Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

An *L*-proline Functionalized Metallo-organic Triangle as Size-Selective Homogeneous Catalyst for Asymmertry Catalyzing Aldol Reactions

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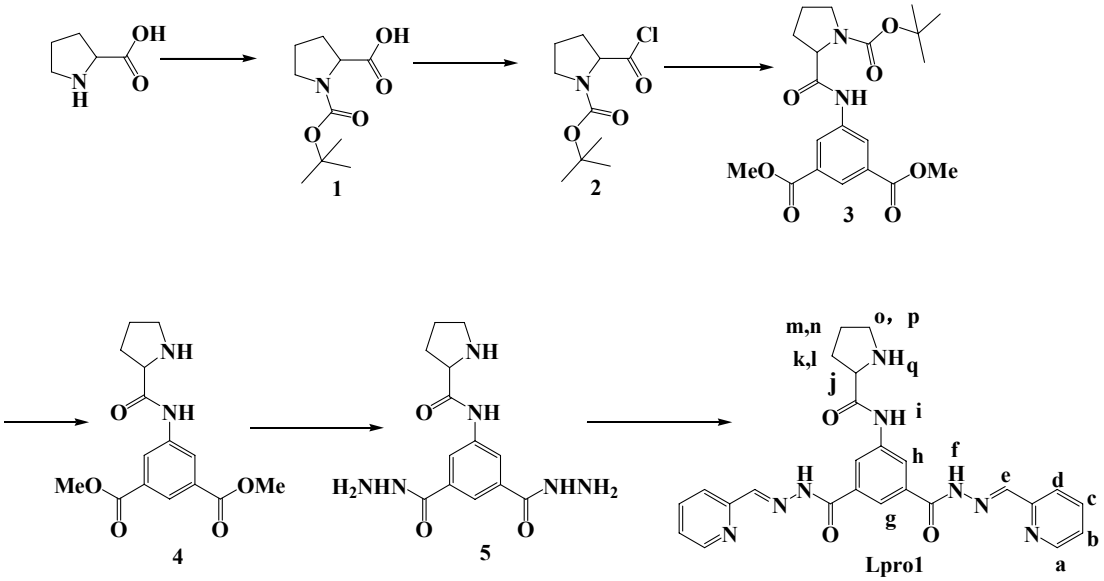
1. Experimental Section.

1.1 Materials and Methods. All chemicals were of reagent grade quality obtained from commercial sources and used without further purification. ^{1}H NMR was measured on a VARIAN INOVA-400 spectrometer with chemical shifts reported as *ppm* (in d_6-DMSO, TMS as internal standard). ESI mass spectra was carried out on a HPLC-Q-Tof MS spectrometer using methanol as mobile phase. The CD spectra was measured on JASCO J-810. HPLC analysis was performed on Agilent 1100 using a Chiralcel AD-H column purchased from Daicel Chemical Industries, Ltd. Products were purified by flash column chromatography on 200-300 mesh silica gel, SiO_2. FT-IR spectra were recorded as KBr pellets on JASCO FT/IR-430. Optical absorption spectra were measured on a TU-1900 Uv/*vis* spectrophotometer at room temperature.

1.2 Procedures for Synthesis



Scheme 1: the synthesis of *L*-**Pro1**

N-Boc-proline (1) : *L*-proline (4.35mmol, 0.5g) was added to a CH_2Cl_2 solution (10 mL) containing triethylamine (0.7 mL), after $(Boc)_2O$ (6.42mmol, 1.4g) was added, the mixture was stirred 2.5 h at room temperature, the white cloudy liquid was turned colorless. The organic phase was washed with 3mL saturation citric acid aqueous solution, 4mL×2 saturation NaCl aqueous solution and water, dried over $MgSO_4$ and evaporated, when it was cooled down, the colorless oil was turned a large white solid, wash with a small amount ethyl ether and dried.

Boc-*L*-ProCl, 0.14 M **in CH_2Cl_2 (2)[S1]:** To a solution of DMF (206 µL, 2.76 mmol) in CH_2Cl_2 (20 mL) at 0°C was added oxalyl chloride (242 µL, 2.76 mmol). A white precipitate formed. Pyridine (222 µL, 2.76 mmol) was added dropwise to the reaction mixture; the precipitate dissolved and the solution turned yellow. *N*-Boc-*L*-proline (594 mg, 2.76 mmol) was then added to the solution. The reaction mixture was stirred for 45 min and used in next step.

Dimethyl 5-(tert-butyl 2-carbamoylpyrrolidine-1-carboxyloyl) benzene-1, 3-dioate (3): To a solution of 5-Amino-isophthalic acid dimethyl ester (144 mg, 0.69 mmol) and NEt_3 (96.0 µL, 0.69 mmol) in CH_2Cl_2 (20 mL) at 0°C was added *N*-Boc-*L*-proline chloride (0.14 M in CH_2Cl_2, 20 mL, 2.76 mmol). The reaction mixture was allowed to warm slowly to RT and stirred at RT for 12 h. The reaction was quenched by addition of 10 % aq. $NaHCO_3$ (20 mL). The phases were separated; the organic layer was washed with sat. aq. $NaHCO_3$(20 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuum, purified by column chromatography (EtOAc/hexanes) and used in next step.

Dimethyl-5-(pyrrolidine-2-carboxamido) benzene-1, 3-dioate (4)[S2]: The **3** was suspended in 1, 4-dioxane (20 mL/mmol). After cooling with an ice bath, a 6 N solution of HCl in 1, 4-dioxane (40 mL/mmol) was added dropwise. The reaction mixture was stirred for 2 h at 0°C and then evaporated in vacuum and used in next step.

5-(pyrrolidine-2-carboxamido) benzene-1, 3-dihydrazide (5) A mixture solution of hydrazine hydrate (80%) (6.5 mmol, 400 mg) and **4** (0.65 mmol, 200 mg) in dry EtOH solution (15 mL) was stirred over 24h at boiling temperature. The white precipitate formed, was collected by filtration, washed with dry EtOH and dried in vacuum and used in next step.

