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#### Short communication

# POSS supported diarylprolinol silyl ether as an efficient and recyclable organocatalyst for asymmetric Michael addition reactions



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#### 1. Introduction

During the past decades, organocatalysis has received growing attention in asymmetric organic transformations [1–4]. A variety of organocatalysts have been explored and applied in a wide range of organic processes, providing efficient access to valuable chiral compounds and intermediates. Among them, the Jørgensen–Hayashi's diarylprolinol silyl ether catalyst [5–7] has emerged as one of the most important organocatalysts for its high efficiency, selectivity, and robustness in asymmetric reactions. Its practical applications, however, suffered from some limitations such as high catalyst loading and difficulties in separating the catalyst from the product. Consequently, immobilization of Jørgensen–Hayashi catalyst onto the supports including polymers [8–13], ionic liquids [14–18], magnetic nanoparticles [19–22], porous materials [23], dendrimers [24] and fluorous tags [25], has been developed to conquer the above-mentioned defects and allow the recycling of the catalyst.

Polyhedral oligomeric silsesquioxanes (POSSs) are a new class of organic–inorganic hybrid materials. A typical POSS molecule is composed of a silicon–oxygen core framework and covered externally by various organic groups, one or more of which is reactive. Owing to the thermally robust cage structure, nanoscale dimensions and multi-functionality, POSSs are considered to be ideal building blocks in many areas of materials chemistry [26,27], and there are also examples of the applications of metal-containing POSS compounds in catalytic reactions [28–30]. In

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#### ABSTRACT

The POSS supported (*S*)- $\alpha$ , $\alpha$ -diphenylprolinol trimethylsilyl ether catalyst was synthesized and applied in the asymmetric Michael addition reactions of aldehydes and arylnitroalkenes, providing the products in good yields with excellent enantioselectivities and good diastereoselectivities. The POSS supported catalyst can be readily recycled and reused for further transformations at least eight cycles without observing significant decrease in yield and stereoselectivity.

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addition, POSS has different solubilities in various solvents, making it possible to utilize POSS as a soluble support. However, chiral-functionalized unit immobilized on silsesquioxanes for asymmetric organocatalysis is still absent in the literature.

In recent years, we have successfully prepared tetraarylphosphonium supported imidazolidinone catalysts and effectively applied them in asymmetric Diels–Alder reaction [31] and 1,3-dipolar cycloaddition [32]. As a continuation of efforts to explore efficient and recyclable organocatalyst, a POSS supported (*S*)- $\alpha$ , $\alpha$ -diphenylprolinol trimethylsilyl ether catalyst (Fig. 1) was designed and synthesized. Next, we employed it in asymmetric Michael addition wishing to run the catalyzed reaction under homogeneous conditions and recover the catalyst **3** by the precipitation method.

#### 2. Experimental

#### 2.1. General

Reactions were monitored by TLC using precoated plates of silica gel HF254 (0.5 mm, Yantai, China). Column chromatography was performed with a silica gel column (200–300 mesh, Yantai, China). NMR spectra were recorded on WIPM 400 spectrometer (<sup>1</sup>H at 400 MHz, <sup>13</sup>C at 100 MHz and <sup>29</sup>Si NMR at 79.5 MHz). IR spectra were recorded on an IR-spectrum one (PE) spectrometer. HPLC were performed with Dionex UltiMate 3000 and equipped with a chiral column (chiralpak AD-H or chiralcel OD-H) using *i*-PrOH/*n*-hexane as an eluent. A UV detector (UVD-3000) was used for the peak detection.

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Fig. 1. Structure of POSS supported (S)- $\alpha$ , $\alpha$ -diphenylprolinol trimethylsilyl ether catalyst.

