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Novel Recycling System for Organic Synthesis via Designer Polymer-Gel Catalysts

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1. Introduction

In modern synthetic organic chemistry, the development of efficient reagent or catalyst recycling systems is regarded as one of the most important topics.[1−6] The use of polymer supports is one of the potential approaches for this purpose, and the immobilization of reagents or catalysts on polymer supports offers a number of important advantages over their traditional homogeneous counterparts.[7−29] For example, their separation from reaction products is easy and their potentiality for the consecutive recycling steps is accessible for a green chemical process. In addition, the immobilization on polymeric supports often causes the stabilization of sensitive catalyst and provides the potential applicability to intelligent materials. Despite these advantages, solid-phase catalyst is commonly difficult to retain or raise the activities relative to their homogeneous counterparts. Because of this significant disadvantage, solid-phase reaction system diminishes its synthetic utility in many cases.

In recent years, much attention has been focused on the creation of reagent or catalyst recycling that exploits multifunctionalized materials via thermomorphic effect (Scheme 1). The use of a biphasic reaction system employing ionic liquids or fluorous solvents to hold efficient catalytic activity is recognized as a potential strategy.[30−74] The main concept of these methods is to utilize the thermomorphic phase behavior and distribution of catalysts in the solvent for efficient recycling without loss of catalytic activity. The popularity of these systems has significantly increased over the past decade.

On the other hand, the use of functionalized polymers to provide an effective reagent or catalyst recycling system has gained attention as an efficient alternative that avoids the use of expensive ionic liquids or fluorous solvents. Much of the efforts in this area have been focused on the soluble polymer catalysis based on the control of liquid/solid or liquid/liquid catalysts separation since the pioneering work of Bayer and Mutter in the early 1970s.[75−84] By using such catalysts, organic reactions can be carried out in a homogeneous manner and, thus,may have similar catalytic activity and selectivity as the homogeneous parent system.

An organic reaction utilizing an amphiphilic molecule or material in water offers several unforeseen reactivities or selectivities because of the strong affinity between substrate and catalyst based on the hydrophobic effect.[85−99] In addition, the use of water is a better choice to carry out organic reactions from the viewpoint of green synthesis because water offers practical advantages over organic solvents: it is cheap, readily available, nontoxic, and nonflammable. Although various organic reactions are carried out in the presence of an amphiphilic molecule such as surfactants, the difficulties in separation of organic products at the end of the reaction often diminish its utility, and subsequent clean up of the dirty water containing surfactants and inorganic agents could also be trouble. In contrast, the use of an insoluble amphiphilic matrix such as a polymer gel has a potentiality for efficient solid-phase catalysis and could open up an innovative approach to the design of an efficient catalyst recycling system.

As an extension of the chemistry of this functionalized polymer catalysis, some exciting approaches to develop an efficient reaction system based on the properties of the polymer chain have appeared. The use of a novel reaction medium provided by a functionalized polymer could bring a new strategy in the design of reagent or catalyst recycling systems. This article will provide an outline of the principle of catalyst recycling via designer gels, mainly focused on the functionalized poly-*N*-isopropylacrylamide-based polymer and its applications in organic synthesis.

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Shiro Ikegami was born in Yamanashi, Japan, in 1936. He received his Ph.D. degree in 1965 from The University of Tokyo (the late Professor Shun-ichi Yamada). After spending 1.5 years as a research fellow granted from The Japan Society for the Promotion of Science (JSPS), he stayed at Purdue University, Indiana, U.S.A., for two years (the late Professor Herbert C. Brown) as a postdoctoral research associate in 1966−1968. After returning to Japan in 1968, he was in the Faculty of Pharmaceutical Sciences, The University of Tokyo, as a research associate and then moved to National Institute of Radiological Sciences, Division of Pharmaceutical Sciences, as senior scientist, where he was for 10 years. In 1978, he moved to School of Pharmaceutical Sciences, Teikyo University, as full Professor. He received The PSJ Award in 1997 from The Pharmaceutical Society of Japan (PSJ) and was PSJ President in 2002. He has retired in March 2006 and become Professor Emeritus. His major research interests were on three major subjects: Design and Synthesis of Bioactive Substances, Carbohydrate Chemistry, and Green Chemistry—Exploitation of New Polymer Catalysts.

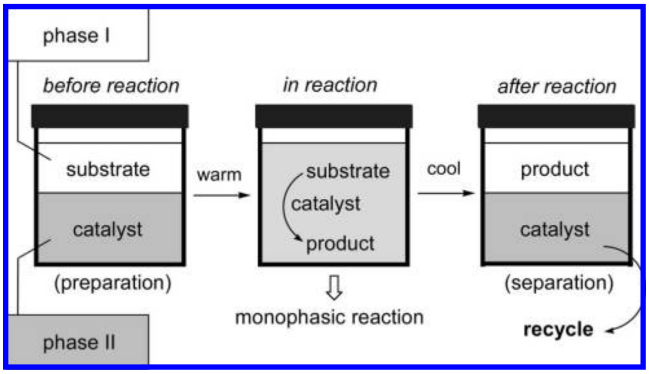
Hiromi Hamamoto was born in Kyoto, Japan, in 1974. He received his B.S. and M.S. degrees from Okayama University and received his Ph.D. degree in 2003 from Osaka University (Professor Yasuyuki Kita). He joined the group of Professor Shiro Ikegami in Teikyo University as a research associate (2003−2007). He is currently a lecturer at Kinki University. His present research focuses on the development of new reagents for use in organic synthesis.

2. Catalyst Recycling on Triphase System

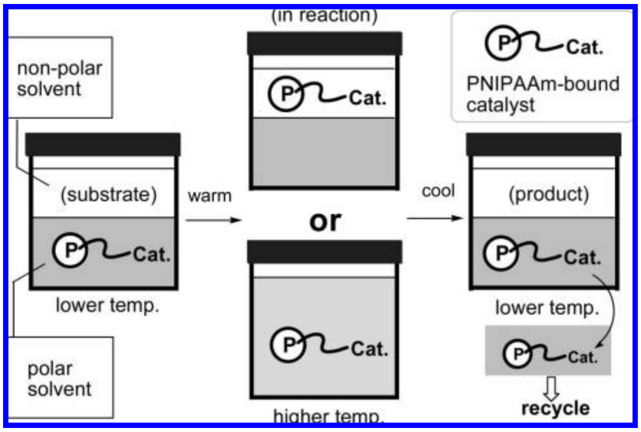
2.1. Properties of PNIPAAm

Poly(*N*-isopropylacrylamide) (PNIPAAm)-based polymers intrinsically show the characteristic temperature-responsive intelligence and have been applied to various fields such as drug-delivery systems, column packing materials, and cell culture substrates by using external temperature changes.[100,101] The PNIPAAm polymers undergo thermally reversible changes between water-soluble and -insoluble states across a lower critical solution temperature (LCST) from 30 to 40 °C.[101] Thus, the polymer chains of PNIPAAm are hydrated below the LCST and dehydrated with aggregation above the LCST. Several efficient applications of soluble PNIPAAm-supported catalyst to biphasic systems have already been reported by Bergbreiter (Scheme 2). The advantages of these applications are highlighted in their recent reviews.[77,81−84] However, the applications of PNIPAAm-based copolymer catalyst in aqueous mediums are still limited.

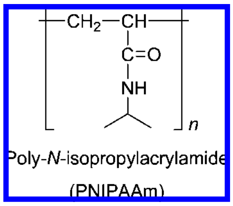
Scheme 1



Scheme 2



2.2. PNIPAAm-Gel in Water



Poly-*N*-isopropylacrylamide (PNIPAAm)

The study of polymer gels and their responses to external environment such as temperature, solvent, or pH, etc. are of special interest because of their potentials as drug-delivery systems, actuators, and separation devices. Frequently studied polymer gels are based on PNIPAAm. The uncross-linked PNIPAAm polymers are dissolved in an aqueous solution, and the turbidity of the solution varies due to dissolution and precipitation of the polymer. When the polymer chains are cross-linked, the conformational changes lead to macroscopic mechanical change of the polymer network. Such conformational change of the polymer chain induces swelling/deswelling transition with the change of external solvent, which could cause the control of absorbency of organic substrates. In many cases, the utility of cross-linked PNIPAAm polymers could be found in water.

