Creating enzyme-mimicking nanopockets in metal-organic frameworks for catalysis

Xiaofei Zhang

INTRODUCTION

Enzymes are generally characterized by their active sites in substrate-binding pockets and can attain exceptional catalytic selectivity for a reaction via a second coordination sphere (1). It is therefore highly desired to construct heterogeneous active sites in an artificial nanopocket where an enzyme-behaving substrate preorganization, transition state stabilization, and cofactor-controlled regulation could take effect via multiple interactions (2–8). Current studies of biomimetic catalysts mainly focus on following the structure of metal cofactors for designing active sites in classic porous catalysts like zeolites (9, 10) but remain forbidden for fabricating the substrate-specific nanopockets owing to the absence of allostERIC effects in the rigid scaffolds.

Different from the traditional porous catalysts, metal-organic frameworks (MOFs) have been recognized as the most appropriate candidate to mimic enzymes, because their ordered arrangement of metal active centers and organic ligands and tunable geometry of cavities or channels provide the confined environment akin to enzymes (11–14). Until now, biomimetic MOF catalysts have widely been constructed by replicating the structure of metal cofactors in different enzymes (15–18), e.g., metalloporphyrin units (15), mono/binuclear copper centers (19, 20), and metal-OH sites (15, 21). However, the allosteric effect in the nanopockets of MOFs, i.e., the conformal change of organic ligands responsible for substrate binding and transition state stabilization, is rarely explored.

Here, we choose zirconium terephthalate UiO-66 containing varied modulators to investigate the effect of stereochemical environment on its catalytic activity, because UiO-66 features high coordination number with benzenedicarboxylic acid (BDC) linkers and remarkable tolerance toward linker deficiency without damaging the whole scaffold structure (13, 22). Aiming at catalytic transfer hydrogenation of alkyl levulinates with isopropanol toward γ-valerolactone (GVL), these modulators endow zirconium sites with enhanced activity and selectivity and good stability. The catalytic activity of UiO-66FC is ~30 times that of UiO-66, also outperforming the state-of-the-art heterogeneous catalysts. Distinct from general consensus on electron-withdrawing or electron-donating effect on the stability. The catalytic activity of UiO-66FC is ~30 times that of UiO-66, also outperforming the state-of-the-art heterogeneous catalysts.

RESULTS

Synthesis and characterization of nanopockets inside UiO-66

Before experiments, we first visualized the nanopockets inside UiO-66, where multiple exposed zirconium sites would bind with substrates and catalyze reactions together with the second coordination sphere effect (Fig. 1A and fig. S1) (15), and the typical three-dimensional (3D) image of two adjacent zirconium sites in the nanopockets was delineated (8). For example, in the case of Zr–O clusters containing two BDC at one zirconium site and two BDC/AC/FC at the other zirconium site, the percentage of buried volume (% Vbur) value around two zirconium centers is 24.0 for UiO-66, 20.5 for UiO-66AC, and 19.3 for UiO-66FC (Fig. 1B and figs. S2 to S4). This result discloses modulator-induced control over spatial congestion near zirconium nodes in the nanopockets.

Armed with the above analysis, we synthesized UiO-66 samples containing varied modulators by dissolution of precursors zirconium (IV) chloride (ZrCl4) and H2BDC in N,N′-dimethylformamide (DMF) solvent followed by addition of different equivalents of FC or AC, which were finally subjected to solvothermal treatment and vacuum drying (figs. S5 to S7). Quantitative measurements manifest an average composition of Zr6O4.95(OH)3.05(BDC)5.34(HCOO)0.37 in pristine UiO-66 (fig. S8), and the molar ratio of BDC to Zr6 cluster is slightly lower than the theoretical value of 6.0 (22), due to small
defects and small amount of FC (0.37) produced during synthesis (22, 23). As for UiO-66AC and UiO-66FC, the average composition is estimated to be $\text{Zr}_6\text{O}_{5.85}(\text{OH})_{2.15}(\text{BDC})_{4.16}(\text{CH}_3\text{COO})_{1.83}$ and $\text{Zr}_6\text{O}_{6.11}(\text{OH})_{1.89}(\text{BDC})_{3.99}(\text{HCOO})_{1.91}$, respectively (figs. S9 and S10) (24). Approximately, almost two BDC molecules in each cluster of UiO-66 are substituted by two AC molecules in UiO-66AC or two FC molecules in UiO-66FC.

The structures of the as-prepared UiO-66, UiO-66AC, and UiO-66FC were fully investigated by various characterization techniques. Powder x-ray diffraction (XRD) patterns reveal that UiO-66, UiO-66AC, and UiO-66FC are of identical cubic close-packed crystal structure (fig. S11) (22). Fourier transform infrared (FTIR) spectra discern organic ligands in all the samples (fig. S12) (25); meanwhile, the mass content of zirconium centers is 27.9 weight % (wt %) for UiO-66, 34.8 wt % for UiO-66AC, and 37.9 wt % for UiO-66FC (table S1). 

The structures of the as-prepared UiO-66, UiO-66AC, and UiO-66FC were fully investigated by various characterization techniques. Powder x-ray diffraction (XRD) patterns reveal that UiO-66, UiO-66AC, and UiO-66FC are of identical cubic close-packed crystal structure (fig. S11) (22). Fourier transform infrared (FTIR) spectra discern organic ligands in all the samples (fig. S12) (25); meanwhile, the mass content of zirconium centers is 27.9 weight % (wt %) for UiO-66, 34.8 wt % for UiO-66AC, and 37.9 wt % for UiO-66FC (table S1). 

The structures of the as-prepared UiO-66, UiO-66AC, and UiO-66FC were fully investigated by various characterization techniques. Powder x-ray diffraction (XRD) patterns reveal that UiO-66, UiO-66AC, and UiO-66FC are of identical cubic close-packed crystal structure (fig. S11) (22). Fourier transform infrared (FTIR) spectra discern organic ligands in all the samples (fig. S12) (25); meanwhile, the mass content of zirconium centers is 27.9 weight % (wt %) for UiO-66, 34.8 wt % for UiO-66AC, and 37.9 wt % for UiO-66FC (table S1). 

N$_2$ adsorption-desorption isotherms show that the specific surface area is 786, 1037, and 1294 m$^2$ g$^{-1}$ for UiO-66, UiO-66AC, and UiO-66FC, respectively, while the pore volume is 0.41, 0.55, and 0.69 cm$^3$ g$^{-1}$, respectively (Fig. 1C and table S2). Notably, the pore size distribution is enlarged up to 2 nm by connecting the neighboring pores (Fig. 1D), disclosing that engineering the zirconium nodes with monocarboxylic modulators tunes the spaces of nanopockets inside UiO-66.
Catalytic transfer hydrogenation of alkyl levulinates with isopropanol

GVL is one of the most important platform molecules, not only serving as a fuel additive and solvent for biomass processing but also acting as a key feedstock for producing many chemicals (26, 27). The most effective method of GVL synthesis is transfer hydrogenation of biomass derived alkyl levulinates using secondary alcohols as hydrogen donor via Meerwein-Ponndorf-Verley (MPV) reduction and subsequent intramolecular lactonization catalyzed by Lewis acid catalysts (26). Thus, transfer hydrogenation of ethyl levulinate (EL; molecular size, 1.01 nm by 0.67 nm) toward GVL with isopropanol as a hydrogen donor is selected as a typical reaction to evaluate the catalytic performances of UiO-66, UiO-66AC, and UiO-66FC (figs. S13 and S14). Note that the side reaction of EL with isopropanol to form isopropyl levulinate (IPL) often occurs (27).

