ACS Catalysis

Subscriber access provided by Northern Illinois University

Article

# Amphiphilic Hyperbranched Polyethoxysiloxane: A Self-Templating Assembled Platform to Fabricate Functionalized Mesostructured Silicas for Aqueous Enantioselective Reactions

Kun Zhang, Juzeng An, Yanchao Su, Jueyu Zhang, Ziyun Wang, Tanyu Cheng, and Guohua Liu

*ACS Catal.*, **Just Accepted Manuscript** • DOI: 10.1021/acscatal.6b01315 • Publication Date (Web): 11 Aug 2016

**Downloaded from http://pubs.acs.org on August 13, 2016**

**Just Accepted**

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a free service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are accessible to all readers and citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.

ACS Publications

ACS Catalysis is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

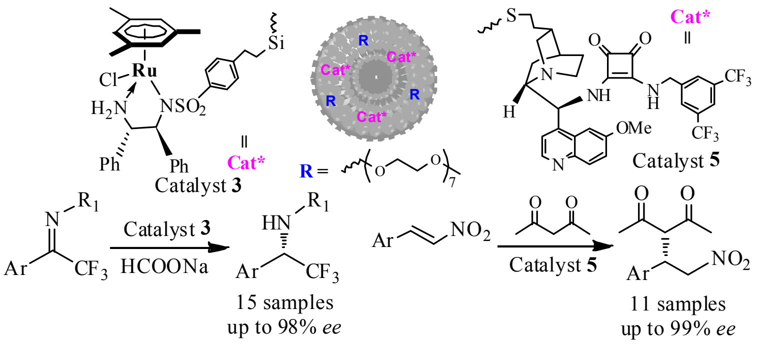
Published by American Chemical Society. Copyright © American Chemical Society. However, no copyright claim is made to original U.S. Government works, or works produced by employees of any Commonwealth realm Crown government in the course of their duties.

# Amphiphilic Hyperbranched Polyethoxysiloxane: A Self-Templating Assembled Platform to Fabricate Functionalized Mesostructured Silicas for Aqueous Enantioselective Reactions

Kun Zhang, Juzeng An, Yanchao Su, Jueyu Zhang, Ziyun Wang, Tanyu Cheng, Guohua Liu*

Key Laboratory of Resource Chemistry of Ministry of Education, Shanghai Key Laboratory of Rare Earth Functional Materials, Shanghai Normal University, Shanghai, China. Tel: + 86 21 64322280; E-mail: ghliu@shnu.edu.cn.

**ABSTRACT:** Fabrication of amphiphilic mesostructured silica as a heterogeneous catalyst is beneficial to facilitate an aqueous reaction due to its highly dispersed nature in water. In this work, by taking advantage of a self-templating assembled strategy, we construct two types of mesostructured silicas as heterogeneous catalysts, chiral ruthenium/diamine-functionalized and chiral cinchonine-based squaramide-functionalized heterogeneous catalysts, through the use of amphiphilic poly(ethyleneglycol) monomethylether-modified hyperbranched polyethoxysiloxane as a silica precursor. As presented in the study, chiral ruthenium/diamine-functionalized catalyst performs an asymmetric transfer hydrogenation of acyclic α-trifluoromethylimines to chiral α-trifluoromethylamines in water while chiral squaramide-functionalized one enables efficiently asymmetric Michael addition of acetylacetone to nitroalkenes in brine. Both highly catalytic performances are attributed to the combined multifunctionalities of well-defined single-site chiral active species, highly dispersed catalytic centers and practical phase-transferred function. Furthermore, both catalysts can also be recovered easily and reused repeatedly for at least seven times without loss of catalytic activity. Such a feature makes this self-templating assembly attracting in construction of various heterogeneous catalysts.



KEYWORDS. *Asymmetric catalysis, heterogeneous catalyst, immobilization, mesoporous material, silica.*

## INTRODUCTION

Development of silica-based immobilizated strategy to fabricate heterogeneous catalysts for enantioselective reactions has obtained great achievements in heterogeneous asymmetric catalysis, where numerous reviews have been well-documented and some have exhibited highly catalytic efficiency.[1] Although many silica-based assembled methods have been explored in construction of various heterogeneous catalysts,[2] direct utilization of a self-templating assembled approach[3] to fabricate a functionalized mesostructured silica as a heterogeneous catalyst for an enantioselective reaction is still rare thus highly desirable. A significant benefit of such a self-templating assembled approach is that various chiral functionalities could be incorporated easily into silicate networks, which is not only simple but also is effective in construction of heterogeneous catalysts. Furthermore, no template-directing assembled reagent means no extraction-step during a self-templating assembled process, which simplifies greatly the synthetic procedure of heterogeneous catalysts. In particular, an obtained heterogeneous catalyst through a self-templating assembly without any template-directing reagents can reflect truly catalytic nature of heterogeneous catalyst itself, as this self-templating assembly eliminates completely the disturbance coming from those residual structure-directing reagents that are employed generally and are difficult to be removed during an assembled method.[4]

As an important amphiphilic silica precursor, poly(ethyleneglycol) monomethylether-modified hyperbranched polyethoxysiloxane (PEG-PEOS), possesses a self-templating ability to construct various mesoporous materials without any template-directing reagents.[5] One pioneering work reported by Zhu and Möller group utilizes this amphiphilic PEG-PEOS molecule under basic conditions to assemble various silica materials with controlled morphology, where mesoporous particles, hollow nanospheres and ultrasmall solid particles could be formed through the adjustment of amounts of hydrophilic PEG fragments in PEG-PEOS molecule.[5d] More importantly, the amounts of PEG-functionality in a self-templating assembled process can be fine-tuned. This feature is beneficial to form an adjustable PEG-functionalized mesoporous silica. Meanwhile, these PEG-functionalities possess a significant benefit in catalysis because they can boost an aqueous catalytic performance due to their additional phase-transfer function in an aqueous reaction condition. In addition, scalable preparation and facile functionality of PEG-PEOS have opened up opportunities in fabrication of various functionalized materials, where self-templating assembly of PEG-PEOS has produced successfully various functionalized nanocapsules for medicine delivery and encapsulation of enzymes.[6] However, to the best of our knowledge, these unique advantages applied in catalysis are not still explored yet. Thus, by utilizing the advantage of amphiphilic mesoporous silica developed by Zhu and Möller group, incorporation of chiral siloxane into amphiphilic PGE-PEOS-based silicate network not only constructs an amphiphilic chiral molecule-functionalized mesostructured silica as a heterogeneous catalyst through a self-templating assembled strategy but also can realize a highly efficient asymmetric catalysis in water, which is of great interest both fundamentally and practically.