Scheme 3

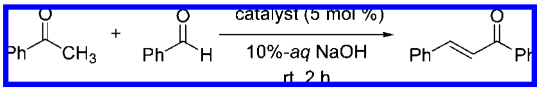


Table 1. Organic Solvent-Free Claisen−Schmidt Reaction

entry	catalyst	yield (%)
1	(none)	8
2	**1**	89
3	**1** (second use)	88
4	**1** (third use)	90
5	**1** (fourth use)	88
6	**1** (fifth use)	89
7	Amberlite IRA-900	6
8	Amberlyst A-26	35

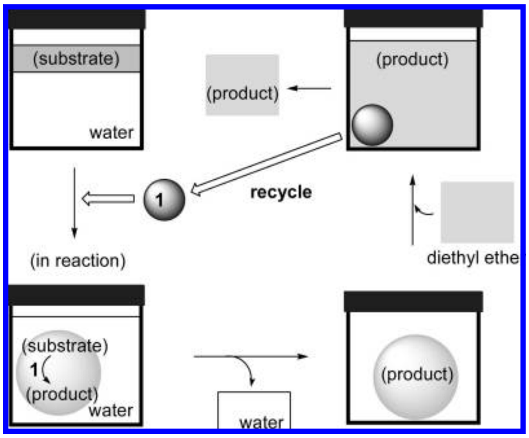
PNIPAAm-gel with a structure in which the PNIPAAm main chain was cross-linked or grafted on quaternized aminoalkyl chain (**1**) could control the absorbency of organic substrates due to external solvent changes.[102] When **1** and 2-octanol were submerged in water, 2-octanol was absorbed into **1**, while the retained oil was thoroughly released by changing the external solvent to diethyl ether. Application of this unique ability to the design of a new recyclable system brought an efficient organic reaction in water. In the **1**-catalyzed Claisen−Schmidt reaction of benzaldehyde and acetophenone (Scheme 3), higher catalytic activity was exerted relative to the quaternary ammonium hydroxide resin of commercially available polystyrene divinylbenzene (Table 1). Additionally, the product is easily isolated by the use of a minimal amount of diethyl ether, and the recovered **1** can be used for consecutive reactions without any significant loss of catalytic efficacy (Scheme 4). High catalytic activity with the simplicity of the recycling steps would be advantageous because a common organic reaction using amphiphilic molecules in water often requires excess amounts of organic solvent or causes many troubles when isolating product from solution. Moreover, similar efficiency could be found in the **1**-catalyzed nitrile Aldol reaction and epoxidation of α,β-enones (Scheme 5).

2.3. Organic Solvent-Free Triphase Oxidation Catalysis

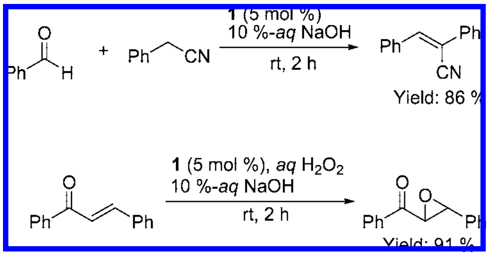
The use of an amphiphatic solid-phase catalyst under an aqueous−organic biphase system or an aqueous system could bring highly reactive catalyst recycle systems. For example, polystyrene−poly(ethylene glycol) (PS−PEG) has been often used for catalyst support and applied to organic reaction in water because they construct effective catalytic sites with high affinity to both hydrophobic and hydrophilic reagents.[103−115] On the other hand, an assembled complex (**2**) of a noncross-linked copolymer of PNIPAAm with an ammonium ion and phosphotungstic acid ($H_3PW_{12}O_{40}$), which is insoluble in water, works as an efficient oxidation catalyst under organic solvent-free conditions, such as in water.[116−118]

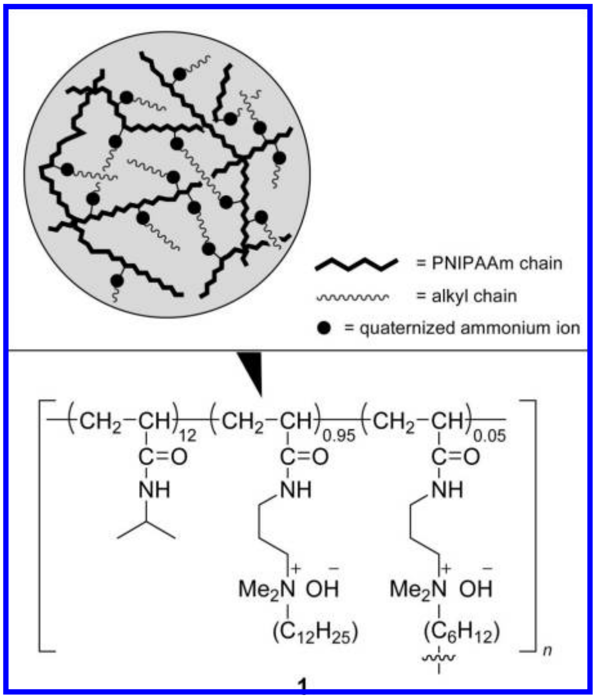
When a series of epoxidations of several allylic alcohols with hydrogen peroxide was performed in the presence of **2**, hydrophobic substrates were converted to the corresponding epoxides in high yields under an organic solvent-free triphasic system, and recovered **2** can be used for consecutive reactions (Scheme 6).[116,118] In the presence of 2.7×10^{-5} mol equiv of **2**, the reaction of phytol with 2 mol equiv of 30% aq. H_2O_2 resulted in the corresponding epoxy alcohol in 94% yield, and Turn of Number (TON) of **2** was approximately 35 000 (Scheme 7). In addition, this system

Scheme 4



Scheme 5





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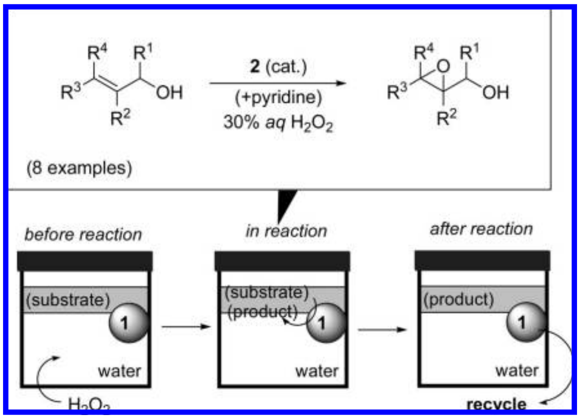
is effective for oxidation of secondary amines (Scheme 8). In the presence of **2**, oxidation of dibenzylamine derivatives with hydrogen peroxide resulted in the corresponding nitrones in good yields.[117,118]

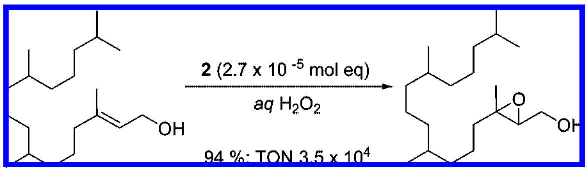
2.4. Organic Solvent-Free Triphase Palladium Catalysis

Similarly, the palladium-type assembled complex of non-cross-linked copolymer of PNIPAAm with a phosphine palladium dichloride (**3**), which is insoluble in water, worked as an efficient catalyst under an organic solvent-free triphasic system.[119,120] It efficiently catalyzed the heterogeneous

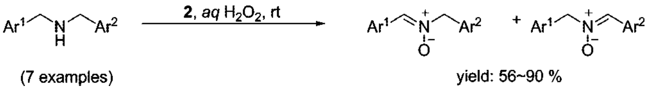
Scheme 6

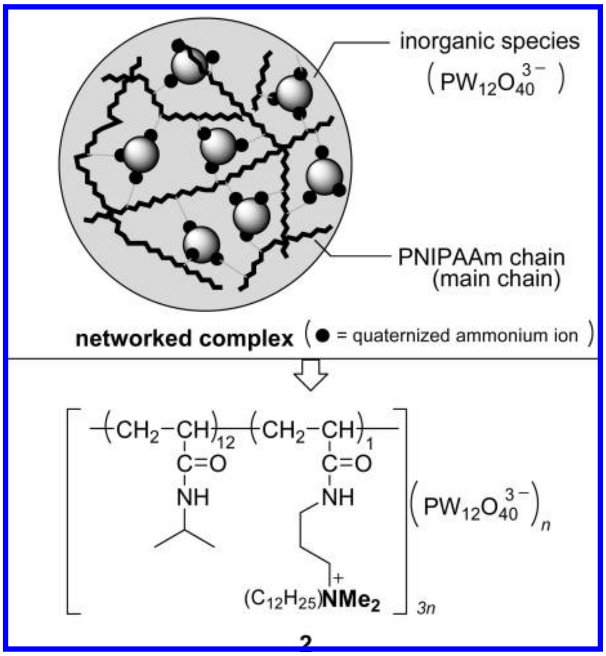


Scheme 7



Scheme 8





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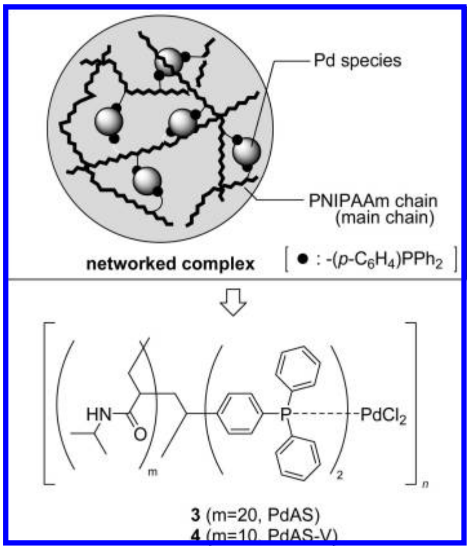
Suzuki–Miyaura reaction of aryl and alkenyl halides, benzylic chlorides with arylboronic and alkenylboronic acids, and alkyl-9-Borabicyclononanes (Scheme 9). Although the reaction takes 96 h to reach completion and required an excess of boronic acid, it should be noted that the highest turnover number TON of **3** reached up to 1 250 000 in use of **3** (8 × 10^{-7} mol %). Additionally, **3** showed outstanding stability in any reaction media such as water or aqueous or anhydrous organic solvents and was reused 10 times without loss of activity. Further tuning of **3** to the highly cross-linking mode provided an efficient recyclable solid-phase catalyst (**4**) for heterogeneous Mizoroki–Heck reaction in water (Scheme 10).[121,122] The methodology of the reaction in toluene as a solvent was demonstrated more effectively, resulted in high TON (1 150 000) of **4** (8 × 10^{-7} mol %: tetraethylammonium (TEA), toluene, 100 °C, 96 h),and could be applied to the synthesis of resveratrol.