***L*-Pro1**: The white solid **5** (0.59 mmol, 180 mg) was added to a dry CH_3OH solution (10 mL) containing 2-pyridinecarboxaldehyde (0.71 mmol, 76 mg). The mixture was stirred for 24h at room temperature. During the reaction, a pale precipitate was formed, which was collected by filtration, washed with CH_3OH, and dried in vacuo. Yield: (calculated from 5-Amino-isophthalic acid dimethyl ester), 243 mg (73%). ^{1}H NMR (d_6-DMSO, *ppm*) δ: 12.86(s, 2H, H_f), 11.33(s, 1H, H_i), 10.00(s, 1H, H_q), 8.81(s, 2H, H_e), 8.71(d, 2H, H_a, J = 4.80 H_z), 8.64(s, 2H, H_g), 8.44(s, 1H, H_h), 8.12(m, 4H, $H_{c,d}$), 7.62(t, 2H, H_b, J = 16.0 Hz), 4.47(t, 1H, H_j, J = 12.0 H_Z), 3.30(t, 2H, $H_{o,p}$, J = 12.0 H_Z), 2.45(m, 1H, H_k), 1.98(m, 3H, $H_{l,\ m,\ n}$).

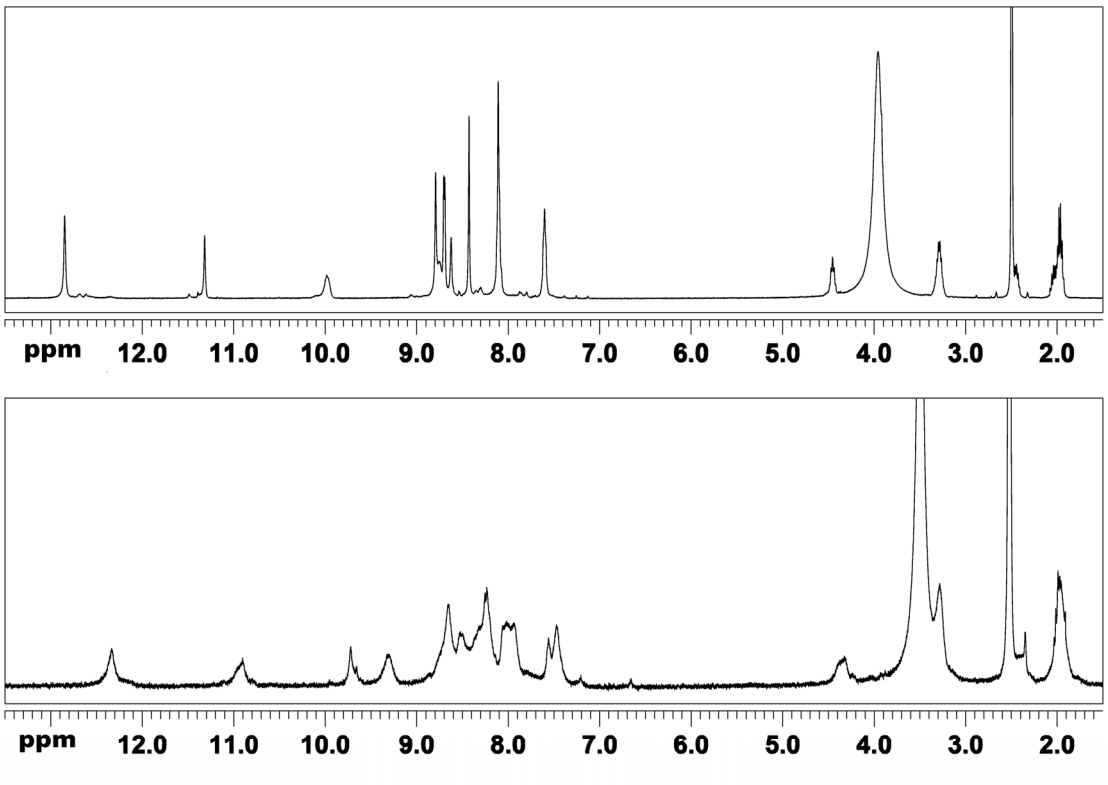
API-MS *m/z*: 485.0975 ([M-H^+]).

Co-**Pro1**[S3]: $Co(NO_3)_2 \cdot 6H_2O$ (87.3mg, 0.3 mmol) and *L*-**Pro1** (145 mg, 0.3 mmol) were dissolved in CH_3OH (10 ml) to give a light red solution. After addition of NH_4PF_6 (97.8mg, 0.6mmol), the orange-yellow precipitates formed were isolated and dried in vacuum. Yield: 55%. ^1H NMR (d_6-DMSO, *ppm*) δ: 12.34(2H, H_f), 10.90(1H, H_i), 9.73(1H, H_q), 9.32(2H, H_e), 8.64(2H, H_a), 8.52(s, 2H, H_g), 8.23(s, 1H, H_h), 8.00(4H, $H_{c,d}$), 7.53(2H, H_b), 4.33(1H, H_j), 3.28(2H, $H_{o,p}$), 2.38(1H, H_k), 1.97(3H, $H_{l,\ m,\ n}$).

