Supporting Information

Chiral Proline-Substituted Porous Organic Cages in Asymmetric Organocatalysis

Ning Xu,[a] Kongzhao Su,[a,b] El-Sayed M. El-Sayed,[a,b,d] Zhanfeng Ju,[a] and Daqiang Yuan*[a,b,c]

[a.] State Key Laboratory of Structural Chemistry, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences, Fuzhou, 350002, Fujian, China.

[b.] University of the Chinese Academy of Sciences, Beijing, 100049, China

[c.] Fujian Science and Technology Innovation Laboratory for Optoelectronic Information of China, Fuzhou, 350002, Fujian, China.

[d.] Chemical Refining Laboratory, Refining Department, Egyptian Petroleum Research Institute, Nasr City, 11727, Egypt.

Corresponding author: ydq@fjirsm.ac.cn

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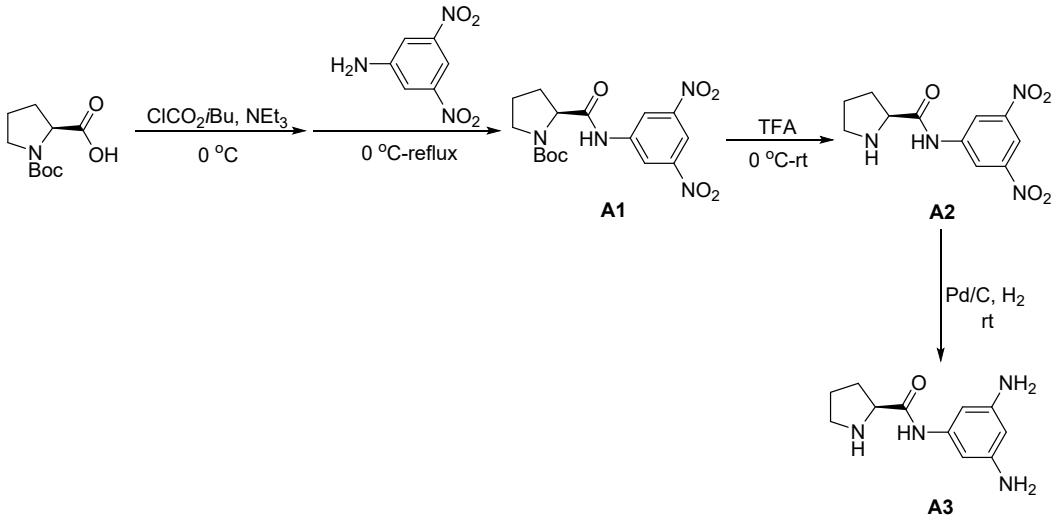
1. General Materials and Measurements

Commercially available reagents were used as received without further purification. Most reagent-grade chemicals were obtained from Adamas Reagent, Ltd. C4RACHO was synthesized according to the procedure in the literature. All the reagent-grade chemicals were commercially available and used directly. FT-IR spectra were collected on KBr pellets in the 4000-400 cm-1 range using a VERTEX70 spectrometer. 1H NMR spectra were recorded on a Bruker Avance 400 spectrometer. High-resolution ESI-TOF-MS spectra were obtained on a MaXis™ 4G instrument from Bruker. Thermogravimetric analyses (TGA) were measured on a NETZSCH STA 449C unit at a heating rate of 10 °C min^{-1} under a nitrogen atmosphere. Circular dichroism (CD) spectra were recorded with a Bio-logic MOS-450 CD Spectrometer at room temperature. Powder X-ray diffraction (PXRD) data were collected on a PANalytical B.V.Empyrean powder diffractometer using a Cu Kα source (λ = 1.5418 Å) over the range of 2θ = 2.0−40.0° with a step size of 0.02° and 2 s per step and MiniFlex 600 spectrometer using Cu Kα radiation over the range of 2θ = 4.0−50.0° with a step size of 0.02° and 2 s per step. Elemental analysis (C, H, N) was performed on an Elementar Vario MICRO elemental analyzer. The sorption isotherm for N_2 was measured using a Micromeritics ASAP 2020 plus analyzer with ultra-high-purity N_2 (99.999% purity) at liquid nitrogen temperature (77 K).

2. Experimental Procedures

2.1 Synthesis of the chiral proline-decorated diamine ligands

2.1.1 Synthesis of (S)-N-(3,5-diaminophenyl)pyrrolidine-2-carboxamide (A3)



Scheme S1. Synthetic route of (S)-N-(3,5-diaminophenyl)pyrrolidine-2-carboxamide.

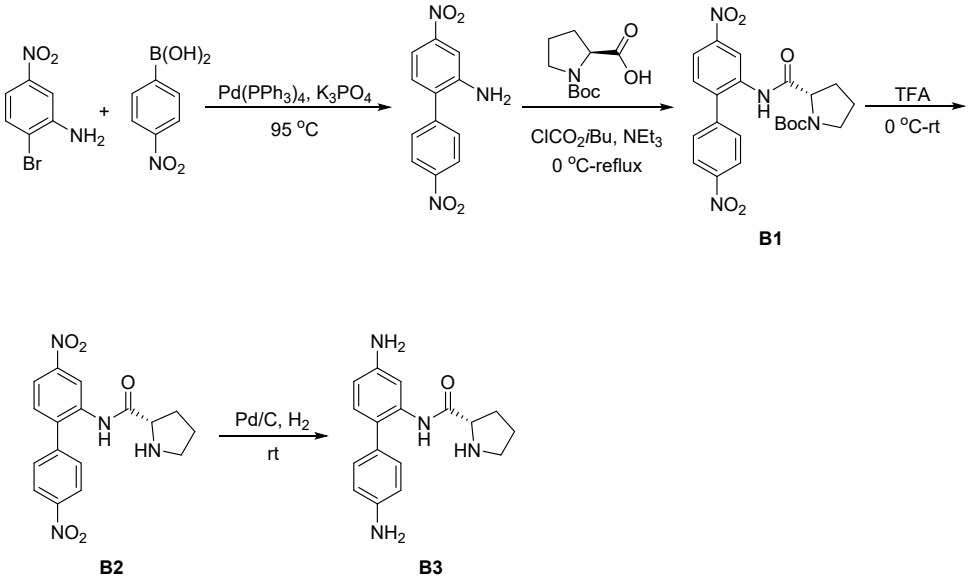
To a solution of Boc-L-proline (1.27 g, 5.9 mmol) in 20 mL dry THF was added triethylamine (0.82 mL, 5.9 mmol) under argon atmosphere. After the mixture was cooled to 0 °C, isobutyl chloroformate (0.78 mL, 6.0 mmol) was added dropwise followed by stirring for 1 h. After that, 2,4-dinitroaniline (0.99 g, 5.4 mmol) was added to the solution in small portions. The resulting mixture was stirred at 0 °C for 1 h, at room temperature for 2 h, and then heated at reflux for 24 h. Upon cooling down, the mixture was filtered and the filtrate was concentrated. The residue was purified by column chromatography with dichloromethane as the

eluent to give compound **A1** as light yellow oil in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 10.62 (s, 1H), 8.67 (s, 2H), 8.61 (s, 1H), 4.58 (s, 1H), 3.43-3.57 (m, 2H), 2.45 (s, 1H), 1.98-2.05 (m, 3H), 1.57 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)= 171.72, 155.88, 148.11, 140.85, 118.16, 112.04, 81.38, 60.46, 47.31, 29.30, 28.31, 24.26. Anal. calcd (%): C, 50.53; H, 5.30; N, 14.73. Found (%): C, 50.45; H, 5.38; N, 14.76. IR (KBr, cm^{-1}) v 3099, 2980, 1657, 1535, 1420, 1344, 1163, 1135, 899, 813, 772, 727. ESI-TOF-MS: calcd. for $C_{16}H_{20}N_4NaO_7$ $[M+Na]^+$ 403.1224, found 403.1212.

The above product **A1** (1.9 g, 5.0 mmol) was dissolved in dry dichloromethane (30 mL) and cooled to 0 °C. Then, trifluoroacetic acid (15 mL) was slowly added to the solution. The mixture was stirred at room temperature for two days and concentrated under reduced pressure. Dichloromethane (10 mL) and H_2O (10 mL) were added, the resulting mixture was basified with NH_4OH and extracted with dichloromethane (3 × 50 mL). The obtained organic layer was collected, washed with brine, and dried over anhydrous $MgSO_4$. After removing the organic solvent under reduced pressure, the residue was purified by column chromatography with dichloromethane/ethyl acetate (3/1, v/v) as the eluent to afford compound **A2** as light yellow solids in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 10.51 (s, 1H), 8.87 (s, 2H), 8.71 (s, 1H), 3.94-3.98 (m, 1H), 3.13-3.19 (m, 1H), 3.00-3.06 (m, 1H), 2.23-2.30 (m, 2H), 1.79-1.84 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)= 174.52, 148.70, 140.17, 118.68, 113.08, 60.80, 47.36, 30.67, 26.30.

Compound **A2** (1.4 g, 5.0 mmol), 5% Pd/C (1.0 g) and dry THF (30 mL) were mixed in a 100 mL round bottom flask. After vacuumized and refilled with H_2 for three times, the mixture was stirred at room temperature for two days. After that, the reaction mixture was filtered through Celite and the filtrate was concentrated to give the product **A3** as white solids in 92% yield, mp: 125.4-127.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm)= 9.41 (s, 1H), 6.09 (d, 2H), 5.54 (s, 1H), 4.70 (s, 4H), 3.56-3.60 (m, 1H), 2.79-2.90 (m, 2H), 1.95-2.04 (m, 1H), 1.67-1.76 (m, 1H), 1.58-1.64 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm)= 172.95, 149.88, 139.75, 96.33, 94.81, 61.24, 47.26, 30.99, 26.48. Anal. calcd (%): C, 59.98; H, 7.32; N, 25.44. Found (%): C, 59.95; H, 7.38; N, 25.46. IR (KBr, cm^{-1}) v 3366, 3303, 3217, 2958, 1666, 1611, 1534, 1493, 1452, 1185, 1080, 922, 835, 712, 681. ESI-TOF-MS: calcd. for $C_{11}H_{16}N_4O$ $[M+H]^+$ 221.1397, found 221.1384.

2.1.2 Synthesis of (S)-N-(4,4'-diamino-[1,1'-biphenyl]-2-yl)pyrrolidine-2-carboxamide (B3)



Scheme S2. Synthetic route of (S)-N-(4,4'-diamino-[1,1'-biphenyl]-2-yl)pyrrolidine-2-carboxamide.

2-Bromo-5-nitroaniline (2.17 g, 10.0 mmol), 4-nitrophenylboronic acid (1.67 g, 10.0 mmol), $Pd(PPh_3)_4$ (0.58 g, 0.5 mmol) and K_3PO_4 (6.37 g, 30.0 mmol) were mixed in a 200 mL Schlenk flask. After vacuumed and refilled with argon for three times, toluene-water-ethanol (30 ml, 20 ml, 10 ml) was added. The mixture was stirred at 95 °C for 24 h and then cooled to room temperature. The organic phase was separated and the aqueous phase was extracted with dichloromethane (3 × 50 mL). The combined organic phases were washed with brine, and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure and purified by column chromatography with petroleum ether/dichloromethane (1/1, v/v) as eluent to afford 4,4'-dinitro-[1,1'-biphenyl]-2-amine in 90% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm)= 8.33 (d, 2H), 7.75 (d, 2H), 7.65 (d, 1H), 7.43-7.46 (m, 1H), 7.29 (d, 1H), 5.75 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm)= 148.82, 147.34, 147.25, 145.23, 131.81, 130.53, 129.64, 124.55, 111.00, 109.70.

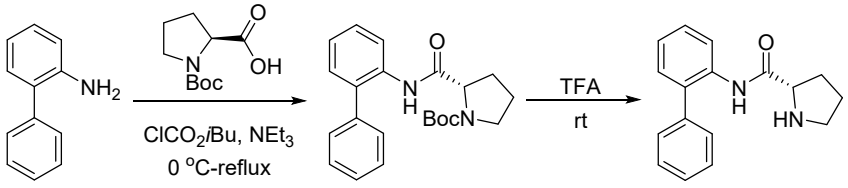
To a solution of Boc-L-proline (1.27 g, 5.9 mmol) in 20 mL dry THF was added triethylamine (0.82 mL, 5.9 mmol) under argon atmosphere. After the mixture was cooled to 0 °C, isobutyl chloroformate (0.78 mL, 6.0 mmol) was added dropwise followed by stirring for 1 h. Subsequently, 4,4'-dinitro-[1,1'-biphenyl]-2-amine (1.4 g, 5.4 mmol) was added to the solution in small portions. The resulting mixture was stirred at 0 °C for 1 h, at room temperature for 2 h, and then heated at reflux for 24 h. After cooling, the mixture was filtered and the filtrate was concentrated. The residue was purified by column chromatography with dichloromethane as the eluent to give compound **B1** as light yellow solids in 80% yield, mp: 62.5-63.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 9.39 (s, 1H), 9.23 (s, 1H), 8.38 (d, 2H), 8.05 (d, 1H), 7.57 (d, 2H), 7.40 (d, 1H), 4.30 (d, 1H), 3.24 (s, 2H), 2.48 (s, 1H), 1.88 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)= 172.99, 153.57, 147.93, 147.68, 142.97, 136.33, 136.21, 130.48, 129.96, 124.06, 118.69, 116.57, 80.61, 70.66, 47.01, 30.64, 27.88, 23.29. Anal. calcd (%): C, 57.89; H, 5.30; N, 12.27. Found (%): C, 57.94; H, 5.21; N, 12.24. IR (KBr, cm^{-1}) *v* 2976, 1693, 1592, 1521, 1389, 1338, 1303, 1158, 1086, 8564, 741, 695. ESI-TOF-MS: calcd. for $C_{22}H_{24}N_4NaO_7$ $[M+Na]^+$ 479.1537, found 479.1539.

To a solution of **B1** (2.74 g, 6.0 mmol) in dry dichloromethane (40 mL) at 0 °C was added trifluoroacetic acid (25 mL). The mixture was stirred at room temperature for two days and concentrated under reduced

pressure. After the addition of dichloromethane (10 mL) and H_2O (10 mL), the resulting mixture was basified with NH_4OH and extracted with dichloromethane (3 × 50 mL). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and then concentrated to dryness. The crude product was purified by chromatography on silica gel with dichloromethane/ethyl acetate (3/1, v/v) as the eluent to afford compound **B2** as white solids in 85% yield, mp: 95.3-96.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm)= 10.21 (s, 1H), 9.37 (d, 1H), 8.40 (d, 2H), 8.03-8.06 (m, 1H), 7.60 (d, 2H), 7.41 (d, 1H), 3.80-3.84 (m, 1H), 2.88-2.94 (m, 1H), 2.55-2.60 (m, 1H), 2.12-2.19 (m, 1H),1.99-2.05 (m, 1H), 1.59-1.75 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm)= 173.85, 148.31, 147.81, 143.13, 135.97, 135.35, 130.39, 130.09, 124.09, 118.45, 115.31, 60.82, 47.09, 30.56, 26.15. Anal. calcd (%): C, 57.30; H, 4.53; N, 15.72. Found (%): C, 57.33; H, 4.54; N, 15.62. IR (KBr, cm^{-1}) *v* 3122, 2867, 1698, 1598, 1512, 1452, 1344, 1081, 904, 855, 732, 700, 614. ESI-TOF-MS: calcd. for $C_{17}H_{16}N_4O_5$ $[M+H]^+$ 357.1154, found 357.1191.

Compound **B2** (1.78 g, 5.0 mmol), 5% Pd/C (1.2 g) and dry THF (40 mL) were mixed in a 100 mL round bottom flask. After vacuumized and refilled with H_2 for three times, the mixture was stirred at room temperature for two days. After that, the reaction mixture was filtered through Celite and the filtrate was concentrated to give the product **B3** as white solids in 96% yield, mp: 83.2-84.6 °C; ^{1}H NMR (400 MHz, DMSO-d_6): *δ* (ppm)= 10.07 (s, 1H), 7.72 (d, 1H), 7.03 (d, 2H), 6.90 (d, 1H), 6.71 (d, 2H), 6.39-6.41 (m, 1H), 5.20 (d, 4H), 3.67-3.72 (m, 1H), 2.85-2.91 (m, 1H), 2.65-2.71 (m, 1H), 2.01-2.08 (m, 1H), 1.85-1.90 (m, 1H), 1.61-1.70 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): *δ* (ppm)= 173.18, 148.19, 147.85, 135.75, 130.80, 130.21, 126.25, 120.90, 114.52, 110.09, 105.76, 61.16, 46.96, 31.02, 26.24. Anal. calcd (%): C, 68.90; H, 6.80; N, 18.90. Found (%): C, 68.85; H, 6.88; N, 18.93. IR (KBr, cm^{-1}) *v* 3438, 3343, 3216, 2967, 2866, 1665, 1606, 1511, 1470, 1288, 1243, 1180, 812, 556. ESI-TOF-MS: calcd. for $C_{17}H_{20}N_4O$ $[M+H]^+$ 297.1710, found 297.1690.

2.1.3 Synthesis of (S)-N-([1,1'-biphenyl]-2-yl)pyrrolidine-2-carboxamide (BPP)



BPP

Scheme S3. Synthetic route of (S)-N-([1,1'-biphenyl]-2-yl)pyrrolidine-2-carboxamide (BPP).

The model catalyst BPP was synthesized followed the synthetic route similar to compound **B2** as white solids in 86% total yield. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm)= 9.95 (s, 1H), 8.42 (d, 1H), 7.46 (t, 2H), 7.35-7.41 (m, 4H), 7.24-7.26 (m, 1H), 7.15 (t, 1H), 3.74-3.77 (m, 1H), 2.80-2.86 (m, 1H), 2.55-2.61 (m, 1H), 2.05-2.14 (m, 1H), 1.94-2.02 (m, 1H), 1.54-1.67 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm)= 173.48, 138.39, 134.91, 132.22, 129.83, 129.25, 128.53, 128.24, 127.48, 123.71, 120.24, 60.84, 46.89, 30.75, 25.91. ESI-TOF-MS: calcd. for $C_{17}H_{18}N_2O$ $[M+H]^+$ 267.1492, found 267.1472.

2.2 Synthesis and characterization of the two chiral POCs

2.2.1 Synthesis of CPOC-401-Pro

(S)-N-(3,5-diaminophenyl)pyrrolidine-2-carboxamide (**A3**) (0.08 mmol, 17.6 mg) and C4RACHO (0.04 mmol, 33 mg) were added into $CHCl_3$ (6 mL) and stirred at 65 °C for 1 day. After cooling to room temperature, Bromobenzene (1.5 mL) was added and slow vapor diffusion of MeOH into the mixture was conducted for two weeks. Red block single crystals of CPOC-401-Pro were obtained in ~52% yield and washed with MeOH. (mp >400 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 16.05 (s, 1H), 10.73 (s, 1H), 10.01 (s, 0.5H), 9.27 (d, 1H), 7.12-7.34 (m, 2.5H), 4.64 (s, 1H), 3.82 (s, 0.5H), 3.04 (s, 1H), 2.05-2.15 (m, 3H), 1.58 (s, 1H), 1.74 (s, 1H), 1.04 (t, 6H). Anal. calcd (%): C, 70.45; H, 6.76; N, 9.39. Found (%): C, 70.21; H, 6.88; N, 9.41. IR (KBr, cm^{-1}) *v* 2953, 2926, 2867, 1620, 1579, 1452, 1293, 1211, 994, 858, 798, 681. ESI-TOF-MS: calcd. for CPOC-401-Pro ($C_{280}H_{320}N_{32}O_{40}$) $[M+5H]^{5+}$ 955.6889, found 955.6886.

2.2.2 Synthesis of CPOC-302-Pro

(S)-N-(4,4'-diamino-[1,1'-biphenyl]-2-yl)pyrrolidine-2-carboxamide (**B3**) (0.10 mmol, 29.6 mg) and C4RACHO (0.05 mmol, 41.2 mg) were added into PhCl (6 mL) and stirred at 100 °C for 12 h. After cooling to room temperature, slow vapor diffusion of MeOH into the mixture was conducted for one week. Red block single crystals of CPOC-302-Pro were obtained in ~65% yield and washed with MeOH. (mp >400 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 16.17 (s, 1H), 10.19 (s, 1H), 9.18 (s, 1H), 8.49 (s, 0.5H), 7.13-7.42 (m, 4.5H), 4.67 (s, 1H), 3.76 (s, 0.5H), 2.95 (s, 0.5H), 2.69 (s, 0.5H), 1.61-2.11 (m, 5H), 1.06 (s, 6H). Anal. calcd (%): C, 73.19; H, 6.59; N, 8.33. Found (%): C, 73.22; H, 6.46; N, 8.19. IR (KBr, cm^{-1}) *v* 2955, 2922, 2863, 1621, 1574, 1525, 1502, 1453, 1294, 1202, 1094, 1003, 799, 748. ESI-TOF-MS: calcd. for CPOC-302-Pro ($C_{492}H_{528}N_{48}O_{60}$) $[M+5H]^{5+}$ 1615.6052, found 1615.6061; $[M+6H]^{6+}$ 1346.5056, found 1346.5064; $[M+7H]^{7+}$ 1154.2915, found 1154.2905.

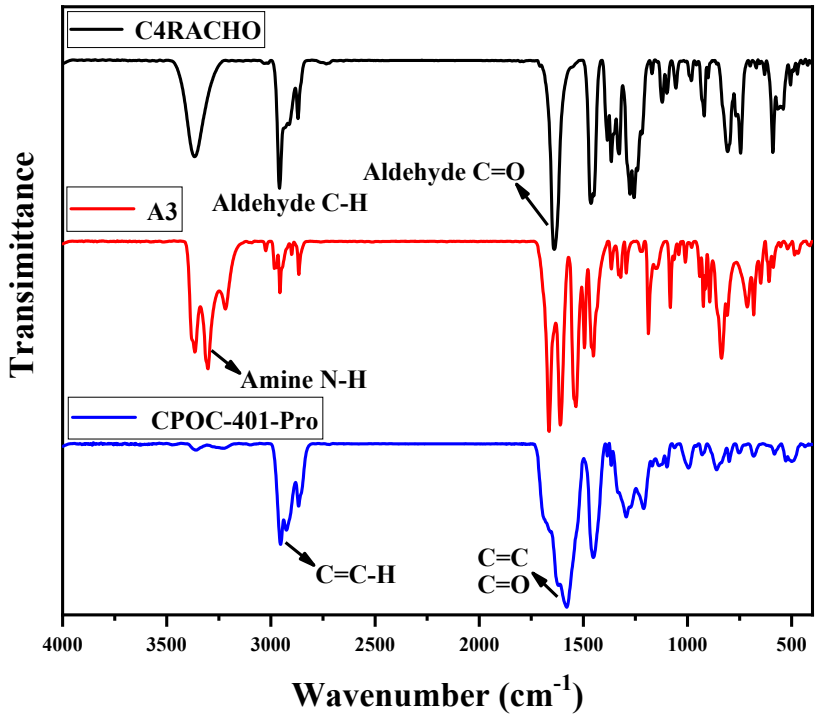


Figure S1. FT-IR spectra of C4RACHO, **A3** and CPOC-401-Pro.

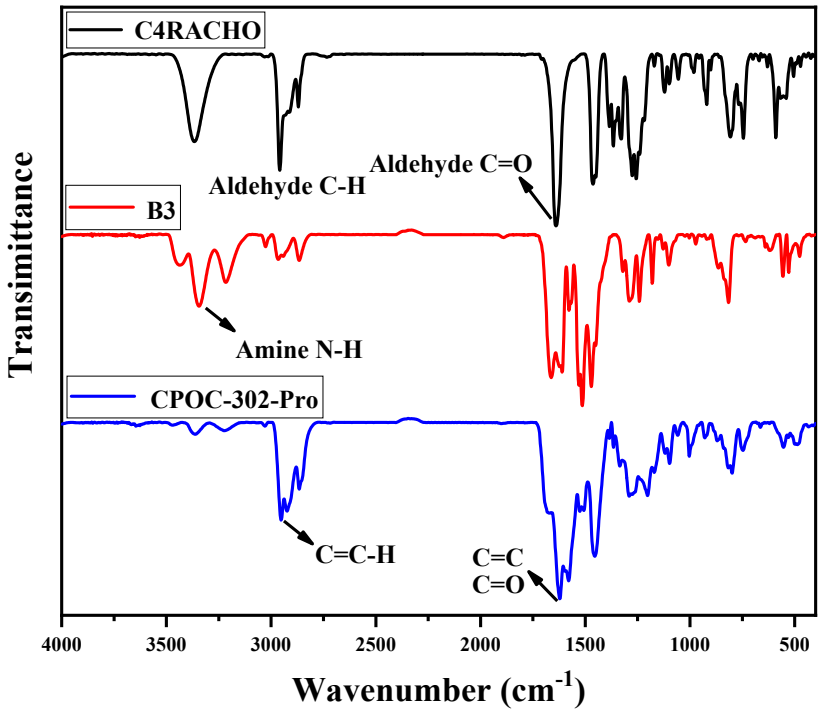


Figure S2. FT-IR spectra of C4RACHO, **B3** and CPOC-302-Pro.

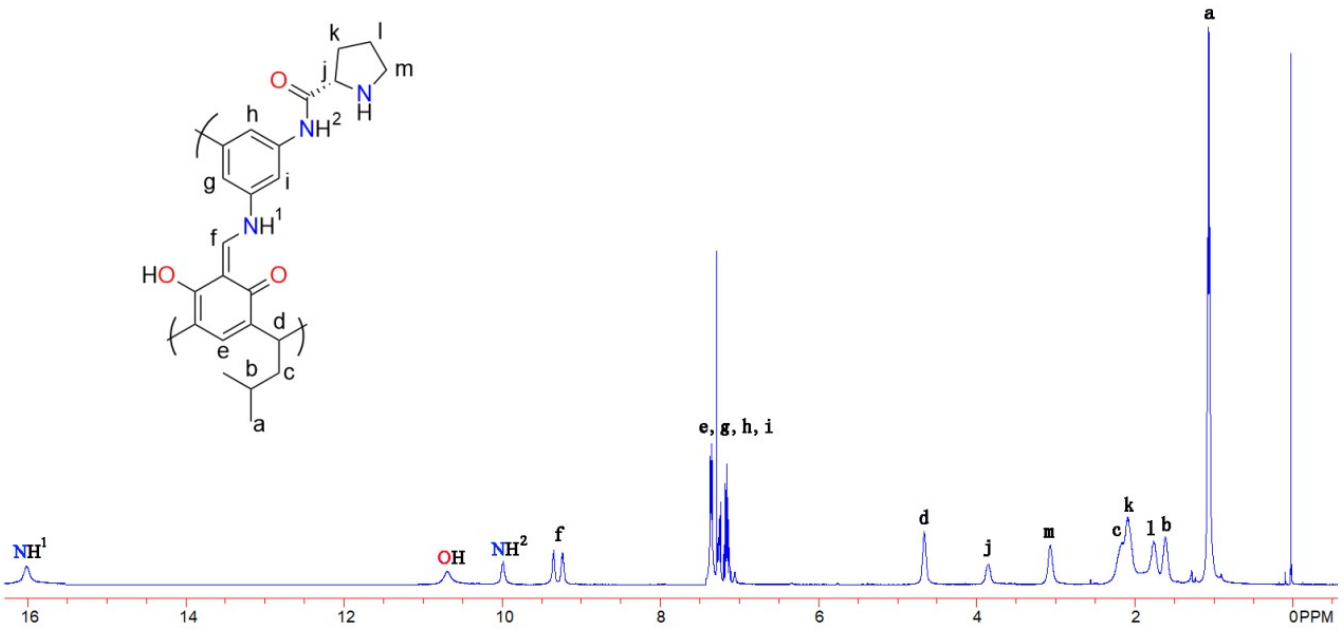


Figure S3. ^{1}H NMR of CPOC-401-Pro ($CDCl_3$, 400 MHz).

