

Asymmetric Cascade Catalysis with Chiral Polyoxometalatebased Frameworks: Sequential Direct Aldol and Epoxidation Reactions

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Abstract: Catalytic asymmetric cascade reactions in which the substrates are transferred through a well-choreographed consecutive independent step by a single catalyst have received an increasing interest. By incorporating a chiral organocatalyst pyrrolidine, an oxidation catalyst polyoxometalate and a Lewis acid catalyst copper(II) into a single porous coordination network (PCN), two enantiomorphs CuW-PYIs with novel Kagomé lattice are achieved and applied in the conversion of aldehyde with ketone into value-added chiral epoxy ketone via a one-pot procedure. The chiral pyrrolidine organocatalysts interact with carbonyl group of ketones throughout the reaction, which is beneficial to achievement of compatibility between reaction intermediates and synergy of the multiple catalytic cycles, thus driving the direct aldol/epoxidation cascade reaction in orderly and asymmetrical way. Moreover, 'twocenter catalysis' principle is well demonstrated in the direct aldol/epoxidation cascade reactions.

Introduction

Catalytic asymmetric cascade reactions have aroused considerable interest because of avoiding time-consuming, costly protecting-group manipulations as well as the isolation of reaction intermediates.^[1] In recent years, many of new cascade reactions utilizing the chiral organocatalysts with one reaction center in a suitable ligand environment have been extensively investigated.^[2] Compared with the one reaction center in many catalytic systems, 'two-center catalysis' is the extension of this strategy in the field of organocatalytic cascade reactions. 'Twocenter catalysis' possesses significant advantages in both high selectivity and reactivity because the reactants are bound and oriented at two different centers (see Scheme 1a).^[3] This discovery can provide a new method to design catalysts for the other cascade reactions. However, the biggest challenge for the successful implementation of 'two-center catalysis' is to realize the consistency of the different catalyzed reaction rates.^[4]

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Enantiomerically enriched epoxy ketones are highly useful intermediates and versatile building blocks in asymmetric organic transformations, in which the carbonyl groups as additional moieties are susceptible to further transformations.^[5] Therefore, a variety of powerful homogeneous organic and organometallic chiral catalysts have been explored for highly efficient and reliable asymmetric epoxidation of α , β -unsaturated aldehydes/ketones to date.^[6] However, the general synthetic procedure for the asymmetric syntheses of chiral epoxy ketones requires two mechanistically distinct catalytic processes: 1) the condensation of aldehydes with ketones to yield α , β unsaturated carbonyl compounds, and 2) the asymmetric epoxidation of α , β - unsaturated carbonyl compounds to afford optical epoxy ketones. It will be a straightforward and valuable synthetic tool for preparing enantiomerically enriched epoxy aldehydes/ketones from readily available light aldehydes and ketones by a well-choreographed consecutive discrete catalytic step with multiple transformations in a same catalyst.^[7]



Scheme 1. (a) The schematic representation of the typical 'two-center catalysis' pattern. (b) The schematic representation of synthetic procedure of CuW-**PYIs**, showing the constitutive of the chiral PCNs and the cascade catalytic process for production of chiral epoxy ketones directly from aldehydes and ketones.

Chiral PCNs as the typical crystalline materials with infinite network structures and a chiral template have attracted much attention for their unique applications in asymmetric catalysis.^[8] The key features of the chiral PCNs are their abilities not only to incorporate multiple modified catalytic sites simultaneously in the building block of PCNs but also to position substrates in

proximity to each other for enhancing their reactivity through a synergistic cooperation between different catalysis sites.^[9] Beyond that, the most important problem in the cascade catalytic processes is how to achieve the compatibility between reaction intermediates and the consistency of the multiple catalytic cycles.^[10]

