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An environmentally friendly, photocontrollable and highly recyclable catalyst for use in a one-pot three-component Mannich reaction

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Graphical Abstract



Highlights

- An azobenzene-containing catalyst supported on zirconium phosphonate was synthesized
- The catalyst catalyzes one-pot three-component Mannich reaction in water
- The catalyzed Mannich reaction could be photo-controllable
- The catalyst could be recycled and recovered easily

Abstract: An environmentally friendly, photocontrollable and highly recyclable catalyst (ZrOPPAZOSO₃H) has been synthesized by the immobilization of 4-[4-(6-phosphonic acid-hexanoxyl)phenylazo]benzenesulfonic acid onto zirconium phosphonate. This catalyst was characterized by Fourier transform infrared, scanning electron microscopy, X-ray powder diffraction, nitrogen adsorption-desorption and UV-Vis analyses. The catalytic activity of ZrOPPAZOSO₃H was investigated towards the one-pot three-component Mannich-type reaction of benzaldehyde, aniline and

cyclohexanone in water at room temperature, and gave excellent yields. Interestingly, the catalytic activity could be regulated by photoirradiation. Furthermore, upon completion of the reaction, the product could be readily separated by extraction, and the water phase reused in the next run. Lastly, the catalyst could be readily recovered by centrifugation and reused up to six times without any discernible impact on its activity.

Keywords: Mannich reaction; Environmentally friendly catalyst; Photocontrollable; Azobenzene; Zirconium phosphonate

1. Introduction

The Mannich reaction involves the reaction of two carbonyl compounds with an amine to give a β -amino-carbonyl compound via a C–C bond-forming reaction in the presence of a proper catalyst [1]. β -Amino-carbonyl compounds are important intermediates in the synthesis of pharmaceutical agents and natural products [2], and the Mannich reaction has therefore attracted considerable interest from numerous research groups. A variety of different catalysts have been developed for the Mannich reaction, including Bronsted acids [3-6], Lewis acids [7-18] and several other organic or inorganic compounds [19-22]. However, most of these methods are conducted in organic solvents [3-7,9-13,15-17,19-22] or organic solvent-water mixtures [14,18]. The development of novel catalysts capable of catalyzing the Mannich reaction of a wide range of substrates in water is therefore highly desired and research in this area has grown considerable, because of the economical and environmental benefits of water. However, the use of water as a solvent has been limited because of the poor

solubility of most organic reactants in water. For example, most of the reported Mannich reactions conducted in water use silyl enol ethers as precursors [23] or have to be performed in the presence of surfactants (such as sodium dodecyl sulfate) [24,25] or ionic liquids [26,27]. Unfortunately, silyl enol ethers have to be prepared from the corresponding carbonyl compounds and the Mannich reactions of these substrates generally require an organic solvent. The use of surfactants or ionic liquids in these reactions can lead to phase separation issues. Several researchers have reported the use of water-soluble catalysts such as heteropoly acids and its salts [28,29] Bi(OTf)₃•4H₂O [30], 5-sulfosalicylic acid [31], calix[n]arene quaternary ammonium salts [32] and boron chelate complexes [33]. However, catalysts of this type can be difficult to recover from the reaction mixture because of their good solubility. Catalysts supported on a stable solid substrate are therefore highly desired because they can be readily recycled [34,35].

To address these challenges, we developed a novel environmentally friendly, recyclable and photocontrollable catalyst (ZrOPPAZOSO₃H, Scheme 1) for a one-pot three-component Mannich reaction in water by tethering a sulfonated azobenzene to zirconium phosphate. It was envisaged that the sulfonic acid group in this catalyst would serve as a catalytic moiety, as well as enhancing the aqueous solubility of the catalyst. The recyclability of the catalyst could be realized by tethering the azobenzene moiety to zirconium phosphate, which is a versatile material with a layered structure. Azobenzene chromophores [36-40] are well-known photoresponsive moieties, and the photoirradiation of these systems can induces trans/cis isomerization

processes, resulting in pronounced changes in their geometry, which can promote or slow down specific reactions. The catalyst developed in this study demonstrated photo-controllability, as well as being environmentally friendly and highly recyclable for the one-pot three-component Mannich reaction of unmodified aldehydes, ketones and amines in water. Indeed, photo-activated or photocontrollable catalysts for Mannich reactions are rarely found in literature and the current system is interesting for further exploring its potential applications in inhibition reactions.