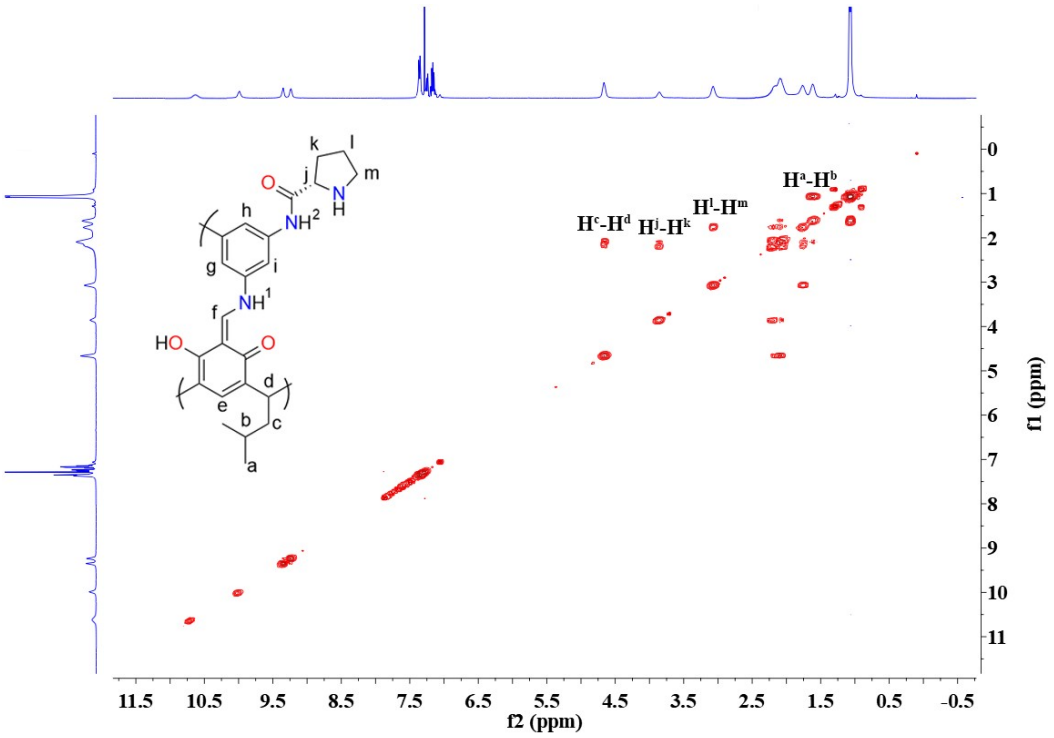


Figure S4. ^{1}H-^{1}H COSY NMR Spectrum of CPOC-401-Pro recorded in $CDCl_3$.

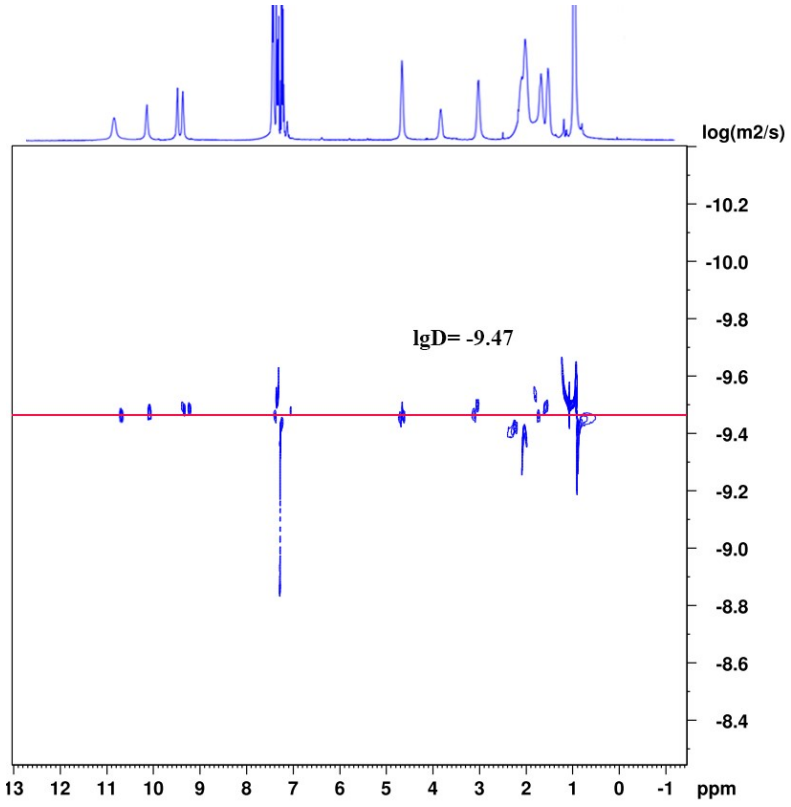


Figure S5. ^{1}H DOSY NMR spectrum of CPOC-401-Pro recorded in $CDCl_3$.

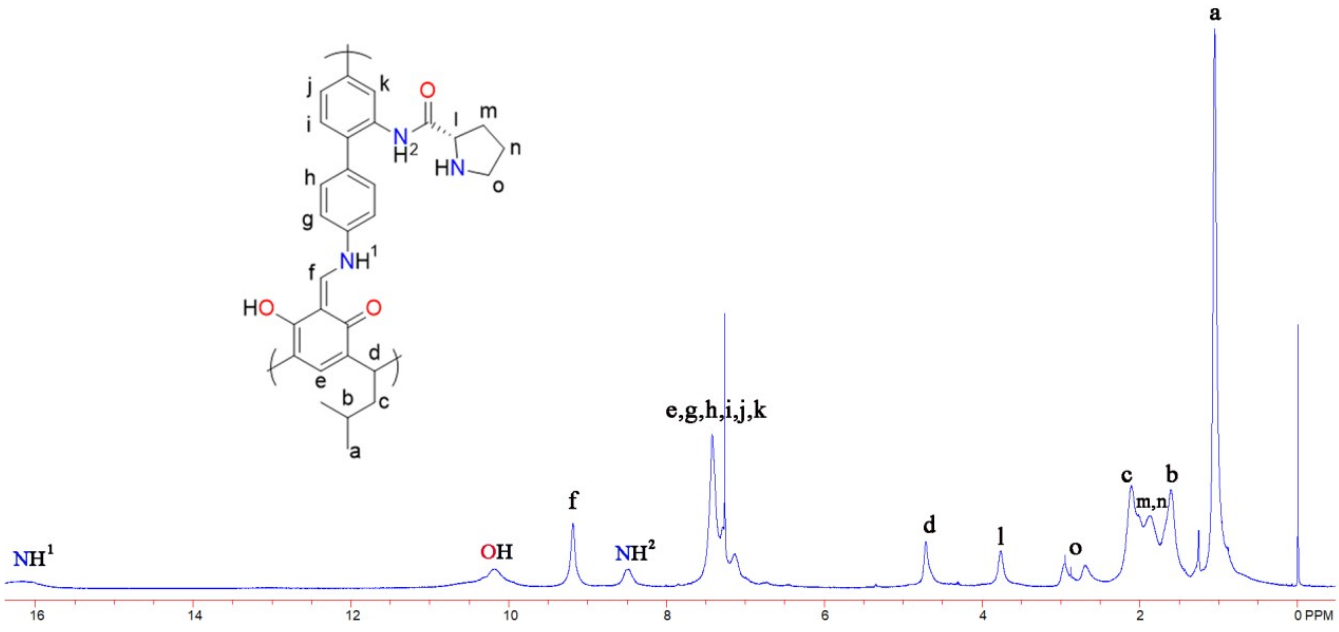


Figure S6. ^{1}H NMR of CPOC-302-Pro ($CDCl_3$, 400 MHz).

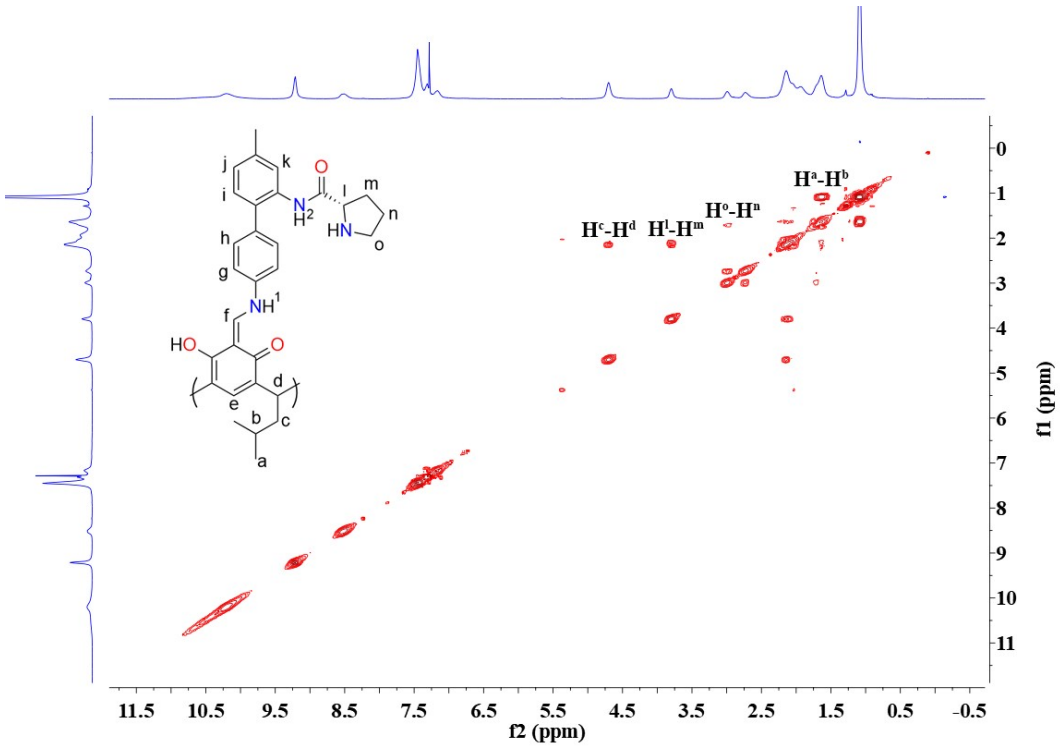


Figure S7. ^{1}H-^{1}H COSY NMR Spectrum of CPOC-302-Pro recorded in $CDCl_3$.

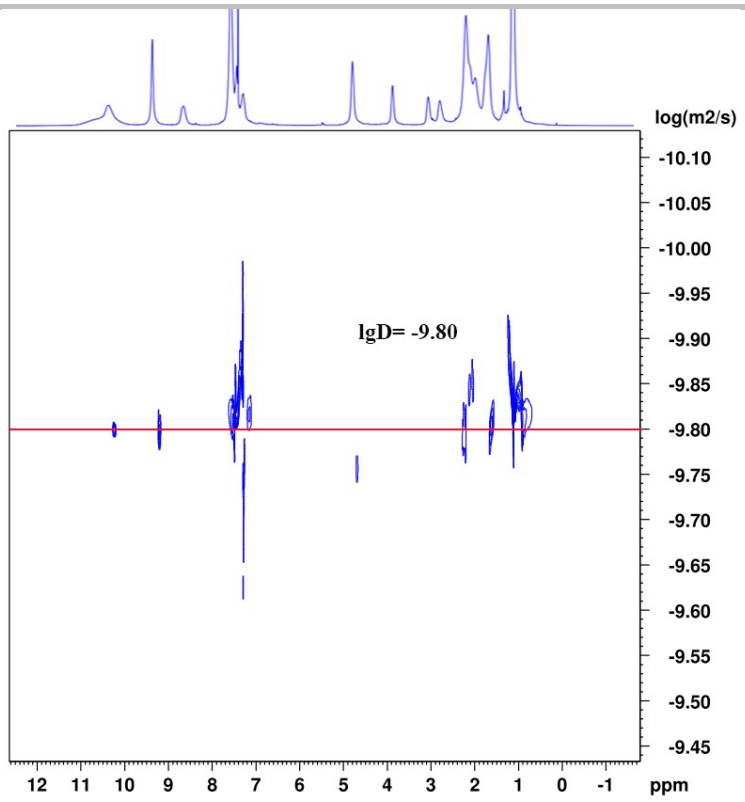


Figure S8. ^{1}H DOSY NMR spectrum of CPOC-302-Pro recorded in $CDCl_3$.

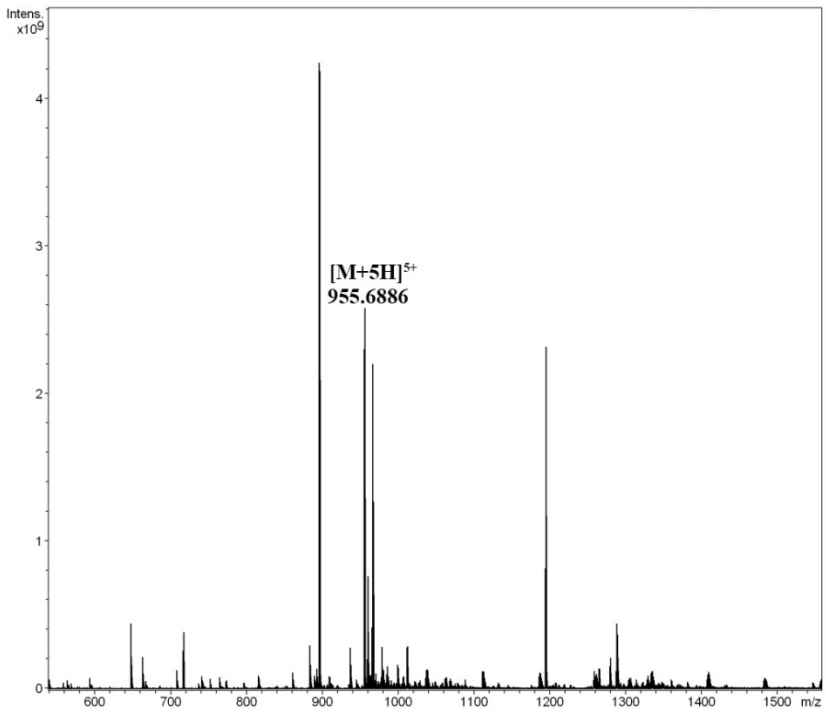


Figure S9. ESI-TOF-MS spectrum of CPOC-401-Pro.

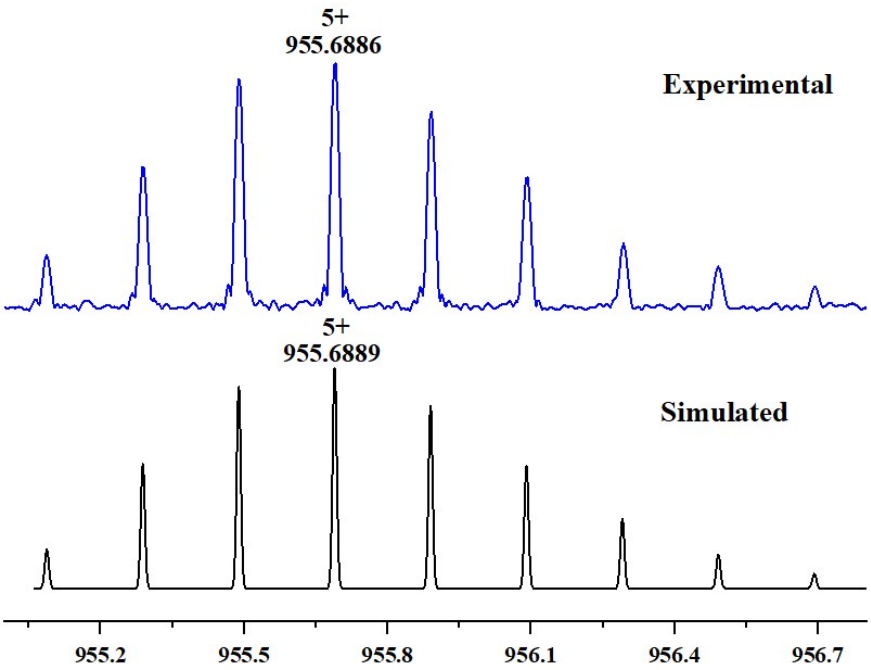


Figure S10. ESI-TOF-MS spectrum of $[M+5H]^{5+}$, M represents the intact assembly of CPOC-401-Pro.

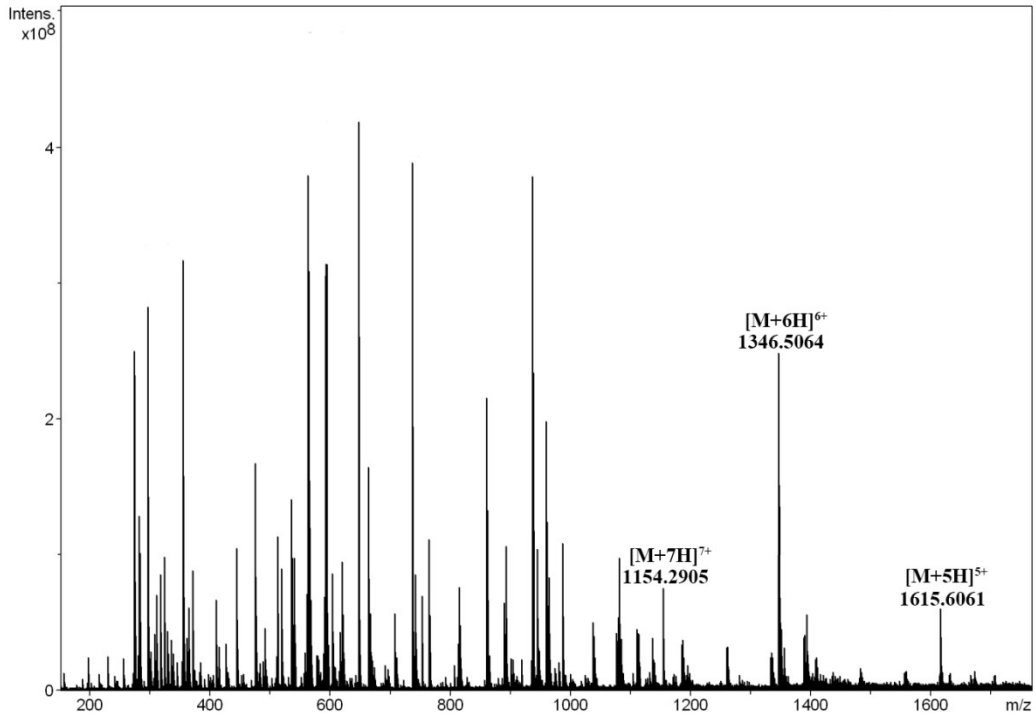


Figure S11. ESI-TOF-MS spectrum of CPOC-302-Pro.

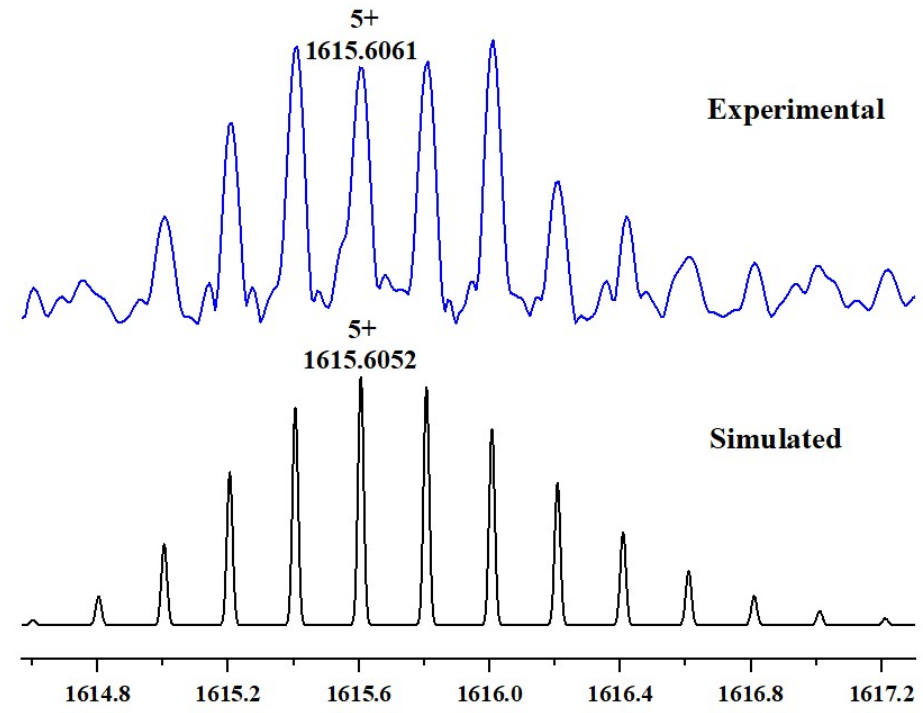


Figure S12. ESI-TOF-MS spectrum of $[M+5H]^{5+}$, M represents the intact assembly of CPOC-302-Pro.

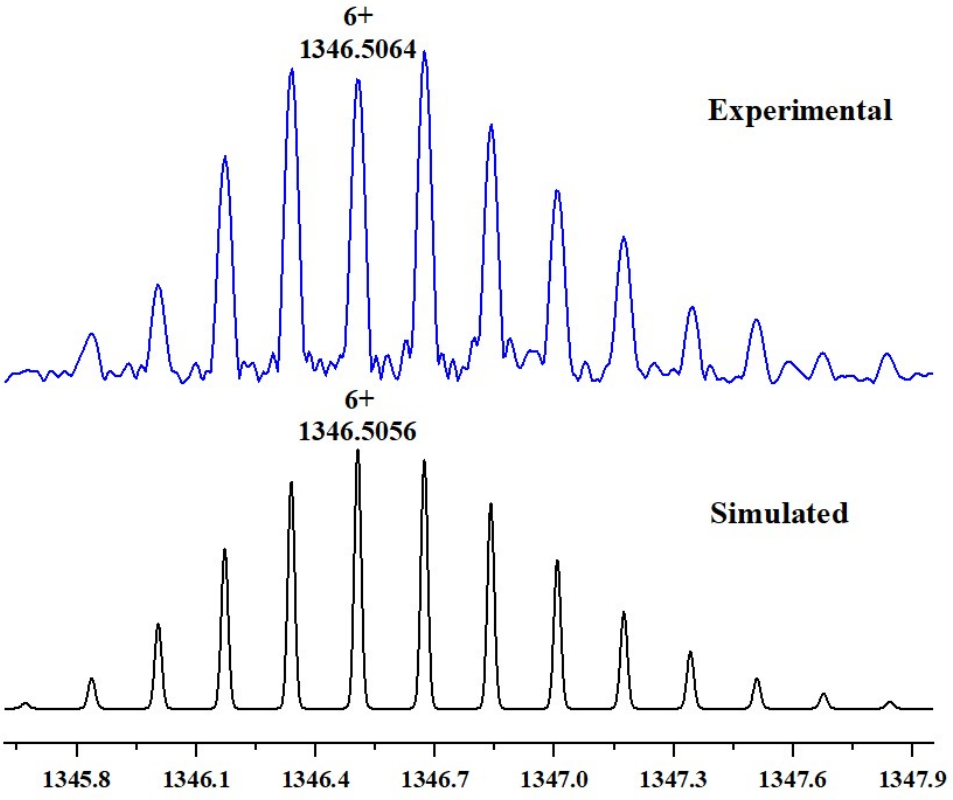


Figure S13. ESI-TOF-MS spectrum of $[M+6H]^{6+}$, M represents the intact assembly of CPOC-302-Pro.

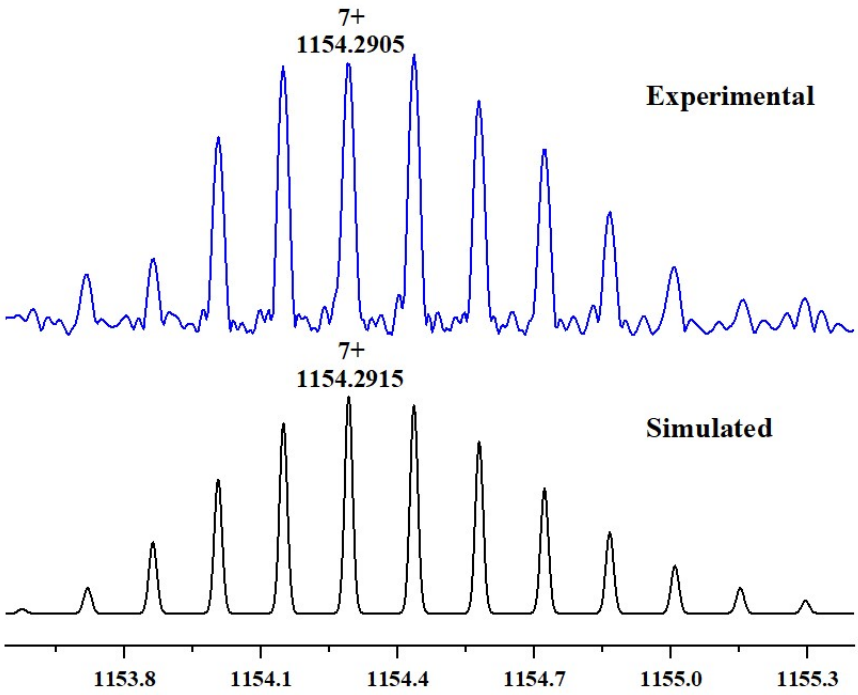


Figure S14. ESI-TOF-MS spectrum of $[M+7H]^{7+}$, M represents the intact assembly of CPOC-302-Pro.

