Supplementary Information for:

**Catalysts Confined in Programmed Framework Pores Enable New Transformations and Tune Reaction Efficiency and Selectivity**

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1. General procedures

All starting materials and solvents were used as received from commercial sources without further purification unless otherwise noted. Several compounds were prepared via literature procedures: (S)-H₂bdc-ProBoc, H₃hmtt, H₃hbtt, H₃hhtt, H₂hdtt and H₂dppdc.² Column chromatography was carried out on silica gel (grade 60, mesh size 230-400, Scharlau). NMR spectra were recorded at room temperature (unless otherwise noted) on Bruker-400 and Bruker-500 Avance instruments, with the use of the solvent proton as an internal standard. High performance liquid chromatography (HPLC) was carried out using a Dionex Ultimate 3000 system equipped with a UV detector.

2. MOF synthesis

[Zn₄O(bdc-Pro)₁₂(bpdc)₁₂(hmtt)₄]₃, [Zn₄O(bdc-Pro)₁₂(bpdc)₁₂(hbtt)₄]₃, [Zn₄O(bdc-Pro)₁₂(bpdc)₁₂(hbt)₄]₃ and [Zn₄O(bdc-Pro)₁₂(dppdc)₁₂(hmtt)₄]₃ were synthesized according to the literature.¹

(a) [Zn₄O(bdc-Pro)₁₂(bpdc)₁₂(hmtt)₄]

H₃hbtt (40.0 mg, 41.2 μmol), H₂bpdc (9.9 mg, 41.2 μmol), (S)-H₂bdc-ProBoc (15.5 mg, 41.2 μmol) and Zn(NO₃)₂·4H₂O (74.0 mg, 283.2 μmol) were dissolved in dry DEF (5 mL) and water (0.175 mL). A solvothermal reaction was carried out in an 85 °C isothermal oven for 24 hours to obtain yellow crystals. The mother liquor was replaced with anhydrous DMF and this process was repeated five times. The DMF was then replaced with fresh anhydrous acetone and the solvent replenished five times within an hour. The acetone-occluded crystals were thermolyzed to generate the title compound by heating the crystals at a rate of 20 °C / min and holding the temperature at 200 °C for 20 hours under a dynamic vacuum.

(b) [Zn₄O(bdc-Pro)₁₂(bpdc)₁₂(hbtt)₄]

H₃hbtt (56 mg, 41.2 μmol), H₂bpdc (9.9 mg, 41.2 μmol), (S)-H₂bdc-ProBoc (15.5 mg, 41.2 μmol), benzoic acid (55 mg, 0.45 mmol) and Zn(NO₃)₂·4H₂O (74.0 mg, 283.2 μmol) were dissolved in dry DEF (5 mL) and water (0.175 mL). The reaction was carried out in an 85 °C isothermal oven for 24 hours to obtain yellow crystals. The mother liquor was replaced with anhydrous DMF and this process was repeated five times. The DMF was then replaced with fresh anhydrous acetone and the solvent replenished five times within an hour. The acetone-occluded crystals were thermolyzed to generate the title compound by heating the crystals at a rate of 20 °C / min and holding the temperature at 200 °C for 20 hours under a dynamic vacuum.

(c) [Zn₄O(bdc-Pro)₁₂(dppdc)₁₂(hbtt)₄]

H₃hbtt (33 mg, 41.2 μmol), H₂dppdc (17.5 mg, 41.2 μmol), (S)-H₂bdc-ProBoc (15.5 mg, 41.2 μmol), benzoic acid (55 mg, 0.45 mmol) and Zn(NO₃)₂·4H₂O (74.0 mg, 283.2 μmol) were dissolved in dry DEF (5 mL) and water (0.175 mL). The reaction was carried out in an 85 °C isothermal oven for 24 hours to obtain yellow crystals. The mother liquor was replaced with anhydrous DMF and this process was repeated five times. The DMF was then replaced with fresh anhydrous acetone and the solvent replenished five times within an hour. The acetone-occluded crystals were thermolyzed to generate the title compound by heating the crystals at a rate of 20 °C / min and holding the temperature at 200 °C for 20 hours under a dynamic vacuum.