2.5. Organic–Aqueous Triphase Oxidation



3 (m=20, PdAS)
4 (m=10, PdAS-V)

Catalysis

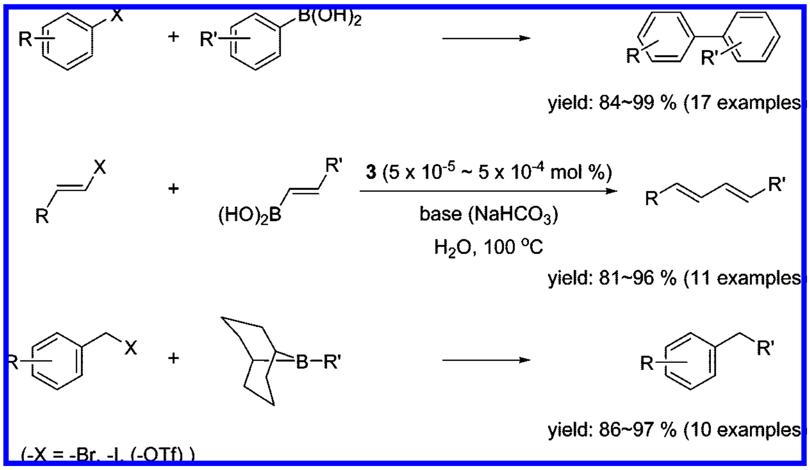
In contrast to the organic solvent-free triphase catalysis system, the organic solvent–aqueous triphase catalysis system is also attractive to construct a green chemical process. The utilization of the PNIPAAm complex with tungsten species **2** for the oxidation of benzilic amines under the toluene–aqueous hydrogen peroxide triphase catalysis system provided an efficient direct transformation to carbonyls (Scheme 11).[123] The catalyst could be recovered by simple filtration and reused without significant loss of activity. Although the reactivity of **2** on the homogeneous system was also examined by using a polar organic solvent such as MeCN or *tert*-butyl alcohol, slightly lower yields were attributable to the production of undesired side products and excess amounts of organic solvents were required for the extractive workup process.

3. Catalyst Recycling via Thermomorphic Effect

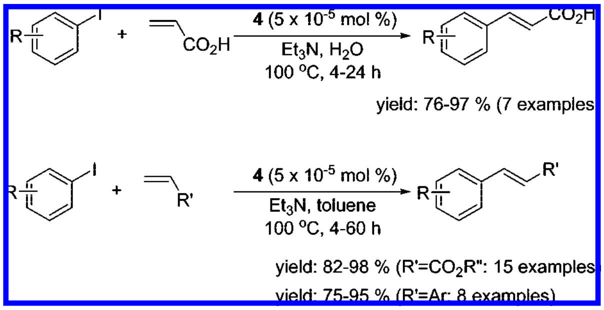
3.1. Thermomorphic Property of PNIPAAm Polymer Gel

Because of their characteristic temperature-responsive intelligence, PNIPAAm polymers and polymer gels could cause drastic mode transfer at several temperatures. For example, the PNIPAAm complex with tungsten species **2** displays the specific transitions owing to temperature changes.[124,125] When **2** is used together with water and the organic substrates, it is insoluble in both phases at room temperature. On heating the organic substrates, they gradually soak into **2** and the absorption completes at around 60 °C, while excess heating to more than 70 °C tends to induce the generation of emulsion species.

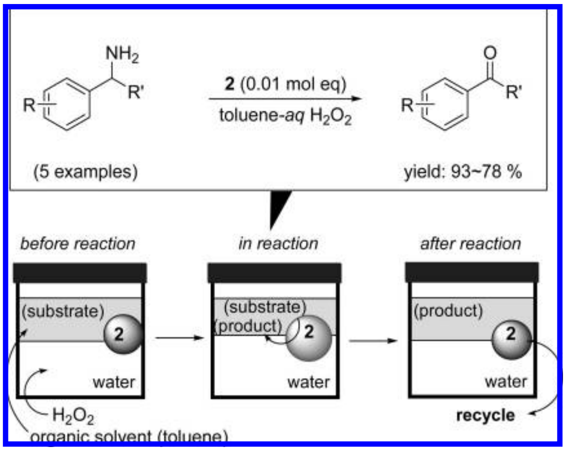
Scheme 9



Scheme 10



Scheme 11



Scheme 12

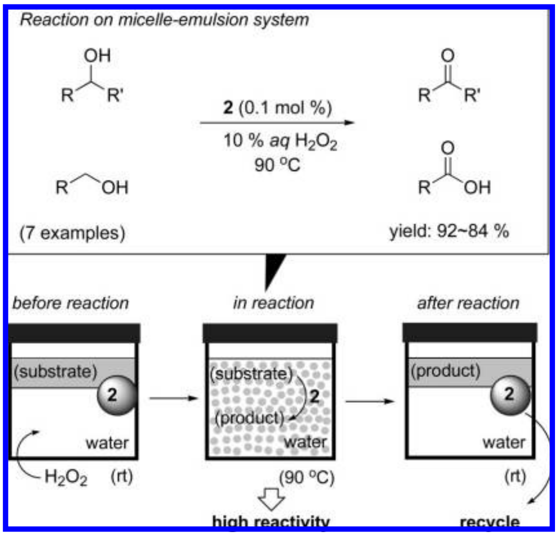


Table 2. Oxidation of 1-Phenyl-1-Propanol Catalyzed by 2

entry	solvent	conditions (at 90 °C)	yield (%)
1	H_2O	emulsion	92
2	H_2O	emulsion	92 (second use)
3	H_2O	emulsion	90 (third use)
4	*t*-BuOH	homogeneous	35
5	CH_3CN	homogeneous	34

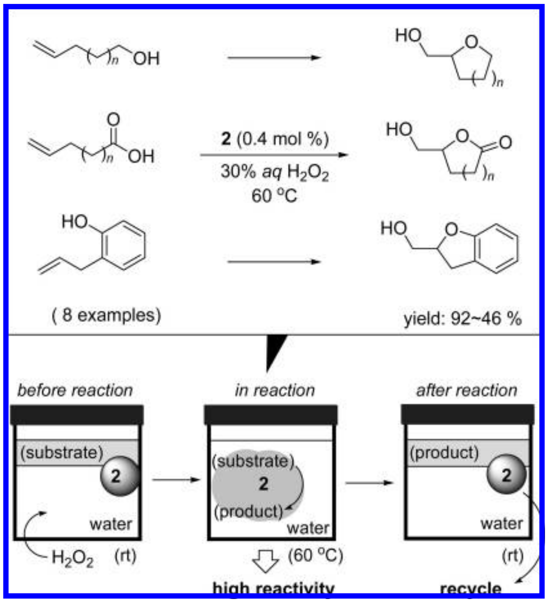
3.2. Thermoregulated Micelle-Emulsion System

A micellar-type system utilizing switchable catalyst based on the characteristic temperature-responsive intelligence of **2** exerted high performances for catalyst recycling with efficient activity as summarized in Scheme 12.[125] In the hydrogen peroxide oxidation of 1-phenyl-1-propanol in water, the thermoregulated formation of a stable emulsion was detected at 90 °C and higher activity was observed. The catalyst was precipitated on cooling and cleanly separated from the reaction mixture after the addition of diethyl ether. The recovered **2** was reused for consecutive reactions without significant loss of catalytic efficacy. Although the reactivity of **2** on a homogeneous system was also examined by using various organic solvents such as *t*-BuOH and CH_3CN, no significant activity was observed in each case and excess amounts of organic solvents were required for the extractive workup process. It is noteworthy that this catalytic system based on micellar-type aggregates in water is more effective than homogeneous systems in both catalytic activity and recyclability (Table 2). In addition, the oxidation using this condition works well for a range of secondary and primary alcohols to yield the corresponding ketones and carboxylic acids, respectively.