2. Experimental details

2.1. Materials and methods

All of the chemicals used in the current study were purchased from Aladdin Co. (Shanghai, China) and used without further purification.

Fourier transform infrared (FT-IR) spectra were recorded on a Perkin-Elmer Model GX Spectrometer (Perkin-Elmer, Waltham, USA) as KBr pellets using polystyrene as a standard. X-ray diffraction (XRD) patterns were recorded on a LabX XRD-6100X-ray Diffractometer (SHIMADZU, City, Japan) with Cu-K_{α} monochromated radiation (λ =1.5406 Å) at 36 kV and 20 mA. The morphological characteristics of the ZrOPPAZOSO₃H catalyst were determined by scanning electron microscopy (SEM; S-4800, Hitachi, Tokyo, Japan). ¹H NMR and ¹³C NMR (300 MHz) spectra were recorded on a Bruker AV-300NMR instrument (Bruker, USA) at ambient temperature using TMS as an internal reference standard. Nitrogen adsorption-desorption analysis was

conducted at 77 K on an Autosorb-1 apparatus (Quantachrome, USA). The specific surface areas and pore diameters were calculated using the BET and BJH models, respectively. UV-Vis spectra were recorded with an UV-4802 spectrophotometer (UNICO Shanghai Instruments Co. Ltd, Shanghai, China) using a CEL-S500 Xe lamp (Beijing Zhongjiao Jinyuan Keji Co., Ltd, Beijing, China) as a light source. Wavelengths of 365 and 440 nm were selected using 365 and 440 nm filters, respectively.

2.2. Synthesis of ZrOPPAZOSO₃H

The synthesis of ZrOPPAZOSO₃H was completed over five steps (Scheme 2).

2.2.1. Synthesis of 4-[(4-Hydroxy)phenylazo]benzenesulfonic acid

4-[(4-Hydroxy)phenylazo]benzenesulfonic acid was synthesized according to a modified version of previous methods reported by Ma, Kumar and Gong [41-43]. Briefly, sulfanilic acid (3.48 g, 20.0 mmol), sodium nitrite (1.52 g, 22.0 mmol) and water (8.0 mL) were added to a 250 mL round-bottomed flask, and the resulting mixture was cooled in an ice bath under stirring. An ice-cold mixture of water (8.0 mL) and conc. HCl (36%, 8.0 mL) was then added to the reaction flask in a dropwise manner, and the resulting diazonium salt solution was stirred for 1 h at 0–5 °C. The diazonium salt solution was added to an ice-cold mixture of phenol (2.48 g, 20.4 mmol) and aqueous NaOH solution (40 mL, 3.0 mol L⁻¹) in a dropwise manner over 45 min. The resulting mixture was stirred at 0 °C for 2 h and then acidified to pH=3 with conc. HCl to give an orange precipitate, which was collected by filtration to give

the crude product. The crude material was then purified by recrystallization from ethanol to give 4.02 g of pure 4-[(4-hydroxy)phenylazo]benzene sulfonic acid as an orange solid. Yield: 71.9 %. ¹H NMR (300 MHz, DMSO- d_6) δ (ppm): 10.4 (s, 1H), 7.83 (d, 2H), 7.76 (s, 4H), 6.96 (d, 2H).

2.2.2. Synthesis of 4-[4-(6-diethylphosphonohexanoxyl)-phenylazo] benzenesulfonic acid

Diethyl (6-bromo-hexanyl)phosphonate was synthesized according to a method reported by Cernetic [44] with some minor modifications. Briefly, 1,6-dibromohexane (10.0 g, 32 mmol) was heated at reflux under nitrogen and treated with triethylphosphite (1.4 mL, 8 mmol), which was added in dropwise manner. The resulting mixture was stirred for 12 h at 148 °C and then cooled to room temperature. The crude product was purified by column chromatography over silica gel eluting with ethyl acetate/petroleum ether (1:10, v/v) to give 1.63 g of diethyl (6-bromohexanyl)-phosphonate as a colorless liquid. Yield: 66.0%. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 4.11 (m, 4H), 3.42 (t, 2H), 1.78 (m, 8H), 1.46–1.26 (unresolved coupling, combined integral, 8H). 4-[4-(6-Diethylphosphonohexanoxyl)-phenylazo]benzene-sulfonic acid was synthesized according to a literature procedure reported by Cernetic and Tamura [44,45]. 4-(4-Hydroxyphenylazo)benzenesulfonic acid (2.50 g, 9.00 mmol), potassium carbonate (3.72 mg, 26.95 mmol) and acetone (60 mL) were added to a 100 mL round-bottomed flask, and the resulting mixture was stirred for 1 h at room temperature. KI (0.15 g, 0.90 mmol) and diethyl (6-bromohexanyl)phosphonate (3.25