(d) [Zn₄O(bdc-Pro)₁₂(dppdc)₁₂(hhtt)₄]

H₃hhtt (40 mg, 41.2 μmol), H₂dppdc (17.5 mg, 41.2 μmol), (S)-H₂bdc-ProBoc (15.5 mg, 41.2 μmol), benzoic acid (55 mg, 0.45 mmol) and Zn(NO₃)₂·4H₂O (74.0 mg, 283.2 μmol) were dissolved in dry DEF (5 mL) and water (0.175 mL). The reaction was carried out in an 85 °C isothermal oven for 24 hours to obtain yellow crystals. The mother liquor was
replaced with anhydrous DMF and this process was repeated five times. The DMF was then replaced with fresh anhydrous acetone and the solvent replenished five times within an hour. The acetone-occluded crystals were thermolyzed to generate the title compound by heating the crystals at a rate of 20 °C / min and holding the temperature at 200 °C for 20 hours under a dynamic vacuum.

(e) \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{dppdc)}_{1/2}\text{hott)}_{4/3}\]

\(\text{H}_3\text{hott}\) (47 mg, 41.2 µmol), \(\text{H}_3\text{dppdc}\) (17.5 mg, 41.2 µmol), (S)-\(\text{H}_2\text{bdc-ProBoc}\) (15.5 mg, 41.2 µmol), benzoic acid (55 mg, 0.45 mmol) and \(\text{Zn(NO}_3\text{)}_2\cdot4\text{H}_2\text{O}\) (74.0 mg, 283.2 µmol) were dissolved in dry DEF (5 mL) and water (0.175 mL). The reaction was carried out in an 85 °C isothermal oven for 24 hours to obtain yellow crystals. The mother liquor was replaced with anhydrous DMF and this process was repeated five times. The DMF was then replaced with fresh anhydrous acetone and the solvent replenished five times within an hour. The acetone-occluded crystals were thermolyzed to generate the title compound by heating the crystals at a rate of 20 °C / min and holding the temperature at 200 °C for 20 hours under a dynamic vacuum.

(f) \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{dppdc)}_{1/2}\text{hott)}_{4/3}\]

\(\text{H}_3\text{hdtt}\) (56 mg, 41.2 µmol), \(\text{H}_3\text{dppdc}\) (17.5 mg, 41.2 µmol), (S)-\(\text{H}_2\text{bdc-ProBoc}\) (15.5 mg, 41.2 µmol), benzoic acid (55 mg, 0.45 mmol) and \(\text{Zn(NO}_3\text{)}_2\cdot4\text{H}_2\text{O}\) (74.0 mg, 283.2 µmol) were dissolved in dry DEF (5 mL) and water (0.175 mL). The reaction was carried out in an 85 °C isothermal oven for 24 hours to obtain yellow crystals. The mother liquor was replaced with anhydrous DMF and this process was repeated five times. The DMF was then replaced with fresh anhydrous acetone and the solvent replenished five times within an hour. The acetone-occluded crystals were thermolyzed to generate the title compound by heating the crystals at a rate of 20 °C / min and holding the temperature at 200 °C for 20 hours under a dynamic vacuum.

3. \(^1\text{H}\) NMR spectroscopic analysis of digested MOF samples

For \(^1\text{H}\) NMR spectroscopy, The desolvated crystals were digested using the following protocol: 23 µL of a 35% DCl solution in D\(_2\)O was mixed with 1 mL of DMSO-d\(_6\) to give a DCl/DMSO-d\(_6\) stock solution. Around 5 mg of MOF was digested in 150 µL of this stock solution together with 450 µL of DMSO-d\(_6\). Spectra were acquired immediately following dissolution. The spectra for \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{bpdc)}_{1/2}\text{hott)}_{4/3}\], \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{bpdc)}_{1/2}\text{hbtt)}_{4/3}\], \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{bpdc)}_{1/2}\text{hott)}_{4/3}\) and \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{dppdc)}_{1/2}\text{hott)}_{4/3}\) were reported previously\(^1\text{a}\). The MOFs made by hdtt are very difficult to digest due to the poor solubility of hdtt ligand in DMSO. The spectra for all the other MOFs are presented below.
Figure S1. $^1$H NMR spectrum of digested [Zn$_4$O(bdc-Pro)$_2$(bpdc)$_{1/2}$(hht)$_{4/3}$] after thermolysis, showing integrals that match with the formula.

Figure S2. $^1$H NMR spectrum of digested [Zn$_4$O(bdc-Pro)$_2$ (dppdc)$_{1/2}$(hbt)$_{4/3}$] after thermolysis, showing integrals that match with the formula.
Figure S3. $^1$H NMR spectrum of digested $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{dppdc})_{1/2}(\text{hht})_{4/3}]$ after thermolysis, showing integrals that match with the formula.