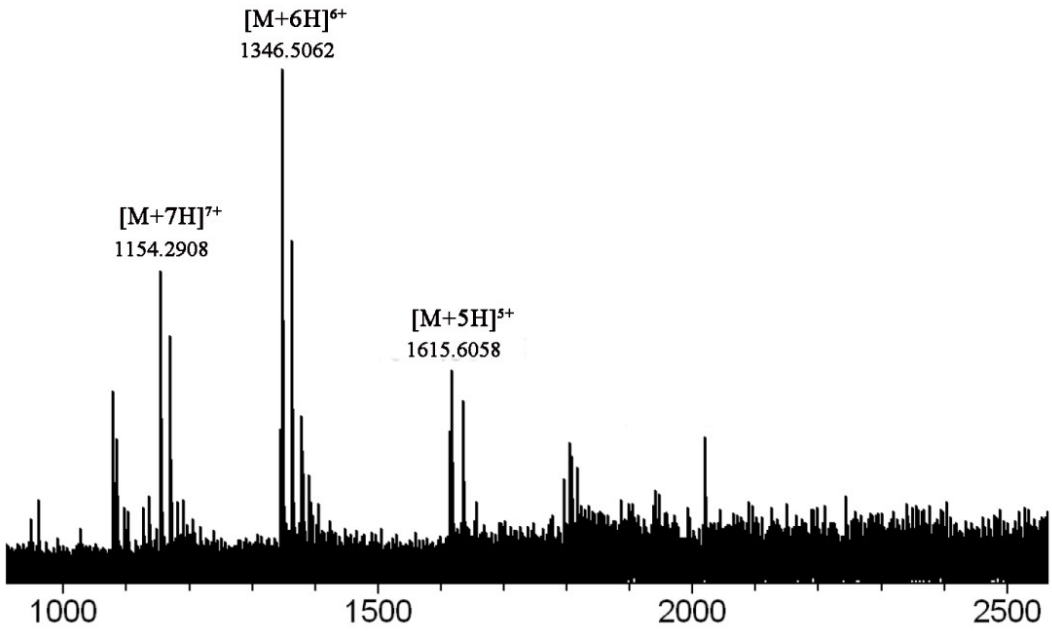


Figure S15. ESI-TOF-MS spectrum of CPOC-302-Pro after five catalytic cycles.

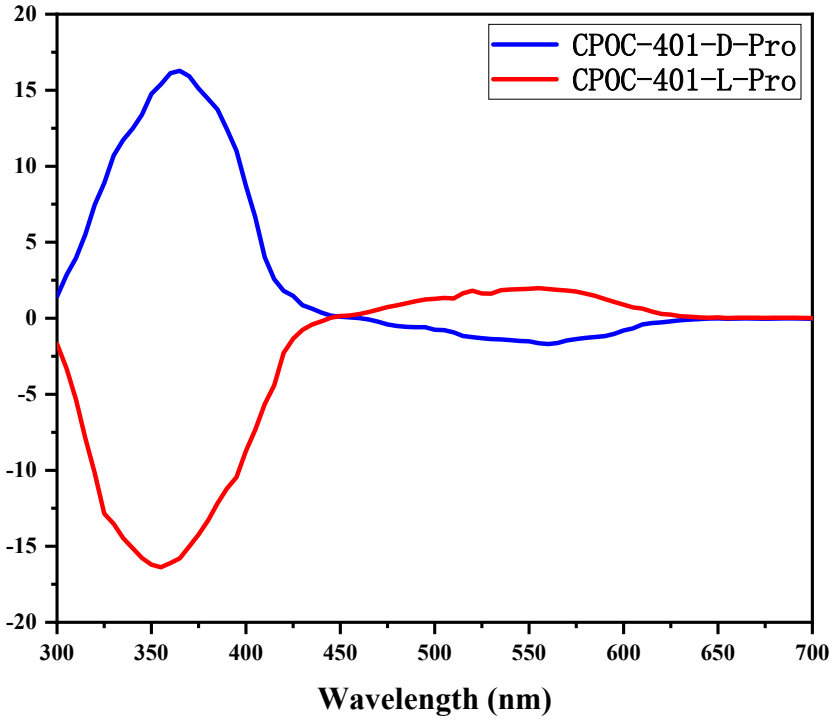


Figure S16. CD spectra of CPOC-401-Pro in $CHCl_3$ at room temperature.

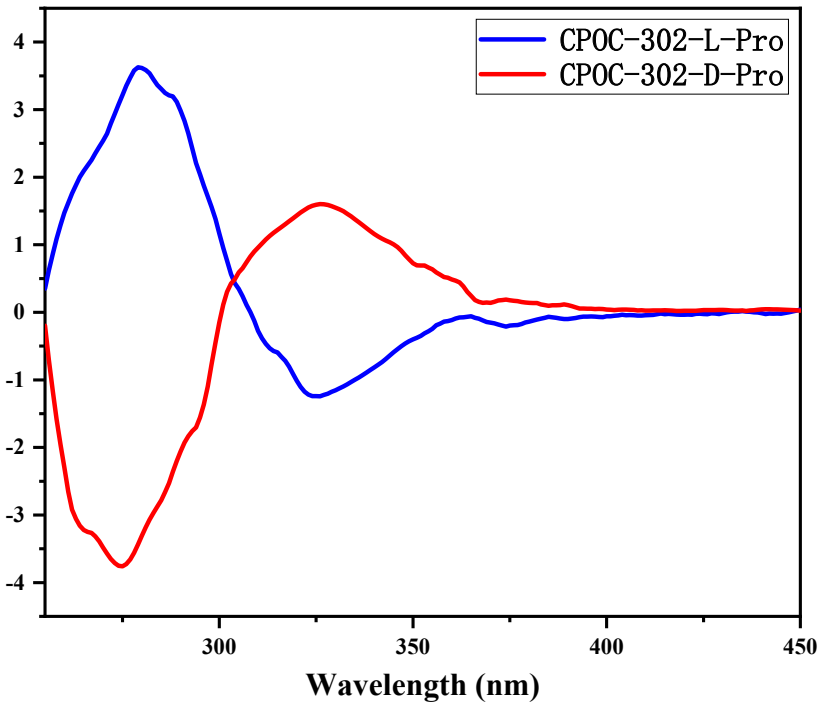


Figure S17. CD spectra of CPOC-302-Pro in $CHCl_3$ at room temperature.

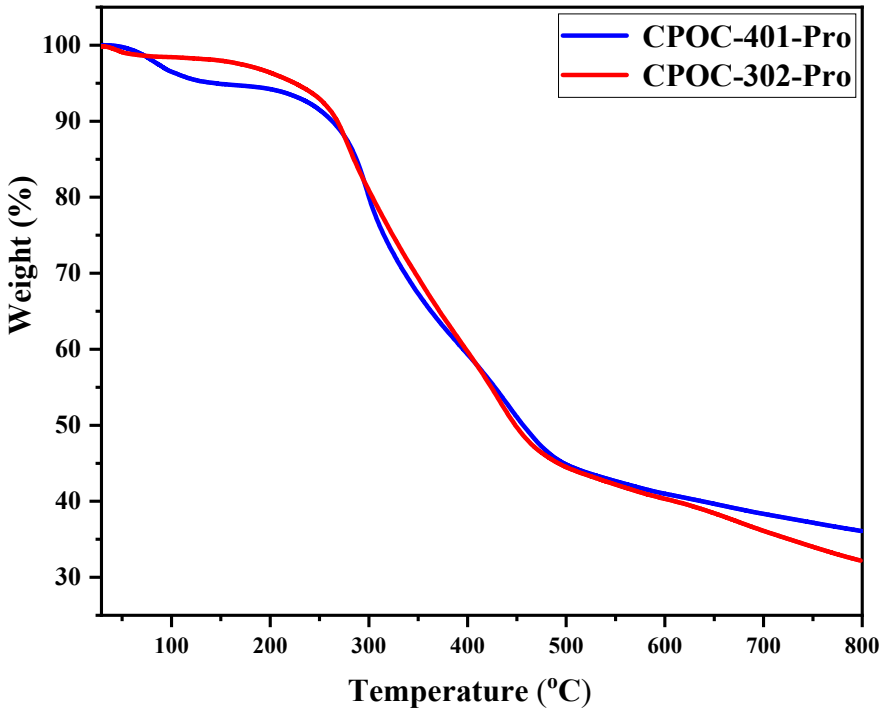


Figure S18. TGA curves of CPOC-401-Pro and CPOC-302-Pro.

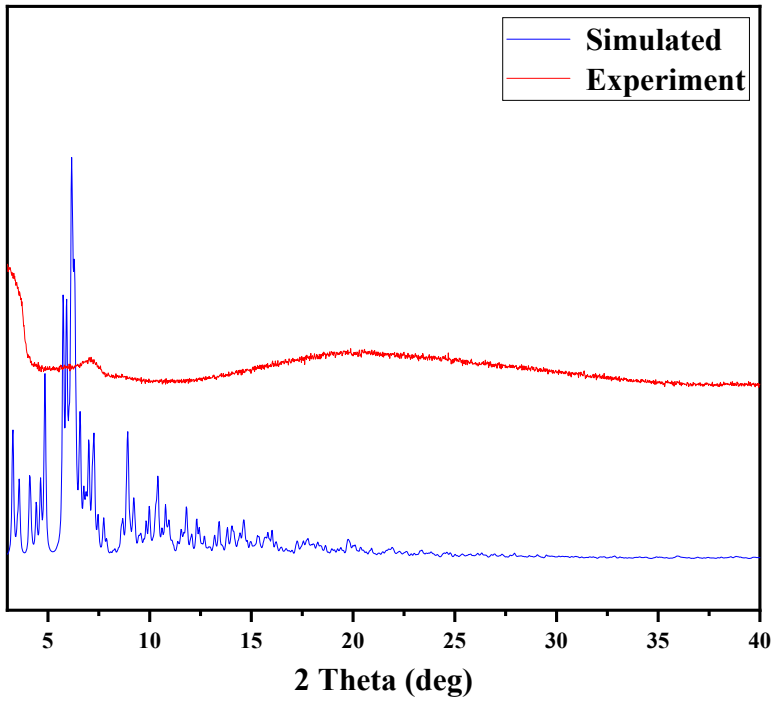


Figure S19. PXRD patterns of CPOC-401-Pro after desolvation.

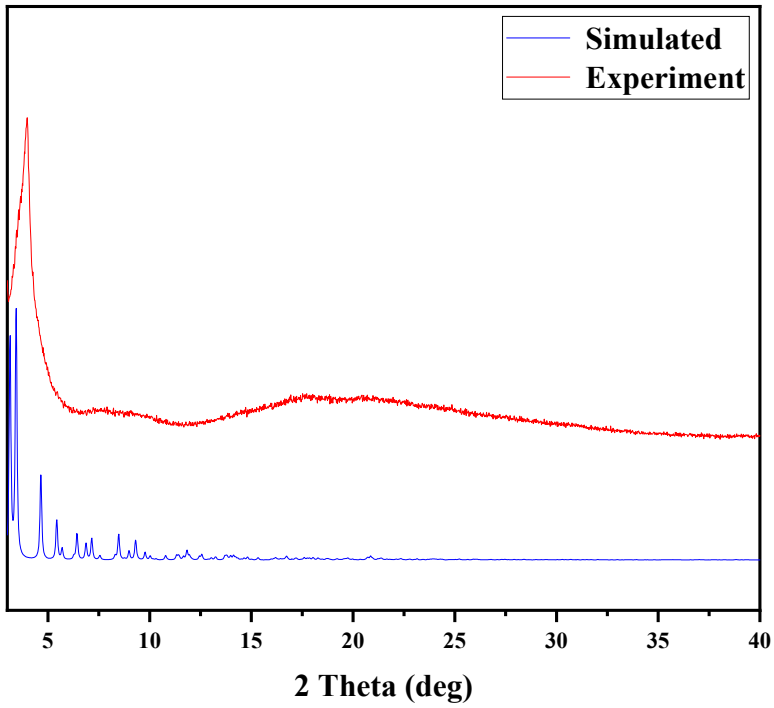
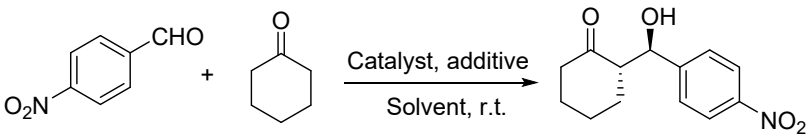


Figure S20. PXRD patterns of CPOC-302-Pro after desolvation.

2.3 Catalytic activity test of the synthesized chiral POCs

Table S1. Optimization of the reaction conditions of asymmetric aldol reaction



Entry[a]	Catalyst	Solvent	Additive	Yield(%)[b]	anti/syn[c]	ee(%)[d]
1	CPOC-302-Pro	Toluene	Acetic acid	65	85:15	79
2	CPOC-302-Pro	Toluene	TFA	Trace	--	--
3	CPOC-302-Pro	Toluene	TsOH	Trace	--	--
4	CPOC-302-Pro	Toluene	PhCOOH	76	87:13	81
5	CPOC-302-Pro	Toluene	4-NBA	88	88:12	82
6	CPOC-302-Pro	$CHCl_3$	4-NBA	75	89:11	79
7	CPOC-302-Pro	DCE	4-NBA	86	83:17	80
8	CPOC-302-Pro	o-Xylene	4-NBA	90	86:14	83
9	CPOC-302-Pro	Mesitylene	4-NBA	83	85:15	83
10	CPOC-302-Pro	THF	4-NBA	64	80:20	82
11	CPOC-302-Pro	CH_3CN	4-NBA	45	75:25	66
12	CPOC-302-Pro	MTBE	4-NBA	95	90:10	86

13	CPOC-302-Pro	MTBE/H_2O=100/1	4-NBA	99	93:7	92
14	CPOC-401-Pro	MTBE/H_2O=100/1	4-NBA	98	88:12	83

[a]Reaction conditions: aldehyde (0.20 mmol), ketone (2.0 mmol), 10 mol% catalyst (related to the proline amount in the material), 4-nitrobenzoic acid (4-NBA) (20 mol%), H_2O (0.01 mL), and MTBE (1.0 mL) at r.t. for 3 days. [b]Isolated yield. [c]Determined by ^{1}H NMR. [d]Determined by chiral HPLC.

2.3.1 General Procedure for asymmetric aldol reaction

In a tube with the aldehyde (0.2 mmol), ketone (2.0 mmol), 4-nitrobenzoic acid (0.04 mmol) and the chiral POCs (10 mol% loading of effective chiral proline groups) was added 1.0 mL MTBE and 0.01 mL H_2O at room temperature. The mixture was stirred for 3 days at room temperature. After the reaction was completed (monitored by TLC), 3.0 mL *n*-hexane was added to the mixture and the catalyst was isolated by centrifugation and thoroughly washed with *n*-hexane for three times. The combined organic phase was concentrated in vacuo and purified by column chromatography on silica gel. ^{1}H NMR spectroscopy was used to determine the diastereoselectivity (dr) value. The enantioselectivity (ee) value was determined by HPLC on a chiral-phase Chiralpak AD-H, OD-H or AS-H column.

Table S2. Performance comparison between CPOC-302-Pro with other chiral porous/supramolecular materials for the model aldol reactions.

Catalyst	yield (%)	anti/syn	ee (%)	Reference
CPOC-302-Pro	99	93:7	92	This work
CMIL-1	81	4:1	66	S1
Cd-TBT	97	1:1	58	S2
IRMOF-Pro	100	3:1	14	S3
Ap@3	72	3.3:1	74	S4
UiO-68-NHPro	97	12:88	0	S5
CZJ-18(Cu)-Pro	95	5:1	88	S6
DMTA-TPB1/4′	95	9:1	92	S7
PAF-1-NHPro	70	10.3:1	71	S8
Co-Pro1	42	6:1	73	S9

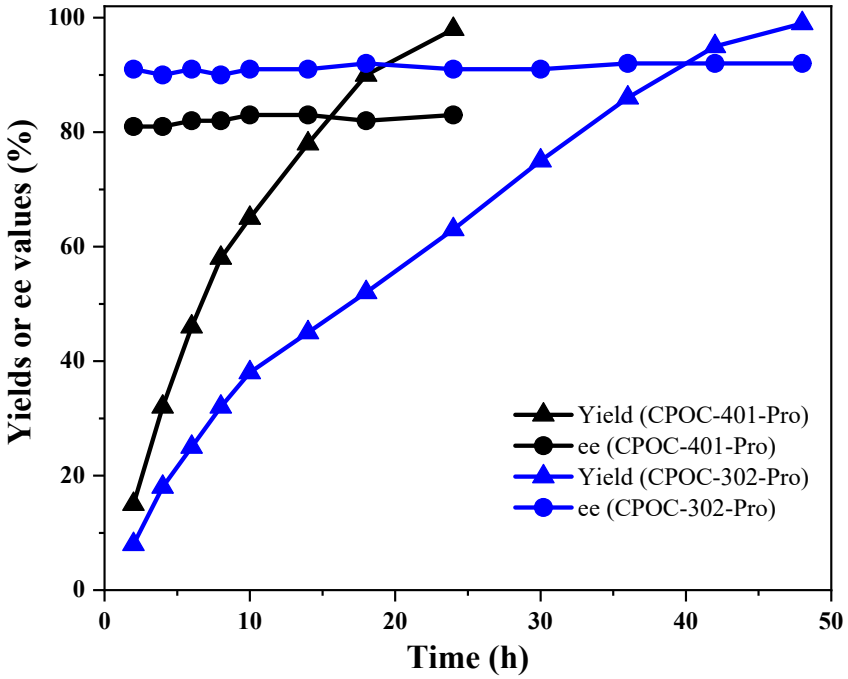
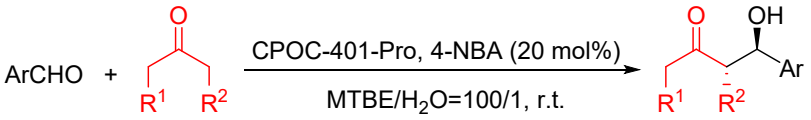
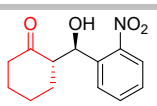


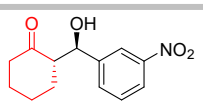
Figure S21. Kinetic results for the asymmetric aldol addition of p-nitrobenzaldehyde with cyclohexanone with 10 mol% loadings of chiral proline groups in the cage catalysts.

Table S3. Substrate Scope of the aldol addition reactions catalyzed by CPOC-401-Pro[a]

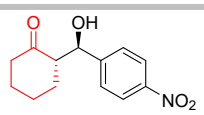




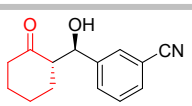
yield = 90%
dr = 87:13
ee = 84%



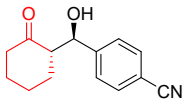
yield = 93%
dr =85:15
ee = 82%



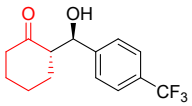
yield = 95%
dr = 90:10
ee =83%



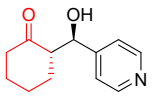
yield = 92%
dr = 83:17
ee = 76%



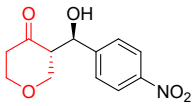
yield = 94%
dr = 92:8
ee = 77%



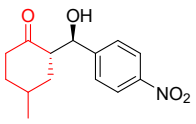
yield = 91%
dr = 89:11
ee = 75%



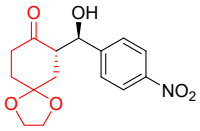
yield = 96%
dr = 78:22
ee = 76%



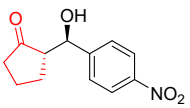
yield = 95%
dr = 75:25
ee = 70%



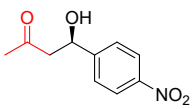
yield = 90%
dr = 86:14
ee = 72%



yield = 97%
dr = 82:18
ee = 76%



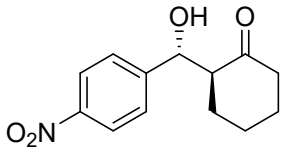
yield = 98%
dr = 79:21
ee = 84%[b]



yield = 90%
ee = 44%[b]

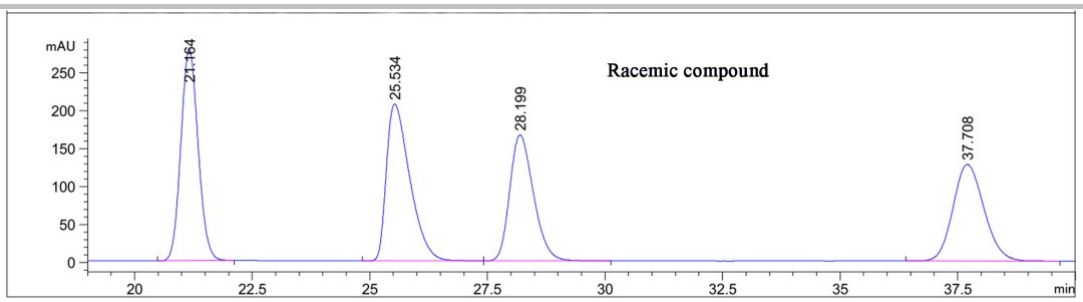
[a]Reaction conditions: aldehyde (0.20 mmol), ketone (2.0 mmol), 10 mol% catalyst (related to the proline amount in the material), 4-NBA (20 mol%), H_2O (0.01 mL), and MTBE (1.0 mL) at r.t. for 3 days. Isolated yield. The above Catalytic products were characterized by ^1H NMR and their ee values were determined by chiral HPLC. [b]Under the 0 °C reaction conditions.

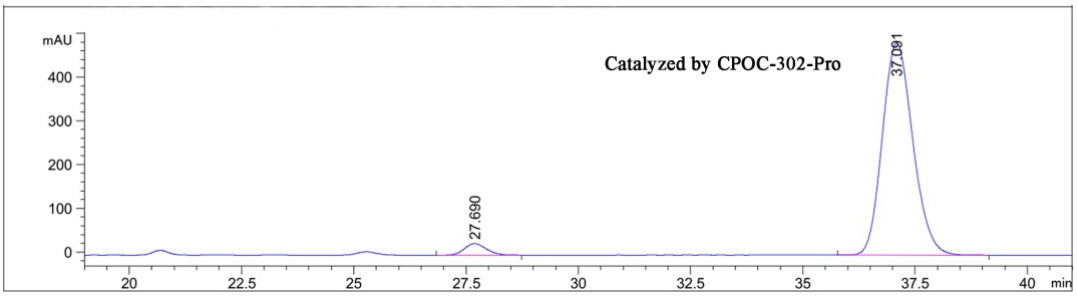
2.3.2 ^1H NMR and HPLC of the catalytic product



(S)-2-((R)-hydroxy(2-nitrophenyl)methyl)cyclohexan-1-one

^1H NMR (400 MHz, CDCl3): δ (ppm)= 8.20 (d, 2H), 7.52 (d, 2H), 4.91 (dd, 1H), 4.13 (d, 1H), 2.58-2.64 (m, 1H), 2.47-2.52 (m, 1H), 2.34-2.42 (m, 1H), 2.09-2.15 (m, 1H), 1.81-1.85 (m, 1H), 1.54-1.70 (m, 3H), 1.33-1.44 (m, 1H). HPLC analysis (Chiralcel AD-H column, n-Hexane/i-PrOH = 90:10, 1.0 mL/min, λ = 254 nm), t_{minor} = 28.2 min, t_{major} = 37.7 min.





Serial Number	Retention Time [min]	Area	Area %
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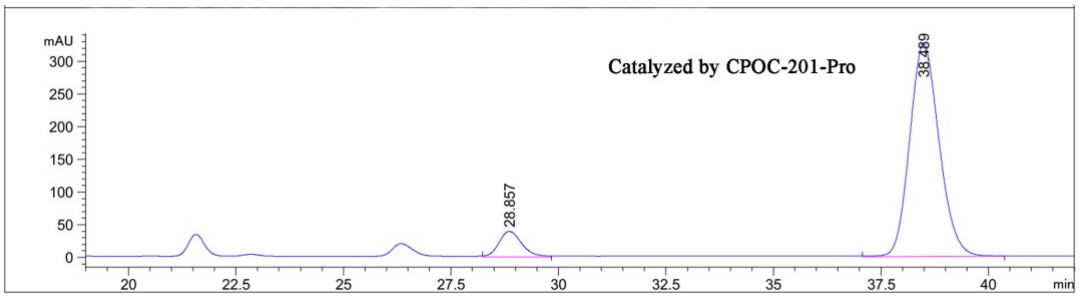
2	37.091	2286381	96.23



Serial Number	Retention Time [min]	Area	Area %
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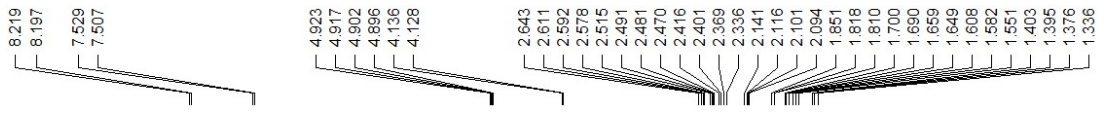
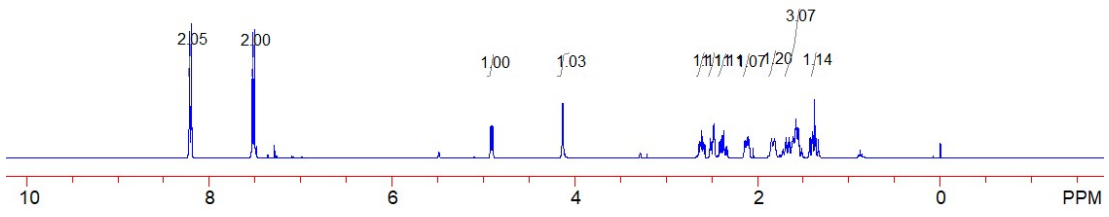
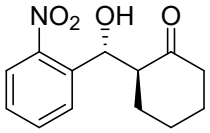
2	38.489	1554331	91.37

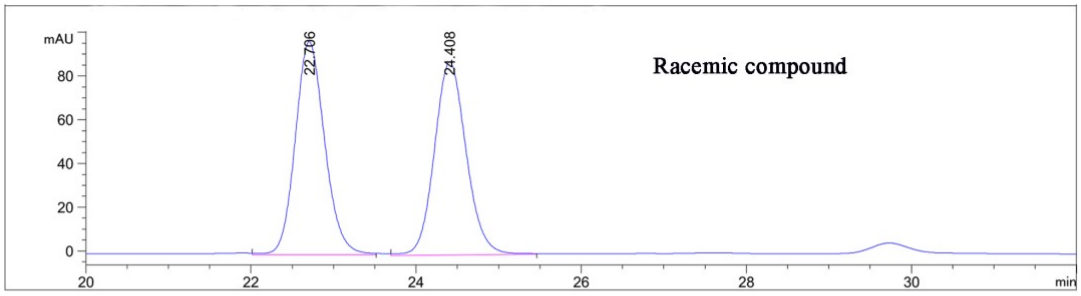


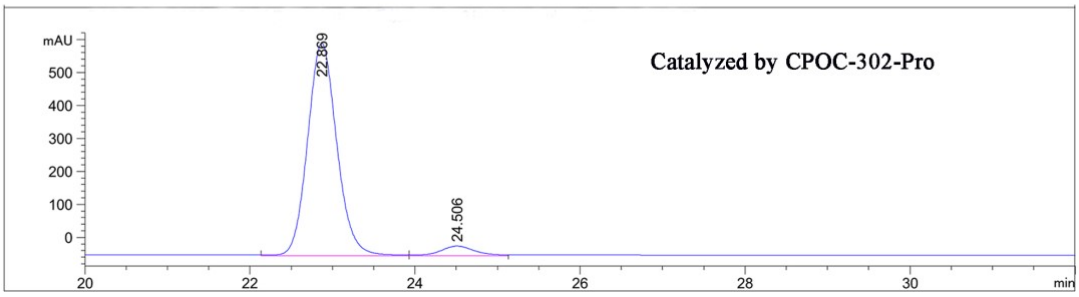




(S)-2-((R)-hydroxy(4-nitrophenyl)methyl)cyclohexan-1-one

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 7.85 (d, 1H), 7.77 (d, 1H), 7.64 (t, 1H), 7.44 (t, 1H), 5.45 (d, 1H), 4.09 (bs, 1H), 2.74-2.80 (m, 1H), 2.43-2.48 (m, 1H), 2.30-2.39 (m, 1H), 2.05-2.13 (m, 1H), 1.83-1.87 (m, 1H), 1.57-1.78 (m, 4H). HPLC analysis (Chiralcel AD-H column, n-Hexane/i-PrOH = 80:20, 0.5 mL/min, λ = 254 nm), t_{major} = 22.7 min, t_{minor} = 24.4 min.