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g, 10.78 mmol) were then added to the flask, and the resultant mixture was heated at reflux with stirring for 48 h. The mixture was cooled to room temperature and filtered to remove the inorganic salts. The filtrate was evaporated to dryness under vacuum to give the crude product as a solid. The crude was purified by recrystallization from ethanol to give 3.30 g of pure 4-[4-(6-diethylphosphonohexanoxyl-phenylazo]-benzenesulfonic acid as an orange solid. Yield: 73.6%. ¹H NMR (300 MHz, DMSO-*d*₆) δ (ppm): 7.90 (d, 2H), 7.79 (d, 4H), 7.13 (d, 2H), 4.08 (t, 2H), 3.96 (m, 4H), 1.68-1.75 (m, 4H), 1.43–1.52 (m, 6H), 1.23 (s, 6H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ (ppm): 162.05, 152.21, 150.77, 146.61, 127.14, 125.10, 122.16, 115.56, 68.43, 61.25, 29.93, 28.81, 25.41, 24.47, 22.48, 16.75.

2.2.3. Synthesis of 4-[4-(6-phosphonic acid-hexanoxyl)phenylazo] benzenesulfonic acid (PAAZOSO₃H)

PAAZOSO₃H was synthesized using methods from the literature with some modifications [44,46,47]. Trimethylsilylbromide (2.12 mL, 16.05 mmol) was added in a dropwise manner to a solution of 4-[4-(6-diethylphosphonohexanoxyl) phenylazo]benzenesulfonic acid (2.0 g, 4.01 mmol) in anhydrous CH₂Cl₂ (20 mL), and the resulting mixture was stirred under N₂ for 6 h at room temperature. The CH₂Cl₂ and excess trimethylsilylbromide were subsequently removed under reduced pressure to give a residue, which was hydrolyzed with water (20 mL) under N₂ over a period of 2 h to give a brown precipitate. The precipitate was collected by filtration and dried under vacuum for 24 h at 50 °C to give 1.49 g of PAAZOSO₃H as a brown solid. Yield: 83.8 %. ¹H NMR (300 MHz, DMSO-*d*₆) δ (ppm): 7.90 (d, 2H), 7.79 (d,

4H), 7.13 (d, 2H), 4.08 (t, 2H), 1.77 (s, 2H), 1.46 (m, 6H), 1.31 (s, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ (ppm): 162.07, 152.22, 150.78, 146.62, 127.39, 125.10, 122.16, 115.56, 68.42, 35.51, 30.22, 28.88, 25.56, 23.17.

2.2.4. Synthesis of inorganic-organic hybrid zirconium phosphonate ZrOPPAZOSO₃H

The ZrOPPAZOSO₃H catalyst was prepared by the direct precipitation method [48-50]. Briefly, a mixture of PAAZOSO₃H (0.30 g, 0.68 mmol), NaH₂PO₄•2H₂O (0.22 g, 1.41 mmol), conc. HCl (36%, 2.0 mL) and DMSO (20.0 mL) was stirred at room temperature until all of the solids completely dissolved. The solution was then treated with 4.0 mL of an aqueous ZrOCl₂•8H₂O solution (0.67 g, 2.09 mmol) in a dropwise manner under stirring, and the resulting mixture was aged at 65 °C for 6 h. The mixture was then cooled to room temperature and filtered to give a solid, which was washed with H₂O until the washings became neutral (pH=7). The washed solid was then dried under vacuum at 50 °C for 24 h to afford 0.93 g of ZrOPPAZOSO₃H as a red-brown solid.