Figure S4. $^1$H NMR spectrum of digested $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{dppdc})_{1/2}(\text{hht})_{4/3}]$ after thermolysis, showing integrals that match with the formula.
4. N$_2$ adsorption isotherm and pore size distribution

N$_2$ adsorption isotherms were measured by a volumetric method using a Quantachrome Autosorb iQ2 instrument. Before the measurements, the sample was activated under dynamic vacuum at 200 °C for 20 h. The pore size distribution of the MOFs was obtained by fitting the data with quenched solid density functional theory (QSDFT).

![Figure S5. N$_2$ adsorption isotherm (left) at 77 K and pore size distribution (right) for [Zn$_4$O(bdc-Pro)$_{1/2}$(dppdc)$_{1/2}$(h htt)$_{4/3}$]. The total pore volume was found to be 1.41 cm$^3$ g$^{-1}$.](image)

![Figure S6. N$_2$ adsorption isotherm (left) at 77 K and pore size distribution (right) for [Zn$_4$O(bdc-Pro)$_{1/2}$(dppdc)$_{1/2}$(h htt)$_{4/3}$]. The total pore volume was found to be 0.65 cm$^3$ g$^{-1}$. A nearly-identical adsorption isotherm was measured following catalysis.](image)

5. X-ray diffraction

All X-ray diffraction experiments were carried out on a Rigaku Spider X-ray diffractometer with Cu-K$_\alpha$ radiation (Rigaku MM007 microfocus rotating-anode generator), monochromated and focused with high-flux Osmic multilayer mirror optics, and a curved image plate detector. PXRD data were obtained from desolvated MOF samples that were ground then fixed to a mount with a minimum amount of Fomblin oil. A very broad scattering peak due to this oil is sometimes observed between 2$\theta$ = 7° and 20°. The two-dimensional images of the Debye rings were integrated with 2DP$^2$ to give 2$\theta$ vs I diffractograms. The predicted powder patterns of the MOFs were generated from their single-crystal structures using Mercury. The structure of [Zn$_4$O(bdc-Pro)$_{1/2}$(dppdc)$_{1/2}$(h htt)$_{4/3}$] determined by SCXRD has been deposited with the CCDC (1885842).
Figure S7. Powder XRD patterns the MOF catalysts prior to catalysis. From top to bottom: [Zn₄O(bdc-Pro)₁/₂(dppdc)₁/₂(hddt)₄/₃], [Zn₄O(bdc-Pro)₁/₂(dppdc)₁/₂(hott)₄/₃], [Zn₄O(bdc-Pro)₁/₂(dppdc)₁/₂(hhtt)₄/₃], [Zn₄O(bdc-Pro)₁/₂(bpdc)₁/₂(hddt)₄/₃], [Zn₄O(bdc-Pro)₁/₂(dppdc)₁/₂(hhtt)₄/₃] together with a simulated powder XRD pattern of MUF-77.
6. Catalysis experiments

6.1 Experimental protocol

**p-aldol reaction:** A stock catalyst solution was prepared with p-nitrobenzaldehyde (158 mg, 1.05 mmol), nitrobenzene (standard, 100 μL), acetone (30 mL).

**m-aldol reaction:** A stock catalyst solution was prepared with m-nitrobenzaldehyde (158 mg, 1.05 mmol), nitrobenzene (standard, 100 μL), acetone (30 mL).

**m-Henry reaction:** A stock catalyst solution was prepared with m-nitrobenzaldehyde (158 mg, 1.05 mmol), nitromethane (3 mL), THF (27 mL).

**Competition reaction between m-aldol and m-Henry reaction:** A stock catalyst solution was prepared with m-nitrobenzaldehyde (158 mg, 1.05 mmol), nitromethane (1.5 mL), Acetone (28.5 mL).