3.3. Thermoregulated Gel-Phase System

The use of the temporally formed specific hydrophobic PNIPAAm gel phase holding the flexible solid state as a specific organic reaction medium provided also the efficient thermomorphic catalysis systems in water (Scheme 13).[126] In the **2**-catalyzed oxidative cyclization with hydrogen peroxide in water, the absorption of organic materials in the catalyst phase was similarly detected at 60 °C, and higher reactivity owing to the hydrophobic effect was observed. The organic materials retained in gel were released by cooling

Scheme 13



the reaction mixture, and the organic/aqueous/solid phases were cleanly separated after the addition of diethyl ether. The recovered **2** could be used for subsequent reactions without any significant loss of catalytic efficacy. The comparison of reactivities on oxidation with conventional tungsten systems showed specific acceleration at higher temperature (60 °C) with generation of the adsorption of the substrate into the PNIPAAm gel phase, whereas undesired further oxidation products were detected with additional heating (70 °C), attributable to the subsequent partial formation of emulsion species (Figure 1). Thus, higher catalytic activity exerted over other versatile tungsten systems with the advantage of easy catalyst recycling was noteworthy. In addition, this system was applicable to the oxidative cyclization of several open-chain precursors noteworthy (see Table 3).

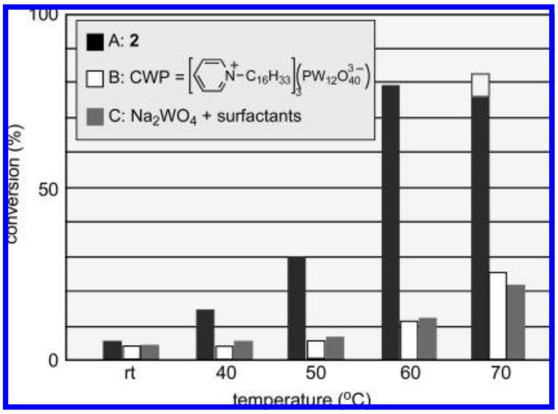
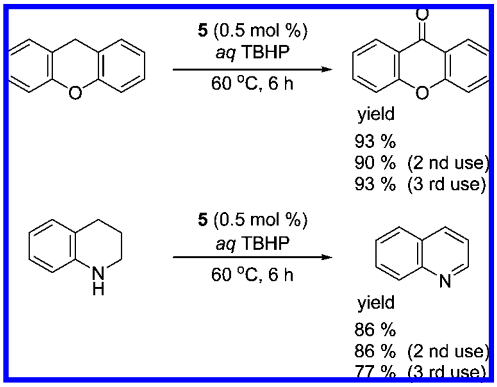


Figure 1.

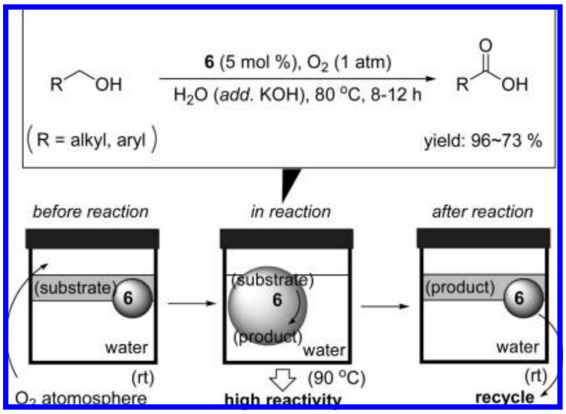
Table 3. Oxidative Cyclization of Pent-4-en-1-ol Catalyzed by 2

entry	solvent	yield (%)
1	H_2O	83
2	H_2O	87 (second use)
3	H_2O	88 (third use)
4	*t*-BuOH	48
5	CH_3CN	25

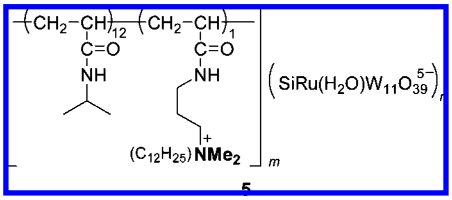
Scheme 14



Scheme 15



A similar thermomorphic catalyst, the PNIPAAm complex with ruthenium substituting polyoxometalate **5**, showed the thermoregulated absorption of organic substrates at 60 °C and provided an efficient recyclable catalyst in aqueous medium again.[127] In **5**-catalyzed benzylic oxidation of xanthene with *tert*-butylhydroxy peroxide (TBHP), the reaction proceeds efficiently to give xanthone (Scheme 14). The catalyst could be easily recovered and reused for subsequent reactions. Additionally, this system is applicable for oxidative dehydrogenation of tetrahydroquinoline.



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In a modification of this concept, the aerobic oxidation system via a thermomorphic catalysis system was designed utilizing cross-linked PNIPAAm-gel immobilized ruthenium catalyst (**6**) (Scheme 15).[124,128,129] Similar to **2**, the absorption of organic materials in the catalyst phase was detected by heating the reaction mixture where the oil-containing polymer gel is more rigid in comparison with polymer complex **2** and could keep a gel form at 90 °C. In **6**-catalyzed aerobic oxidation of primary alcohols, high activity was exerted and the corresponding carboxylic acids were obtained in good yields. The catalyst was easily separated from the reaction mixture after cooling, and the recovered catalyst could also be used for consecutive reactions without any significant loss of catalytic efficacy. The reusability of this catalyst for 10 cycles was still excellent. In addition, this system is also applicable for oxidative coupling reaction of naphthols with molecular oxygen in water (Scheme 16). Again, this ther-

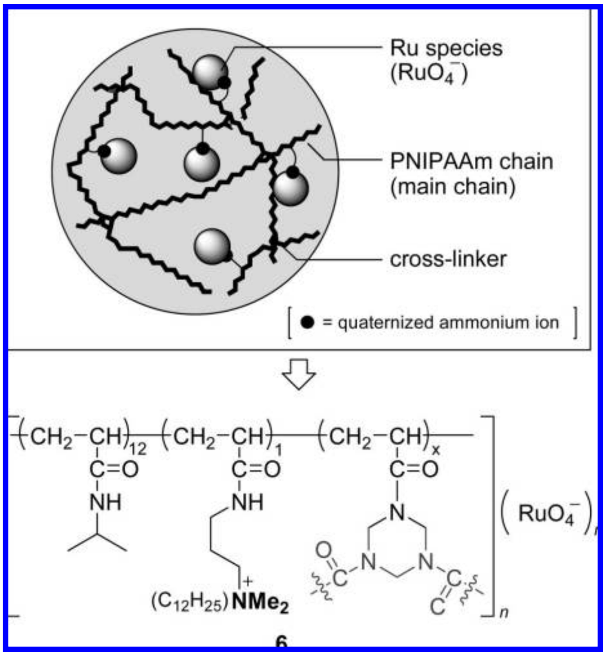
Table 4. Aerobic Oxidation of 4-Methylbenzyl Alcohol in Water

entry	catalyst	yield (%)
1	**6**	94
2	**6** (second use)	96
3	**6** (third use)	91
4	**6** (fourth use)	95
5	**6** (fifth use)	96
6	**6** (10th use)	92
7	TPAP[a]	41
8	PSP[b]	56

[a] TPAP (n-$Pr_4N^+RuO_4^-$). [b] PSP (polymer-supported perruthenate: Amberlyst 26 and RuO_4^-).

momorphic system brought a remarkable acceleration of the reactivity and an ease of catalyst recycling by using the catalyst intelligence (Table 4).

In this context, polyethylene glycol (PEG)-containing PNIPAAm immobilized perruthenate catalyst **7** was successfully used in the aerobic oxidation of alcohols in organic medium.[129] PEG-PNIPAAm Ru catalyst **7** exhibited efficient catalytic activity in the oxidation of 4-methylbenzyl alcohol, though PEG-free-PNIPAAm Ru catalyst diminished their catalytic activity. Investigation of the effects of water presence in the oxidation process indicated that the hydrophilic PEG component on **7** somehow plays an important role in the removal of water generated during the course of the oxidation from the catalytic site in an identical phase among a hydrophobic PNIPAAm gel environment at high temperature. In addition, the holding water would be released after cooling due to the loss of hydrophobicity on the PNIPAAm chain. The catalyst could be recovered by simple filtration and reused without significant loss of activity (Scheme 17).



