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## Facile construction of functionalized periodic mesoporous organosilica for Ir-catalyzed enantioselective reduction of $\alpha$ -cyanoacetophenones and $\alpha$ -nitroacetophenones†

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**A facile method to construct chiral organoiridium-functionalized periodic mesoporous organosilica is developed. The heterogeneous catalyst displays excellent catalytic efficiency in the enantioselective reduction of  $\alpha$ -cyanoacetophenones and  $\alpha$ -nitroacetophenones in aqueous medium because of the hydrophobic nature and uniformly distributed active iridium species. The catalyst could be conveniently recovered and reused eight times without loss of its catalytic activity.**

Great achievements have been made in immobilization of chiral organometallic complexes using periodic mesoporous organosilicas (PMOs) as supports for constructing heterogeneous chiral catalysts.<sup>1</sup> Such achievements are due to the similarity of physical properties of PMOs to those of inorganosilica mesoporous materials, such as large specific surface area and pore volume, tunable pore dimension, well-defined pore arrangement, as well as high thermal and mechanical stabilities.<sup>2</sup> Furthermore, the potential hydrophobicity of PMOs due to the intrinsic organosilicate inner surface significantly promotes organic transformation in biphasic reaction media.<sup>3</sup> In general, immobilization of chiral organometallic complexes within the PMO network can be achieved either by a post-grafting strategy or by a co-condensation strategy,<sup>1a,b</sup> which have led to many highly efficient heterogeneous chiral catalysts in various asymmetric reactions. From the synthetic methods, assembly of a PMO-based heterogeneous chiral catalyst often requires chiral ligand-derived siloxanes, regardless of the strategy employed.<sup>4</sup> However, preparation of a pure chiral siloxane derived from a chiral ligand is very difficult because of the tedium of its purification by silica gel column chromatography. Thus, exploration of an alternative means to directly anchor a chiral ligand for constructing heterogeneous chiral catalysts is highly desirable.

In our effort to assemble heterogeneous catalysts through various chiral siloxanes,<sup>5</sup> we utilize a post-coordination method in the present contribution. That is, a chiral ligand was directly

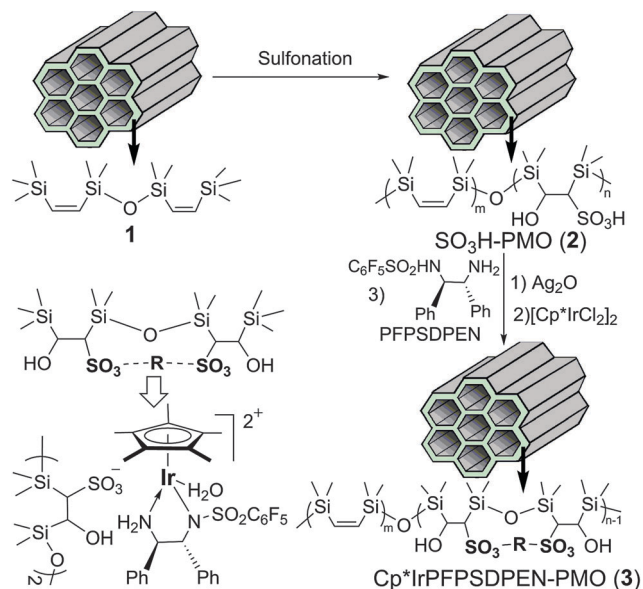
anchored onto a metal-functionalized PMO. No chiral ligand-derived siloxane is necessary in this process. Taking advantage of the post-coordination method and the hydrophobic feature of the PMO network, we conveniently construct a hydrophobic, chiral organoiridium-functionalized heterogeneous catalyst through the direct post-coordination of commercial (*R,R*)-pentafluorophenyl-sulfonyl-1,2-diphenylethylenediamine (PFPSDPEN) onto an organoiridium-functionalized PMO. As expected, the high hydrophobicity and uniformly distributed active iridium species greatly promote the enantioselective reduction of  $\alpha$ -cyanoacetophenones and  $\alpha$ -nitroacetophenones in aqueous medium. In addition, the heterogeneous catalyst could be recovered and reused at least eight times without loss of its catalytic activity.