For comparison, also prepared organic 4-[4-6-zirconium we benzenesulfonic phosphate-hexanoxyl]phenylazo] acid (ZrOPAZOSO₃H) and inorganic zirconium phosphonate. ZrOPAZOSO₃H was prepared by the direct precipitation method according to literature procedures [48-50]. Briefly, a mixture of PAAZOSO₃H (0.50 g, 1.13 mmol), conc. HCl (36%, 2.0 mL) and DMSO (20 mL) was stirred at room temperature until all of the solids completely dissolved. The solution was then treated with 4.0 mL of an aqueous ZrOCl₂•8H₂O solution (0.40 g, 1.24 mmol) in a dropwise manner under stirring, and the resulting mixture was aged

at 65 °C for 6 h. The mixture was cooled to room temperature and filtered to give a solid, which was washed with H₂O until the washings became neutral (pH=7). The washed solid was then dried under vacuum at 50 °C for 24 h to afford 0.63 g of ZrOPAZOSO₃H as a brown solid. Inorganic zirconium phosphonate was prepared according to previous reports [48-50].

2.3. Spectroscopic characterization and photoisomerization studies

Spectroscopic characterization and photoisomerization experiments for PAAZOSO₃H, ZrOPPAZOSO₃H and ZrOPAZOSO₃H were conducted in DMSO using a 1.0 cm path length quartz cuvette at room temperature in all cases. Suspensions of ZrOPPAZOSO₃H and ZrOPAZOSO₃H were maintained with magnetic stirrers and irradiated at 365 nm, followed by 440 nm. The kinetic properties of the photoisomerization (trans→cis) reactions were analysed using kinetic Eq. (1), as follows [37]:

$$\ln \frac{A_0 - A_\infty}{A_t - A_\infty} = kt \tag{1}$$

where A_0 , A_t and A_{∞} are the absorbance wavelengths at 365 and 440 nm of the azobenzene chromophores at times 0, t and the photostationary state, respectively, and k is the rate constant of the photoisomerization process.

2.4. Mannich reaction

All of the Mannich reactions were performed in a 3.0 mL quartz cell (1.0 cm optical path length) equipped with a magnetic stirrer. Typically, ZrOPPAZOSO₃H (18.9 wt% with respect to benzaldehyde), benzaldehyde (53.0 mg, 0.5 mmol), aniline (46.5 mg, 0.5 mmol), cyclohexanone (53.9 mg, 0.55 mmol) and H₂O (3.0 mL) were charged 10

into the quartz cell, and the resulting mixture was irradiated at 365 nm under stirring for 5 h at room temperature. The progress of the reaction was monitored by thin layer chromatography. The desired product formed as a white precipitate over time and was extracted from the reaction mixture with ethyl acetate (3×5.0 mL). The combined organic extracts were evaporated to dryness under vacuum to give the Mannich reaction product as colorless crystals. The catalyst remained in the water phase. Typical procedure for the recycling and recovery of the catalyst

2.5. Recycling of the ZrOPPAZOSO₃H catalyst

The water phase containing the ZrOPPAZOSO₃H catalyst was readily recycled following the extraction of the product with ethyl acetate. Most notably, the water phase could be used directly in a subsequent run following the addition of fresh reactants.

2.6. Recovery of the ZrOPPAZOSO₃H catalyst

The catalyst was readily recovered by centrifugation following by filtration upon completion of the recycling runs.

3. Results and discussion

FT-IR spectra of PAAZOSO₃H, ZrOPPAZOSO₃H and ZrOPAZOSO₃H are shown in Fig. 1. The strong and broad absorption bands centered around 3440 cm⁻¹ in the spectra of PAAZOSO₃H, ZrOPPAZOSO₃H and ZrOPAZOSO₃H were attributed to O– H stretching vibrations. The absorption bands at 2936 and 2862 cm⁻¹ were attributed to the C–H stretching vibrations. The sharp absorption bands at 1601 and 1501 cm⁻¹

were assigned to C=C stretching vibrations. A sharp absorption band was observed at 1034 cm⁻¹ in the spectra of ZrOPPAZOSO₃H and ZrOPAZOSO₃H, which was attributed to the stretching vibrations of the P–O–Zr bonds. Notably, the intensity of this peak was much stronger in the ZrOPPAZOSO₃H spectrum than it was for ZrOPAZOSO₃H, thereby proving the structural formation of ZrOPPAZOSO₃H and ZrOPAZOSO₃H [51].

