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Organic–Inorganic Hybrid Polymer-Encapsulated Magnetic Nanobead Catalysts

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Abstract: A new strategy for the encapsulation of magnetic nanobeads was developed by using the in situ self-assembly of an organic–inorganic hybrid polymer. The hybrid polymer of $\{[Cu(bpy)(BF_4)_2(H_2O)_2](bpy)\}_n$ (bpy = 4,4′-bipyridine) was constructed on the surface of amino-functionalized magnetic beads and the resulting hybrid-polymer-encapsulated beads were utilized as catalysts for the oxidation of silyl enolates to provide the corresponding α-hydroxy carbonyl compounds in high yield. After the completion of the reaction, the catalyst was readily recovered by magnetic separation and the recovered catalyst could be reused several times. Because the current method did not require complicated procedures for incorporating the catalyst onto the magnetic beads, the preparation and the application of various other types of organic–inorganic hybrid-polymer-coated magnetic beads could be possible.

Keywords: chelates · heterogeneous catalysis · hybrid polymer · magnetic properties · oxidation · sustainable chemistry

Introduction

The beautiful frameworks produced by the assembly of organic and inorganic molecules have received much attention because the resulting architectural porosity and/or large surface area provide a basis for exploring functions, such as, molecular recognition, gas storage, and catalysis.[1,2] Monodisperse magnetic nanoparticles are also quite fascinating because of their diverse uses, including biochemical applications involving separation and purification protocols.[3] Combining both these exciting characteristics could result in greater effort directed toward the development of such advanced materials. Herein we describe the construction of an organic–inorganic hybrid polymer on the surface of iron-oxide-derived magnetic beads and the use of such beads in a recyclable catalysis system based on magnetic separation.

Results and Discussion

A self-assembled organic–inorganic hybrid polymer consisting of metal cations (M) and hybridized ligands (X–X) was designed by using the appropriate functional group (X) and was immobilized on magnetic beads (Figure 1). In the

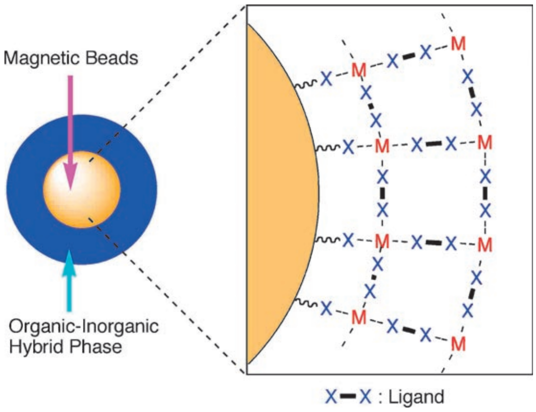

Figure 1. Structure of organic–inorganic hybrid-polymer-encapsulated magnetic beads (HP-MB). Counteranions are omitted for clarity.

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course of our recent efforts to apply organic–inorganic hybrid polymers in organic synthesis, we succeeded in the catalytic synthesis of α-hydroxy ketones by using $\{[Cu(bpy)(BF_4)_2(H_2O)_2](bpy)\}_n$ ("Cu-bpy" where bpy = 4,4′-bipyridine).[4–6] Thus we attempted to construct the Cu-bpy hybrid-polymer-encapsulated magnetic beads (HP-MB) in this study.

Amino-functionalized magnetic beads (≈200 nm diameter, ≈130 $\mu mol\,g^{-1}$ NH_2 content, ≈40 $emu\,g^{-1}$ magnetic susceptibility, and 15 $m^2\,g^{-1}$ specific surface area) containing approximately 70 % iron oxide[7] were mixed with $Cu(BF_4)_2$ (10 equivalents to the amine content) and bpy (20 equivalents to the amine content) in EtOH. The resulting mixture was gently agitated at ambient temperature for eight hours. The excess of added reagents was readily washed out with EtOH after making the beads cohere under an external magnetic field. The extreme simplicity of the preparation of these HP-MB self-assembled magnetic beads was remarkable. Although superparamagnetic nanoparticle-supported catalysts have been studied recently, the synthesis of the materials described in those reports involved several complicated transformations.[8]

Although the magnetic beads thus obtained did not show any obvious change in color, characteristic changes to the surfaces of the magnetic beads were observed in SEM images. As shown in Figure 2, small projections were observed to stick out from the spherical surface of the magnetic beads. These projections were probably the result of anisotropic growth of the crystalline Cu-bpy hybrid polymer.