# 2.2. Synthesis of POSS supported (S)- $\alpha$ , $\alpha$ -diphenylprolinol trimethylsilyl ether catalyst

3-azidopropylheptaphenyl POSS 1 (3.0 g, 2.9 mmol), 2 (1.6 g, 4.3 mmol) and dry tetrahydrofuran (40 mL) were charged to a 100 mL three-neck round-bottomed flask equipped with a magnetic stirrer. The system was degassed and purged with nitrogen, then CuBr (41.5 mg, 0.29 mmol) and N,N,N',N',N''-pentamethyldiethylenetriamine (PMDETA) (60.3 µL, 0.29 mmol) were added. The reaction mixture was stirred at room temperature for 30 h and dropped into dilute hydrochloric acid (1 wt.%, 30 mL). The resultant mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>  $(20 \text{ mL} \times 3)$  and dried over Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvent, the residue was washed with methyl tert-butyl ether (MTBE) (50 mL) and dried in vacuo at 50 °C for 24 h to give the desired product as a white solid which was pure enough to be used for the catalytic reactions (3.62 g, 88%). IR: 3358, 3198, 2933, 1659, 1594, 1459, 1134, 1106, 1028 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>):  $\delta$  – 0.09 (s, 9H), 0.85 (t, J = 8.0 Hz, 2H), 1.85–1.90 (m, 2H), 1.98 (br, 1H), 2.02–2.15 (m, 2H), 2.76 (dd, *J* = 12.0, 4.0 Hz, 1H), 3.21 (dd, *J* = 16.0, 4.0 Hz, 1H), 3.95 (dd, I = 16.0, 8 Hz, 1H), 4.27 (t, I = 8.0 Hz, 2H), 4.48 (dd, I = 12.0, 4.0 Hz, 1H), 4.53 (s, 2H), 7.31–7.46 (m, 31H), 7.61 (s, 1H), 7.74–7.76 (m, 14H);  $^{13}\text{C}$  NMR (100 MHz, DMSO-d\_6):  $\delta$  143.0, 139.0, 133.6, 131.4, 129.1, 129.0, 128.3, 128.1, 127.9, 127.5, 81.3, 76.3, 60.9, 50.5, 33.0, 28.3, 23.1, 13.4, 7.5, 2.3;  $^{29}\text{Si}$  NMR (79.5 MHz, DMSO-d\_6):  $\delta$  - 56.43, - 69.63, -69.95; HRMS (ESI) calcd for [C<sub>68</sub>H<sub>70</sub>N<sub>4</sub>O<sub>14</sub>Si<sub>9</sub>]<sup>+</sup>: 1419.2885, found 1419.2960.

#### 2.3. General procedure for the asymmetric Michael addition reactions

To a solution of aldehyde (0.3 mmol) in  $CH_2Cl_2$  (1 mL) was added aryInitroalkene (0.2 mmol) and POSS supported organocatalyst (57 mg, 0.04 mmol). The homogeneous reaction mixture was stirred at 10 °C until complete conversion of the starting materials (monitored by TLC). MTBE (10 mL) was added to the mixture and a precipitate formed. After filtration, the solid was separated and washed with MTBE to afford the recycled catalyst with quantitative yield. The filtrate was concentrated and purified by column chromatography on silica gel to give the Michael adduct as an oil. The syn/anti ratio was determined by <sup>1</sup>H NMR spectroscopy of the crude mixture and the enantiomeric excess (ee) of the adduct was determined by HPLC on a chiral phase.

#### 3. Results and discussion

#### 3.1. Preparation of POSS supported catalyst

The synthetic route of POSS supported catalyst **3** was depicted in Scheme 1. The intermediate 3-azidopropylheptaphenyl POSS **1** [33] and pyrrolidine moiety **2** [13] were prepared according to the established procedure, respectively. Then a CuAAC reaction between **1** and **2** was performed to give **3** in good yield, which is soluble in typical organic solvents, such as toluene, CHCl<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, CH<sub>3</sub>CN, EtOAc, THF, and insoluble in Et<sub>2</sub>O, MTBE or H<sub>2</sub>O. This solubility allowed a simple recovery of POSS support catalyst **3** when precipitated with a poor solvent.



Scheme 1. Synthesis of the POSS supported (S)- $\alpha$ , $\alpha$ -diphenylprolinol trimethylsilyl ether catalyst.

#### 3.2. Optimizing of the asymmetric Michael addition conditions

To evaluate the catalytic capacity of our POSS supported catalyst, the Michael addition of aldehydes with arylnitroalkenes, which is a powerful tool for carbon–carbon bond formation and affords synthetically useful  $\gamma$ -nitro carbonyl compounds, was carried out. The reaction between propionaldehyde and nitrostyrene was selected as the model reaction for optimizing the reaction conditions with **3** as the catalyst (Table 1).