Table 1 summarizes the catalytic results. Without a catalyst, there is no transfer hydrogenation of EL with isopropanol (Table 1, entry 13). When UiO-66 is used as the catalyst, the conversion rate of EL and selectivity of GVL are 12.9 and 77.4%, respectively, at 150°C for 3 hours (Table 1, entry 1, and figs. S15 and S16). Under identical condition, UiO-66AC exhibits an enhanced catalytic performance, and the conversion rate of EL and selectivity of GVL increase to 86.3 and 98.9%, respectively (Table 1, entry 5, and figs. S17 and S18). UiO-66FC substantially enhances both the conversion rate of EL and selectivity of GVL to 99.7 and 99.3%, respectively (Table 1, entry 8, and figs. S19 and S20). To make the evaluation on catalytic performance more meaningful, the catalytic performance of different catalysts is further compared at the same conversion rate of EL (~52.9%). Note that the similar selectivity of GVL around 79% is obtained (Table 1, entries 2, 4, and 7), but the reaction time is distinct with each other, and it is 16.5 hours for UiO-66, 1.58 hours for UiO-66AC, and 0.5 hours for UiO-66FC. Notably, the catalytic activity of UiO-66FC is ~30 times that of pure UiO-66 under identical reaction condition. In addition to catalytic activity, the considerable difference in selectivity of GVL is also found over different catalysts at the same reaction time due to the formation of side product IPL. Note that as-formed IPL could further be converted to GVL via MPV reduction. Similarly, when IPL is used as the substrate, the catalytic activity strongly correlates with the modulated spaces of nanopockets in UiO-66 and follows the same order: UiO-66 < UiO-66AC < UiO-66FC (figs. S21 to S23 and table S3). Moreover, when EL is used as the substrate, the almost complete conversion to GVL is also achieved over different catalysts by prolonging the reaction time up to 72 hours for UiO-66, 6.25 hours for UiO-66AC, and 3 hours for UiO-66FC (Table 1, entries 3, 6, and 8).

As contrast samples, commercial zirconium isopropoxide complex displays only 3.5% conversion rate of EL and 22.9% selectivity of GVL (Table 1, entry 10, and fig. S24). UiO-66FC-derived hydrous zirconia (28) that inherits the morphology and porosity of UiO-66FC shows 9.4% conversion rate of EL and 78.1% selectivity of GVL (Table 1, entry 11, and figs. S25 to S28), while commercial and crystalline ZrO2 exhibits only 2.1% conversion rate of EL and 50.0% selectivity of GVL (Table 1, entry 12, and figs. S29 and S30). Above results suggest that the catalytic activity and selectivity of GVL strongly correlate with the modulated spaces of nanopockets in UiO-66. To verify the correlation, we tested a substrate of carbonyl-containing 2-triphenylenecarboxaldehyde that has a considerably larger molecular size of 1.28 nm by 1.08 nm (fig. S31). The conversion rate was found to be merely 2.1, 15.9, and 16.8% for UiO-66, UiO-66AC, and UiO-66FC, respectively, at 160°C for 4 hours (Table 1, entries 26 to 28, and fig. S32). Such a low activity is attributed to the fact that 2-triphenylenecarboxaldehyde is hard to be tuned in the nanopockets, indicating the critical role of nanopockets inside UiO-66 on catalytic transfer hydrogenation of EL.

Other alkyl levulinates including methyl levulinate (ML), propyl levulinate (PL), and butyl levulinate (BL) were also chosen as the substrates to produce GVL (fig. S14). Evidently, the catalytic activity and selectivity of GVL over different catalysts follow the same order: UiO-66 < UiO-66AC < UiO-66FC (Table 1, entries 14 to 16, 18 to 20, and 22 to 24; and figs. S33 to S35). Specifically, the conversion rate is 99.7% for ML, 93.0% for PL, and 94.1% for BL with the use of UiO-66FC, and the corresponding selectivity of GVL is 98.6, 98.5, and 99.5%.

In addition to alkyl levulinates, typical carbonyl-containing substrates including furfural, 2'-fluoroacetoephone, and 4,5-dihydro-3(2H)-thiophenone were examined so that the influence of tunable spaces of nanopockets on the transfer hydrogenation capability could be shown (fig. S36). Markedly, the yield of all hydrogenation products is in the order of UiO-66 < UiO-66AC < UiO-66FC (Table 1, entries 29 to 37, and figs. S37 to S39). Together, the tunable spaces of nanopockets have the universal effect on catalyzing transfer hydrogenation reactions, giving rise to distinct transformation performances of alkyl levulinates toward GVL over UiO-66, UiO-66AC, and UiO-66FC.

Stability is another key parameter to evaluate the performance of catalysts. During the five successive cycles, both conversion rate of EL and selectivity of GVL remain almost unchanged over the UiO-66FC catalyst (fig. S40). Such a high stability is further proved by morphology and crystal structure survey, where no obvious difference between the fresh and used catalysts is observed (figs. S41 and S42). In addition, there is almost no substantial binding energy shift of Zr 3d level in UiO-66FC before and after the reaction (fig. S43). Note that for transfer hydrogenation of a wide range of alkyl levulinates toward GVL, the overall catalytic performance of UiO-66FC is superior to that of all the reported heterogeneous catalysts (table S4).

Theoretical elucidation of reaction pathway

We started the catalytic mechanism study by determining the dominating step of the tandem process, namely, transfer hydrogenation and intramolecular lactonization. The time-dependent conversion rate of EL and selectivity of possible products are recorded over UiO-66FC at 150°C. Only GVL and by-product IPL (4a in Table 1) are discerned without the hydrogenation intermediate ethyl 4-hydroxypentanoate (4-HEP; 2a in Table 1) during the whole reaction process (fig. S44), demonstrating that 4-HEP quickly converts to GVL and transfer hydrogenation is dominating in the tandem process, which is consistent with the findings in the literature (29, 30).

On the basis of these results and reported literatures (31, 32), we proposed the whole reaction pathway of transfer hydrogenation of EL (Fig. 2A) and further calculated the reaction energy of each step at the exposed zirconium active sites in UiO-66FC cluster [Zr6O6.11(OH)1.89(BDC)3.99(HCOO)1.91], where two terephthalates and two FC molecules are attached (Fig. 2, B and C) (33, 34). Overall, two isopropanol molecules sequentially participate as hydrogen donors for transfer hydrogenation of EL.

