Editor's choice paper

# An amphiphilic and photoswitchable organocatalyst for the aldol reaction based on a product-imprinted polymer

An-xun Zheng [a], Cheng-bin Gong [a,*], Wei-jing Zhang [a], Qian Tang [a], Hai-rong Huang [a], Cheuk-fai Chow [b,*], Qian Tang [a,*]

[a] The Key Laboratory of Applied Chemistry of Chongqing Municipality, College of Chemistry and Chemical Engineering, Southwest University, Chongqing, 400715, China
[b] Department of Science and Environmental Studies, The Education University of Hong Kong, Hong Kong

## ARTICLE INFO

## ABSTRACT

A series of amphiphilic molecularly imprinted polymers (MIP1, MIP2, MIP3, MIP4, MIP5, and MIP6) containing hydrophobic photoresponsive sites and hydrophilic catalytically active sites were fabricated using bifunctional monomers. These polymers were characterized by scanning electron microscopy, $N_2$ adsorption–desorption analysis, Fourier Transform infrared spectroscopy, thermal gravimetric analysis, and ultraviolet–visible spectroscopy. The catalytic activity of the amphiphilic molecularly imprinted polymer was investigated towards the aldol reaction between p-nitroaldehyde and acetone (a molecular enlargement reaction) in a mixed solvent of DMSO and water at room temperature. The polymer catalyst MIP3 performs best, and displayed good conversions with low catalyst loading (5 mol% of L-hydroxyproline with respect to the aldehyde) and photoswitching properties (photo-regulated conversion difference of 20%). Compared with the corresponding non-imprinted polymer, a higher binding capacity, higher conversion, and better photoswitching properties were obtained when the molecularly imprinted polymer was used as the catalyst, illustrating the importance of the specific cavities in the molecularly imprinted polymer.

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## 1. Introduction

Molecular imprinting is a well-known methodology for generating specific recognition sites with memory of the shape, size, and functionality of templates, and has many promising characteristics such as good selectivity towards template, physical robustness, thermal stability, as well as low cost and easy preparation [1–3]. These outstanding properties make molecularly imprinted polymers (MIPs) very promising candidates for various applications such as separation processes [4–8], biotechnology [9,10], chemical sensors [11–14], and catalysis [15–39]. For the application of MIPs in catalysis, substrates and substrate analogues [16,17,19,21,24,26,27,29,31,32,36–38], transition-state analogues [20,22,25,30,33], product analogues [35], and catalysts [18] have been used as templates. The use of catalyst as template is scarce. The catalytically active sites are generally contained in the MIP and are usually used to catalyze reduction [16,35,37,38], hydrolysis [17,20,31,36], degradation [21,25–27], and oxidation [5] reactions. Most of these are molecular decrease reactions compared with their corresponding reactants. However, to the best of our knowledge, there have been limited reports of MIP-catalyzed molecular enlargement reactions with respect to the reactants.

The aldol reaction is a molecular enlargement reaction through the formation of carbon–carbon bond. L-proline or L-hydroxyproline has been extensively used as a catalyst to catalyze the aldol reaction. However, several challenges need to be addressed. A high catalyst loading (up to approximately 30 mol% with respect to the aldehyde) is usually required owing to the low catalytic activity of L-proline [40]. The catalytic efficiency of L-proline in water is typically poor [41], therefore, L-proline-catalyzed aldol reaction is typically carried out in organic solvents (DMSO, in general). The separation of the product and recycling of the catalyst is difficult [42]. Polymer-supported L-hydroxyproline has been used to facilitate the separation of the product and recovery of the catalyst [43,44] in an aldol reaction in an aqueous medium. The polymer formed a micro-reaction environment or compartments to promote the reaction [44]. The hydrophobic, structured compartments were believed to isolate the L-hydroxyproline catalytic site from the bulk medium. Gong

* Corresponding authors.
E-mail addresses: gongcbtq@swu.edu.cn (C.-b. Gong), cfchow@ied.edu.hk (C.-f. Chow), qiantang@swu.edu.cn (Q. Tang).