**Homogeneous catalyst:** Me₂bdc-Pro was used as a homogenous analog of the catalytic bdc-Pro linker.

**Typical protocol:**

In a typical experiment, 1.0 mL of stock solution was added to a 1.5 mL HPLC sample vial together with a pre-weighed quantity of desolvated catalyst. The mass of catalyst was chosen so that it contained 10 mol% of prolinyl groups relative to p- or m-nitrobenzaldehyde. The reaction mixture was allowed to stand in the autosampler of the HPLC at 20 °C. During the reaction, 2.0 μL of the supernatant was subjected to HPLC analysis every two hours over the initial 12 hours of the reaction and then again after 24 h. HPLC analysis was carried out under the following conditions: Lux amylose-1 column; mixed solvent of CH₃CN and deionized water (50:50 v/v); flow rate of 0.5 ml/min. Products were detected according their absorption of 254 nm UV light. The conversion of nitrobenzaldehyde was calculated by comparing the ratio of its peak area and that of the nitrobenzene standard. The ee value of each reaction is reported based on the excess of the enantiomer with shorter retention time measured after a reaction time of 24 h. Figures S8-S12 show representative HPLC chromatograms.

![Figure S8. A typical HPLC chromatogram (Lux amylose-1) of the p-aldol reaction mixture. Peak 1 (6.33 min): acetone; Peak 2 (11.51 min): enantiomer 1 of the aldol adduct; Peak 3 (12.93 min): enantiomer 2 of the aldol adduct; Peak 4 (15.91 min): nitrobenzene; Peak 5 (17.60 min): p-nitrobenzaldehyde; Peak 6 (24.69 min): product of the elimination of H₂O from the initial aldol product.](image-url)
Figure S9. A typical HPLC chromatogram (Lux amylose-1) of the m-aldol reaction mixture. Peak 1 (6.29 min): acetone; Peak 2 (9.35 min): enantiomer 1 of the aldol adduct; Peak 3 (10.87 min): enantiomer 2 of the aldol adduct; Peak 4 (17.96 min): m-nitrobenzaldehyde; Peak 5 (22.12 min): product of the elimination of H₂O from the initial aldol product.

Figure S10. A typical HPLC chromatogram (Lux amylose-1) of the Henry reaction mixture. Peak 1 (6.96 min): CH₃NO₂; Peak 2 (11.0 min): enantiomer 1 of the Henry adduct; Peak 3 (12.58 min): enantiomer 2 of the Henry adduct; Peak 4 (16.39 min): nitrobenzene; Peak 5 (18.70 min): m-nitrobenzaldehyde.

Figure S11. A typical HPLC chromatogram (Lux amylose-1) of the competition reaction between m-aldol and m-Henry reaction after 24 hours. Peak 1 (6.28 min): acetone; Peak 2 (6.70 min): CH₃NO₂; Peak 3 (9.26 min): enantiomer 1 of the aldol adduct; Peak 4 (10.48 min): enantiomer 1 of the Henry adduct; Peak 5 (10.81 min): enantiomer 2 of the aldol
adduct; Peak 6 (11.98 min): enantiomer 2 of the Henry adduct; Peak 7 (17.85 min): m-nitrobenzaldehyde; Peak 8 (22.11 min): product of the elimination of H₂O from the initial aldol product.

**Figure S12.** Typical HPLC chromatograms indicating enantioselectivity. (a) p-aldol reaction catalysed by [Zn₄O(bdc-Pro)₁/₂(dppdc)₁/₂(hmtt)₄/₃] after 24 hours. (b) p-aldol reaction catalysed by [Zn₄O(bdc-Pro)₁/₂(dppdc)₁/₂(hott)₄/₃] after 24 hours. Peak 1: acetone; Peak 2: enantiomer 1 of the aldol adduct; Peak 3: enantiomer 2 of the aldol adduct; Peak 4: p-nitrobenzaldehyde; Peak 5: product of the elimination of H₂O from the aldol product.

### 6.2 Calculation of the observed initial rate for aldol reactions

The rate of the aldol reaction, \( r \), based on the consumption of nitrobenzaldehyde (NBA) can be expressed as a function of reaction rate constant \( k \) and the concentration of NBA and acetone by assuming the reaction order of NBA is unity:

\[
\frac{d[NBA]}{dt} = k[NBA][acetone]^a
\]

Here, \( a \) is the reaction order of acetone. Since the reaction is carried out in the presence of a very large excess of acetone, the above equation can be simplified as

\[
\frac{d[NBA]}{dt} = k_{obs}[NBA]
\]

where \( k_{obs} \) is the pseudo first-order observed rate constant.
Therefore

\[ \ln[\text{NBA}] = \ln[\text{NBA}]_0 - k_{\text{obs}} t \]

Here, \([\text{NBA}]_0\) is the initial concentration of nitrobenzaldehyde and \(t\) is time. Plotting \(\ln([\text{NBA}]/[\text{NBA}]_0)\) as a function of time over the initial 12 hours of the reaction yields a line with slope \(k_{\text{obs}}\) estimated by least squares fitting.

