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Development of a New Triphase Catalyst and Its Application to the Epoxidation of Allylic Alcohols

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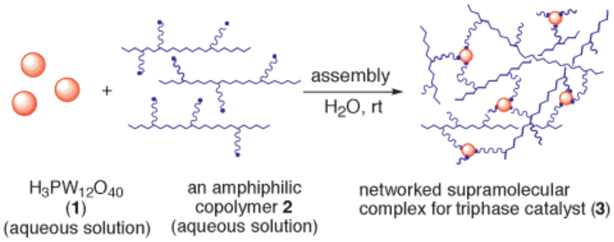
ABSTRACT



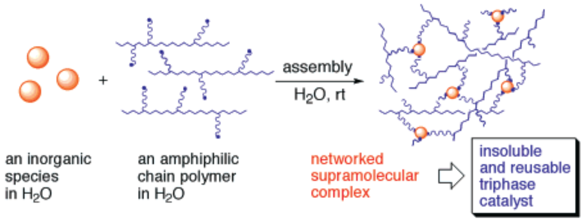
A new triphase catalyst has been developed. When an aqueous solution of $H_3PW_{12}O_{40}$ (1) was added to a solution of the amphiphilic chain copolymer 2, a new self-assembled and macroporous complex 3 was formed. This complex was effective as a catalyst in the epoxidation of allylic alcohols. Even in the use of 2.7 × 10^{-5} mole equiv of the catalyst, the epoxidation with aqueous H_2O_2 proceeded without organic solvents to give the corresponding epoxy alcohols in high yields.

The development of green chemistry is a challenging goal in recent organic chemistry. As Anastas and Warner[1] have proposed for green chemistry, it is important to realize reaction systems, in water solvent instead of an organic solvent, to use safe reagents, to decrease hazardous inorganic and organic waste, and to use a minimal amount of reusable catalysts.

One promising reaction system for achieving these goals is the use of triphase catalysis.[2] By using triphase catalysts, the procedure can be simplified, providing an easier workup and isolation of products and quantitative recovery of the catalyst. So far, cross-linked polystyrene resins and silica gel have been utilized as supports for immobilizing the catalysts. However, the reactivity of these catalysts is low; therefore, larger amounts of the catalysts are required. In addition, the use of an organic solvent is generally essential.[3] Therefore, improvement of triphase catalysts has been investigated recently.[4]

Hence, we planned to develop a new and more effective triphase catalyst. Our concept is as follows: A complexation of a water-soluble inorganic reagent and an amphiphilic polymer could be used as substrates of the triphase catalyst. When the inorganic reagent reacts with the amphiphilic polymer in aqueous solution, they could form a self-assembled and networked suprapolymer complex[5] (Scheme 1), which would be insoluble. This amphiphilic complex could have affinity to both the organic substrates and the

Scheme 1. Hypothesis of Formation of the Networked Supramolecular Complex for a New Triphase Catalyst



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(2) Regen, S. L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 421−429.

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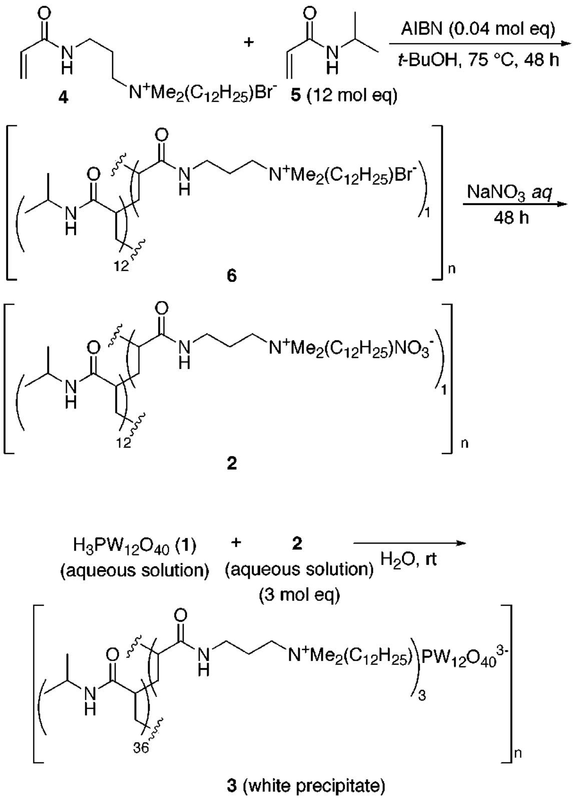
aqueous solution. It would be possible to use the complex as a triphase catalyst without an organic solvent. Moreover, the complex would possess pores that could be formed by the self-assembly of the inorganic species and the amphiphilic polymer. The surface area of the catalyst would be sufficiently wide such that the substrates and reactants could be contacted on the catalyst efficiently.

