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A Porous Cu(II)-MOF with Proline Embellished Cavity: Cooperative Catalysis for the Baylis-Hillman Reaction

Dinesh De, Tapan K. Pal, and Parimal K. Bharadwaj*

Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur 208016, India

Supporting Information

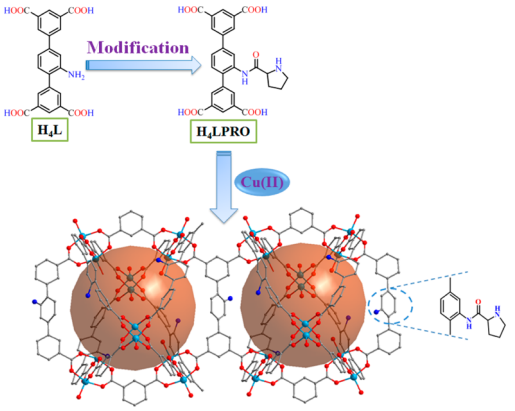
ABSTRACT: L-Proline has been covalently attached in a rigid linear ligand, H_4L, having an isophthalate moiety at each terminal to form the chiral ligand, H_4LPRO. This linker has been used for the construction of a porous MOF, $L_{Cu}PRO$. The free L-proline moiety in the cavity of the framework in the presence of imidazole as a cocatalyst functions synergistically to catalyze the Baylis−Hillman reaction between α,β-unsaturated carbonyl compounds and aromatic aldehydes. High porosity of the framework is proven by the nitrogen adsorption isotherm.

Transition metal complexes have been extensively used as homogeneous catalysts over the years. These metal ions can be used with linkers of different topologies to construct porous metal−organic frameworks (PMOFs). When the metal ions in these PMOFs possess open coordination sites, they can be used along with the coordination space to efficiently act as heterogeneous catalysts.[1] Moreover, in PMOFs, a functional group can sometimes be integrated in the ligand to furnish a unique catalytic site.[2] Incorporation of urea and pyrrolidine in PMOFs are well documented.[3] Importantly, with the incorporation of a chiral group in the ligand, the derived MOF will become homochiral.[4] Motivated by supramolecularly organized homogeneous chiral catalysis reactions, the employment of chiral functional group in the linkers to have homochiral organocatalytic PMOFs is quite fascinating and has been reported in the literature.[5]

Most of the natural amino acids are cheap and may be considered as an enantiopure ligand for the construction of the chiral MOFs.[6] But their flexible nature poses problems in constructing MOFs with large cavities. An easier way would be the attachment of a chiral amino acid covalently to a rigid linker. Inspired by the excellent structure of our earlier framework L_{Cu},[7] we have modified the ligand H_4L into an enantiopure ligand H_4LPRO by attaching a proline group (see Scheme 1) which has been used in many asymmetric reactions.[8] There are few L-proline (hereafter only proline) based homochiral MOFs reported in the literature. Thus, proline incorporation in MOF was performed by post-synthetic coordination on open metal sites in MIL-101[9] and post-synthetic amide coupling[10] or post-synthetic click reactions.[11] In a recent report, the proline moiety has been covalently attached to a linker prior to MOF construction for heterogeneous catalysis of asymmetric aldol reactions.[12]

Herein, we report the synthesis of the enantiopure ligand H_4LPRO (Scheme 1) for the construction of a noninterpenetrated homochiral MOF, $L_{Cu}PRO$. This MOF has been characterized by single crystal X-ray diffraction, powdered X-ray diffraction, digestion NMR, and solid state circular dichroism (CD) spectra (Supporting Information (SI)). The porous $L_{Cu}PRO$ together with cocatalytic amount of imidazole has been used to explore the Baylis−Hillman (BH) reaction between an aldehyde and an α,β-unsaturated carbonyl compound to form α-methylene-β-hydroxy carbonyl derivatives. The BH reaction has emerged as a synthetically highly versatile process[13] with atom economical carbon−carbon bond formation at the α position with respect to the activated alkene. A number of studies are reported in the literature on the homogeneous catalysis of the BH reactions. Here, we show the BH reaction being catalyzed by a Cu-MOF acting as a heterogeneous catalyst.