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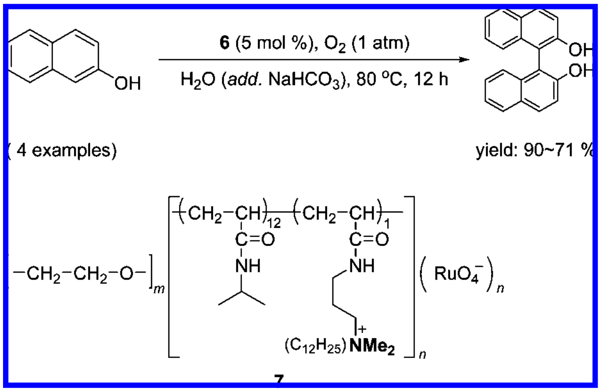
4. Ionic Polymer-Gel Catalysis

Ionic liquids have attracted growing interest as alternatives to replace volatile organic solvents in catalysis. Their ionic natures with nonvolatility and thermal stability make them highly suitable for various transition metal catalysis.[40−58] However, traditional ionic liquid mediated reaction systems require large amounts of expensive ionic liquid, which makes them unattractive under economical consideration. In addition, the high viscosity of ionic liquids can induce a mass transfer limitation if the chemical reaction is fast. Several approaches to provide supported ionic liquid catalysts, which combine the advantages of ionic liquids with those of heterogeneous support materials, were investigated as an extension of ionic catalysis chemistry. The frequently used supports for this purpose are modified silica gel, and this methodology is one effective strategy for heterogenization of homogeneous ionic liquid catalysis system to date.[130−132]

Scheme 16



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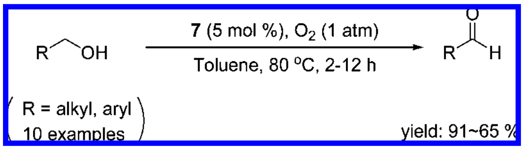
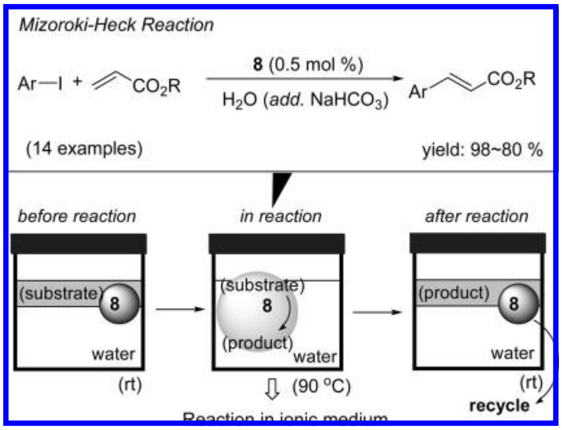
Scheme 17



The concept of a PNIPAAm-based thermomorphic catalysis system was further extended to ionic heterogeneous reactions. Ionic polymer supported palladium **8** prepared from cross-linked PNIPAAm-gel and palladium acetate works as an attractive catalyst for the Mizoroki−Heck reaction in water (Scheme 18, Table 5).[133] In the **8**-catalyzed reaction of iodobenzene with butyl acrylate, the reaction proceeded at an inner ionic polymer gel phase owing to the absorption of organic materials by heating. Thus, significant enhancement of catalyst activity and stability was detected relative to PNIPAAm-gel Pd catalyst with low ionic matrix content. The catalyst was easily separated from the reaction mixture after cooling, and the recovered catalyst could also be used for consecutive reactions without loss of catalytic

Scheme 18



Scheme 19

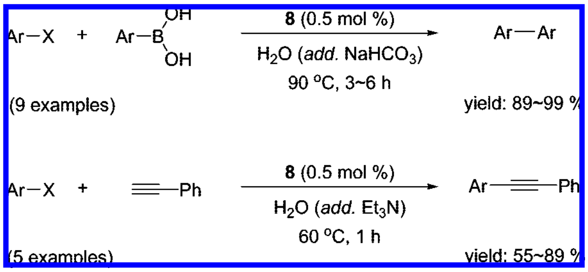


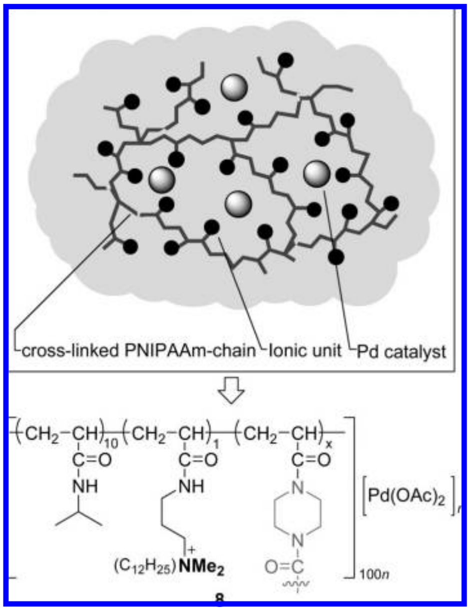
Table 5. Mizoroki−Heck Reaction of Iodobenzene with Butyl Acrylate in Water

entry	catalyst[a]	yield (%)
1	**8**	97
2	**8** (second use)	90
3	**8** (third use)	93
4	**8** (fourth use)	96
5	**8** (fifth use)	92
6	PNIPAAm-Pd[b]	23
7	Pd (OAc)$_2$	25

[a] 0.5 mol %. [b] PNIPAAm-Pd: PNIPAAm-gel Pd catalyst with low ionic matrix content.

efficacy. In addition, this system is also applicable for Suzuki−Miyaura coupling and copper-free Sonogahira coupling in water (Scheme 19).

5. Catalyst Preparation



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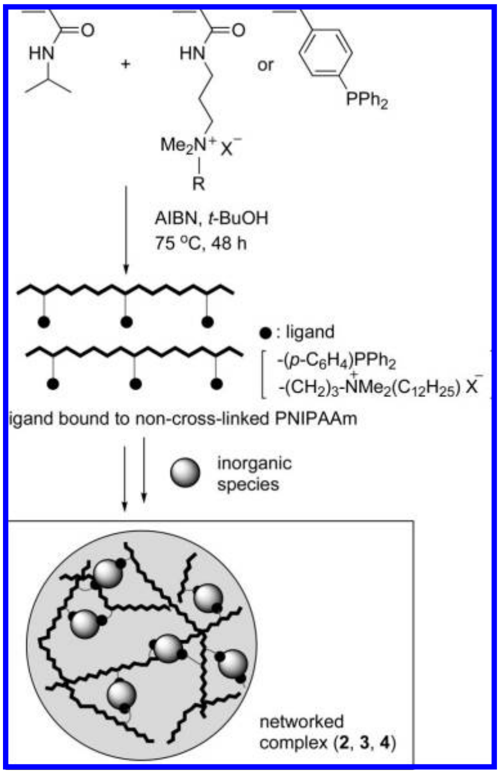
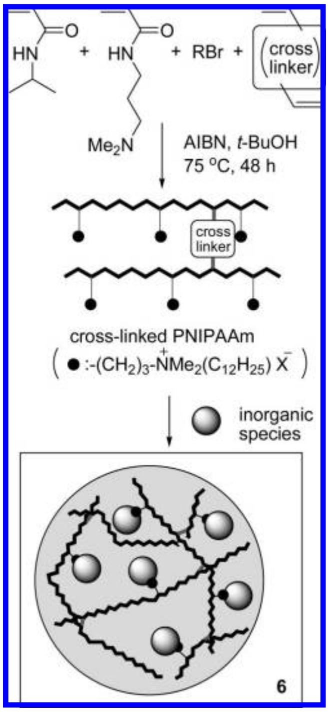
PNIPAAm-based catalysts described in this article were prepared in two ways mainly. Polymer complex type catalysts (such as **2**−**5**) were prepared by a self-assembly process of inorganic species with a noncross-linked PNIPAAm chain, which is synthesized by radical polymerization of *N*-isopropylacrylamide and the corresponding monomers (ionic acrylamide or diphenylstyrylphosphine) using Azobisisobutyronitrile (AIBN) as an initiator (Scheme 20).[116,118−122] On the other hand, PNIPAAm-gel immobilized type catalysts (such as **6**, **8**) were prepared by the treatment of inorganic species and cross-linked PNIPAAm-gel, which is synthesized by radical polymerization of *N*-isopropylacrylamide and the corresponding monomers in the presence of a cross-linking agent (Scheme 21).[102,127,128,133] Formation of the ammonium salt derived from *N*-(*N*,*N*-dimethylaminopropyl)acrylamide and alkyl halide was achieved in situ during the polymerization process.

Scheme 20



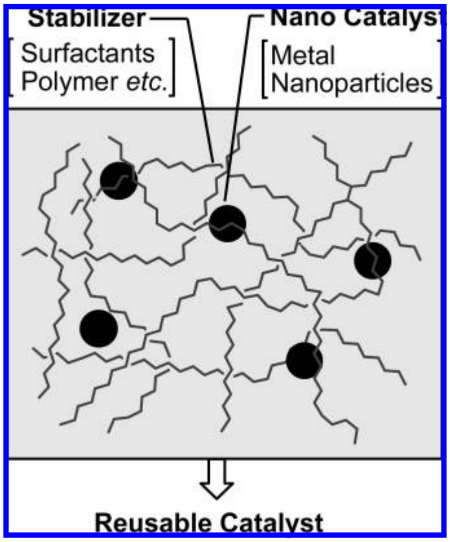
Scheme 21



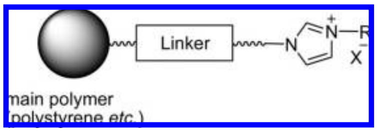
6. Polymer-Gel Related Advanced Catalysis

Recent progress in the heterogeneous catalysis brought various efficient advanced catalysts. Utility of polymer gels could often be found in the design of those catalysis systems.