As efforts to construct various silica-based heterogeneous catalysts for enantioselective reactions,[7] in this contribution, we employ an amphiphilic PEG-PEOS as a silica precursor and a self-templating strategy as an assembled approach, constructing two types of chiral ruthenium/diamine-functionalized and chiral cinchonine-based squaramide-functionalized mesostructured silicas as heterogeneous catalysts. The advantage of this approach is a facile self-templating sol–gel process without any additives and the benefit of both heterogeneous catalysts is efficient in enantioselective reactions in an environmentally friendly medium.

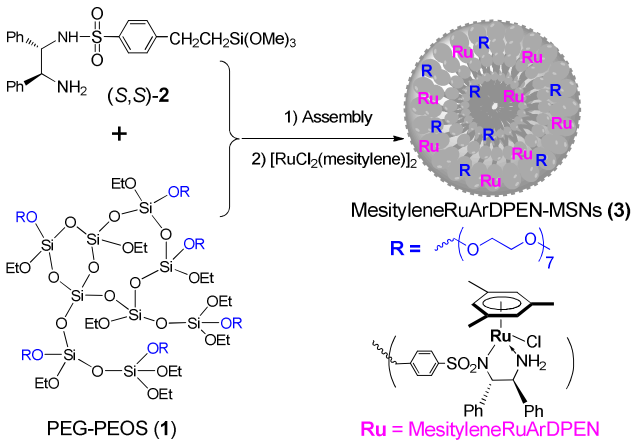
## EXERIMENTAL SECTION

**Preparation of of the heterogeneous Catalyst 3**. In a typical procedure, 1.0 g (0.36 mmol) of PEG-PEOS was dispersed in 20.0 mL of deionized water and was treated by ultrasonic irradiation for 10 min. Then an ammonia aqueous solution (25%) (1.20 mL) was added to adjust the ammonia concentration to 0.7 M. The mixture was kept under gentle stirring (500 rpm) at 25 °C for 3 h. After that, 0.10 g (0.20 mmol) of (*S*,*S*)-ArDPEN-derived silica (**2**) was added to the solution. The reaction mixture was stirred at 25 °C with a stirring speed of 500 rpm for another 24 h. The solids were collected by centrifugation and washed repeatedly with excess distilled water. The solid was filtered, rinsed with ethanol again, and then dried at 60 °C under reduced pressure overnight to afford ArDPEN-functionalized mesostructured nanoparticles (ArDPEN-MSNs) (0.65 g) in the form of a white powder. The collected solids (0.50 g) were suspended in 20.0 mL of dry $CH_2Cl_2$ again and 0.10 g of (0.17 mmol) $[RuCl_2(mesitylene)]_2$ were added. The resulting mixture was stirred at 25 °C for 24 h. The mixture was filtered through filter paper and then rinsed with excess $CH_2Cl_2$. After Soxhlet extraction for 10 h in $CH_2Cl_2$ to remove homogeneous and unreacted starting materials, the solid was dried at ambient temperature under vacuum overnight to afford catalyst **3** (0.45 g) as a light−yellow powder. ICP analysis showed that the Ru loading-amount was 20.65 mg (0.204 mmol) per gram catalyst. IR (KBr) cm$^{-1}$: 3432.6 (s), 3057.8 (w), 2858.2 (w), 1633.7 (m), 1499.8 (w), 1458.6 (w), 1392.1 (w), 1325.5 (w), 1167.2 (s), 1092.2 (s), 950.7 (m), 800.8 (m), 700.6 (m), 567.5 (m), 467.4 (m). $^{13}$C CP/MAS NMR (161.9 MHz): 147.8, 138.2, 128.1 ($\underline{C}$ of Ph and Ar groups), 105.0, 102.7 ($\underline{C}$ of mesitylene ring), 76.3−71.0 ($\underline{C}$H of −NCHPh), 65.5−56.5 ($\underline{C}H_2$ of $-OCH_2CH_2O-$), 29.9 ($\underline{C}H_2$ of $-CH_2Ar$), 23.2−12.5 ($\underline{C}H_3$ of mesitylene and $\underline{C}H_3$ of $-CH_2CH_3$), 9.1 ($\underline{C}$ of $-CH_2Si$) ppm. $^{29}$Si MASNMR (79.4 MHz): $T^2$ (δ = −59.8 ppm), $T^3$ (δ = −69.3 ppm), $Q^3$ (δ = −102.5) ppm, $Q^4$ (δ = −112.2 ppm).

**General procedure for asymmetric reaction.** A typical procedure was as follows. The catalyst **3** (19.56 mg, 4.0 μmol of Ru, based on ICP analysis, 2.0 mol%), (α-trifluoromethylimines (0.20 mmol), HCOONa (68.0 mg, 1.0 mmol, 5.0 equiv) and 2.0 mL of $H_2O$ were added sequentially to a 5.0 mL round−bottom flask. The mixture was then stirred at 40 °C for 12−24 h. During this period, the reaction was monitored constantly by TLC. After completion of the reaction, the catalyst was separated by centrifugation (10,000 rpm) for the recycling experiment. The aqueous solution was extracted with ethyl ether (3 × 3.0 mL). The combined ethyl ether extracts were washed with $NaHCO_3$ and brine, and then dehydrated with $Na_2SO_4$. After evaporation of ethyl ether, the residue was purified by silica gel flash column chromatography to afford the desired product. The yields were determined by $^1$H-NMR, and the ee values were determined by a HPLC analysis using a UV-Vis detector and a Daicel OD–H or OB–H or AD–H chiralcel column (Φ 0.46 × 25 cm).

## RESULTS AND DISCUSSION

### Synthesis and structural characterization of the heterogeneous catalyst 3



**SCHEME 1.** Preparation of the heterogeneous catalyst **3.**

Self-templating assembly of chiral MesityleneRuArDPEN-functionality (MesityleneRuArDPEN:[8] ((η$^6$-mesitylene)RuC1[N-((*S*,*S*)-2-amino-1,2-diphenylethyl)-4-ethylbenzenesulfonamide], where ArDPEN = N-((*1S,2S*)-2-amino-1,2-diphenylethyl)-4-ethylbenzenesulfonamide) within the PEG-PEOS-based silicate network produced the ruthenium/diamine-functionalized mesostructured nanoparticles, abbreviated as MesityleneRuArDPEN-MSNs (**3**), as outlined in Scheme 1. Firstly, the amphiphilic silica precursor PEG-PEOS (**1**) was synthesized according to the reported method.[5] The self-templating assembly of **1** and **2** then gave the chiral ArDPEN-functionalized mesostructured nanoparticles (ArDPEN-MSNs), which was coordinated with $[RuCl_2(mesitylene)]_2$ to form crude heterogeneous catalyst. Finally, this crude heterogeneous was treated with a Soxhlet extraction, affording the pure catalyst **3** as a light-yellow powder (see SI in Figures S1-S5).

