

Supporting Information for

Blocking bimolecular activation pathways leads to different regioselectivity in metal-organic framework catalysis

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1. General experimental

All of the solvents were purchased from Fisher and used without further purification unless further notice. NMR spectra were recorded on a Bruker NMR 400 NB spectrometer at 400 MHz and referenced to the proton resonance resulting from incomplete deuteration of chloroform-*d* (δ 7.26) or DMSO-*d*₆ (δ 2.49). Thermogravimetric analysis (TGA) was performed in air using a Shimadzu TGA-50 equipped with a S2 platinum pan and heated at a rate of 3°C per minute. Single-crystal X-ray diffraction and powder X-ray diffraction (PXRD) patterns were collected on a Bruker SMART APEX II diffractometer using Cu radiation. The PXRD patterns were processed with the APEX 2 package using PILOT plug-in. The conversions were determined by ¹H NMR with mesitylene as an internal standard or by integrations of HPLC traces. The *ee* values were determined by chiral HPLC.

2. Synthesis and characterization of ligand and MOFs

3-Formyl-4-hydroxy-5-*t*-butylbenzoic acid. 4-Bromo-2-*t*-butylphenol (4.73 g, 20.7 mmol) was dissolved in 50 mL of *N,N*-dimethylformamide and the solution was degassed for 30 minutes. CuCN (2.31 g, 25.8 mmol) was then added and the solution was heated to reflux under nitrogen. After 2 days, the solution was cooled down, diluted with dichloromethane and washed with water and brine. The organic layer was then dried over anhydrous MgSO₄. After removal of the solvent, the resulting oil was dissolved in a 1:1 mixture of 6M NaOH (aq) and ethanol and heated to reflux overnight. The solution was cooled down, poured to an ice/HCl mixture and extracted with ethyl acetate. The organic layer was then washed with brine and dried over anhydrous MgSO₄. After removal of the solvent, the resulting solid was dissolved in 100 mL of trifluoroacetic acid and hexamethylenetetraamine (4.35 g, 31.0 mmol) was added to the solution.

The solution was heated to reflux for 18 hours, then 100mL of 33% H₂SO₄ was added and the solution was refluxed for another 3 hours. The solution was then cooled down, extracted with diethyl ether (2 × 100mL) and washed with water and brine. The organic layer was dried over anhydrous MgSO₄ and concentrated in vacuo. The resulting oil was then dissolved in 2M NaOH (aq), filtered, and poured to an ice/HCl mixture. The resulting solid was filtered out and purified by column chromatography on silica gel (hexanes: ethyl acetate: acetic acid = 10:1:0.2 v/v/v) to afford 1.01g of white solid (22% yield for 3 steps) as the product. ¹H NMR (CDCl₃, δ, 400MHz) 12.31 (s, 1H), 9.96 (s, 1H), 8.26 (s, 2H), 1.46 (s, 9H).

(R, R)-N, N'-Bis(3-carboxyl-5-*t*-butylsalicylidene)-1,2-cyclohexanediamine (H₂L). 3-Formyl-4-hydroxy-5-*t*-butylbenzoic acid (205.5mg, 0.925mmol) and (R, R)-1,2-cyclohexanediamine (52.85mg, 0.463mmol) was dissolved in 20mL of tetrahydrofuran. The solution was then allowed to stir at room temperature for 3 days and the solvent was removed in vacuo. The resulting solid was dissolved in ethanol and then precipitated out by addition of water. The solid was filtered out and dried in air to afford 239 mg of yellow powder (99% yield) as the product. ¹H NMR (DMSO-*d*₆, δ, 400MHz) 15.02 (s, 2H), 12.49 (br, 2H), 8.60 (s, 2H), 7.79 (d, 2H, J=2.0Hz), 7.76 (d, 2H, J=2.0Hz), 3.56 (d, 2H, J=9.6Hz), 1.4-2.0 (m, 8H), 1.31 (s, 18H).

(R, R)-N, N'-Bis(3-carboxyl-5-*t*-butylsalicylidene)-1,2-cyclohexanediamino cobalt(III) acetate [Co(H₂L)(OAc)]. A suspension of H₂L (104.95mg, 0.20mmol) in 4 mL of toluene (suspension A) and a solution of Co(OAc)₂·4H₂O (62.86mg, 0.25mmol) in 4mL methanol (solution B) were degassed separately. Solution B was then added to suspension A dropwise under nitrogen atmosphere and the resulting mixture was allowed to react for 1 hour. The solvent was then removed in vacuo and the resulting orange solid was dispersed in 10 mL of dichloromethane. 0.25mL of glacial acetic acid was then added and the suspension was exposed to air and allowed to stir until the solvent evaporated. The resulting solid was dispersed in water, filtered and dried in air to afford 108 mg of dark brown powder (85% yield) as the product. Samples for elemental analysis were recrystallized from chloroform. ESI-MS: *m/z* 579.10 [M-OAc]⁺, 693.18 [M+Na+CH₃OH]⁺. Elemental analysis: calcd. for [Co(H₂L)(OAc)·H₂O·0.3CHCl₃]: C, 56.02; H, 6.01; N, 4.05; found: C, 55.69; H, 6.31; N, 4.08.

Methyl 3-formyl-4-hydroxy-5-*t*-butylbenzoate. 3-Formyl-4-hydroxy-5-*t*-butylbenzoic acid (114.5mg, 0.52mmol) was dissolved in 30 mL of methanol. A few drops of concentrated

H₂SO₄ were added and the solution was heated to reflux overnight. The solution was neutralized by sodium bicarbonate after cooling down, and the solvent was removed in vacuo. The residue was then extracted with water/ethyl acetate and the organic layer was dried of MgSO₄. Removing solvent on rotovap resulted in 55 mg of white solid (45%) as the product. ¹H NMR (CDCl₃, δ, 400MHz) 12.19 (s, 1H), 9.92 (s, 1H), 8.19 (d, 1H, J=2.0Hz), 8.17 (d, 1H, J=2.0Hz), 3.92(s, 3H), 1.43 (s, 9H).

(R, R)-N, N'-Bis(3-methoxycarbonyl-5-*t*-butylsalicylidene)-1,2-cyclohexanediamine (Me₂-L). Methyl 3-formyl-4-hydroxy-5-*t*-butylbenzoate (55.0mg, 0.233mmol) and (R, R)-1,2-cyclohexanediamine (13.22mg, 0.116mmol) was dissolved in 15mL of tetrahydrofuran. The solution was then allowed to stir at room temperature for 3 days and the solvent was removed in vacuo, resulting in 56 mg of yellow solid (96% yield) as the product. ¹H NMR (CDCl₃, δ, 400MHz) 14.59 (br, 2H), 8.30 (s, 2H), 7.92 (d, 2H, J=2.0Hz), 7.73 (d, 2H, J=2.0Hz), 3.83 (s, 6H), 3.36 (d, 2H, J=9.6Hz), 1.6-2.2 (m, 8H), 1.40 (s, 18H).