Ethylenylene-bridged PMO functionalized with chiral Cp\*IrPFPSDPEN, abbreviated as Cp\*IrPFPSDPEN-PMO (**3**), (Cp\*IrPFPSDPEN: Cp\* = pentamethyl cyclopentadiene, PFPSDPEN = (*R,R*)-pentafluorophenylsulfonyl-1,2-diphenylethylenediamine), was prepared as outlined in Scheme 1. First, ethylenylene-bridged PMO (**1**) was obtained through the co-condensation of 1,2-bis(triethoxysilyl)-ethylene according to a reported method.<sup>5b</sup> Epoxidation of double bonds (–C=C–) followed by conversion of the resulting epoxide with bisulfite ions then afforded **2** in the form of a white powder.<sup>7</sup> Finally, continuous ion exchanges with Ag<sub>2</sub>O<sup>8</sup> and then with (Cp\*IrCl<sub>2</sub>)<sub>2</sub> (ref. 9) followed by direct complexation of PFPSDPEN led to the crude heterogeneous catalyst **3**. This was subjected to Soxhlet extraction to clear its nanochannels and to obtain its pure form as a light-gray powder (see ESI† in the experimental and in Fig. S1–S5).

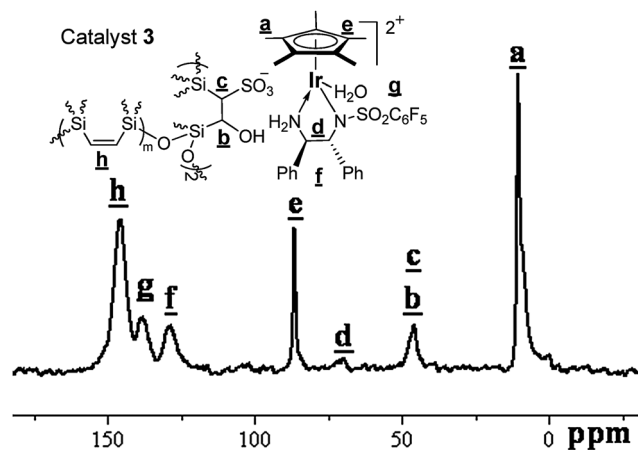
Incorporation of well-defined, single-site, active iridium centers within the PMO network could be proven by solid-state <sup>13</sup>C cross-polarization (CP)/magic angle spinning (MAS) NMR spectroscopy. As shown in Fig. 1, catalyst **3** produced strong, characteristic carbon signals of SiCH=CHSi groups at ~145 ppm, corresponding to the main ethylenylene-bridged organosilica embedded within the PMO network. Additional weak carbon signals observed between ~43 and ~51 ppm are attributed to the SiCHOH and SiCHSO<sub>3</sub>H groups, indicating that sulfonation occurred.<sup>7</sup> Both observations reveal that only a fraction of –C=C– double bonds underwent sulfonation during synthesis (corresponding to weak carbon signals), while those

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Scheme 1 Preparation of catalyst **3**.

embedded within the pore walls were inaccessible for sulfonation (corresponding to strong carbon signals). Signals for carbon atoms of NCHPh groups (between  $\sim 69$  and  $\sim 73$  ppm) and for carbon atoms of the aromatic ring (at  $\sim 129$  and  $\sim 138$  ppm) of the chiral PFPSDPEN moiety could be observed clearly (marked in the spectra). Peaks at  $\sim 87$  and  $\sim 11$  ppm are ascribed to the carbon atoms of the Cp ring and to the carbon atoms of the  $\text{CH}_3$  groups attached to the Cp ring, respectively. These peaks are absent in the spectrum of **2**,<sup>7</sup> suggesting the formation of the  $\text{Cp}^*\text{IrPFPSDPEN}$  complex. Chemical shifts of **3** are similar to those of its homogeneous counterpart,  $\text{Cp}^*\text{IrPFPSDPEN}$ ,<sup>6a</sup> demonstrating that **3** had the same well-defined single-site active species of  $\text{Cp}^*\text{IrPFPSDPEN}$ . Its solid-state  $^{29}\text{Si}$  MAS NMR spectrum further demonstrates its organosilicate network and the composition of active  $\text{Cp}^*\text{IrPFPSDPEN}$  (see ESI† in Fig. S2). Here, two strong T signals, corresponding to  $\text{T}^2(\text{R-Si}(\text{OSi})_2(\text{OH}))$  and  $\text{T}^3(\text{R-Si}(\text{OSi})_3)$  ( $\text{R} = \text{Cp}^*\text{IrPFPSDPEN}$ -functionalized alkyl-linked groups or ethylene-bridged groups), reveal that  $\text{R-Si}(\text{OSi})_2(\text{OH})$  and  $\text{R-Si}(\text{OSi})_3$  comprise the main organosilicate network.<sup>10</sup> Similar to those of the