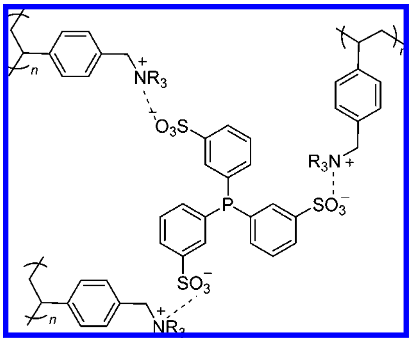
Scheme 22



Scheme 24



Scheme 25

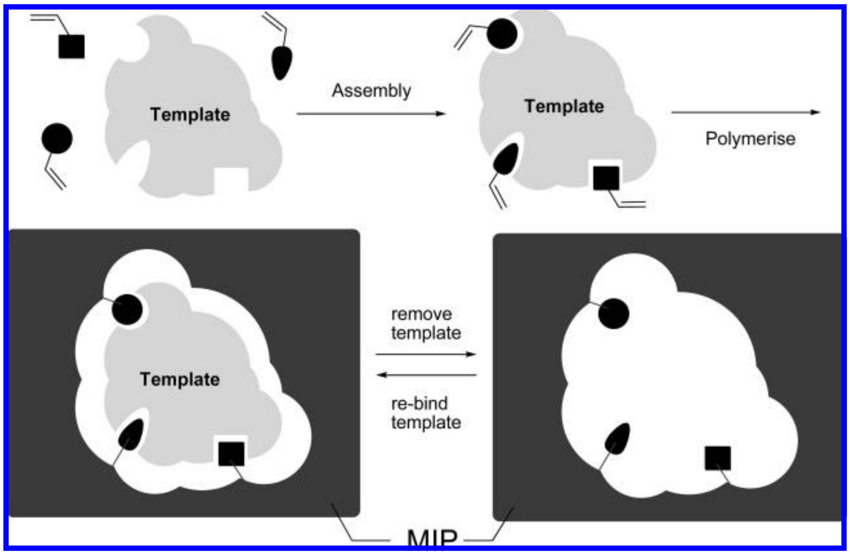


The leading examples are cited in the catalytic system based on nanoparticle chemistry, imprinted polymer chemistry, and polymer-supported ionic liquid synthesis.

Nanoparticle catalysts have attracted attention in recent years because of their unique properties.[134−137] They often classified into "semiheterogeneous catalyst" by means of the frontier catalyst between homogeneous and heterogeneous. Progress has been made in the efficiency and selectivity of reactions and recovery of the catalysts. Usually, metallic nanoparticles are kinetically unstable with respect to agglomeration to the bulk metal and must, therefore, be stabilized by additives (Scheme 22). Polymer is a suitable stabilizer of metallic nanoparticles and makes it possible to use metallic nanoparticles as versatile reusable catalysts. The frequently used polymer for nanoparticles stabilization is poly(*N*-vinyl-2-pyrrolidone) (PVP).[135] Akashi reported the use of PNIPAAm or polystyrene microspheres having PNIPAAm branches on their surfaces for the stabilization of several nanoparticles such as Pt colloids, Au/Pt bimetallic colloids, and Ag colloids.[138−142] The temperature-dependent property of the PNIPAAm chain affected the stability of the nanoparticles, and the catalytic activities are controlled by temperature. In addition, another PNIPAAm polymer related composite was reported by Li.[143] PNIPAAm networks modified Au nanoparticles for nanocomposite entrapment was investigated. The synthesized Au nanoparticles−copolymer hybrids possess clearly thermosensitive properties and exhibit "inspire" and "expire" water behavior in response to temperature changes in aqueous solution. An application of polyacrylamide type gel for palladium nanocluster catalyzed reaction was reported by Corain.[144,145]

Molecularly imprinted polymers (MIPs) are intelligent polymer gels and are well-established as molecular recognition materials but are now being increasingly considered for enzyme-like catalysis.[146−152] Generally, MIPs are synthesized from functional monomers using radical polymerization or polycondensation. Molecular imprinting allows for producing a memory of the transition state of a catalytic reaction by polymerization and subsequent removal of the template (Scheme 23). A sharp-selective reaction space provides a molecule similar to that of the catalytic transition state. Though the frequently used polymer in this field is functional polymethacrylic acid cross-linked with divinylbenzene or ethylene glycol bis-methacrylate, polyacrylamide type polymer gels could also be usable. The synthesis and hydrolytic catalytic characterization of imprinted acrylamide based on

Scheme 23



microgels incorporating arginine and tyrosine derivatives as additional functional monomers is reported by Resmini.[153] A novel type of peroxidase-like imprinted nanogels incorporating hemin, acrylamide, and 4-vinylpyridine as functional monomers was prepared by Li.[154,155] The thus-obtained MIP showed greater catalytic activity in the oxidation reaction of homovanilic acid under aqueous conditions due to the high absorption potentiality toward substrate.

Polymer-supported ionic liquid is often used for the heterogenization of ionic liquids.[130−132] The frequently used polymeric ionic liquid is polystyrene having imidazolium salt branches (Scheme 24).[156−160] Attractive catalytic activities were found in such as a nucleophilic substitution reaction including fluorination and Mizoroki−Heck reaction. A polymeric ionic medium, polyionic gel, was also utilized for metal scavenging and catalysis by Wagner (Scheme 25).[161,162]

7. Conclusion

As this review shows, the use of designer polymer-gel catalysts based on the functionalized PNIPAAm could bring a new strategy in the design of catalyst recycling systems. Various types of organic reaction systems were provided and many utilities could be found relative to common systems. Recent development and the evolution of polymer-gel chemistry would promise the creation of more excellent catalysts at present and even in the near future. Furthermore, this strategy must be contributive to not only the scientific development along “Green Chemistry” but also in the industrial production involving asymmetric synthesis.

8. Abbreviations for Catalysts

1: PAGCL-OH
2: PAG-PW (PWAA, abbreviation used in published papers)
3: PAGPPS-PdCL (PdAS, abbreviation used in published papers)
4: PAGPPS(V)-PdCl (PdAS-V, abbreviation used in published papers)
5: PAG-SiWRu
6: PAGTCl-Ru
7: PAGPEG-Ru
8: iPAGPCL-PdAc

