Communication

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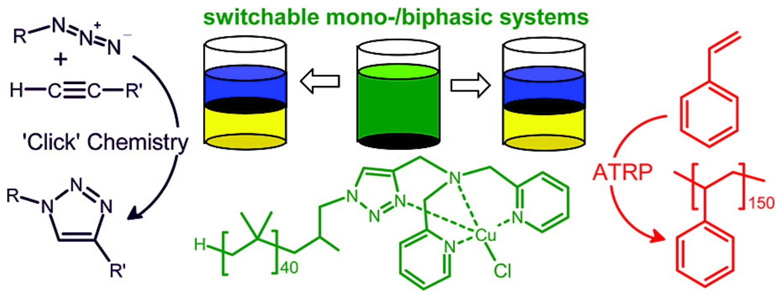

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Self-Separating Homogeneous Copper (I) Catalysts

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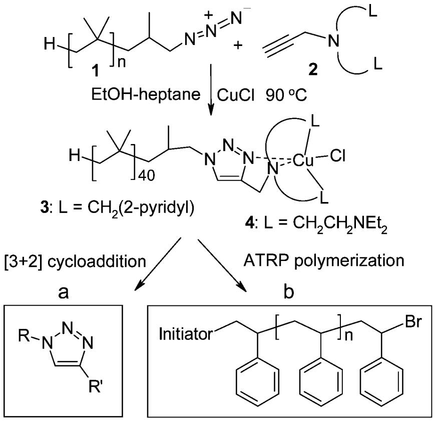
Strategies that use the properties of macromolecular or biphasic systems to control reaction rates or effect separations are routinely used in nature and are of increasing interest in homogeneous catalysis. Encapsulation strategies,[1,2] biphasic systems,[3,4] or strategies where autonomous control features are built into a catalyst so that a catalyst makes itself,[5] controls its reaction rate without external cooling or heating,[6] or separates itself from products[7] are examples where molecular engineering has been successfully used to facilitate catalytic processes. Here we describe a system where the self-separating properties of a macromolecular homogeneous transition metal catalyst facilitates its synthesis and isolation and later facilitates its separation from macromolecular products in two different sorts of reactions.

Copper−amine complexes can be used to effect a variety of carbon−carbon or carbon−heteroatom bond-forming reactions.[8−10] Thus, methods to more efficiently synthesize, purify, and separate such complexes are of interest and are potentially useful in homogeneous catalysis chemistry. Inspired by Fokin and Sharpless' recent Cu(I)-catalyzed [3+2] chemistry,[11] we have developed polyisobutylene (PIB)-supported Cu(I) catalysts where the polymer provides both a means to isolate the catalyst and a means to separate the catalyst from products by gravity-based separations in subsequent reactions.

Much attention has recently been given to the Cu(I)-catalyzed "click" formation of 1,4-disubstituted-1,2,3-triazoles as a selective and efficient synthetic procedure in all sorts of reactions including the synthesis of macromolecules[12] and synthesis of metal−ligand complexes.[11,13−15] A recent report has shown that syntheses of such complexes can be autocatalytic and that the product ligands stabilize the reactive Cu(I) species under aerobic aqueous conditions.[11] We have prepared similar polymer-supported Cu(I) complexes whose synthesis was autocatalytic and was carried out in a fashion that affords an easily separable solution of catalyst for use in subsequent catalytic chemistry. This chemistry (Scheme 1) uses polyisobutylene oligomers that we have shown separate phase selectively into nonpolar alkane solvents in thermomorphic or latent-biphasic solvent systems.[16]

Scheme 1. Synthesis and Applications of a PIB-Supported Cu(I) Catalyst[a]



[a] Reagents and conditions: a, RN_3, R′C≡CH, 90 °C, 12 h; b. ethyl 2-bromoisobutyrate, styrene, tin (II) 2-ethylhexanoate, heptane 110 °C, 21 h.

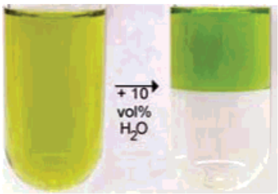
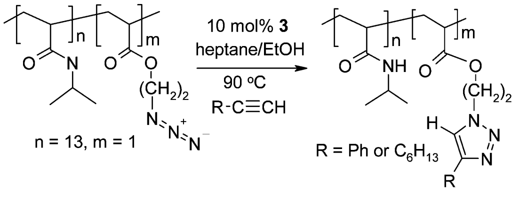


Figure 1. Phase-selective solubility of a PIB−Cu(I) complex in a heptane/90% EtOH/H_2O mixture after addition of 10 vol % H_2O to a monophasic heptane/EtOH solution. UV analysis showed >99.6% of the copper complex was in the heptane phase of the product biphasic mixture.

