**Supporting information**

# Asymmetric aldol reaction catalyzed by amino acid tetrapeptides (L-Pro-L-Pro-L-Phe-L-Phe-OMe)

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**Content**

## S1 Experimental

### S1.1 Chemicals and agents.

Unless otherwise stated, all reagents were purchased from commercial sources and used without purification. Boc-L-phenylalanine, methyl-3-phenyl-L-alaninate, isobutyl chloroformate, 4-methylmorpholine, N,N'-dicyclohexylcarbodiimide, cyclohexanone, 4'-methylacetophenone, 4'-(trifluoromethoxy)-acetophenone, α-tetralone, 1-acetonaphthone, acetophenone, 1-cyclohexylethan-1-one, 2-cyclohexen-1-one, 4-fluoroacetophenone, 4-methoxyacetophenone, 2-acetonaphthone were purchased from Sahn Chemical Technology Co., Ltd. Boc-L-Proline dipeptide, 4-phenyl-2-butanone, p-tolualdehyde, 4-bromo-2-hydroxybenzaldehyde, 2-imidazolecarboxaldehyde, vanillin, 4-bromobenzaldehyde, benzaldehyde were purchased from Aladdin Chemical Co., Ltd. (Shanghai, China). All solvents used in the reactions were of analytical grade, carefully dried, and distilled before use.

### S 1.2 Characterization

The $^{1}H$ NMR spectra (500 MHz) were recorded using a Bruker AVANCE III-500 instrument at room temperature. IR spectra were obtained with a Perkin-Elmer FTIR-100 spectrophotometer. The characteristics were recorded using scanning electron microscope (Thermoscientific ApreoS LoVac, USA, SEM). The crystal structure of the catalyst was analyzed by X - ray diffraction (Rigaku Corporation, TTRIII, Japan, XRD). The absolute configuration of products was determined by JASCO PU-2089 high performance liquid chromatograph (HPLC) system equipped with UV-vis (JASCO-UV-2070), circular dichroism (JASCO-CD-2095) detectors and a column of AD-H using a solution of hexane/2-propanol as eluent at a flow rate of 1 mL $min^{-1}$. A solution of product (1.00 mg $mL^{-1}$) was injected into the chromatographic system through an intelligent sampler (JASCO AS-2055)

**Table S1** Solubility test of L-Phe-L-Phe-OMe and L-Pro-L-Pro-L-Phe-L-Phe-OMe

| solvent | L-Phe-L-Phe-OMe | L-Pro-L-Pro-L-Phe-L-Phe-OMe |
|---|---|---|
| petroleum ether | — | — |
| $CCl_4$ | — | — |
| $CH_2Cl_2$ | — | — |
| THF | — | — |
| isopropanol | — | — |
| $CHCl_3$ | — | — |
| pyridine | + | — |
| triethylamine | — | — |
| acetone | — | — |
| DMF | — | — |
| MeOH | — | — |
| DMSO | + | + |
| Hexafluoroisopropanol | ++ | ++ |
| $H_2O$ | — | — |