Single-site chiral MesityleneRuArDPEN active center incorporated in the silicate network of **3** could be confirmed by solid-state $^{13}$C CP/ MAS NMR spectroscopy. As shown in Figure 1, catalyst **3** showed the carbon signals around ~74 ppm and ~128 ppm, which were corresponded to carbon atoms of the $–N\underline{C}H\underline{C}_6H_5$ groups in ArDPEN moiety. Peaks at 105.0 and 102.7 ppm in the spectrum of **3** ascribed the characteristic carbon atoms of the aromatic ring in mesitylene moiety, whilst peak at 20.8 ppm was attributed to the characteristic carbon atom of the $\underline{C}H_3$ groups attached to the aromatic ring in mesitylene moiety. However, these observed characteristic peaks in the spectrum of its parent ArDPEN-MSNs were absent, indicating the formation of the chiral MesityleneRu-ArDPEN complex as a single-site active center. Furthermore, the chemical shift values in catalyst **3** were similar to those of its homogeneous MesityleneRuTsDPEN,[8] elucidating both well-defined single-site chiral active species. This judgment could be validated by a XPS investigation (see SI in Figure S2), where catalyst **3** had the same Ru $3d_{5/2}$ electron binding energy as its homogeneous MesityleneRuTsDPEN (281.41 eV versus 281.44 eV). These findings confirmed that immobilization of chiral MesityleneRuTsDPEN-functionality within its PEG-PEOS-based silicate network through a self-templating sol–gel process followed by a complexation approach could retain the original chemical environment of its homogeneous MesityleneRuTsDPEN, which is crucial to control its enantioselective performance discussed below.

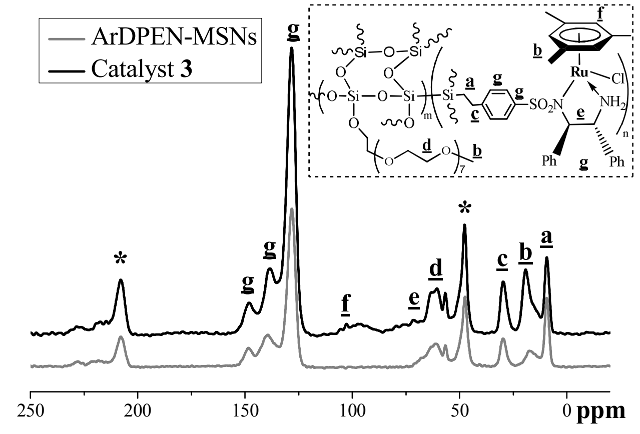


FIGURE 1. The solid-state $^{13}$C MAS NMR spectra of ArDPEN-MSNs and catalyst **3**.

The $^{29}$Si MAS NMR spectrum further demonstrated the main silicate compositions of **3** (see SI in Figure S3), where catalyst **3** presented two groups of typical silica signals (Q signals for inorganosilica and T signals for organosilica). As compared these values with those typical ones in the literature,[9] the strong $T^3$ signal at −68.9 ppm was attributed to $R–Si(OSi)_3$ species (R = alkyl-linked PEG-functionality and MesityleneRuArDPEN-functionality), while the $Q^3–Q^4$ signals at −102.3 and −110.2 ppm ascribed $(HO)Si(OSi)_3$ and $Si(OSi)_4$ species, respectively. These observations demonstrated that catalyst **3** possessed mainly the inorganosilicate networks of $(OH)Si(OSi)_3$ and $Si(OSi)_4$ with the organosilicate $R–Si(OSi)_3$ species as its main part of silica walls.[9]

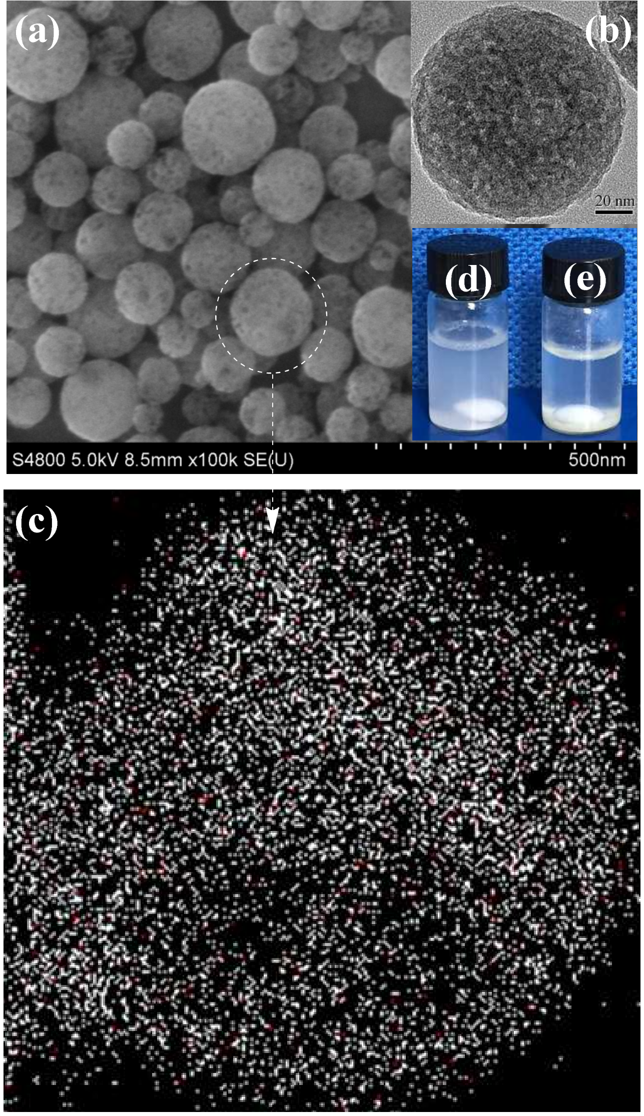


FIGURE 2. (a) SEM images of **3**, (b) TEM images of **3**, and (c) SEM image with a chemical mapping of **3** showing the distribution of Si (white) and Ru (red), (d and e) the dispersive situations in water as indicated catalyst **3** (d) and its parallel analogue **3'** (e).