Polyoxometalates (POMs) are the appropriate candidates to design and construct tailored PCNs due to their versatility, accessibility, excellent physical properties and potential applications in the catalysis.^[11] A promising way to combine the organic and inorganic catalytic components synergistically is to introduce effective oxidation catalyst POMs into the appropriate chiral PCNs, that would be to increase the stability and the efficiency of the corresponding functions.^[12] Recently, we have successfully developed the asymmetric dihydroxylation and asymmetric epoxidation/cycloaddition tandem reactions catalyzed solely by POM-based chiral metal-organic frameworks.^[13] Based on our previous work, this paper reported two new enantiomorphs of POM-based PCNs (POM/PCNs), CuW-PYI1 and CuW-PYI2, which were prepared by Keggintype PW₁₂O₄₀³⁻ anions, copper(II) ions and *L- or D-*pyrrolidine-2vl-imidazole (PYI) under solvothermal conditions. CuW-PYIs displayed two-dimensional (2D) Kagomé topologies. In the network the chiral organocatalyst pyrrolidine, oxidation catalyst polyoxometalate and Lewis acid catalyst copper(II) were orderly distributed and spatial matching, which will be beneficial for the high efficiency and enantioselectivity in the conversion of aldehyde and ketone into value-added epoxy ketone via a onepot procedure (see Scheme 1b).

Results and Discussion

Structural Description.

CuW-PYI1 was synthesized by the solvothermal reaction of $H_3PW_{12}O_{40}$ ·7 H_2O , $Cu(NO_3)_2$ ·3 H_2O and *L*-BCIP in a mixed solvent of alcohol and water with a yield of 68%. CuW-PYI2 was prepared similarly to CuW-PYI1, except that using D-BCIP in place of L-BCIP. Single crystal structural analysis revealed that both CuW-PYI1 and CuW-PYI2 shared the same cell dimensions and crystallized in a chiral space group R_3 . Both the asymmetric unit of CuW-PYI1 and CuW-PYI2 consisted of two $PW_{12}O_{40}^{3-}$ anions and three $[Cu(PYI)_2]^{2+}$ cations (see Figure S1, S2). In the crystal structure of CuW-PYI1, there were two crystallographically independent copper ions, which coordinated with two nitrogen atoms from two L-PYI1 units and two oxygen atoms from different PW12Q403- anions and adopted a distorted quadrilateral geometry (see Figure 1a). Because the axial positions of the copper ion were empty, the special coordination mode would help to enhance the Lewis acidity of the copper(II) center and afford the possibility of CuW-PYIs as Lewis acid catalysts. [14] Besides, the copper ions were well-positioned within the channels, which was beneficial to interact with substrate molecules that entered into the framework channels.

Chiral **PYI** groups were in-situ generated with the butoxycarbonyl of **BCIP** removed in the reaction. The **PYI**

groups coordinated with copper ions and tightly surrounded the $PW_{12}O_{40}^{3^-}$ anions in a fan configuration. The arrangement patterns of the **PYI** groups in the CuW–**PYI1** and CuW–**PYI2** were the mirror image inversion (see Figure 1b). Compared with our previous structures, the pyrrolidine N atoms were not protonated and no hydrogen bonds were found between the pyrrolidine N atoms and the imbedded $PW_{12}O_{40}^{3^-}$ anion in CuW–**PYI1**.^[13] As a result, the bared pyrrolidine N atoms were potentially functionalized as asymmetric catalytic active sites to stabilize the potential transition state in both asymmetric direct aldol reaction and epoxidation of α , β - unsaturated carbonyl compounds.^[14,6a] Moreover, the unique redox property of $PW_{12}O_{40}^{3^-}$ could act as the cooperative catalytic sites to activate oxidants for generating the epoxidation.^[15]



Figure 1. (a) Plot of the connections between the $PW_{12}O_{40}^{3^-}$ and the copper centers of CuW–**PYI**1. (b) Representation of the mirror image structures of CuW–**PYI**1 (left) and CuW–**PYI**2 (right). (c) The 2D open sheet of CuW–**PYI**1 viewed down the *c*-axis. (color scheme: carbon, orange; nitrogen, blue; copper green; $PW_{12}O_{40}^{3^+}$, polyhedron), H atoms are omitted for clarity. (d) A schematic representation of the 2D Kagomé topological network of CuW–**PYI**1.