(R, R)-N, N'-Bis(3-methoxycarbonyl-5-*t*-butylsalicylidene)-1,2-cyclohexanediamino cobalt(III) acetate [Co(Me₂L)(OAc)]. A solution of Me₂L (56mg, 0.11mmol) in 4 mL of toluene (solution A) and a solution of Co(OAc)₂·4H₂O (76mg, 0.30mmol) in 4mL methanol (solution B) were degassed separately. Solution B was then added to solution A dropwise under nitrogen atmosphere and the resulting mixture was allowed to react for 1 hour. The solvent was then removed in vacuo and the resulting orange solid was dissolved in 10 mL of dichloromethane. 0.25mL of glacial acetic acid was then added and the suspension was exposed to air and allowed to stir until the solvent evaporated. The resulting solid was dispersed in water, filtered and dried in air to afford 70 mg of dark brown powder (94% yield) as the product. Samples for elemental analysis were recrystallized from chloroform. ¹H NMR (DMSO-*d*₆, δ, 400MHz) 8.17 (d, 1H, J=2.4Hz), 8.16 (d, 1H, J=2.4Hz), 7.99 (d, 1H, J=1.4Hz), 7.96 (d, 1H, J=1.4Hz), 7.81 (d, 1H, J=2.4Hz), 7.75 (d, 1H, J=2.4Hz), 3.78 (s, 6H), 2.99 (m, 2H), 1.7-2.0 (m, 7H), 1.65 (s, 9H), 1.59 (s, 9H), 1.13 (s, 4H). ¹³C NMR (DMSO-*d*₆, δ, 100.7MHz) 177.81, 170.94, 170.42, 166.92, 166.88, 164.68, 164.59, 143.10, 141.76, 137.44, 137.27, 130.09, 129.71, 120.16, 119.97, 114.23, 113.26, 70.88, 70.44, 51.84, 51.75, 36.06, 30.30, 30.24, 29.96, 29.67, 24.75, 24.10. Elemental analysis: calcd. for [Co(Me₂L)(OAc)·H₂O·0.5CHCl₃]: C, 55.67; H, 6.16; N, 3.76; found: C, 55.70; H, 6.31; N, 4.08.

Zn₄O[CoL(OAc)]₃·17DMF·30EtOH (MOF 1). Zn(NO₃)₂·6H₂O (5 mg, 16.8 μmol) and Co(H₂L)(OAc) (5mg, 7.83 μmol) were added to a screw-capped glass vial. 0.25mL of *N,N*-dimethylformamide (DMF) and 0.5mL of ethanol were then added. The vial was capped and placed in an oven at 60 °C for 3 days. Black cubic crystals (5mg, 40% yield) were obtained. Solvent content determined by ¹H NMR/TGA: DMF 25.1%, EtOH 29.2%; calculated from proposed formula: DMF 25.8%, EtOH 28.8%.

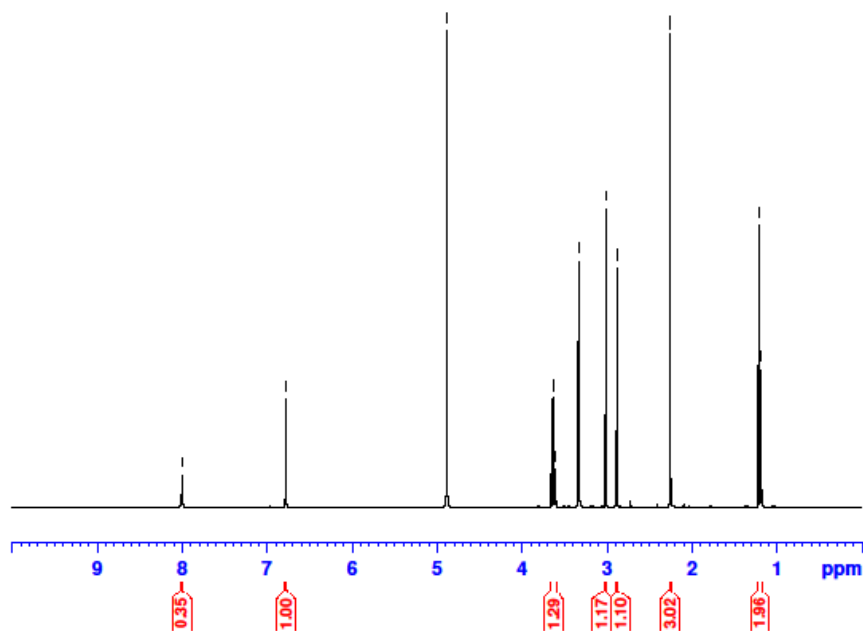


Figure S1. ¹H NMR spectroscopic determination of solvent content of MOF 1. Mesitylene was added as an internal standard.

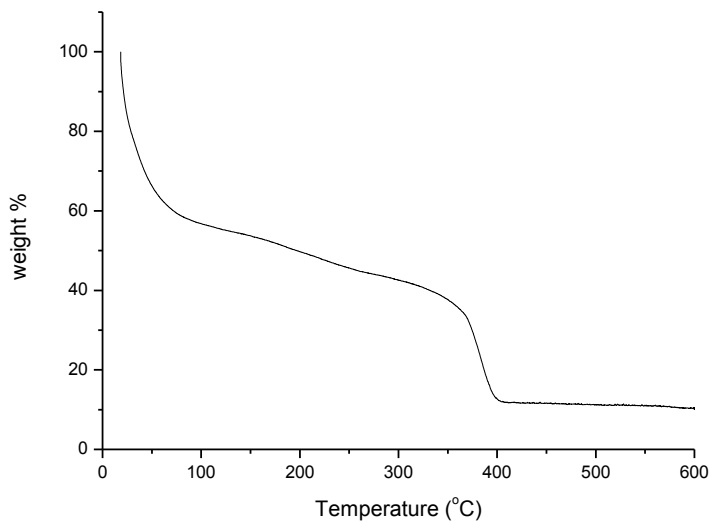


Figure S2. Thermogravimetric analysis (TGA) curve for MOF 1. The sample was heated to 600°C at a rate of 3°C/min.

Zn₄(OH)₂[CoL(OAc)][CoL(OH₂)₂]₄·24DBF·14H₂O (MOF 2). Zn(NO₃)₂·6H₂O (2 mg, 6.72 μmol) and Co(H₂L)(OAc) (2 mg, 3.13 μmol) were added to a polypropylene vial. 40 μL of *N,N*-di-*n*-butylformamide (DBF) was then added. The vial was placed in a large capped vial in an oven at 60 °C for 5 days. Needle-like black crystals (0.5mg, 11% yield) were obtained. Solvent content determined by ¹H NMR/TGA: DBF 50.7%, H₂O 5.7%; calculated from proposed formula: DBF 50.9%, H₂O 5.3%.

