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# Construction of Pyridine-Based Chiral Ionic Covalent Organic Frameworks as a Heterogeneous Catalyst for Promoting Asymmetric Henry Reactions

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rganic cationic ionic liquids (OCILs) have offered a promising template as an efficient homogeneous catalyst.<sup>1</sup> However, the procedure for the most OCIL-involved reactions is complicated, in particular for the separation of products from the reaction mixture and recovery of OCILs. Furthermore, the recycling of OCILs is normally not environmentally benign.<sup>2,3</sup> "Immobilization" of OCILs via the host-guest encapsulation seems to be an optimal strategy, which can not only remain the catalytic function of OCILs, but also simplify the workup procedure leading to a "greener" process. Introduction into the rigid supports such as porous materials and polymers has offered a possible strategy to immobilize OCILs.4-6 However, the OCILs-immobilized catalysts reported so far had rather low catalytic performance.<sup>7–9</sup> Thus, it is still a challenge for the immobilization of OCILs, which can facilitate the heterogeneous catalytic procedure with high catalytic performance.

In an effort to immobilize OCILs and make chiral covalent organic framework (COF)-based heterogeneous catalysts,<sup>10</sup> we prepared the pyridine-based COFs via the condensation of the predesigned monomer 2,4,6-(4'-triaminophenyl) pyridine (TPP) with 2-hydroxyl tribenzaldehyde (HTD). So far, three strategies for the preparation of chiral COFs were summarized in literature including postsynthesis, direct synthesis, and chiral induction synthesis.<sup>11–14</sup> Herein, the chiral auxiliary was introduced by the post modification of pyridine unit leading to the pyridinium salts in COFs. The ionized COFs remained the highly crystalline structure with the chiral auxiliary arranged in an ordered manner in the framework.

As a proof of concept, the resultant chiral OCIL-based COFs as heterogeneous catalysts were employed to catalyze asymmetric Henry addition<sup>15</sup> reactions of nitromethane with substituted benzaldehydes. Even though the heterogeneous catalysts involving metal complex,<sup>8</sup> sieve,<sup>16</sup> organic polymer, and etc. have been utilized for Henry reaction, these complexes always had rather low yield (15-82.4%) and stereoselectivity  $(7-40\% \ ee)$ . Interestingly, with the heterogeneous catalysts involving the chiral COFs first employed for the enantioselective Henry reactions, excellent yields and stereoselectivity (up to 97% yield and 92% ee, respectively) were realized. Furthermore, the catalysts can be easily recovered and recycled without a notable loss of the catalytic performance. The proposed catalytic mechanism suggested that the synergistic effect between the pyridinium salts and the COF template played a critical role in promoting the enantioselective Henry reactions. Herein, we report our preliminary studies on the first examples of chiral OCIL-based COFs as heterogeneous catalysts in asymmetric synthesis.

The solvothermal synthesis of TPP-HTD COF starting from TPP and HTD via imine formation was performed in mixed solvent systems with acetic acid as the catalyst (Figure 1a). It

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**Figure 1.** (a) Synthesis of TPP-HTD COF and CCLSM-1. (b,c) PXRD Patterns of TPP-HTD COF and CCLSM-1. (d) Representation of AA and AB Stacking Modes of TPP-HTD COF.

was found that the mixed solvent containing 1,2-dichlorobenzene and *n*-butanol in a ratio of 1:5 (v/v) resulted in the construction of TPP-HTD COF with a high crystallinity successfully (Table S1 and Figure S1). The post modification of TPP-HTD COF with (S)-prolinol bromoacetate in acetonitrile at room temperature leading to the generation of pyridinium salts furnished the chiral ionic COF, CCLSM-1 (the immobilized OCILs based on COFs).

The powder X-ray diffraction (PXRD) analysis was performed to determine the crystalline structure of TPP-HTD COF (Figures 1b, S2, and S3). As shown in Figure 1b, the experimental PXRD pattern of TPP-HTD COF displayed five prominent diffraction peaks at  $2\theta = 5.47^{\circ}$ ,  $9.55^{\circ}$ ,  $11.08^{\circ}$ ,  $14.63^{\circ}$  and  $25.35^{\circ}$ , which could be assigned to the (100), (110), (200), (3-10), and (101) facets of the crystalline, respectively. The Pawley-refined PXRD profile of AA stacking is highly consistent with the experimental pattern with Rwp<sub>TOP</sub> = 4.37%. Thus, comparison of the experimental and the simulated PXRD patterns suggested that TPP-HTD COF adopted the eclipsed AA stacking mode (Figure S4 and Figure 1d). Interestingly, the PXRD pattern of the chiral ionic COF, CCLSM-1, indicated the good crystallinity of the post synthesized product and analogous diffraction facets to its precursor was observed. However, due to the presence of the chiral auxiliary in the channel of the 2D COFs, the pore size of CCLSM-1 is expected to be reduced, and thus, it was shown that the main peaks in the PXRD image of CCLSM-1 shifted  $0.16^{\circ}$  toward the right side (Figure 1c).