Serial Number	Retention Time [min]	Area	Area %
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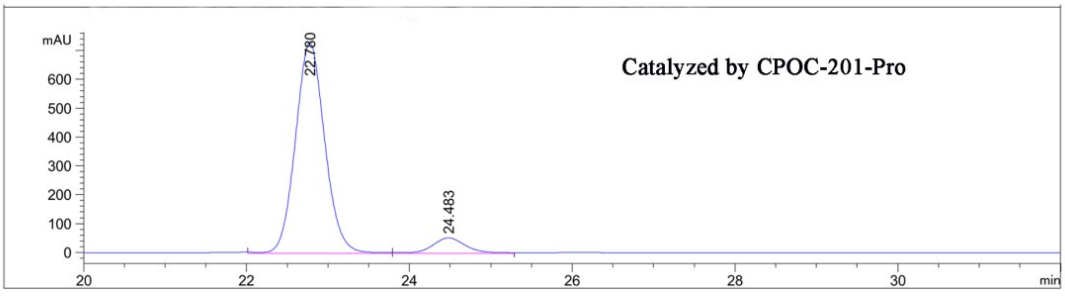
2	24.506	87240	5.18



Serial Number	Retention Time [min]	Area	Area %
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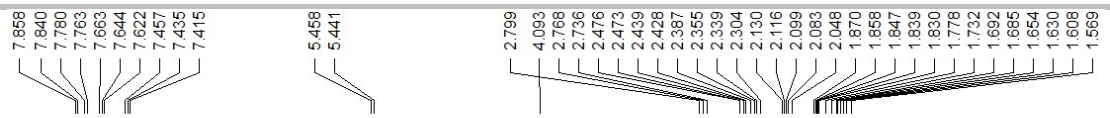
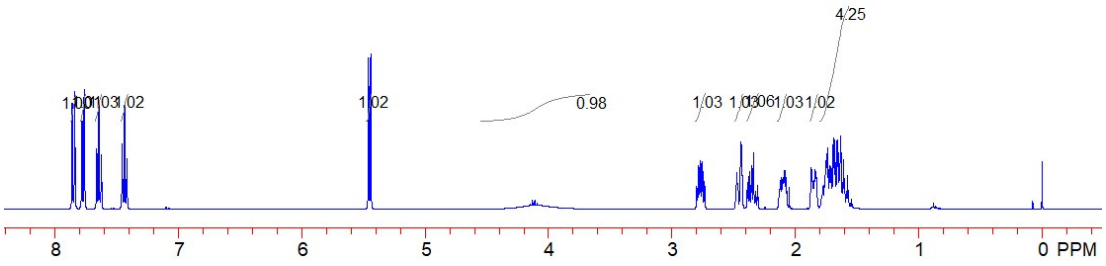
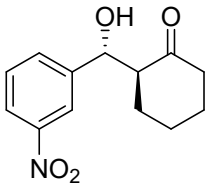
2	24.483	157221	7.90

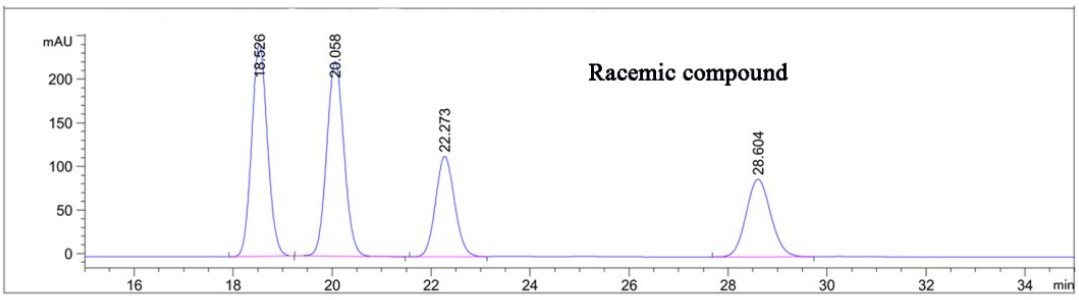


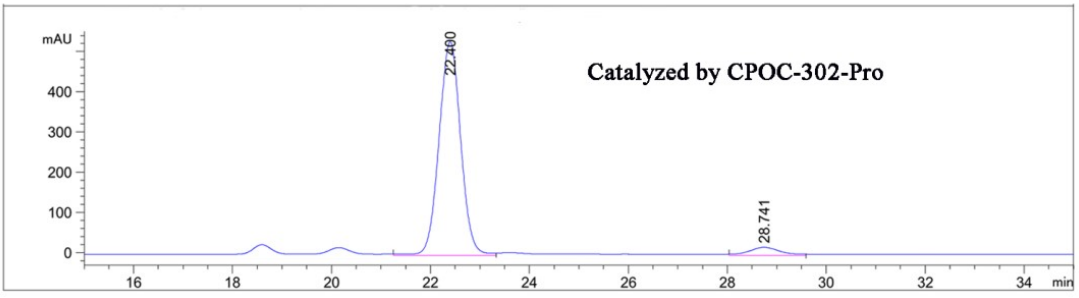




(S)-2-((R)-hydroxy(3-nitrophenyl)methyl)cyclohexan-1-one

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 8.22 (s, 1H), 8.15-8.18 (m, 1H), 7.68 (d, 1H), 7.54 (t, 1H), 4.91 (dd, 1H), 4.17 (d, 1H), 2.62-2.67 (m, 1H), 2.48-2.53 (m, 1H), 2.38-2.42 (m, 1H), 2.10-2.15 (m, 1H), 1.81-1.85 (m, 1H), 1.55-1.71 (m, 3H), 1.38-1.42 (m, 1H). HPLC analysis (Chiralcel AD-H column, n-Hexane/i-PrOH = 90:10, 1.0 mL/min, λ = 254 nm), t_{major} = 22.3 min, t_{minor} = 28.6 min.





Serial Number	Retention Time [min]	Area	Area %
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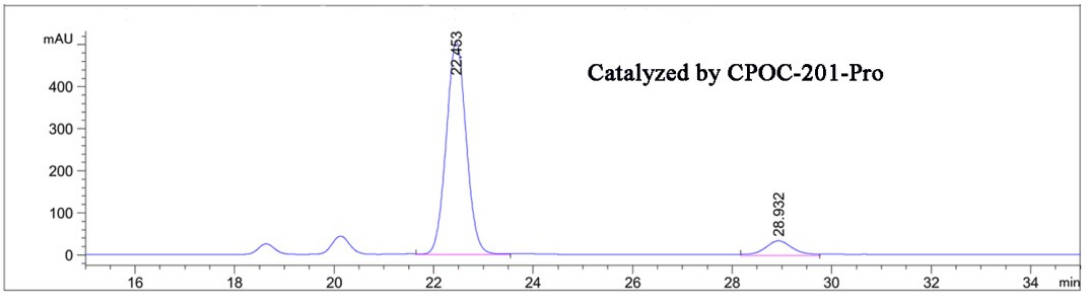
2	28.741	92884	5.42



Serial Number	Retention Time [min]	Area	Area %
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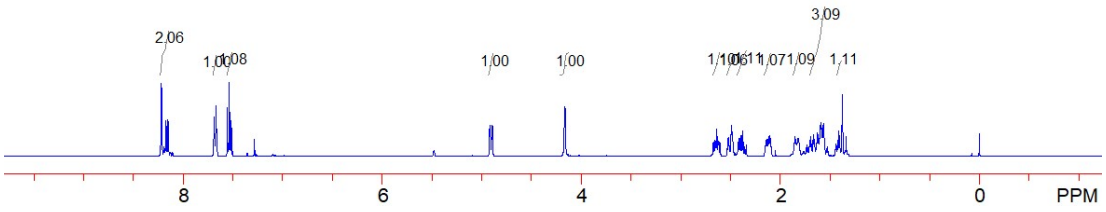
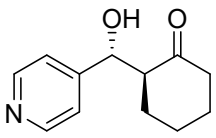
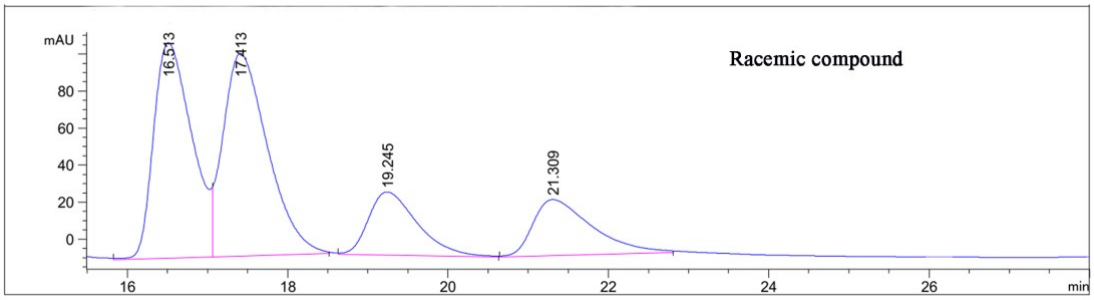
2	28.932	139239	8.92

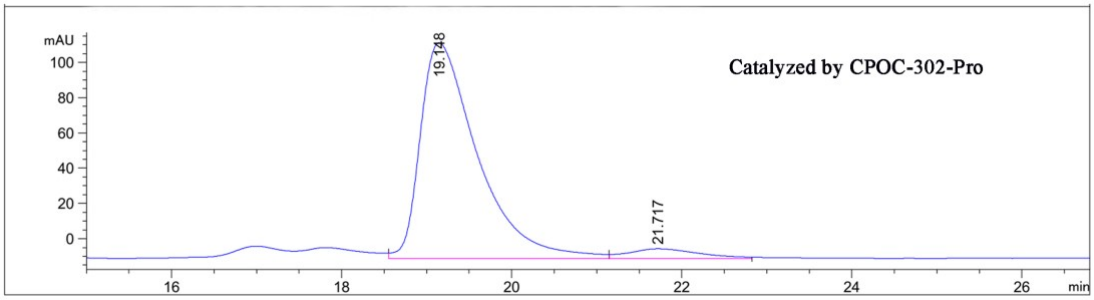




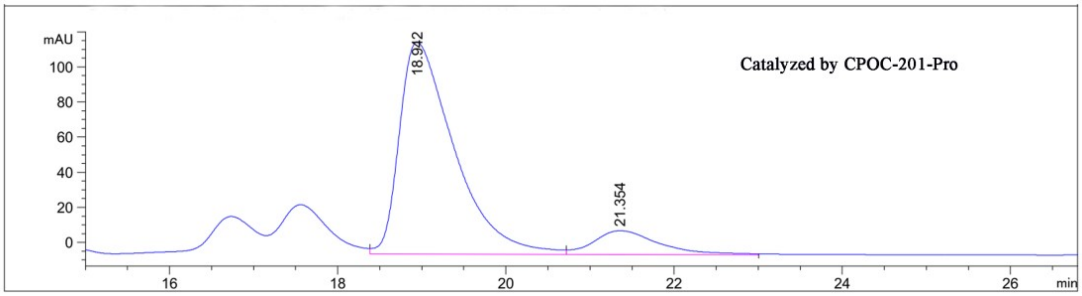
(S)-2-((R)-hydroxy(pyridin-4-yl)methyl)cyclohexan-1-one

^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm)= 8.54-8.56 (m, 2H), 7.26-7.27 (m, 2H), 4.82 (d, 1H), 4.40 (s, 1H), 2.58-2.64 (m, 1H), 2.45-2.50 (m, 1H), 2.32-2.40 (m, 1H), 2.08-2.12 (m, 1H), 1.82-1.85 (m, 1H), 1.55-1.69 (m, 1H), 1.36-1.43 (m, 1H). HPLC analysis (Chiralcel OD-H column, n-Hexane/i-PrOH = 90:10, 1.0 mL/min, λ = 254 nm), t_{major} = 19.2 min, t_{minor} = 21.3 min.

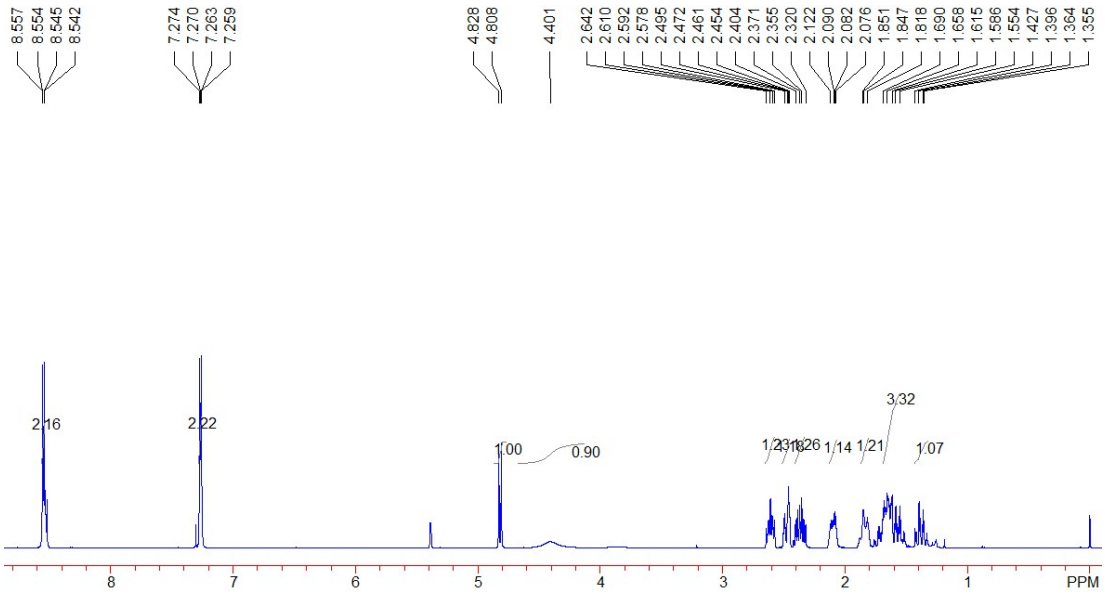


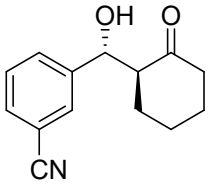


Serial Number	Retention Time [min]	Area	Area %
1	19.148	5724669	94.68
2	21.717	321526	5.32



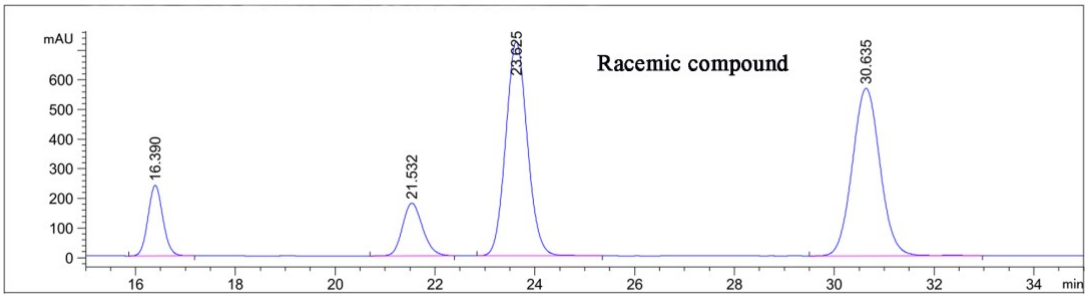
Serial Number	Retention Time [min]	Area	Area %
1	18.942	5472777	88.16
2	21.354	735248	11.84

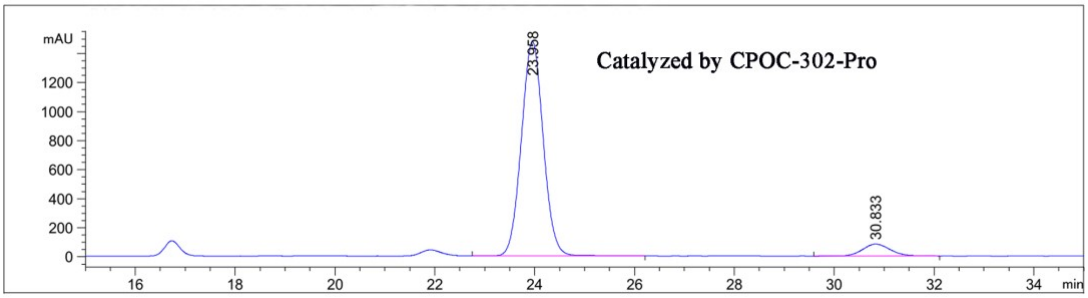




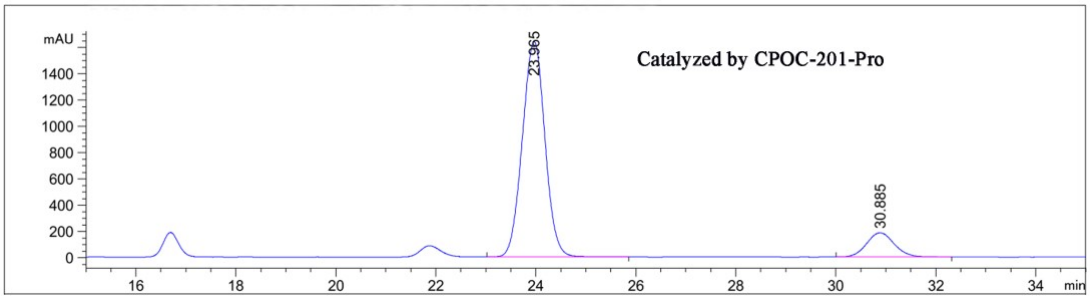
3-((R)-hydroxy((S)-2-oxocyclohexyl)methyl)benzonitrile

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 7.65 (s, 1H), 7.56-7.61 (m, 2H), 7.45-7.48 (m, 1H), 4.82 (d, 1H), 4.12 (s, 1H), 2.55-2.62 (m, 1H), 2.47-2.52 (m, 1H), 2.33-2.41 (m, 1H), 2.09-2.14 (m, 1H), 1.81-1.85 (m, 1H), 1.53-1.70 (m, 3H), 1.26-1.37 (m, 1H). HPLC analysis (Chiralcel AD-H column, n-Hexane/i-PrOH = 90:10, 1.0 mL/min, λ = 220 nm), t_{major} = 23.6 min, t_{minor} = 30.6 min.

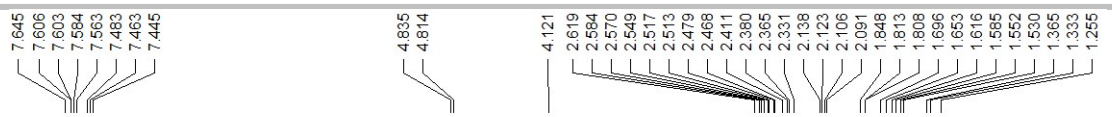


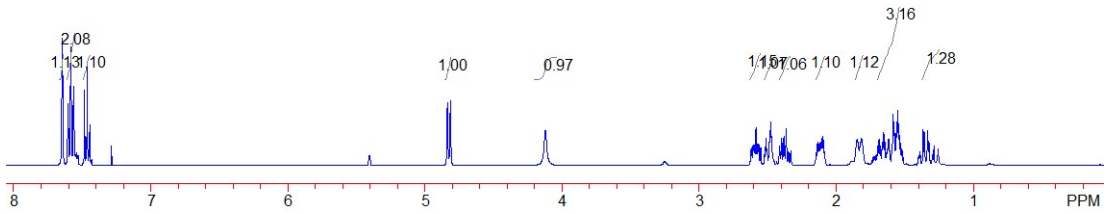


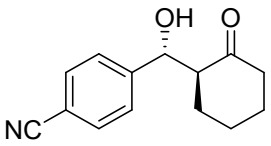
Serial Number	Retention Time [min]	Area	Area %
1	23.958	4498071	93.38
2	30.833	318736	6.62



Serial Number	Retention Time [min]	Area	Area %
1	23.965	5152551	87.94
2	30.885	706541	12.06

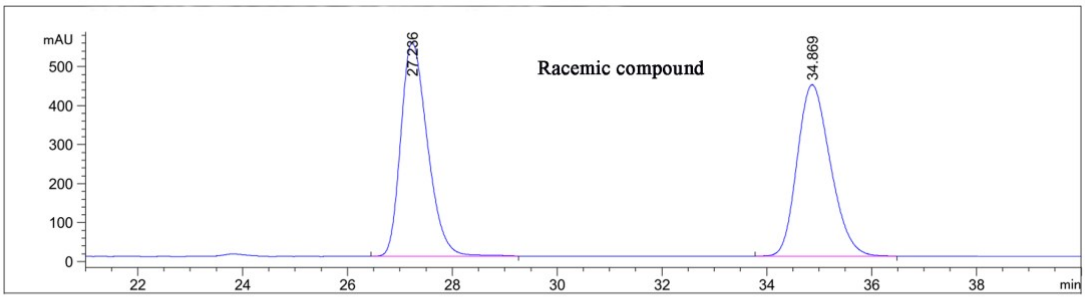


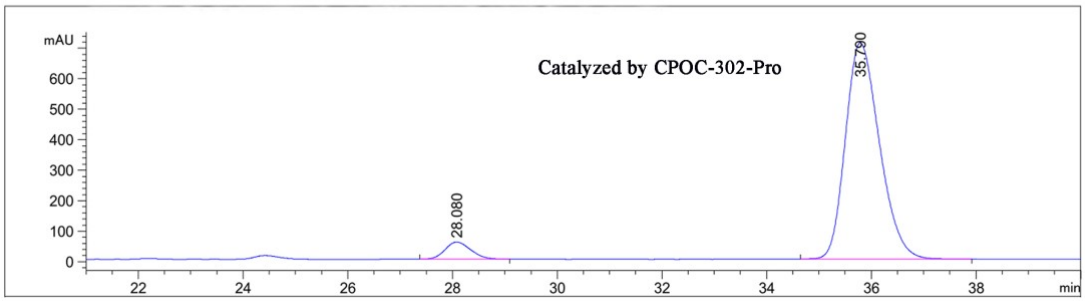




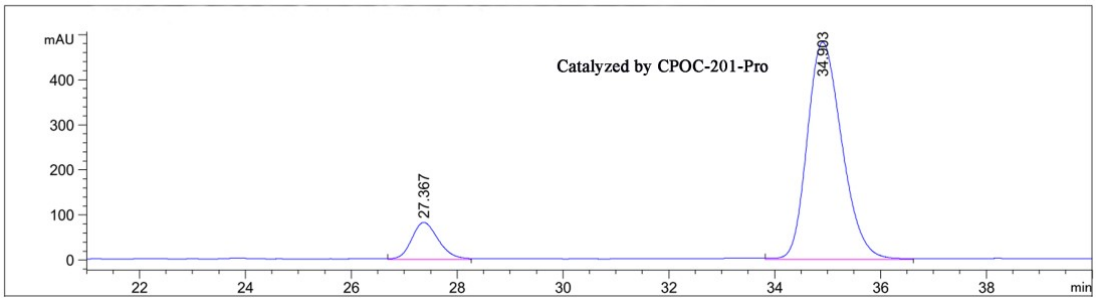
4-((R)-hydroxy((S)-2-oxocyclohexyl)methyl)benzonitrile

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 7.65 (d, 2H), 7.45 (d, 2H), 4.84 (dd, 1H), 4.09 (d, 1H), 2.46-2.61 (m, 2H), 2.32-2.40 (m, 1H), 2.09-2.13 (m, 1H), 1.81-1.84 (m, 1H), 1.53-1.69 (m, 3H), 1.33-1.37 (m, 1H). HPLC analysis (Chiralcel AD-H column, n-Hexane/i-PrOH = 90:10, 1.0 mL/min, λ = 220 nm), t_{minor} = 27.2 min, t_{major} = 34.9 min.