### 6.2.1 Reaction kinetics plots for the catalysts of \([\text{Zn}_4\text{O}(\text{bdc-Pro})_{1/2} (\text{bpdc})_{1/2} (\text{hxtt})_{4/3}]\)

Table S1. Summarized results of \(p\)-aldol and \(m\)-aldol reactions catalyzed by \([\text{Zn}_4\text{O}(\text{bdc-Pro})_{1/2} (\text{bpdc})_{1/2} (\text{hxtt})_{4/3}]\).

| Entry | Catalyst linker set     | Initial rate (L mol\(^{-1}\) day\(^{-1}\)) | Conversion at 24 h (%) | e.e. (%) |
|-------|-------------------------|---------------------------------------------|------------------------|---------|
|       |                         | \(p\)-aldol\(^b\) | \(m\)-aldol\(^b\) | \(p\)-aldol | \(m\)-aldol | \(p\)-aldol | \(m\)-aldol |
| 1     | bdc-Pro/bpdc/hmtt       | 0.69 | 0.72 | 52.3 | 46.5 | -3.5 | -4.0 |
| 2     | bdc-Pro/bpdc/hbtt       | 0.68 | 0.73 | 51.4 | 48.1 | 4.5 | 1.8 |
| 3     | bdc-Pro/bpdc/hhtt       | 2.42 | 1.76 | 90.2 | 80.0 | 3.0 | -3.6 |
| 4     | bdc-Pro/bpdc/hott       | 2.12 | 1.38 | 91.0 | 71.6 | 6.1 | 4.4 |
| 5     | bdc-Pro/bpdc/hdtt       | 0.54 | 0.54 | 45.5 | 38.3 | 2.9 | -3.3 |
| 6     | Me\(_2\)bdc-Pro\(^c\)   | 0.05 | 0.19 | 5.3 | 18.1 | 9.7 | 21.4 |

\(^a\) \(p\)-Aldol reaction is between \(p\)-nitrobenzaldehyde and acetone. \(^b\) \(m\)-Aldol reaction is between \(m\)-nitrobenzaldehyde and acetone. \(^c\) Control reaction using the dimethyl ester of the catalytic linker (Me\(_2\)bdc-Pro) under homogenous conditions.

Figure S13. Reaction kinetics plot for the \(p\)-aldol reaction catalysed by \([\text{Zn}_4\text{O}(\text{bdc-Pro})_{1/2} (\text{bpdc})_{1/2} (\text{hxtt})_{4/3}]\).
Figure S14. Reaction kinetics plot for the $p$-aldol reaction catalysed by [Zn$_4$O(bdc-Pro)$_{1/2}$+(bpdc)$_{1/2}$+4(hbt)]$_4$.

Figure S15. Reaction kinetics plot for the $p$-aldol reaction catalysed by [Zn$_4$O(bdc-Pro)$_{1/2}$+(bpdc)$_{1/2}$+4(hbt)]$_4$.
Figure S16. Reaction kinetics plot for the 1,3-aldol reaction catalysed by [Zn₄O(bdc-Pro)$_{1/2}$(bpdc)$_{1/2}$(hott)$_{4/3}$].

Figure S17. Reaction kinetics plot for the 1,3-aldol reaction catalysed by [Zn₄O(bdc-Pro)$_{1/2}$(bpdc)$_{1/2}$(hdt)$_{4/3}$].
**Figure S18.** Reaction kinetics plot for the \( m \)-aldol reaction catalysed by \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{(bpdc)}_{1/2}\text{(hmtt)}_{4/3}]\).

**Figure S19.** Reaction kinetics plot for the \( m \)-aldol reaction catalysed by \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{(bpdc)}_{1/2}\text{(hbbt)}_{4/3}]\).
Figure S20. Reaction kinetics plot for the *m*-aldol reaction catalysed by [Zn₄O(bdc-Pro)₁/₂(bpdc)₁/₂(hhtt)₄/₃].

Figure S21. Reaction kinetics plot for the *m*-aldol reaction catalysed by [Zn₄O(bdc-Pro)₁/₂(bpdc)₁/₂(hott)₄/₃].
**Figure S22.** Reaction kinetics plot for the \( m \)-aldol reaction catalysed by \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{(bpdc)}_{1/2}\text{(hdtt)}_{4/3}]\).  