First, isopropanol coordinates with one zirconium site to form an isopropanol anion by proton transfer from its hydroxyl group to...
Table 1. Transfer hydrogenation of various alkyl levulinates, aldehydes, and ketones via MPV reduction by different catalysts.*

| Entry | Substrate | Catalysts | T (°C) | t (hours) | Conv. † (%) | Sel. of 3a † (%) |
|-------|-----------|-----------|--------|-----------|-------------|-----------------|
|       | Substrate I: Ethyl levulinate (EL) |            |        |           |             |                 |
| 1     | EL        | UiO-66    | 150    | 3         | 12.9        | 77.4            |
| 2     | EL        | UiO-66    | 150    | 16.5      | 52.9        | 79.4            |
| 3     | EL        | UiO-66    | 150    | 72        | 99.3        | 99.2            |
| 4     | EL        | UiO-66AC  | 150    | 1.58      | 52.9        | 79.3            |
| 5     | EL        | UiO-66AC  | 150    | 3         | 86.3        | 98.9            |
| 6     | EL        | UiO-66AC  | 150    | 6.25      | 99.1        | 99.0            |
| 7     | EL        | UiO-66FC  | 150    | 0.5       | 52.9        | 79.5            |
| 8     | EL        | UiO-66FC  | 150    | 3         | 99.7        | 99.3            |
| 9     | EL        | UiO-66FC-R‡ | 150   | 3         | 76.3        | 95.4            |
| 10    | EL        | Zirconium isopropoxide | 150 | 3 | 3.5 | 22.9 |
| 11    | EL        | Hydrous zirconia§ | 150 | 3 | 9.4 | 78.1 |
| 12    | EL        | Commercial zirconia | 150 | 3 | 2.1 | 50.0 |
| 13    | EL        | Without catalyst | 150 | 3 | - | - |
|       | Substrate II: Methyl levulinate (ML) |            |        |           |             |                 |
| 14    | ML        | UiO-66    | 160    | 3         | 14.6        | 65.9            |
| 15    | ML        | UiO-66AC  | 160    | 3         | 95.4        | 96.9            |
| 16    | ML        | UiO-66FC  | 160    | 3         | 99.7        | 98.6            |
| 17    | ML        | UiO-66FC-R² | 160   | 3         | 76.6        | 85.5            |
|       | Substrate III: Propyl levulinate (PL) |            |        |           |             |                 |
| 18    | PL        | UiO-66    | 160    | 5         | 18.9        | 63.0            |
| 19    | PL        | UiO-66AC  | 160    | 5         | 86.5        | 87.3            |
| 20    | PL        | UiO-66FC  | 160    | 5         | 93.0        | 98.5            |
| 21    | PL        | UiO-66FC-R² | 160   | 5         | 83.7        | 98.2            |
|       | Substrate IV: Butyl levulinate (BL) |            |        |           |             |                 |
| 22    | BL        | UiO-66    | 160    | 5         | 16.6        | 62.0            |
| 23    | BL        | UiO-66AC  | 160    | 5         | 88.5        | 87.0            |
| 24    | BL        | UiO-66FC  | 160    | 5         | 94.1        | 99.5            |
| 25    | BL        | UiO-66FC-R² | 160   | 5         | 84.0        | 97.9            |
|       | Substrate V: 2-Triphenylenecarboxaldehyde |            |        |           |             |                 |
| 26    | 2-Triphenylenecarboxaldehyde | UiO-66 | 160 | 4 | 2.1 | - |

*continued on next page
| Entry | Catalysts | T (°C) | t (hours) | Conv. † (%) | Sel. of 3a † (%) |
|-------|-----------|--------|-----------|-------------|-----------------|
| 27    | UiO-66AC  | 160    | 4         | 15.9        | -               |
| 28    | UiO-66FC  | 160    | 4         | 16.8        | -               |

**Substrate VI: Furfural**

| Entry | Catalysts | T (°C) | t (hours) | Conv. † (%) | Sel. of 3a † (%) |
|-------|-----------|--------|-----------|-------------|-----------------|
| 29    | UiO-66    | 150    | 3         | 34.0        | -               |
| 30    | UiO-66AC  | 150    | 3         | 86.6        | -               |
| 31    | UiO-66FC  | 150    | 3         | 99.9        | -               |

**Substrate VII: 2′-Fluoroacetophenone**

| Entry | Catalysts | T (°C) | t (hours) | Conv. † (%) | Sel. of 3a † (%) |
|-------|-----------|--------|-----------|-------------|-----------------|
| 32    | UiO-66    | 150    | 3         | 29.8        | -               |
| 33    | UiO-66AC  | 150    | 3         | 85.6        | -               |
| 34    | UiO-66FC  | 150    | 3         | 98.6        | -               |

**Substrate VIII: 4,5-Dihydro-3(2H)-thiophenone**

| Entry | Catalysts | T (°C) | t (hours) | Conv. † (%) | Sel. of 3a † (%) |
|-------|-----------|--------|-----------|-------------|-----------------|
| 35    | UiO-66    | 150    | 3         | 18.7        | -               |
| 36    | UiO-66AC  | 150    | 3         | 66.4        | -               |
| 37    | UiO-66FC  | 150    | 3         | 93.6        | -               |

*Reaction condition: 1 ml of isopropanol, 3 ml of 1,4-dioxane, 68 mg of UiO-66, 54 mg of UiO-66AC, 50 mg of UiO-66FC, 49.6 mg of UiO-66FC-R, 40 mg of zirconium isopropoxide, 43.4 mg of hydrous zirconia, or 25.6 mg of commercial ZrO2 is used as catalyst, while 40 µl of ML, 50 µl of EL, 40 µl of PL, or 40 µl of BL is used as substrate; 41 mg of UiO-66, 33 mg of UiO-66AC, or 30 mg of UiO-66FC is used as catalyst, while 50 µl of furfural, 50 µl of 2′-fluoroacetophenone, 50 µl of 4,5-dihydro-3(2H)-thiophenone, or 30 µl of 2-triphenylencarboxaldehyde is used as substrate. Note that the varied catalyst weight is selected to ensure the same amount of zirconium active centers. †Conversion rate and selectivity of target product are determined by gas chromatography. ‡UiO-66FC-R is prepared by completely removing FC inside UiO-66FC. §Hydrous zirconia is prepared by completely removing FC and BDC ligands in UiO-66FC using NaOH solution.