The crystal structure of CuW-PYI1 could be described as a 2D Kagomé lattice topology (see Figure 1c). The copper ions as a quasi-planar 4-connected building unit were positioned at the lattice points and bridged by the $PW_{12}O_{40}^{3-}$ ligands, thereby generating the trigonal and large hexagonal windows within the layer (Cu^{...}Cu diagonal distances are of 19.96 Å in hexagonal windows) (see Figure 1d). Each $PW_{12}O_{40}^{3-}$ anion as an equilateral triangle ligand coordinated with three copper ions by terminal oxygen atoms of the same {W3O10} clusters. It was worth mentioning that the $PW_{12}O_{40}^{3-}$ anions were imbedded in the triangular cavities and alternately distributed on the each side of the 2D layer (see Figure S3), thus realizing catalysis sites distributed at the molecular scale, which should avail to contact with the substrate molecules. The corresponding structures of CuW-PYI2 were shown in Figure S4-S7 in the Supporting Information.

The layer of CuW-**PYI1** displayed a honeycomb-like pattern, and the layers packed in an eclipsed arrangement along the *c*-axis to furnish 1D chiral channels with porosity of 8.5% (749.1 $Å^3$,

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calculated from PLATON analysis^[16]) (see Figure 2a,b). The accessible pores provided the possibility of adsorption suitable substrates within the channels. As can be seen from the Figure 2c, the Kagomé lattice exhibited an interlayer separation of 10.40 Å, which can exactly accommodate one $PW_{12}O_{40}^{3}$ molecule (about 10.40 Å in diameter) into the cavities. Remarkably, the first layer and the third layer interacted through the O…O interactions in a concerted manner with O…O distances in the expected range from 3.08 to 3.40 Å, thus furnishing the sextuplet $\text{PW}_{12}\text{O}_{40}{}^{3\text{-}}$ embrace (see Figure 2d). The suitable interlayer separation of 20.56 Å between the first and the third layer can exactly hold the middle layer. To the best of our knowledge, the metal-organic frameworks and inorganic Kagomé compounds have been extensively reported.^[17] However, the POM-based compounds with Kagomé lattice topology are still scarce.^[18]



Figure 2. (a) Layers of CuW-**PYI1** pack along the crystallographic c-axis. (b) The stacking pattern of CuW-**PYI1** showing the 1D channels along the c axis with $PW_{12}O_{40}^{3^-}$ anions omitted. (c) Layers of CuW-**PYI1** pack along the crystallographic *b*-axis. The middle layer (green) is held in place by direct O...O interactions with the first and third layers. (d) Sextuplet POM embrace. The middle layer has been deleted.

Powder XRD, CD and EPR characterization.

The PXRD of CuW–**PYI**s showed the good correspondence between the calculated and the experimental patterns suggesting the high purity of the bulk samples (see Figure 3a, Figure S8). CD of the bulk sample of CuW–**PYI1** presented two Cotton effects at 248 nm (θ = 32.0 mdeg) and 320 nm (θ = -56.7 mdeg) (Figure 3b), respectively. The Cotton effect at 248 nm arose from the asymmetric groups, which had an about 12 nm blue-shifted relative to the chiral **PYI** precursor. The other new strong Cotton effect at about 320 nm was assigned to the characteristic oxygen-to-tungsten charge-transfer bands of PW₁₂O₄₀^{3–} anion.^[19] The CD spectrum of CuW–**PYI**2 was almost a mirror image of CuW–**PYI1** giving opposite Cotton effects at 248 nm (θ = -24.4 mdeg) and 320 nm (θ = 73.2 mdeg), which showed that they were enantiomers.

EPR spectroscopic studies of CuW-PYI1 were conducted on crystalline samples with microwave frequency 9.45 GHz at 100 K to gain more information about the nature of the copper catalysts. The complex exhibited an anisotropic EPR spectrum with poorly resolved copper hyperfine features and a narrower transition at the effective g value of 2.098 (see Figure 3c), which was consistent with a quadrilateral geometry for the copper(II) complex and in accordance with the crystal structure of CuW-PYI1.^[20] The EPR parameter g > 2.0023 was characteristic of $d_{x^2 \cdot y^2}^{2 \cdot 2}$ orbital of unpaired electron ground state in axial symmetry of Cu^{II} coordination sphere.^[21] To mimic the catalysis process, we also studied the EPR of CuW-PYIs in the catalysis process with ketones (100 mmol), aldehydes (10 mmol) and t-butylhydroperoxide (TBHP) (20 mmol). EPR spectra of recovered solids from the catalytic system seemed identical with that of the fresh catalyst. The results indicated that the valence state of Cu^{II} maintained in the catalytic process, which supported our proposed mechanism of 'two-center catalysis' in cascade asymmetric direct aldol/epoxidation reactions by CuW-PYIs.