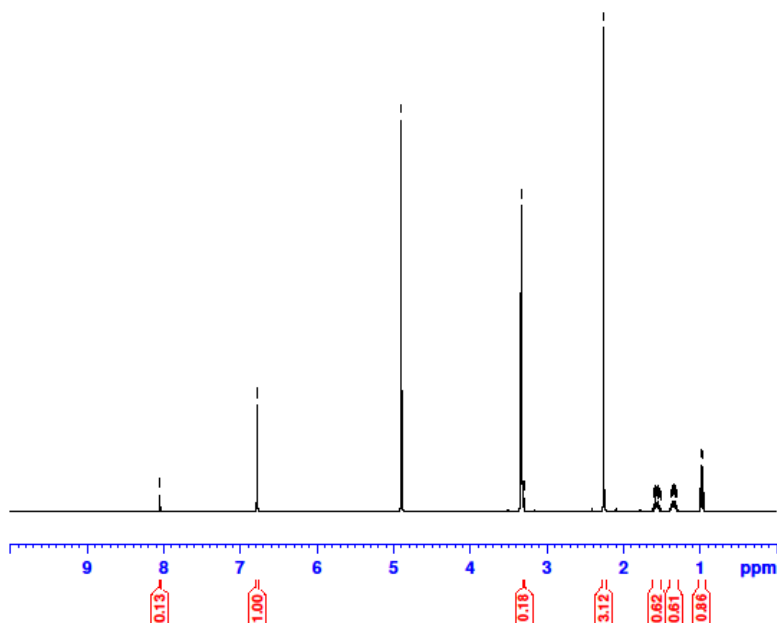


Figure S3. ¹H NMR spectroscopic determination of solvent content of MOF 2. Mesitylene was added as an internal standard.

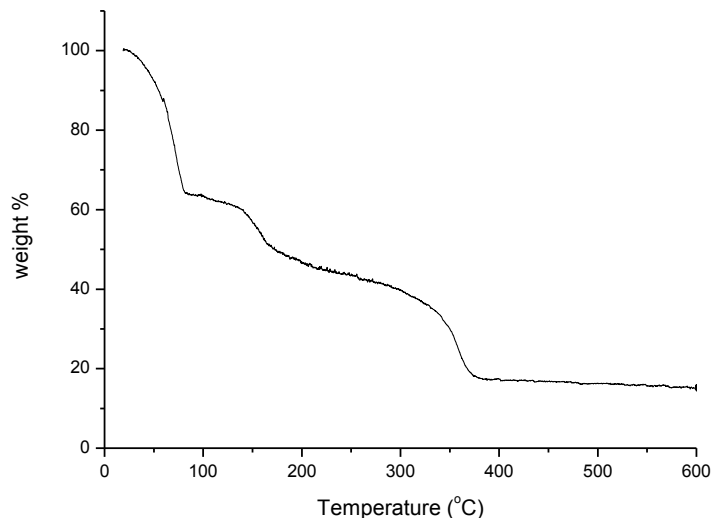


Figure S4. Thermogravimetric analysis (TGA) curve for MOF **2**. The sample was heated to 600°C at a rate of 3°C/min.

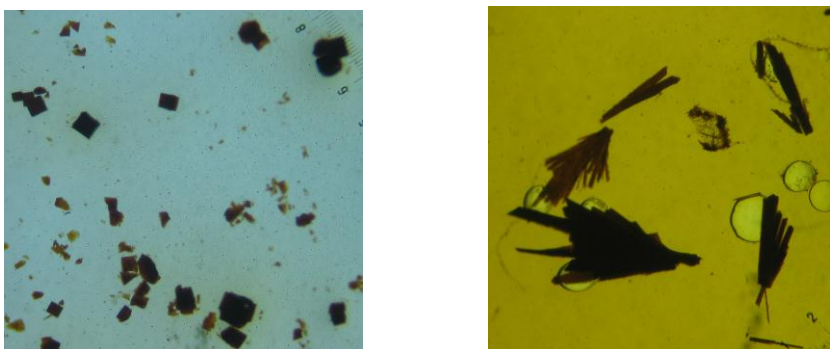


Figure S5. Photographs of MOF **1** (left) and MOF **2** (right) under a microscope showing cubic and needle-like morphologies for **1** and **2**, respectively.

3. Single crystal X-ray structure determination

All crystallographic measurements were made on a Bruker SMART Apex II CCD-based X-ray diffractometer system operated at 1600 watts (Cu-target X-ray tube). The crystals were mounted inside a capillary tube (0.5 mm ID) with small amount of mother liquid to prevent solvent loss from the crystal frameworks. The frames were integrated with the Bruker SAINT© build in APEX II software package using a narrow-frame integration algorithm, which also corrects for the Lorentz and polarization effects. Absorption corrections were applied using SADABS. Structures were solved by direct methods and refined to convergence by least squares method on F2 using the SHELXTL software suite.

Due to the relatively weak diffraction and low resolution ($>1.3 \text{ \AA}$) (which is not uncommon for this kind of framework with very large solvent accessible void space), as well as ligand disorders due to rotation of C-C bond between carboxylate group and benzene ring (which is also a common phenomenon for MOFs built from 2-connected dicarboxylate ligands), restraints (SIMU and DELU) on displacement parameters, and DFIX for bond lengths are applied, and all the phenyl rings are constrained to ideal six-membered rings. SQUEEZE subroutine of the PLATON software suite was applied to remove the scattering from the highly disordered guest molecules. The resulting new HKL files were used to further refine the structures. Non-hydrogen atoms (except Zn and Co) are refined isotropically.

Table S1. Crystal data and structure refinement for MOF 1 and MOF 2.

Compound	MOF 1	MOF 2
Empirical formula	$\text{Zn}_4\text{O}[\text{CoL}(\text{OAc})]_3 \cdot 17\text{DMF} \cdot 30\text{EtOH}$	$\text{Zn}_4(\text{OH})_2[\text{CoL}(\text{OAc})][\text{CoL}(\text{OH}_2)_2]_4 \cdot 24\text{DBF} \cdot 14\text{H}_2\text{O}$
Formula weight	4811.89	7412.63
Temperature (K)	293	293
Wavelength (\AA)	1.54178	1.54178
Crystal system	cubic	orthorhombic
Space group	$F432$	$I222$
Unit cell dimensions	a = 41.5687(2) b = 41.5687(2) c = 41.5687(2) $\alpha = 90$ $\beta = 90$ $\gamma = 90$	a = 17.9269(9) b = 19.2699(10) c = 50.450(3) $\alpha = 90$ $\beta = 90$ $\gamma = 90$
Volume (\AA^3)	71828.9(6)	17427.8(15)
Z	4	2
Density (calcd. g/cm^3)	0.362	0.601
Absorption coeff. (mm^{-1})	1.506	2.408
F(000)	7672.0	3106.0
Crystal size (mm)	$0.4 \times 0.4 \times 0.4 \text{ mm}$	$0.5 \times 0.2 \times 0.1 \text{ mm}$
Crystal color & shape	black block	black needle-like
θ range data collection	1.84 – 36.30	1.75 – 36.42
Limiting indices	$-31 \leq h \leq 22, -29 \leq k \leq 31, -29 \leq l \leq 30$	$-13 \leq h \leq 13, -14 \leq k \leq 14, -36 \leq l \leq 38$
Reflection collected	25931	16349
Independent reflections	1459	4129
R(int)	0.0945	0.0596
Data/restraints/parameters	1459/38/39	4129/88/194
Goodness-of-fit on F^2	1.811	1.451
Final R indices [$I > 2\sigma(I)$]	R1 = 0.1222, wR2 = 0.3281	R1 = 0.0839, wR2 = 0.2247

