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Authors: Guohua Liu; Xiaomin Shu; Liang Li; Gengwei Zhang; Cuibao Li; Tanyu Cheng; Ronghua Jin

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### A Cinchona Alkaloid-Functionalized Mesostructured Silica for Construction of Enriched Chiral β-Trifluoromethyl-β-Hydroxy Ketones over An Epoxidation-Relay-Reduction Process

Cuibao Li, Xiaomin Shu, Liang Li, Genwei Zhang, Ronghua Jin, 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 200234, P. R. China

Abstract: A cinchona alkaloidfunctionalized heterogeneous catalyst is prepared through a thiol-ene click of reaction chiral N-(3,5ditrifluoromethylbenzyl)quininium bromide and a mesostructured silica obtained by co-condensation of 1,2bis(triethoxysilyl)ethane 3and (triethoxysilyl)propane-1-thiol. Structural analyses and

characterizations disclose its welldefined chiral single-site active center, and electron microscopy images reveal its monodisperse property. As a heterogenous catalyst, it enables an efficient asymmetric epoxidation of β-trifluoromethyl-β,βachiral disubstituted, where those obtained chiral products can be converted easily into enriched chiral β-trifluoromethylβ-hvdroxy ketones through a sequential epoxidation-relay-reduction process. this heterogeneous Furthermore, catalyst can be recovered conveniently

and reused in asymmetric epoxidation of 4,4,4-trifluoro-1,3-diphenylbut-2enone, showing an attractive feature in a practical construction of enriched chiral  $\beta$ -CF<sub>3</sub>-substituted molecules.

**Keywords:** Asymmetric catalysis • Heterogeneous catalyst • Immobilization • Silica • Supported catalysts

#### Introduction

Construction of enriched chiral  $\beta$ -trifluoromethylated aromatic ketones with CF<sub>3</sub>-bearing chiral tertiary carbon center is highly desirable because these ketones as synthetic building blocks can be converted easily into various biologically active organic molecules in fluorine chemistry.<sup>[1]</sup> So far, strategy for enantioselective construction of these ketones with CF<sub>3</sub>-bearing chiral tertiary carbon center empolys mainly  $\beta$ -trifluoromethyl- $\beta$ , $\beta$ -disubstituted enones as prochiral substrates, which includes enantioselective reduction,<sup>[2]</sup> enantioselective aldol reaction,<sup>[3]</sup>

Professor Guohua Liu
 Key Laboratory of Resource Chemistry of Ministry of Education, Shanghai
 Key Laboratory of Rare Earth Functional Materials, Shanghai Normal
 University
 Address: No.100 Guilin Rd.
 Fax: (+) (0086)2164322511
 E-mail: ghliu@shnu.edu.cn

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/asia.200xxxxxx.((Please delete if not appropriate)) enantioselective tandem reduction-isomerition reaction,[4] asymmetric epoxidation<sup>[5]</sup> and so on.<sup>[6]</sup> Among these methods, asymmetric epoxidation is accepted extensively as a powerful and reliable organic transformations for construction of these ketones with CF<sub>3</sub>-bearing chiral tertiary carbon center, as it is not only useful to prepare enriched chiral epoxides<sup>[5]</sup> but also can be used to convert into various chiral β-trifluoromethyl- $\beta$ -hydroxy ketones.<sup>[5b,7]</sup> Although tremendous efforts have been made in asymmetric epoxidation,<sup>[8]</sup> its application in construction of enriched chiral epoxides from achiral βtrifluoromethyl- $\beta$ , $\beta$ -disubstituted enones is still rare.<sup>[5]</sup> Only two successful examples enable asymmetric epoxidation of achiral B-trifluoromethyl-B.B-disubstituted enones to enriched chiral epoxides, where Shibata group<sup>[5a]</sup> reported a methylhydrazine-induced asymmetric epoxidation of βtrifluoromethyl- $\beta$ , $\beta$ -disubstituted enones through the use of chiral cinchona alkaloid as a catalyst while Chen<sup>[5b]</sup> group peformed this asymmetric transformation through the utilization of a pentafluorinated quinidine-based catalyst under hydrogen peroxide condition. Despite of both highly catalytic performances, their practical applications are still hindered greatly due to the inherent drawbacks of expensive chiral ligands and complicated product isolation. Therefore, development of an immobilization strategy to overcome these limitations is an unmet challenge both in fundamental research and practical application.