Scheme 1. Modification of the Ligand and Crystal Structure of $L_{Cu}PRO$



The ligand H_4LPRO was synthesized in four steps via the reaction of *N*-(*tert*-butoxycarbonyl)-L-proline and L_1 by slightly modifying a procedure described by Telfer et al.[12a] (Scheme S1, SI). The ligand, H_4LPRO, reacts with $Cu(NO_3)_2{\cdot}3H_2O$ (1:3 molar ratio) solvothermally to form blue colored block shaped crystals of $L_{Cu}PRO$ (Scheme 1). Structural analysis by X-ray crystallography divulges that the framework is isoreticular with our previously reported PMOF, L_{Cu}.[7] In the present case, due to heavy disordering, the proline side chain in the PMOF $L_{Cu}PRO$ could not be located in the electron density map and thus could not be established by single crystal X-ray structural analysis. Its presence in the PMOF has been established by the combination of ^1H NMR and ESI-MS analysis of a digested sample of the

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PMOF (in D_2SO_4/DMSO-d_6). The ^{1}H NMR spectroscopy (Figure S5, SI) unambiguously reveals that the **H_4LPRO** ligand does not decompose during the MOF synthesis and matches perfectly with that of the pure ligand, **H_4LPRO** in DMSO-d_6 (Figure S2, SI). The integrity of the linker is further corroborated by the ESI-MS analysis of the digested sample (Figure S6, SI), which shows a prominent peak at m/z 519 corresponding to $[\mathbf{H_4LPRO} + H]^+$.

The parent PMOF $\mathbf{L_{Cu}}$ crystallizes in the trigonal space group $R\bar{3}m$. In the case of the PMOF $\mathbf{L_{Cu}PRO}$, the diffraction data could be found to be consistent with the trigonal space group $R\bar{3}$. This trigonal space group cannot be the true space group due to the chirality of the proline moiety. But because of the lack of long-range order of the chiral side arm and the rigid architecture of the remaining part of the molecule, the structure equates to a nonchiral space group with statistical disordering of the proline group over four sites.[12] The asymmetric unit consists of half of the $\mathbf{LPRO}^{4-}$ ligand and Cu_2 paddle-wheel SBU. Each Cu(II) ion in the SBU exhibits square pyramidal coordination geometry with equatorial coordination from four different bridging carboxylates and an aqua ligand bound axially (Figure 1a).

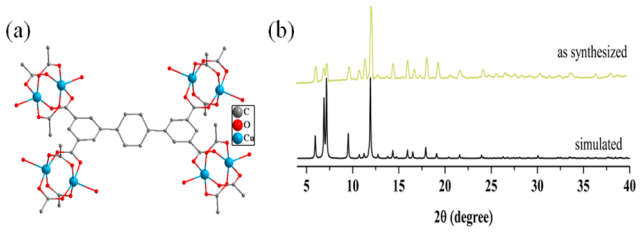


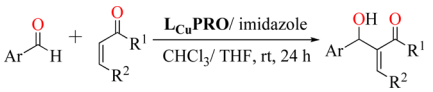
Figure 1. (a) Coordination environment around Cu^{2+} ions in $\mathbf{L_{Cu}PRO}$ (H atoms and side proline part of the ligand **H_4LPRO** are not shown). (b) PXRD pattern simulated from the CIF file (bottom) and PXRD pattern of as synthesized $\mathbf{L_{Cu}PRO}$ (top).

The Cu···Cu distance in the SBU is 2.658(1) Å, which compares well with the similar reported structure.[14] All Cu−O bond lengths are comparable to the literature known Cu(II)-containing complexes.[15] These SBUs are propagated in all directions without any interpenetration, forming a robust structure with large cages (Scheme 1) of dimension 14.072 Å (distance refers to atom-to-atom connection) occupied by DMF and water as guests. The framework is also porous like $\mathbf{L_{Cu}}$ and exhibits a void volume of ∼63.1% (including the proline side-group; 62.2% for $\mathbf{L_{Cu}}$) as calculated by PLATON.[16] The experimental powder X-ray diffraction (PXRD) pattern for bulk samples of $\mathbf{L_{Cu}PRO}$ matched closely to the simulated pattern (generated from the CIF file) confirming the bulk phase purity (Figure 1b).