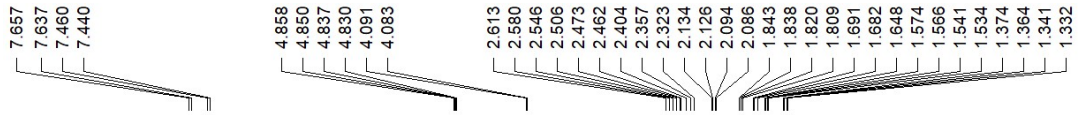


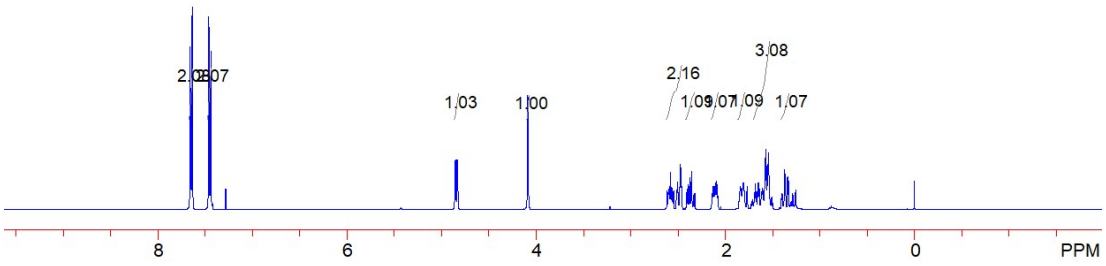


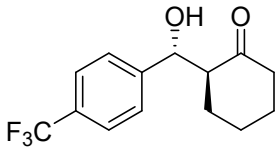
Serial Number	Retention Time [min]	Area	Area %
1	28.080	191464	5.64
2	35.790	3200451	94.36



Serial Number	Retention Time [min]	Area	Area %
1	27.367	293189	11.75
2	34.903	2202461	88.25

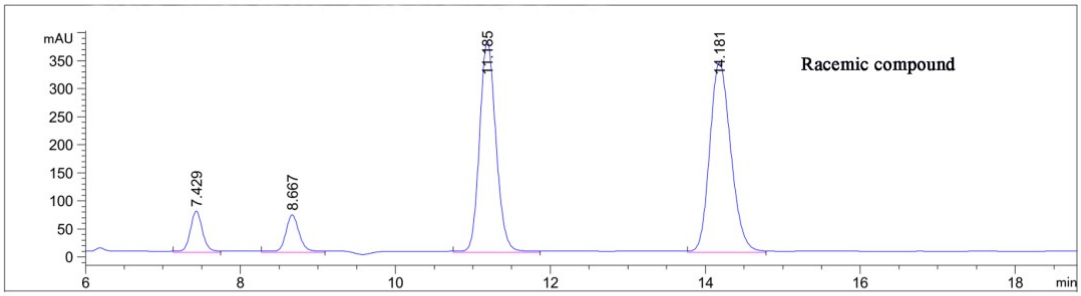


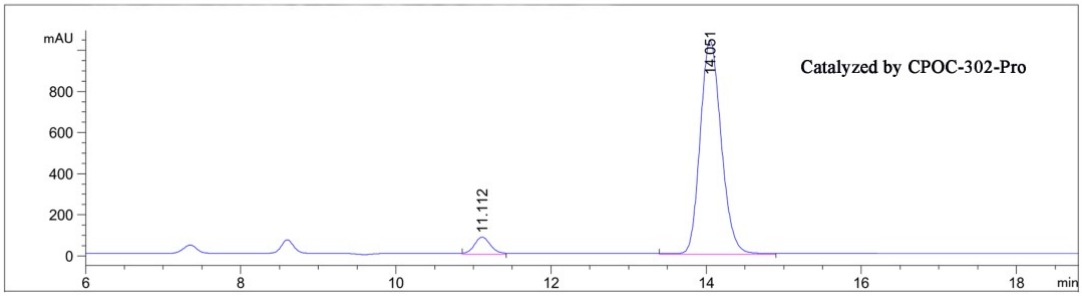




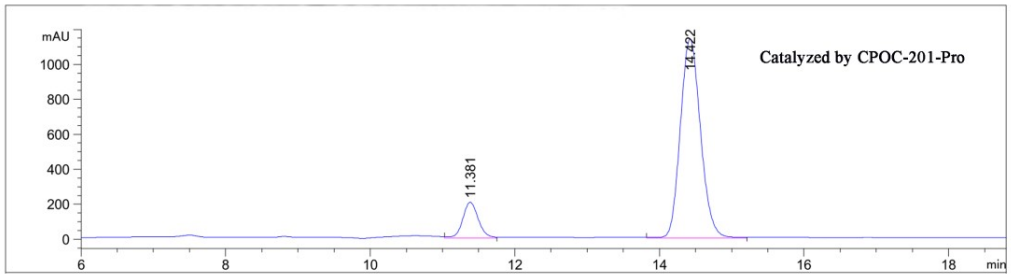
(S)-2-((R)-hydroxy(4-(trifluoromethyl)phenyl)methyl)cyclohexan-1-one

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 7.61 (d, 2H), 7.45 (d, 2H), 4.85 (d, 1H), 4.06 (s, 1H), 2.56-2.63 (m, 1H), 2.47-2.52 (m, 1H), 2.32-2.41 (m, 1H), 2.07-2.14 (m, 1H), 1.79-1.84 (m, 1H), 1.64-1.69 (m, 1H), 1.53-1.61 (m, 2H), 1.32-1.38 (m, 1H). HPLC analysis (Chiralcel AD-H column, n-Hexane/i-PrOH = 90:10, 1.0 mL/min, λ = 220 nm), t_{minor} = 11.2 min, t_{major} = 14.2 min.

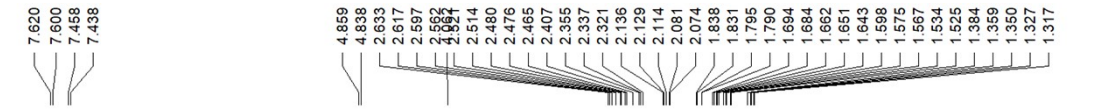


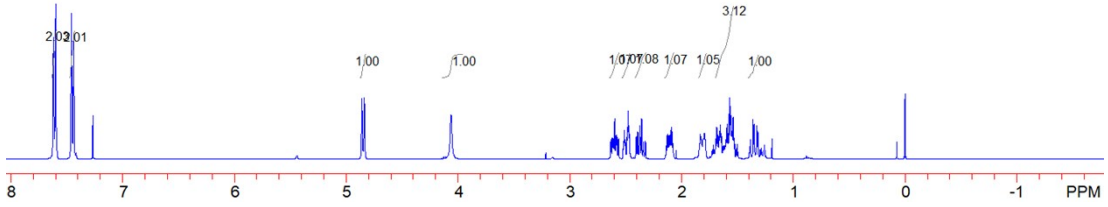


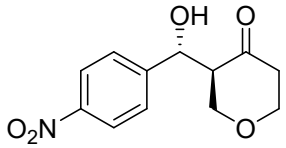
Serial Number	Retention Time [min]	Area	Area %
1	11.112	124667	5.95
2	14.051	1969261	94.05



Serial Number	Retention Time [min]	Area	Area %
1	11.381	309841	12.26
2	14.422	2216971	87.74

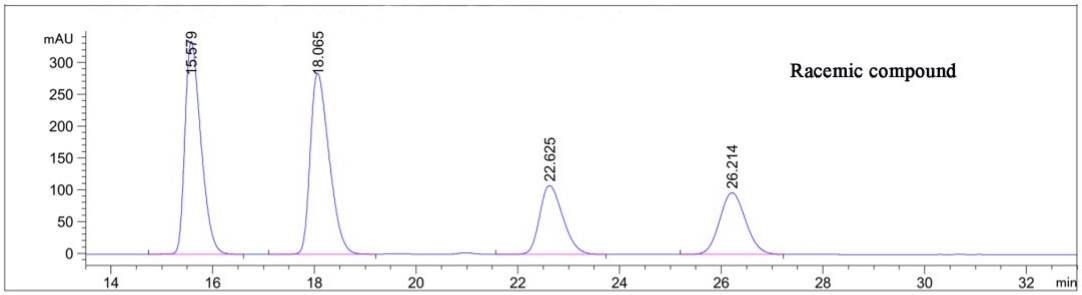


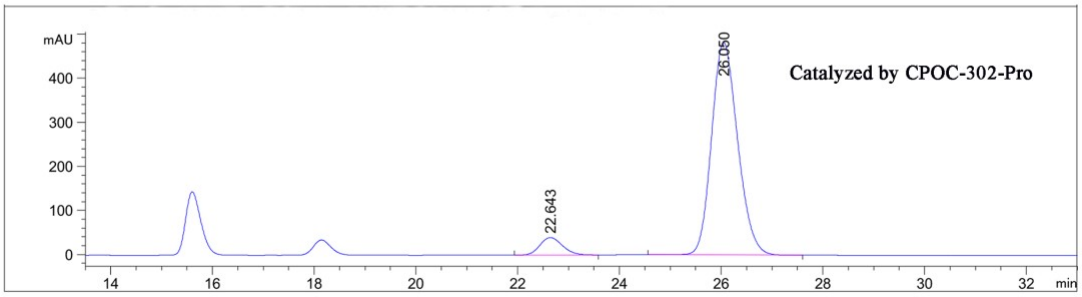




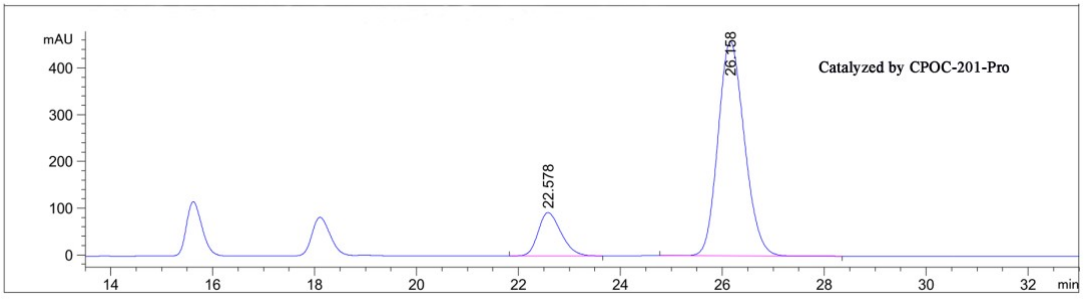
(S)-3-((R)-hydroxy(4-nitrophenyl)methyl)tetrahydro-4H-pyran-4-one

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 8.23 (d, 2H), 7.53 (d, 2H), 5.00 (dd, 1H), 4.18-4.24 (m, 1H), 3.87 (d, 1H), 3.70-3.77 (m, 2H), 3.44-3.49 (m, 1H), 2.87-2.93 (m, 1H), 2.65-2.73 (m, 1H), 2.52-2.57 (m, 1H). HPLC analysis (Chiralcel AD-H column, n-Hexane/i-PrOH = 90:10, 1.0 mL/min, λ = 254 nm), t_{minor} = 22.6 min, t_{major} = 26.2 min.

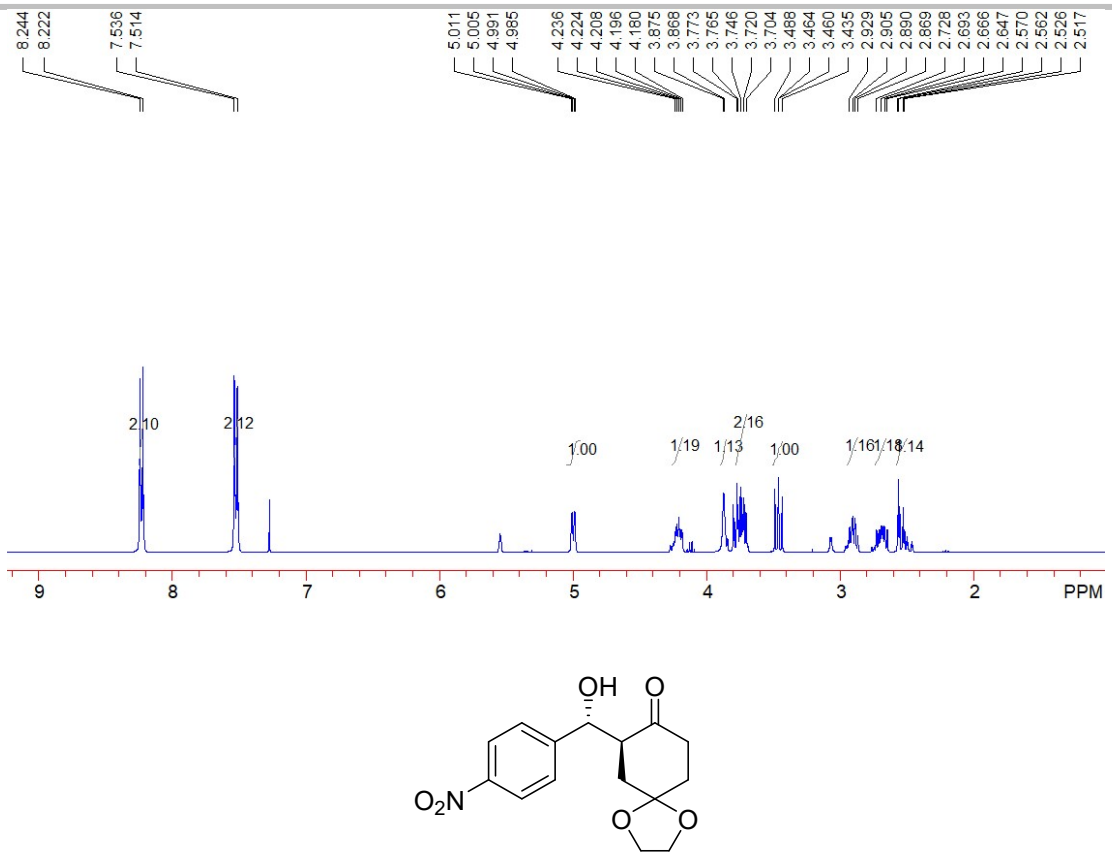




Serial Number	Retention Time [min]	Area	Area %
1	22.643	121308	6.60
2	26.050	1715741	93.40

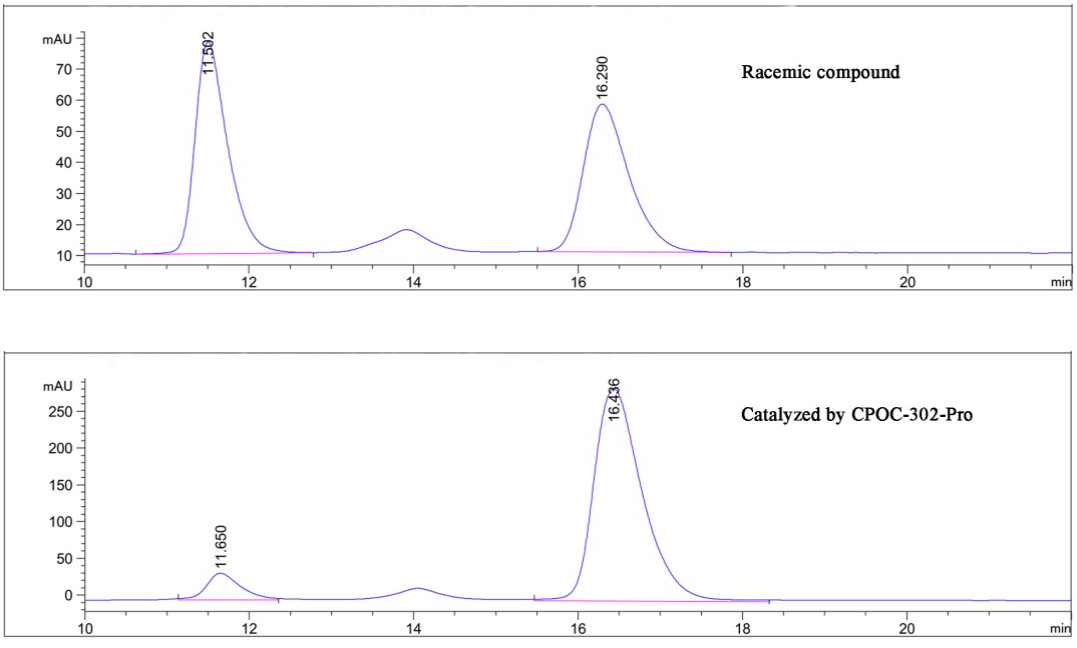


Serial Number	Retention Time [min]	Area	Area %
1	22.578	287445	14.80
2	26.158	1654121	85.20

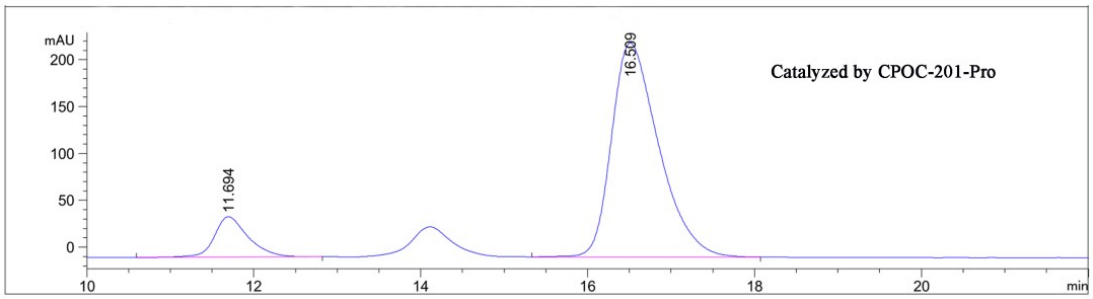


(S)-7-((R)-hydroxy(4-nitrophenyl)methyl)-1,4-dioxaspiro[4.5]decan-8-one

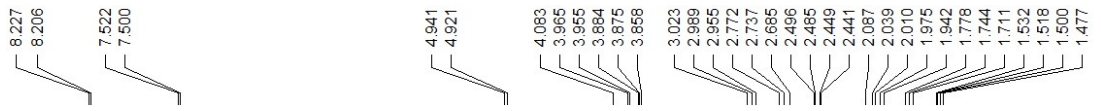
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 8.22 (d, 2H), 7.51 (d, 2H), 4.93 (d, 1H), 4.08 (s, 1H), 3.86-3.97 (m, 4H), 2.96-3.02 (m, 1H), 2.69-2.77 (m, 1H), 2.44-2.50 (m, 1H), 1.94-2.09 (m, 2H), 1.71-1.78 (m, 1H), 1.48-1.53 (m, 1H). HPLC analysis (Chiralcel AS-H column, n-Hexane/i-PrOH = 70:30, 1.0 mL/min, λ = 254 nm), t_{minor} = 11.5 min, t_{major} = 16.3 min.

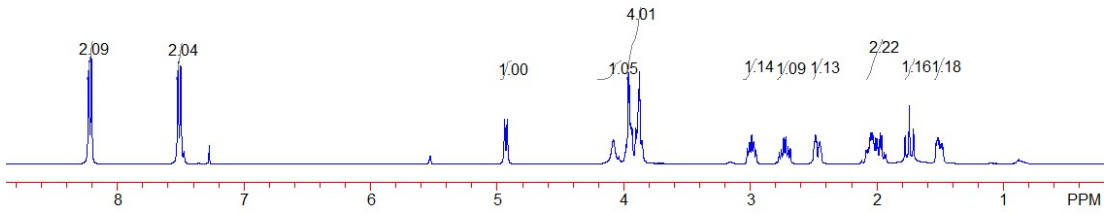


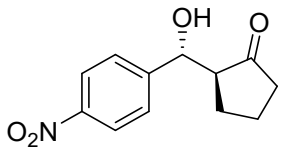
Serial Number	Retention Time [min]	Area	Area %
1	11.650	106101	8.20
2	16.436	1187551	91.80



Serial Number	Retention Time [min]	Area	Area %
1	11.694	121668	11.96
2	16.509	895758	88.04

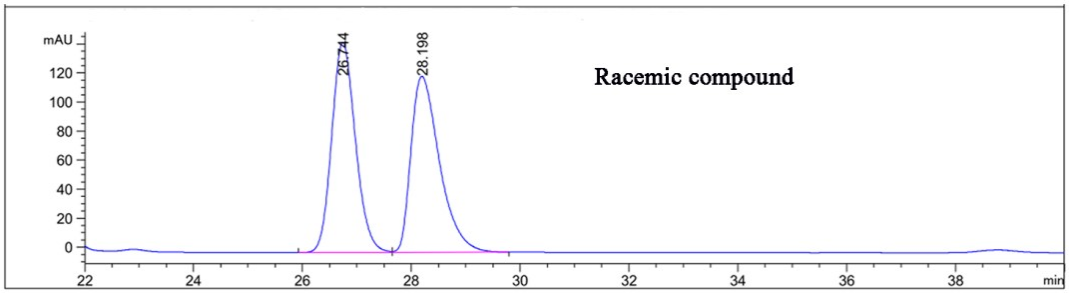


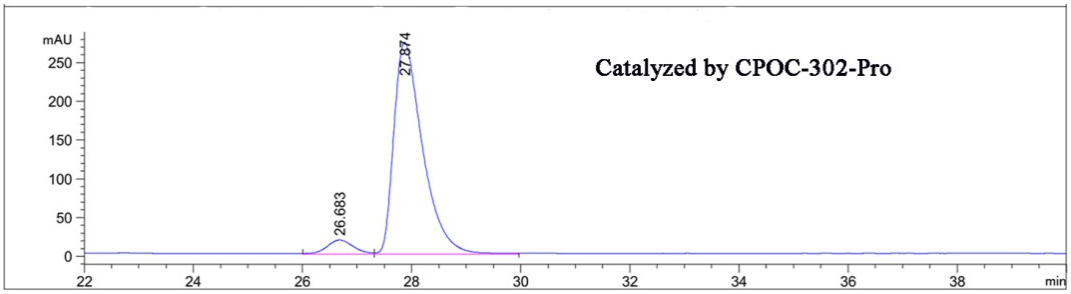




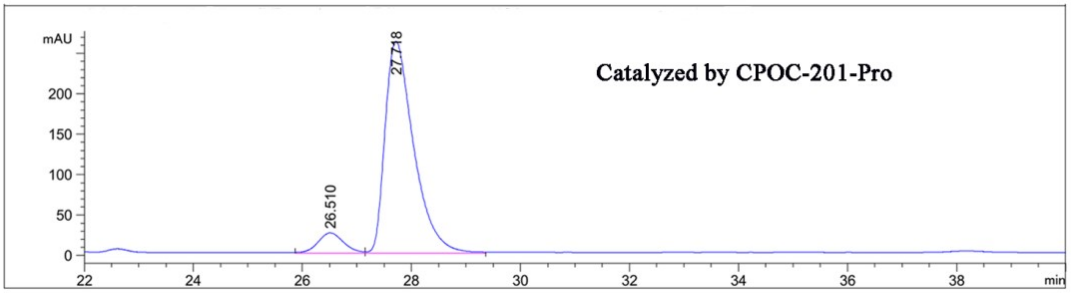
(S)-2-((R)-hydroxy(4-nitrophenyl)methyl)cyclopentan-1-one

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 8.20-8.23 (m, 2H), 7.51-7.55 (m, 2H), 5.43 (t, 1H), 2.61 (d, 1H), 2.36-2.52 (m, 2H), 2.11-2.19 (m, 1H), 1.96-2.07 (m, 2H), 1.70-1.76 (m, 2H). HPLC analysis (Chiralcel AD-H column, n-Hexane/i-PrOH = 90:10, 1.0 mL/min, λ = 254 nm), t_{minor} = 26.7 min, t_{major} = 28.2 min.

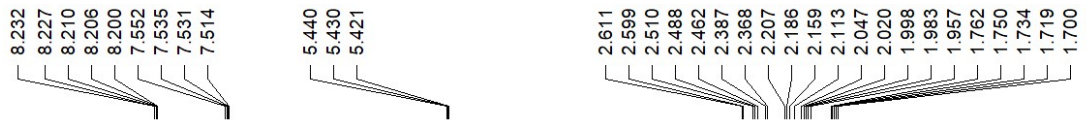


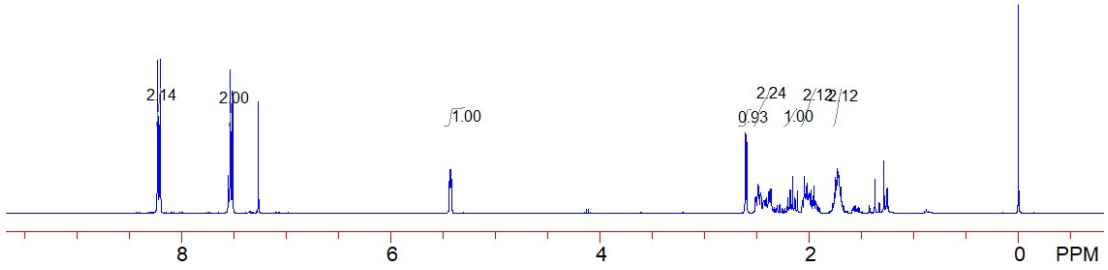


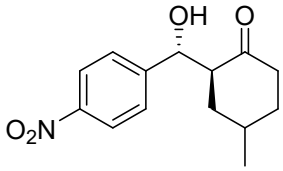
Serial Number	Retention Time [min]	Area	Area %
1	26.683	76968	6.90
2	27.874	1038201	93.10



Serial Number	Retention Time [min]	Area	Area %
1	26.510	82909	7.94
2	27.718	961706	92.06

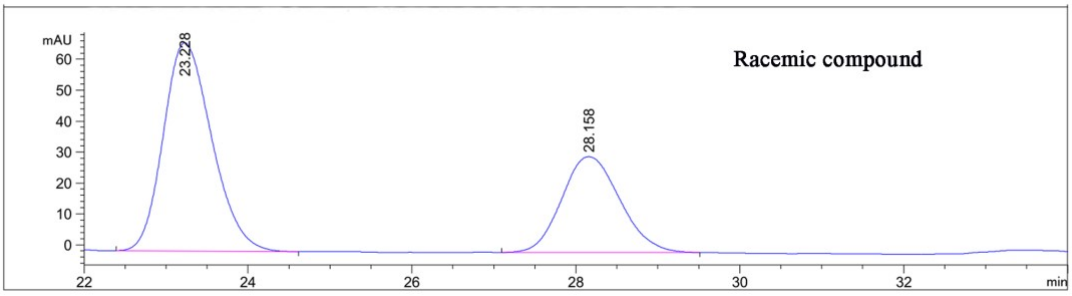


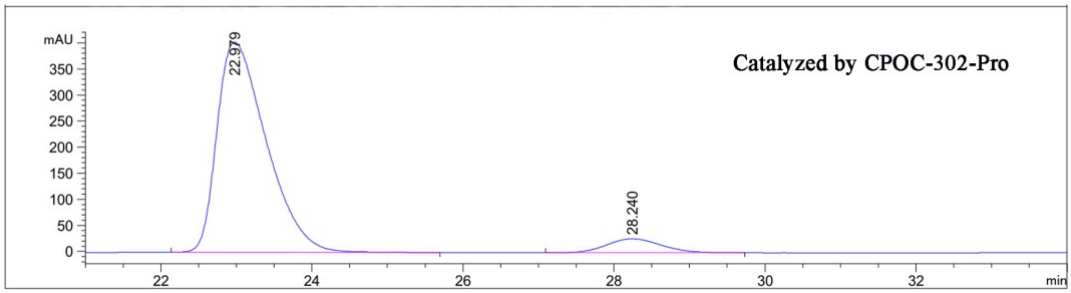




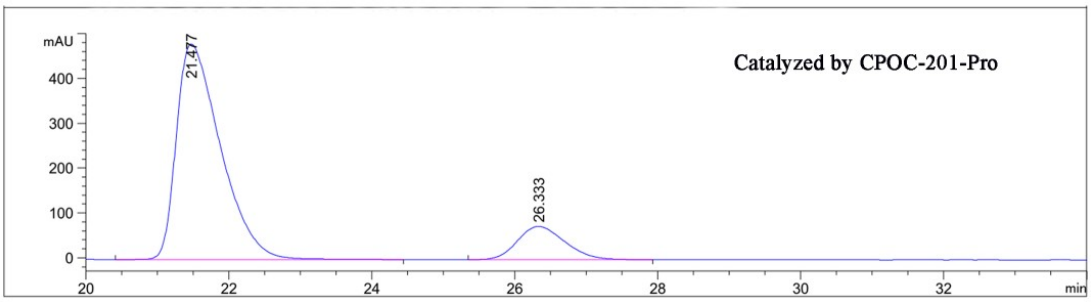
(2S)-2-((R)-hydroxy(4-nitrophenyl)methyl)-4-methylcyclohexan-1-one

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 8.22 (d, 2H), 7.51 (d, 2H), 4.94 (d, 1H), 3.98 (s, 1H), 2.72-2.78 (m, 1H), 2.39-2.59 (m, 2H), 2.09-2.10 (m, 1H), 1.92-1.98 (m, 1H), 1.77-1.81 (m, 1H), 1.56-1.63 (m, 1H), 1.26-1.34 (m, 1H), 1.06 (d, 3H). HPLC analysis (Chiralcel OD-H column, n-Hexane/i-PrOH = 90:10, 1.0 mL/min, λ = 254 nm), t_{minor} = 23.2 min, t_{major} = 28.2 min.