9. References

(1) Gladysz, J. A. *Pure Appl. Chem.* **2001**, *73*, 1319.
(2) Gladysz, J. A. *Chem. Rev.* **2002**, *102*, 3215.
(3) Ley, S. V.; Baxendale, I. R. *Chem. Rec.* **2002**, *2*, 377.
(4) Cole-Hamilton, D. J. *Science* **2003**, *299*, 1702.
(5) Baker, R. T.; Kobayashi, S.; Leitner, W. *Adv. Synth. Catal.* **2006**, *348*, 1337.
(6) Horvath, I. T.; Anastas, P. T. *Chem. Rev.* **2007**, *107*, 2169.
(7) Akelah, A.; Sherrington, D. C. *Chem. Rev.* **1981**, *81*, 557.
(8) Ciardelli, F.; Braca, G.; Carlini, C.; Sbrana, G.; Valentini, G. *J. Mol. Catal.* **1982**, *14*, 1.
(9) Challa, G. *J. Mol. Catal.* **1983**, *2*, 1.
(10) Akelah, A.; Sherrington, D. C. *Polymer* **1983**, *24*, 1369.
(11) Hodge, P. *Chem. Soc. Rev.* **1997**, *26*, 417.
(12) Shuttleworth, S. J.; Allin, S. M.; Sharma, P. K. *Synthesis* **1997**, 1217.
(13) Ley, S. V.; Baxendale, I. R.; Bream, R. N.; Jackson, P. S.; Leach, A. G.; Longbottom, D. A.; Nesi, M.; Scott, J. S.; Storer, R. I.; Taylor, S. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3815.
(14) Shuttleworth, S. J.; Allin, S. M.; Wilson, R. D.; Nasturica, D. *Synthesis* **2000**, 1035.
(15) de Miguel, Y. R.; Brule, E.; Margue, R. G. *J. Chem. Soc., Perkin Trans. 1* **2001**, 3085.
(16) Clapham, B.; Reger, T. S.; Janda, K. D. *Tetrahedron* **2001**, *57*, 4637.
(17) Eames, J.; Watkinson, M. *Eur. J. Org. Chem.* **2001**, 1213.
(18) McNamara, C. A.; Dixon, M. J.; Bradley, M. *Chem. Rev.* **2002**, *102*, 3275.
(19) Benaglia, M.; Puglisi, A.; Cozzi, F. *Chem. Rev.* **2003**, *103*, 3401.
(20) Gelbard, G. *Ind. Eng. Chem. Res.* **2005**, *44*, 8468.
(21) Dioos, B. M. L.; Vankelecom, I. F. J.; Jacobs, P. A. *Adv. Synth. Catal.* **2006**, *348*, 1413.
(22) Cozzi, F. *Adv. Synth. Catal.* **2006**, *348*, 1367.
(23) Dennis, P. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 1175.
(24) Kirschning, A.; Monenschein, H.; Wittenberg, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 650.
(25) Tzschucke, C. C.; Markert, C.; Bannwarth, W.; Roller, S.; Hebel, A.; Haag, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 3964.
(26) Yoshida, J.; Itami, K. *Chem. Rev.* **2002**, *102*, 3693.
(27) Jas, G.; Kirschning, A. *Chem.—Eur. J.* **2003**, *9*, 5708.
(28) Kirschning, A.; Jas, G. *Top. Curr. Chem.* **2004**, *242*, 209.
(29) Kirschning, A.; Solodenko, W.; Mennecke, K. *Chem.—Eur. J.* **2006**, *12*, 5972.
(30) Behr, A.; Henze, G.; Schomaecker, R. *Adv. Synth. Catal.* **2006**, *348*, 1485.
(31) Sheldon, R. A. *Green Chem.* **2005**, *7*, 267.
(32) Jessop, P. G.; Heldebrant, D. J.; Li, X.; Eckert, C. A.; Liotta, C. L. *Nature* **2005**, *436*, 1102.
(33) Blaser, H.-U.; Studer, M. *Green Chem.* **2003**, *5*, 112.
(34) Wang, Y.; Jiang, J.; Jin, Z. *Catal. Sur. Asia* **2004**, *8*, 119.
(35) Liu, S.; Xiao, J. *J. Mol. Catal., A: Chem.* **2007**, *270*, 1.
(36) Afonso, C. A. M.; Branco, L. C.; Candeias, N. R.; Gois, P. M. P.; Lourenco, N. M. T.; Mateus, N. M. M.; Rosa, J. N. *Chem. Commun.* **2007**, *26*, 2669.
(37) Sheldon, R. A. *Green Chem.* **2005**, *7*, 267.
(38) Behr, A.; Henze, G.; Schomaecker, R. *Adv. Synth. Catal.* **2006**, *348*, 1485.
(39) Jessop, P. G.; Heldebrant, D. J.; Li, X.; Eckert, C. A.; Liotta, C. L. *Nature (London)* **2005**, *436*, 1102.
(40) Welton, T. *Chem. Rev.* **1999**, *99*, 2071.
(41) Earle, M. J.; Seddon, K. R. *Pure Appl. Chem.* **2000**, *72*, 1391.
(42) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772.
(43) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667.
(44) Sheldon, R. *Chem. Commun.* **2001**, 2399.
(45) Zhao, D.; Wu, M.; Kou, Y.; Min, E. *Catal. Today* **2002**, *74*, 157.
(46) Handy, S. T. *Chem.—Eur. J.* **2003**, *9*, 2938.
(47) Welton, T. *Coord. Chem. Rev.* **2004**, *248*, 2459.
(48) Picquet, M.; Poinsot, D.; Stutzmann, S.; Tkatchenko, I.; Tommasi, I.; Wasserscheid, P.; Zimmermann, J. *Top. Catal.* **2004**, *29*, 139.
(49) Wilkes, J. S. *J. Mol. Catal., A: Chem.* **2004**, *214*, 11.
(50) Jain, N.; Kumar, A.; Chauhan, S.; Chauhan, S. M. S. *Tetrahedron* **2005**, *61*, 1015.
(51) Lin, I. J. B.; Vasam, C. S. *J. Organomet. Chem.* **2005**, *690*, 3498.
(52) Muzart, J. *Adv. Synth. Catal.* **2006**, *348*, 275.
(53) Heintz, A.; Wertz, C. *Pure. Appl. Chem.* **2006**, *78*, 1587.
(54) Misao, W.; Can, T. H. *Acc. Chem. Res.* **2006**, *39*, 897.
(55) Afonso, C. A. M.; Branco, L. C.; Candeias, N. R.; Gois, P. M. P.; Lourenco, N. M. T.; Mateus, N. M. M.; Rosa, J. N. *Chem. Commun.* **2007**, 2669.
(56) Binnemans, K. *Chem. Rev.* **2007**, *107*, 2592.
(57) Parvulescu, V. I.; Hardacre, C. *Chem. Rev.* **2007**, *107*, 2615.
(58) Weingaertner, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 654.
(59) Zhu, D. W. *Synthesis* **1993**, 953.
(60) Horvath, I. T.; Rabai, J. *Science* **1994**, *266*, 72.
(61) Studer, A.; Hadida, S.; Ferritto, R.; Kim, S.-Y.; Jeger, P.; Wipf, P.; Curran, D. P. *Science* **1997**, *275*, 823.
(62) Cornils, B. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2057.
(63) Horvath, I. T. *Acc. Chem. Res.* **1998**, *31*, 641.
(64) de Wolf, E.; van Koten, G.; Deelman, B.-J. *Chem. Soc. Rev.* **1999**, *28*, 37.
(65) Barthel-Rosa, L. P.; Gladysz, J. A. *Coord. Chem. Rev.* **1999**, *190−192*, 587.
(66) Curran, D. P. *Pure Appl. Chem.* **2000**, *72*, 1649.
(67) Kitazume, T. *J. Fluorine Chem.* **2000**, *105*, 265.
(68) Luo, Z.; Zhang, Q.; Oderaotoshi, Y.; Curran, D. P. *Science* **2001**, *291*, 1766.
(69) Gladysz, J. A.; Curran, D. P. *Tetrahedron* **2002**, *58*, 3823.
(70) Sandford, G. *Tetrahedron* **2003**, *59*, 437.
(71) Zhang, W. *Tetrahedron* **2003**, *59*, 4475.
(72) Begue, J.; Bonnet-delpon, D.; Crousse, B. *Synlett* **2004**, 18.
(73) Pagliaro, M.; Ciriminna, R. *J. Mater. Chem.* **2005**, *15*, 4981.
(74) Dandapani, S. *QSAR Comb. Sci.* **2006**, *25*, 681.
(75) Mutter, M.; Hagenmaier, H.; Bayer, E. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 811.
(76) Bayer, E.; Mutter, M. *Nature (London)* **1972**, *237*, 512.
(77) Bergbreiter, D. E.; Case, B. L.; Liu, Y.-S.; Caraway, J. W. *Macromolecules* **1998**, *31*, 6053.
(78) Wentworth, P., Jr.; Janda, K. D. *Chem. Commun.* **1999**, 1917.
(79) Toy, P. H.; Janda, K. D. *Acc. Chem. Res.* **2000**, *33*, 546.
(80) Dickerson, T. J.; Reed, N. N.; Janda, K. D. *Chem. Rev.* **2002**, *102*, 3325.