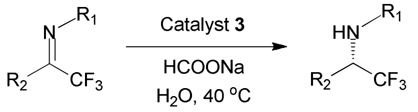
The morphology, pore structure and ruthenium distribution of catalyst **3** were further investigated by means of scanning electron microscopy (SEM), transmission electron microscopy (TEM), and nitrogen adsorption-desorption techniques. As shown in Figure 2, the SEM image (Figure 2a) revealed that catalyst **3** was composed of the monodisperse nanoparticles while the TEM image (Figure 2b) demonstrated its mesostructure confirmed by its nitrogen adsorption-desorption isotherm of catalyst **3** due to its typical IV character with an H1 hysteresis loop (see SI in Figure S4), where both observations were similar to those of its corresponding pure material.[5d] In particular, the TEM image with a chemical mapping technique disclosed that the ruthenium centers were uniformly distributed within its silicate network (Figure 2c). This finding, together with the highly dispersive nature in water (catalyst **3** relative to its parallel analogue **3'** in Figures 2d-2e), will govern its catalytic performance discussed below.

These characterizations and analyses expatiate that amphiphilic poly(ethyleneglycol) monomethylether-modified hyperbranched polyethoxysiloxane as a self-templating silica precursor could assemble steadily a heterogeneous catalyst, where the well-defined single-site chiral ruthenium/diamine-functionality and PEG-functionality were incorporated into the silicate network of monodisperse nanoparticles.

### Catalytic property of the heterogeneous catalyst

Chiral α-trifluoromethylamines as an important motif can be transferred into various biologically active molecules in medical and fluorine chemistry,[10] where direct construction of these chiral α-trifluoromethylamines through asymmetric transfer hydrogentation (ATH) have also been involved.[7a, 11, 12] With the heterogeneous catalyst **3** on hand, we investigated its ATH in water using 4-methoxy-N-(2,2,2-trifluoro-1-phenylethylidene)aniline as a model reaction at first, where the reaction was carried out with $HCO_2Na$ as a hydrogen source and 2.0 mol% of **3** as a catalyst according to the reported method.[7a] It was found that the ATH of 4-methoxy-N-(2,2,2-trifluoro-1-phenylethylidene)aniline catalyzed by **3** gave (*S*)-4-methoxy-N-(2,2,2-trifluoro-1-phenylethyl)aniline with 95% yield and 96% *ee*. Such an *ee* value was markedly better than that attained with its homogeneous counterpart (Mesitylene-RuTsDPEN) in water (Entry 1 vs Entry 1 in brackets), suggesting the amphiphilic benefit of the designed catalyst **3**.

TABLE 1. Asymmetric transfer hydrogenation of α-trifluoromethylimines.[a]



| **Entry** | **R$_1$** | **R$_2$** | **Time (h)** | **Yield (%)[b]** | **Ee. (%)[b]** |
|---|---|---|---|---|---|
| 1 | Ph | PMP | 16(24) | 95 (86) | 96(89)[c] |
| 2 | Ph | PMP | 16 | 93 | 95[d] |
| 3 | Ph | PMP | 24 | 55 | 83[e] |
| 4 | *p*-FPh | PMP | 16 | 93 | 96 |
| 5 | *p*-ClPh | PMP | 16 | 93 | 98 |
| 6 | *p*-BrPh | PMP | 16 | 91 | 94 |
| 7 | *m*-BrPh | PMP | 16 | 94 | 96 |
| 8 | *p*-$CF_3$Ph | PMP | 12 | 97 | 98 |
| 9 | *p*-MePh | PMP | 24 | 84 | 98 |
| 10 | *p*-MeOPh | PMP | 16 | 89 | 95 |
| 11 | 2-thienyl | PMP | 28 | 78 | 97 |
| 12 | Ph | *p*-MePh | 16 | 90 | 96 |
| 13 | *p*-FPh | *p*-MePh | 16 | 93 | 96 |
| 14 | *p*-BrPh | *p*-MePh | 16 | 90 | 95 |
| 15 | Ph | Ph | 18 | 95 | 94 |
| 16 | Ph | *p*-ClPh | 12 | 92 | 94 |
| 17 | Ph | 1-naphthyl | 18 | 91 | 96 |

[a] Reaction conditions: catalyst 3 (19.56 mg, 4.0 μmol of Ru based on ICP analysis), α-trifluoromethylimines (0.20 mmol), 1.0 mmol of HCOONa in 2.0 mL of water, and reaction time (12-28 h). [b] The ee values were determined chiral HPLC analysis (see SI in Figure S8). [c] Data were obtained using the homogeneous MesityleneRuTsDPEN as catalyst. [d] Data were obtained using the mixed PEG plus the homogeneous MesityleneRuTsDPEN as catalyst. [e] Data were obtained using its parallel analogue **3'** as a catalyst.

Based on its highly catalytic performance in the ATH of 4-methoxy-N-(2,2,2-trifluoro-1-phenylethylidene)aniline, a series of aryl–substituted substrates were further investigated under the same reaction conditions. As shown in Table 1, it was found that all tested substrates could be transferred into the responding chiral aryltrifluoromethylamines with high yields and enantioselectivities. It was noteworthy that the structural and electronic properties of substituents in the aromatic ring at $R_2$ group did not affect significantly their enantioselectivities, where the reactions with various electron–withdrawing and electron–donating substituents in the aromatic ring at $R_2$ group were equally efficient (Entries 4–10). But the slightly effects on yields could be observed, which the reactions with electron–withdrawing substituents in the Ar moiety at $R_2$ group had slightly higher yields than those of electron–donating substituents (Entries 4–8 versus entries 9-10). In addition, the thienyl-substituted substrate could be also converted in a highly enantioselective performance (Entry 11). Besides the general *p*-methoxyphenyl (PMP) protection group, other protection groups, such as p-tolyl, Ph, and 1-naphthyl, could also be used in this asymmetric reaction with high enantioselectivities (Entries 12–17).

To gain insight into the catalytic nature of **3** and to eliminate the factors affecting catalytic performance, a few controlled experiments were investigated. Firstly, we performed a hot-filtration experiment, eliminating the possible disturbance coming from residual homogeneous catalyst *via* a non-covalent physical adsorption. In this case, catalyst **3** was filtered from the reaction mixture during the ATH of 4-methoxy-N-(2,2,2-trifluoro-1-phenylethylidene)aniline after 8 h, and the reaction was then continued to react at 40 °C for another 8 h. The result showed that 75% yield and 87% *ee* of chiral product (*S*)-4-methoxy-N-(2,2,2-trifluoro-1-phenylethyl)aniline could be obtained in the first 8 h, but both conversion and *ee* value in the second 8 h had no appreciable change (see SI in Figure S8). This finding suggests that there is no disturbance coming from residual homogeneous catalyst *via* a non-covalent physical adsorption.