Figure 3. (a) PXRD diagrams of CuW-PYI1. (b) CD spectra of crystals of CuW-PYI1 (red line) and CuW-PYI2 (black line), respectively. Inset: CD spectrum of *L*-PYI. (c) X-band EPR powder spectrum of CuW-PYI1 (black) and CuW-PYI1 acquired from the cascade reaction system (red) at 110 K with 9.45 GHz. Reaction conditions: ketones (200 mmol), aldehydes (20 mmol), CuW-PYIs (0.2 mmol), TBHP (40 mmol), 40 °C, 3 days. (d) IR spectra of fresh and TBHP-oxidized CuW-PYI1. (e) IR spectra of cinnamaldehyde, fresh and cinnamaldehyde-incorporated CuW-PYI1, respectively. (f) IR spectra of benzaldehyde, fresh and benzaldehyde-incorporated CuW-PYI1, respectively.

Asymmetric epoxidation.

The asymmetric epoxidation reaction was initially employed using cinnamaldehyde and TBHP oxidant, along with CuW-**PYI**s

(0.1% mol ratio) in a heterogeneous reaction at 40 °C for 120 h, which showed a satisfactory yield (80.5%) and an excellent enantioselectivity (85.8% ee) for (2R,3S)-3-Phenyloxirane-2carbaldehyde (Table 1, entry 1). As shown in Table 1 (entries 2-5), when the catalysts were applied to the other α , β -unsaturated ketones, which also converted to the corresponding chiral epoxy ketones with decent yields and enantioselectivities. The control experiment showed that L-PYI as homogenous catalyst with one organocatalytic reaction center could initiate the reaction and afford the (2S,3R)-configured product with a 35.6% yield and a 38.4% ee under similar reaction conditions because it takes place by an iminium mechanism.^[6a] The use of L-PYI and CuHPW₁₂O₄₀ as homogeneous catalyst also obtained a 56.5% conversion and a 35.7% ee. The blank experiment under identical conditions gave only 7% of yield for 3-Phenyloxirane-2carbaldehyde. The higher efficiency and enantioselectivity catalyzed by CuW-PYI1 may be attributed to the orderly distribution and spatial matching of chiral PYI moieties and $\mathsf{PW}_{12}\mathsf{O}_{40}{}^{3\text{-}}$ anions that simultaneously effectively bound and oriented with cinnamylaldehyde and TBHP, respectively.

Table 1. Yields and enantiomer excess (ee) in the asymmetric epoxidation reactions of olefins. $^{\left[a\right] }$

R ¹ R ² Epoxidation CuW-PYIs, TBHP						
Entry Substrate Yield [%] ^(b) Ee [%] ^(c)						
R^1 R^2						
1 H H 80.5(82.6) 85.8(-80.4)						
2 H CH ₃ 78.5(77.6) 76.8(-85.4)						
3 H phenyl 75.4(78.7) 79.4(-70.8)						
4 4-NO ₂ CH ₃ 82.5(83.8) 78.5(-81.2)						
5 4-NO ₂ phenyl 76.5(77.6) 74.5(-75.8)						
6 styrene 73.8(71.9) 35.4(-36.7)						

[a] Reaction conditions: substrates (5 mmol), CuW-PYIs (0.05 mmol), TBHP (70% in decane, 10 mmol), 40 °C, 120 h. [b] The yields were determined by 1H NMR spectroscopy. [c] The ee values were determined by chiral HPLC on a Chiralcel AD column. The yields and ee values catalyzed by CuW-PYI2 were listed in the parentheses.