**Fig. 2. Reaction pathway of transfer hydrogenation of EL with isopropanol.** (A) Scheme of reaction pathway for transfer hydrogenation of EL with isopropanol. (B) Zr–O cluster model containing two terephthalates at one zirconium site and two BDC/AC/FC at the other zirconium site. (C) Relative energy for each step of transfer hydrogenation of EL with isopropanol over UiO-66FC. (D) Kinetic isotope effect (KIE) experiments on transfer hydrogenation of EL over UiO-66FC using isotopic deuterium CH3CHOHCD3 and CH3CDOHCH3 as hydrogen sources at 150°C. (E) Relative energy for rate-determining step of transfer hydrogenation of EL with isopropanol over UiO-66 and UiO-66AC. Color scheme: Zr (green), C (brown), H (light pink), and O (red).
The adjacent $\mu_2$-oxygen (35), while the other exposed zirconium site reacts with the carbonyl group in the acetyl group of EL (step I in Fig. 2A) (36). The reduction of EL via hydride transfer undergoes a six-membered ring transition state (TS-1 in Fig. 2A), where O group of isopropanol anion additionally shares the same zirconium coordination site with EL and H atom at its $\alpha$-carbon simultaneously binds with carbon in the acetyl group of EL. The formation of TS-1 needs to overcome an energy barrier of 17.5 kcal mol$^{-1}$ (Fig. 2C).

Second, another isopropanol attacks the zirconium site to replace as-formed acetone from the isopropanol anion (step III in Fig. 2A), and this reaction is exothermic with an energy of $\sim$13.5 kcal mol$^{-1}$ (step III in Fig. 2C). Next, another six-membered ring transition state is formed through the proton transfer between hydroxyl in isopropanol and carbonyl in reduced EL with an energy barrier of 7.4 kcal mol$^{-1}$ (TS-2 in Fig. 2, A and C), and 4-HPE is then produced with an energy of $\sim$5.8 kcal mol$^{-1}$ (step IV in Fig. 2, A and C).

Last, as-produced 4-HPE desorbs from the zirconium site, while the isopropanol anion keeps coordinated with an energy of 5.4 kcal mol$^{-1}$ (step V). The hydride transfer of the first six-membered ring transition state (TS-1) is the rate-determining step of the whole reaction process.

To validate the above theoretical analysis, kinetic isotope effect (KIE) experiments were performed on transfer hydrogenation of EL using isotope-labeled (CH$_3$)$_2$CHOH and (CH$_3$)$_2$CDOH as hydrogen donors at 150°C. The corresponding KIE $k_{H}/k_{D}$ value is 1.09 and 2.15 over UiO-66-FC, respectively (Fig. 2D), indicating that breaking of the C-H bond at $\alpha$-carbon in isopropanol is rate limiting (37).

To deeply understand the influence of different modulators around zirconium sites on transfer hydrogenation of EL with isopropanol, we constructed similar Zr-O clusters containing two terephthalates at one zirconium site and two BDC/AC at the other zirconium site in UiO-66 and UiO-66AC (Fig. 2B) (36). Notably, the energy barrier for forming the first six-membered ring transition state is 21.2 kcal mol$^{-1}$ over UiO-66 and 19.8 kcal mol$^{-1}$ over UiO-66AC (Fig. 2E), considerably higher than 17.5 kcal mol$^{-1}$ over UiO-66FC.

**Allosteric effect of organic ligands at transition state**

The energy barrier of six-membered ring transition state is known to strongly depend on its strain energy (38), which could be estimated by using the dihedral angle ($\theta$) (39); a larger dihedral angle presents a lower energy barrier. Thus, the dihedral angle of the six-membered ring transition state was built by the secondary carbon and oxygen atoms in isopropanol and carbonyl group in the acetyl group of EL (Fig. 3A). The value is 68.2$^\circ$ for UiO-66, 71.4$^\circ$ for UiO-66AC, and 73.4$^\circ$ for UiO-66FC, manifesting that UiO-66FC promotes the formation of the six-membered ring transition state much more than UiO-66 and UiO-66AC do.

A close scrutiny of the reaction pathway reveals that the conformation of modulators is changed during the formation of the first six-membered ring transition state (figs. S45 to S47), which is distinguished by the dihedral angle (Fig. 3B) (39). The dihedral angle is established by two zirconium atoms with two carbon atoms in two benzene rings (UiO-66), two carbon atoms in two methyl groups (UiO-66AC), or two hydrogen atoms in two FC groups (UiO-66FC).

Specifically, the value is altered from 133.9$^\circ$ in step I to 138.8$^\circ$ in TS-1 for UiO-66, 140.8$^\circ$ in step I to 148.9$^\circ$ in TS-1 for UiO-66AC, and 146.3$^\circ$ in step I to 153.5$^\circ$ in TS-1 for UiO-66FC. Moreover, 3D topological steric maps of TS-1 are visualized. The fraction of the coordination sphere occupied by the substrates, $V_{burr}$, was estimated to be 30.4 for UiO-66, 26.0 for UiO-66AC, and 25.3 for UiO-66FC, respectively (figs. S48 to S50). In short, because of the highest degree of freedom, the FC modulator easily changes its conformation to promote the formation of six-membered ring transition state of the largest dihedral angle at the active zirconium sites, thus leading to the lowest energy barrier for producing GVL.

**Multiple weak interactions at transition state**

Analogously to the allosteric effectors in enzymes, the multiple interactions offered by BDC/AC/FC ligands stabilize as-formed first six-membered ring transition state. As indicated in Fig. 3C, many atomic distances shorter than 3 Å between the transition state and BDC/AC/FC are discerned (36), uncovering the existence of strong van der Waals forces (see movies S1 to S3). To evidence the importance of such interactions, both substrates and modulators are replaced. Because isotope effect is a powerful tool for evaluating the interactions between molecules (40, 41), the isotope isopropanol- $d_7$CD$_3$CDOHCD$_3$ was used in transfer hydrogenation of EL. The obtained $k_{H}/k_{D}$ value is 2.28 over UiO-66FC (Fig. 3D), larger than 2.15 for isopropanol-$d_1$CH$_3$CDOHCH$_3$, indicating that the multiple interactions between substrates and BDC/FC do occur in nanospectacles of UiO-66FC.

In addition, FC modulators inside UiO-66FC were completely removed to prepare contrast sample (42), denoted as UiO-66FC-R (figs. S51 to S57). When used as catalyst, the conversion rate is 76.6% for ML, 76.3% for EL, 83.7% for PL, and 84.0% for BL (Table 1, entries 9, 17, 21, and 25; and figs. S55 to S61). The catalytic performance of different samples for transfer hydrogenation of different alkyl levulinate follows the same order of UiO-66 < UiO-66FC-R < UiO-66AC < UiO-66FC under identical condition. Moreover, the catalytic performance of different samples for transfer hydrogenation of different alkyl levulinate is lower than that obtained over UiO-66FC under identical condition (Table 1, entries 1, 5, 8, 9, and 14 to 25). The energy barrier for forming the first six-membered ring transition state is calculated to be 20.3 kcal mol$^{-1}$ over the UiO-66FC-R cluster (figs. S62 to S64), lower than that over UiO-66 but higher than that over UiO-66AC and UiO-66FC, which is consistent with the order of catalytic performance of different samples for transfer hydrogenation of different alkyl levulinate. In addition, because of the larger free space around active zirconium sites in UiO-66FC-R (figs. S54 and S56 and table S2), its dihedral angle value gets to 74.3$^\circ$ (fig. S65), higher than that of all other UiO-66 samples (Fig. 3A); however, the catalytic performance is considerably worse in respect with UiO-66AC and UiO-66FC, suggesting that the interactions between the rate-determining six-membered ring transition state and BDC/AC or BDC/FC are crucial for producing GVL.