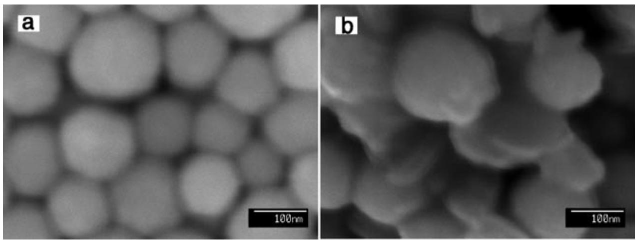
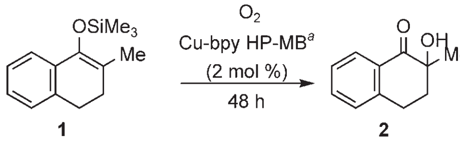


Figure 2. Scanning electron microscope (SEM) images of: a) original amino-functionalized magnetic beads, and; b) Cu-bpy organic–inorganic hybrid-polymer-encapsulated magnetic beads.

To our delight, the newly prepared Cu-bpy HP-MB showed high catalytic activity for the aerobic oxidation of silyl enolates. Thus, based on the NH_2 functionality of the parent magnetic beads, only 2 mol % of the Cu-bpy HP-MB was enough to catalyze the reaction of **1** to provide α-hydroxy ketone **2** in 92 % yield (Table 1,entry 2). The effects of amounts of $Cu(BF_4)_2$ and bpy in the preparation of HP-MB on the catalytic activity of the oxidation were examined. The HP-MB prepared by using ten equivalents of $Cu(BF_4)_2$ showed the highest catalytic activity (Table 1, entry 2).

ICP analysis of the HP-MB used in entry 2 in Table 1 showed that the 2 mol % NH_2 functionality on the parent magnetic beads resulted in 6 mol % Cu atoms and that the organic–inorganic phase formed on the beads was quite thin. It was also noteworthy that the catalytic activity of Cu-bpy HP-MB was higher than that of free $\{[Cu(bpy)(BF_4)_2(H_2O)_2](bpy)\}_n$ (48 h, 53 %) under the current conditions, suggesting that the catalytic oxidation took place on the surface of the hybrid polymer. Importantly, magnetic beads treated with $Cu(BF_4)_2$ without the bpy ligand gave a significant amount of the protonated product of **1**. Moreover, instead of the use of amino-functional magnetic beads, when a commercially available amino-methylated polystyrene was applied as the support, the catalytic activity of the resulting "polymer-supported HP" in the oxidation of **1** decreased to provide α-hydroxy ketone **2** with a yield of only 20 %. This fact could be reasonably explained by considering the incorporation of the HP into the polymer matrix in the conventional support. Based on these results, we can conclude that the organic–inorganic hybrid phase formed on the surface of the magnetic beads was crucial for catalytic activity, and this is an advantage of the use of the magnetic beads.

Table 1. Cu-bpy HP-MB as oxidation catalyst.