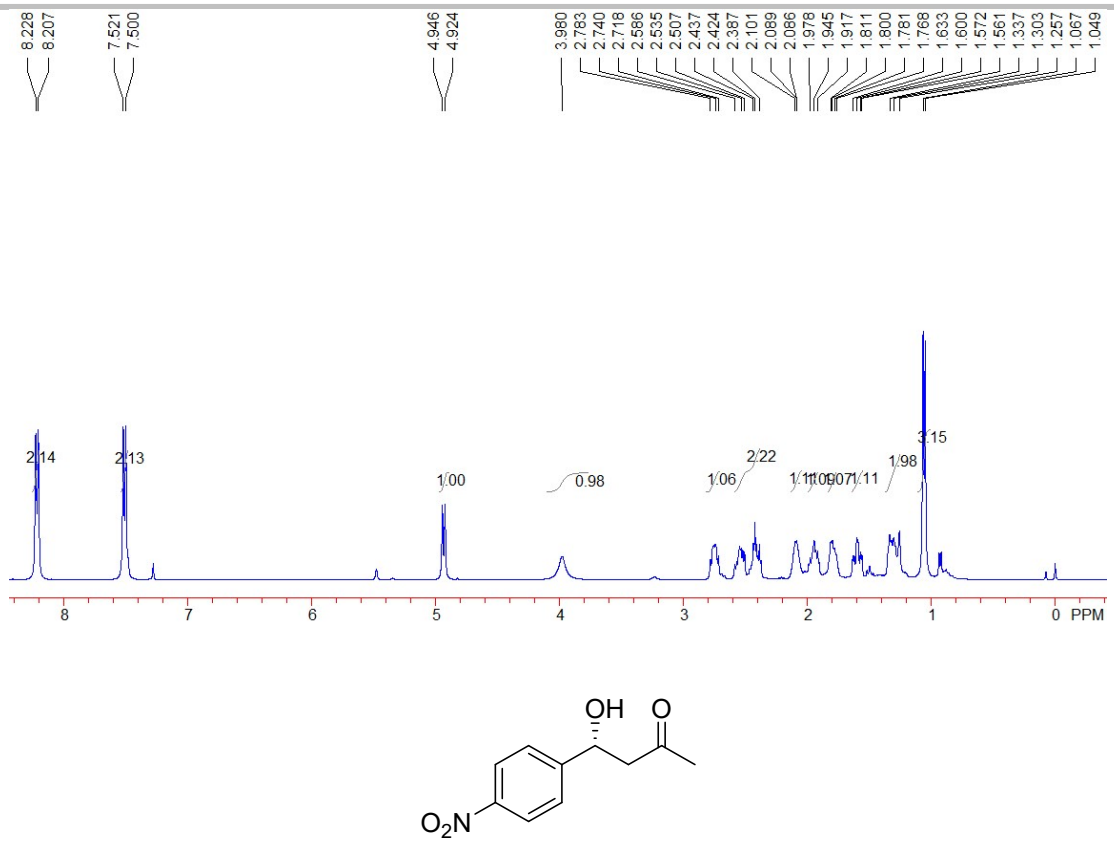




Serial Number	Retention Time [min]	Area	Area %
1	22.979	1826091	93.15
2	28.240	134333	6.85

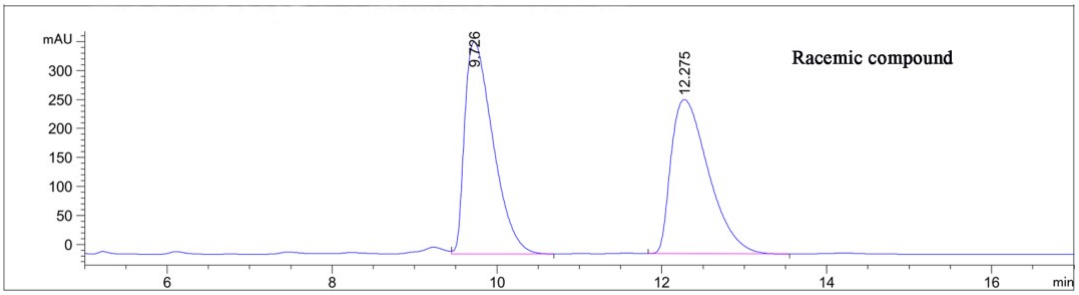


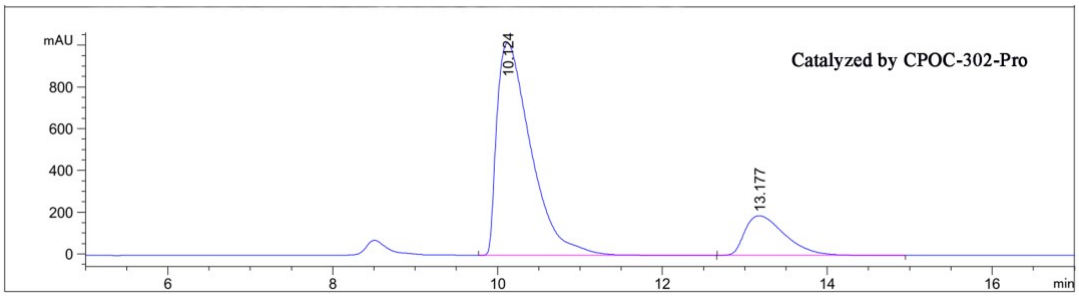
Serial Number	Retention Time [min]	Area	Area %
1	21.477	2059801	85.81
2	26.333	340666	14.19



(R)-4-hydroxy-4-(4-nitrophenyl)butan-2-one

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 8.22 (d, 2H), 7.55 (d, 2H), 5.25-5.29 (m, 1H), 3.63 (d, 1H), 2.85-2.87 (m, 2H), 2.23 (s, 3H). HPLC analysis (Chiralcel AS-H column, n-Hexane/i-PrOH = 70:30, 1.0 mL/min, λ = 254 nm), t_{major} = 9.7 min, t_{minor} = 12.3 min.





Serial Number	Retention Time [min]	Area	Area %
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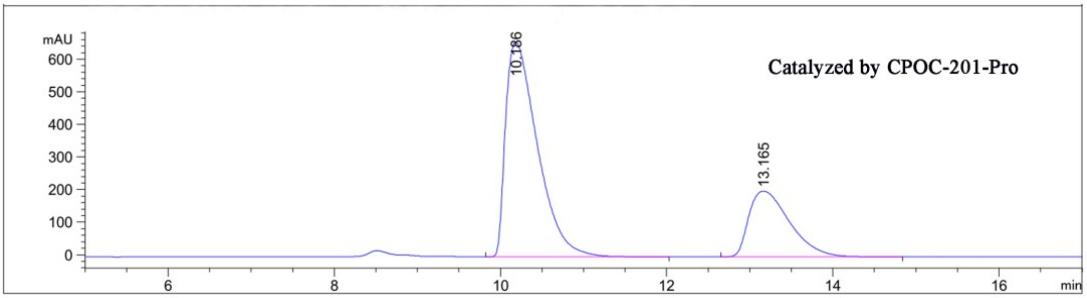
2	13.177	630295	17.85



Serial Number	Retention Time [min]	Area	Area %
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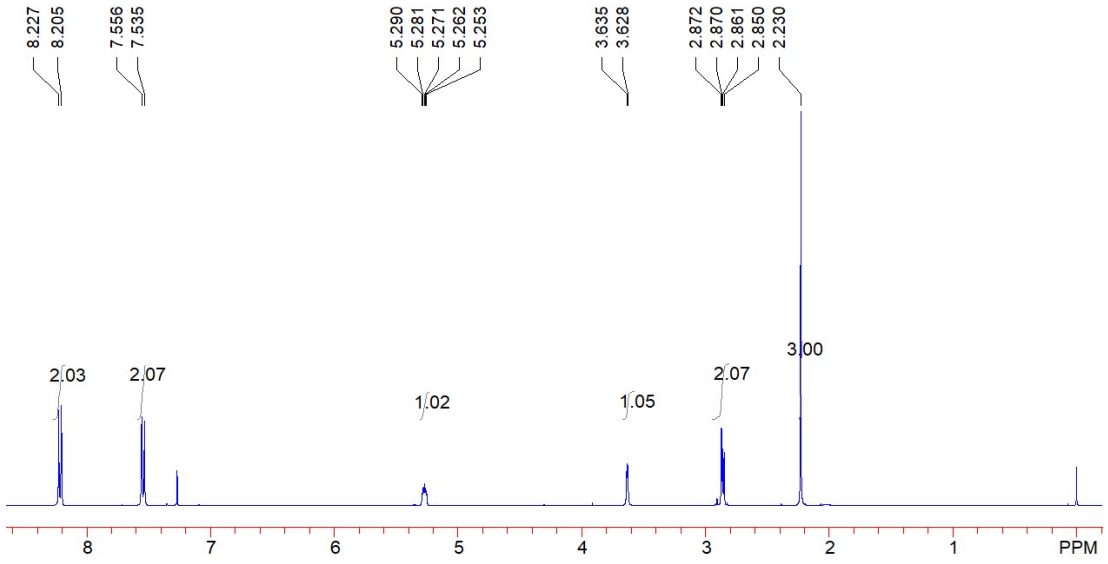
2	13.165	684886	28.14



2.4 2D NOESY experiments

For NOESY experiments with the mixture of CPOC-302-Pro and the reactant (*p*-nitrobenzaldehyde or cyclohexanone), 0.05 mmol of the reactant was added to a solution of CPOC-302-Pro (20 mg CPOC-302-Pro in 1.0 mL $CDCl_3$). After stirring for half an hour at room temperature, the mixture was carried out for the NOESY experiments.

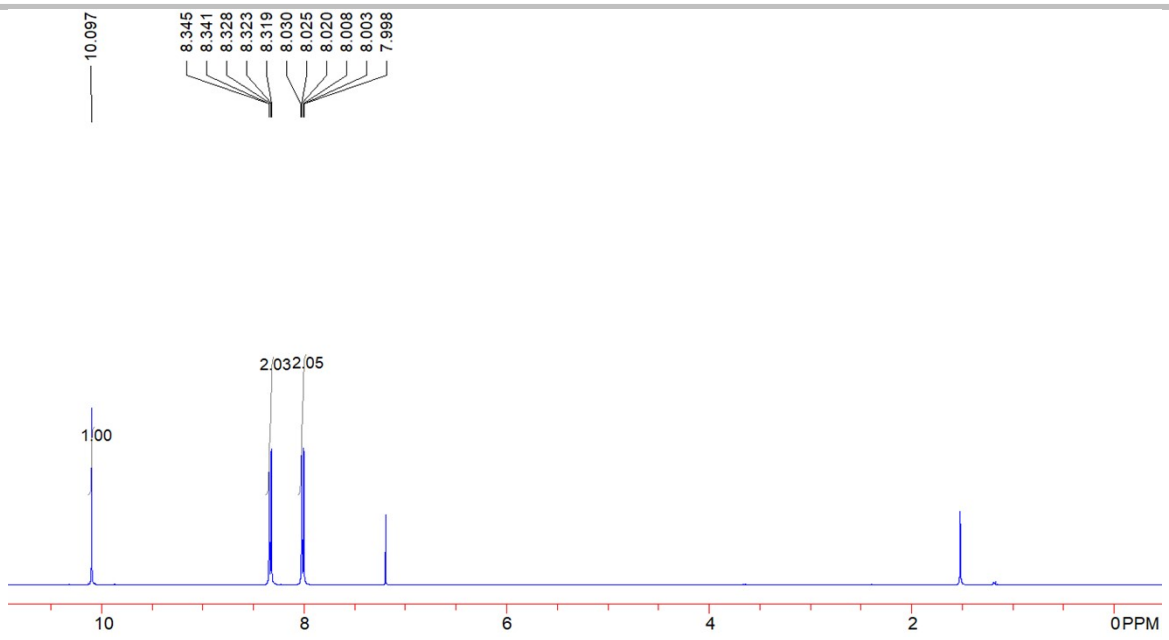


Figure S22. ^{1}H NMR spectrum of *p*-nitrobenzaldehyde ($CDCl_3$, 400 MHz).

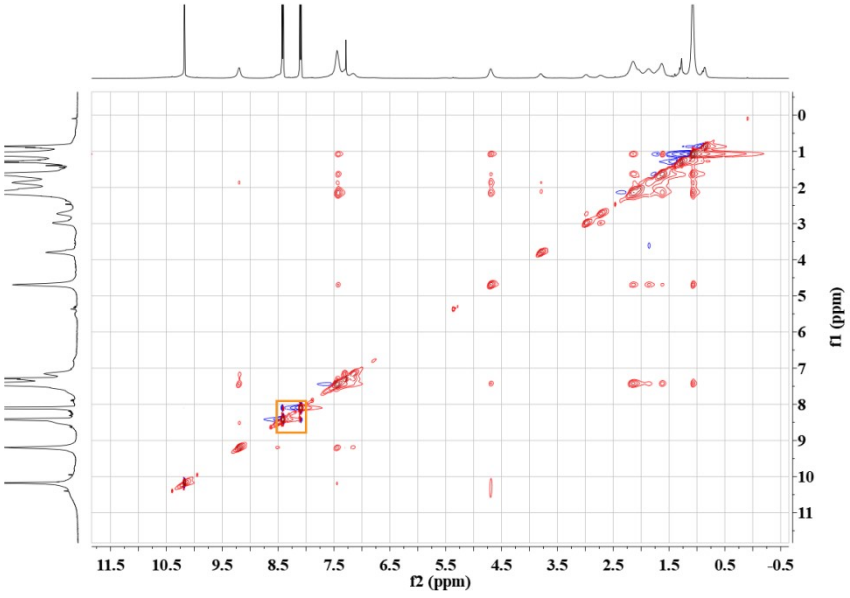


Figure S23. 2D NOESY NMR spectrum (400 MHz, $CDCl_3$, 298 K) of the mixture of CPOC-302-Pro and *p*-nitrobenzaldehyde. Expansion of marked area (in orange rectangle) is reported below.

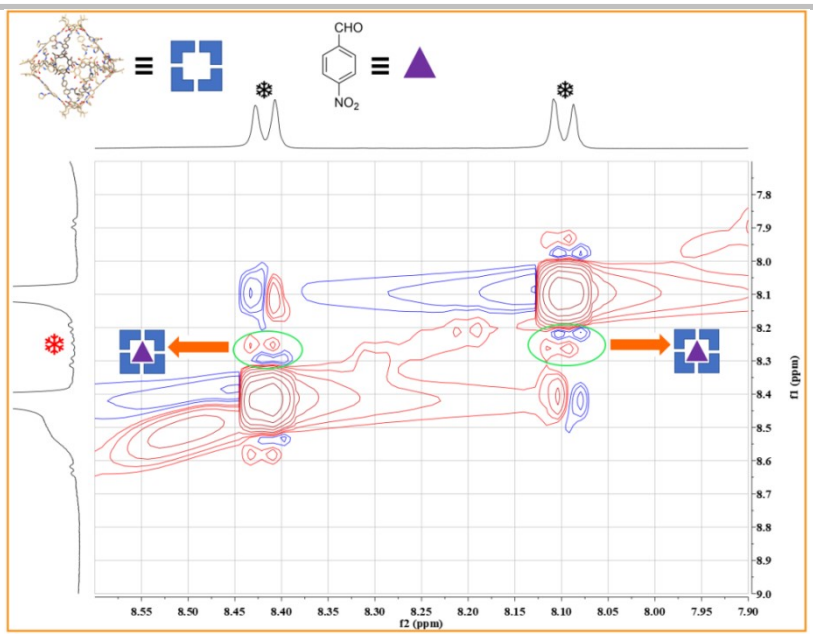


Figure S24. Enlarged view of the orange rectangle in the 2D NOESY NMR spectrum of the mixture of CPOC-302-Pro and *p*-nitrobenzaldehyde. Exchange peaks between aromatic protons of *p*-nitrobenzaldehyde outside the cavity (indicated with black snowflakes) and inside the cavity (indicated with a red snowflake) are shown.

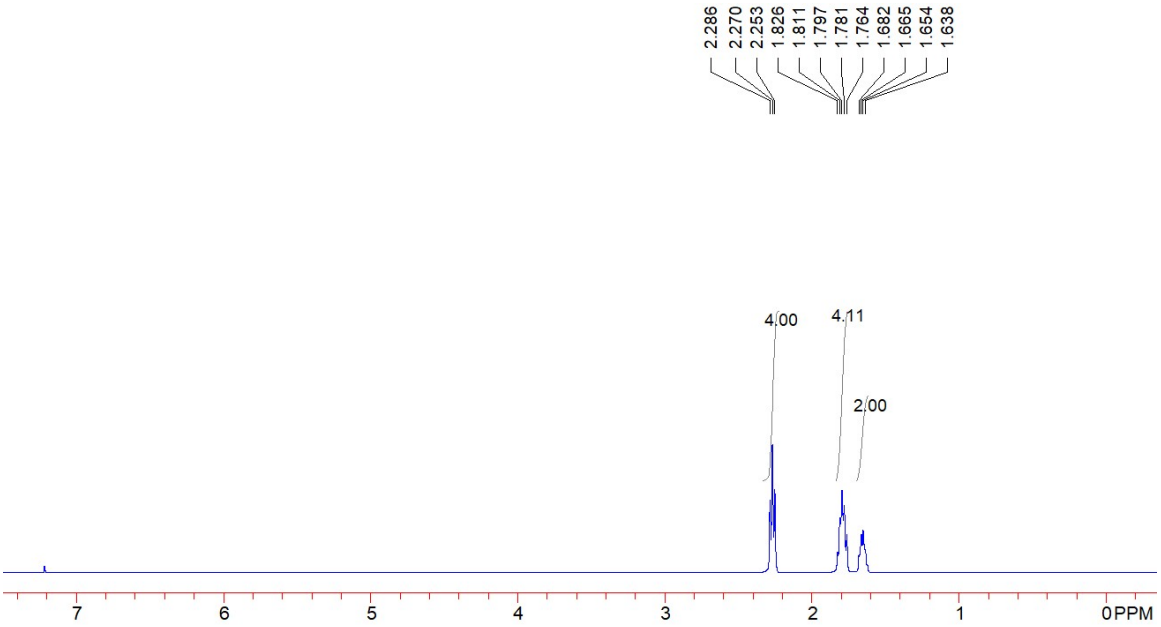


Figure S25. ^{1}H NMR spectrum of cyclohexanone ($CDCl_3$, 400 MHz).

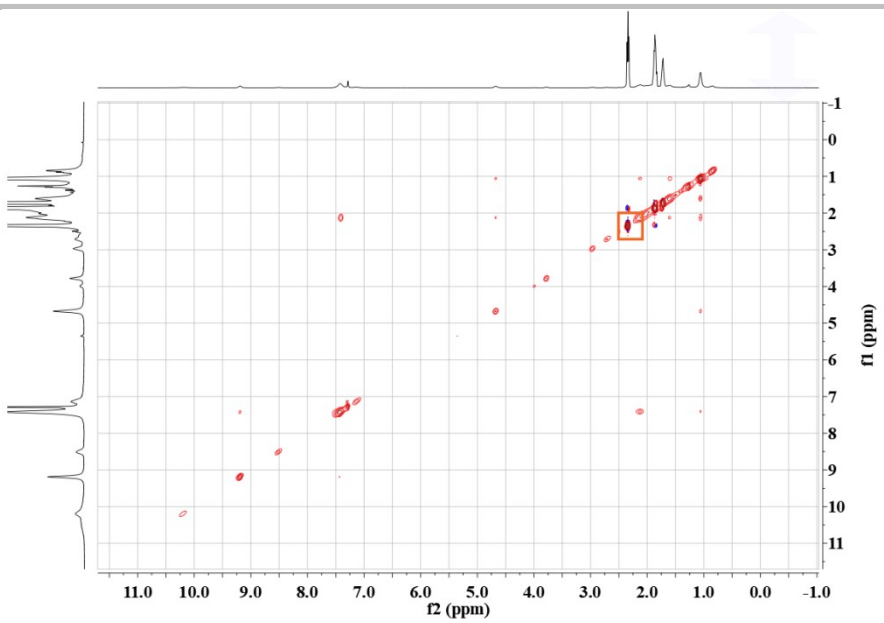


Figure S26. 2D NOESY NMR spectrum (400 MHz, $CDCl_3$, 298 K) of the mixture of CPOC-302-Pro and cyclohexanone. Expansion of marked area (in orange rectangle) is reported below.

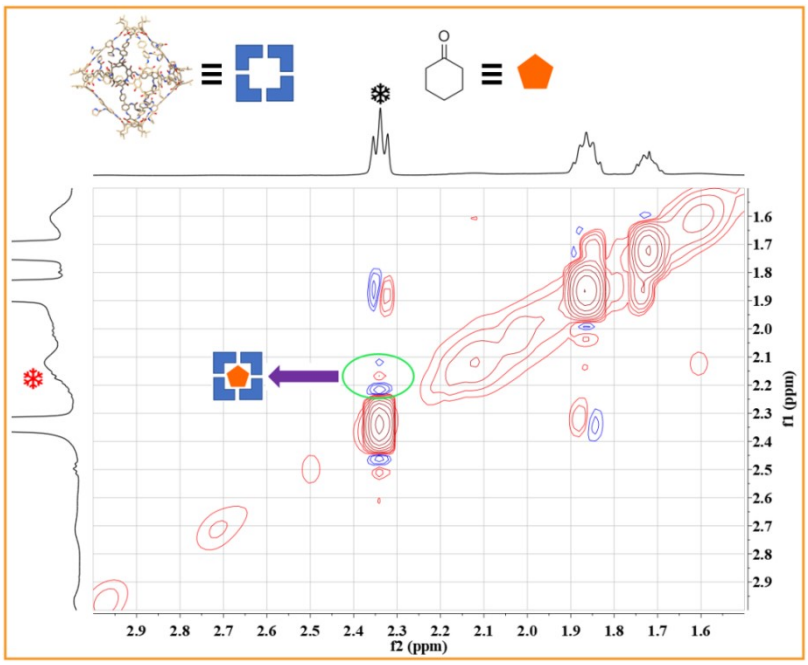
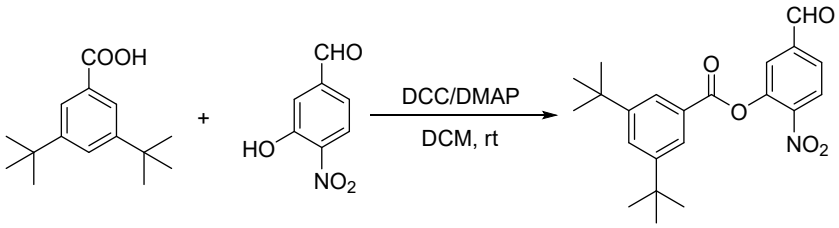


Figure S27. Enlarged view of the orange rectangle in the 2D NOESY NMR spectrum of the mixture of CPOC-302-Pro and cyclohexanone. Exchange peaks between methylene protons (the α position) of cyclohexanone outside the cavity (indicated with a black snowflakes) and inside the cavity (indicated with a red snowflake) are shown.

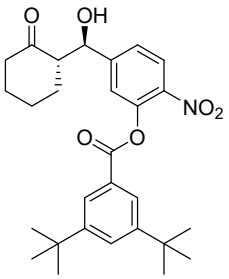
2.5 Size selectivity study of CPOC-302-Pro

Synthesis of 5-formyl-2-nitrophenyl-3,5-di-tert-butylbenzoate



To a solution of 3,5-di-tert-butylbenzoic acid (703 mg, 3.0 mmol) in dry dichloromethane (12 mL) was added DCC (680 mg, 3.3 mmol), DMAP (403 mg, 3.3 mmol) under 0 °C and stirred for 1 h. 3-hydroxy-4-nitrobenzaldehyde (501 mg, 3.0 mmol) in 10 mL dichloromethane was added slowly and the mixture was stirred at room temperature for 12 h. After the reaction was completed, the reaction mixture was filtered and the obtained solution was concentrated under reduced pressure. The crude product was purified by chromatography on silica gel with petroleum ether/ethyl acetate (5/1, v/v) as the eluent to afford the product 5-formyl-2-nitrophenyl 3,5-di-tert-butylbenzoate as white solids in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 10.12 (s, 1H), 8.26 (d, 1H), 8.04 (d, 2H), 7.95 (d, 2H), 7.76 (s, 1H), 1.39 (s, 18H).

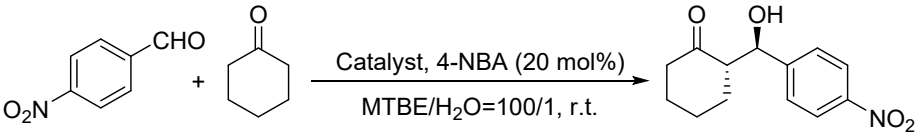
For size selectivity study, two sets of reactions were performed. The procedures are similar to the above catalytic reactions. Under the optimal reaction conditions, 0.20 mmol 5-formyl-2-nitrophenyl 3,5-di-tert-butylbenzoate and 2.0 mmol cyclohexanone were reacted at room temperature in presence of model catalyst BPP and CPOC-302-Pro, respectively. After two days, the corresponding product was isolated by fast column chromatography with petroleum ether/ethyl acetate (6/1, v/v) as the eluent.



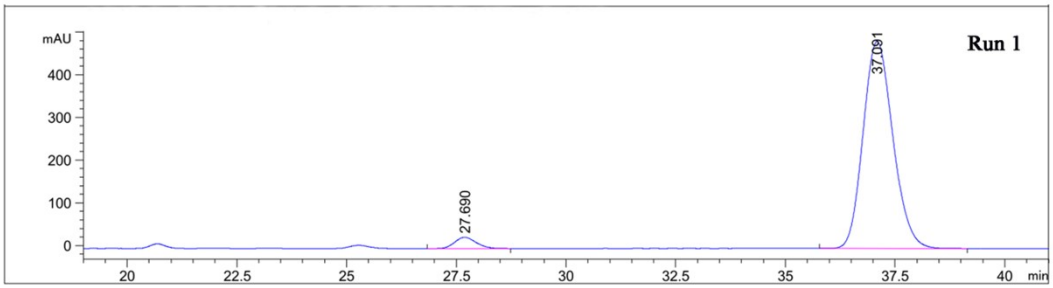
5-((R)-hydroxy((S)-2-oxocyclohexyl)methyl)-2-nitrophenyl 3,5-di-tert-butylbenzoate

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)= 8.12 (d, 1H), 8.04 (d, 2H), 7.74 (t, 1H), 7.40 (d, 1H), 7.35 (d, 1H), 5.49 (s, 1H), 3.30 (s, 1H), 2.64-2.69 (m, 1H), 2.38-2.50 (m, 2H), 2.08-2.13 (m, 1H), 1.87-1.90 (m, 1H), 1.54-1.75 (m, 4H), 1.38 (s, 18H).

