Journal of Catalysis 335 (2016) 62–71

Contents lists available at ScienceDirect

Journal of Catalysis

journal homepage: www.elsevier.com/locate/jcat

Thermo-responsive self-assembled metallomicelles accelerate asymmetric sulfoxidation in water

Yaoyao Zhang [a,b], Rong Tan [a,b,*], Guangwu Zhao [a,b], Xuanfeng Luo [a,b], Chen Xing [a,b], Donghong Yin [a,b,c,*]

[a] *Key Laboratory of Chemical Biology and Traditional Chinese Medicine Research (Ministry of Education), Hunan Normal University, Changsha 410081, PR China*
[b] *Key Laboratory of the Assembly and Application for Organic Functional Molecules, Hunan Normal University, Changsha 410081, PR China*
[c] *Technology Center, China Tobacco Hunan Industrial Corporation, NO. 426 Laodong Road, Changsha, Hunan 410014, PR China*

ARTICLE INFO

Article history:
Received 5 September 2015
Revised 8 November 2015
Accepted 2 December 2015
Available online 11 January 2016

Keywords:
Thermo-responsive
Micellar catalysis
Chiral salen Ti^{IV} complex
Asymmetric sulfoxidation
Water

ABSTRACT

A series of novel chiral salen Ti^{IV} catalysts with thermo-responsive surfactant properties were prepared by covalently appending a chiral salen Ti^{IV} complex on the hydrophobic block of thermo-responsive amphiphilic copolymers of poly(N-isopropylacrylamide-*co*-N,N-dimethyl acrylamide) (poly (NIPAAM-*co*-DMAAM)). Characterization results suggested self-assembly behavior of the catalysts in water at room temperature. The self-assembled metallomicelles induced a micellar catalytic approach in asymmetric sulfoxidation in water using H_2O_2 as an oxidant, leading to significant rate acceleration and remarkable high selectivity. Quantitative conversion (>99%) of methyl phenyl sulfide with up to 96% chemoselectivity and 95% enantioselectivity was achieved over 0.5 mol% of **$PN_{70}D_7$-C** even within 30 min, whereas neat complex was far less efficient (9% conversion with 72% chemoselectivity and 79% enantioselectivity). Moreover, the catalysts could be easily recovered by thermo-controlled separation and be efficiently reused for several cycles.

1. Introduction

Asymmetric oxidation of prochiral sulfides catalyzed by chiral salen Ti^{IV} complexes is of great importance in organic synthesis, since the obtained enantiopure sulfoxides are valuable chiral intermediates for the synthesis of fine chemicals and many pharmaceuticals [1–6]. Organic solvents are commonly used to ensure high reactivity of the transformation. As the demand for environmentally friendly methods increases, water as a solvent is of great interest. Apart from the advantages of being safe, nontoxic, environmentally benign, and inexpensive, water often enhances reaction rate and selectivity in a wide variety of organic reactions [7–13]. However, success of performing the asymmetric sulfoxidation in water has been hindered by poor water-solubility of sulfides and catalysts. An efficient way to solve the problem is to introduce surfactants additives or surfactant-like catalysts [14,15]. Generally, amphiphilic surfactants spontaneously self-assemble in water to form micelles with hydrophobic core and hydrophilic surface. Hydrophobic core sequestered organic reactants from surrounding aqueous environment through hydrophobic affinity, while hydrophilic surface guaranteed water-solubility of the aggregates. The micellar systems thus often result in high local concentration of reactants within the micelle, leading to an acceleration of reaction and/or causing selective effects [16–22]. Lately, we have observed a sixfold increase in reaction rate for the asymmetric epoxidation of unfunctionalized olefins in water using chiral salen Mn^{III} complex-based micellar system [23].

