Once the distillation was finished, the azeotropic distillation was repeated. Upon cooling to room temperature, the black solid was washed with toluene (2 × 30 mL) under argon into a predried (in vacuo) 150-mL coarse-fritted funnel. The toluene (60 mL) used to wash the Cu/C was removed by rotatory evaporation and analyzed for any remaining copper. The fritted funnel was turned upside down under vacuum for 5 h until the Cu/C fell from the frit into the collection flask. The collection flask was then dried in vacuo in a preheated 110–115°C sand bath for 18 h. Using these specific amounts, the catalyst loading was 0.344 mmol Cu^{II}/g catalyst, or 2.2 wt. % Cu.

Representative asymmetric hydrosilylation: conversion of isophorone into (*R*)-3,3,5-trimethylcyclohexanone (Table 2, entry 6): Cu/C (134.4 mg, 0.05 mmol), NaOPh (24.0 mg, 0.20 mmol), and DTBM-segphos (2.4 mg, 0.002 mmol) were added to a flame-dried, argon-purged 10-mL round-bottom flask. Toluene (2 mL) was added and allowed to stir for 90 min. PMHS (240 μL, 4 mmol H⁻) was then added dropwise and allowed to stir for 30 min. Isophorone (300 μL, 2 mmol) was added neat and the reaction was allowed to stir at room temperature until shown to be complete by TLC analysis (3 h; 4:1 hexanes/EtOAc). The reaction mixture was filtered and washed with Et₂O (3 × 5 mL) to remove the Cu/C. The reaction mixture was quenched with aqueous NaOH (15 mL, 3 M) and allowed to stir at room temperature for 3 h. The residue was purified by flash chromatography (4:1 hexanes/EtOAc) to afford the title product (196.3 mg, 70% yield due to volatility) as a clear oil. Analysis of the residue by GC showed 98.9% *ee* by using a ChiralDex-BDM column with 75°C isotherm, *R*_t = 41.47 (minor) and 44.94 (major) min. The product matched previously reported spectral data.

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- [30] Isolation of the catalyst after treatment with *n*BuLi in THF at room temperature followed by exposure to air over time did not lead to any observable physical change; thus, the catalyst appears to be nonpyrophoric, as is the case with Ni⁰/C.