As shown in Figure 3d, a new v(O-O) band at 827 cm⁻¹ was found in the IR spectrum of the catalyst CuW-PYI1 impregnated with TBHP, which confirmed that the active intermediate peroxotungstate was formed during the epoxidation process.^[22] The C=O stretching vibration at 1672 cm⁻¹ in the IR spectrum of the catalyst impregnated with a CH2Cl2 solution of cinnamaldehyde was presented, which had a red-shifted about 11 cm⁻¹ relative to the 1683 cm⁻¹ of the free cinnamaldehyde. The results suggested cinnamaldehyde molecules were absorbed in the cavity of CuW-PYI1 and activated by pyrrolidine nitrogen atoms (Figure 3e). In contrast to the previously reported results,^[13] CuW-PYIs were poor catalysts in asymmetric epoxidation of styrene under the same reaction conditions, which may be attributed to no formation of hydrogen bonds between the terminal oxygen atoms of the POM and the pyrrolidine nitrogen atoms (Table 1, entry 6).[23] These results provided an experimental support for our previous speculation that the formation of hydrogen bonds played a key role in driving the catalytic reaction to proceed in an enantioselective manner. The higher enantioselectivity of epoxy ketones obtained by catalyst CuW-**PYI**s benefited from the formation of covalent bonding between the chiral amino group of **PYI** and the carbonyl group of α , β - unsaturated carbonyl compounds, which provided additional steric orientation and drove the catalysis occurred in a enantioselective manner. Meanwhile, the excellent catalytic activities were attributed to the synergetic interactions between the chiral amines and the inorganic POM clusters.

Mechanistically, we deduced that the formation of iminium (IM) intermediates between the chiral amino groups of **PYIs** and the carbonyl groups of α , β - unsaturated carbonyl compounds initially activated the substrates and enforced the catalysis to proceed in an enantioselective manner,^[24,6a] next, the olefin double bond directly attacked the peroxooxygen groups in a spiro fashion responsible for the epoxidation of cinnamylaldehydes and followed by hydrolysis of the IM intermediates.^[11e]

One-Pot Asymmetric Cascade Reactions.

Proline compounds are particularly favorable organocatalysts for the catalytic cascade reactions due to their flexibility and diversity of combinations of EN and IM activation.^[2a] Substantial experiments have demonstrated that they can effectively promote aldehydes and ketones reaction by formation of EN intermediates between the pyrrolidine moieties of proline and the carbonyl groups of ketones providing the enantiomerically enriched direct aldol products.^[14,24b] It is clear from the crystal structures of CuW-**PYI**s that the chiral directors, Lewis acid and oxidation catalyst coexistence within a confined space, which would provide a particular environment for the efficient conversion of aldehyde with ketone into the chiral epoxy ketone via the combination of EN and IM activation in the asymmetric cascade direct aldol/epoxidation reaction.

Table 2. Yields and enantiomer excess (ee) in the direct aldol/epoxidation cascade reactions between aldehydes and ketones. $^{\rm [a]}$

		+ $\underbrace{\bigwedge_{\text{Sub. B}}^{0}}_{\text{Sub. B}} R^2 \overline{Cu^2}$	One-pot W-PYIs, TBHP	↓ ↓ R ²
Entry	Sub. A (R ¹)	Sub. B(R ²)	Yield [%] ^[b]	ee [%] ^[c]
7	Н	CH ₃	68.5(66.6)	78.5(-72.9)
8	4-CH ₃		67.5(65.6)	75.4 (-70.6)
9	4-Cl		69.4(68.7)	79.4(-73.3)
10	4-NO ₂		72.5(70.8)	76.4(-77.5)
11	Н	Phenyl	70.5(74.5)	77.3(-79.4)
12	4-CH ₃		67.8(64.3)	78.4(-75.6)
13	4-Cl		69.2(66.6)	75.3(-77.4)
14	4-NO ₂		71 3(69 8)	86 2(-78 7)

[a] Reaction conditions: ketones (50 mmol), aldehydes (5 mmol), CuW-**PYIs** (0.05 mmol), TBHP (10 mmol), 40 °C, 120 h. [b] The yields were determined by ¹H NMR spectroscopy. [c] The ee values were determined by chiral HPLC on a Chiralcel AD columns. The yields and ee values catalyzed by CuW-**PYI**2 were listed in the parentheses.