2.6 Catalytic recycle test of CPOC-302-Pro



Run	catalyst	Time (d)	yield (%)	anti/syn	ee (%)
1	CPOC-302-Pro	2	99	93:7	92
2	CPOC-302-Pro	2	96	93:7	92
3	CPOC-302-Pro	2	95	92:8	92
4	CPOC-302-Pro	2	93	92:8	92
5	CPOC-302-Pro	2	90	91:9	90



Serial Number	Retention Time [min]	Area	Area %
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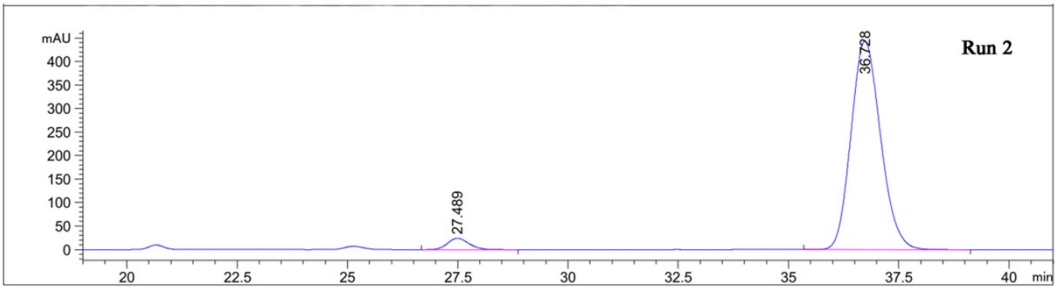
2	37.091	2286381	96.23



Serial Number	Retention Time [min]	Area	Area %
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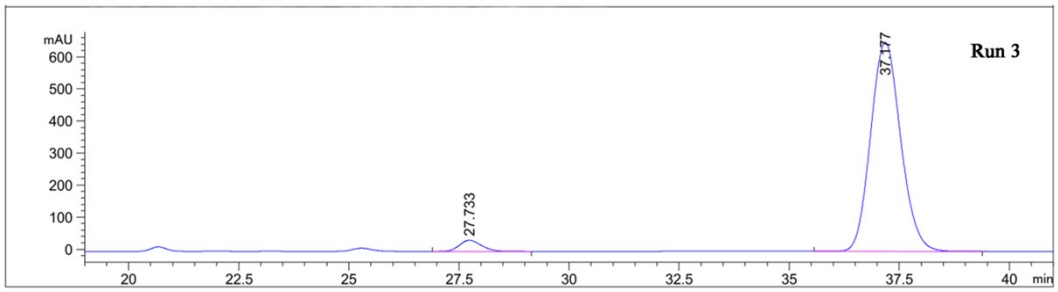
2	36.728	2066973	96.21



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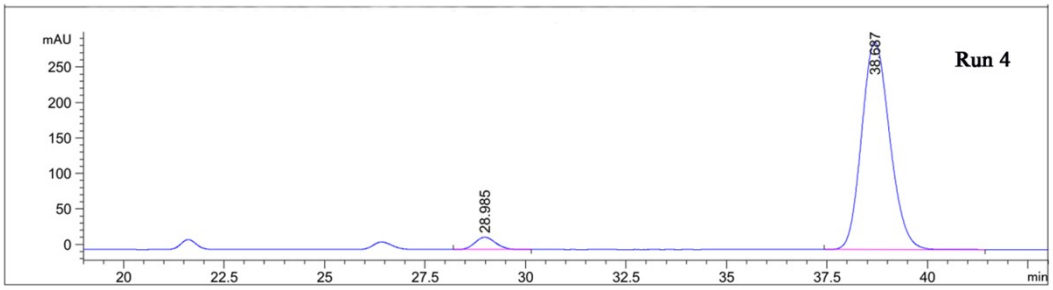
2	37.177	3082045	96.20



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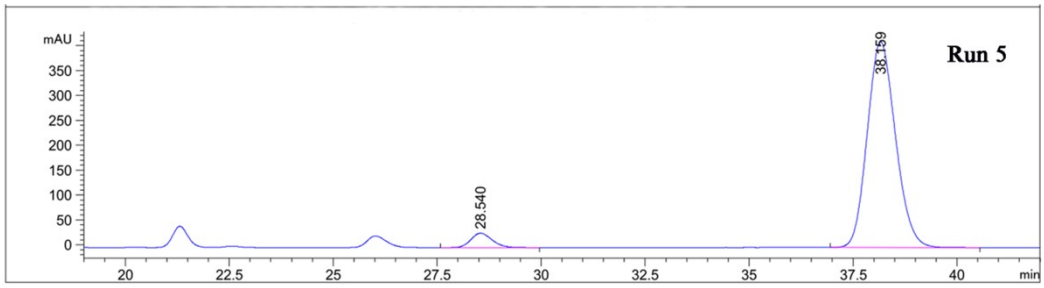

Serial Number	Retention Time [min]	Area	Area %
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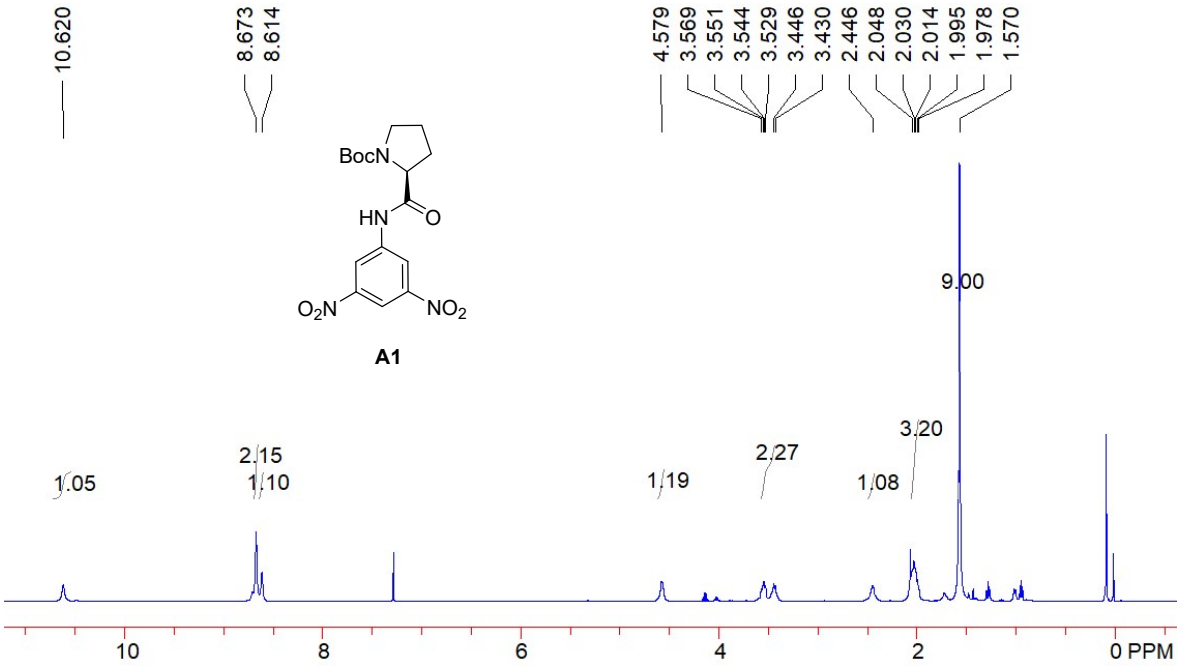
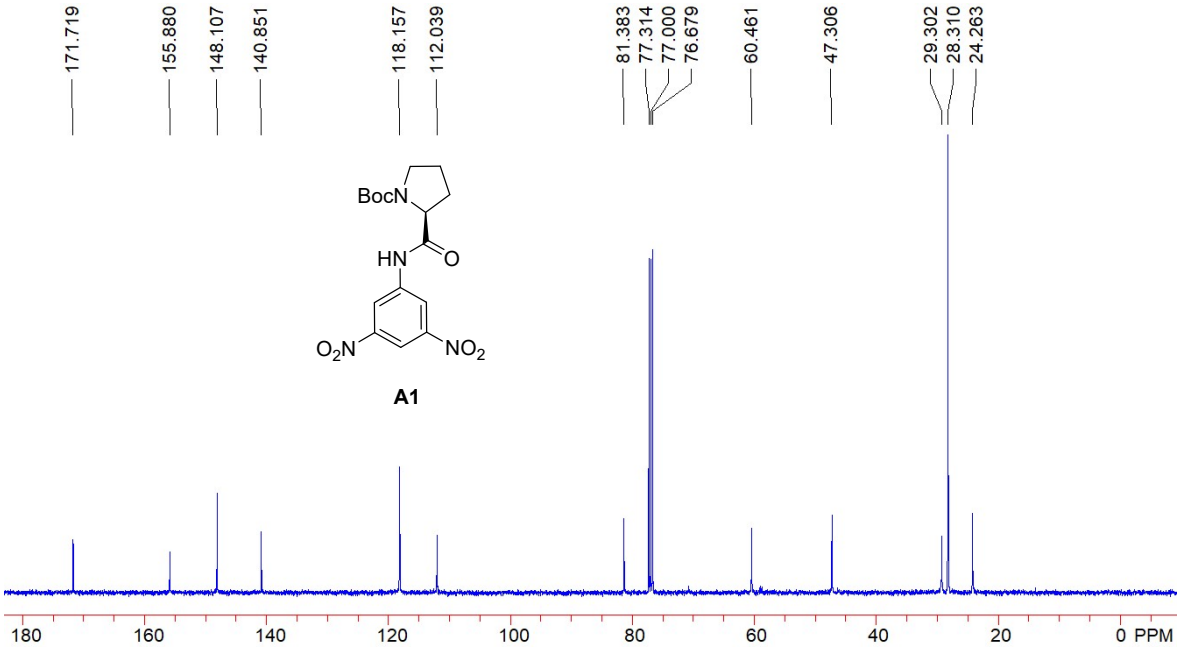
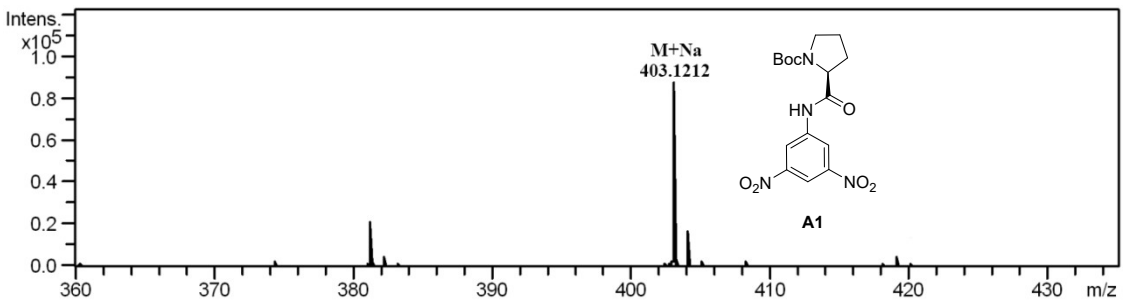
2	38.159	1947361	95.02

