Green Chemisty

A Recyclable Catalytic System Based on a Temperature-Responsive Catalyst**

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In modern synthetic organic chemistry, the development of an efficient reagent or catalyst recycling system is regarded as one of the most important topics.[1] A great deal of effort has been invested in devising methodologies for this purpose. Although various types of recyclable catalytic systems have been explored by using solid reagents and catalysts, it is difficult to retain or raise their activities relative to those of their homogeneous counterparts. Recently, much attention has been focused on the creation of catalytic systems that exploit stimuli-responsive materials. The use of a biphasic system comprising ionic liquids or fluorous solvents and an organic solvent and that can be mixed by changing the temperature is a potential strategy (Figure 1 A).[2–4]

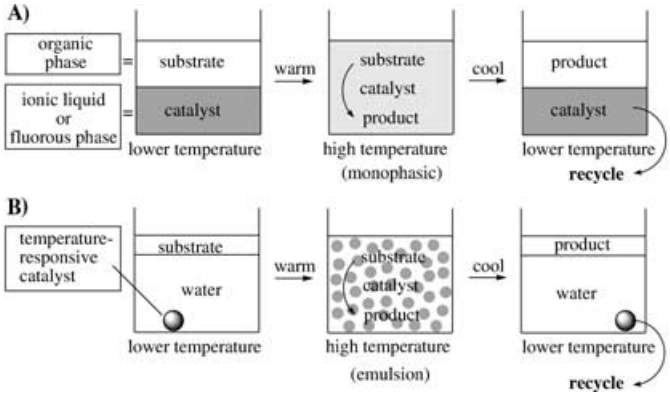
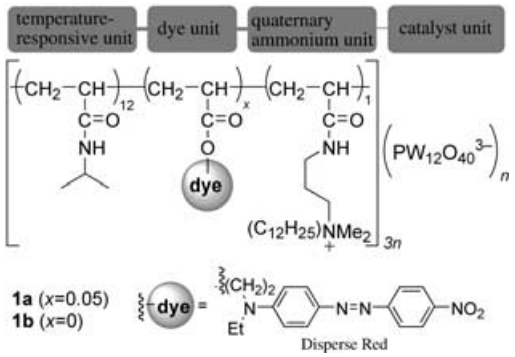


Figure 1. Simplified representation of thermomorphic catalysis. A) Use of a biphasic system comprising ionic liquids or fluorous solvents and an organic solvent. B) Use of a recyclable micellar-type reaction system.

Previously, we investigated the self-assembly of poly(*N*-isopropylacrylamide)-based (PNIPAAm-based) polymer ligands and an inorganic species.[5] This process afforded a networked supramolecular complex in which the polymers are cross-linked by the inorganic species. The complex thus obtained is insoluble in water and functions as an efficient triphase catalyst. In contrast, PNIPAAm polymers intrinsically have temperature-responsive behavior and have been applied to various fields such as drug-delivery systems, column-packing materials, and cell-culture substrates by changing the temperature.[6–8] PNIPAAm polymers undergo thermally reversible changes between water soluble and insoluble states across a lower critical solution temperature (LCST) from 30 to 40 °C. Thus, the polymer chains of NIPAAm are hydrated below the LCST and dehydrated with aggregation above the LCST.[7] The efficient application of soluble PNIPAAm-supported catalysts to biphasic systems has already been reported by Bergbreiter et al.[9]

Colloidal aggregation, such as emulsions formed by amphiphilic molecules in water, has been regarded as an attractive reaction media.[10] This work focuses much attention on the use of the specific hydrophobic species formed by PNIPAAm as a novel organic reaction media in water and provides a recyclable micellar-type reaction system based on PNIPAAm (Figure 1 B). In many cases, the use of a recyclable polymeric catalyst would be advantageous when isolating the product from solution and when removing surfactants that cause environmental pollution.