Secondly, we utilized a parallel experiment to test the function of PEG molecule in a homogeneous catalysis system, indicating the role of PEG-functionality in catalyst **3** in a heterogeneous catalysis system. In this case, the ATH of 4-

methoxy-N-(2,2,2-trifluoro-1-phenylethylidene)aniline catalyzed by its homogeneous MesityleneRuTsDPEN in the presence of PEG molecule were investigated. It was found that the reaction afforded the corresponding chiral products with 93% yield and 95% ee, which was obviously better than that attained in the absence of PEG molecule (Entry 2 vs Entry 1 in brackets). This phenomenon should be due to fact that the enhanced yield from 86% to 93% was attributed to the phase-transfer-function of the PEG molecule in this homogeneous catalysis system, suggesting that the PEG-functionality in the heterogeneous catalyst **3** should function as the similar role in the case of **3-**catalyzed asymmetric reaction in water.

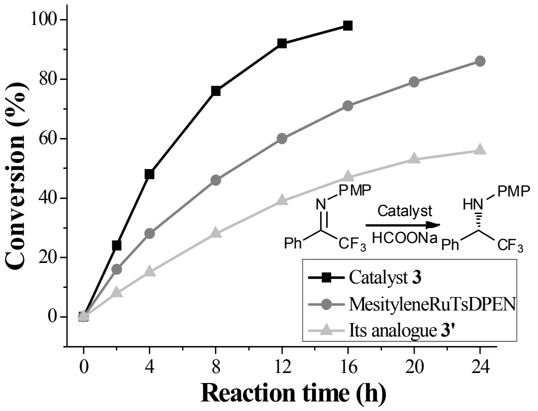


FIGURE 3. Comparison of the asymmetric transfer hydrogenation of 4-methoxy-N-(2,2,2-trifluoro-1-phenylethylidene)aniline catalyzed by **3**, its analogue **3'**, and the homogeneous MesityleneRuTsDPEN. Reactions were carried out at substrate-to-catalyst mole ratio of 50 in water.

Finally, we employed a comparable $SiO_2$-based Mesitylene-RuArDPEN-functionalized inorganosilicate analogue as a parallel catalyst (this inorganosilicate analogue **3'** has no PEG-functionality in its silicate network), judging the function of PEG-functionality in catalyst **3**. In the case, its comparable analogue **3'** was synthesized through the self-templating assembly of POES[5a] and **2** followed by the similar complexation with $[RuCl_2(mesitylene)]_2$ (see SI in experimental and Figure S6). The results showed that the ATH of 4-methoxy-N-(2,2,2-trifluoro-1-phenylethylidene)aniline catalyzed by its analogue **3'** within 24 h only afforded the corresponding chiral products in 55% yield with 83% ee (Entry 3). This observation suggested that the absence of PEG-functionality in the silicate nework of **3'** was responsible for its poor catalytic performance, confirming the ability of PEG-functionality in catalyst **3.** A direct evidence could be offered to support this view through a kinetic investigation in the ATH of 4-methoxy-N-(2,2,2-trifluoro-1-phenylethylidene)aniline. As shown in Figure 3, the ATH of 4-methoxy-N-(2,2,2-trifluoro-1-phenylethylidene)aniline catalyzed by catalyst **3**, by its homogeneous MesityleneRuTsDPEN and by its inorganosilicate analogue **3'** under the same reaction conditions were performed. It was found that the reaction catalyzed by catalyst **3** had an initial activity (TOF value) remarkedly higher than that achieved with its analogue **3'**, even higher than that of its homogeneous counterpart MesityleneRuTsDPEN (the initial TOFs within 2 h were 6.0, 2.0 and 4.0 molmol$^{-1}$h$^{-1}$, respectively). These observations demonstrated that the designed heterogeneous catalyst **3** possessed a highly efficient asymmetric transfer hydrogenation of α-trifluoromethylimines, where the combined functionalities, such as well-defined chiral single-site active species verified by $^{13}$C CP/MAS NMR spectra, uniformly distributed ruthenium center confirmed by SEM image, highly dispersive nature in water indicated at Figure 2d, as well as benefit of PEG-functionality in silicate network discuss above, made their cooperative contributions in its catalytic performance in water.

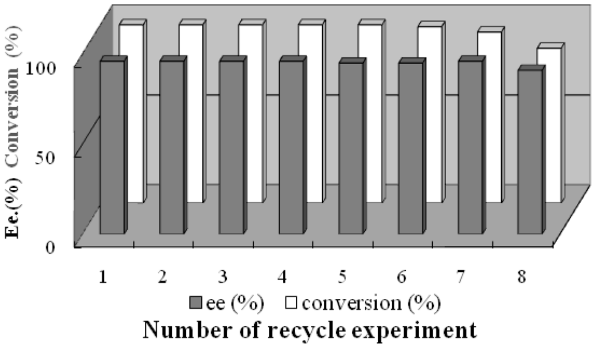
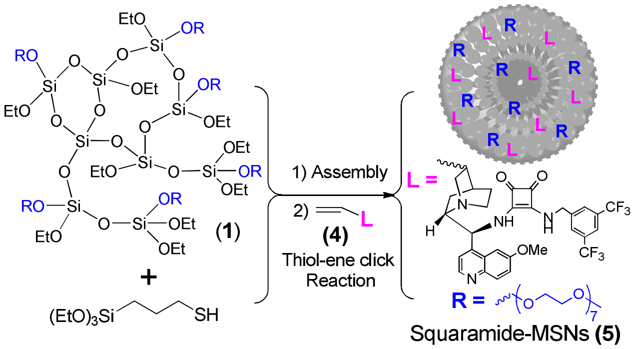


FIGURE 4. Reusability of catalyst **3** using 4-methoxy-N-(2,2,2-trifluoro-1-(4-fluorophenyl)ethylidene)aniline as a substrate.

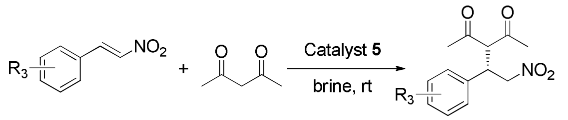
Another important consideration for the design of catalyst **3** is its ease of separation by centrifugation, and the recycled catalyst can retain its catalytic activity and enantioselectivity after multiple recycles. It was found that catalyst **3** could be recovered through high-speed centrifugation and recycled repeatedly. As shown in Figure 4, in seven consecutive reactions, catalyst **3** still afforded 95% conversion and 96% ee in the ATH of 4-methoxy-N-(2,2,2-trifluoro-1-(4-fluorophenyl)ethylidene)aniline (see SI in Table S1 and in Figure S9).