Mesostructured silica nanoparticles, especially periodic mesoporous organosilicas as a kind of idea supports, have been well-documented in immobilization of various chiral molecules for asymmetric catalysis,<sup>[9]</sup> Recently, we also found that ethylene-bridged mesoporous nanoparticles (MNPs) could be applied successfully to asymmetric transfer hydrogenation of various ketones, leading to excellent catalytic and enantioselective performances that are benefited from highly hydrophobic nature of ethenebridged organosilicate walls.<sup>[10]</sup> This significent feature facilitates an aqueous enantioselective reaction because hydrophobic nature enhances reaction rate in a biphasic reaction medium. Thus, taking consideration of ethylenebridged MNPs as a support, it is reasonable to expect that chiral cinchona alkaloid anchored onto such а mesostructured silica enables an efficient asymmetric epoxidation of  $\beta$ -trifluoromethyl- $\beta$ , $\beta$ -disubstituted enones.

As an ongoing research aimed at developing heterogeneous catalysts for enantioselective reactions,<sup>[11]</sup> in this contribution, we utilize the ethylene-bridged mesoporous nanoparticles to anchor N-(3,5-ditrifluoromethylbenzyl)quininium bromide through a thiol-ene click approach, constructing a cinchona alkaloid-functionalized mesoporous organosilica. As a heterogeneous catalyst, it not only displays a highly enantioselective epoxidation of achiral  $\beta$ -trifluoromethyl- $\beta$ , $\beta$ disubstituted enones but also converts epoxides into chiral βtrifluoromethyl-\beta-hydroxy ketones through a sequential epoxidation-relay-reduction process. As demonstrated in the study, the superior catalytic performance is attributed to salient hydrophobicity and confined chiral cinchona alkaloid catalytic nature. Furthermore, this heterogeneous catalyst can be recovered conveniently and reused repeatedly for at least eight times without loss of its catalytic activity in asymmetric epoxidation of 4,4,4-trifluoro-1,3-diphenylbut-2-enone.

#### **Results and Discussion**

Synthesis and structural characterization of the heterogeneous catalyst



Scheme 1. Preparation of catalysts 3.

Ethylene-bridged chiral cinchona alkaloid-functionalized mesoporous nanoparticles, abbreviated as Cinchona@Et@MNPs (3), were constructed as outlined in Scheme 1. Firstly, co-condensation of 1,2-bis(triethoxysilyl)ethane and 3-(triethoxysilyl)propane-1-thiol

using cetyl-trimethylammonium bromide (CTAB) as a structure-directing template<sup>[12]</sup> gave mercapto-functionalized mesoporous nanoparticles (SH@Et@MNPs (1)) in the form of a white powder. Thiol-ene click reaction<sup>[13]</sup> of SH@Et@MNPs (1) and N-(3,5-ditrifluoromethylbenzyl)quininium bromide (2) then led to the crude heterogeneous catalyst, Cinchona@Et@MNPs (3). Finally, this crude one was Soxhlet extracted strictly, affording its pure catalyst **3** as a light-yellow powder (see SI in experimental section and in Figure S1-3).