Moreover, the influence of concentration of FC in UiO-66 on transfer hydrogenation of EL toward GVL is investigated by preparing two contrast samples with less and more FC compared with UiO-66FC. Thermogravimetric analysis (TGA) and $^1$H nuclear magnetic resonance (NMR) measurements manifest that a low average composition of Zr$_6$O$_{6.00}$(OH)$_{2.00}$(BDC)$_{4.15}$(HCOO)$_{1.70}$ (denoted as UiO-66FC-L) and a high average composition of Zr$_6$O$_{5.98}$(OH)$_{2.02}$(BDC)$_{3.85}$(HCOO)$_{2.26}$ (denoted as UiO-66FC-H) are successfully obtained in UiO-66 (figs. S65 and S67). UiO-66FC-L and UiO-66FC-H are of identical cubic close-packed crystal structure and porous nature, while organic ligands in both samples are observed (figs. S68 to S71). Transmission electron microscopy (TEM) images show that the average size of as-synthesized samples is 100 to 200 nm for...
Fig. 3. Conformations of substrates and modulators in the nanopockets for transfer hydrogenation of EL with isopropanol. (A) The first six-membered ring transition state over UiO-66, UiO-66AC, and UiO-66FC and corresponding dihedral angle (θ). (B) Front views of step I and TS-1 over UiO-66, UiO-66AC, and UiO-66FC in Fig. 2 (C and E) and corresponding dihedral angle (θ) built by two zirconium centers and two modulators. (C) The interactions between the first six-membered ring transition state and BDC/AC/FC. The blue dashed lines stand for the atomic distance shorter than 3 Å between them. (D) KIE experiments on transfer hydrogenation of EL over UiO-66FC using isotopic deuterium CD₃CDOHCD₃ as hydrogen source at 150°C with respect to CH₃CDOHCH₃ in Fig. 2D. (E) Fourier transform magnitude of Zr K-edge extended x-ray absorption fine structure (EXAFS) spectra in R-space collected on different samples (not corrected for phase shift). (F) Fourier transform magnitude of Zr K-edge EXAFS spectra in R-space collected on different samples under the reaction of EL with isopropanol (not corrected for phase shift). (G) The average coordination number of Zr—O bonds for different samples. Color scheme: Zr (green), C (brown), H (light pink), and O (red).
and 7.1 for UiO-66FC (table S7). Under the operando condition of EL, Zr─O bonds was calculated to be 7.4 for UiO-66, 7.2 for UiO-66AC, and 7.1 for UiO-66FC (table S7). Under the operando condition of EL, Zr─O bonds was calculated to be 7.4 for UiO-66, 7.2 for UiO-66AC, and 7.1 for UiO-66FC (table S7). Under the operando condition of EL, Zr─O bonds was calculated to be 7.4 for UiO-66, 7.2 for UiO-66AC, and 7.1 for UiO-66FC (table S7).

The average coordination number of the local chemical environment around zirconium atoms (Fig. 3, E and G, and figs. S86 to S88) (23). The average coordination number of the local chemical environment around zirconium atoms (Fig. 3, E and G, and figs. S86 to S88) (23). The average coordination number of the local chemical environment around zirconium atoms (Fig. 3, E and G, and figs. S86 to S88) (23). The average coordination number of the local chemical environment around zirconium atoms (Fig. 3, E and G, and figs. S86 to S88) (23).

Third, we performed x-ray photoelectron spectroscopy (XPS) spectra display that there is no obvious binding energy shift of Zr 3d level in UiO-66FC-L, UiO-66FC, and UiO-66FC-H (fig. S74). When used as catalysts (table S5), the conversion rate is 45.8% for UiO-66FC-L, 81.5% for UiO-66FC, and 69.7% for UiO-66FC at 150°C for 1 hour of reaction, and the corresponding selectivity of GVL is 78.6, 88.1, and 94.8% in turn. With further prolonging reaction time up to 3 hours, the conversion rate is 78.5% for UiO-66FC-L, 99.7% for UiO-66FC, and 98.4% for UiO-66FC-H, and the corresponding selectivity of GVL is 83.9, 99.3, and 98.5% in turn. Compared with UiO-66FC, UiO-66FC-L displays the low conversion rate and selectivity of GVL at the same reaction time. As contrast, UiO-66FC-H shows a lower conversion rate but higher selectivity of GVL at the reaction time of 1 hour. The former might be attributed to the increased particle size of UiO-66FC-H for lengthening the diffusion and transfer pathway of the substance and product, while the latter might strongly correlate with the conformational change of more FC in the nanopocket for promoting the formation of GVL. At a reaction time of 3 hours, UiO-66FC-H exhibits the similar conversion rate and selectivity of GVL with respect to UiO-66FC. Together, the modulator FC in UiO-66 strongly correlates with the excellent catalytic activity and selectivity of GVL.

Electronic and chemical properties of zirconium sites

Despite the overwhelming evidence to support the nanopocket-dominant reaction paths, we carried out further experiments trying to exhaust other factors that could potentially affect the catalytic activity. First, our XPS spectra display that there is no obvious binding energy shift of Zr 3d level in UiO-66, UiO-66AC, and UiO-66FC (fig. S75). The calculated charge distribution of zirconium sites in different samples is also almost same (fig. S76). These results indicate that the difference in catalytic activity is unlikely caused by varied charge of zirconium active centers.

Second, it is known that the high Lewis acidity of active metal sites is beneficial for activating the carbonyl groups and promoting the transfer hydrogenation reaction (26, 36). Because of the similar Lewis acidity for UiO-66FC, UiO-66AC, and UiO-66 (fig. S77), we prepared another contrast sample by using an electron-withdrawing TFA as the modulator, denoted as UiO-66TFA with an average composition of Zr₆O₆.17(OH)₁.83(BDC)₃.86(CF₃COO)₂.11 (figs. S78 to S82). The XPS and temperature-programmed desorption of ammonia (NH₃-TPD) measurements indicate the higher Lewis acidity of active zirconium sites in UiO-66TFA (fig. S83). When used as the catalyst for transfer hydrogenation of ML or EL toward GVL, the order of catalytic performance is UiO-66 < UiO-66TFA < UiO-66AC < UiO-66FC (figs. S84 and S85 and table S6). This highlights the significance of the type of monocarboxylate modulators around zirconium sites in the nanopocket for catalytic transfer hydrogenation reactions rather than their Lewis acidity.

Third, we performed x-ray absorption fine structure results disclose that FC modulator in nanopockets substantially promotes the interaction with EL and isopropanol for producing GVL compared with BDC and AC, which is in good agreement with the experimental and theoretical results.

DISCUSSION

In summary, we have demonstrated that MOFs exhibit great potential to mimic enzymes for constructing the substrate-specific nanopockets, in which the allosteric effect of organic ligands happens and multiple interactions act while strongly correlating with the formation of low energy barrier transition state for transfer hydrogenation reactions. Viewed in perspective, apart from metal or nonmetallic active centers, judicious selection of versatile organic ligands in the nanopockets of MOFs or other framework materials will markedly enrich the toolbox toward artificial catalysis by approximation.