The advantages of micellar catalysis encouraged us to prepare surfactant-type chiral salen Ti^{IV} catalyst for aqueous asymmetric sulfoxidation by appending hydrophobic chiral salen Ti^{IV} complex on a hydrophilic block. We envisioned that the amphiphilic catalyst should form micellar aggregates in water, thereby creating a microenvironment with high local concentration of chiral salen Ti^{IV} complex in the hydrophobic core along with a hydrophilic surface ensuring the water-solubility of the whole aggregate. High local concentration of chiral salen Ti^{IV} complexes confined in the hydrophobic domain may enforce a cooperative reaction pathway resulting in enhanced reaction rates and higher selectivities [24,25]. Furthermore, the hydrophobic microenvironment would exclude excess H_2O_2 from catalyst and sulfoxide, potentially minimizing the undesired over-oxidation of sulfoxide to sulfone, and also preventing the oxidative decomposition of chiral salen Ti^{IV}

---

* Corresponding authors at: Key Laboratory of Chemical Biology and Traditional Chinese Medicine Research (Ministry of Education), Hunan Normal University, Changsha 410081, PR China and Key Laboratory of the Assembly and Application for Organic Functional Molecules, Hunan Normal University, Changsha 410081, PR China. Fax: +86 731 88872531 (R. Tan).

E-mail addresses: yiyangtanrong@126.com (R. Tan), yindh@hunnu.edu.cn (D. Yin).

http://dx.doi.org/10.1016/j.jcat.2015.12.012
0021-9517/© 2015 Elsevier Inc. All rights reserved.

complex during sulfoxidation. Therefore, a surfactant-type chiral salen Ti^{IV} catalyst should allow for the efficient and selective asymmetric sulfoxidation in water. However, the surfactant-type catalysts are commonly different to recover from the aqueous organic system due to amphiphilicity, which would restrict their further development and applications. If the hydrophilic blocks are thermo-sensitive chain, being able to undergo hydrophilic-to-hydrophobic transformation at their lower critical solution temperature (LCST), facile recovery of the catalyst can be expected.

Herein, well-defined thermo-responsive copolymers of poly (NIPAAM-*co*-DMAAM), featuring a terminated amino (—NH_2) group on DMAAM chain, were synthesized *via* reversible addition – fragmentation chain transfer (RAFT) polymerization techniques. Covalently appending chiral salen Ti^{IV} complex on the DMAAM block of poly (NIPAAM-*co*-DMAAM) provided the Ti-salen catalysts with thermo-responsive surfactant properties. The resulted catalysts exhibited thermo-responsive micellization behavior in asymmetric sulfoxidation in water. At reaction temperature (25 °C), they were amphiphilic and self-assembled to form micelles, leading to a significant increase in the activity, chemo- and enantioselectivity as a result of the "micellar catalysis". Almost quantitative conversion (>99%) of sulfides with excellent chemo- (87–99%) and enantioselectivity (72–95%) was observed over the micellar system. The reactivity was even significant higher than that obtained in organic solvent or neat conditions. After reaction, the catalysts switched to double hydrophobic block compounds upon heating above its LCST, which would collapse and precipitate for facile recovery. More attractively, activity switching was repeatable even seven heating/cooling cycles. Furthermore, catalytic performance (activity, stability and enantioselectivity) of the thermo-responsive catalysts could be regulated by controlling the molar ratio of NIPAAM to DMAAM in poly(NIPAAM-*co*-DMAAM).

2. Experimental

2.1. Materials and reagents

Tetra-isopropyl titanate and methyl aryl sulfides were obtained by J&K. N,N-Azobis(isobutyronitrile) (AIBN), NIPAAm, DMAAM, 2-aminoethanethiol hydrochloride, and L(+)-tartaric acid were purchased from Acros. 2-Tert-butylphenol was purchased from Alfa Aesar. Other commercially available chemicals were laboratory grade reagents from local suppliers. All solvents were purified by standard procedures. NIPAAm and DMAAM were purified by recrystallization from *n*-hexane and dried in vacuo before use. Asymmetric chiral salen ligand of (*R*,*R*)-N-(3,5-di-tert-butylsalicylidene)-N′-[3-tert-butyl-5-chloromethyl- salicylidene]-1,2-cyclohexanediamine) was synthesized as described earlier [26]. Traditional chiral ((*R*,*R*)-salen)Ti^{IV}(O^{i}pr)$_2$ complex (denoted as neat complex, as shown in Chart 1) was prepared according to the described procedures [27].