Initially, a screening of the solvents at 25 °C for 24 h with 10 mol% of **3** was investigated (Table 1, entries 1–5), the results showed that dichloromethane was the choice of solvent to give the highest yield and ee value (Table 1, entry 1). The reaction proceeded with the best diastereoselectivity when performed in trichloromethane, however,

Table 1

Optimization of Michael addition reaction conditions between propional dehyde and nitrostyrene. $^{\rm a}$ 

H <sup>O</sup>	+	NO <sub>2</sub> _ca	atalyst 3	н Ц	) NO2		
Entry	Loading (mol%)	Solvent	Temp. (°C)	Time (h)	Yield <sup>b</sup> (%)	dr <sup>c</sup> (syn/anti)	ee <sup>d</sup>
1	10	$CH_2Cl_2$	25	24	69	82:18	96
2	10	CHCl <sub>3</sub>	25	24	26	97:3	68
3	10	THF	25	24	67	68:32	83
4	10	CCl <sub>4</sub>	25	24	30	76:24	70
5	10	Toluene	25	24	Trace	n.d.	n.d.
6	5	$CH_2Cl_2$	25	24	Trace	n.d.	n.d.
7	15	$CH_2Cl_2$	25	24	75	78:22	92
8	20	$CH_2Cl_2$	25	24	78	86:14	97
9	30	$CH_2Cl_2$	25	24	77	84:16	96
10	20	$CH_2Cl_2$	0	24	58	89:11	98
11	20	$CH_2Cl_2$	10	24	65	90:10	99
12	20	CH <sub>2</sub> Cl <sub>2</sub>	10	48	80	92:8	99
13	20	$CH_2Cl_2$	10	72	82	92:8	99
14	20	$CH_2Cl_2$	10	96	82	91:9	99

<sup>a</sup> Reaction conditions: nitrostyrene (0.2 mmol), propionaldehyde (0.3 mmol), **3** (0.001–0.06 mmol), solvent (1 mL).

<sup>b</sup> Yield of isolated product.

<sup>c</sup> Determined by <sup>1</sup>H NMR spectroscopy.

<sup>d</sup> Determined by HPLC analysis on a chiral phase (chiralcel OD-H).

#### Table 2

Scope of catalyst **3** in the Michael addition reaction.<sup>a</sup>

$H \xrightarrow{O} R + Ar \xrightarrow{NO_2} NO_2 \xrightarrow{3(20 \text{ mol}\%)} H \xrightarrow{O} H \xrightarrow{Ar} NO_2$							
Entry	Product	Yield <sup>b</sup>	dr <sup>c</sup>	ee <sup>d</sup>			
1		80	92:8	99			
2		86	89:11	>99			
3		81	92:8	98			
4 <sup>e</sup>		<10	n.d.	n.d.			
5°		85	97:3	99			
6		80	98:2	>99			
7		88	84:16	97			
8		80	82:18	96			
9		88	83:17	98			
10 <sup>f</sup>		90	84:16	96			
11		85	83:17	>99			
12		86	86:14	>99			
13		88	89:11	>99			

<sup>a</sup> Reaction conditions: nitroalkene (0.2 mmol), aldehyde (0.3 mmol), 3 (0.04 mmol), CH<sub>2</sub>Cl<sub>2</sub> (1 mL), 10 °C, 48 h.
 <sup>b</sup> Yield of isolated product.
 <sup>c</sup> Determined by <sup>1</sup>H NMR spectroscopy.
 <sup>d</sup> Determined by HPLC analysis on a chiral phase (chiralpak AD-H or chiralcel OD-H).
 <sup>e</sup> 96 h reaction time was used.
 <sup>f</sup> 24 h reaction time was used.

<sup>f</sup> 24 h reaction time was usEd.)

### Table 3 Recycling of catalyst 3 in the Michael addition reaction.<sup>a</sup>

$H \xrightarrow{O} + VO_2 \xrightarrow{3 (20 \text{ mol}\%)} H \xrightarrow{O} + VO_2 \xrightarrow{3 (20 \text{ mol}\%)} H \xrightarrow{O} + VO_2$						
Cycle	Yield <sup>b</sup>	dr <sup>c</sup>	ee <sup>d</sup> (%)			
1	78	92:8	99			
2	75	90:10	97			
3	78	88:12	98			
4	71	86:14	96			
5	72	87:13	98			
6	72	87:13	96			
7	71	88:12	97			
8	70	87:13	97			

 $^a\,$  Reaction conditions: nitrostyrene (0.2 mmol), propionaldehyde (0.3 mmol), 3 (0.04 mmol), CH\_2Cl\_2 (1 mL), 10  $^\circ$ C, 48 h.