MATERIALS AND METHODS

Reagents

Anhydrous ZrCl₄ (98%) was obtained from Acros. EL (99%), furfural (99.5%), and sodium hydroxide (96%) were purchased from Aladdin Chemical Co. Ltd. AC (99.7%), 2'-fluoroacetophenone (97%), and TFA (99%) were bought from Alfa Aesar. Zirconium isopropoxide (99.9%), and 4,5-dihydro-3(2H)-thiophenone (98%) were obtained from Energy Chemical. Deuteron oxide (99.9 atomic % D), difluoroacetic acid (98%), FC (98%), and sodium trifluoroacetate (98%) were produced from Innochem. BL (98%) and BDC (99%) were received from Macklin. Ethanol (Analytical Reagent), DMF (Analytical Reagent), isopropanol (Analytical Reagent), and 1,4-dioxane (AR) were produced by Modern Oriental (Beijing) Technology Development Co. Ltd. Isopropanol-d₃ (CH₃CHOHCH₃ (99 atomic % D) and ML (99%) were acquired from Sigma-Aldrich. Hydrochloric acid (HCl) (36 to 38%; Guaranteed Reagent) was offered by Sinopharm Chemical Reagents Co. Ltd. PL (98%) and 2-triphenylenecarboxaldehyde (98%) were made by Tokyo Chemical Industry Co., Ltd.. Isopropanol-2-d₃ CH₃CD(OH)CH₃ (99 atomic % D) and isopropanol-1,1,1,3,3,3,3-d₇ (99 atomic % D) were supplied by Shanghai JDbio. All the chemicals were used without further purification.

Characterization

Scanning electron microscopy measurements were performed on a Hitachi S-8220 scanning electron microscope operated at 8 kV. Powder XRD patterns were recorded on D/MAX-TTRIII (Cross Beam Optics) with Cu Ka radiation (λ = 1.542 Å) operating at 40 kV and 200 mA. N₂ adsorption-desorption isotherms were obtained using BET (Brunauer-Emmett-Teller) instrument (ASAP 2420-4, Micromeritics) at 77 K in high vacuum. The samples were degassed at 120°C for 16 hours before the measurement. The XPS measurements were carried out on an ESCALAB250Xi spectrometer at a pressure of 3 × 10⁻⁹ mbar using Al Kα as the excitation source (hv = 1486.6 eV) and operated at 15 kV and 20 mA. FTIR spectra were recorded on a Spectrum One spectrometer in the spectral range of 400 to 4000 cm⁻¹ using the KBr disk method. NH₃-TPD was performed on an Autochem II 2920 chemisorption analyzer. The contents of Zr sites in UiO-66 were determined by inductively coupled plasma
In a typical procedure, 0.307 g of H₂BDC and 0.432 g of ZrCl₄ were dissolved in 50 ml of DMF solution. Then, 1.43 ml of HCl was added into the above solution. To ensure the complete dissolution of reagents, mild heating and stirring were applied for synthesis process. Subsequently, the above mixture was placed in a preheated oven at 120°C for 3 days. Last, the powders were collected via centrifugation and thoroughly washed three times with DMF and ethanol in turn, followed by drying at 80°C under vacuum for 12 hours.

**Synthesis procedures**

### Synthesis of UiO-66

In a typical procedure, 2.70 g of H₂BDC and 1.90 g of ZrCl₄ were dissolved in 45 ml of DMF solution. Then, 0.5 ml of H₂O was added to form a clear solution, and, moreover, 10 ml of TFA was also added. Subsequently, the above mixture was placed in a preheated oven at 120°C for 3 days. Last, the powders were collected via centrifugation and thoroughly washed three times with DMF and ethanol in turn, followed by drying at 80°C under vacuum for 12 hours.

### Synthesis of UiO-66TFA

In a typical procedure, 0.615 g of H₂BDC and 0.862 g of ZrCl₄ were dissolved in 45 ml of DMF solution. Then, 0.2 ml of H₂O was added to form a solution, and, moreover, 14 ml of AC was also added. Subsequently, the above mixture was placed in a preheated oven at 120°C for 3 days. Last, the powders were collected via centrifugation and thoroughly washed three times with DMF and ethanol in turn, followed by drying at 80°C under vacuum for 12 hours.

### Synthesis of UiO-66AC

In a typical procedure, 0.307 g of H₂BDC and 0.432 g of ZrCl₄ were dissolved in 45 ml of DMF solution. Then, 0.2 ml of H₂O was added to form a clear solution, and, moreover, 7 ml of AC was also added. Subsequently, the above mixture was placed in a preheated oven at 120°C for 3 days. Last, the powders were collected via centrifugation and thoroughly washed three times with DMF and ethanol in turn, followed by drying at 80°C under vacuum for 12 hours.

### Synthesis of UiO-66FC

In a typical procedure, 0.307 g of H₂BDC and 0.432 g of ZrCl₄ were dissolved in 45 ml of DMF solution. Then, 0.2 ml of H₂O was added to form a clear solution, and, moreover, 7 ml of AC was also added. Subsequently, the above mixture was placed in a preheated oven at 120°C for 3 days. Last, the powders were collected via centrifugation and thoroughly washed three times with DMF and ethanol in turn, followed by drying at 80°C under vacuum for 12 hours.

### Synthesis of porous hydrous zirconia derived from UiO-66FC

The porous hydrous zirconia was synthesized according to the reported procedure with minor modifications (28). In a typical process, 200 mg of UiO-66FC powders were added into 25 ml of 0.5 M NaOH aqueous solution and subsequently reacted under vigorous stirring at room temperature for 2.5 hours. The obtained powders were collected via centrifugation and thoroughly washed three times with water and ethanol in turn, followed by drying at 80°C under vacuum for 12 hours.

### Synthesis of UiO-66FC-R

The UiO-66FC-R was synthesized according to the reported procedure with minor modifications (42). In a typical procedure, 100 mg of UiO-66FC powders was dispersed in 10 ml of deionized H₂O. Then, 0.1 ml of HCl was added into the above mixture. Subsequently, the mixture was heated in an oil bath at 90°C for 12 hours under vigorous stirring. Last, the powders were recovered via centrifugation and thoroughly washed three times with H₂O and ethanol in turn, followed by drying at 80°C under vacuum for 12 hours.

### Synthesis of UiO-66FC with different FC contents

To obtain UiO-66FC with various FC contents, the FC used in the synthesis process is systematically regulated, while other conditions remain unchanged. In a typical procedure, 0.307 g of H₂BDC and 0.430 g of ZrCl₄ were dissolved in 50 ml of DMF solution. Then, 0.2 ml of H₂O was added to form a clear solution, and, moreover, various amounts of FC were added. Specifically, 3.5 ml of FC was used for UiO-66FC with lower FC content, denoted as UiO-66FC-L, or 14 ml of FC was used for UiO-66FC with higher FC content, denoted as UiO-66FC-H. Subsequently, the above mixture was placed in a preheated oven at 120°C for 3 days. Last, the powders were collected via centrifugation and thoroughly washed three times with DMF and ethanol in turn, followed by drying at 80°C under vacuum for 12 hours to finally obtain UiO-66FC-L or UiO-66-FC-H.