2.2. Methods

FT-IR spectra were obtained as potassium bromide pellets with a resolution of 4 cm^{-1} and 32 scans in the range 400–4000 cm^{-1} using an AVATAR 370 Thermo Nicolet spectrophotometer. Number-average molecular weight (M_n) of polymers was obtained by gel permeation chromatograph (GPC). Analyses were performed on an Alltech Instrument (Alltech, America) using THF as the solvent eluting at a flow of 1 mL min^{-1} through a Jordi GPC 10000 A column (300 mm × 7.8 mm) equipped with an Alltech ELSD 800 detector. The system was calibrated with standard polystyrenes. The detection temperature is 40 °C and column temperature is 30 °C. The LCST of copolymers in water was determined by transmittance measurements using a UV–vis Agilent 8453 spectrophotometer. The complex concentration was 1 wt%, and the heating rate was 5 °C/min. NMR spectra of samples were recorded at a Varian-500 spectrometer with TMS as an internal standard. Morphologies of the self-assembled aggregates were observed by TEM on a Microscope JEM-2100F at an accelerating voltage of 200 kV. Samples were prepared by depositing aqueous solution (0.5 mg mL^{-1}) onto a carbon-coated copper grid, followed by removal of excess solution by blotting the grid with filter paper. The samples were dried for 72 h at room temperature in a desiccator containing dried silica gel. After that, the samples were negatively stained by phosphotungstic acid and dried for another 72 h before examination. The content of titanium contents in the samples was determined by inductively coupled plasma mass spectrometry (ICP-MS) on a NexION 300X analyzer (Perkin-Elmer Corp.). Dynamic light scattering (DLS) was performed using a MS2000 Laser Particle Size Analyzer (Malvern, UK). The sample solutions for measurements were prepared for concentrations of 0.5 mg mL^{-1} followed by filtering through a 0.45 lm disposable polyamide (PA) membrane to free it from dust particles. Light transmittance was fixed at 633 nm with the scattering angle of 90°. The mean diameters of self-assemblies were obtained from the number distribution curves produced by the particle analyzer. Optical rotation of samples was measured in dichloromethane on a WZZ-2A Automatic Polarimeter.

2.3. Preparation of surfactant-like chiral salen Ti^{IV} catalysts

2.3.1. Synthesis of poly(NIPAAM-co-DMAAM)

Poly(NIPAAM-*co*-DMAAM) with various length of PDMAAM block was prepared *via* RAFT techniques, as shown in Scheme 1. Monomers of NIPAAm and DMAAM with different molar feed (91 mmol of NIPAAm and 9 mmol of DMAAM for $PN_{70}D_7$, 95 mmol of NIPAAm and 5 mmol of DMAAM for $PN_{80}D_4$, 97 of mmol

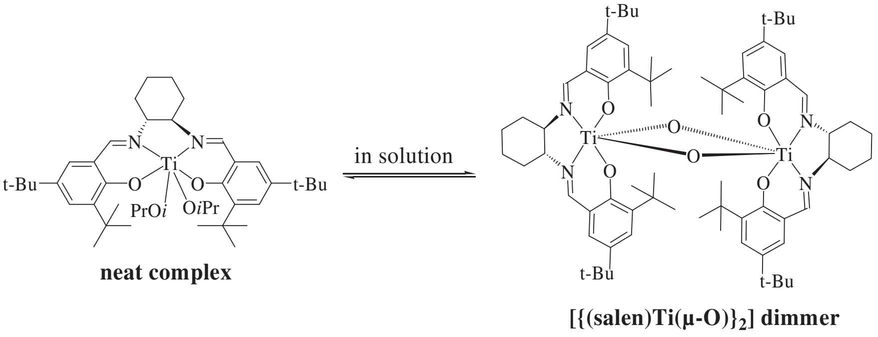

Chart 1. The concentration-dependent equilibrium between monomeric and dimeric species in solution.