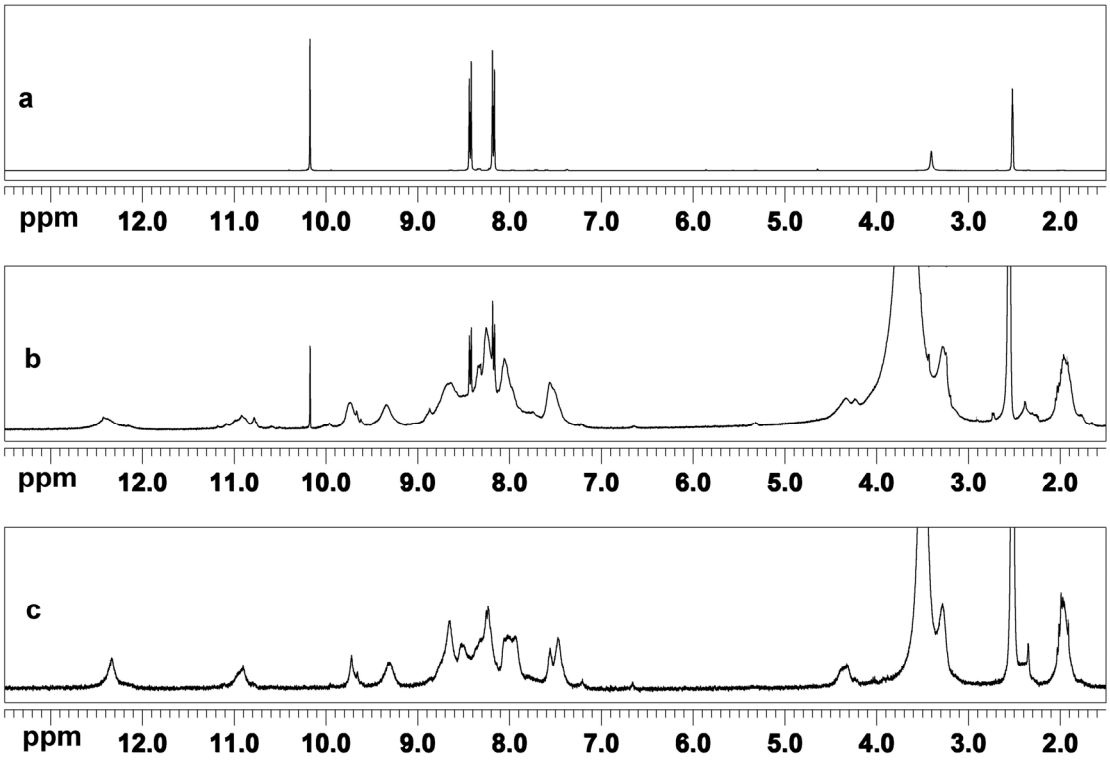
1.3 General procedure for the Aldol reaction

Cyclohexanone (5.2 mL, 5.0 mmol), aldehyde (0.5 mmol) were added to a d_6-DMSO solution of Co-**Pro1** (0.0075 mmol)/*L*-**Pro1** (0.025 mmol), the mixture was stirred for several days at room temperature. The conversion and distereoselectivity were directly determined by ^1H NMR analysis of the reaction solution. The crude product was purified by flash column chromatography(hexane/EtOAC=4:1) to give pure aldol adduct. HPLC analysis Chiralcel AD-H.

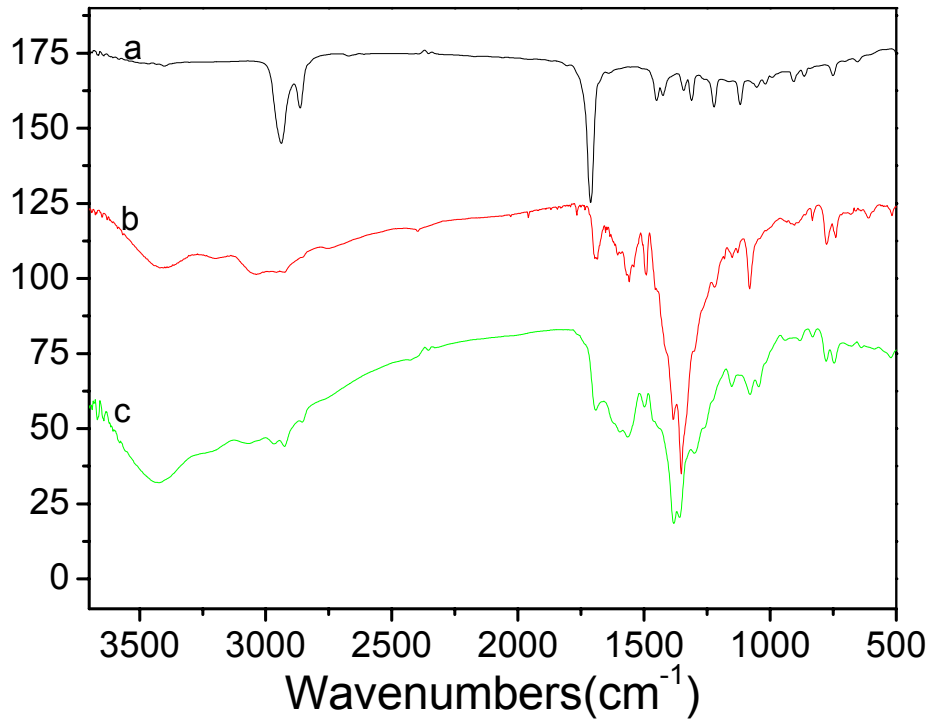
2. Figure S1. ^{1}H NMR spectra of Ligand *L*-**Pro1** (top) and Compound Co-**Pro1** (bottom) in d_6-DMSO.



3. Figure S2. ^{1}H NMR spectra of the free 4-nitrobenzaldehyde (a); compound Co-**Pro1** in presence of equimolar 4-nitrobenzaldehyde (b) and compound Co-**Pro1** (c) in d_6-DMSO.