Figure 1 showed the <sup>29</sup>Si magic angle spinning (MAS) NMR spectra of 1 and catalyst 3, where both only produced one group of T signals that were derived from organosilica. These exclusive T signals demonstrated that all Si species in catalyt **3** were bonded to carbon atoms.<sup>[14]</sup> As compared these isomer values of Si species with those standard values in the literature,<sup>[14]</sup> both T signals around -59.5 and -67.2 ppm in catalyst 3 were responded to  $T^2$  [RSi(OSi)<sub>2</sub>(OH)] and  $T^3$  $[RSi(OSi)_3]$  (R = alkyl-linked cinchona alkaloid or ethylenebridged groups) species. These observation expatiated that catalyst 3 possessed an organosilicate network with R-Si(OSi)<sub>2</sub>(OH) and [R-Si(OSi)<sub>3</sub>] species as its main orgnaosilicate wall. Furthermore, the absence of signals from -90 to -120 ppm means no inorganosilica species for Qseries, indicating that no carbon-silicon bonds cleaved during the co-condensation process



Figure 1. Solid-state <sup>29</sup>Si CP/MAS NMR spectra of 1 and catalyst 3.



Figure 2. Solid-state <sup>13</sup>C CP/MAS NMR spectra of **1** and catalyst **3**.

Anchoring chiral cinchona alkaloid-functionality on the ethylene-bridged silicate network of 3 could be confirmed by

solid-state <sup>13</sup>C cross-polarization (CP) MAS NMR spectroscopy. As shown in Figure 2, both 1 and catalyst 3 produced strong carbon signals of -SiCH<sub>2</sub> groups at ~6 ppm, which ascribed their ethylene-bridged silica embedded in their silicate networks. In contrast catalyst 3 with its parent 1, the characteristic carbon signals between 162 and 112 ppm in the spectrum of 3 were assigned to the carbon atoms of the aromatic ring while peaks between 75 and 49 ppm ascribed the carbon atoms of cyclic alkyl groups in the part of chiral moiety. These observed chemical shifts of catalyst 3 were absent in the spectrum of 1, suggesting that the single-site chiral cinchona alkaloid-functionality had been anchored successfully onto 1 through this thiol-ene click reaction as these chemical shifts were same as those of its homogeneous counterpart.  $^{[8a]}$  In addition, the peaks around ~14, ~30 and ~60 ppm for methyl (or methylene) groups without/with connection to nitrogen atom in CTAB moiety could be observed clearly that were attributed to the residual CTAB molecule in catalyst 3.<sup>[15]</sup>



Figure 3. The TG/DTA curves of catalyst 3.



Figure 4. Nitrogen adsorption-desorption isotherms of 1 and catalyst 3.

Figure 3 exhibited the TG/DTA curves of catalyst **3**. It was found that an endothermic peak around 356 K with 13.45% of weight loss was due to the release of physical adsorption water. Two exothermic peaks around 455 K and 1050 K with 28.21% of the total weight loss could be assigned to the oxidation of the organic moieties including propyl-linked thiol, alkyl-linked cinchona alkaloid, ethylene-bridged groups

and the residual CTAB surfactant.<sup>[15]</sup> After the elimination of the contribution coming from water, the total weight loss of the organic moieties was 32.59%. In sharp contrast to the TG/DTA curve of SH@Et@MNPs (1) with 22.07% of the total weight loss for the similar organic moieties (see SI in Figure S2), the actual loss of cinchona alkaloid was 10.52%, meaning that the loading amount of chiral cinchona alkaloid was 105.20 mg (0.166 mmol) per gram catalyst.



Figure 5. (a) SEM images of **3**, (b) TEM images of **3**, and (c) TEM image with a chemical mapping of **3** showing the distribution of Si (white) and S (red).

Its mesostructural morphology of catalyst **3** were further characterized using nitrogen adsorption–desorption technique, X-ray diffraction (XRD), scanning electron microscopy (SEM) and transmission electron microscopy (TEM). As shown in Figure 4, the heterogeneous catalysts **3** displayed the type IV nitrogen adsorption-desorption isotherms with the H<sub>2</sub> hysteresis loop while the low-angle XRD pattern (see SI in Figure S3) exhibited the well resolved peaks at  $2\theta = 0.8^{\circ}$ - $1.0^{\circ}$ , indicating the ordered mesoporous structure. The SEM image (Figure 5a) revealed that catalyst **3** was composed of the uniformly distributed nanopartiles with a particle size of about 130 nm, while the TEM image (Figure 5b) verified its mesostructural morphology. It was noteworthy that the sulphur atoms in catalyst **3** were uniformly distribution within its organosilicate network observed in a TEM image with a chemical mapping technique (Figure 5c). This finding suggested that the uniformly chiral cinchona alkaloid-functionalities in catalyst **3** play an important role to dominate its catalytic performance discussed below.