### NH₃-TPD experiments

NH₃-TPD experiments were performed on different samples for testing their Lewis acidity. Typically, the catalysts were charged into the quartz reactor, and the temperature was increased from room temperature to 150°C at a rate of 10°C min⁻¹ under He with a flow of 50 cm³ min⁻¹, and then, the catalyst was kept at 150°C for 2 hours. After that, the temperature was decreased to 50°C. NH₃/He (5/95; 50 cm³ min⁻¹) was pulsed into the reactor at 50°C until the acid sites were saturated with NH₃. Then, the sample was blown by He with a flow of 50 cm³ min⁻¹ for 20 min. When the baseline was stable, the sample was heated from 50° to 300°C at a heating rate of 10°C min⁻¹ with the carrier gas rate of 50 cm³ min⁻¹.

### MPV reduction and cyclization reactions

In a typical procedure, different alkyl levulinates or carbonyl compounds, isopropanol (1 ml), 1,4-dioxane (3 ml), and the catalyst were charged into a 15-ml pressure bottle equipped with a magnetic stirrer. After sealing, the reaction mixture was stirred at a defined temperature for the desired time. After the reaction, the obtained products were analyzed quantitatively by gas chromatography (Shimadzu, GC-2014 Plus).

### Theoretical calculations

#### Relative energy for transfer hydrogenation of EL with isopropanol toward GVL

All calculations were carried out with the Gaussian 09 software (43). The PBE0 functional (44) was adopted for all calculations in combination with the D3BJ dispersion correction (45). For geometry optimization and frequency calculations, the LanL2DZ Effective Core Potential and basis set (46) were used for Zr and 6-31G(d) for others (47, 48). The single-point energy calculations were performed with a larger basis set combination, in which the def2-TZVP basis set (49) was used for Zr and 6-31+11+G(d,p) (50, 51) for others. The Solvation Model based on Density implicit solvation model (52) was used to account for the solvation effect when performing single-point energy calculations.

Note that in the model, the zirconium terephthalate UiO-66, each Zr₆O₅(OH)₉ octahedron is coordinated by maximally 12 terephthalate linkers, Zr₆O₅(OH)(CO₂)₁₂, with large octahedral and small tetrahedral cages in close-packed metal structures (12), and the whole composition of theoretical UiO-66 can be denoted as Zr₆O₅(OH)(BDC)₆ (22). The average composition of UiO-66 sample is obtained by combining TGA and ¹H NMR results, and it is Zr₆O₅(HCOO)₀.37 (fig. S8). It is easily concluded that each Zr₆O₅(OH)₄...
octahedron is coordinated by about 11 terephthalate linkers, and a monodecarboxylated UiO-66 cluster with two exposed Zr sites is build up for density functional theory calculation (36). To keep the computational expense within the feasible limits, most of the terephthalates in the UiO-66 cluster were replaced by formates except for four linkers positioned closest to the two active zirconium sites. Similarly, the average composition of UiO-66AC and UiO-66FC is obtained by combining TGA and 1H NMR results, and they are Zr2O5.85(OH)2.15(BDC)4.14(CH3COO)2.83 for UiO-66AC and Zr6O5.11(OH)1.28(BDC)3.99(HCOO)1.91 for UiO-66FC (figs S9 and S10). Note that nearly two BDC linkers are replaced by AC or FC in one UiO-66 cluster on average, and thus, UiO-66AC and UiO-66FC clusters are approximately constructed by substituting two terephthalic linkers by two AC and two FC, respectively.

Topological steric maps of UiO-66 series

Topographic steric maps provided a 3D image of catalytic pocket, namely, the region of the catalyst where the substrate bound and reacted. The percentage of buried volume (% Vbur) was introduced to quantify the fraction of the coordination sphere around a metal center that was occupied by the organic ligand. Because the % Vbur focused on space occupation around the metal rather than specific features of a given class of ligands, it could be used to build property-structure relationship for any class of catalysts and ligands.

The steric distribution of nanopockets in UiO-66 series was visualized using a web-based SambVca software developed by Falivene et al. (www.molnc.unisa.it/OMTools/sambvc2a1/index.html) (6, 53). Once the metal center was set to the equivalent of sea level and the whole complex was oriented to maximize exposure of the metal center from the top, altimetric contours offered a qualitative description of the catalytic pocket. A coloring scheme from deep blue to dark red was used to indicate the regions in catalytic pocket where there was space available to host the substrate below or above the sea level.

The optimized zirconium cluster models containing two terephthalates at one active zirconium site and two BDC/AC/FC at the other zirconium site in the nanopockets of UiO-66 were set for UiO-66, UiO-66AC, and UiO-66FC. The midpoint of two Zr atoms, which coordinated with BDC, AC, and FC, was chosen as the center, and the calculation sphere radius was set to 10 Å to ensure that all the steric effects of ligands were included. The nodes were oriented with the midpoint of abovementioned two Zr atoms at the origin, along with the negative direction of the z axis and one of these two Zr atoms in the xz plane. The distance of the coordination point from the center of the sphere was set to 0, and the mesh spacing for numerical integration was set to 0.1 Å. The six O atoms above the sea level and directly connected with these two Zr atoms were not included in the calculations, while the H atoms were included. Each node was visualized along the z axis to depict the steric contributions of each ligand.

**SUPPLEMENTARY MATERIALS**

Supplementary material for this article is available at https://science.org/doi/10.1126/sciadv.add5678

**REFERENCES AND NOTES**

1. S. Martí, M. Roca, J. Andrés, V. Moliner, E. Silla, J. Turhón, J. Bertrán. Theoretical insights in enzyme catalysis. *Chem. Soc. Rev.* 33, 98–107 (2004).

2. S. H. M. Leenders, R. Gramage-Doria, D. de Bruin, J. N. H. Reek. Transition metal catalysis in confined spaces. *Chem. Soc. Rev.* 44, 433–448 (2015).
44. S. Grimme, Semiempirical hybrid density functional with perturbative second-order correlation. J. Chem. Phys. 132, 401–407 (2015).

45. W. J. Hehre, R. Ditchfield, J. A. Pople, Self-consistent molecular orbital methods. J. Chem. Phys. 28, 1107–1108 (1958).

46. T. Clark, J. Chandrasekhar, G. W. Spitznagel, P. von Ragué Schleyer, Efficient diffuse basis sets for use in molecular orbital studies of organic molecules. Theoret. Chim. Acta 28, 213–222 (1973).

47. F. Wei, S. Schirrmeister, S. Grimmer, Accurate ab initio parametrization of density functional dispersion correction (DFT-D) for the 94 elements H-Pu. J. Chem. Phys. 132, 154104 (2010).