R indices (all data)

R1 = 0.1927, wR2 = 0.3434

R1 = 0.1027, wR2 = 0.2389

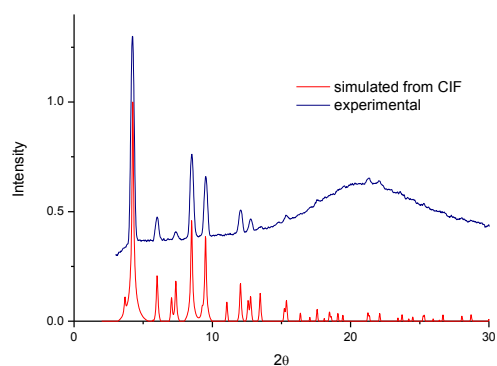


Figure S6. Simulated and experimental powder X-ray patterns of MOF **1**. The broad peak around 20 deg is from quartz capillary tube.

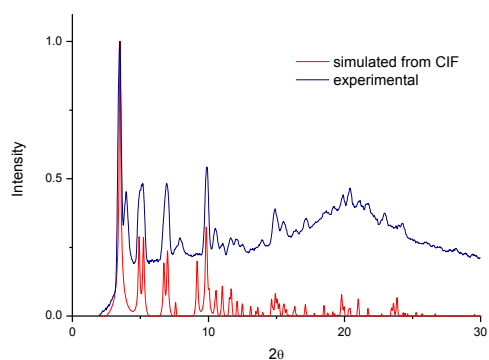


Figure S7. Simulated and experimental powder X-ray patterns of MOF **2**. The broad peak around 20 deg is from quartz capillary tube.

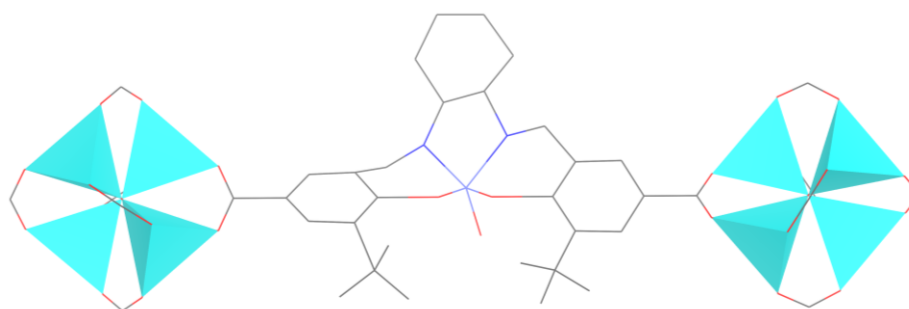


Figure S8. Stick and polyhedron model of MOF **1** showing the Zn₄O SBUs and the dicarboxylate bridging ligand.

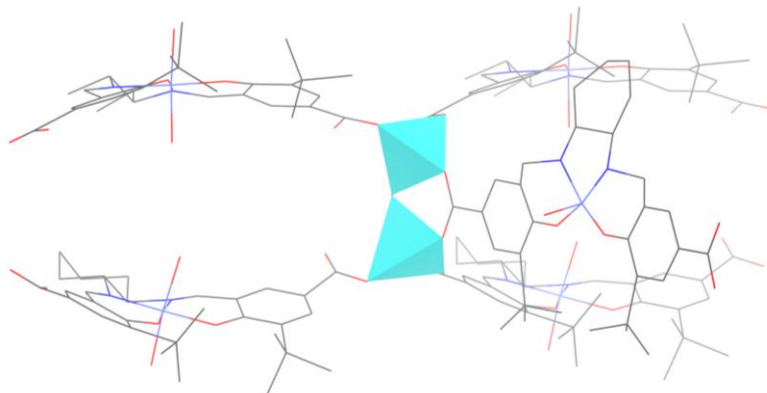


Figure S9. Stick and polyhedron model of MOF 2 showing the Zn₂(OH) SBU and coordinating ligands.

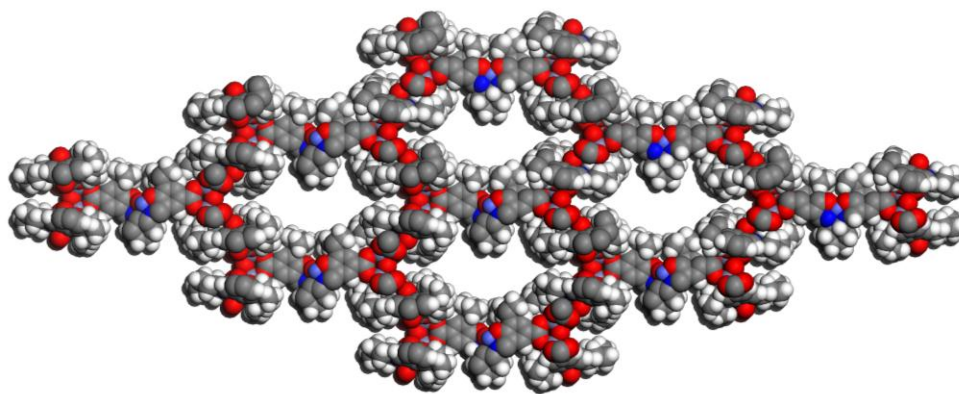


Figure S10. Space-filling model of MOF 2 as viewed along the [100] direction.