In line with this hypothesis, we report here the synthetic development of a new triphase catalyst that consists of an inorganic species and an amphiphilic chain copolymer. This new triphase catalyst was successfully applied to the epoxidation of allylic alcohols in 30% aqueous H_2O_2 without an organic solvent at room temperature.

The new triphase catalyst with the structure **3** was prepared as shown in Scheme 2. Phosphotungstic acid[6,7] (**1**) as an inorganic species and poly(*N*-isopropylacrylamide)-derived polymer[8] (**2**) as an amphiphilic polymer were used for the preparation of **3**. In the structure of **3**, the quaternary ammonium salts moiety of **2** is cross-linked by trivalent $PW_{12}O_{40}^{3-}$.

Scheme 2. Preparation of the New Triphase Catalyst **3** Complexed of Phosphotungstic Acid (**1**) and the Amphiphilic Copolymer **2**



Copolymer **2** was easily synthesized from **4** and *N*-isopropylacrylamide (**5**). A mixture of **4** and 12 mole equiv of **5** was copolymerized in the presence of 0.04 mole equiv of AIBN in *t*-BuOH for 2 days to give the polymer **6** in 86% yield. The polymer **6** was converted into the nitrate **2** by an addition of 20 mole equiv of aqueous $NaNO_3$ to **6**.[9] Complex **3** was prepared on the basis of the synthetic protocol of Ishii's $[\pi\text{-}C_5H_5N(CH_2)_{15}CH_3]_3PW_{12}O_{40}$ complex.[6f] When an aqueous solution of **1** (608 mg in 116 mL of H_2O) was added to an aqueous solution of 3 mole equiv of **2** (334 mg in 33 mL H_2O) at room temperature, the compounds **1** and **2** self-assembled to give the white insoluble precipitate **3** simultaneously. After being stirred for 7 days at the same temperature, the precipitate was filtered on a glass filter (pore size 20−30 μm), washed with water, and freeze-dried to give **3** in 95% yield (870 mg) as white lumps. The complex **3** was insoluble in H_2O and normal organic solvents such as MeOH, EtOH, *i*-PrOH, AcOEt, Me_2CO, CH_2Cl_2, Et_2O, and hexane.

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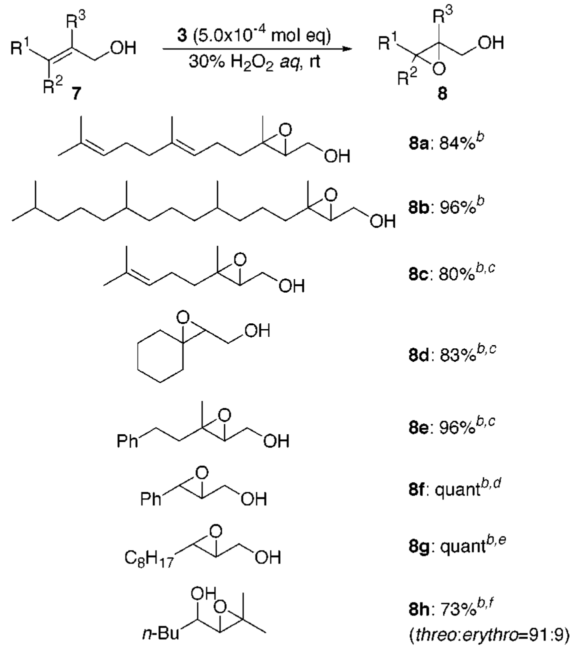
(9) Jacobs and co-workers reported the Amberlite IRA-900-supported Venturello catalyst converted into NO_3^- was effective for the enhancement of selectivity of epoxidation. See ref 7a.