**SCHEME 2.** Preparation of the heterogeneous catalyst **5.**

More importantly, by utilizing amphiphilic PEG-PEOS silica precursor as a self-templating assembled platform, it is also convenient to immobilize others chiral molecules for construction of functionalized heterogeneous catalysts. As shown in Scheme 2, chiral cinchonine-based squaramide-functionalized mesostructured nanoparticles, abbreviated as Squaramide-MSNs (**5**) (chiral squaramide (**4**):[13] 3-((3,5-bis(trifluoromethyl)benzyl)amino)-4-(((1*S*)-(6-methoxyquinolin-4-yl)((2*S*)-5-vinylquinuclidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione), could also be fabricated steadily through this self-templating assembled approach. Similar to the preparation of catalyst **3**, the self-templating assembly of (triethoxysilyl)propanethiol and amphiphilic PEG-PEOS (**1**) led to the mercapto-functionalized mesostructured nanoparticles (SH-MSNs), which the reaction with chiral squaramide (**4**) by a thiol-ene click reaction[14] produced the heterogeneous catalyst **5** as a white powder (see SI in Figure S1, S3-S7). A benefit of this heterogeneous catalyst **5** was that it enabled a highly efficient asymmetric Michael addition of acetylacetone to nitroalkenes in brine, where various substrates could be transferred smoothly to the responding chiral products within twenty minute reaction time as shown in Table 2. Taking the asymmetric Michael addition of acetylacetone to nitrostyrene as an example, it was found that the enantioselective reaction catalyzed by catalyst **5** afforded (*S*)-3-(2-nitro-1-phenylethyl)pentane-2,4-dione in 95% yield with 99% *ee* value, which was comparable to that of its homogeneous counterpart (entry 1 versus 1 in the bracket).[13c] As expected, the highly dispersed chiral active centers and phase-transfer-featured PEG-functionality could enhance cooperatively enantioselective Michael addition of acetylacetone to nitroalkenes in aqueous medium. Furthermore, it was found that the structural and electronic properties did not affect significantly their enantioselectivities regardless of electron–withdrawing and electron–donating substituents in the Ar moiety at $R_3$ group (Entries 2–11). Also, catalyst **5** could be recovered through high-speed centrifugation and recycled repeatedly, where the recycled catalyst **5** still afforded 92% conversion and 97% ee after a continuous eight times recycle in the enantioselective Michael addition of acetylacetone to nitrostyrene (see SI in Tabel S2 and in Figure S11).

TABLE 2. Asymmetric Michael addition of acetylacetone to nitroalkenes.[a]



| Entry | $R_1$ | Time (minute) | Yield (%)[b] | Ee. (%)[b] |
|---|---|---|---|---|
| 1 | 4-H | 20 | 95 (98) | 99(99)[c] |
| 2 | 4-F | 20 | 97 | 99 |
| 3 | 4-Cl | 20 | 96 | 97 |
| 4 | 3-Cl | 20 | 95 | 99 |
| 5 | 2-Cl | 20 | 93 | 99 |
| 6 | 4-Br | 20 | 94 | 99 |
| 7 | 4- $CF_3$ | 20 | 97 | 99 |
| 8 | 4-Me | 20 | 95 | 99 |
| 9 | 4-OMe | 20 | 97 | 99 |
| 10 | 3-OMe | 20 | 95 | 98 |
| 11 | 2-OMe | 20 | 93 | 96 |

[a] Reaction conditions: catalyst **5** (36.26 mg, 5.0 μmol of squaramide based on TG analysis), nitroalkenes (1.0 mmol), acetylacetone (2.0 mmol), 5.0 mL brine, reaction time (20 minute). [b] Determined by chiral HPLC analysis (see SI in Figure S10). [c] Data were obtained using its homogeneous squaramide as a catalyst.

In conclusions, we utilize a self-templating assembled approach to develop two functionalized mesostructured silicas as heterogeneous catalysts. As presented in this study, chiral ruthenium/diamine-functionalized heterogeneous catalyst displays high catalytic activity and enantioselectivity in the asymmetric transfer hydrogenation of α-trifluoromethylimines to chiral aryltrifluoromethylamines, while chiral squaramide-functionalized heterogeneous catalyst enables asymmetric Michael addition of acetylacetone to nitroalkenes in brine to afford chiral products with highly catalytic efficiency. As designed, the combined functionalities, such as well-defined single-site active species, highly dispersed nanoparticles, as well as phase-transfer-function PEG-functionality, contribute cooperatively the catalytic performance in an environmentally friendly medium. Furthermore, both catalysts could be recovered and reused repeatedly without any obvious effect on its catalytic performance. The outcomes from the study suggest that a simple self-templating assembled approach could be used to construct various chiral organomolecule-functionalized mesostructured silicas for highly efficient asymmetric catalysis.

## ASSOCIATED CONTENT

### Supporting Information

Experimental procedures and analytical data of chiral products are available free of charge via the Internet at http://pubs.acs.org.

## AUTHOR INFORMATION

### Corresponding Author

ghliu@shnu.edu.cn

## ACKNOWLEDGMENT

We are grateful to China National Natural Science Foundation (21402120), and Shanghai Sciences and Technologies Development Fund (13ZR1458700), Shanghai Municipal Education Commission (14YZ074) for financial supports.

## REFERENCES

(1) (a) Kleitz, F. in Handbook of Asymmetric Heterogeneous Catalysis. Wiley-VCH, Weinheim, **2008**, pp. 178; (b) De Vos, D. E.; Dams, M.; Sels, B. F.; Jacobs, P. A. *Chem. Rev.* **2002**, *102*, 3615-3640; (c) Minakata, S.; Komatsu, M. *Chem. Rev.* 2009, **109**, 711724; (d) Bartók, M. *Chem. Rev.* **2010**, *110*, 1663-1705; (e) Mehdi, A.; Reye, C.; Corriu. R. *Chem. Soc. Rev.* **2011**, *40*, 563574; (f) Yang, H. Q.; Zhang, L.; Zhong, L.; Yang, Q. H.; Li, C. *Angew. Chem. Int. Ed.* **2007**, *46*, 6861-6865; (g) Thomas, J. M.; Raja, R. *Acc. Chem. Res.* **2008**, *41*, 708-720; (h) Cheng, T. Y.; Zhao, Q. K.; Zhang, D. C.; Liu, G. H. *Green Chem.* **2015**, *17*, 2100-2122.