**Figure S23.** Reaction kinetics plot for the \( p \)-aldol reaction catalysed by the dimethyl ester of the catalytic linker (Me₂bdc-Pro) under homogenous conditions.
Figure S24. Reaction kinetics plot for the \textit{m}-aldol reaction catalysed by the dimethyl ester of the catalytic linker (Me₂bdc-Pro) under homogenous conditions.
6.2.2 Reaction kinetics plots for the catalysts of \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{dppdc)}_{1/2}\text{hxtt)}_{4/3}\)

Table S2. Aldol Reaction of acetone and \(p\)-nitrobenzaldehyde catalyzed by \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{dppdc)}_{1/2}\text{hxtt)}_{4/3}\).

| Entry | Catalyst linker set | Initial rate \((\text{L mol}^{-1} \text{ day}^{-1})\) | Conversion at 24 h \(\%\) | e.e. \(\%\) |
|-------|---------------------|---------------------------------|-----------------|--------|
| 1     | bdc-Pro/dppdc/hmtt  | 0.37                            | 27.7            | -0.3   |
| 2     | bdc-Pro/dppdc/hbtt  | 0.66                            | 51.1            | 4.7    |
| 3     | bdc-Pro/dppdc/h htt  | 1.21                            | 70.9            | 19.4   |
| 4     | bdc-Pro/dppdc/h ott | 1.20                            | 72.9            | 27.7   |
| 5     | bdc-Pro/dppdc/hdtt  | 0.18                            | 15.6            | 1.3    |

Figure S25. Reaction kinetics plot for the \(p\)-aldol reaction catalysed by \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{dppdc)}_{1/2}\text{hxtt)}_{4/3}\).
Figure S26. Reaction kinetics plot for the $\rho$-aldol reaction catalysed by $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{(dppdc)}_{1/2}\text{(hbt)}_{4/3}]$.