With the insoluble complex **3** in hand, the epoxidation of allylic alcohols in aqueous H_2O_2 at room temperature was examined under the triphase conditions. When the epoxidation of farnesol (**7a**) with 2 mole equiv of 30% aqueous H_2O_2 without an organic solvent was carried out in the presence of 5.0×10^{-4} mole equiv of **3** at room temperature for 13 h, we were pleased to find that the pure 2,3-epoxy alcohol **8a** was obtained in 84% isolated yield (Scheme 3). In this reaction, C(6)−(7) and C(10)−(11) alkenes in **7a** were intact under the oxidation conditions. Also, the epoxidation of phytol (**7b**), which is an allylic alcohol with a hydrophobic long chain (C20), proceeded efficiently. A 25-mL flask equipped with a magnetic stirring bar was charged with 2.52 mmol of **7b**, 5.05 mmol of 30% aqueous H_2O_2, and 1.26 μmol of **3**. After the mixture was stirred vigorously at room temperature for 7 h, AcOEt (Et_2O and CH_2Cl_2 can be used) was added, and **3** was filtered. The organic layer was separated, washed with saturated aqueous $Na_2S_2O_3$, dried in vacuo, and purified by flash column chromatography to give the epoxy alcohol **8b** in 96% isolated yield.[10] Since some epoxides were sensitive to the acid-catalyzed hydrolytic cleavage, an addition of a trace amount of aqueous pyridine was effective.[11] When the reaction of geraniol (**7c**) was carried out in the presence of 5.0×10^{-4} mole equiv of **3** and 6.0×10^{-3} mole equiv of 0.04 M aqueous pyridine solution at room temperature for 15 h, the desired 2,3-epoxygeraniol **8c** was afforded in 80% yield. Under the reaction conditions, the C(6)−(7) double bond was also intact. The reaction of 2-cyclohexylidene-ethanol (**7d**), which possessed an exocyclic allylic alcohol, proceeded for 12 h to give **8d** in 83% yield. Moreover, when the reaction of (*E*)-3-methyl-5-phenyl-pent-2-en-1-ol (**7e**) was carried out in the presence of 5.0×10^{-4} mole equiv of **3** and 6.0×10^{-3} mole equiv of aqueous pyridine solution at room temperature for 13 h, the desired epoxy alcohol **8e** was afforded in 96% yield. With disubstituted allylic alcohols, the reaction of (*E*)-2-undecen-1-ol (**7g**) gave **8g** in quantitative yield. Furthermore, when the diasteroselective epoxidation of 2-methyl-2-octen-4-ol (**7h**) was carried out, the *threo*-selective epoxy alcohol **8h** was obtained in 73% yield (*threo*/*erythro* 91:9).

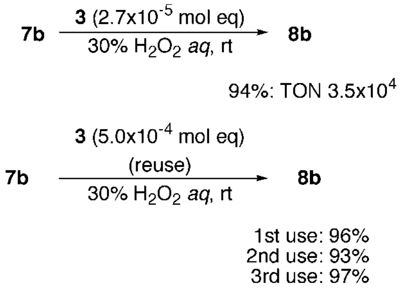
Scheme 3. Epoxidation of Various Allylic Alcohols with 30% Hydrogen Peroxide Catalyzed by Insoluble Tungsten-Amphiphilic Copolymer-Assembled Triphase Catalyst 3[a]



[a] Reaction conditions: allylic alcohols (2.52 mmol), 30% aqueous H_2O_2 (5.05 mmol) and **3** (1.26 μmol) at room temperature unless otherwise specified. [b] Isolated yield. [c] Pyridine (0.0151 mmol; 0.378 mL aq soln) was added to **3** prior to use. [d] Pyridine (0.242 mmol; 0.378 mL aq soln) was added to **3** (5.05μmol) prior to use. [e] Pyridine (0.0604 mmol; 0.378 mL aq soln) was added to **3** (5.05 μmol) prior to use. [f] Pyridine (0.0604 mmol; 0.378 mL aq soln) was added to **3** prior to use. The diastereomeric ratio of **8h** was determined by ^{1}H NMR analysis; see: Iseki, Y.; Kudo, M.; Mori, A.; Inoue, S. *J. Org. Chem.* **1992**, *57*, 6329−6331.

It was possible to decrease the amount of catalyst **3**. The reaction of **7b** with 2 mole equiv of 30% aqueous H_2O_2 in the presence of 2.7×10^{-5} mole equiv (27 ppm) of **3** at room temperature proceeded to give **8b** in 94% yield (Scheme 4). The turnover number (TON) of the catalyst **3** was approximately 35000, while that of tungsten catalysts supported by polystyrene beads or silica gel was a few hundred.[7] That is, turnover efficiency of **3** was hundreds of times higher than that of other polymer-supported tungsten catalysts.