Compared to that of TPP, the Fourier Transform Infrared (FT-IR) spectra of TPP-HTD COF and CCLSM-1 (Figure 2a) exhibited a new absorption band at 1620 cm<sup>-1</sup>, which corresponded to the stretching vibrations of C==N groups, indicative of the presence of the Schiff-base linkages in the TPP-HTD COF and chiral ionic COF, CCLSM-1. The



Figure 2. (a) FT-IR spectra of TPP, TPP-HTD COF, and CCLSM-1. (b) Raman spectra of CCLSM-1.

absorptions at 1460 cm<sup>-1</sup> are characteristic for the vibrations of aromatic C=N groups in pyridine units. The FT-IR spectrum of CCLSM-1 also showed the vibration absorptions of pyridinium C-N bonds at 1280 cm<sup>-1</sup> and the ester C-O units at 1050 cm<sup>-1</sup>, which were absent in the spectrum of TPP-HTD COF, indicating that the pyridinium salts were successfully formed by the post modification of the pyridine moieties in TPP-HTD COF with the bromoacetate derivative. The Raman spectrum of CCLSM-1 (Figure 2b) exhibited the characteristic out-of-plane vibrations of methylene at 1335  $cm^{-1}$  and the antisymmetric vibration of C–N (pyridine) at 1449 cm<sup>-1</sup> further suggesting the presence of the chiral prolinol group introduced into COFs. The N<sub>2</sub> sorption measurement at 77 K was performed to analyze the pore characters of TPP-HTD COF and chiral ionic COF, CCLSM-1 (see Figure S4 and the corresponding discussions). The structures of TPP-HTD COF and CCLSM-1 were further characterized by <sup>13</sup>C NMR in their solid states (Figures S5 and S6). Furthermore, the zeta potential and potential distribution of TPP-HTD COF and CCLSM-1 were obtained in the Figure S7, which displayed the significant potential increase from the TPP-HTD COF to the ionic CCLSM-1. The thermal stability of the TPP-HTD COF and CCLSM-1 was investigated by the thermogravimetric analysis (TGA), and the results showed that the as-synthesized ionized COF had the similar thermal stability with the TPP-HTD COF (Figure S8). And the TPP-HTD COF has good chemical stability (Figure S9). Especially, CCLSM-1 exhibited Cotton effects in the solid-state circular dichroism (CD) spectra (Figure S10). The X-ray photoelectron spectroscopy (XPS) spectra provided an insight into the presence of different nitrogen forms in the TPP-HTD COF and CCLSM-1, and the bromine element in the ionic CCLSM-1. The results indicate the successfully partial formation of pyridinium salts in CCLSM-1 which are in good agreement with the pore size distribution results obtained for CCLSM-1 (see Figure S12, Table S3, and the corresponding discussions).

The scanning electron microscopy (SEM) images of TPP-HTD COF and CCLSM-1 suggested that the TPP-HTD COF was synthesized as island-like sheets and the as-synthesized the chiral ionic COF, CCLSM-1, was obtained as spherical particles with diameters of ~400 nm probably due to the presence of the electrostatic interaction between layers (Figure 3). The high resolution transmission electron microscopy (HRTEM) image of CCLSM-1 displayed two different types of lattice fringe spacing (Figure 3: D1 and D2). The lattice fringe spacing with a value of 0.306 nm actually represented the interlamellar spacing of TPP-HTD COF and the one with 0.244 nm suggested that of CCLSM-1, respectively, which were both in good agreement with those obtained from PXRD refinement.



**Figure 3.** (a,b) SEM images of CCLSM-1 and TPP-HTD COF. Inset: zoomed-in image within the annotated area. (c) HRTEM images of CCLSM-1. Inset: the lattice of CCLSM-1. Right: the distributions of the lattice distance on the line D1 and D2.

Next, the asymmetric catalytic performance of the resulted OCIL-based chiral COF catalyst was investigated. The asymmetric Henry addition reaction of nitromethane with a representative series of aromatic aldehydes involving CCLSM-1 as heterogeneous catalysts (10 mol %) was evaluated at rt. Nitromethane was employed both as the reactant and the solvent. The catalytic results with different substrates are summarized in Table S5.