The TGA curve of $\mathbf{L_{Cu}PRO}$ (Figure S9, SI) shows a weight loss of 24.35% due to the removal of guest lattice DMF and coordinated and lattice water molecules and is stable up to ∼300 °C. The compound is insoluble and stable in common organic solvents as confirmed from PXRD measurements (Figure S10, SI). To measure the permanent porosity of $\mathbf{L_{Cu}PRO}$, the activated $\mathbf{L_{Cu}PRO}$ was subjected to the nitrogen gas sorption measurements at 77 K. The desolvated $\mathbf{L_{Cu}PRO}$ exhibits an initial type-I isotherm up to the relative pressure of 0.7 and afterward shifted to type-IV[17] as in the case of $\mathbf{L_{Cu}}$ (Figure S11, SI). The calculated Brunauer−Emmett−Teller (BET) surface area is found to be 920 $m^2\ g^{-1}$ with a pore volume of 0.82 $cm^3\ g^{-1}$. Thus, the surface area and pore volume are lower than those of $\mathbf{L_{Cu}}$ (BET surface area 1952 $m^2\ g^{-1}$ and pore volume 0.98 $cm^3\ g^{-1}$). The reduced surface area and pore volume in $\mathbf{L_{Cu}PRO}$ are considerably influenced by the flexible proline groups which project into the channels of the structure and occupy the free space.

The presence of free proline moiety in the framework led us to explore the catalytic activity of the Baylis−Hillman reaction. Our interest in the Baylis−Hillman reaction is due to the fact that it is atom economical and forms specific carbon−carbon bonds along with the generation of functional groups for further use.[18] This reaction can be done by using a Lewis base, typically a tertiary amine like DABCO or a tertiary phosphine. But the reactions suffer from low reaction rates, and therefore, Lewis bases in combination with catalyst components capable of activating the carbonyl functions are used to accelerate the reaction rate.[19] The amino acid, L-proline provides extensive opportunities as a homogeneous organo-catalyst in various organic transformations.[8] However, homogeneous catalysts are very often difficult to recover, and/or they decompose during the catalytic reaction. In order to surmount these limitations, researchers have developed methods to fix the catalyst in a solid support. In recent times, the supported-proline moiety is found to be a good heterogeneous catalyst.[20] In this regard, we sought to explore the possibility of synergistic effects between two distinct cocatalytic entities, $\mathbf{L_{Cu}PRO}$ and imidazole. The methyl vinyl ketone (MVK)-based BH reaction (Table 1) is currently a subject of extensive

Table 1. Results Obtained for the Baylis−Hillman Reactions Catalyzed by $\mathbf{L_{Cu}PRO}$/ Imidazole[a]



entry	Ar	R^1, R^2	catalyst	% yield[b]
1	4-NO_2Ph	CH_3, H	$\mathbf{L_{Cu}PRO}$/imidazole	75
2	3-NO_2Ph	CH_3, H	$\mathbf{L_{Cu}PRO}$/imidazole	69
3	2-NO_2Ph	CH_3, H	$\mathbf{L_{Cu}PRO}$/imidazole	66
4	4-FPh	CH_3, H	$\mathbf{L_{Cu}PRO}$/imidazole	62
5	Ph	CH_3, H	$\mathbf{L_{Cu}PRO}$/imidazole	50
6	4-CH_3Ph	CH_3, H	$\mathbf{L_{Cu}PRO}$/imidazole	41
7	4-NO_2Ph	C_2H_5, H	$\mathbf{L_{Cu}PRO}$/imidazole	64
8	4-NO_2Ph	OCH_3, H	$\mathbf{L_{Cu}PRO}$/imidazole	57
9	4-NO_2Ph	$-(CH_2)_3-$	$\mathbf{L_{Cu}PRO}$/imidazole	61
10	4-NO_2Ph	CH_3, H	**H_4LPRO**/imidazole	32
11	4-NO_2Ph	CH_3, H	imidazole	trace
12	4-NO_2Ph	CH_3, H	$\mathbf{L_{Cu}PRO}$	trace