et al. [18] pioneered a photoswitchable catalyst based on MIP for the aldol reaction using L-proline as the template and photoresponsive 4-[(4-methacryloyloxy)phenylazo]-benzenesulfonic acid as the functional monomer. When the azobenzene chromophores were in the *trans* form, the catalyst (L-proline) was bound by the MIP, and the reaction was turned off; when the azobenzene chromophores were in *the cis* form, the catalyst was released into the solution containing the reactants to catalyze the aldol reaction, and the reaction was turned on. Although photoswitchable properties were realized, the catalyst loading was high (40 mol% of L-proline with respect to 4-nitrobenzaldehyde) and the solvent (DMSO) was organic. Herein, by combining the hydrophobic, structured compartments provided by polymer, specificity of MIP, and the photoresponsiveness of azobenzene, we prepared a MIP-based catalyst for aldol reaction (a molecular enlargement reaction). We used a hydrophobic and photoresponsive azobenzene derivative and a hydrophilic catalytically active and functionalized L-hydroxyproline as bifunctional monomers, and the reaction product as a template. The amino group and carboxyl group of L-hydroxyproline was expected to act as a catalytic unit and a recognition unit, respectively. The hydroxyl group of L-hydroxyproline was functionalized with a polymerizable carbon–carbon double bond for the formation of polymer catalyst. The reaction product, 4-hydroxy-4-(4-nitrophenyl) butan-2-one (HNBO), between *p*-nitrobenzaldehyde and acetone was used as the template. Thus the specific cavity in MIP can recognize *p*-nitrobenzaldehyde and provide enough space for reactants. This MIP-catalyzed aldol reaction proceeded in a mixed solvent of DMSO: $H_2O$ (3 mL, 1:1, v/v) with lower catalyst loading, good conversion, and photoswitching properties.

## 2. Experimental

### 2.1. Materials and instrumentation

Thionyl chloride (99.0%) and methacrylic acid (98.5%, AR grade) were purchased from Chengdu Kelong Chemical Reagent Company, Chengdu, China. *p*-Nitrobenzaldehyde (99.0%) was purchased from Shanghai Dibai Chemical Technology Company, Shanghai, China. L-Hydroxyproline (99.0%), phenol (99.0%), trifluoroacetic acid (TFA, 99.0%), ethylene glycol dimethacrylate (EGDMA, AR grade), and other chemical reagents were purchased from Aladdin Co., Shanghai, China, and used as received. All of the solvents were of analytical-reagent grade, commercially available, unless otherwise noted. Azodiisobutyronitrile (AIBN) was recrystallized in methanol prior to use.

^{1}H NMR and ^{13}C NMR were measured using a Bruker AV-600 NMR instrument at an ambient temperature using tetramethylsilane as an internal standard. Ultraviolet–visible (UV–vis) spectra were recorded with an UV-4802 spectrophotometer (UNICO (Shanghai) Instruments Co., Ltd., China). A CEL S-500 Xe light was used as the light source (Au Light Inc., Beijing, China), and 365 and 440 nm light wavelengths were selected using filters, respectively. Fourier transform infrared spectroscopy (FTIR) spectra were recorded in the 4000–400 cm$^{-1}$ region with a Perkin-Elmer Model GX spectrometer (USA) using a KBr pellet method. Thermal stability of materials was evaluated using a SDT Q600 thermal analyzer (USA) at a heating rate of 10 °C min$^{-1}$ up to 750 °C under flowing nitrogen (100 mL min$^{-1}$). Nitrogen adsorption–desorption analysis was conducted at 77 K on an Autosorb-1 apparatus (Quantachrome, USA). Specific surface areas and pore diameters were calculated using the Brunauer-Emmett-Teller (BET) and Barrett-Joyner-Halenda (BJH) models, respectively. Morphologies of the MIP and non-imprinted polymer (NIP) were identified by scanning electron microscopy (SEM; JSM-7800F, JEOL, Japan). Dynamic light
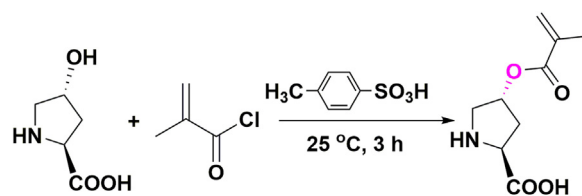