4. Figure S3. IR spectra of Cyclohexanone (a), Co-**Pro1** adsorbing Cyclohexanone (b) and the free Co-**Pro1** (c).



5. ^{1}H-NMR spectra of all the crude Aldol products of entry 1

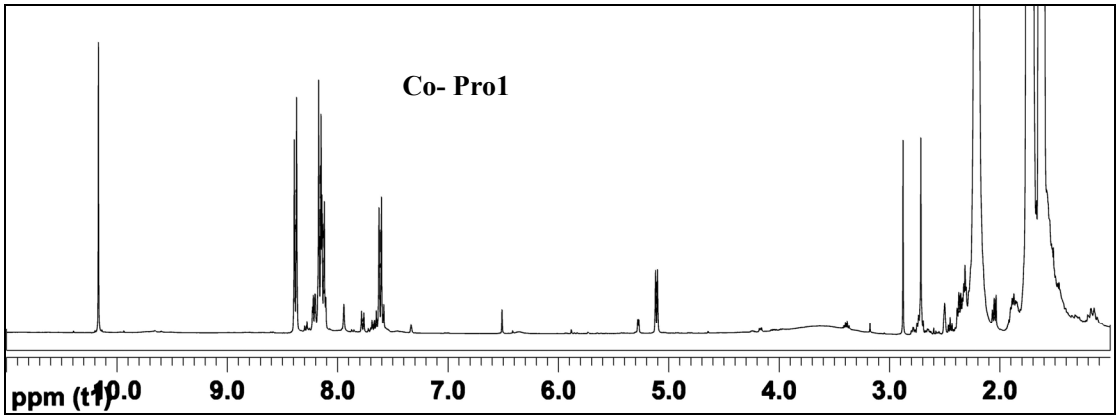


Figure S4a ^{1}H-NMR spectra of the crude product of 2-(Hydroxy-(4-nitrophenyl)methyl)-cyclohexan-1-one catalyzed by Co-**Pro1**.

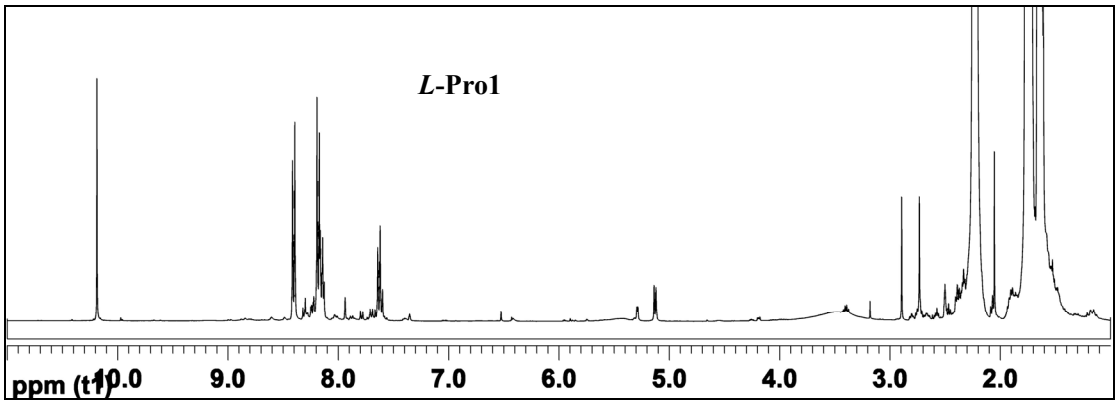


Figure S4b. ^{1}H-NMR spectra of the crude product of 2-(Hydroxy-(4-nitrophenyl)methyl)-cyclohexan-1-one catalyzed by *L*-**Pro1**.

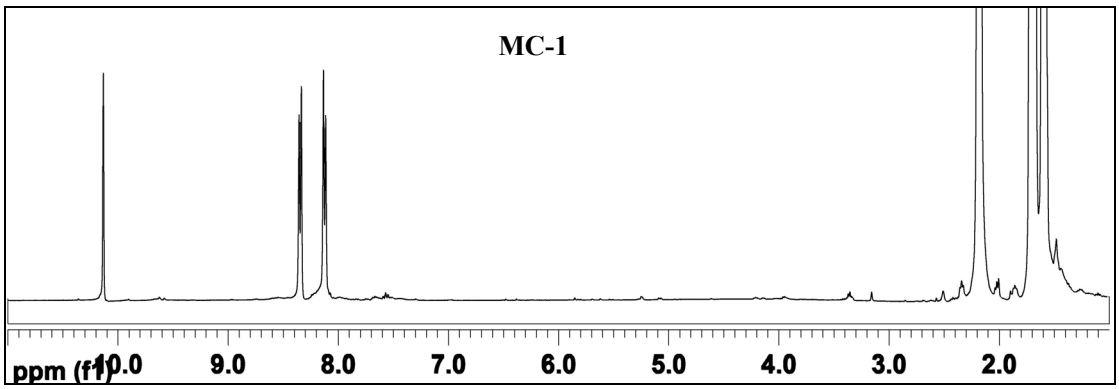


Figure S4c. ^{1}H-NMR spectra of the crude product of 2-(Hydroxy-(4-nitrophenyl)methyl)-cyclohexan-1-one catalyzed by **MC-**1.

6. ^{1}H-NMR spectra of all the crude Aldol products of entry 2

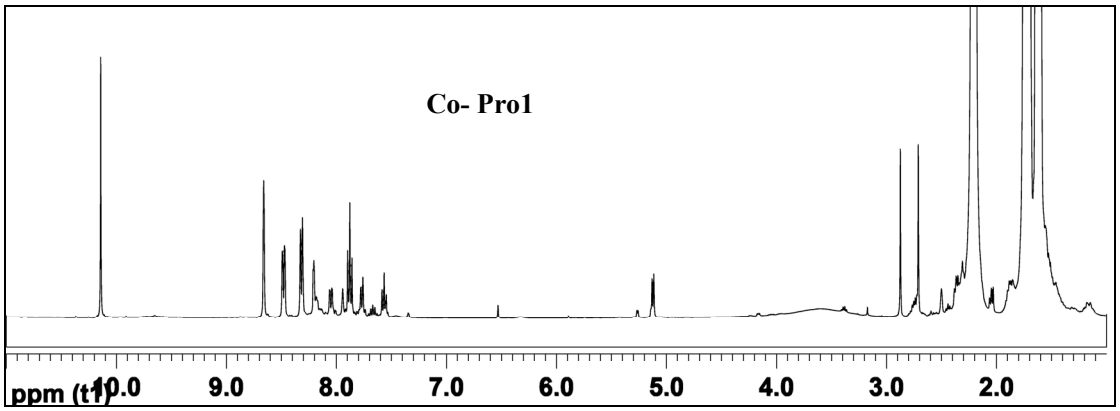


Figure S5a. ^{1}H-NMR spectra of the crude product of 2-(Hydroxy-(3-nitrophenyl)methyl)-cyclohexan-1-one catalyzed by Co-**Pro1**.