48. P. J. Hay, W. R. Wadt, Ab initio effective core potentials for molecular calculations. Potentials for K to Au including the outermost core orbitals. J. Chem. Phys. 82, 299–310 (1985).

49. W. J. Hehre, D. J. ageing, J. A. Pople, Self-consistent molecular orbital methods. XII. Further extensions of Gaussian—Type basis sets for use in molecularorbital studies of organic molecules. J. Chem. Phys. 56, 2257–2261 (1972).

50. A. D. Becke, Density-functional exchange-energy approximation with correct asymptotic behavior. Phys. Rev. A 38, 3098–3100 (1988).

51. J. Parr, W. Yang, Density-functional theory of covalent bonding. Phys. Rev. B 13, 4864–4869 (1976).

52. P. J. Hay, W. R. Wadt, Ab initio effective core potentials for molecular calculations. Potentials for K to Au including the outermost core orbitals. J. Chem. Phys. 82, 299–310 (1985).

53. A. D. Becke, Density-functional exchange-energy approximation with correct asymptotic behavior. Phys. Rev. A 38, 3098–3100 (1988).

54. J. Parr, W. Yang, Density-functional theory of covalent bonding. Phys. Rev. B 13, 4864–4869 (1976).

55. S. Bordiga, F. Bonino, K. P. Lillerud, C. Lamberti, X-ray absorption spectroscopies: Useful tools to understand metallicorganic frameworks structure and reactivity. Chem. Soc. Rev. 39, 4885–4927 (2010).

56. D. K. S. Hadd, H. Zhao, Z. Wang, J. X. Wang, Porous Ti/Zr microspheres for efficient transfer hydrogenation of biomass-derived levulinic acid to γ-valerolactone. ACS Omega 2, 1047–1054 (2017).

57. C. Xie, J. Song, B. Zhou, J. Hu, Z. Zhang, P. Zhang, Z. Jiang, B. Han, Porous hafnium phosphonate: Novel heterogeneous catalyst for conversion of levulinic acid and esters into γ-valerolactone. ACS Sustainable Chem. Eng. 4, 6231–6236 (2016).

58. M. Chia, J. A. Dumesic, Liquid-phase catalytic transfer hydrogenation and cyclization of levulinic acid and its esters to γ-valerolactone over metal oxide catalysts. Chem. Commun. 47, 12233–12235 (2011).

59. Z. Xue, J. Jiang, G. Li, W. Zhao, J. Wang, T. Mu, Zirconium-cyanuric acid coordination polymer: Highly efficient catalyst for conversion of levulinic acid to γ-valerolactone. Cat. Soc. Technol. 6, 5374–5379 (2016).

60. H. Li, S. Fang, S. Yang, Direct catalytic transformation of biomass derivatives into biofuel component γ-valerolactone with magnetic nickel-zirconium nanoparticles. ChemPlusChem 81, 135–142 (2016).

61. A. H. Valekar, K.-H. Cho, S. K. Chitale, D.-Y. Hong, G.-Y. Cha, U.-H. Lee, D. W. Hwang, C. Serre, J.-S. Chang, Y. K. Hwang, Catalytic transfer hydrogenation of ethyl levulinate to γ-valerolactone over zirconium-based metal-organic frameworks. Green Chem. 18, 4542–4552 (2016).

62. H. Li, S. Fang, S.Yang, Direct conversion of sugars and ethyl levulinate into γ-valerolactone with superparamagnetic acid-base bifunctional ZrFeOx nanocatalysts. ACS Sustainable Chem. Eng. 4, 236–246 (2016).

63. J. F. Kurisngal, Y. Rachuri, A. S. Palakkal, R. S. Pillai, Y. Gu, Y. Choe, D.-W. Park, Water-tolerant DUT-series metal-organic frameworks: A theoretical-experimental study for the chemical fixation of CO2 and catalytic transfer hydrogenation of ethyl levulinate to γ-valerolactone. ACS Appl. Mater. Interfaces 11, 44158–44179 (2019).

64. M. Liu, S. Li, G. Fan, L. Yang, F. Li, Hierarchical flower-like bimetallic NiCu catalysts for catalytic transfer hydrogenation of ethyl levulinate into γ-valerolactone. Ind. Eng. Chem. Res. 58, 10317–10327 (2019).

65. H. Li, T. Yang, Z. Fang, Biomass-derived mesoporous Hf-containing hybrid for efficient Meeerwein-Ponndorf-Reduction at low temperatures. Appl. Catal. Environ. 227, 79–89 (2018).

66. Y. Sha, Z. Xiao, H. Zhou, K. Yang, Y. Song, N. Li, R. He, K. Zhi, Q. Liu, Direct use of hemic acid mixtures to construct efficient Zr-containing catalysts for Meerwein-Ponndorf-Reduction reactions. Green Chem. 19, 4829–4837 (2017).

67. S. Zhou, F. Dai, Z. Xiang, T. Song, D. Liu, F. Liu, H. Qi, Zirconium-lignosulfonate polyphenolic polymer for highly efficient hydrogen transfer of biomass-derived oxygenates under mild conditions. Appl. Catal. Environ. 248, 31–43 (2019).

68. Y. Kuwahara, H. Kango, H. Yamashita, Catalytic transfer hydrogenation of biomass-derived levulinic acid and its esters to γ-valerolactone over sulfonic acid-functionalized UO6-66. ACS Sustainable Chem. Eng. 5, 1141–1152 (2016).

69. X. Tang, Z. Li, X. Zeng, Y. Jiang, S. Liu, T. Lei, Y. Sun, L. Lin, In situ catalytic hydrogenation of biomass-derived methyl levulinate to γ-valerolactone in methanol. ChemSusChem 8, 1601–1607 (2015).

Acknowledgments Funding: We acknowledge financial support from the National Key Research and Development Program of China (2021YFA1100403 to G.L. and 2021YFA1100302 to Z.T.), Strategic Priority Research Program of Chinese Academy of Sciences (XDB36000000 to Z.T. and G.L.), National Natural Science Foundation of China (92006204, 21890381, and 21721002 to Z.T.; 22173024, 21721020, and 51672053 to G.L.), Beijing Natural Science Foundation (22182070 to G.L.), and Youth Innovation Promotion Association CAS (2016036 to G.L.) and Beijing Synchrotron Radiation Facility. Author contributions: Z.T. and G.L. proposed the research direction and guided the project. X.Z. designed and performed the experiments and characterization. C.Y. designed and performed some supplementary experiments. X.Z. and F.A. carried out XAS experiments and analyzed the experimental results. C.C. and C.X. took part in the theoretical calculation. C.Y., C.C., and X.X. took part in the discussion of experimental data and gave some suggestions. Z.T., G.L., and X.Z. drafted the manuscript. All the authors commented on the manuscript. X.Z. and C.Y. contributed equally to this work. Competing interests: The authors declare that they have no competing interests. Data and materials availability: All data needed to evaluate the conclusions in the paper are present in the paper and/or the Supplementary Materials.