Scheme 4 Epoxidation Catalyzed by 2.7×10^{-5} Mole Equiv (27 ppm) of Triphase Catalyst **3**, and the Epoxidation Promoted by Recovered Triphase Catalyst



Moreover, **3** was effective as a reusable catalyst as shown in Scheme 4. When the reaction of **7b** and 2 mole equiv of 30% H_2O_2 in the presence of 5.0×10^{-4} mole equiv of **3** was carried out for 12 h at room temperature, the product **8b** was given in 96% yield. In the presence of the recovered catalyst, the second reaction of **3** with H_2O_2 proceeded for 12 h at room temperature to give **8b** in 93% yield. Again,

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[10] When the reaction of **7b** with aqueous H_2O_2 was carried out in the presence of 4.0×10^{-4} mole equiv of $(Bu_4N)_3PW_{12}O_{40}$ in place of **3**, **8b** was not obtained.

[11] It was reported that pH control in aqueous media was important for tungsten-catalyzed epoxidation; see refs 6d,e and 7b.

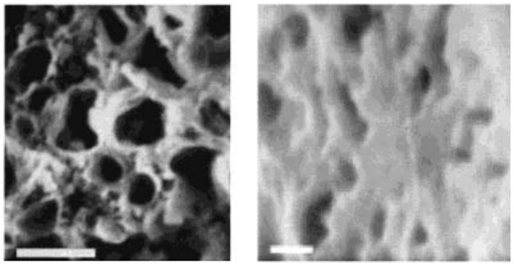

Figure 1. Scanning electron micrographs (SEM) of **3**: (left) 1000×, scale bar = 10 μm; (right) 12000×, scale bar = 500 nm.

the recovered catalyst was reusable; that is, the third reaction afforded **8b** in 97% yield.

To obtain further information on the structure of the catalyst, we analyzed **3** by several spectroscopic measurements. One complex unit of **3**·$22H_2O$ corresponds to formula $C_{276}H_{563}N_{42}O_{101}PW_{12}$; calculated % of elementary analysis was C 39.8, H 6.3, N 7.1; found % was C 39.6, H 6.6, N 7.2.[12] The infrared spectrum of **3** exhibited strong vibrations at 1080 (P═O), 978 (W═O), 897, and 818 cm^{-1}, while that of **1** exhibited them at 1080, 982, 893 and 808 cm^{-1}. The result suggests the structure of the phosphotungstic acid unit of **3** was similar to that of **1**.

A scanning electron microscope (SEM) study was also performed (Figure 1). The compound **3** was treated with gold vapor by the sputter-coating method. We were pleased to find that the complex **3** had macropores, whose diameter was about 1−10 μm (Figure 1 left), and hundreds a nanometer or less (Figure 1 right). These facts mean that the surface area and the reactive sites of an amphiphilic complex of **3** are extensive. Therefore, the substrates and reagents could infiltrate into the amphiphilic complex **3** effectively. The existence of macropores should be one reason why 2.7×10^{-5} mole equiv of **3** could work efficiently as a triphase catalyst, although **3** was insoluble in solvent. Further investigations as to whether **3** is not only a macroporous complex but also a mesoporous complex and whether **2** is cross-linked by $PW_{12}O_{40}^{3-}$ are currently in progress.

In conclusion, we have developed a new triphase catalyst prepared from the self-assembly of an aqueous solution of an inorganic species and an amphiphilic polymer. Even in the presence of only 2.7×10^{-5} mole equiv (27 ppm) of the triphase catalyst without an organic solvent, the epoxidation of an allylic alcohol with aqueous H_2O_2 gave the desired epoxy alcohol in excellent yield. Again, the catalyst was easily prepared and purified, and it was insoluble, recoverable, and reusable. Moreover, it was a macroporous complex. Since this new triphase catalyst exhibited great potentiality, applications to other reactions involving asymmetric synthesis are currently being studied.

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[12] It is natural for complex **3** to possess $22H_2O$ in one complex unit, because *n* in **1**·nH_2O is ca. 40−60 (purchased from Wako Pure Chemical Industries, Ltd., Japan) and complete evaporation of water from **3** should be difficult.