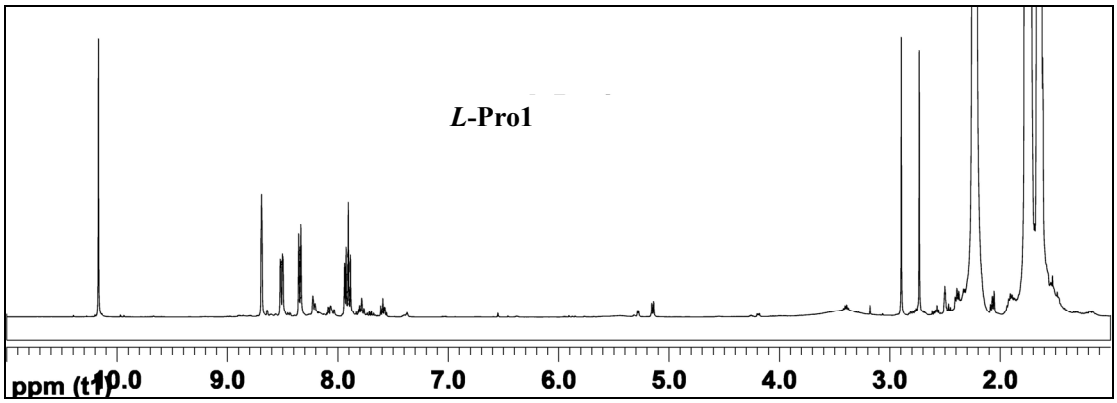


Figure S5b. ^{1}H-NMR spectra of the crude product of 2-(Hydroxy-(3-nitrophenyl)methyl)-cyclohexan-1-one catalyzed by *L*-**Pro1**.

7. ^{1}H-NMR spectra of all the crude Aldol products of entry 3

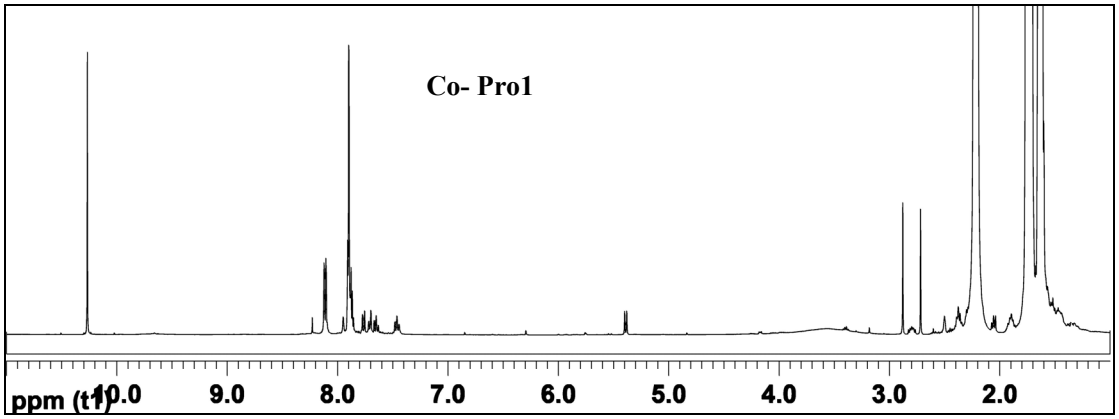


Figure S6a. ^{1}H-NMR spectra of the crude product of 2-(Hydroxy-(2-nitrophenyl)methyl)-cyclohexan-1-one catalyzed by Co-**Pro1**.

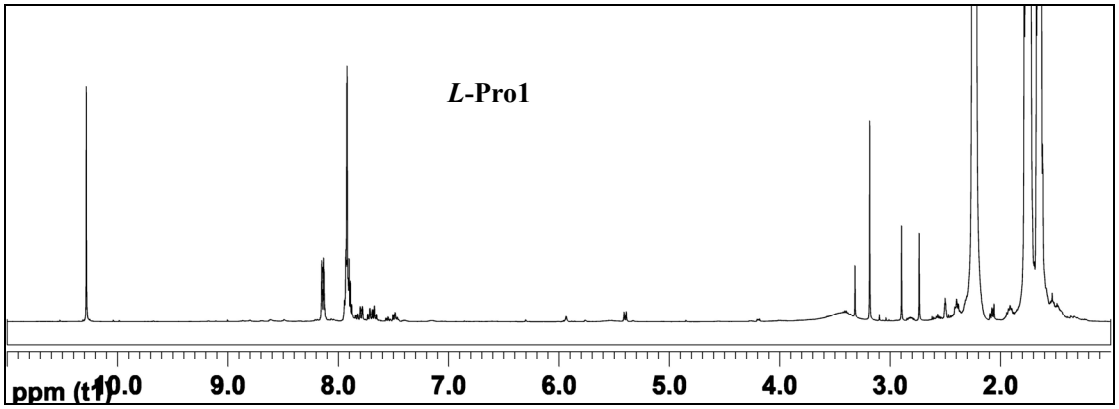


Figure S6b. ^{1}H-NMR spectra of the crude product of 2-(Hydroxy-(2-nitrophenyl)methyl)-cyclohexan-1-one catalyzed by *L*-**Pro1**.