#### Catalytic performance of the heterogeneous catalyst

#### Catalytic properties

Cinchona alkaloids are well-known as an efficient chiral catalyst to catalyze asymmetric epoxidation of various enones,<sup>[5, 16]</sup> As presented in this study, we examined the enantioselective performance of catalyst 3 in the asymmetric epoxidation of 4,4,4-trifluoro-1,3-diphenylbut-2-enone at first, where the methylhydrazine-induced epoxidation with 5.0 mol% of 3 as a catalyst under air atmosphere was investigated according to the reported method.<sup>[5a]</sup> It was found that the asymmetric epoxidation of 4,4,4-trifluoro-1,3diphenylbut-2-enone catalyzed by **3** gave phenyl((2R,3R)-3phenyl-3-(trifluoromethyl)oxiran-2-yl)methanone in a 96% yield with excellent diastereoselectivity (50:1) and enantioselectivity of 96% ee (Entry 1, Table 1), which was comparable to that of its homogeneous counterpart.<sup>[5a]</sup> Based on this excellent catalysis, direct transformation of 4,4,4trifluoro-1,3-diphenylbut-2-enone to (S)-4,4,4-trifluoro-3hydroxy-1,3-diphenylbutanone was performed through a

Table 1. The epoxidation-relay-reduction of  $\beta$  -trifluoromethyl-  $\beta,\beta$  -disubstituted enones.  $^{[a]}$ 

sequential epoxidation-relay-reduction process.<sup>[5a,5b]</sup> The results showed that this epoxidation-relay-reduction could afford the reductive products of (*S*)-4,4,4-trifluoro-3-hydroxy-1,3-diphenylbutanone in a quantitatively with the retained 96% *ee* value (Entry 1, Table 1). This finding offered an opportunity to test its enantiospecificity (%*es*) [%*es* = 100 (product *ee*)/(chiral intermediate *ee*)]. As observed, this enantioselective epoxidation-relay-reduction had excellent enantiospecificity (100%), indicating the superiority of this enantioselective relay reaction.

Having obtained an efficient epoxidation-relay-reduction, we further investigated its applicability with a series of  $\beta$ trifluoromethylated enones. As shown in Table 1, various  $\beta$ trifluoromethylated enones could be transformed steadily to the responding chiral products with high yields and enantioselectivities as shown in column 8-9 in Table 1. In order to compare their enantiospecificities, the single-step enantioselective epoxidation of  $\beta$ -trifluoromethylated enones to chiral epoxides<sup>[5a]</sup> catalyzed by **3** was also performed in column 5-7 in Table 1. As expected, these enantioselective epoxidation-relay-reduction had excellent enantiospecificities (more than 99%), confirming the benefit in the practical construction of enriched chiral β-CF<sub>3</sub>-substituted compounds. Also, it was found that the structures and electronic properties of substituents on the aromatic rings at  $R_1$  or  $R_2$ groups did not affect their enantiospecificity, where the asymmetric reactions with various electron-withdrawing and -donating substituents on the aryl moiety at  $R_1$  or  $R_2$  were equally efficient (Entries 2-12).

Entry	6a-6l	6a-6l (R <sub>1</sub> , R <sub>2</sub> )			7a-71 <sup>[b]</sup>	<b>7a-7l</b> <sup>[b]</sup>		8a-8l	
		$\mathbb{R}^1$	R <sup>2</sup>	Yield	% <i>ee</i> <sup>[c]</sup>	<b>dr</b> <sup>[d]</sup>	Yield	%ee <sup>[c]</sup>	
1	6a	Ph	Ph	96	96	50:1	95	96	>99
2	6b	p-FPh	Ph	95	94	100:1	96	94	>99
3	6c	p-ClPh	Ph	95	94	50:1	95	94	>99
4	6d	p-BrPh	Ph	93	94	50:1	94	95	>99
5	6e	p-MePh	Ph	97	96	50:1	93	97	>99
6	6f	p-MeOPh	Ph	94	96	100:1	94	97	>99
7	6g	Ph	p-FPh	95	95	100:1	95	96	>99
8	6h	Ph	p-ClPh	94	92	100:1	95	96	>99
9	6i	Ph	p-BrPh	93	94	100:1	93	97	>99
10	6i	Ph	<i>n</i> -MePh	96	96	25:1	93	96	>99