(81) Bergbreiter, D. E. *Chem. Rev.* **2002**, *102*, 3345.
(82) Bergbreiter, D. E.; Hughes, R.; Besinaiz, J.; Li, C.; Osburn, P. L. *J. Am. Chem. Soc.* **2003**, *125*, 8244.
(83) Bergbreiter, D. E.; Li, J. *Top. Curr. Chem.* **2004**, *242*, 113.
(84) Bergbreiter, D. E.; Sung, S. D. *Adv. Synth. Catal.* **2006**, *348*, 1352.
(85) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159.
(86) Li, C.-J. *Chem. Rev.* **1993**, *93*, 2023.
(87) Lubineau, A.; Auge, J.; Queneau, Y. *Synthesis* **1994**, 741.
(88) Schwuger, M.-J.; Stickdorn, K.; Schomaecker, R. *Chem. Rev.* **1995**, *95*, 849.
(89) Tascioglu, S. *Tetrahedron* **1996**, *52*, 11113.
(90) Kobayashi, S.; Manabe, K. *Acc. Chem. Res.* **2002**, *35*, 209.
(91) Jenner, G. *Tetrahedron* **2002**, *58*, 5185.
(92) Oehme, G.; Grassert, I.; Paetzold, E.; Fuhrmann, H.; Dwars, T.; Schmidt, U.; Iovel, I. *Kinet. Catal.* **2003**, *44*, 766.
(93) Otto, S.; Engberts, J. B. F. N. *Org. Biomol. Chem.* **2003**, *1*, 2809.
(94) Wei, W.; Keh, C. C. K.; Li, C.-J.; Varma, R. S. *Clean Technol. Environ. Policy* **2004**, *6*, 250.
(95) Dwars, T.; Paetzold, E.; Oehme, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 7174.
(96) Li, C.-J. *Chem. Rev.* **2005**, *105*, 3095.
(97) Chechik, V. *Annu. Rep. Prog. Chem., Sect. B: Org. Chem.* **2006**, *102*, 357.
(98) Lindstroem, U. M.; Andersson, F. *Angew. Chem., Int. Ed.* **2006**, *45*, 548.
(99) Holmberg, K. *Eur. J. Org. Chem.* **2007**, 731.
(100) Schild, H. G. *Prog. Polym. Sci.* **1992**, *17*, 163.
(101) Heskins, M.; Guillet, J. E. *J. Macromol. Sci. Chem.* **1968**, *2*, 1441.
(102) Hamamoto, H.; Kudoh, M.; Takahashi, H.; Ikegami, S. *Org. Lett.* **2006**, *8*, 4015.
(103) Shibatomi, K.; Nakahashi, T.; Uozumi, Y. *Synlett* **2000**, 1643.
(104) Uozumi, Y.; Nakao, R. *Angew. Chem., Int. Ed.* **2003**, *42*, 194.
(105) Otomaru, Y.; Senda, T.; Hayashi, T. *Org. Lett.* **2004**, *6*, 3357.
(106) Nakao, R.; Rhee, H.; Uozumi, Y. *Org. Lett.* **2005**, *7*, 163.
(107) Arumugam, S.; Vutukuri, D. R.; Thayumanavan, S.; Ramamurthy, V. *J. Am. Chem. Soc.* **2005**, *127*, 13200.
(108) Kobayashi, Y.; Tanaka, D.; Danjo, H.; Uozumi, Y. *Adv. Synth. Catal.* **2006**, *348*, 1561.
(109) Kim, J. W.; Kim, J.-H.; Lee, D.-H.; Lee, Y.-S. *Tetrahedron Lett.* **2006**, *47*, 4745.
(110) Schoenfelder, D.; Nuyken, O.; Weberskirch, R. *J. Org. Chem.* **2005**, *69*, 4648.
(111) Uozumi, Y.; Suzuka, T.; Kawade, R.; Takenaka, H. *Synlett* **2006**, 2109.
(112) Nakai, Y.; Kimura, T.; Uozumi, Y. *Synlett* **2006**, 3065.
(113) Bortenschlager, M.; Schoellhorn, N.; Wittmann, A.; Weberskirch, R. *Chem.*—*Eur. J.* **2007**, *13*, 520.
(114) Yamada, Y. M. A.; Arakawa, T.; Hocke, H.; Uozumi, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 704.
(115) Li, J.; Zhang, Y.; Han, D.; Jia, G.; Gao, J.; Zhong, L.; Li, C. *Green Chem.* **2008**, *10*, 608.
(116) Yamada, Y. M. A.; Ichinohe, M.; Takahashi, H.; Ikegami, S. *Org. Lett.* **2001**, *3*, 1837.
(117) Yamada, Y. M. A.; Tabata, H.; Takahashi, H.; Ikegami, S. *Synlett* **2002**, 2031.
(118) Yamada, Y. M. A.; Tabata, H.; Ichinohe, M.; Takahashi, H.; Ikegami, S. *Tetrahedron* **2004**, *60*, 4087.
(119) Yamada, Y. M. A.; Takeda, K.; Takahashi, H.; Ikegami, S. *Org. Lett.* **2002**, *4*, 3371.
(120) Yamada, Y. M. A.; Takeda, K.; Takahashi, H.; Ikegami, S. *J. Org. Chem.* **2003**, *68*, 7733.
(121) Yamada, Y. M. A.; Takeda, K.; Takahashi, H.; Ikegami, S. *Tetrahedron Lett.* **2003**, *44*, 2379.
(122) Yamada, Y. M. A.; Takeda, K.; Takahashi, H.; Ikegami, S. *Tetrahedron* **2004**, *60*, 4097.
(123) Hamamoto, H.; Suzuki, Y.; Takahashi, H.; Ikegami, S. *Tetrahedron Lett.* **2007**, *48*, 4239.
(124) Hamamoto, H.; Ikegami, S. *J. Synth. Org. Chem., Jpn.* **2008**, *66*, 205.
(125) Hamamoto, H.; Suzuki, Y.; Yamada, Y. M. A.; Tabata, H.; Takahashi, H.; Ikegami, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 4536.
(126) Hamamoto, H.; Suzuki, Y.; Takahashi, H.; Ikegami, S. *Adv. Synth. Catal.* **2007**, *349*, 2685.
(127) Hamamoto, H.; Suzuki, Y.; Takahashi, H.; Ikegami, S. Unpublished results, 2008.
(128) Hamamoto, H.; Kudoh, M.; Takahashi, H.; Ikegami, S. Unpublished results, 2008.
(129) Hamamoto, H.; Kudoh, M.; Takahashi, H.; Natsugari, H.; Ikegami, S. *Chem. Lett.* **2007**, *36*, 632.
(130) Riisager, A.; Fehrmann, R.; Haumann, M.; Wasserscheid, P. *Eur. J. Inorg. Chem.* **2006**, 695.
(131) Mehnert, C. P. *Chem.*—*Eur. J.* **2005**, *11*, 50.
(132) Riisager, A.; Fehrmann, R.; Haumann, M.; Wasserscheid, P. *Top. Catal.* **2006**, *40*, 91.
(133) Hamamoto, H.; Kudoh, M.; Takahashi, H.; Ikegami, S. Unpublished results, 2008.
(134) (a) Schmid, G. *Chem. Rev.* **1992**, *92*, 1709. (b) Toshima, N. In *Fine Particles Science and Technology*; Pellizzetti, E., Ed.; Kluwer: Dordrecht, The Netherlands, 1996; pp 371−383.
(135) Roucoux, A.; Schulz, J.; Patin, H. *Chem. Rev.* **2002**, *102*, 3757.
(136) Widegren, J. A.; Finke, R. G. *J. Mol. Catal., A: Chem.* **2003**, *191*, 187.
(137) Astruc, D.; Lu, F.; Aranzaes, J. R. *Angew. Chem., Int. Ed.* **2005**, *44*, 7852.
(138) Chen, C.-W.; Akashi, M. *Langmuir* **1997**, *13*, 6465.
(139) Chen, C.-W.; Serizawa, T.; Akashi, M. *Chem. Mater.* **2002**, *14*, 2232.
(140) Chen, C.-W.; Serizawa, T.; Akashi, M. *Chem. Mater.* **1999**, *11*, 1381.
(141) Chen, C.-W.; Serizawa, T.; Akashi, M. *Langmuir* **1999**, *15*, 7998.
(142) Chen, C.-W.; Akashi, M. *Polym. Adv. Technol.* **1999**, *10*, 127.
(143) Li, D.; He, Qiang; Cui, Y.; Wang, K.; Zhang, X.; Li, J. *Chem.*—*Eur. J.* **2007**, *13*, 2224.
(144) Corain, B.; Burato, C.; Centomo, P.; Lora, S.; Meyer-Zaika, W.; Schmid, G. *J. Mol. Catal., A: Chem.* **2005**, *225*, 189.
(145) Burato, C.; Centomo, P.; Rizzoli, M.; Biffis, A.; Campestrini, S.; Corain, B. *Adv. Synth. Catal.* **2006**, *348*, 255.
(146) Brady, P. A.; Sanders, J. K. M. *Chem. Soc. Rev.* **1997**, *26*, 327.
(147) Welbes, L. L.; Borovik, A. S. *Acc. Chem. Res.* **2005**, *38*, 765.
(148) Becker, J. J.; Gagne, M. R. *Acc. Chem. Res.* **2004**, *37*, 798.
(149) Alexander, C.; Davidson, L.; Hayes, W. *Tetrahedron* **2003**, *59*, 2025.
(150) Wulff, G. *Chem. Rev.* **2002**, *102*, 1.
(151) Whitcombe, M. J.; Alexander, C.; Vulfson, E. N. *Synlett* **2000**, 911.
(152) Marx, S.; Avnir, D. *Acc. Chem. Res.* **2007**, *40*, 768.
(153) Maddock, S. C.; Pasetto, P.; Resmini, M. *Chem. Commun.* **2004**, 536.
(154) Cheng, Z.; Zhang, L.; Li, Y. *Chem.*—*Eur. J.* **2004**, *10*, 3555.
(155) Chen, Z.; Hua, Z.; Wang, J.; Guan, Y.; Zhao, M.; Li, Y. *Appl. Catal., A* **2007**, *328*, 252.
(156) Shinde, S. S.; Lee, B. S.; Chi, D. Y. *Tetrahedron Lett.* **2008**, *49*, 4245.
(157) Kim, D. W.; Jeong, H.-J.; Lim, S. T.; Sohn, M.-H.; Chi, D. Y. *Tetrahedron* **2008**, *64*, 4209.
(158) Kim, D. W.; Hong, D. J.; Jang, K. S.; Chi, D. Y. *Adv. Synth. Catal.* **2006**, *348*, 1719.
(159) Kim, D. W.; Chi, D. Y. *Angew. Chem., Int. Ed.* **2004**, *43*, 483.
(160) Altava, B.; Burguete, M. I.; Garcia-Verdugo, E.; Karbass, N.; Luis, S. V.; Puzary, A.; Sans, V. *Tetrahedron Lett.* **2006**, *47*, 2311.
(161) Thiot, C.; Schmutz, M.; Wagner, A.; Mioskowski, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 2868.
(162) Thiot, C.; Wagner, A.; Mioskowski, C. *Org. Lett.* **2006**, *8*, 5939.

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