Figure S27. Reaction kinetics plot for the $\rho$-aldol reaction catalysed by $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{(dppdc)}_{1/2}\text{(hbt)}_{4/3}]$.  

```markdown
| Equation | $y = A + B \times x$ |
|----------|----------------------|
| Adj. R-Sq. | 0.99667 |

| Initial rate | Value | Standard Err |
|--------------|-------|--------------|
| A            | 0.0116 | 0.00557      |
| B            | -0.6645 | 0.01716     |


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Figure S28. Reaction kinetics plot for the $\beta$-aldol reaction catalysed by $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{(dppdc)}_{1/2}\text{(hdt)}_{4/3}]$.

Figure S29. Reaction kinetics plot for the $\beta$-aldol reaction catalysed by $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{(dppdc)}_{1/2}\text{(hdt)}_{4/3}]$. 

\begin{verbatim}
Equation   \quad y = A + B \times x
Adj. R-Squ 0.982
\hline
Value  |  Standard E
Initial rate A | -0.075  | 0.0235
Initial rate B | -1.198  | 0.0724
\end{verbatim}
Table S3. Aldol reaction of acetone and \textit{m}-nitrobenzaldehyde catalyzed by \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{dppdc)}_{1/2}\text{hmtt})_{4/3}\].

| Entry | Catalyst linker set | Initial rate (L mol\(^{-1}\) day\(^{-1}\)) | Conversion at 24 h (%) | e.e. (%) |
|-------|---------------------|------------------------------------------|-------------------------|----------|
| 1     | bdc-Pro/dppdc/hmtt  | 0.47                                     | 34.3                    | -2.65    |
| 2     | bdc-Pro/dppdc/hhtt  | 1.7                                      | 80.6                    | 0.4      |
| 3     | bdc-Pro/dppdc/hott  | 1.33                                     | 70.7                    | 11.4     |
| 4     | bdc-Pro/dppdc/hdtt  | 0.49                                     | 36.3                    | -2.78    |

Figure S30. Reaction kinetics plot for the \textit{m}-aldol reaction catalysed by \([\text{Zn}_4\text{O(bdc-Pro)}_{1/2}\text{dppdc)}_{1/2}\text{hmtt})_{4/3}\].

Equation: \(y = A + B \times x\)

|          | Value    | Standard Error |
|----------|----------|----------------|
| Ln(C/Co) A | 0.01419  | 0.00723        |
| Ln(C/Co) B | -0.4706  | 0.02228        |

Equation: \(y = A + B \times x\)

|          | Value    | Standard Error |
|----------|----------|----------------|
| Ln(C/Co) A | -0.13801 | 0.03723        |
| Ln(C/Co) B | -1.69629 | 0.11471        |
Figure S31. Reaction kinetics plot for the $m$-aldol reaction catalysed by $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{dppdc})_{1/2}(\text{hott})_{4/3}]$.

Figure S32. Reaction kinetics plot for the $m$-aldol reaction catalysed by $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{dppdc})_{1/2}(\text{hott})_{4/3}]$.

Figure S33. Reaction kinetics plot for the $m$-aldol reaction catalysed by $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{dppdc})_{1/2}(\text{hott})_{4/3}]$.

6.3 Calculation of the observed initial rate for Henry reactions

The rate of the Henry reaction, $r$, based on the consumption of m-nitrobenzaldehyde (mNBA) can be expressed as a function of reaction rate constant $k$ and the concentration of mNBA and nitromethane by assuming the reaction order of mNBA is unity:

$$ r = -\frac{d[\text{mNBA}]}{dt} = k[\text{mNBA}][\text{nitromethane}]^a $$
Here, \( a \) is the reaction order of nitromethane. Since the reaction is carried out in the presence of a very large excess of nitromethane, the above equation can be simplified as

\[
\frac{d[mNBA]}{dt} = k_{obs}[mNBA]
\]

where \( k_{obs} \) is the pseudo first-order observed rate constant.

Therefore

\[
\ln[mNBA] = \ln[mNBA]_0 - k_{obs}t
\]

Here, \([mNBA]_0\) is the initial concentration of m-nitrobenzaldehyde and \( t \) is time. Plotting \( \ln([mNBA]/[mNBA]_0) \) as a function of time over the initial 12 hours of the reaction yields a line with slope \( k_{obs} \) estimated by least squares fitting.

**Table S4.** Henry reaction of nitromethane and m-nitrobenzaldehyde catalyzed by \([\text{Zn}_4\text{O(bdc-Pro)}]_{1/2}(\text{dppdc})_{1/2}(\text{hmtt})_{4/3}\).

| Entry | Catalyst linker set | Initial rate (L mol\(^{-1}\) day\(^{-1}\)) | Conversion at 24 h (%) | e.e. (%) |
|-------|---------------------|---------------------------------|------------------------|----------|
| 1     | bdc-Pro/dppdc/hmtt   | 0.10                            | 8.2                    | 8.2      |
| 2     | bdc-Pro/dppdc/hhtt   | 0.064                           | 6.7                    | -9.8     |
| 3     | bdc-Pro/dppdc/hott   | 0.023                           | 2.6                    | -2.0     |
| 4     | bdc-Pro/dppdc/hdtt   | 0.015                           | 1.5                    | -2.2     |