11	6k	Ph	p-MeOPh	95	96	100:1	94	96	>99
12	61	Ph	biphenyl	92	93	50:1	91	99	>99

<sup>[</sup>a] Reaction conditions: catalyst **3** (30.12 mg, 5.0 µmol of cinchona alkaloid 5.0%, based on TG analysis), trifluoromethylated enones (0.10 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (39.10 mg, 0.12 mmol, 1.2 equiv) in 5.0 nL (0.017 M) of methyl *tert*-butyl ether (MTBE) were added hydrazine (6.5 µL, 0.12 mmol, 1.2 equiv) at ambient temperature (25 °C). The mixture was then stirred at room temperature (25 °C) under air atmosphere for 6-18 h. After that, Zn (13.0 mg, 0.2 mmol, 2 equiv) and NH<sub>4</sub>Cl (8.0 mg, 0.15 mmol, 1.5 equiv) in 1.0 mL of EtOH was added, and the mixture was tirred at 40 °C for 2 h. [b] Data were obtained in single-step reactions. [c] The *dr* values were determined by <sup>1</sup>H NMR of the crude products (see SI in Figures S7). [d] The *ev* values were determined by chiral HPLC analysis (see SI in Figures S4-5). [e] The *ev* equals (*ee* of product)/(*ee* of chiral intermediate).

#### Investigating reaction rate of asymmetric epoxidation

Another aim in the design of the heterogeneous catalyst 3 expects to obtain a highly efficient epoxidation through the overcoming the intrinsic limitation of slow diffusion during the catalytic process. As observed, the single-step asymmetric epoxidation of 4,4,4-trifluoro-1,3-diphenylbut-2enone catalyzed by 3 could be completed within 6 h although its reaction time was longer than 4 h obtained with its homogeneous counterpart. This result suggested that this asymmetric epoxidation has a relatively fast reaction rate as a generally heterogeneous catalyst often needs an obviously longer reaction time than its corresponding homogeneous counterpart due to the slow diffusion. This observation indicated that the hydrophobic benefit of the organosilicate network in the designed catalyst 3 could promote the singlestep asymmetric epoxidation. In order to confirm the hydrophobic benefit of catalyst 3, this enantioselective epoxidation catalyzed a parallel inorganosilicate analogue 3' was compared, where its analogue 3' could be obtained through the co-condensation of tetraethoxysilane (instead of 1,2-bis(triethoxysilyl)ethane) and 3-(triethoxysilyl)propane-1-thiol following the similar synthetic process. Differented from catalyst 3 with organosilicate ethylene-bridged units as the silica network, this comparable inorganosilicate analogue 3' had inorganosilicate Si-O-Si-linked units as its silica network. It was found that the asymmetric epoxidation catalyzed by 3' was markedly slower than that attained with catalyst 3 (12 h for 3' versus 6 h for catalyst 3). This phenomenon demonstrated that the hydrophobic nature of 3 is beneficial to draw 4,4,4-trifluoro-1,3-diphenylbut-2-enone into the catalytically activity center in nanochannels from aqueous system, thereby accelerating reaction rates.<sup>[10]</sup> This judgment could further be proved by a kinetic investigation as shown in Figure 6, where the asymmetric epoxidation of 4,4,4-trifluoro-1,3-diphenylbut-2-enone catalyzed by its homogeneous counterpart, catalyst 3 and its analogue 3' were performed. The results showed that the enantioselective reaction catalyzed by 3 resulted in an initial activity higher than that achieved with its inorganosilicate analogue **3**' (the initial TOFs were 4.0 molmol<sup>-1</sup>h<sup>-1</sup> for **3**' versus 6.6 molmol<sup>-1</sup>h<sup>-1</sup> for **3**).