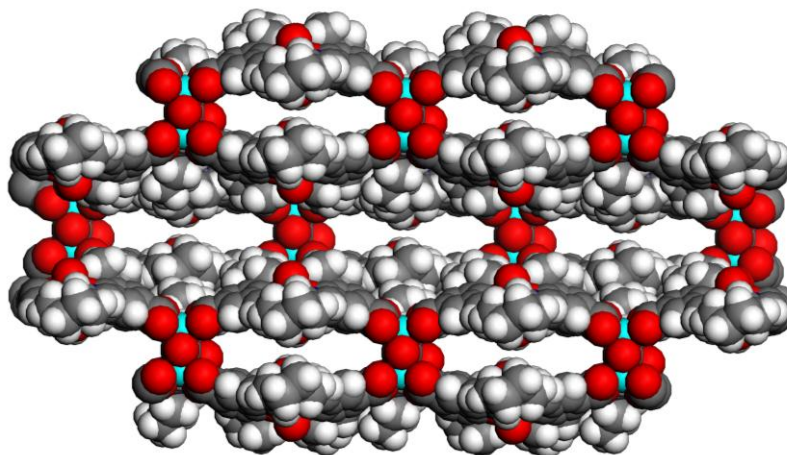


Figure S11. Space-filling figure of MOF 2 as viewed along the [001] direction.

4. Representative procedure for dye uptake measurements

Fresh crystals of MOF 1 (1.93 mg) were briefly dried on a piece of filter paper and soaked in an ethanol solution of Brilliant Blue R-250 (25mM, 0.5mL) overnight. The dye solution

was carefully removed by syringe and the crystals were then washed with water until the washing was colorless. The solid remained was then dissolved in a mixture of 2 mL methanol and 10 μ L 2M HCl(aq). The resulting solution was diluted by 10 times to fit in the detection range of the spectrometer. Absorption measurements were performed on a Shimadzu UV2401-PC UV-Vis spectrophotometer and the concentration of the dye was calculated by comparing the absorption with a standard curve.

5. Ring-opening reactions of epoxy alcohols

Representative procedure. *t*-Butyl methyl ether (TBME) was dried with sodium and stored in a dry box before use. Fresh crystals of MOF **1** (8.0 mg, 0.005mmol) were briefly dried on a piece of filter paper and washed with dichloromethane for 3 times. The crystals were then washed by 1mL \times 3 of dry TBME. Another 1.5mL of dry TBME was added to the sample and the suspension was cooled in an ice bath to 0°C. 4,5-Epoxy-1-pentanol (**3**, 48.5 μ L, 0.5mmol) was added to the suspension and the mixture was allowed to stir for 6 hours at 0 °C. Benzoic anhydride (0.17 g, 0.75 mmol, 1.5 equiv.), 4-dimethylaminopyridine (0.061g, 0.5 mmol, 1 equiv.) and dichloromethane (1mL) were then added to the mixture and the mixture was stirred for an additional hour. The reaction mixture was diluted with 20 mL of ethyl acetate and washed with 2 \times 20mL 2M HCl, 20mL saturated NaHCO₃ (aq), and 20mL brine. The organic layer was then dried over anhydrous MgSO₄ and the solvent was removed in vacuo. The resulting oil was dissolved in chloroform-*d* and 28.0 μ L of mesitylene was added as an internal standard. After taking the crude ¹H NMR spectrum, the solution was concentrated again and purified by flash chromatography (hexanes: diethyl ether = 8:1 v/v). The mixture of **3'** and **4b'** was obtained as colorless oil. The ratio and ee values of each component were determined by chiral HPLC. HPLC conditions: Chiralcel[®] OJ column, Hex:iPrOH = 95:5, 0.5mL/min: **4a'** 15.48/16.06 min, **4b'** 19.69/20.71 min, **3'** 29.10/30.34 min.

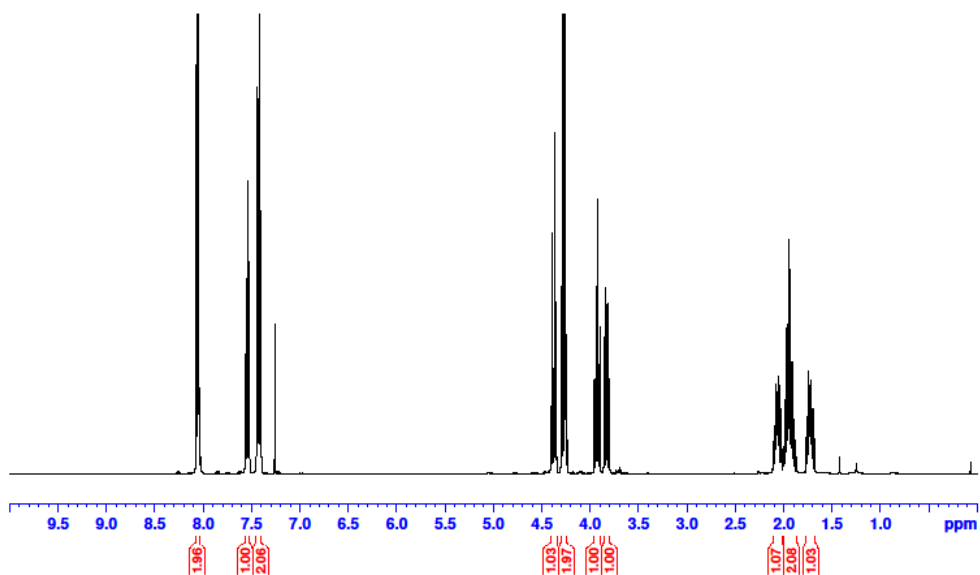


Figure S12. ¹H NMR spectrum of compound 4b'.

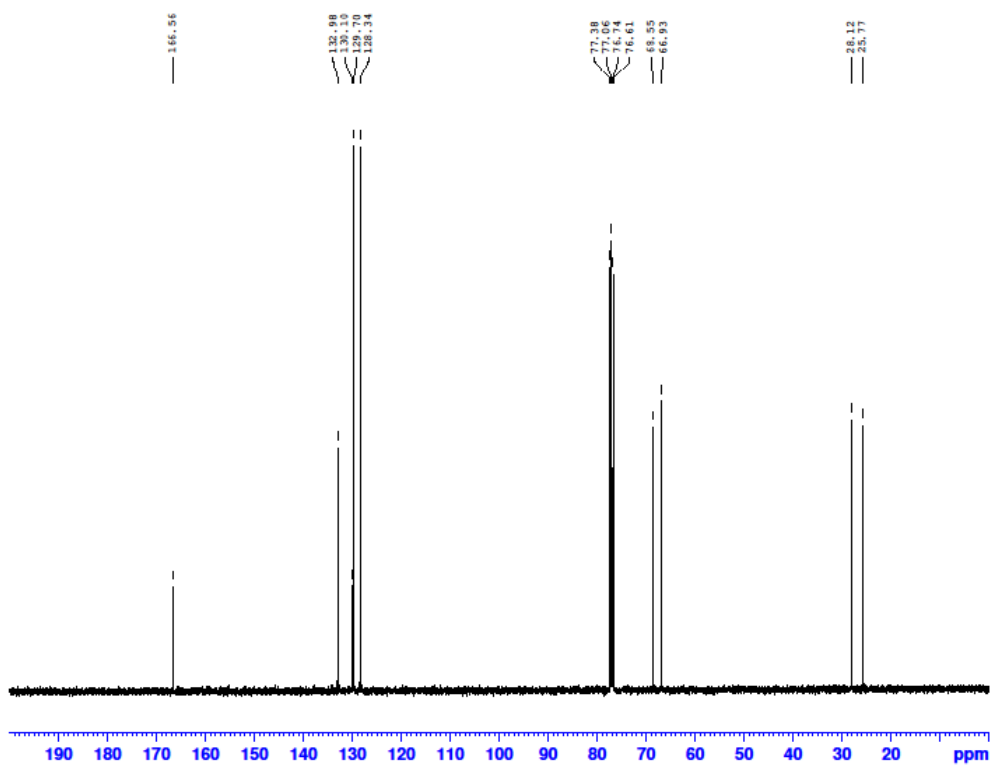


Figure S13. ¹³C NMR spectrum of compound 4b'.