As shown in Table S5 (entry 1), in the presence of CCLSM-1, the Henry reaction of nitromethane with benzaldehyde furnished the desired nitroaldol product in good yield (85%) with decent enantioselectivities (69% enantiomeric excess, ee). The aromatic aldehydes (entries 2-7) bearing electronwithdrawing moieties under the same conditions led to the nitroaldols in good to excellent yields (72-97%) with good to excellent enantioselectivities obtained (72-92% ee). The highest yield of 97% was realized for 4-nitro benzaldehyde with the greatest enantioselectivity (92% ee). Interestingly, it was shown that in the presence of an electron-donating unit at the para-position of the aromatic aldehyde, the nitroaldol products were obtained in a poor yield with low enantioselectivities (entries 7 and 8). For a comparison, the Henry reaction of nitromethane with 4-nitro benzaldehyde in the absence of CCLSM-1 was investigated, and it was shown that only trace amounts of the nitroaldol product resulted (entry 8). In the presence of TPP-HTD COF, the precursor to CCLSM-1, under the same conditions, the desired product was only obtained in 12%.

As is shown above, the catalytic performance of the immobilized OCIL remained and thus it would be of interest to further examine the recyclability of the heterogeneous OCIL-based COF catalysts. The recyclable performance of CCLSM-1 was then investigated by evaluating the Henry reaction of nitromethane with 4-nitro benzaldehyde. After the reaction, the catalysts were recovered by simple filtration and dried for the second cycle. The residual weights of dry CCLSM-1 catalyst were recorded after each cycle, and up to 5 cycles performed. The results are summarized in Table 1 and

# Table 1. Recycling Performance of CCLSM-1 in Asymmetric Henry Reactions<sup>a</sup>

cycle	residual weight (mg)	time (h)	yield <sup>b</sup> (%)	% ee <sup>c</sup>
1	26.0	24	97	92
2	25.9	24	96.2	90
3	25.9	24	95.5	89
4	25.8	24	95	89
5	25.7	24	95	89

<sup>*a*</sup>All reactions were carried out with 0.5 mmol *p*-nitrobenzaldehyde and 2 mL nitromethane. <sup>*b*</sup>Isolated yield after chromatographic purification. <sup>*c*</sup>Determined by chiral HPLC.

demonstrated in Figure S13. As is shown, almost no weight loss of the heterogeneous catalysts can be observed and the yield of the nitroaldol product remained excellent (above 95%) after 5 cycles. The enantioselectivities only slightly reduced (shown in cycles 3-5). The overall results suggested that the immobilized OCIL in COF exhibited excellent recyclability as shown in Figure S13.

The influence of the amount of the chiral moiety introduced at the pyridine nitrogen of the initial COF on the catalytic performance under the same reaction conditions have also been evaluated in Figure S14 (see the detailed discussions in SI).

To further understand the role of the immobilized OCIL in COF played in the promoting the Henry reaction and the sense of the asymmetric induction imparted, a plausible catalytic cycle was proposed involving the transition model (Figure 4), which is based on the previously reported steric and electronic considerations.<sup>17–19</sup>



Figure 4. Plausible catalytic mechanism of CCLSM-1 for Henry addition reaction.

As shown, the ionic pyridinium bromide has a resonance structure which can be stabilized by the two-dimensional framework with widely expanded  $\pi$ -conjugations. It is believed that the chiral OCIL-based COF actually played a dual role in promoting the asymmetric Henry addition reactions. First, nitromethane was deprotonated by the residual basic pyridine unit in the framework. The static charge interaction between the negative charged oxygen of the nitromethane and the pyridinium unit can favorably occur from the bottom due to the steric interaction above induced by the presence of the chiral prolinol moiety. The nucleophilic attack of the nitromethane to Si-face of the aromatic aldehyde followed by

protonation furnished the nitroaldol products mainly with the absolute R configuration.

In summary, "immobilization" of OCILs in COF was realized by the post modification of the pyridine-based COF via the formation of pyridinium salts with the chiral prolinol bromoacetate derivative leading to the highly crystalline chiral ionic COFs, CCLSM-1. The resultant chiral ionic COF material as a heterogeneous catalyst not only remained the catalytic function of OCILs, but also simplify the workup procedure leading to a "greener" process, as demonstrated in asymmetric Henry reactions. Up to 97% yield and 92% ee were realized, and the catalysts can be readily recovered and recycled without loss of the catalytic performance. A plausible catalytic cycle was proposed to further understand the role that the immobilized OCIL in COF played in promoting the Henry reaction and the sense of the asymmetric induction imparted. The results suggested that the immobilization of OCILs by the post modification of COFs is an optimal strategy, which can facilitate the heterogeneous catalytic procedure involving OCILs. Expanding of this methodology in catalyzing various asymmetric organic reactions is in progress.

# ASSOCIATED CONTENT

## **Supporting Information**

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c00175.

Characterization data of all the monomers, linkages and the COFs such as liquid and solid NMR, TGA, EDS, CD spectra and crystal data of COFs and the HPLC profile and <sup>1</sup>H NMR characterization of catalytic product (PDF)

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#### Notes

The authors declare no competing financial interest.

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