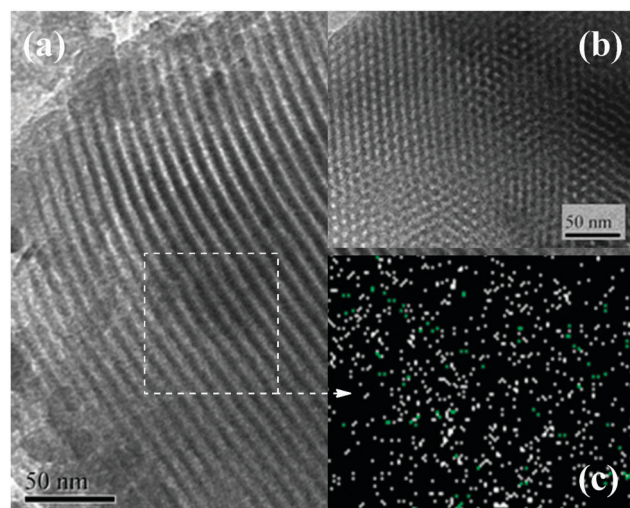
Fig. 1  $^{13}\text{C}$  CP/MAS NMR spectrum of catalyst **3**.

parent counterpart, weak  $\text{T}^1(\text{R}(\text{HO})_2\text{SiOSi})$ ,  $\text{Q}^3((\text{HO})\text{Si}(\text{OSi})_3)$ , and  $\text{Q}^4(\text{Si}(\text{OSi})_4)$  signals could be observed in this case.<sup>7</sup>

In addition, catalyst **3** produced a IV-type nitrogen adsorption-desorption isotherm with a  $\text{H}_2$  hysteresis loop (see ESI† in Fig. S3) while its small-angle X-ray diffraction (XRD) pattern (see ESI† in Fig. S4) exhibited a well-resolved peak at  $2\theta = 0.8^\circ$ – $1.0^\circ$ , indicating its ordered dimensional-hexagonal ( $P6mm$ ) mesoporous channels.<sup>5b,7</sup> Transmission electron microscopy (TEM) images further confirmed the ordered dimensional-hexagonal pore arrangements (Fig. 2a and b). It is worth mentioning that the TEM image with a chemical mapping revealed that the iridium active centers were uniformly distributed within the PMO network (Fig. 2c), demonstrating the formation of site-isolated active species proved by its  $^{13}\text{C}$  CP/MAS NMR spectrum.

Table 1 summarizes the general applicability of catalyst **3** in the enantioselective reduction of  $\alpha$ -cyanoacetophenones and  $\alpha$ -nitroacetophenones in aqueous medium, in which the asymmetric reaction with the hydrogen source  $\text{HCO}_2\text{H}$  and 0.25 mol% PMO as a catalyst was carried out according to a reported method.<sup>6a</sup> In general, high conversions, no side products, and high enantioselectivities were obtained for all tested substrates. Taking enantioselective reduction of benzoylacetoneitrile as a example, it was found that catalyst **3** produced (*R*)-3-hydroxy-3-phenylpropanenitrile with  $>99\%$  conversion and 96% ee value. Such an ee value is slightly higher than that of  $\text{Cp}^*\text{IrPFPSDPEN}$  (entry 1 vs. entry 1 in brackets, Table 1), even higher than that obtained with the mixed  $\text{SO}_3\text{H-PMO}$  (**2**) and its homogeneous  $\text{Cp}^*\text{IrPFPSDPEN}$  as a catalyst (entry 2), indicating that the coordination environment of catalyst **3** remained in its original homogeneous situation that could be confirmed by X-ray photoelectron spectroscopy (XPS) investigation (see ESI† in Fig. S5). In addition, the asymmetric reaction could be run at much higher substrate-to-catalyst mole ratios without apparently affecting its ee value, as exemplified by the enantioselective reduction of benzoylacetoneitrile at a substrate-to-catalyst mole ratio of 600 (entry 3, Table 1).

It is noteworthy that the electronic properties of substituents at the Ar moiety of acetophenones did not affect enantioselectivities,

Fig. 2 TEM images of catalyst **3** viewed along the [100] (a) and [001] (b) directions. (c) TEM image with a chemical mapping of **3**, showing the distribution of Si (white) and Ir (green).