(2) (a) Zhang, X. M.; Zhao, Y. P.; Peng, J.; Yang, Q. H. *Green Chem.* **2015**, *17*, 1899–1906. (b) Bai, S. Y.; Yang, H. Q.; Wang,

P.; Gao, J. S.;Li, B.;Yang Q. H; Li, C. *Chem. Commun.* **2010**, *46*, 8145–8147; (c) Liu, P. N.; Deng, J. G.; Tu, Y. Q.; Wang, S. H. *Chem. Commun.* **2004**, 2070–2071; (d) Haraguchi, N.; Nishiyama A.; Itsuno, S. *J. Polym. Sci., Polym. Chem. Ed.* **2010**, *48*, 3340–3349; (e) Haraguchi, N.; Tsuru, K.; Arakawa Y.; Itsuno, S. *Org. Biomol. Chem.* **2009**, *7*, 69–75; (f) Li, X. G.; Wu, X. F.; Chen, W. P.; Hancock, F. E.; King F., Xiao, J. L. *Org. Lett.* **2004**, *6*, 3321–3324.

(3) (a) Liu, P.; Dong, Y.; Du, P.; Mu, B. *Ind. Eng. Chem. Res.* **2012**, *51*, 3350-3355; (b) Tang, D.; Hu, S.; Dai, F.; Yi, R.; Gordin, M. L.; Chen, S.; Song, J.; Wang, D. *ACS Appl. Mater. Interfaces* **2016**, *8*, 6779-6783; (c) Xia, C.; Alshareef, H. N. *Chem. Mater.* **2015**, *27*, 4661-4668; (d) Qiao, Y.; Wang, Y.; Yang, Z.; Lin, Y.; Huang, J. *Chem. Mater.* **2011**, *23*, 1182-1187.

(4) Cauda, V.; Schlossbauer, A.; Kecht, J.; Zürner, A.; Bein, T. *J. Am. Chem. Soc.* **2009**, *131*, 11361-11370.

(5) (a) Jaumann, M.; Rebrov, E. A.; Kazakova, V. V.; Muzafarov, A. M.; Goedel, W. A.; Möller, M. *Macromol. Chem. Phys.* **2003**, *204*, 1014-1026; (b) Zhu, X.; Jaumann, M.; Peter, K.; Möller, M. *Macromolecules* **2006**, *39*, 1701-1708; (c) Sakamoto, S.; Shimojima, A.; Miyasaka, K.; Ruan, J.; Terasaki, O.; Kuroda, K. *J. Am. Chem. Soc.* **2009**, *131*, 9634-9635; (d) Wang , H.; Agrawal, G.; Tsarkova, L.; Zhu, X.; Möller, M. *Adv. Mater.* **2013**, *25*, 1017-1021.

(6) (a) Zhang, C.; Yan, K.; Hu, C.; Zhao, Y.; Chen, Z.; Zhu, X.; Möller. M. *J. Mater. Chem. B.* **2015**, *3*, 1261-1267; (b) Agrawal, G.;Ülpenich, A.; Zhu, X.; Möller, M.; Pich, A. *Chem. Mater.* **2014**, *26*, 5882-5891; (c) Wu, J.; Zhao, L.; Xu, X.; Bertrand, N.; Choi, W.; Yameen, B.; Shi, J.; Shah, V.; Mulvale, M.; MacLean, J. L.; Farokhzad, O. C. *Angew. Chem. Int. Ed.* **2015**, *54*, 9218-9223; (d) Garofalo, C.; Capuano, G.; Sottile, R.; Tallerico, R.; Adami, R.; Reverchon, E.; Carbone, E.; Izzo, L.; Pappalardo, D. *Biomacromolecules* **2014**, *15*, 403-415; (e) Lee, S. H.; Moroz, E.; Castagner, B.; Leroux, J. C. *J. Am. Chem. Soc.* **2014**, *136*, 12868-12871.

(7) (a) Wu, M.; Cheng, T. Y.; Ji, M.; Liu, G. H. *J. Org. Chem.* **2015**, *80*, 3708-3713; (b) Wu, M.; Kong, L. Y.; Wang, K. W.; Jin, R. H.; Cheng, T. Y.; Liu, G. H. *Catal. Sci. Technol.* **2015**, *5*, 1750-1757; (c) Xia, D. Q.; Cheng, T. Y.; Xiao, W.; Liu, K. K.; Wang, Z. L.; Liu, G. H.; Li, H. X.; Wang, W. *ChemCatChem* **2013**, *5*, 1784-1789; (d) Zhang, D. C.; Gao, X. S.; Cheng, T. Y.; Liu, G. H. *Sci. Rep.* **2014**, *4*, 5091-5098; (e) Gao, X. S.; Liu, R.; Zhang, D. C.; Wu, M.; Cheng, T. Y.; Liu, G. H. *Chem. Eur. J.* **2014**, *20*, 1515-1519; (f) Liu, R.; Cheng, T. Y.; Kong, L. Y.; Chen, C.; Liu, G. H.; Li, H. X. *J. Catal.* **2013**, *307*, 55-61; (g) Zhang, H. S.; Jin, R. H.; Yao, H.; Tang, S.; Zhuang, J. L.; Liu**,** G. H.; Li, H. X. *Chem. Commun.* **2012**, *48*, 7874-7876; (h) Gao, F.; Jin, R. H.; Zhang, D. C.; Liang, Q. X.; Ye, Q. Q.; Liu, G. H. *Green Chem.* **2013**, *15*, 2208-2214; (i) Cheng, T. Y.; Zhao, Q. K.; Zhang, D. C.; Liu, G. H. *Curr. Org. Chem.* **2015**, *19*, 667-680.

(8) (a) Hashiguchi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 7562-7563; (b) Ohkuma, T.; Tsutsumi, K.; Utsumi, N.; Arai, N.; Noyori, R.; Murata, K. *Org. Lett.* **2007**, *9*, 255-257.

(9) Krőcher, O. ; Kőppel, R. A. ; Frőba, M. ; Baiker, A. *J. Catal.* **1998**, *178*, 284-298.

(10) (a) Nie, J.; Guo, H. C.; Cahard, D.; Ma, J. A. *Chem. Rev.* **2011**, *111*, 455-529; (b) Lim, J.; Taoka, B.; Otte, R. D.; Spencer, K.; Marshall, C. G.; Young, J. R. *J. Med. Chem.* **2011**, *54*, 7334-7349; (c) O'Shea, P. D.; Chen, C. Y.; Gauvreau, D.; Hughes, F.; Gosselin, G.; Nadeau, C.; Volante, R. P. *J. Org. Chem.* **2009**, *74*, 1605-1610; (d) Zhang, N.; Ayral-Kaloustian, S.; Nguyen, T.; Afragola, J.; Hernandez, J.; Lucas, R.; Gibbons, J.; Beyer, C. *J. Med. Chem.* **2007**, *50*, 319-327; (e) Imamoto, T.; Iwadate, N.; Yoshida, K. *Org. Lett.* **2006**, *8*, 2289-2292; (f) Goulioukina, N. S.; Bondarenko, G. N.; Lyubimov, S. E.; Davankov, V. A.; Gavrilov, K. N.; Beletskaya, I. P. *Adv. Synth. Catal.* **2008**, *350*, 482-492.