Fig. 2 shows the XRD patterns of zirconium phosphonate, ZrOPAZOSO₃H and ZrOPPAZOSO₃H. The characteristic diffraction peak of zirconium phosphonate at 2θ =8.0° was consistent with the formation of a layered structure with an interlayer distance of 1.1 nm. Weak diffraction peaks were observed for ZrOPAZOSO₃H and ZrOPPAZOSO₃H at 2θ =8.0°, which demonstrated that these materials had layered structures. The broad diffraction peaks around 2θ =21° were indicative of the amorphous nature of ZrOPAZOSO₃H and ZrOPPAZOSO₃H. ZrOPPAZOSO₃H gave a diffraction peak around 2θ =33°, which was consistent with the formation of some crystalline material [52].

Fig. 3 shows SEM images of ZrOPAZOSO₃H (Fig. 3A) and ZrOPPAZOSO₃H (Fig. 3B). A comparison of the SEM images of these two materials revealed that ZrOPPAZOSO₃H was composed of smaller and looser particles with a more flake-like morphology (Fig. 3B), with the length of each flake being about 200 nm.

Fig. 4 shows the UV-Vis spectra and spectral changes for DMSO solutions of PAAZOSO₃H, ZrOPAZOSO₃H and ZrOPPAZOSO₃H following alternate periods of irradiation at 365 and 440 nm. Fig. 4A shows the UV-Vis spectra and spectral changes

of a DMSO solution of the azobenzene monomer PAAZOSO₃H upon its irradiation at 365 nm. UV irradiation at 365 nm induced a *trans* \rightarrow *cis* photoisomerization reaction, resulting in a decrease in the absorbance at 358 nm. Subsequent irradiation at 440 nm reversed this process and returned the solution back to its original state (Fig. 4B), demonstrating that these photoinduced isomerization processes are completely reversible. ZrOPAZOSO₃H and ZrOPPAZOSO₃H showed similar reversible photoisomerization phenomenon (Fig. 4C-F), thereby illustrating that the azobenzene chromophores tethered zirconium phosphonate maintained to reversible photoisomerization properties. However, the rate constants (k) of ZrOPAZOSO₃H and ZrOPPAZOSO₃H were smaller than that of PAAZOSO₃H (Table 1). The rate constants decreased according to the order $k_{PAZOSO3H} > k_{ZrOPAZOSO3H} > k_{ZrOPAZOSO3H}$. This order was attributed to the growing rigidity of the environment, which would hinder the reorientation of the azobenzene chromophores.

Fig. 5(A and B) show the nitrogen adsorption–desorption isotherms of ZrOPAZOSO₃H and ZrOPPAZOSO₃H and their corresponding pore size distributions. The textural parameters of ZrOPAZOSO₃H and ZrOPPAZOSO₃H were calculated using the BJH method at 77 K. The adsorption isotherms of ZrOPAZOSO₃H and ZrOPPAZOSO₃H were both typical Type IV isotherms. The pore size distribution of ZrOPAZOSO₃H gave three narrow peaks at 1.18, 1.67 and 2.32 nm, as well as a broad peak between 3.72 and 4.80 nm, which had a maximum at 4.20 nm. The pore size distribution of ZrOPAZOSO₃H gave three narrow peaks at 1.09, 1.38 and 1.72 nm, as well as two broad peaks in the range of 2.42–2.88 and 3.81–5.54 nm, with

maximum values at 2.19 and 4.50 nm, respectively. These results demonstrated that the pores of ZrOPAZOSO₃H and ZrOPPAZOSO₃H were between micro and mesoporous. The surface areas and total pore volumes of ZrOPAZOSO₃H and ZrOPPAZOSO₃H were determined to be $10.02 \text{ m}^2 \text{ g}^{-1}$ and $0.0252 \text{ cm}^3 \text{ g}^{-1}$, and 47.74 m² g⁻¹ and 0.1429 cm³ g⁻¹, respectively. The pore size, surface area and total pore volume properties of ZrOPPAZOSO₃H were larger than those of ZrOPAZOSO₃H. These differences were attributed to the addition of inorganic NaH₂PO₄•2H₂O, which would have promoted the formation of some crystalline material.