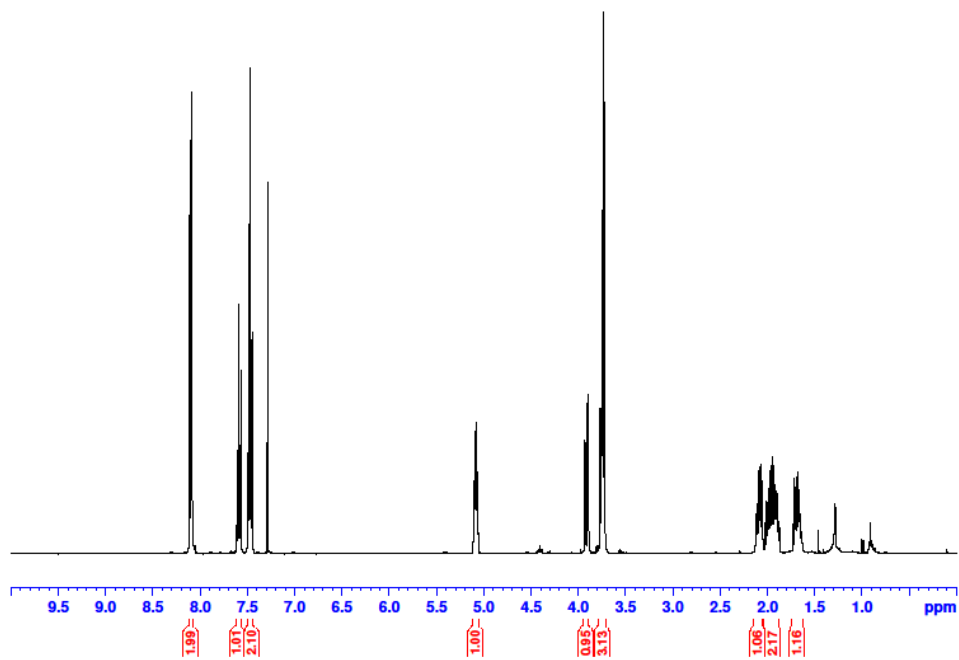


Figure S14. ¹H NMR spectrum of compound 4a'.

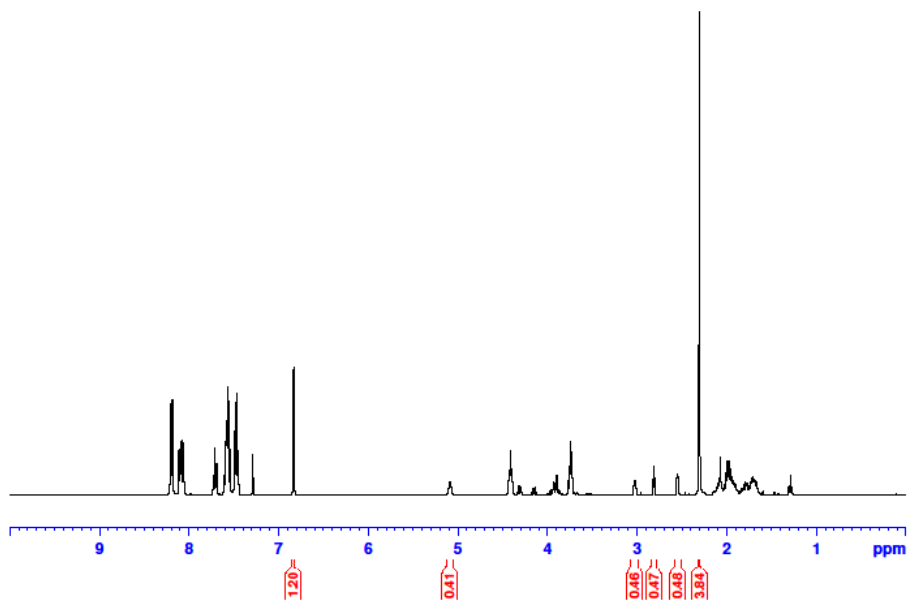


Figure S15. ¹H NMR spectrum of reaction mixture catalyzed by Co(L-Me₂)OAc.

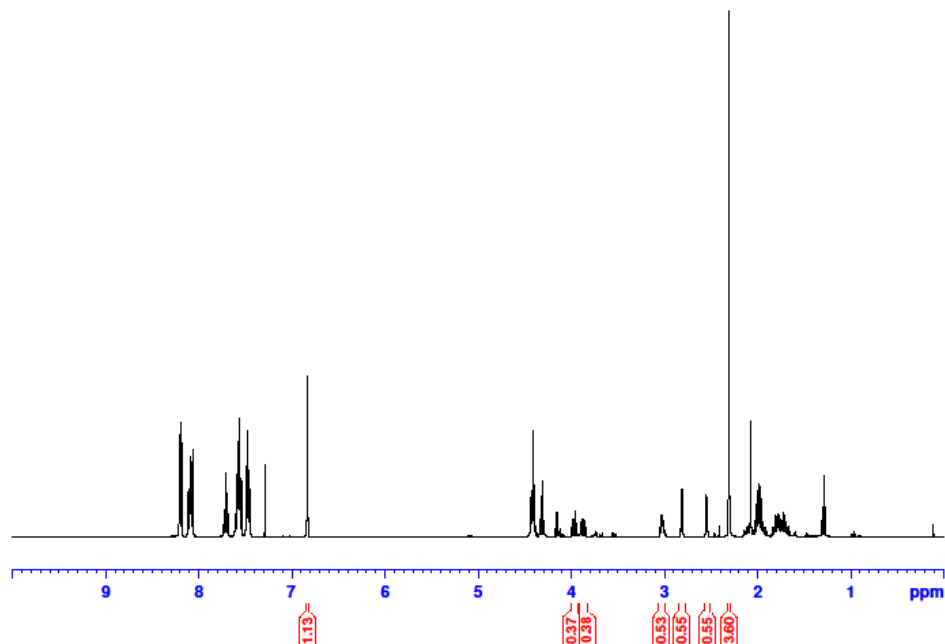


Figure S16. ¹H NMR spectrum of reaction mixture catalyzed by **1**.