[a]Reaction conditions: aldehyde (0.1 mmol), carbonyl (0.2 mmol) in 1 mL of $CHCl_3$/THF (1:1), cat. $\mathbf{L_{Cu}PRO}$ (10 wt %), and imidazole (10 mol %), 25 °C for 24 h. [b]Isolated yields after silica gel chromatography.

investigation in asymmetric catalysis.[18,21] In analogy to Shi et al.,[22] we seek the combination of a nucleophilic catalyst, imidazole, with $\mathbf{L_{Cu}PRO}$ for the BH reaction. Among the variety of BH reactions, that of MVK with 4-nitrobenzaldehyde is chosen as a model reaction (entry 1). As shown in Table 1, imidazole (10 mol %) in the absence of $\mathbf{L_{Cu}PRO}$ (entry 11) catalyzes the reaction between MVK and aldehyde (<4% yield, 48 h) very sluggishly. Also, the use of $\mathbf{L_{Cu}PRO}$ alone (entry 12) provides no product in the same time length. Yet, when the two are employed together (entry 1), a facile reaction occurs (75% yield, 24 h). Notably, the product is nearly racemic (Figure S12, SI), indicating the influence of the L-proline chirality to be minimal.[22]

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Based on these results, a range of aromatic aldehydes were employed in the coupling of MVK under optimized reaction conditions using $\mathbf{L_{Cu}PRO}$ with imidazole as the catalytic system. The results are listed in Table 1. The corresponding adducts are obtained in good yields. For 3-nitrobenzaldehyde, 2-nitrobenzaldehyde, and 4-fluorobenzaldehyde, similar results are obtained (entries 2−4). However, for benzaldehyde or 4-methylbenzaldehyde, the products are obtained only in moderate yields (entries 5 and 6). Further, we have extended different α,β-unsaturated carbonyls such as ethyl vinyl ketone, methyl acrylate, and cyclohexenone for the model BH reaction (entries 7−9). In each case, the yield is fair to good. The formation of the desired product was confirmed by the ^{1}H NMR and ^{13}C NMR (Figures S18−S35, SI), and improvement of the reaction is monitored by TLC. It should be pointed out that, in all cases, the products are obtained with very low ee values (5−8%).

To demonstrate the heterogeneous nature of $\mathbf{L_{Cu}PRO}$, the filtration test was performed (see SI), which authenticated no catalytically active species leached into the liquid phase, and the conversion was only possible with the solid catalyst ($\mathbf{L_{Cu}PRO}$) along with cocatalyst. After being recovered using filtration and washing, $\mathbf{L_{Cu}PRO}$ could be subsequently used in the successive runs. The catalytic activity of $\mathbf{L_{Cu}PRO}$ experienced only a slight degradation after three cycles (see Figure S16, SI); meanwhile, it always retained its crystallinity, as determined by PXRD (Figure S17, SI). N_2 gas sorption measurement at 77 K of recovered $\mathbf{L_{Cu}PRO}$ after three catalytic cycles does not show any significant adsorption, presumably due to collapse of the framework during activation (Figure S36, SI).

In summary, we report herein one enantiopure organic ligand $\mathbf{H_4LPRO}$ with a flexible L-proline-functionalized side group and rigid isophthalate units at each terminal, which has been rationally designed and employed to construct the chiral PMOF $\mathbf{L_{Cu}PRO}$. The L-proline-functionalized PMOF along with imidazole nucleophile have been found to function synergistically as cocatalysts for the ketone-based Baylis−Hillman reaction. To the best of our knowledge, it is the first Baylis−Hillman reaction catalyzed by a PMOF functionalized with L-proline.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.6b01211.

Experimental details, characterization procedures, crystallographic data with refinement details, selected bond lengths and angles, TGA, PXRD patterns, N_2 sorption isotherms (PDF)

X-ray crystallographic information for CCDC No. 1480085 (CIF)

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■ AUTHOR INFORMATION

Corresponding Author

*E-mail: pkb@iitk.ac.in.

Notes

The authors declare no competing financial interest.

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