| 5     | Me\(_2\)bdc-Pro\(^a\) | n.r.\(^b\)                     | n.r.                   | n.r.     |

\(^{a}\) Control reaction using the dimethyl ester of the catalytic linker (Me\(_2\)bdc-Pro) under homogenous conditions. \(^{b}\) No product formation is observed by HPLC or TLC after 24 h.

**Figure S34.** Reaction kinetics plot for the Henry reaction catalysed by \([\text{Zn}_4\text{O(bdc-Pro)}]_{1/2}(\text{dppdc})_{1/2}(\text{hmtt})_{4/3}\).
Figure S35. Reaction kinetics plot for the Henry reaction catalysed by [Zn₄O(bdc-Pro)₁/₂(dppdc)₁/₂(hht)⁴/₃].

Figure S36. Reaction kinetics plot for the Henry reaction catalysed by [Zn₄O(bdc-Pro)₁/₂(dppdc)₁/₂(hht)⁴/₃].
Figure S37. Reaction kinetics plot for the Henry reaction catalysed by $[\text{Zn}_4\text{O(bdc-Pro)}]_{1/2}(\text{dppdc})_{1/2}(\text{hddt})_{4/3}$.

Figure S38. TLC plate for the Henry reaction after 24 h showing that the reaction is not catalyzed by Me$_2$bdc-Pro under homogeneous conditions but it is catalyzed by heterogeneous MOF catalysts. The eluent is a mixture of ethyl acetate and n-hexane (v/v=1:3).

Table S5. Control experiments for Henry reaction.

| Henry stock solution$^a$ | Additive | Catalyst (10 mol%) | Result (after 24 hours) |
|--------------------------|----------|-------------------|------------------------|
| 1                        | 1 mL     | -                 | Me$_2$bdc-Pro          | n. r.      |
| 2                        | 1 mL     | Zn(NO$_3$)$_2$(H$_2$O)$_4$ (2 mg) | Me$_2$bdc-Pro          | n. r.      |
| 3                        | 1 mL     | -                 | $[\text{Zn}_4\text{O(bdc)}]_{1/2}(\text{dppdc})_{1/2}(\text{hddt})_{4/3}$ | n. r.      |
| 4                        | 1 mL     | -                 | $[\text{Zn}_4\text{O(bdc-Pro)oc)}]_{1/2}(\text{bpdpc})_{1/2}(\text{hddt})_{4/3}$ | n. r.      |

$^a$ The preparation of the Henry stock solution is described on Page S7.
7. Microscopy images, XRD and $^1$H NMR spectra of MOFs after catalysis

Figure S39. Optical microscopy images of $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{dppdc})_{1/2}(\text{hhtt})_{4/3}]$ crystals before (left) and after (right) catalysis. The transparency and integrity of the crystals are very well maintained after catalysis.

Figure S40. Powder XRD patterns of the MOF catalysts after the Henry reaction. From top to bottom: $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{bpdc})_{1/2}(\text{hmtt})_{4/3}]$, $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{bpdc})_{1/2}(\text{hhtt})_{4/3}]$, $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{bpdc})_{1/2}(\text{hhtt})_{4/3}]$, $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{bpdc})_{1/2}(\text{hhtt})_{4/3}]$, $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{bpdc})_{1/2}(\text{hhtt})_{4/3}]$, $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{bpdc})_{1/2}(\text{hhtt})_{4/3}]$, $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{bpdc})_{1/2}(\text{hhtt})_{4/3}]$, and $[\text{Zn}_4\text{O(bdc-Pro)}_{1/2}(\text{dppdc})_{1/2}(\text{hhtt})_{4/3}]$. 
Figure S41. $^1$H NMR spectrum of the digested MOF catalyst, [Zn$_4$O(bdc-Pro)$_{1/2}$bpdc)$_{1/2}$(hmtt)$_{4/3}$], after an aldol reaction.

Figure S42. $^1$H NMR spectrum of the digested MOF catalyst, [Zn$_4$O(bdc-Pro)$_{1/2}$bpdc)$_{1/2}$(hmtt)$_{4/3}$], after a Henry reaction.
Figure S43. $^1$H NMR spectrum of the digested MOF catalyst, [Zn$_4$O(bdc-Pro)$_{1/2}$(bpdc)$_{1/2}$(hbtt)$_{4/3}$], after a Henry reaction.

Figure S44. $^1$H NMR spectrum of the digested MOF catalyst, [Zn$_4$O(bdc-Pro)$_{1/2}$(bpdc)$_{1/2}$(hbtt)$_{4/3}$], after a Henry reaction.
Figure S45. $^1$H NMR spectrum of the digested MOF catalyst, [Zn₄O(bdc-Pro)$_{1/2}$(bpdc)$_{1/2}$(hott)$_{4/3}$], after a Henry reaction.

Figure S46. $^1$H NMR spectrum of the digested MOF catalyst, [Zn₄O(bdc-Pro)$_{1/2}$(dppdc)$_{1/2}$(hmtt)$_{4/3}$], after a Henry reaction.
Figure S47. $^1$H NMR spectrum of the digested MOF catalyst, $[\text{Zn}_4\text{O}(\text{bdc-Pro})_{1/2}(\text{dppdc})_{1/2}(\text{hbt})_{4/3}]$, after a Henry reaction.

Figure S48. $^1$H NMR spectrum of the digested MOF catalyst, $[\text{Zn}_4\text{O}(\text{bdc-Pro})_{1/2}(\text{dppdc})_{1/2}(\text{hbt})_{4/3}]$, after a Henry reaction.
Figure S49. $^1$H NMR spectrum of the digested MOF catalyst, [Zn$_4$O(bdc-Pro)$_{1/2}$(dppdc)$_{1/2}$($h$ott)$_{4/3}$], after a Henry reaction.

8. References

(1) Liu, L. J.; Zhou, T. Y.; Telfer, S. G. Modulating the Performance of an Asymmetric Organocatalyst by Tuning Its Spatial Environment in a Metal-Organic Framework. J. Am. Chem. Soc. 2017, 139, 13936-13943.

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