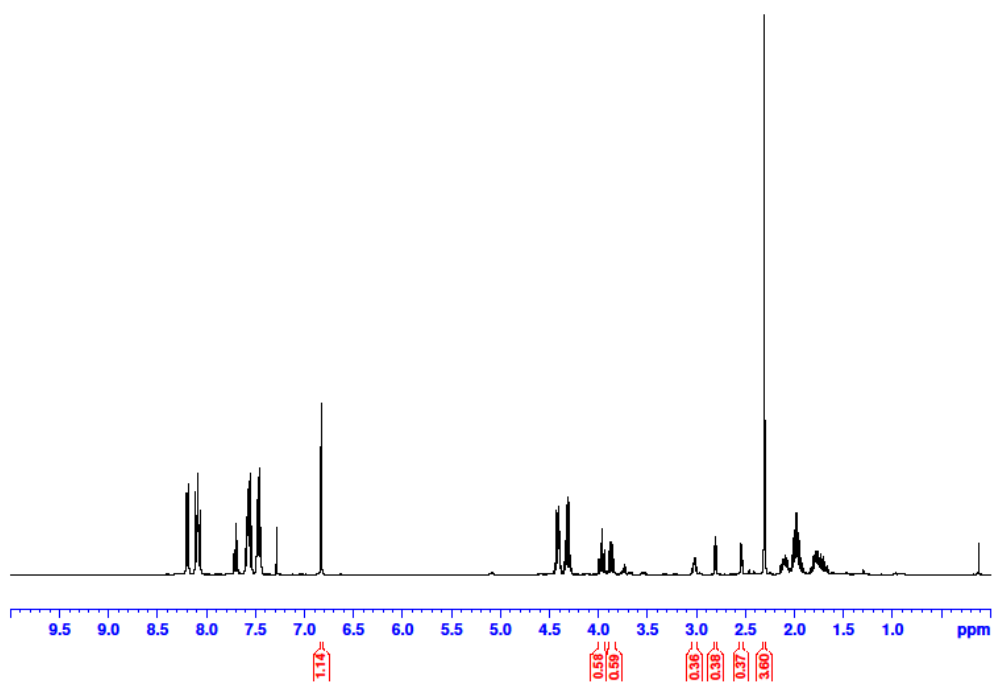


Figure S17. ¹H NMR spectrum of reaction mixture catalyzed by **2**.

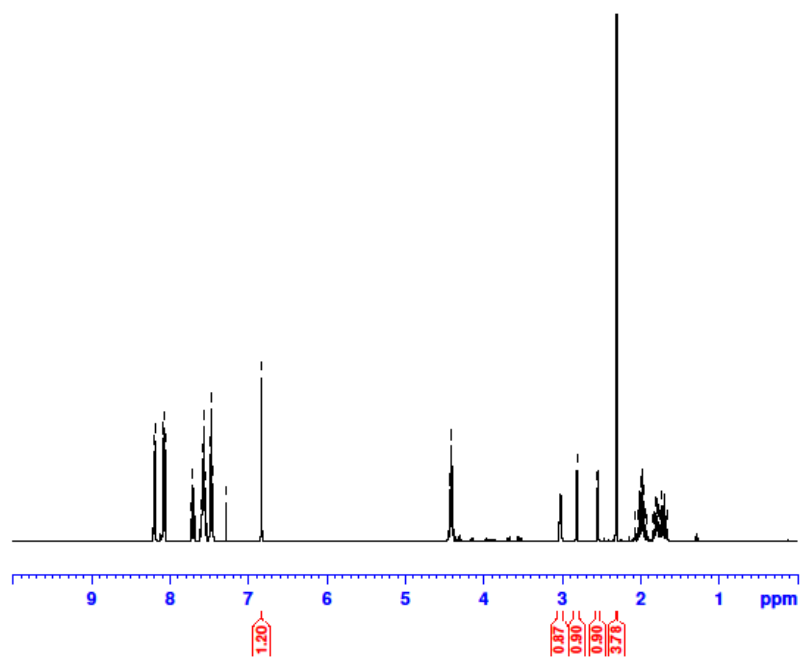
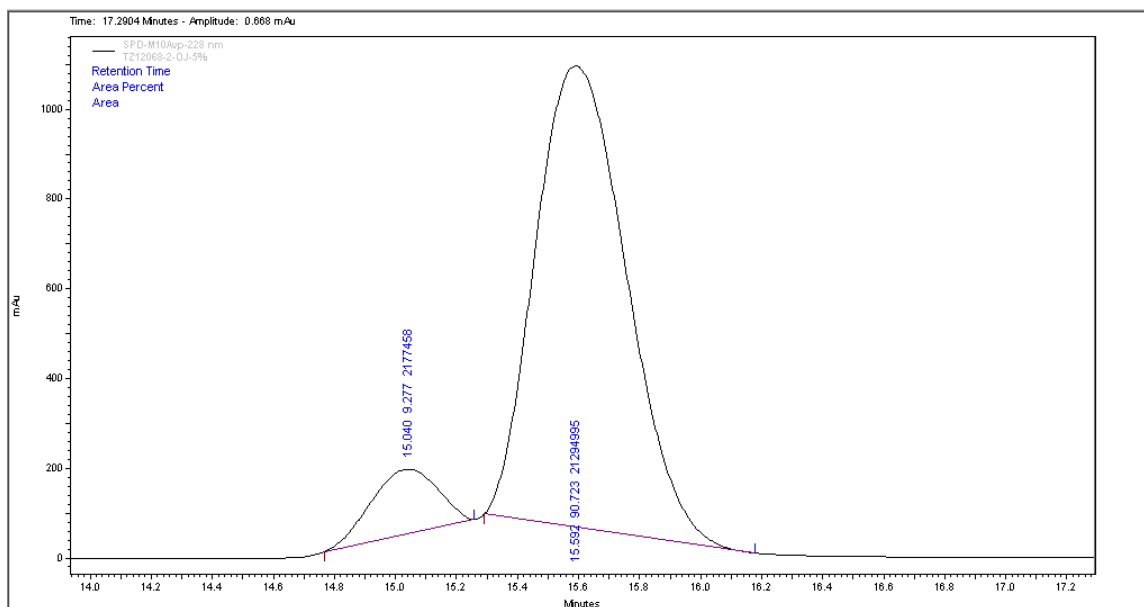


Figure S18. ¹H NMR spectrum of reaction mixture catalyzed by MOF-5.