A Cu(I)-catalyzed "click" [3+2] cycloaddition formed 1,4-disubstituted-1,2,3-triazole bound Cu(I) complexes **3** and **4**. The phase-selective solubility of PIB facilitated isolation of a solution of either polymer-supported Cu(I) complex via a liquid−liquid separation without column chromatography. The [3+2] cycloaddition was carried out with CuCl in a miscible heptane/EtOH mixture. After 16 h the PIB−azide **1** had been completely consumed, and addition of 10 vol % water produced a biphasic mixture where the Cu(I) complex **3** was visually in the less dense heptane phase (Figure 1). While both PIB complexes **3** and **4** could be prepared and isolated as a heptane solution using a stoichiometric mixture of CuCl and the PIB−azide, it was also possible to prepare the Cu-free triazole ligand if the cycloaddition in Scheme 1 were carried out with 10 mol % CuCl. In this case, a filtration (SiO_2) removed the paramagnetic copper salts to yield the Cu-free PIB−triazole ligands present in the Cu complexes **3** or **4** as ^1H NMR characterizable products. However, if the Cu(I) complexes **3** or **4** were to be used in a subsequent catalytic reaction, isolation of a heptane solution of **3** or **4** by a biphasic liquid/liquid separation sufficed. Such solutions were storable for months under nitrogen with no sign of decomposition.

Heptane solutions of the Cu(I) complexes **3** and **4** proved to be effective recyclable catalysts both for synthesis of themselves and for other Cu(I)-catalyzed [3+2] cycloaddition modification reactions of other polymers (eq 1). Complete conversion of the starting azide occurred in these reactions.



(1)

Cu(I)-catalyzed atom transfer radical polymerization(ATRP) is another reaction catalyzed by Cu(I)−amine complexes. Such

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Figure 2. Monophasic polymerization and subsequent separation of **3** and **5** and a polystyrene product: (a) reaction scheme; (b) separated product mixture.

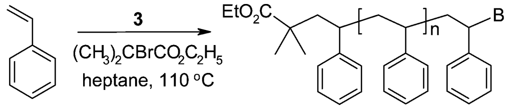
Table 1. Recyclable ATRP Polymerization Results for Styrene Polymerization Using **3** and **5** as Recoverable Catalysts

cycle	% yield[a]	M_n (calc)[b]	M_n[c]	M_w/M_n[c]
1	51.8	18000	23000	1.11
2	59.3	20000	22000	1.14
3	61.1	21000	24000	1.15
4	43.0	15000	17000	1.25
5	47.3	16000	17000	1.26

[a] The yield was based on the mass of the recovered polymer. [b] The M_n(calc) = $[\text{monomer}]_o/[\text{initiator}]_o$ x yield x monomer molecular weight. [c] The M_n and M_w/M_n values were determined by GPC using a Viscotek triple detector system with a GMHx1 column.

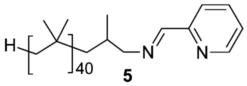
polymerizations are controlled radical polymerizations and afford excellent control of the product polymer's polydispersity and molecular weight. They are especially useful in the synthesis of block copolymers or in controlling a polymer's end-group structure. While various groups have described new, very active catalysts[17−19] or described strategies to separate the Cu(I) catalysts from the polymer products,[20−25] contamination of products by the transition metal catalysts remains an issue of concern.

Cu-catalyzed ATRP polymerizations are an example of an approach to catalysis where the catalyst self-separates from its products. Given that polystyrene is insoluble in heptane and that **3** is very soluble in heptane, we expected that this polymerization would illustrate how a system could be designed to self-separate itself after a reaction, owing to the differential solubilities of the catalyst and the product polymer. When a polymerization was carried out in a heptane/styrene mixture using $(CH_3)_2CBrCO_2Et$ as an initiator with **3** as a catalyst (eq 2), the polymerization proceeded to form a viscous suspension. If the polymerization were stopped at an intermediate point, centrifugation produced a biphasic mixture where the colored catalyst was clearly present in the upper heptane phase. UV−visible analysis showed no detectable PIB-bound copper complex in the product phase. ICP-MS analysis of the product phase showed ca. 3% of the copper present in **3** was present in the product polymer phase.



(2)

To ensure the copper remained coordinated to a PIB ligand and in the form of Cu(I), an additional 0.5 equiv (relative to **3**) of a PIB ligand (**5**) was added, and the polymerizations were carried out in the presence of a Sn(II) carboxylate known to reduce any Cu(II) formed by adventitious oxidation back to Cu(I). Polymerizations of styrene or methyl methacrylate used $(CH_3)_2CBrCO_2Et$ as the initiator with **3** as the source of copper. The reactions were typically carried out to about 50% conversion. As can be seen in Figure 2, copper was sequestered in the heptane phase at the end of the reaction. As shown in Table 1, the catalyst was recyclable and it behaved in this system just as a low-molecular weight analogue with minimal leaching of the copper (I) complex.