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As shown in Table 2 (entries 7-14), the cascade reactions could be smoothly completed within a single workup stage by a reaction mixture of benzaldehyde, acetone and TBHP with catalyst CuW-PYI1 at 40 °C. The target (2R, 3S)-3-Phenyloxirane-2-carboxaldehyde was obtained in a 68.5% yield and a 78.5% ee. The control experiment showed under identical condition without CuW-PYI1, no reaction happened. CuW-PYI1 solids could be easily recycled from the reaction suspension by filtration, and be reused at least three runs with slight decrease in yield (from 68.5% to 65.6% yield) and enantioselectivity (from 78.5% to 74.2% ee). In order to verify the heterogeneity, the experiment was carried out by gravity filtration to remove the catalyst after reaction 60 hours. The results demonstrated the reaction nearly was terminated in the next another 60 hours, which suggested that CuW-PYI1 was a true heterogeneous catalyst. The index of PXRD patterns of the CuW-PYI1 bulky samples filtered from the catalytic reaction after three runs was agreed well with the fresh samples, which indicated the crystallinity maintained (Figure 3a). As expected, CuW-PYI2 solids exhibited similar catalytic activities and gave products with opposite chirality in the asymmetric cascade direct aldol/epoxidation reaction. In addition, to test the generality of the catalysis, some other benzaldehydes bearing an electronwithdrawing or electron-attracting substituent and ketones were screened. The results showed that all of the aldehydes and ketones were converted to the corresponding chiral epoxy ketones with decent yields and enantioselectivities.



Scheme 2. The diagram for potential mechanism of 'two-center catalysis' in cascade asymmetric direct aldol/epoxidation reactions by CuW-**PYI**s.

One broad C-O stretching vibration at 1690 cm⁻¹ was presented in the IR spectrum of the catalyst CuW-**PYI1** impregnated with benzaldehyde in acetonitrile solution, which had a red shift of 11 cm⁻¹ from 1701 cm⁻¹ of the free benzaldehyde (see Figure 3f).^[14a] The result unambiguously demonstrated the absorbance of benzaldehyde and possible activation of the substrate by the unsaturated Cu^{II} in the channel of CuW-**PYI1**. CuW-**PYIs** belonged to a particular class of the two-center catalysts, in which the chiral amine groups as Lewis-

basic centers can activate the carbonyl groups of ketones leading to the nucleophilic EN intermediates (A), meanwhile Cu^{II} ions as Lewis-acidic centers were available to activate benzaldehyde molecules resulting in the electrophile carbocations (B).^[14b] Then the nucleophilic EN intermediates attacked the electrophile carbocations furnishing the β - hydroxyl IM intermediates (C), and further converted into the α , β unsaturated IM intermediates (D) smoothly under heating conditions. Simultaneously, TBHP molecules were activated by POMs forming peroxotungstate intermediates (E); then, the olefin double bond directly attacked the peroxooxygen groups in a spiro fashion forming the epoxidation of cinnamylaldehydes (F) lastly, the IM intermediates hydrolyzed furnishing the chiral products (Scheme 2) and the catalytic cycle was accomplished. In conclusion, the orderly, asymmetrical and efficient conversion of aldehyde with ketone into value-added chiral epoxy ketone in the direct aldol/epoxidation cascade reaction was largely attributed to the chiral pyrrolidine organocatalysts, which interacted with carbonyl groups of ketones throughout the reaction, thus achieving of compatibility between the reaction intermediates and synergy of the multiple catalytic cycles.

Conclusions

In summary, we have developed a new strategy to construct functionalized chiral polyoxometalate materials and explored them in the asymmetric cascade reactions for preparing optical epoxy ketones from the readily available light aldehydes and ketones. CuW–**PYI**s exhibited the unusual 2D Kagomé topology. In the crystal structures of CuW–**PYI**s, the chiral director, Lewis acid and oxidation catalyst coexist within a confined space, which provided a particular environment for the efficient conversion of aldehyde with ketone into the chiral epoxy ketone via the combination of EN and IM activation in the asymmetric cascade direct aldol/epoxidation reaction. The results demonstrated that the chiral POM-based PCNs were excellent catalysts for creating enantiomeric compounds by a wellchoreographed consecutive discrete catalytic step with multiple transformations.

Experimental Section

General Methods and Materials.