The catalytic properties of ZrOPPAZOSO₃H were evaluated using the one-pot three-component Mannich reaction of benzaldehyde, aniline and cyclohexanone at room temperature as a model reaction (Scheme 3). The experimental conditions for this transformation, including the solvent, amount of catalyst, reaction time and molar ratio of reactants, were fully optimized (Table 2).

Excellent yields were obtained in MeOH (97.2%), EtOH (98.0%) and H_2O (94.5%) (Table 2, entries 1–5). Water was selected as the best solvent for further investigation because it is environment-friendly. Furthermore, preliminary results revealed that polar solvents were beneficial for this reaction.

Optimization experiments revealed that yield increased as the amount of catalyst increased (Table 2, entries 6–11), with an 18.9 wt% loading of the ZrOPPAZOSO₃H catalyst with respect to benzaldehyde giving the highest yield (94.5%). To illustrate the efficiency of the catalyst, we conducted the same reaction in the absence of ZrOPPAZOSO₃H (Table 2, entry 6). This reaction failed to afford any of the desired

material. These results indicated that the presence of ZrOPPAZOSO₃H was critical to the success of this reaction. The same reaction was also carried out using zirconium phosphate as a catalyst to rule out the possibility that the catalysis was caused by the zirconium phosphate support (Table 2, entry 12). This reaction gave a much lower yield (8.6%) of the Mannich product. Using organic ZrOPAZOSO₃H as the catalyst (Table 2, entry 13), we obtained a yield of 67.9%. These results therefore demonstrate that the inorganic-organic hybrid zirconium phosphate catalyst gave the best results in terms of the yield of the desired product.

The yield also increased as the reaction time increased and reached a maximum after 5 h (Table 2, entries 1, 14–18). The highest yield was obtained with a molar ratio of benzaldehyde:aniline:cyclohexanone=1.0:1.0:1.1 (Table 2, entries 1, 19–24).

Notably, the activity of the ZrOPPAZOSO₃H catalyst could be photocontrolled (Fig. 6). For example, yields of 60.6, 94.5, 50.7 and 36.6% were obtained under the same conditions for experiments conducted at ambient conditions (namely, under natural light), under irradiation at 365 and 440 nm, and in the dark, respectively. Similar trends were also observed when ZrOPAZOSO₃H, PAAZOSO₃H, and 4-hydroxyl-[4-(6-phosphonic acid-hexanoxyl)phenylazobenzene (PAAZOOH, ESI, Fig. S1) were used as the catalyst. The reason for this trend can be explained as follows. At ambient conditions, azobenzene chromophores exist in both *trans* and *cis* form, and moderate yield was obtained (ESI, Fig. S2). Irradiation at 365 nm would induce the *trans* \rightarrow *cis* isomerization of the substrate (Scheme 1), thereby bringing the sulfonic acid farther away from the zirconium phosphate and promoting the reaction.

Most of the azobenzene chromophores would exist in their *trans* form upon irradiation at 440 nm, moving the sulfonic acid closer to the zirconium phosphate, the interaction between sulfonic acid and hydroxyl groups of zirconium phosphate would probably result in a reduction in the rate of the reaction. The lowest yield was obtained in the dark because of the near-complete conversion of the *cis* form to the *trans* form [53]. Therefore, photocontrolled catalyzed Mannich reaction was realized. When zirconium phosphate and benzene sulfonic acid (BSA) without photosensitive azobenzene were used as the catalyst, slightly higher yield was obtained under UV or visible light irradiation compared to the case in the dark. This was probably caused by the slightly elevated temperature (about 8°C) upon photoirradiation. Compared with the Mannich reaction results using PAAZOSO₃H and BSA as the catalysts, lower yields were obtained when PAAZOOH was used as the catalyst. This illustrated that sulfonic acid plays important role in the catalysed Mannich reaction.

It is noteworthy that the catalyst could be readily recycled and recovered following the reaction. Upon completion of the catalyzed Mannich reaction, the solid product was easily separated from the reaction system by extraction with ethyl acetate. The remaining aqueous solution could be used directly in the next reaction run by simply adding the required reactants. The recovery of the catalyst was also easy. After completion of the reaction and the subsequent isolation of the product, the catalyst in the aqueous phase was simply obtained by centrifugation for future use (ESI, Fig. S3). It's clearly that the supported ZrOPPAZOSO₃H and ZrOPAZOSO₃H can be easily aqueous non-supported recovered from solvent. However, the materials

(PAAZOSO₃H, PAAZOOH, and BSA) cannot be recovered from the aqueous solvent by simple centrifugation. As shown in Fig. 7, the catalyst continued to afford an excellent yield (91.8%) after six runs, which represents a better performance than several previously reported catalysts [26,35,54].