Entry	$Cu(BF_4)_2$ [equiv]	bpy [equiv]	Yield [%][b]
1	5	10	89
2	10	20	92
3	20	40	74
4	100	200	36

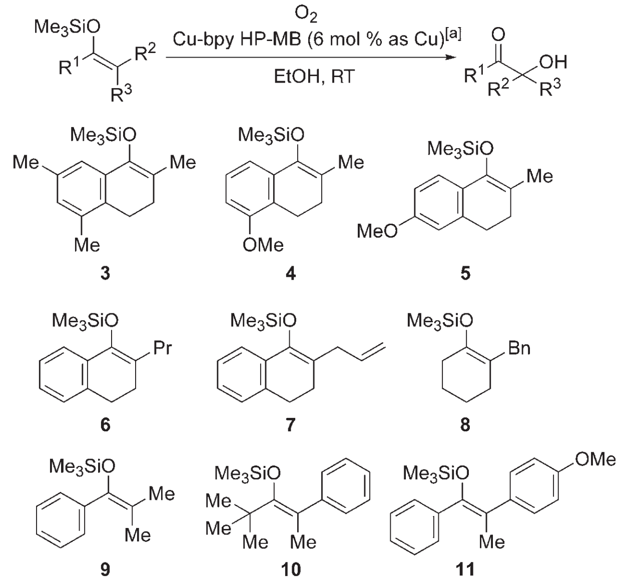
[a] Catalyst amount as the monomeric structure based on the functionality on the parent magnetic beads. [b] Yield of isolated product after treatment with $P(OEt)_3$.

The scope and generality of the new direct method is summarized in Table 2. Various substrates were converted to α-hydroxy ketones in good yields under mild conditions. In particular, not only cyclic ketones, but acyclic ketones were also transformed to the corresponding α-hydroxy ketones, with chemical yields higher than those obtained by using free Cu-bpy (Table 2, entries 7 and 9).[4a]

The Cu-bpy HP-MB was readily recovered by using an external magnetic field in air, and the recovered catalyst could be recycled. For example, after the reaction of $Cu(BF_4)_2$ and bpy (10 and 20 equivalents, respectively, entry 2 in Table 1), the magnetic beads were quantitatively recovered by magnetic separation, and the catalyst was repeatedly reused to give the α-hydroxy ketone **2** (2nd use: 92 % (48 h), 3rd use: 89 % (48 h), 4th use: 85 % (48 h), 5th use: 84 % (48 h)).

The extremely simple preparation procedure for the HP-MB compounds allows us to use high throughput screening to determine the most efficient catalysts. The catalytic activities of a series of metal salts-bpy HP-MBs are correlated in Figure 3. The cationic Cu^{II}-bpy HP-MB catalysts ($Cu(BF_4)_2$ and $Cu(OTf)_2$) showed similar high catalytic activities. Interestingly, the readily prepared $Co(BF_4)_2$-bpy HP-MB catalyst provided the adduct **2** with a yield of 65 %, although the

Table 2. Synthesis of α-hydroxy ketones by using Cu-bpy HP-MB catalyst.



Entry	Substrate	Time [h]	Yield [%][b]
1	**3**	48	93
2	**4**	48	90
3	**5**	48	89
4	**6**	72	75
5	**7**	48	75
6	**8**	48	90
7	**9**	72	>99 (79)[c]
8	**10**	48	>99
9	**11**	72	78 (62)[c]

[a] Catalyst amount is based on the monomeric structure. [b] Yield of isolated product after treatment with $P(OEt)_3$. [c] Yield in parentheses was obtained by using 10 mol% free $\{[Cu(bpy)(BF_4)_2(H_2O)_2](bpy)\}_n$.[9]