Elemental analyses (EA) of C, H and N were performed on a Vario EL III elemental analyzer. ICP analyses were performed on a Jarrel-AshJ-A1100 spectrometer. FT-IR spectra were recorded from a solid sample pelletized with KBr on JASCO FT/IR-430. Powder XRD diffractograms were obtained on a Riguku D/Max-2400. Circular dichroism (CD) spectra were obtained from a solid sample pelletized with KBr on JASCO J-810. EPR spectra were obtained at 110K using a Bruker ESP-380E FTEPR spectrometer operating at 9.44 GHz (X-band) with 100 kHz modulation, microwave power 2.04 mW and modulation amplitude 1 G. ¹H and ¹³C NMR spectra were recorded on a Varian INOVA-400 MHz type (¹H, 400 MHz; ¹³C, 400 MHz) spectrometer. The chemical shifts are reported in ppm relative to CDCl₃ (δ = 7.26) for ¹H NMR and relative to the central

CDCl₃ resonance (δ = 77.0) for ¹³C NMR. Optical rotation was measured on a PerkinElmer 241 polarimeter. HPLC analysis was performed on Agilent 1150 using a ChiralPAk OD-H column or AD-H column purchased from Daicel Chemical Industries, Ltd. Products were purified by flash column chromatography on 200-300 mesh silica gel, SiO₂.

Synthesis. All reagents were used as purchased without further purification. *L*- and *D*- N-*tert*-butoxy-carbonyl-2-(imidazole)-1-pyrrolidine (*L*- or *D*-**BCIP**),^[25] and H₃PW₁₂O₄₀·nH₂O^[26] were prepared according to the literatures and confirmed by IR and ¹HNMR, respectively.

Synthesis of CuW-PYI1. CuW-PYI1 was synthesized by the selfassembly under hydrothermal conditions (see Scheme S1): $H_{3}PW_{12}O_{40}\text{-}7H_{2}O$ (200 mg, 0.067 mmol), $Cu(NO_{3})_{2}\text{-}3H_{2}O$ (72.5 mg, 0.3 mmol) and L-N-tert-butoxy-carbonyl-2-(imidazole)-1-pyrrolidine (L-BCIP) (50.0 mg, 0.2 mmol) was added in mixed water (4 mL) and alcohol (4 mL) and stirred at pH 3.0 for 6 h, then sealed in a 25 mL Teflon-lined autoclave and maintained at 130 °C for 72 h (see Scheme S1). After cooling the autoclave to room temperature, yellow block single crystals of CuW-PYI1 were separated, washed with water and air-dried. (Yield: ca. 68% based on H₃PW₁₂O₄₀·7H₂O). EA and ICP calcd (%) for C48H78N18P2Cu3W24O80:C 8.41, H 1.15, N 3.68, P 0.90, Cu 2.78, W 64.39; Found: C 8.43, H 1.12, N 3.64, P 0.92, Cu 2.76, W 64.40. IR (KBr): four characteristic asymmetric vibrations resulting from PW₁₂O₄₀³⁻ anions: ν (W=O_t) (922 cm⁻¹), ν (W-O_b) (887 cm⁻¹), ν (W-O_c) (794 cm⁻¹), and $v(P-O_a)$ (1078 cm⁻¹); four characteristic vibrations resulting from **PYI** molecules: υ(N-O) (1229 cm⁻¹), υ(ring) (1473 cm⁻¹), δ(C-H, in plane)(1181 cm⁻¹), and δ (N-O) (841 cm⁻¹).

Synthesis of CuW–**PYI**2. The preparation of CuW–**PYI**2 was similar to that of CuW–**PYI**1, except that using *D*–**BCIP** in place of *L*–**BCIP**. (Yield: ca. 65% based on H₃PW₁₂O₄₀-7H₂O). EA and ICP calcd (%) for C₄₈H₇₈N₁₈P₂Cu₃W₂₄O₈₀: C 8.41, H 1.15, N 3.68, P 0.90, Cu 2.78, W 64.39; Found: C 8.40, H 1.13, N 3.67, P 0.89, Cu 2.79, W 64.43. IR (KBr): four characteristic asymmetric vibrations resulting from PW₁₂O₄₀⁻³ anions: v(W=O₁) (923 cm⁻¹), v(W-O_b) (888 cm⁻¹), v(W-O_c) (795 cm⁻¹), and v(P-O_a) (1079 cm⁻¹); four characteristic vibrations resulting from **PYI** molecules: v(N-O) (1230 cm⁻¹), v(ring) (1474 cm⁻¹), δ (C-H, in plane) (1182 cm⁻¹), and δ (N-O) (842 cm⁻¹).