**Table 1** Enantioselective reduction of  $\alpha$ -cyano and  $\alpha$ -nitroacetophenones<sup>a</sup>

$\text{Ar}-\text{C}(=\text{O})-\text{CH}_2-\text{X} \xrightarrow[\text{0.2 M, pH = 2.0 or 3.5, rt}]{\text{Catalyst 3, 5 equiv HCO}_2\text{H, H}_2\text{O}} \text{Ar}-\text{CH}(\text{OH})-\text{CH}_2-\text{X}$					
X = CN, NO <sub>2</sub>					
Entry	Ar	X	Time	Conv. <sup>b</sup> (%)	ee <sup>b</sup> (%)
1	Ph	CN	12	99	96(94) <sup>c</sup>
2	Ph	CN	14	99	92 <sup>d</sup>
3	Ph	CN	24	92	95 <sup>e</sup>
4	<i>p</i> -FPh	CN	12	99	93
5	<i>m</i> -ClPh	CN	12	99	93
6	<i>p</i> -BrPh	CN	12	99	93
7	<i>p</i> -MePh	CN	12	99	97
8	<i>m</i> -MeOPh	CN	12	99	94
9	2-Furyl	CN	12	99	96
10	2-Thiophenyl	CN	15	99	98
11	Ph	NO <sub>2</sub>	10	99	97
12	<i>p</i> -FPh	NO <sub>2</sub>	10	99	96
13	<i>p</i> -ClPh	NO <sub>2</sub>	10	99	93
14	<i>p</i> -MePh	NO <sub>2</sub>	10	99	96
15	<i>p</i> -MeOPh	NO <sub>2</sub>	15	99	96

<sup>a</sup> Reaction conditions: catalyst 3 (20.0 mg, 2.0  $\mu\text{mol}$  of Ir, based on the ICP analysis),  $\alpha$ -cyanoacetophenones ( $\alpha$ -nitroacetophenones) (0.80 mmol) and the aqueous solution of formic acid (5.0 equiv. 1.0 M formate solution, 0.2 M overall concentration, for X = CN, pH = 3.5; for X = NO<sub>2</sub>, pH = 2.0), at room temperature (25 °C) for 10–24 h. <sup>b</sup> Determined by chiral HPLC analysis (see ESI† in Fig. S11 and S13). <sup>c</sup> Data in the bracket were obtained using the homogeneous Cp\*IrPFPSDPEN as a catalyst. <sup>d</sup> Data were obtained using the mixed SO<sub>3</sub>H-PMO (2) and its homogeneous Cp\*IrPFPSDPEN as a catalyst. <sup>e</sup> Data were obtained using catalyst 3 with a substrate-to-catalyst mole ratio of 600.

that is, various electron-withdrawing and electron-donating substituents of the Ar moiety led to the same efficiency (entries 4–10). The asymmetric reaction was also suitable for the enantioselective reduction of  $\alpha$ -nitroacetophenones. Similarly, high conversions, no side products, and high enantioselectivities could also be obtained with several  $\alpha$ -nitroacetophenones (entries 11–15).

It is worth mentioning that the asymmetric reaction catalyzed by 3 has the reaction rate higher than that attained with its homogeneous counterpart, Cp\*IrPFPSDPEN.<sup>6a</sup> For example, we found that the enantioselective reduction of benzoylacetone nitrile catalyzed by 3 could reach completion within 12 h, whereas the reaction catalyzed by Cp\*IrPFPSDPEN required 24 h. Notably, the greatly enhanced reaction rate attained with 3 is due to the uniformly distributed single-site iridium active species and the highly hydrophobic PMO network (see ESI† in Fig. S6–S9). To confirm this conclusion, the kinetic profile of the enantioselective reduction of benzoylacetone nitrile catalyzed by 3 and by Cp\*IrPFPSDPEN were investigated. The results show that the initial activity of 3 was higher than that of Cp\*IrPFPSDPEN; the initial TOF values were 94.2 and 39.0 mol (mol<sup>-1</sup> h<sup>-1</sup>), respectively (see ESI† in Fig. S10).

Important considerations in the design of any heterogeneous catalyst are ease of separation by simple filtration and retention of catalytic activity and enantioselectivity of the recovered catalyst after multiple cycles. We found that 3 could be recovered easily and reused in eight consecutive reactions for enantioselective reduction of benzoylacetone nitrile. In the eighth recycle, catalyst 3 still afforded the desired products with 98.2% conversion and 95.2% ee value (see ESI† in Table S1 and Fig. S12). Apparently, the high recyclability should be due to the low leaching of Ir, in which

the amount of Ir in the eighth recycle is 30.09 mg per gram of catalyst and only 6.7% of Ir was lost.

In conclusion, by taking advantage of a direct post-coordination method, we conveniently constructed one ethylene-bridged, hydrophobic, chiral organoiridium-functionalized heterogeneous catalyst. This catalyst displays excellent catalytic activity and high enantioselectivity in the enantioselective reduction of  $\alpha$ -cyanoacetophenones and  $\alpha$ -nitroacetophenones in aqueous medium. As presented in this study, the excellent catalytic activity and high enantioselectivity are attributed to the high hydrophobicity and uniformly distributed single-site iridium active species within the PMO material, which significantly promote organic transformation in aqueous medium. In addition, the heterogeneous catalyst could be recovered and reused at least eight times without loss of its catalytic activity. This strategy here offers a facile means to construct a hydrophobic chiral organometal-functionalized PMO with high catalytic performance.

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