The scope of this newly developed ZrOPPAZOSO₃H-catalyzed Mannich reaction was evaluated using a wide range of substituted benzaldehydes and aniline under the optimized conditions. As shown in Table 3, the reaction proceeded smoothly with aromatic aldehydes bearing an electron-donating group (e.g., OCH₃ or CH₃) at their 4-position. Anilines bearing an electron-withdrawing group (e.g., CN, NO₂ or Cl) at their 4-position also reacted smoothly. Moderate yields (56-78%) were obtained, which were lower than the results using non-substituted reactants. The possible reason for this could be ascribed to their bad solubility in water. Significant increase in yield was obtained if a small fraction of ethanol was added into this reaction system.

4. Conclusions

In this study, we have described our initial efforts towards the development of a novel environmentally friendly, photo-controllable and recyclable catalyst for the three-component Mannich reaction of benzaldehyde, aniline and cyclohexanone in water. The catalyst developed in this study is based on the combination of sulfonic acid with an azobenzene chromophore and zirconium phosphonate. This new catalyst photo-controllably catalyzed the one-pot, three-component Mannich reaction of aldehydes, amines and ketones in water.

Furthermore, this catalyst can be readily recycled and reused. The environmentally friendly, photocontrollable and recyclable properties of this catalyst could make it possible to use this system in other acid-catalyzed organic reactions.

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Figure Captions



Fig. 1. FT-IR spectra of PAAZOSO₃H, ZrOPPAZOSO₃H, and ZrOPAZOSO₃H.

Fig. 2. High-angle XRD patterns of zirconium phosphonate, ZrOPAZOSO₃H and ZrOPPAZOSO₃H.





Fig. 3. SEM images of $ZrOPAZOSO_{3}H(A)$ and $ZrOPPAZOSO_{3}H(B)$.

Fig. 4. UV-Vis spectra and spectral changes for a solution of PAAZOSO₃H in DMSO $(1.0 \times 10^{-5} \text{ mol } \text{L}^{-1})$ upon irradiation at 365 nm (A) and 440 nm (B). UV-Vis spectra and spectral changes for a solution of ZrOPAZOSO₃H in DMSO (0.2 mg mL⁻¹) upon irradiation at 365 nm (C) and 440 nm (D). UV-Vis spectra and spectral changes for a solution of ZrOPPAZOSO₃H in DMSO (0.2 mg mL⁻¹) upon irradiation at 365 nm (E) and 440 nm (F).













Fig. 5. Nitrogen adsorption-desorption isotherms of $ZrOPAZOSO_3H$ (A) and $ZrOPPAZOSO_3H$ (B) at 77 K. Insets: the corresponding pore size distributions calculated using the BJH method.





Fig. 6. Photocontrolled catalytic activities of ZrOPPAZOSO₃H, ZrOPAZOSO₃H, zirconium phosphate, PAAZOSO₃H, benzene sulfonic acid, and PAAZOOH towards the Mannich reaction. Reaction conditions: catalyst (10 mg), benzaldehyde (53.0 mg, 0.50 mmol), aniline (46.5 mg, 0.50 mmol), cyclohexanone (53.9 mg, 0.55 mmol) and H_2O (3.0 mL).



Fig. 7. Recyclability of the ZrOPPAZOSO₃H catalyst for the Mannich reaction of benzaldehyde, aniline and cyclohexanone in water at 25 °C for 5 h under irradiation at 365 nm.



Scheme Captions



Scheme 1 Chemical structure of ZrOPPAZOSO₃H and its photoisomerization.

Scheme 2 Synthetic route for ZrOPPAZOSO₃H.



Scheme 3 ZrOPPAZOSO₃H-catalyzed one-pot three-component Mannich reaction.