<sup>b</sup> Yield of isolated product.

<sup>c</sup> Determined by <sup>1</sup>H NMR spectroscopy.

<sup>d</sup> Determined by HPLC analysis on a chiral phase (chiralcel OD-H).)

the ee was only 68% (Table 1, entry 2). In toluene, only trace amount of product was observed (Table 1, entry 5). Next, the influence of catalyst amount on the Michael addition was examined, which reveals that the most suitable amount of catalyst used was 20 mol%, as higher or lower catalyst loadings seemed to be detrimental either for yield or stereoselectivity (Table 1, entries 1, 6-9). The effect of temperature, a universally crucial factor, was also tested (Table 1, entries 8, 10, 11). It is found that 10 °C is the optimal temperature for the reaction, which resulted in 65% yield, 90:10 dr and 99% ee. In order to further improve the efficiency of the catalytic reaction, we prolonged the reaction time from 24 to 48, 72 and 96 h, respectively (Table 1, entries 11–14). The best result (80% yield, 92:8 dr, 99% ee) was obtained when 48 h was employed and more longer time did not give more better result. This result, to our delight, is comparable to that obtained when using non-supported diarylprolinol silyl ether as a reaction catalyst [7]. Thus, the conditions for entry 12 were taken as optimized conditions for the Michael addition of propionaldehyde to nitrostyrene.

## 3.3. Catalytic activity of catalyst **3** in the asymmetric Michael addition reactions

The substrate scope of the asymmetric Michael reaction was investigated with a variety of aldehydes and arylnitroalkenes catalyzed by POSS supported Jørgensen-Hayashi catalyst 3 in dichloromethane (Table 2). In general, all aldehydes efficiently undergo Michael addition reactions with different arylnitroalkenes, giving the corresponding products in excellent yields (80-90%) and enantioselectivities (>96% ee), together with good diastereoselectivities (82:18 to 98:2 dr). When less hindered aldehydes and the nitroalkene without substituent on the benzene ring was employed (Table 2, entries 1-3), the diastereoselectivity was a little higher than that with either an electron-withdrawing or -donating group on the benzene ring (Table 2, entries 7-10) or with a naphthyl substituent (Table 2, entry 11), while the yield and enantioselectivity remained at the same level. A NO2 group on the benzene is likely to facilitate the reaction, providing the corresponding product in 90% yield within a 24 h reaction time (Table 2, entry 10). Iso-valeraldehyde, a branched aldehyde, was also investigated and gave a very low conversion even prolonged the reaction time to 96 h (Table 2, entry 4). When changing the benzene ring to NO<sub>2</sub> substituted benzene (Table 2, entry 5) or naphthyl substituent (Table 2, entry 6), however, the products were obtained in good yield with the highest dr values owing to the steric effect. Nitroalkene with heterocyclic substituent, such as the 2-furyl or 2-thienyl group, can also be used as substrate in this process, providing the product in excellent yield and stereoselectivity (Table 2, entries 12, 13).

#### 3.4. Recycling and reuse of catalyst 3

With the success of the above reactions, we continued our study by exploring the recyclability of the catalyst. After the reaction, the POSS supported catalyst can be easily separated and collected quantitatively from substrates and products through precipitation by adding MTBE to the reaction mixture. As shown in Table 3, no significant decrease in catalytic activity was observed when POSS-supported catalyst **3** was recovered and reused in further reactions. Good diastereoselectivities of 87:13 dr and 97% ee of the product were obtained even in the 8th cycle (Table 3, cycle 8).

#### 4. Conclusions

In conclusion, we have synthesized a POSS supported  $(S)-\alpha,\alpha$ diphenylprolinol trimethylsilyl ether catalyst and employed it in the asymmetric Michael addition reactions of aldehydes and arylnitroalkenes, providing the products in good yields with excellent enantioselectivities and good diastereoselectivities. Most importantly, the POSS supported Jørgensen–Hayashi catalyst can be readily recovered and reused for further transformations at least eight cycles without observing significant decrease in yield and stereoselectivity.

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