To design a new recyclable catalytic system from micellar-type aggregates, a dye-labeled catalyst comprising a phosphotungstic acid ($H_3PW_{12}O_{40}$), a PNIPAAm polymer, and a Disperse Red moiety was synthesized (Scheme 1).[5d] Using



Scheme 1. Design of thermomorphic polymer-supported $PW_{12}O_{40}^{3-}$ complex **1**.

this model catalyst **1a**, we investigated the effect of temperature on phase transformation in the presence of an organic substrate and solvent. Although **1a** was insoluble in most solvents at room temperature, the formation of a stable emulsion was observed in water at high temperature (Figure 2 A). Furthermore, an optical micrograph of the mixture at 80 °C showed the presence of hydrophobic beads in water, while such species could not be observed at room temperature (Figure 3). In contrast, **1a** was insoluble in nonpolar solvents such as toluene or octane and soluble in polar organic solvent such as MeCN or *tert*-butyl alcohol at high temperature (Figures 2 B and C).

The results mentioned above prompted us to develop a new reaction system based on the thermomorphic catalyst **1b** for the oxidation of primary and secondary alcohols with hydrogen peroxide.[11] In the oxidation of 1-phenyl-1-propanol in water, the thermoregulated formation of a stable

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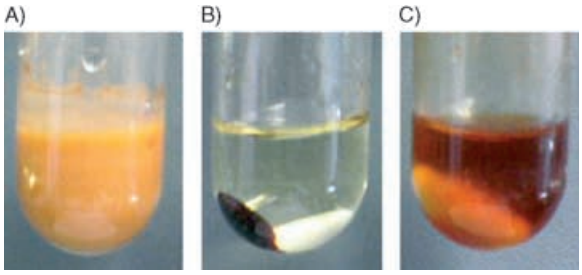


Figure 2. Photographs of a mixture of **1a** and 1-phenyl-1-propanol at 80°C: A) in water; B) in toluene; C) in *t*BuOH.

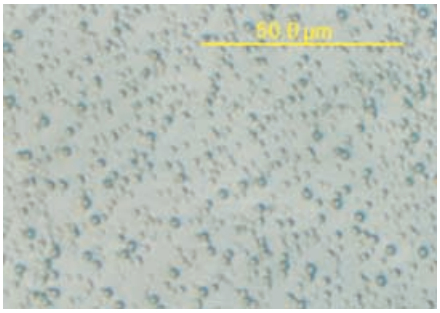
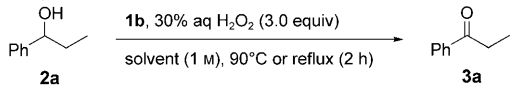


Figure 3. Optical micrograph of a mixture of **1a** and 1-phenyl-1-propanol in water at 80°C.

Table 1: Solvent effect on the oxidation of 1-phenyl-1-propanol (**2a**) catalyzed by **1b**.



Entry	Solvent	*c*(**1b**) [mol%]	Yield [%][a]	Reaction system
1	H_2O	0.0	<1	–
2	H_2O	0.5	92	emulsion
3	H_2O[b]	0.1	92	emulsion
4	toluene	0.5	10	heterogeneous
5	*n*-C_8H_{18}	0.5	18	heterogeneous
6	$C_2H_4Cl_2$	0.5	12	heterogeneous
7	*t*BuOH	0.5	35	homogeneous
8	CH_3CN	0.5	34	homogeneous

[a] Yield of isolated products. [b] 10% aq H_2O_2 (1.5 equiv).

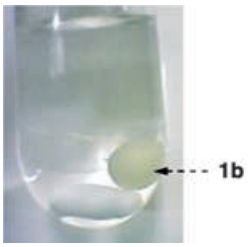
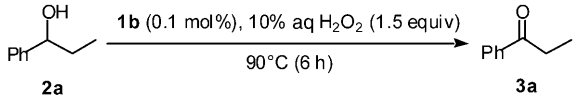


Figure 4. Photograph of recovered **1b**.



yield after 1st use: 92 %; 2nd use: 92 %; 3rd use: 90 %

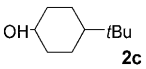
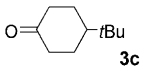
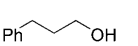
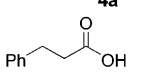
Scheme 2. Oxidation of 1-phenyl-1-propanol by recycled **1b**.