(11) (a) Giacalone, F.; Gruttadauria, M.; Agrigento, P.; Noto, R. *Chem. Soc. Rev.* **2012**, *41*, 2406-2447; (b) Abe, H.; Amii, H.; Uneyama, K. *Org. Lett.* **2001**, *3*, 313-315; (c) Suzuki, A.; Mae, M.; Amii, H.; Uneyama, K. *J. Org. Chem.* **2004**, *69*, 5132-5134; (d) Chen, M. W.; Duan, Y.; Chen, Q. A.; Wang, D. S.; Yu, C. B.; Zhou, Y. G. *Org. Lett.* **2010**, *12*, 5075-5077; (e) Genoni, A.; Benaglia, M.; Massolo, E.; Rossi, S. *Chem. Commun.* **2013**, *49*, 8365-8367; (f) Mikami, K.; Murase, T.; Zhai, L.; Kawauchi, S.; Itoh, Y.; Ito, S. *Tetrahedron Lett.* **2010**, *51*, 1371-1373; (g) Henseler, A.; Kato, M.; Mori, K.; Akiyama, T. *Angew. Chem. Int. Ed.* **2011**, *50*, 8180-8183; (h) Dai, X. Y.; Cahard, D. *Adv. Synth. Catal.* **2014**, *356*, 1317-1328.

(12) (a) Martins, J. E. D.; Clarkson, G. J.; Wills, M. *Org. Lett***.** **2009**, *11*, 847-850; (b) Wu, X. F.; Li, X. H.; Zanotti-Gerosa, A.; Pettman, A.; Liu, J.; Mills, A. J.; Xiao, J. L. *Chem. Eur. J.* **2008**, *14*, 2209-2222; (c) Wu, X. F.; Liu, J.; Tommaso, D. D.; Iggo, J. A.; Catlow, C. R.; Bacsa, J.; Xiao, J. L. *Chem. Eur. J.* **2008**, *14*, 7699-7715; (d) Liu, P. N.; Deng, J. G.; Tu, Y. Q.; Wang, S. H. *Chem. Commun.* **2004**, 2070-2071; (e) Cortez, N. A.; Aguirre, G.; Parra-Hake, M.; Somanathan, R. *Tetrahedron: Lett.* **2009**, *50*, 2281-2291; (f) He, Y. M.; Fan, Q. H. *ChemCatChem* **2015**, *7*, 398–400; (g) Yang, Z. S.; Chen, F.; He, Y. M.; Yang, N. F.; Fan, Q. H. *Catal. Sci. Technol.* **2014**, *4*, 2887–2890; (h) Liu, P. N.; Gu, P. M.; Wang, F. Tu, Y. Q. *Org. Lett***.** **2004**, *6*, 169-172; (i) Wu, X. F.; Li, X. G.; Hems, W.; King, F.; Xiao, J. L. *Org. Biomol. Chem.* **2004**, *2*, 1818-1821; (j) Wu, J. S.; Wang, F.; Ma, Y. P.; Cui, X.; Cun, L. F.; Zhu, J.; Deng, J. G. Yu, B. L. *Chem. Commun.* **2006**, 1766–1768.

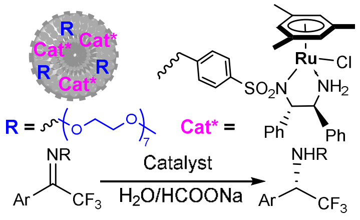
(13) (a) Malerich, J. P.; Hagihara, K.; Rawal, V. H. *J. Am. Chem. Soc.* **2008**, *130,* 14416-14417; (b) Jiang, H.; Paixão, M. W.; Monge, D.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2010**, *132*, 2775-2783; (c) Bae, H. Y.; Some, S.; Oh, J. S.; Lee, Y. S.; Song, C. E. *Chem. Commun.* **2011**, *47*, 9621-9623; (d) Yang, W.; Du, D. M. *Org. Lett.* **2010**, *12*, 5450-5453; (e) Enders, D.; Hahn, R.; Atodiresei, I. *Adv. Synth. Catal.* **2013**, *355*, 1126-1136; (f) Pham, T. S.; Gönczi, K.; Kardos, G.; Süle, K.; Hegedüs, L.;Kállay, M.; Kubinyi, M.; Szabó, P.; Petneházy, I.; Tőke, L.; Jászay, Z. *Tetrahedron: Asymmetry* **2013**, *24*, 1605-1614; (g) Dong, Z.; Qiu, G.; Zhou, H.; Dong, C. *Tetrahedron: Asymmetry* **2012**, *23*, 1550-1556; (h) Dai, L.; Wang, S.; Chen, F. *Adv. Synth. Catal.* **2010**, *352*, 2137-2141; (i) Mailhol, D.; del Mar Sanchez Duque, M.; Raimondi, W.; Bonne, D.; Constantieux, T.; Coquerel, Y.; Rodriguez, J. *Adv. Synth. Catal.* **2012**, *354*, 3523-3532; (j) Yang, K. S.; Nibbs, A. E.; Turkmen, Y. E.; Rawal, V. H. *J. Am. Chem. Soc.* **2013**, *135*, 16050-16053; (k) Bera, K.; Namboothiri, I. N. N. *Chem. Commun.* **2013**, *49*, 10632l-10634; (l) Wang, Y. F.; Chen, R. X.; Wang, K.; Zhang, B. B.; Li, Z. B.; Xu, D. Q. *Green Chem.* **2012**, *14*, 893-895; (m) Ren, X. C.; He, C. Y.; Feng, Y. L.; Chai, Y. H.; Yao, W.; Chen, W. P.; Zhang, S. Y. *Org. Biomol. Chem.* **2015**, *13*, 5054-5060.

(14) Tucker-Schwartz, A. K.; Farrell, R. A.; Garrell, R. L. *J. Am. Chem. Soc.* **2011**, *133*, 11026-11029.

# Graphical Abstract:

## Amphiphilic Hyperbranched Polyethoxysiloxane: A Self-Templating Assembled Platform to Fabricate Functionalized Mesostructured Silicas for Aqueous Enantioselective Reactions

Kun Zhang, Juzeng An, Yanchao Su, Jueyu Zhang, Ziyun Wang, Tanyu Cheng, Guohua Liu*



Two amphiphilic mesostructured silica-based heterogeneous catalysts are fabricated through a self-templating assembled strategy, which enable highly efficient enantioselective reactions in an environmentally friendly medium.