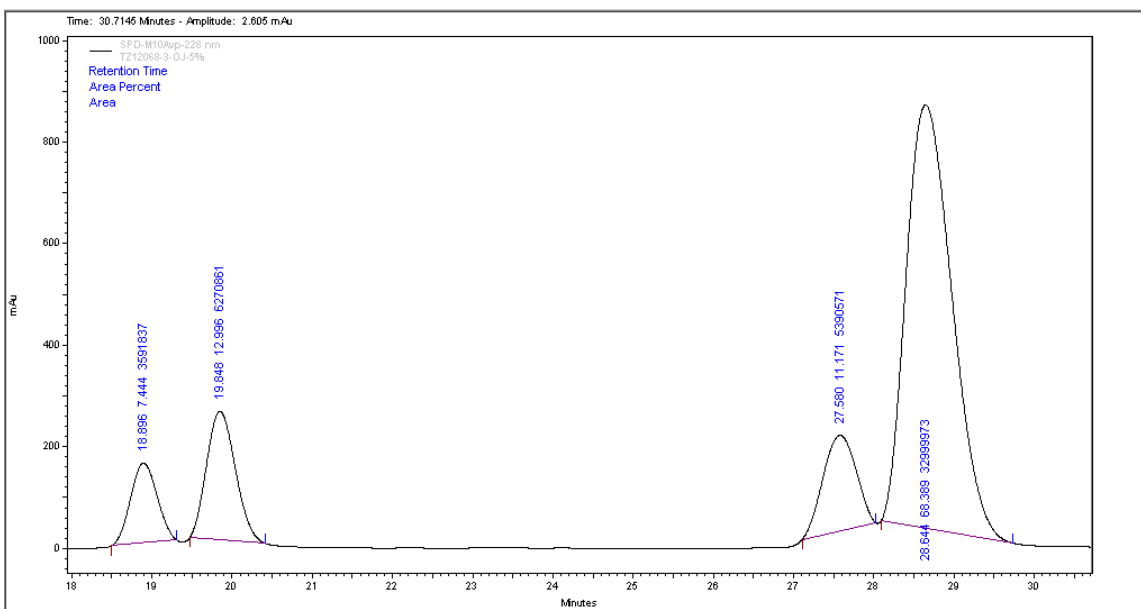


Figure S19. HPLC chromatograms of **4a'** (top) and **3'** and **4b'** (bottom) catalyzed by Co(L-Me₂)OAc.

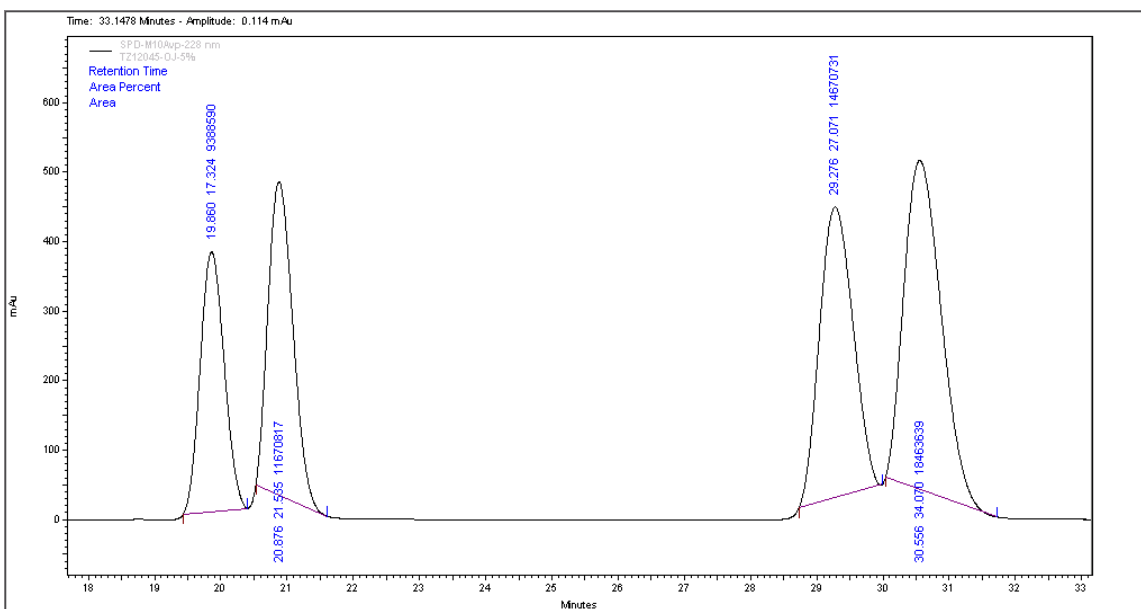


Figure S20. HPLC chromatograms of **3'** and **4b'** catalyzed by **1**.

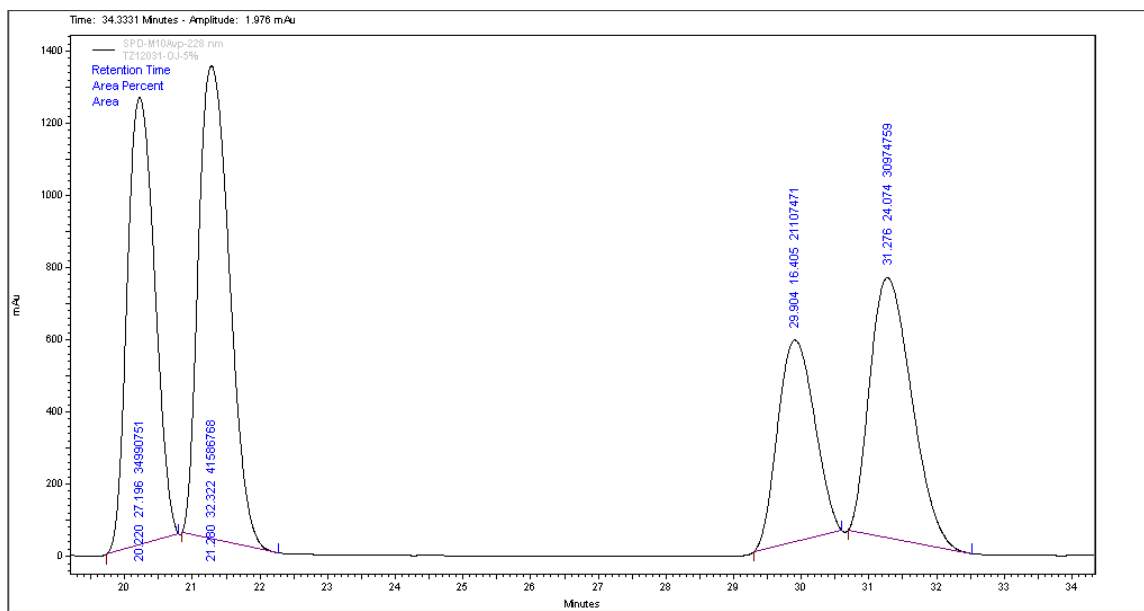


Figure S21. HPLC chromatograms of **3'** and **4b'** catalyzed by **2**.