8. ^{1}H-NMR spectra of all the crude Aldol products of entry 4

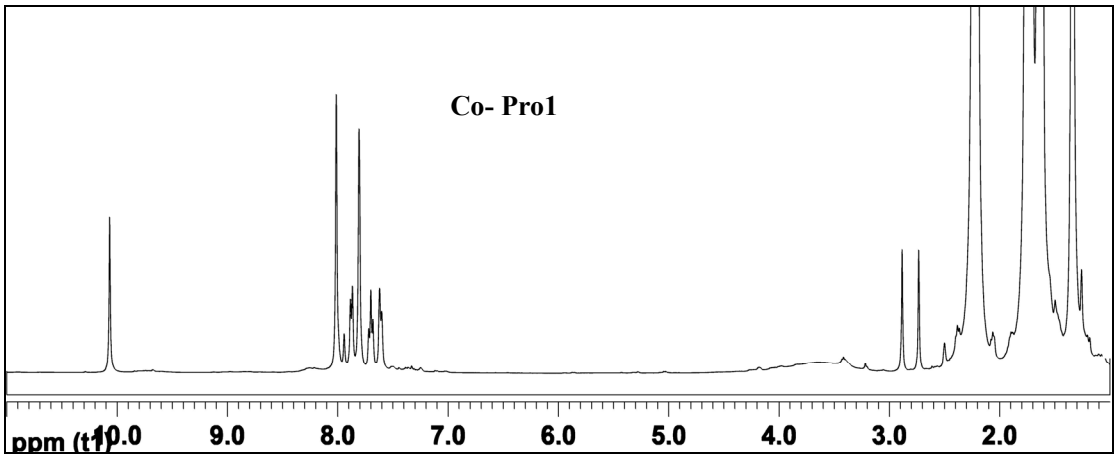


Figure S7a. ^{1}H-NMR spectra of the crude product of 2-(Hydroxy-(3-phenylene-(3, 5-di-tert-butylbenzoyl))methyl)cyclohexan-1-one catalyzed by Co-**Pro1**.

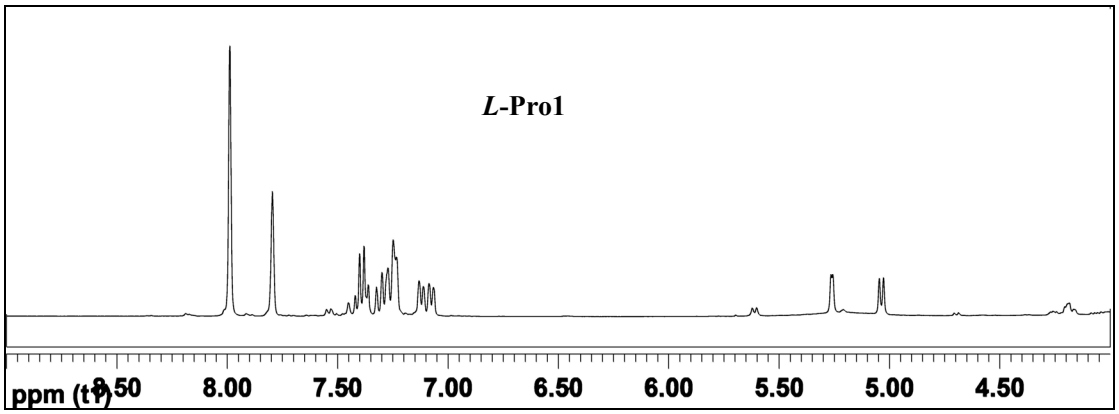


Figure S7b. ^{1}H-NMR spectra of 2-(Hydroxy-(3-phenylene-(3, 5-di-tert-butylbenzoyl))-methyl)- cyclohexan-1-one catalyzed by *L*-**Pro1**.

9. HPLC chromatograms of the Aldol products of entry 1

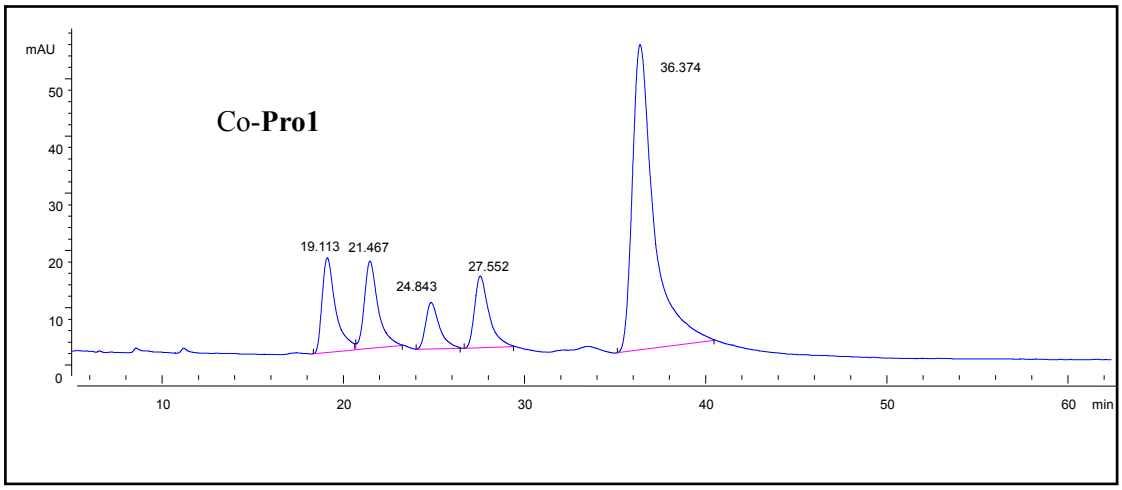


Figure S8a. HPLC chromatogram of 2-(Hydroxy-(4-nitrophenyl)methyl)cyclohexan-1-one catalyzed by **Co-Pro1**. HPLC analysis: Chiralcel AD-H (Hexane/i-PrOH = 90/10, flow rate: 1.0 mL/min, λ = 254 nm, 20°C).