Figure 6. Comparison of the enantioselective epoxidation-reduction of 4,4,4-trifluoro-1,3-diphenylbut-2-enone catalyzed by its homogeneous counterpart (2), catalyst 3 and its inorganosilicate analogue 3'. Reactions were carried out using 5 mol% of catalysts.

#### Catalyst recycling and reuse

In addition to the aim for construction of optically pure  $\beta$ trifluoromethyl-β-hydroxy ketones, an important consideration is the ease of separation for the heterogeneous catalyst 3, and the recycled heterogeneous catalyst 3 can retain its reactivity and enantioselectivity after multiple recycling. As observed, the heterogeneous catalyst 3 could be recovered easily from the reaction system by simple centrifugation. As shown in Table 2, in eight consecutive reactions, the recycled heterogeneous catalyst 3 still produced chiral products with 91% yield and 95% ee in the asymmetric epoxidation of 4,4,4-trifluoro-1,3-diphenylbut-2-enone to phenyl((2R,3R)-(3-phenyl-3-(trifluoromethyl)oxiran-2yl)methanone.

Table 2. Reusability of catalyst 3 for asymmetric epoxidation of 4,4,4-trifluoro-1,3-diphenylbut-2-en-1-one to phenyl ((2R,3R)-3-phenyl-3-(trifluoromethyl)oxiran-2-yl)methanone.
b]

Run time	1	2	3	4	5	6	7	8
% Conversion	98	96	95	95	95	95	94	91
% ee	96	96	96	96	96	96	96	95

[a] Reaction conditions: catalyst **3** (301.20 mg, 5.0  $\mu$ mol of cinchona alkaloid 5.0%, based on TG analysis), trifluoromethylated enones (1.0 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (1.20 mmol, 1.2 equiv) in 20.0 mL (0.017 M) of methyl *tert*-butyl ether (MTBE) were added hydrazine (1.2 mmol, 1.2 equiv) at ambient temperature (25 °C). The mixture was then stirred at room temperature (25 °C) under air atmosphere for 6 h. [b] Determined by chiral HPLC analysis (see SI in Figure S6).

#### Conclusion

In conclusions, we develop an ethylene-bridged chiral cinchona-functionalized mesoporous silica, which enables an efficiently epoxidation-relay-reduction, converting achiral  $\beta$ trifluoromethyl- $\beta$ , $\beta$ -disubstituted enones to chiral βtrifluoromethyl-\beta-hydroxy ketones with up to 99% ee and more than 99% enantiospecificity. As presented in this study, hydrophobic periodic mesoporous organosilica, uniformly distributed active species, and confined cinchona alkaloid catalytic nature are responsible for its highly catalytic performance. Furthermore, the heterogeneous catalyst could also be recovered easily and reused repeatedly eight times without obvious effect on its reactivity in the enantioselective epoxidation of 4,4,4-trifluoro-1,3-diphenylbut-2-enonee, affording a practical approach for construction of valuable chiral β-CF<sub>3</sub>-substituted molecules.