Compounds	Rate constants (s ⁻¹)		
Compounds	<i>trans→cis</i>	<i>cis→trans</i>	
PAAZOSO ₃ H	$(1.89\pm0.04)\times10^{-2}$	$(3.18\pm0.04)\times10^{-2}$	
ZrOPAZOSO ₃ H	$(2.60\pm0.06)\times10^{-3}$	$(19.69\pm0.40)\times10^{-3}$	
ZrOPPAZOSO ₃ H	$(1.45\pm0.04)\times10^{-3}$	$(20.66 \pm 1.26) \times 10^{-3}$	

Table 1 Rate constants for the $trans \rightarrow cis$ and $cis \rightarrow trans$ isomerization

processes of PAAZOSO ₃ H, ZrOPAZOSO ₃ H and ZrOPPAZOSO ₃ H.
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Table 2 Effects of the solvent, amount of catalyst, reaction time and molar ratio of the reactants on the ZrOPPAZOSO₃H-catalyzed one-pot three-component

Entry	1:2:3	Solvent	Catalyst amount	Reaction time	Yield ^b
	(molar ratio)		(wt%)	(h)	(%)
1	1.0:1.0/1.1 ^a	H ₂ O	18.9	5	94.5
2	$1.0:1.0/1.1^{a}$	MeOH	18.9	5	97.2
3	$1.0:1.0/1.1^{a}$	EtOH	18.9	5	98.3
4	$1.0:1.0/1.1^{a}$	THF	18.9	5	85.1
5	$1.0:1.0/1.1^{a}$	CH_2Cl_2	18.9	5	84.7
6	$1.0:1.0/1.1^{a}$	H_2O	0	5	0
7	$1.0:1.0/1.1^{a}$	H_2O	13.2	5	60.3
8	$1.0:1.0/1.1^{a}$	H_2O	15.1	5	62.7
9	$1.0:1.0/1.1^{a}$	H_2O	17.0	5	82.1
10	$1.0:1.0/1.1^{a}$	H_2O	20.8	5	92.2
11	$1.0:1.0/1.1^{a}$	H_2O	22.6	5	93.8
12	$1.0:1.0/1.1^{a}$	H_2O	10 mg ^c	5	8.6
13	$1.0:1.0/1.1^{a}$	H_2O	10 mg ^d	5	67.9
14	$1.0:1.0/1.1^{a}$	H_2O	18.9	2	34.3
15	$1.0:1.0/1.1^{a}$	H_2O	18.9	3	52.5
16	$1.0:1.0/1.1^{a}$	H_2O	18.9	4	83.2
17	$1.0:1.0/1.1^{a}$	H_2O	18.9	6	94.2
18	$1.0:1.0/1.1^{a}$	H_2O	18.9	7	94.9
19	1.0:1.0:1.0	H_2O	18.9	5	90.3
20	1.0:1.0:1.05	H_2O	18.9	5	93.2
21	1.0:1.0:1.2	H_2O	18.9	5	93.9
22	1.0:1.05:1.0	H_2O	18.9	5	90.8
23	1.0:1.1:1.0	H_2O	18.9	5	89.3
24	1.0:1.1:1.1	H_2O	18.9	5	94.2

Mannich reaction.

^a Reaction conditions: benzaldehyde (53.0 mg, 0.50 mmol), aniline (46.5 mg, 0.50 mmol),

cyclohexanone (53.9 mg, 0.55 mmol) and solvent (3.0 mL) with irradiation at 365 nm.

^b Isolated yields.

^c Zirconium phosphate as the catalyst.

^d ZrOPAZOSO₃H as the catalyst.

Table 3 Three-component Mannich reactions of different benzaldehydes and

R ₁ -	-CHO + R ₂ -	Ŋ_NH₂ +	ZrOPPAZOSO ₃ H ,H₂O 25 ºC, 365 nm	R ₂ NH O R ₁ 5
Entry	R ₁	R ₂	Products	Yields (%) ^b
1	$4-NO_2$	4-H	5a	78.0
2	4-CN	4-H	5b	63.0
3	4-OCH ₃	4-H	5c	61.0
4	4-H	4-Cl	5d	56.0
5	4-H	4-CH ₃	5e	63.0

anilines with cyclohexanone.^a

^a Reaction conditions: Benzaldehyde (0.50 mmol), aniline (0.50 mmol), cyclohexanone

(0.55 mmol), $ZrOPPAZOSO_3H$ (10.0 mg) and H_2O (3.0 ml).

^b Isolated yield.