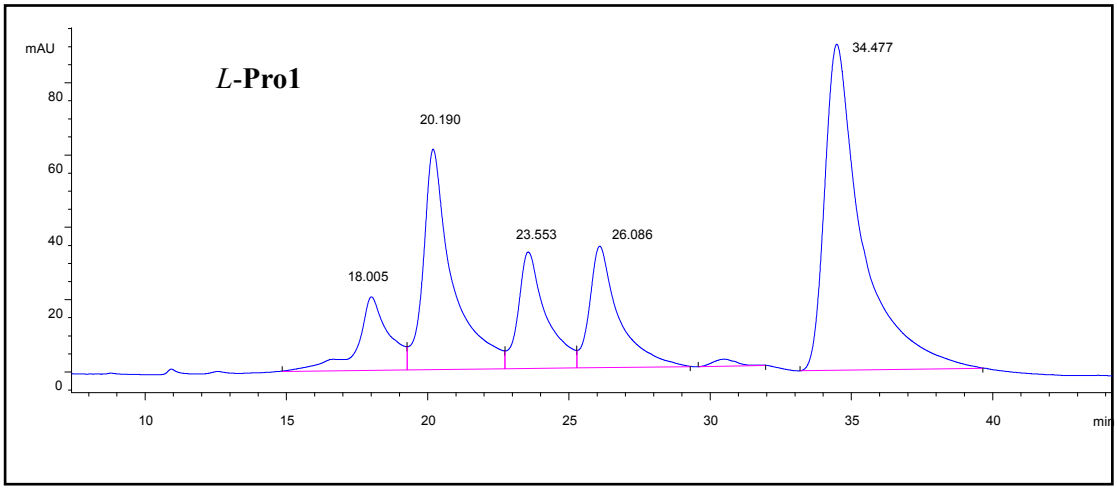


Figure S8b. HPLC chromatogram of 2-(Hydroxy-(4-nitrophenyl)methyl)cyclohexan-1-one catalyzed by *L*-**Pro1**. HPLC analysis: Chiralcel AD-H (Hexane/i-PrOH = 90/10, flow rate: 1.0 mL/min, λ = 254 nm, 20^{0}C).

10. HPLC chromatograms of the Aldol products of entry 2

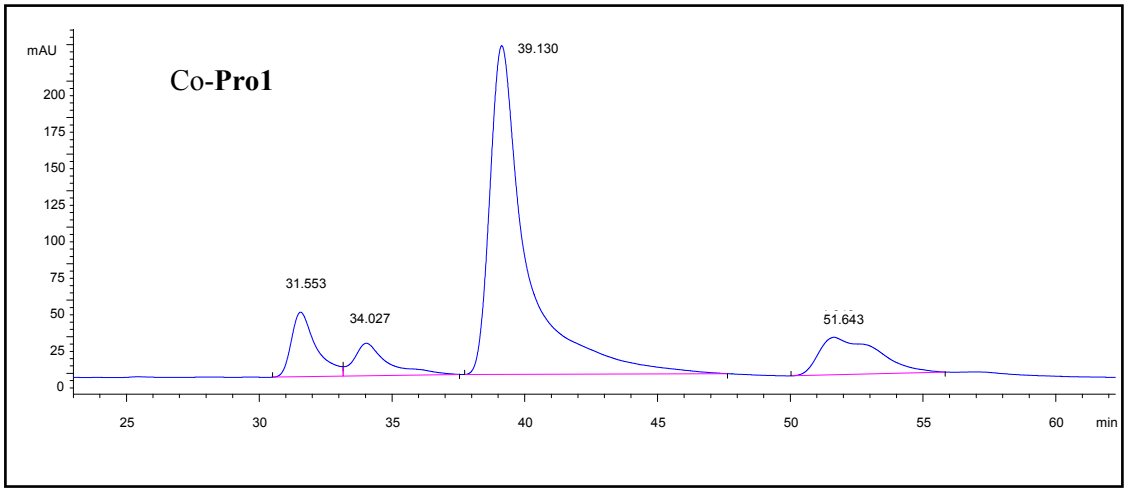


Figure S9a. HPLC chromatogram of 2-(Hydroxy-(3-nitrophenyl)methyl)cyclohexan-1-one catalyzed by Co-**Pro1**. HPLC analysis: Chiralcel AD-H (Hexane/i-PrOH = 90/10, flow rate: 1.0 mL/min, λ = 254 nm, 20^0C).