**Scheme 1.** Synthetic route for methacryloyl-*trans*-4-hydroxy-proline.

scattering (DLS) was performed on a NanoBrook Omni (Brookhaven Instruments, Newoyork, USA). The ee was measured at 20 °C with an Agilent high performance liquid chromatography (HPLC) 1200 series system equipped with quaternary pump (G1311A), variable wavelength detector (G1314A), and autosampler (G1313A). The mobile phase used for HPLC experiments was a mixture of *n*-hexane and isopropanol (85:15, v:v), and all separations were carried out on a Daicel AD-H chiral column with a flow rate of 0.8 mL min$^{-1}$. The detecting wavelength of the UV detector was set at 270 nm.

### 2.2. Synthesis of methacryloyl chloride

Thionyl chloride (25.00 g, 0.21 mol) and five drops of DMF were introduced into a 50 mL three-necked flask connected with a tail gas absorber, to which methacrylic acid (17.22 g, 0.20 mol) was added dropwise under magnetic stirring. After then, the mixture was heated to 50 °C and kept for 5 h. Methacryloyl chloride (colorless oil, b.p. 96–98 °C, yielded 90%) was obtained by atmospheric distillation.

### 2.3. Synthesis of 4-hydroxy-4-(4-nitrophenyl) butan-2-one (the template)

The template, 4-hydroxy-4-(4-nitrophenyl) butan-2-one (HNBO), was synthesized according to a method reported by Al-Momani [42] with some modification. *p*-Nitrobenzaldehyde (6.00 g, 39.70 mmol) and DMSO (20 mL) were introduced into a 250-mL flask. A solution of L-hydroxyproline (0.46 g, 3.51 mmol) in 40 mL acetone was added. The mixture was stirred for 48 h at room temperature and then concentrated. The residue was dissolved in water (150 mL), and the aqueous layer was extracted with ethyl acetate (3 × 40 mL). Combined organic layers were washed with saturated NaCl solution (2 × 50 mL), and dried over MgSO$_4$. The solvent was removed under reduced pressure and the crude product was purified via column chromatography (petroleum ether/ethyl acetate of 5:1, v/v). HNBO was obtained as a light yellow solid in 85% yield. ^{1}H NMR (600 MHz, CDCl$_3$) $\delta$ (ppm): 8.21 (d, 2H, *J* = 8.4 Hz), 7.54 (d, 2H, *J* = 8.4 Hz), 5.27 (m, 1H, *J* = 3.6–12.0 Hz), 3.55 (s, 1H), 2.86 (d, 2H, *J* = 4.2 Hz), 2.22 (s, 3H).

### 2.4. Synthesis of methacryloyl-trans-4-hydroxyproline (the catalyst monomer)

The catalyst monomer was designed by functionalizing the catalyst L-hydroxyproline with a polymerizable carbon–carbon double bond. The catalyst monomer, methacryloyl-*trans*-4-hydroxyproline (MAHP), was synthesized according to previous methods with some modification using L-hydroxyproline and methacryloyl chloride as the reactants (Scheme 1) [45,46]. TFA (3.0 g) was placed in a 50-mL three-necked flask, to which L-hydroxyproline (0.50 g, 3.80 mmol) was added slowly in an ice bath under stirring. After then, the mixture was stirred at room temperature till L-hydroxyproline dissolved. To the viscous solution, *p*-toluene sulfonic acid (0.13 g, 0.76 mmol) was added. Methacryloyl chloride (0.81 g, 7.80 mmol) was then added dropwise under an ice-salt bath. The reaction system was stirred at room temperature