X-ray Crystallographic Analysis.

Crystals with dimensions 0.30×0.24×0.18 mm for CuW-PYI1 and 0.28×0.25×0.21 mm for CuW-PYI2 were stuck on a glass fiber, and intensity data were collected at 153 K on a Bruker Smart APEX II CCD diffractometer with graphite-monochromated Mo-Ka radiation (λ = 0.71073 Å), respectively. Routine Lorentz polarization and Multi-scan absorption correction were applied to intensity data. Their structures were determined and the heavy atoms were found by direct methods using the SHELXTL-97 program package.^[27] The remaining atoms were found from successive full-matrix least-squares refinements on F^2 and Fourier syntheses.^[28,29] Positions of the hydrogen atoms attached to carbon and nitrogen atoms were geometrically placed. All hydrogen atoms were refined isotropically as a riding mode using the default SHELXTL parameters. For CuW-PYI1, of 128 reflections, 5729 unique reflections ($R_{int} = 0.0672$) were considered observed [I>2 σ (I)]. The final cycle of refinement including atomic coordinates and the anisotropic thermal parameters converged to $R_1 = 0.0611$ and $wR_2 = 0.1680$ [I>2 σ (I)]. For CuW-PYI2, of 12394 reflections, 5568 unique reflections (R_{int} = 0.0686) were considered observed [I> $2\sigma(I)$]. The final cycle of refinement including atomic coordinates and the anisotropic thermal parameters converged to $R_1 = 0.0576$ and $wR_2 = 0.1395$ [I>2 σ (I)]. CCDC 1478772 and 1478773 contain the supplementary crystallographic data for this

paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Catalysis.

General Procedure for the Organocatalytic Epoxidation of *a*,*β*-**Unsaturated Aldehydes/Ketones.** The catalyst (0.05 mmol, 1 mol %) was added to a solution of the *a*,*β*-unsaturated aldehydes or ketones (5 mmol) followed by the addition of TBHP (70% in decane) (10 mmol, 2 equiv.) at 40 °C. After reaction five days the crude reaction mixture was passed through a silica gel FC column (ether/pentane) to give the corresponding *a*,*β*-epoxy aldehydes/ketones. The stereochemistry of the chiral amine-catalyzed asymmetric epoxidation reactions was established by comparison of the optical rotation of 3-Phenyloxirane-2-carboxaldehyde with the literatures^(6a,30) {[a] _D²⁵ +14.3 (c 0.48, CHCl₃) for (*2R*,3S)-3-Phenyloxirane-2-carbaldehyde; [a]_D²⁵ -20.4 (c = 0.55, CHCl₃) for (*2S*,*3R*)-3-Phenyloxirane-2-carbaldehyde}, which revealed that the stereochemistry of the 3-Phenyloxirane-2-carboxaldehyde derived were (*2R*,3S) and (*2S*,*3R*) by CuW–**PYI**1 and CuW–**PYI**2, respectively.

Typical one-pot procedure for the transformation of aldehydes with ketones to chiral epoxy ketones using the CuW-PYIs. The aldehydes (5 mmol) and ketones (50 mmol) were added in 2 mL solvent of DMSO and stirred for 15 mins, the catalyst (0.05 mmol) and TBHP (70% in decane, 10 mmol) were added and the mixture was stirred for several days at 40°C. The mixture was extracted with ethyl acetate ($2mL \times 3$), and the organic layer was dried with anhydrous MgSO₄, filtered, and concentrated to give pure epoxy ketones after column chromatography (ether/pentane). The conversion was directly determined by ¹H NMR analysis of the reaction solution. The *ee* was determined by chiral HPLC analysis.

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Entry for the Table of Contents

FULL PAPER

Two enantiomorphs CuW-**PYI**s with novel Kagomé lattice were prepared from a chiral organocatalyst, an oxidation catalyst polyoxometalate and a Lewis acid catalyst. They showed the satisfactory yields and enantioselectivities in the cascade Direct aldol/ epoxidation reactions by synergism of the multiple catalytic sites.



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Asymmetric Cascade Catalysis with Chiral Polyoxometalate-based frameworks: Sequential Direct aldol and Epoxidation Reactions

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