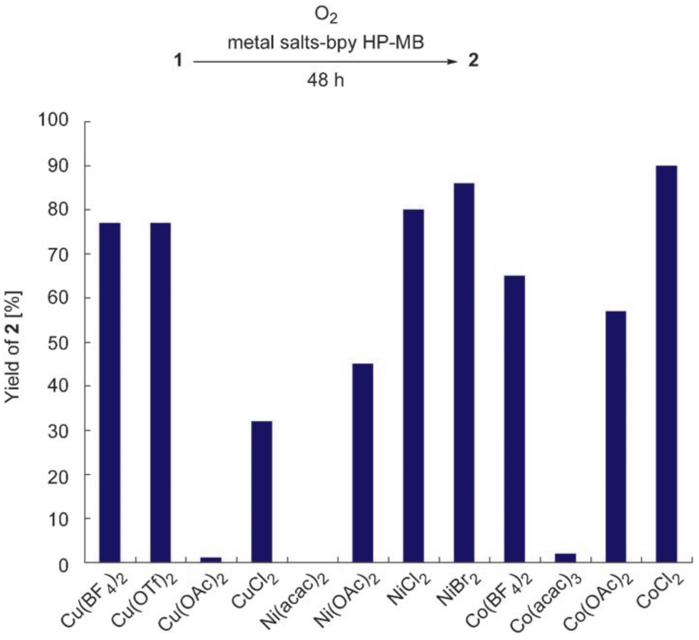


Figure 3. High throughput screening (HTS) of HP-MB catalysts (yields were determined by GC-MS).

original Co-bpy hybrid polymer was hard to obtain without use of the magnetic beads. Among the HP-MB catalysts we examined, the $CoCl_2$-derived catalyst showed the highest catalytic activity to provide the adduct in 90% yield. These results show that the quick preparation and easy manipulation of HP-MB catalysts enables a combinatorial approach to explore the new efficient catalysts.

Conclusion

In conclusion, we have demonstrated the application of organic–inorganic hybrid-polymer-encapsulated magnetic beads in catalysis. The advantages of the current method are catalyst recycling and the easy manipulation afforded by the magnetic beads. Because the method currently studied did not require complicated procedures for incorporating the catalyst onto the magnetic beads, the preparation and the applications of various other types of organic–inorganic hybrid-polymer-coated magnetic beads are now in progress.

Experimental Section

Analytical TLC was performed on precoated (0.25 mm) silica gel plates. Column chromatography was conducted with 70–230 mesh silica gel. All experiments were carried out by using standard-grade oxygen (1 atm). Silyl enolate of 2-benzylcyclohexanone (entry 6 in Table 2) was prepared by treating 2-benzylcyclohexanone with bromomagnesium diisopropylamide in ether, followed by silylation (TMSCl, Et_3N, HMPA).[10] The other silyl enolates were prepared by treatment of the corresponding ketones with lithium diisopropylamide in THF, followed by silylation (TMSCl, Et_3N). Other chemicals were used as purchased.

Preparation of Cu-bpy HP-MB: Amino-functionalized magnetic beads (600 μL, ≈130 $\mu mol\,g^{-1}$ NH_2 content) purchased from Ademtech SA (Cat. No. 02220) were mixed with 4,4′-bipyridyl (2.5 mg, 15.6 μmol) in MeOH (750 μL) and $Cu(BF_4)_2{\cdot}6H_2O$ (1.9 mg, 7.8 μmol) in H_2O (150 μL). The resulting mixture was gently agitated at ambient temperature for 8 h to give the Cu-bpy HP-MB. Excess reagents were washed out with H_2O (1.5 mL) and EtOH (3×1.5 mL) after making the beads cohere under an external magnetic field.

SEM: The Cu-bpy HP-MB was dried in vacuo before SEM images were recorded. The dried solid was carefully picked up and applied to the stainless-steel stubs by using carbon tape. After an osmium coating was formed (7 Pa, 10 mA, 5 s), the SEM image was obtained under vacuum ($<2.5\times10^{-4}$ Pa) by using a JSM-6330F instrument.

Cu-bpy-HP-MB-catalyzed synthesis of α-hydroxyketone (entry 2, Table 1): To a solution of Cu-bpy HP-MB (0.78 μmol as $-NH_2$) in EtOH (1.5 mL) was added silyl enolate **1** (9.1 mg, 39 μmol). The mixture was agitated at room temperature for 48 h under oxygen atmosphere (1 atm). After treating with $P(OEt)_3$ (7 μL, 39 μmol), the Cu-bpy HP-MB was recovered by promoting cohesion under an external magnetic field. From the organic phase, the solvents were evaporated in vacuo, and the residues were purified by column chromatography on silica gel to give α-hydroxyketone **2**.

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