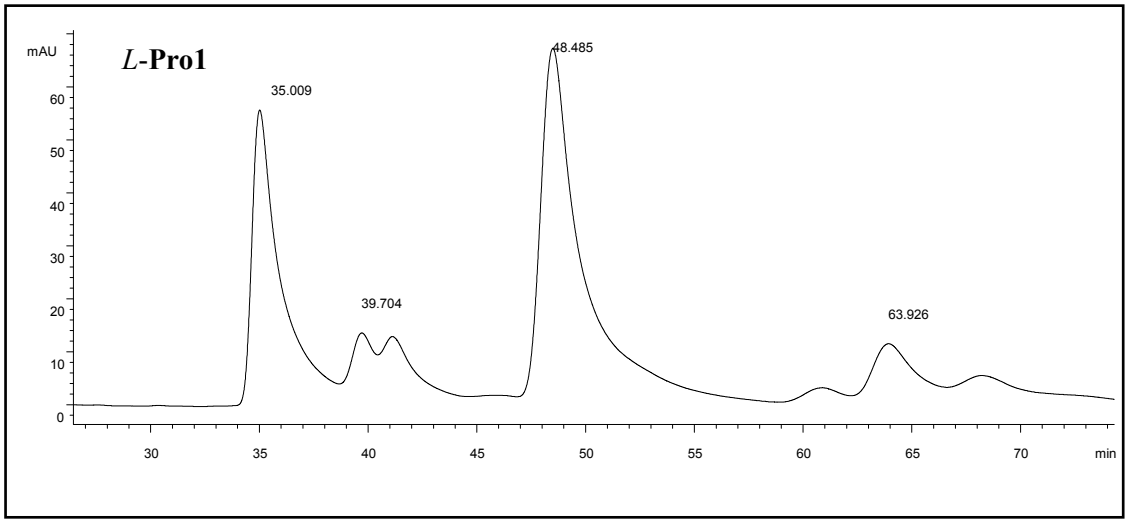


Figure S9b. HPLC chromatogram of 2-(Hydroxy-(3-nitrophenyl)methyl)cyclohexan-1-one catalyzed by *L*-**Pro1**. HPLC analysis: Chiralcel AD-H (Hexane/i-PrOH = 90/10, flow rate: 1.0 mL/min, λ = 254 nm, 20^0C).

11. **Figure S8** HPLC chromatograms of the Aldol products of entry 3

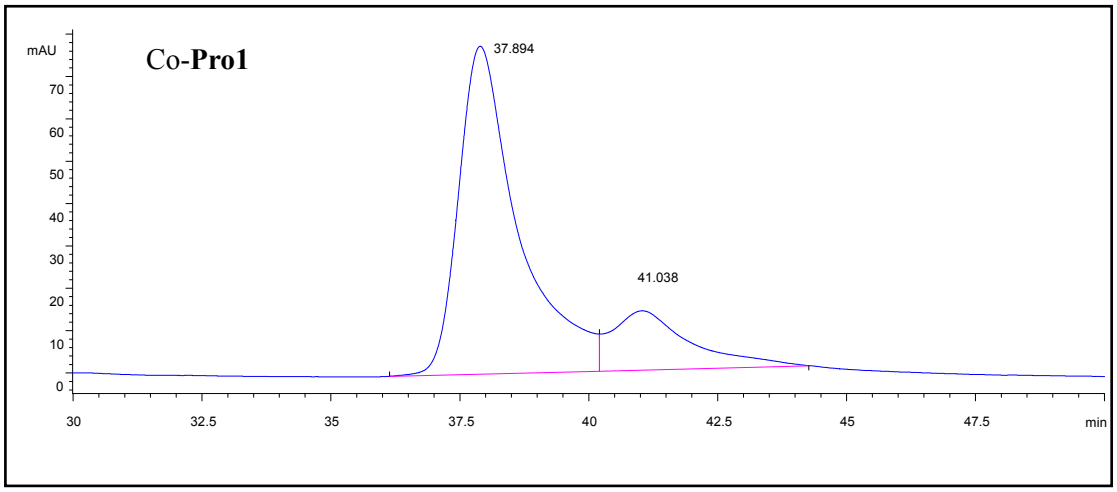


Figure S10a. HPLC chromatogram of 2-(Hydroxy-(2-nitrophenyl)methyl)cyclohexan-1-one catalyzed by Co-**Pro1**. HPLC analysis: Chiralcel AD-H (Hexane/i-PrOH = 95/5, flow rate: 1.0 mL/min, λ = 254 nm, 20^{0}C).

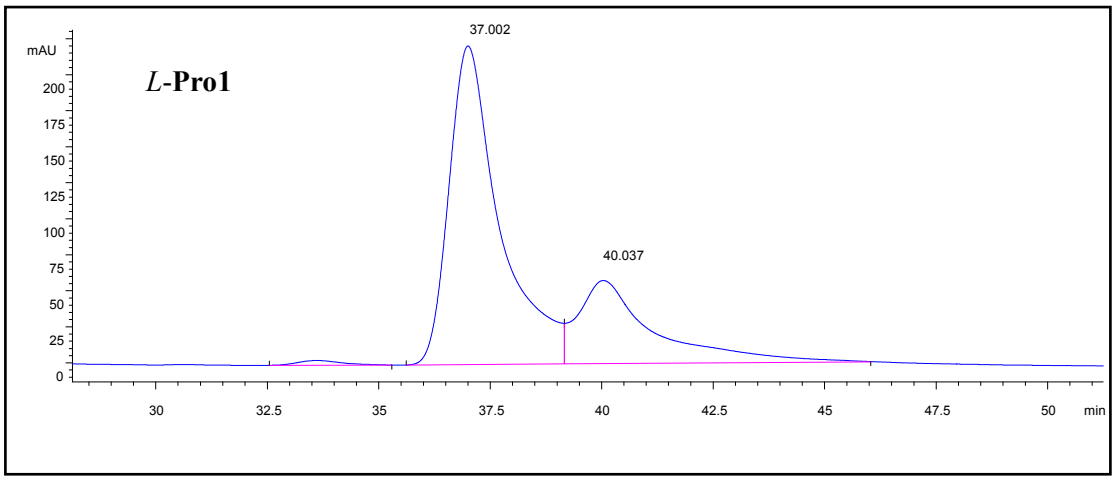


Figure S10b. HPLC chromatogram of 2-(Hydroxy-(2-nitrophenyl)methyl)cyclohexan-1-one catalyzed by *L*-**Pro1**. HPLC analysis: Chiralcel AD-H (Hexane/i-PrOH = 95/5, flow rate: 1.0 mL/min, λ = 254 nm, 20^{o}C)

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S2. J. Bitta and S. Kubik, *Org. lett.*, 2001, **17**, 2637.
S3. H. M. Wu, C. He, Z. H. Lin, Y. Liu, and C. Y. Duan, *Inorg. Chem.* 2009, **48**, 408.