emulsion was detected at 90°C and higher activity was observed. In contrast, the oxidation hardly proceeded in the absence of catalyst (Table 1, entries 1 and 2). Furthermore, the oxidation proceeded smoothly even when only 0.1 mol% of **1b** was present (entry 3). Recovery of catalyst was very easy; **1b** precipitated on cooling and cleanly separated from the reaction mixture after the addition of diethyl ether (Figure 4). The ^{31}P NMR spectrum of recovered **1b** was unchanged relative to that of **1b** before the reaction and no other species was evident.[11,12] Moreover, recovered **1b** could also be used for consecutive reactions without any significant loss of catalytic efficacy (Scheme 2). The reaction was also carried out in various organic solvents (Table 1, entries 4–7). However, no significant activity was observed in each case. It is noteworthy that this catalytic system based on micellar-type aggregates in water is more effective than homogeneous systems.[13]

Having obtained these results, we extended our catalytic system to the oxidation of other alcohols. Oxidation of the secondary alcohols **2b–e** afforded the corresponding ketones **3b–e** in good yields (Table 2). However, the oxidation of the primary alcohols, **2f** and **2g**, with 3.0 equivalents of hydrogen peroxide afforded selectively the corresponding carboxylic acids **4a** and **4b**.

In summary, we have designed a unique and facile recyclable reaction system based

Table 2: Oxidation of primary and secondary alcohols catalyzed by **1b**.

Entry	Substrate	Product	10% aq H_2O_2 [equiv]	Yield [%][a] (1st use)	(2nd use)	(3rd use)
1[b]	 **2b**	 **3b**	1.5	92	89	90
2[b]	 **2c**	 **3c**	1.5	88	87	87
3[c]	 **2d**	 **3d**	1.5	93	93	89
4[c]	 **2e**	 **3e**	1.5	92	88	90
5[c]	 **2f**	 **4a**	3.0	89	90	87
6[d]	 **2g**	 **4b**	3.0	84	80	81

[a] Yield of isolated products. [b] **1b** (0.1 mol%), 90°C (6 h). [c] **1b** (0.2 mol%), 90°C (6 h). [d] **1b** (0.4 mol%), 90°C (8 h).

on a thermomorphic catalyst comprising PNIPAAm. Formation of a stable emulsion, derived from hydrophobic PNIPAAm at high temperature, raises the catalytic activity in the oxidation of alcohols with hydrogen peroxide. Moreover, the catalyst is easily recovered and reused. The results described herein highlight the potential use of PNIPAAm in the field of organic synthesis. Further investigation into the catalytic properties of temperature-responsive catalysts are currently in progress.

Experimental Section

General procedure for the catalytic reaction: A mixture of **1b** (80 mg, 0.01 mmol) and **2** (10 mmol) in 10% aq H_2O_2 (4.5 mL, 15 mmol) was heated to 90°C and stirred for 6 h. After the reaction mixture had been allowed to cool to room temperature, Et_2O (2.5–5 mL) was added and this mixture stirred for 5–10 min. The organic and aqueous phases were removed, and recovered **1b** was washed with ether and distilled water, which were then added to the aqueous phase. The aqueous phase was extracted three times with Et_2O and the combined organic extracts were washed with brine. The organic phase was then dried over $MgSO_4$ and concentrated under reduced pressure. The residual crude reaction mixture was purified by silica-gel column chromatography to give the pure products of **3**. Recovered **1b** was dried under vacuum for 12 h and reused for subsequent catalytic experiments.

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[12] The absence of the dye-labeled polymer unit of **1a** in both organic and aqueous phases after oxidation catalyzed by **1a** indicates that tungsten leaching is negligible. Furthermore, the recovered aqueous phase did not show any catalytic activities for the oxidation of alcohols in the presence of surfactant and hydrogen peroxide.

[13] The oxidation of alcohol in water was not accelerated by the presence of $(Bu_4N)_3[PW_{12}O_{40}]$: Yields = 9% (in H_2O), < 5% (in toluene), 55% (in *t*BuOH); conditions: catalyst 0.5 mol%, solvent 1M, H_2O_2 1.5 equiv, 90°C, 2 h.