5

These studies show that the use of mixed-solvent systems where the products, catalysts, or byproducts self-separate from one another at the end of a reaction is a consequence of a product polymer's phase-selective solubility is a useful approach for polymer synthesis or modification. The specific catalyst discussed has been shown to be effective as a catalyst for its own formation and as a recyclable catalyst in synthesis and modification of other sorts of polymers using two quite different Cu(I)-catalyzed reactions. Extensions of related sorts of PIB-bound catalysts in other cycloaddition reactions and other polymerizations is currently under investigation.

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Supporting Information Available: Synthesis and characterization of polymers; procedures for ligand synthesis and catalysis. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Takeuchi, M.; Akiyama, R.; Kobayashi, S. *J. Am. Chem. Soc.* **2005**, *127*, 13096−13097.
(2) Poe, S. L.; Kobašlija, M.; McQuade, D. T. *J. Am. Chem. Soc.* **2006**, *128*, 15586−15587.
(3) Horváth, I. T. *Acc. Chem. Res.* **1998**, *31*, 641−650.
(4) Joó, F. *Acc. Chem. Res.* **2002**, *35*, 738−745.
(5) Hill, C. L.; Zhang, X. *Nature* **1995**, *373*, 324−326.
(6) Davies, D. M.; Stringer, E. L. *Langmuir* **2003**, *19*, 1927−1928.
(7) Motoyama, Y.; Mitsui, K.; Ishida, T.; Nagashima, H. *J. Am. Chem. Soc.* **2005**, *127*, 13150−13151.
(8) Wang, S.-Y.; Ji, S.-J.; Loh, T.-P. *J. Am. Chem. Soc.* **2007**, *129*, 276−277.
(9) Ouali, A.; Laurent, R.; Caminade, A.; Majoral, J.-P.; Taillefer, M. *J. Am. Chem. Soc.* **2006**, *128*, 15990−15991.
(10) Cabrera, S.; Gomez-Arrayás, R.; Carretero, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 16394−16395.
(11) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596−2599. Chan, T. R.; Hilgraf, R.; Sharpless, K. B.; Fokin, V. V. *Org. Lett.* **2004**, *6*, 2853−2855.
(12) Malkoch, M.; Thibault, R. J.; Drockenmuller, E.; Messerschmidt, M.; Voit, B.; Russell, T. P.; Hawker, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 14942−14949.
(13) Dai, Q.; Gao, W.; Liu, D.; Kapes, L. M.; Zhang, X. *J. Org. Chem.* **2006**, *71*, 3928−3934.
(14) Detz, R. J.; Heras, S. A.; de Gelder, R.; van Leeuwen, P. W. N. M.; Hiemstra, H.; Reek, J. N. H.; van Maarseveen, J. H. *Org. Lett.* **2006**, *8*, 3227−3230.
(15) Mindt, T. L.; Struthers, H.; Brans, L.; Anguelov, T.; Schweinsberg, C.; Maes, V.; Tourwé, D.; Schibli, R. *J. Am. Chem. Soc.* **2006**, *128*, 15096−15097.
(16) Li, J.; Sung, S.; Tian, J.; Bergbreiter, D. E. *Tetrahedron* **2005**, *61*, 12081−12092.
(17) Jakubowski, W.; Min, K.; Matyjaszewski, K. *Macromolecules* **2006**, *39*, 39−45.
(18) Percec, V.; Guliashvili, T.; Ladislaw, J. S.; Wistrand, A.; Stjerndahl, A.; Sienkowska, M. J.; Monteiro, M. J.; Sahoo, S. *J. Am. Chem. Soc.* **2006**, *128*, 14156−14165.
(19) Tang, H.; Arulsamy, N.; Radosz, M.; Shen, Y.; Tsarevsky, N. V.; Braunecker, W. A.; Tang, W.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2006**, *128*, 16277−16285.
(20) Honigfort, M. E.; Brittain, W. J. *Macromolecules* **2003**, *36*, 3111−3114.
(21) Hong, S. C.; Matyjaszewski, K. *Macromolecules* **2002**, *35*, 7592−7605.
(22) Shen, Y.; Zhu, S.; Pelton, R. *Macromolecules* **2001**, *34*, 3182−3185.
(23) Ding, S.; Xing, Y.; Radosz, M.; Shen, Y. *Macromolecules* **2006**, *39*, 6399−6405.
(24) Shen, Z.; Chen, Y.; Frey, H.; Stiriba, S.-E. *Macromolecules* **2006**, *39*, 2092−2099.
(25) Faucher, S.; Okrutny, P.; Zhu, S. *Macromolecules* **2006**, *39*, 3−5.

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