#### **Experimental Section**

Preparation of the heterogeneous Catalyst 3. In a typical synthesis, a dry 50 mL round-bottom flask was charged with SH@Et@MNPs (1) (0.50 g), chiral cinchona alkaloid (2) (309.0 mg, 0.50 mmol), and 2.0 mol% of 2,2-dimethoxy-1,2diphenylethanone photoinitiator, backfilled with argon, and irradiated for 27 h with a 15 W blacklight ( $\lambda_{max} = 365$  nm). The resulting solid was filtered through filter paper and rinsed with excess methanol and dichloromethane. After Soxlet extraction in dichloromethane solvent for 12 h to remove any homogeneous and unreacted starting materials, the solid was dried overnight at 60°C under vacuum to afford the heterogeneous catalyst (3) (0.58 g) as a light-yellow powder. IR (KBr) cm<sup>-1</sup>: 3425.3 (s), 2919.9 (w), 2849.9 (w), 1490.1 (w), 1411.6 (m), 1167.5 (s), 1037.1 (s), 872.7 (m), 767.9 (m), 698.3 (m), 445.5 (m). <sup>13</sup>C CP MAS NMR (161.9 MHz): 162.1–112.2 (<u>C</u> of Ar, Ph and CF<sub>3</sub>), 73.2–49.0 ( $\underline{C}$  of cyclic alkyl groups in cycling group connected to N atom, of -CHOH, and of -OCH3, and C of -NCH2 and -NCH3 in CTAB molecule), 46.5-31.2 (C of -SCH2CH2CH2Si, and of -CH2CH2CH2NCH3), 23.5 (C of -SCH2CH2CH2Si, of -CH2CH2-, and of cyclic alkyl groups in cycling group without connected to N atom in CTAB molecule), 13.3 (13.4 ( $\underline{C}$  of  $-CH_2\underline{C}H_3$  in CTAB molecule), 5.9 ( $\underline{C}$  of  $-\underline{C}H_2Si$ ) ppm. <sup>29</sup>Si MAS/NMR (79.4 MHz): T<sup>2</sup> ( $\delta$  = -59.5 ppm), T<sup>3</sup> ( $\delta$  = -67.2 ppm). Elemental analysis (%): C 18.15, H 2.83, N 0.56, S 0.88.

General procedure for the enantioselective epoxidation-relay-reduction of βtrifluoromethyl- $\beta$ , $\beta$ -disubstituted enones. A typical procedure was as follows: To a stirred suspension of catalyst 3 (30.12 mg, 5.0 µmol of cinchona alkaloid 5.0%, based on TG analysis), trifluoromethylated enones (0.10 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (39.10 mg, 0.12 mmol, 1.2 equiv) in 5.0 mL (0.017 M) of methyl tert-butyl ether (MTBE) were added hydrazine (6.5 µL, 0.12 mmol, 1.2 equiv) at ambient temperature (25 °C). The mixture was then stirred at the same temperature under air atmosphere for 6-18 h. During this period, the reaction was monitored constantly by TLC. When the reaction was completed, catalyst was separated by centrifugation (10,000 rpm) for the recycling experiment. Aqueous solution was added Zn (13.0 mg, 0.2 mmol, 2 equiv) and NH<sub>4</sub>Cl (8.0 mg, 0.15 mmol, 1.5 equiv) in 1.0 mL of EtOH, and the mixture was stirred at 40 °C for 2 h. The reaction was then quenched with water. Aqueous layer was extracted with ethyl ether (3  $\times$  3.0 mL). The combined ethyl ether extracts were washed with NaHCO\_3 and brine, and then dehydrated with Na<sub>2</sub>SO<sub>4</sub>. 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 <sup>1</sup>H-NMR, and the ee values were determined by a HPLC analysis using a UV-Vis detector and a Daicel chiralcel column ( $\Phi$  0.46  $\times$  25 cm).

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# **Entry for the Table of Contents** (Please choose one layout only) Layout 2:

Heterogeneous Asymmetric Catalysis

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ACinchonaAlkaloid-FunctionalizedMesostructuredSilicaforConstructionGenrichedChiralβ-Trifluoromethyl-β-HydroxyKetonesoverKetonesoverAnEpoxidation-Relay-ReductionProcessF



A cinchona alkaloid-functionalized mesostructured silica enables an efficient asymmetric epoxidation of achiral  $\beta$ -trifluoromethyl- $\beta$ , $\beta$ -disubstituted, where these chiral products can be converted conveniently into enriched chiral  $\beta$ -trifluoromethyl- $\beta$ -hydroxy ketones

through a sequential epoxidationrelay-reduction process. The superior catalytic performance are attributed to hydrophobic mesoporous organosilica network, uniformly distributed active species, and confined cinchona alkaloid catalytic nature.