2.7 ^{1}H, ^{13}C NMR spectra and mass spectra of the precursor moleculars





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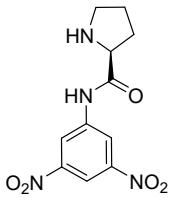
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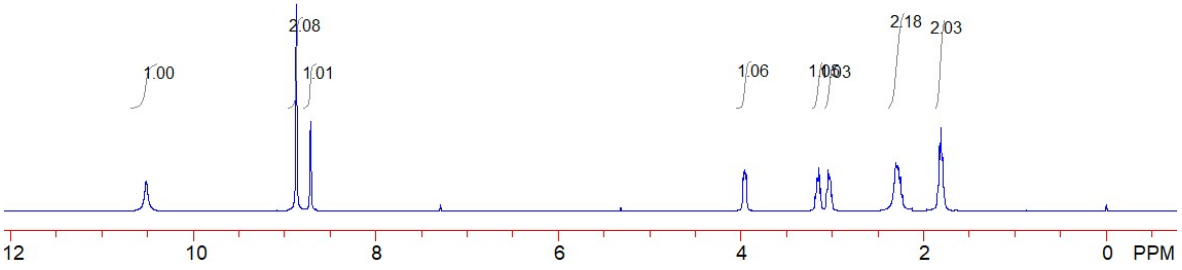
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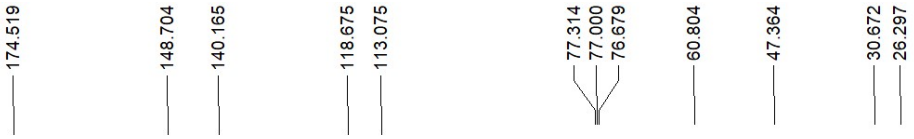
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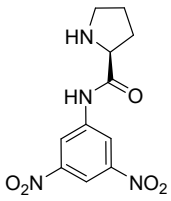
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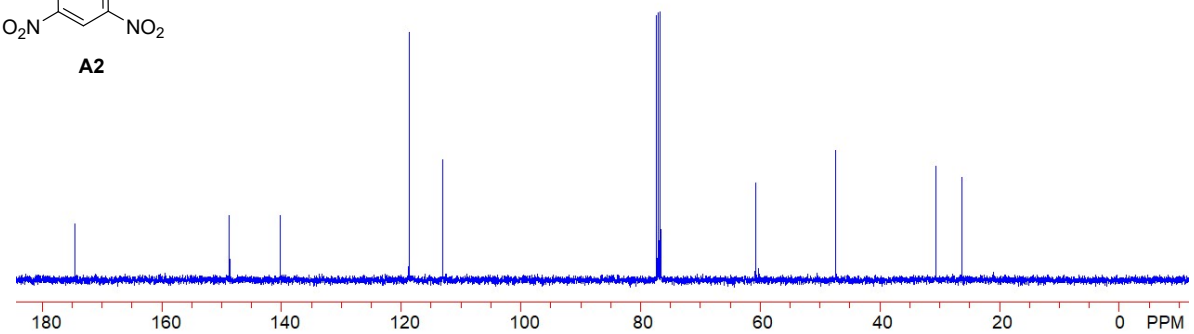
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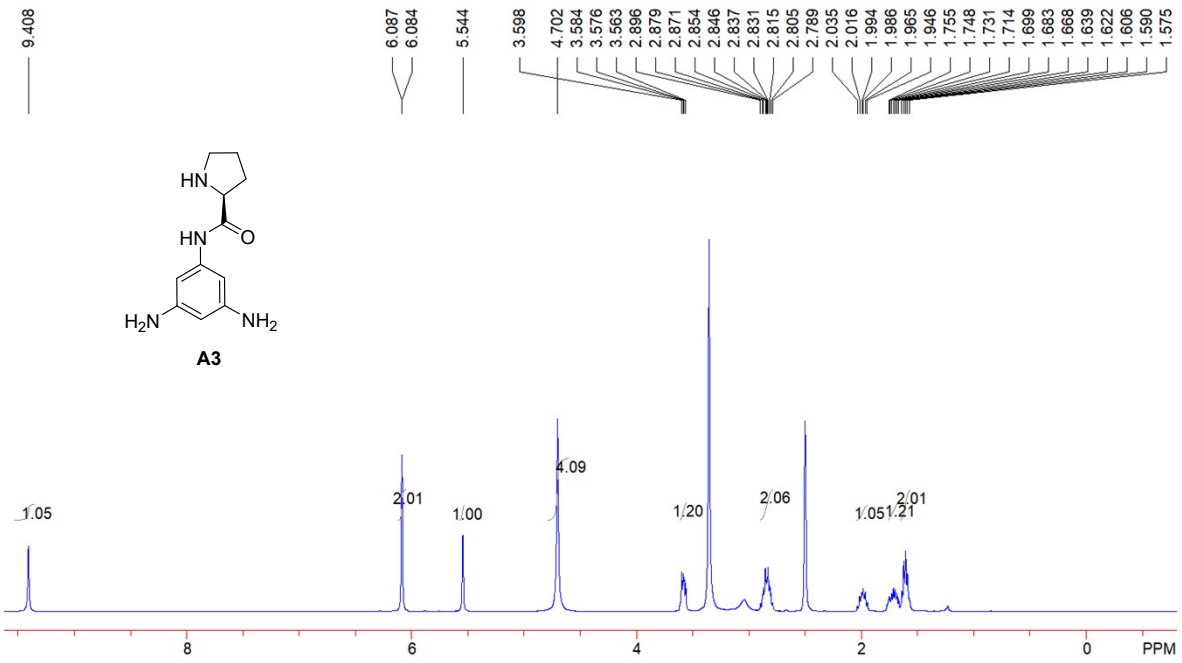
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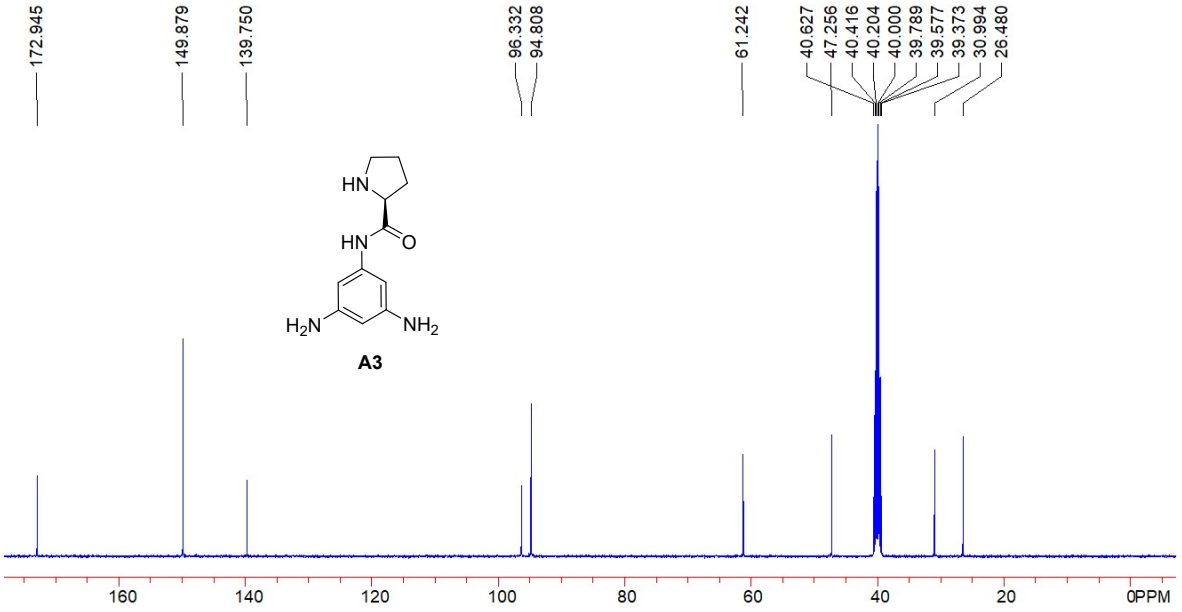
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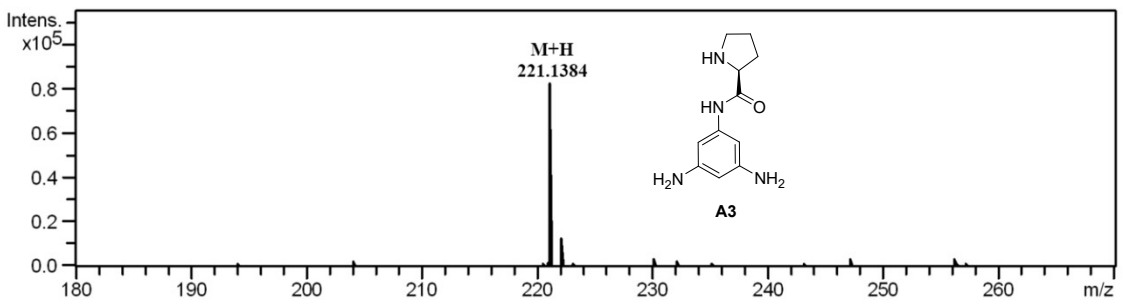
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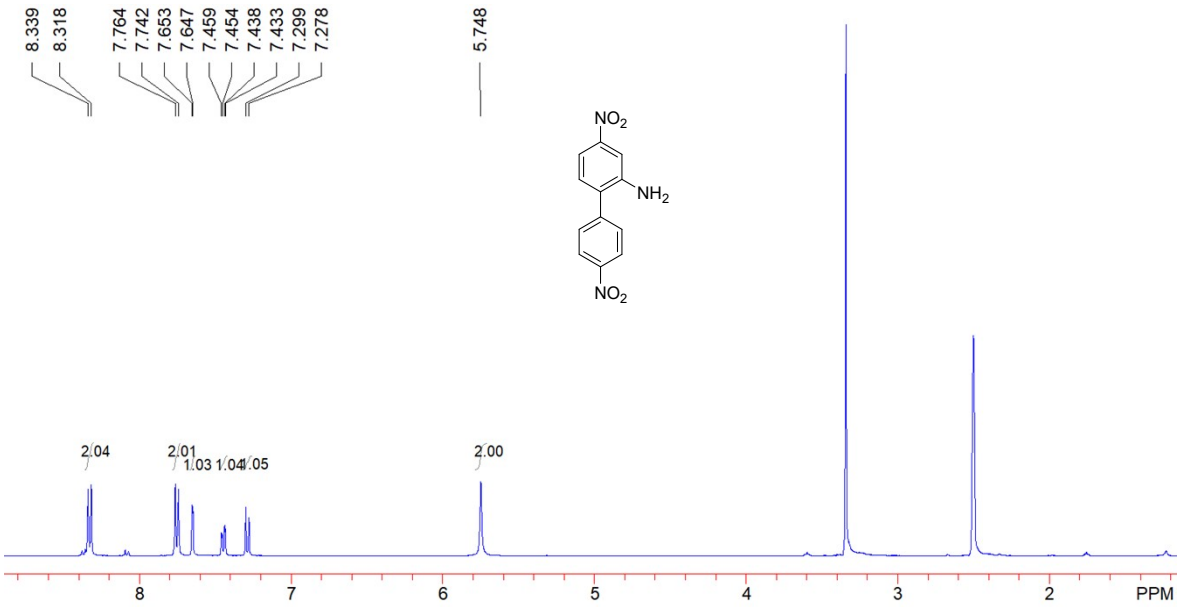
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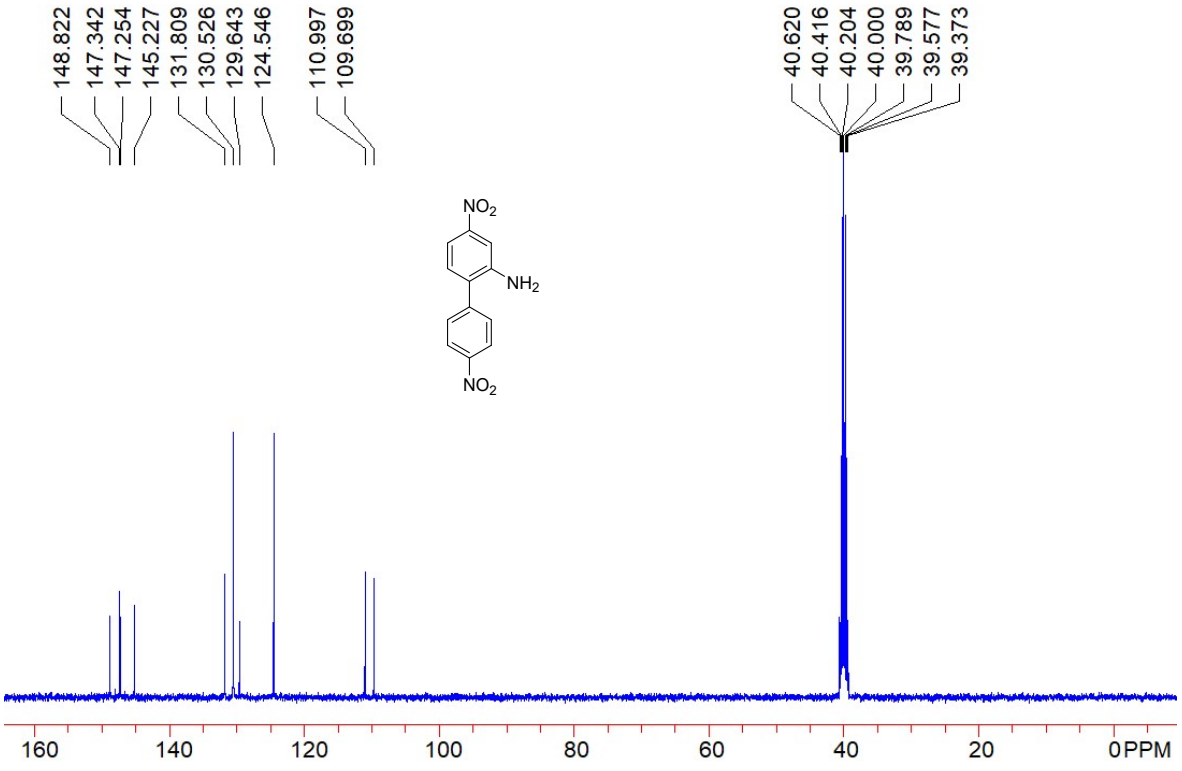
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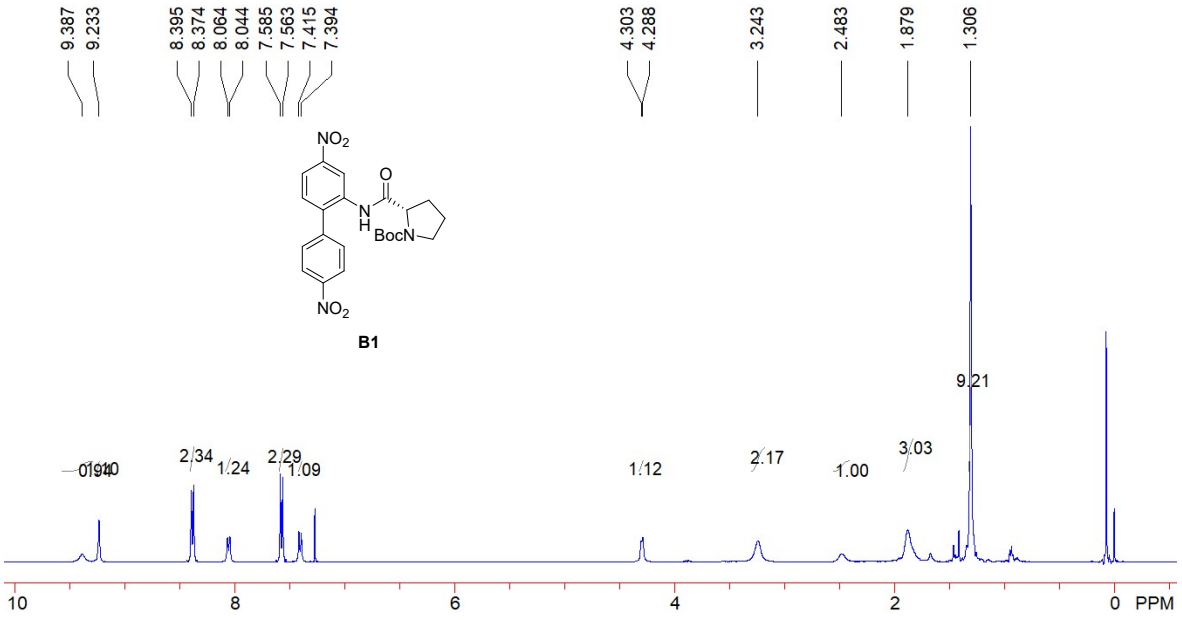
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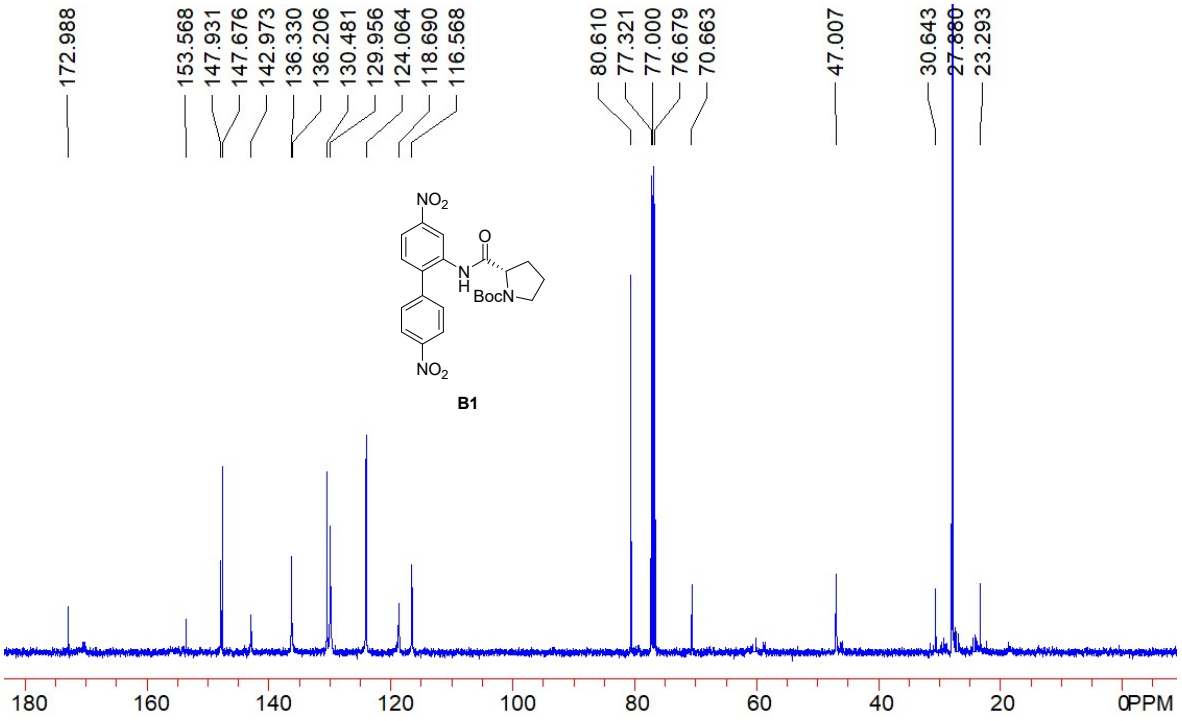
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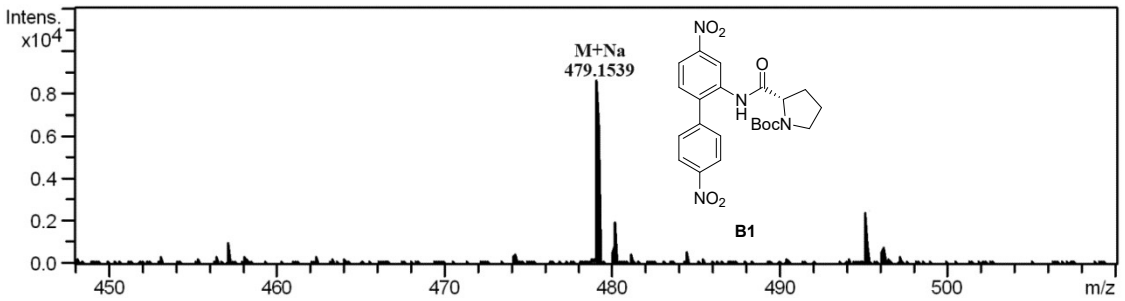
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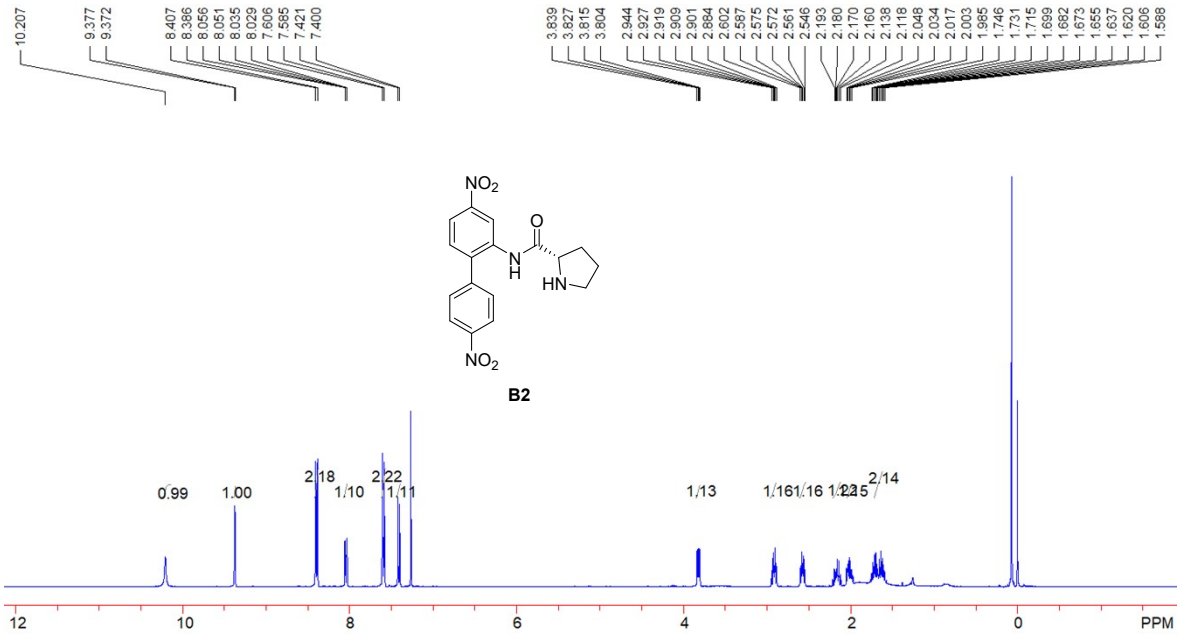
m/z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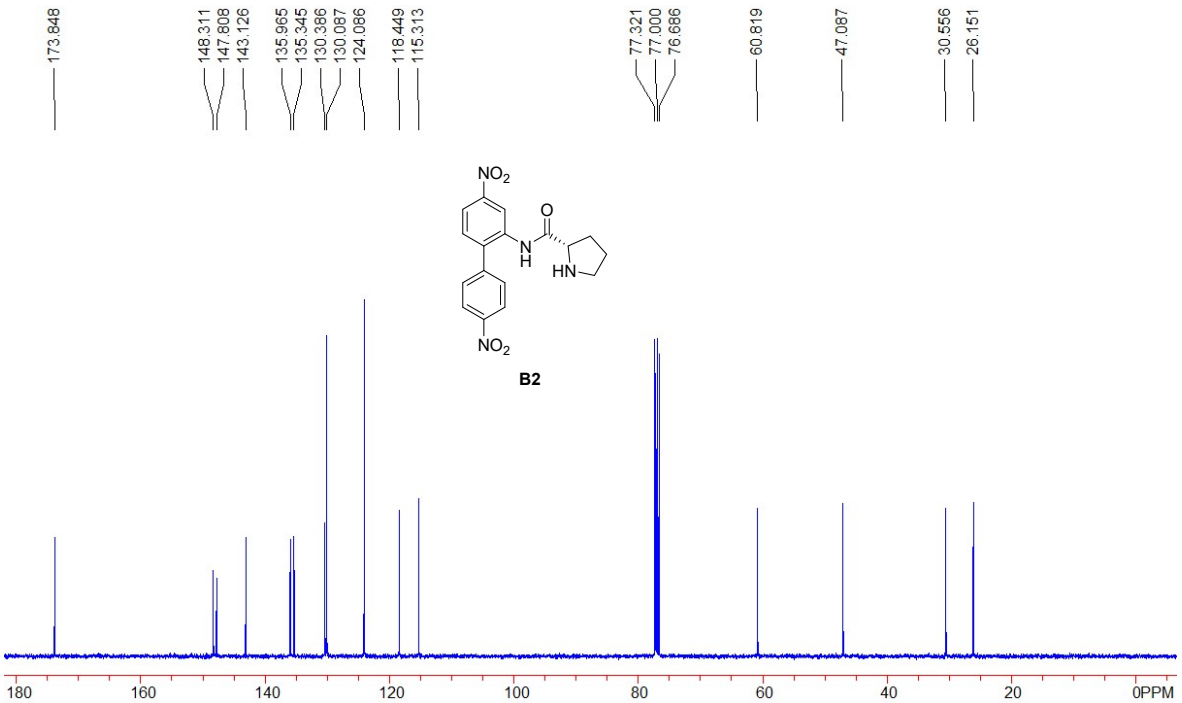
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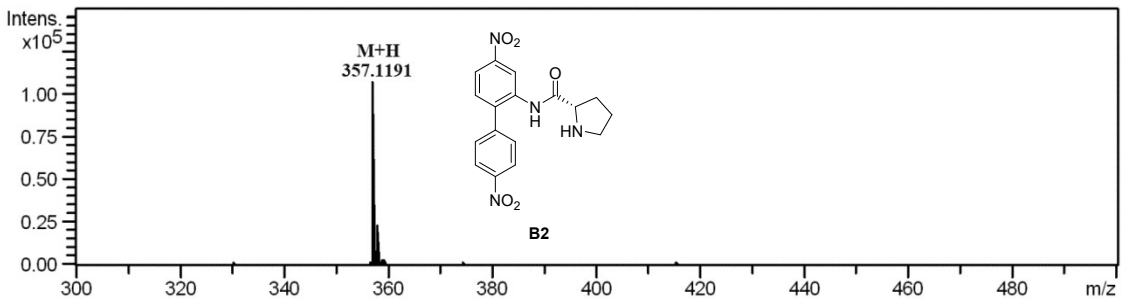
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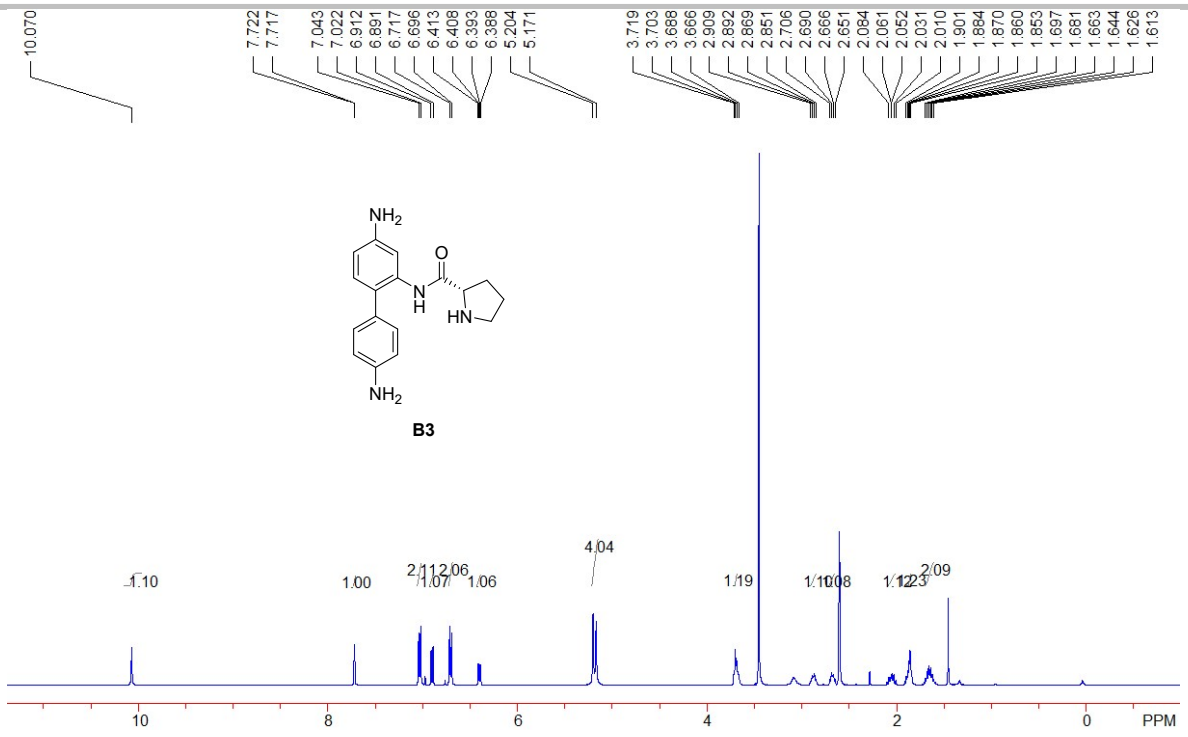
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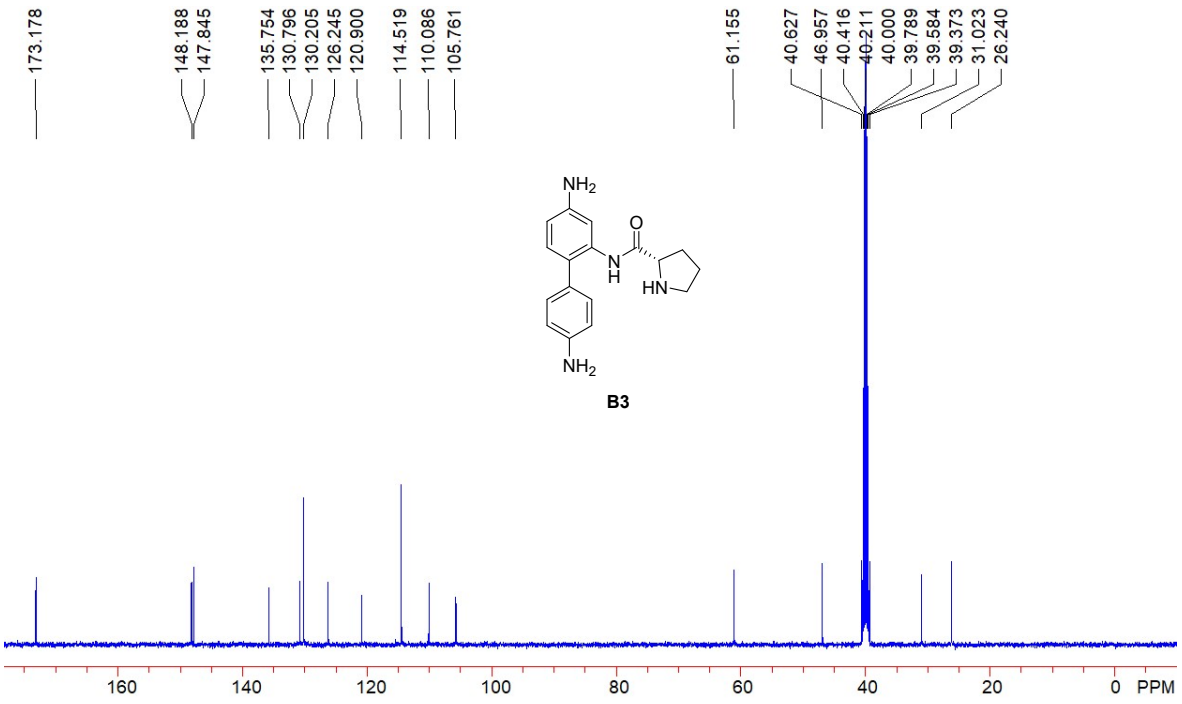
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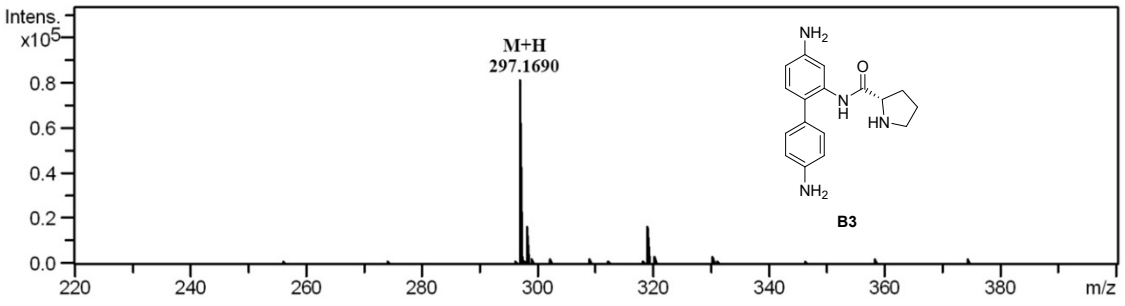
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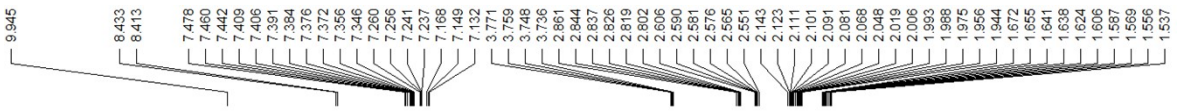
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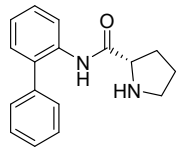
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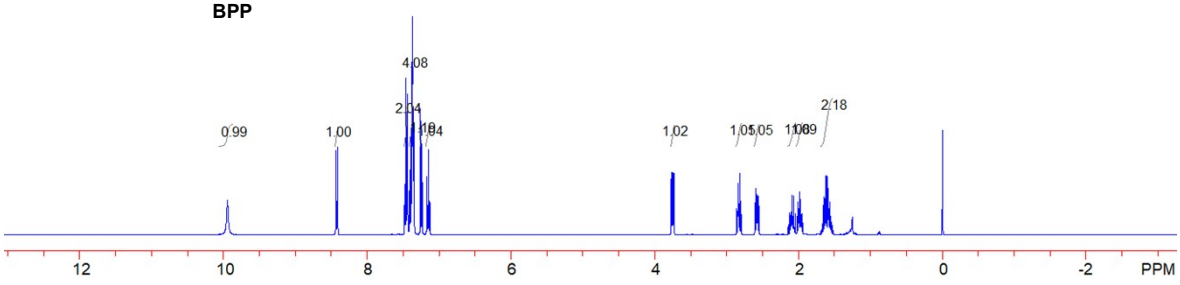
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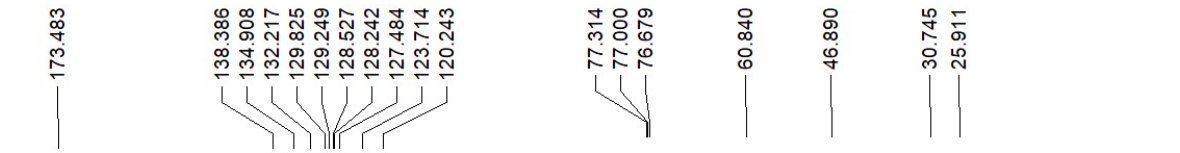
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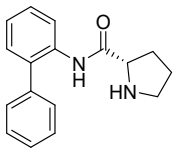
O
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180
160
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0 PPM

3. Single Crystal Determination and Results

Single-crystal X-ray data of CPOC-302-Pro and CPOC-401-Pro were collected at 100.0(1) K on XtaLAB Synergy R, HyPix equipped with Hybrid Pixel Array detector. Data reduction was performed with CrysAlisPro package.[S10]

The structures of CPOC-302-Pro and CPOC-401-Pro were solved by *SHELXD*-2018 and *SHELXT*-2018, respectively, and the refinements were done by full-matrix least-squares on F^2 (*SHELXL*-2018) with the graphical interface Shelxle.[S11] The atoms in the cage framework were refined anisotropically, including constraints, restraints and rigid bodies where necessary. H atoms attached to carbon, nitrogen, and hydroxyl oxygen atoms were positioned geometrically and constrained to ride on their parent atoms. The two crystals were weakly diffracting, immediately losing solvent after removal from the mother liquor. Hence, the quality of the data is far more than sufficient to locate the substituted group. Meanwhile, the structure features large solvent-accessible volumes within the cage. The contents of these volumes are highly disordered and the residual electron density peaks are not arranged in an interpretable pattern. Consequently, the *SQUEEZE* function[S12] of *PLATON* was employed to remove the contribution of the electron density, which gave a potential solvent-accessible void of 33021 and 18897 Å^3 per unit cell (a total of approximately 6593 and 2594 electrons). The resultant files were used in further refinement. The detailed crystal data and cell parameters are summarized in Table S3. The geometry optimized structures of CPOC-302-Pro and CPOC-401-Pro were modeled using CP2K software, and the overlay of the X-ray and GFN-xTB optimized structure by CP2K shows a remarkable agreement (Figure S15)

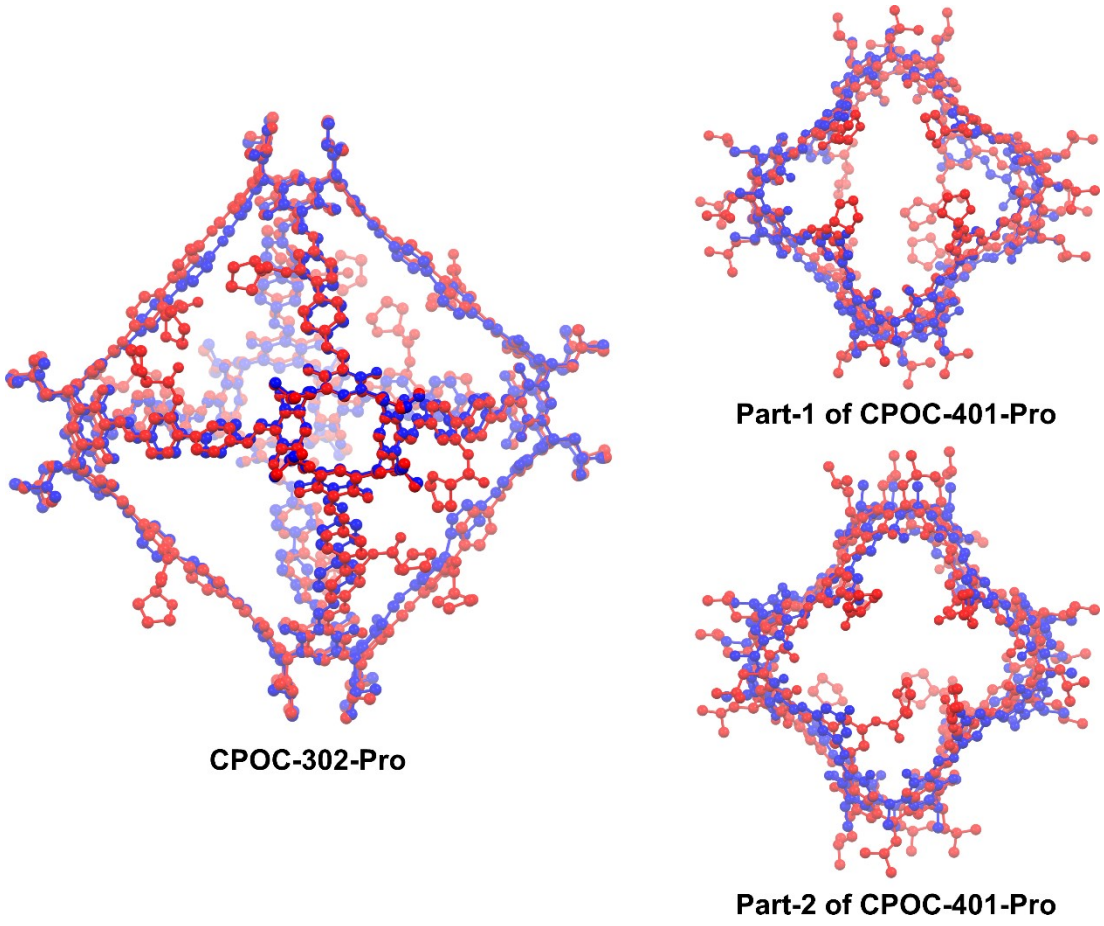

Figure S22. The overlapping image of the crystal structure (blue) and optimized structure (red) of CPOC-302-Pro and CPOC-401-Pro.

Table S4. Crystal Data and Structural Refinement for CPOC-302-Pro and CPOC-401-Pro.

	CPOC-302-Pro	**CPOC-401-Pro**
CCDC No.	2113144	2113665
Empirical formula	$C_{492}H_{528}N_{48}O_{60}$	$C_{280}H_{320}N_{32}O_{40}$
Formula weight	8073.59	4773.66
Temperature (K)	100.0(1)	100.0(1)
Wavelength (Å)	1.54184	1.54184
Crystal system	trigonal	triclinic
Space group	*P*3*c*1	*P*1
***a* (Å)**	32.5182(19)	28.4101(12)
***b* Å)**	32.5182(19)	30.2731(13)
***c* (Å)**	51.424(4)	32.7364(15)
***α* (°)**	90	82.444(4)
***β* (°)**	90	81.795(4)
***γ* (°)**	120	63.273(4)
Volume (Å^3)	47092(7)	24818(2)
Z	2	2
Calculated density (g cm^{-3})	0.569	0.639
Absorption coefficient (mm^{-1})	0.302	0.347
F_{000}	8592	5088
Crystal size (mm^3)	0.10×0.05×0.03	0.23×0.18×0.15
θ range for data collection (°)	2.327 to 77.023□	2.075 to 78.085
Reflections collected	183245	330746
Independent reflections	58296	142785
Max. and min. transmission	0.92486 and 1.00000	0.87204 and 1.00000
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data / restraints / parameters	58296 / 2020 / 1336	142785 / 15362 / 4273
Goodness-of-fit on F^2	0.793	1.377
Final *R* indices [I□2σ(I)]	$R1$ = 0.1220, $wR2$ = 0.2206	$R1$ = 0.2292, $wR2$ = 0.4808
R indices (all data)	$R1$ = 0.4055, $wR2$ = 0.3757	$R1$ = 0.3500, $wR2$ = 0.5579
Largest diff. peak and hole (e Å^{-3})	0.309 and -0.157	1.624 and -0.875
Absolute structure parameter	0.2(3)	0.53(12)

[a]$R_1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b]$wR_2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$

4. Geometry Optimized Models

The initial structures of CPOC-302-Pro and CPOC-401-Pro were token from their crystal structures and modified using Materials Studio to add the substituent group. The geometry optimizations were employed the GFN1-xTB method[S13, S14] with Grimme's D3 van der Waals dispersion correction using the CP2K code[S15]. GFN-xTB is a method of self-consistent, third-order, density functional tight-binding (DFTB3), suitable for the calculation of structures, vibrational frequencies, and non-covalent interactions in large molecular systems. Only atomic coordinates of the periodic systems were optimized, and the cell parameters were fixed.) A convergence threshold of 3.0×10^{-6} Hartree was used for all self-consistent field (SCF) calculations. The structural optimizations were considered converged if the maximum force on all atoms falls below 4.5×10^{-4} Hartree $Bohr^{-1}$.

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