Notice: ++ dissolve, + slight soluble, - insoluble

**Table S2** Effects of solvent, time and catalyst dosage on asymmetric Aldol reaction [a]

| Entry | Catalyst (mg) | Time (d) | solvent | Yield (%)[b] | *ee* (%)[c] | syn/anti[c] |
|---|---|---|---|---|---|---|
| 1 | 2 | 7 | MeOH | 88 | 4 (2R, 1'R) | 56/44 |
| 2 | 4 | 7 | MeOH | 90 | 6 (2R, 1'R) | 75/25 |
| 3 | 6 | 7 | MeOH | 91 | 9 (2R, 1'R) | 89/11 |
| 4 | 8 | 7 | MeOH | 92 | 11 (2R, 1'R) | 99/1 |
| 5 | 10 | 7 | MeOH | 94 | 13 (2R, 1'R) | 99/1 |
| 6 | 12 | 7 | MeOH | 95 | 98 (2R, 1'R) | 99/1 |
| 7 | 14 | 7 | MeOH | 95 | 98 (2R, 1'R) | 99/1 |
| 8 | 12 | 1 | MeOH | - | - | - |
| 9 | 12 | 2 | MeOH | - | - | - |
| 10 | 12 | 3 | MeOH | - | - | - |
| 11 | 12 | 4 | MeOH | 20 | 95 (2R, 1'R) | 98/1 |
| 12 | 12 | 5 | MeOH | 24 | 96 (2R, 1'R) | 99/1 |
| 13 | 12 | 6 | MeOH | 54 | 95 (2R, 1'R) | 99/1 |
| 14 | 12 | 7 | MeOH | 95 | 99 (2R, 1'R) | 99/1 |
| 15 | 12 | 8 | MeOH | 95 | 99 (2R, 1'R) | 99/1 |
| 16 | 12 | 7 | MeOH | 95 | 99 (2R, 1'R) | 99/1 |
| 17 | 12 | 7 | THF | 91 | 99 (2R, 1'R) | 99/1 |
| 18 | 12 | 7 | $CH_2Cl_2$ | 92 | 99 (2R, 1'R) | 99/1 |
| 19 | 12 | 7 | $CHCl_3$ | 92 | 99 (2R, 1'R) | 99/1 |
| 20 | 12 | 7 | toluene | 45 | 99 (2R, 1'R) | 99/1 |

[a] The reaction was performed with cyclohexanone (0.6 mmol), paranitroanisole (0.5 mmol), L-Pro-L-Pro-L-Phe-L-Phe-OMe at 25 °C. [b] Isolated yields. [C] For R enantiomer, determined by chiral HPLC analysis (Chiralpak AD-H) with hexane/isopropanol (90/10, v/v) as the eluent.

**Table S3** Effect of different catalysts on catalytic performance [a]

| Entry | Catalyst | Yield (%)[b] | *ee* (%)[c] | syn/anti[c] |
|---|---|---|---|---|
| 1 | L-Pro-L-Pro-L-Phe-L-Phe-OMe (12.0 mg, 4.6 mmol%) | 95 | 99 (2R, 1'R) | 99/1 |
| 2 | L-Pro-L-Phe-L-Phe-OMe (9.7 mg, 4.6 mmol%) | 90 | 89 (2R, 1'R) | 991 |
| 3 | L-Phe-L-Phe-OMe (7.5 mg, 4.6 mmol%) | 12 | 26(2R, 1'R) | 75/25 |
| 4 | L-Pro-L-Pro (4.8 mg, 4.6 mmol%) | 91 | 88(2R, 1'R) | 90/10 |
| 5 | L-Phe (3.8 mg, 4.6 mmol%) | 10 | 13 (2R, 1'R) | 62/38 |
| 6 | L-Phe-OMe (4.1 mg, 4.6 mmol%) | 9 | 16 (2R, 1'R) | 60/40 |

[a]The reaction was performed with cyclohexanone (0.6 mmol), paranitroanisole (0.5 mmol), and MeOH (1mL) at 25 °C 7d. [b] Isolated yields. [C] For R enantiomer, determined by chiral HPLC analysis (Chiralpak AD-H) with hexane/isopropanol (90/10, v/v) as the eluent.

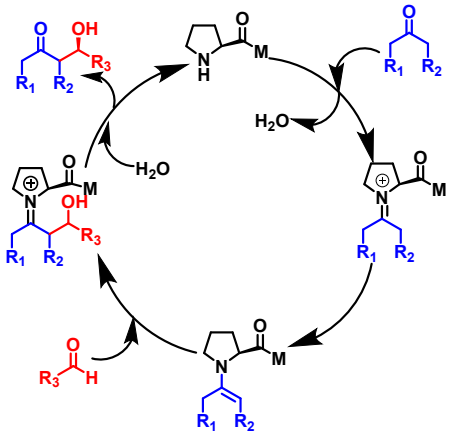



**Figure S1** Mechanism diagram of L-proline involved in hydroxyl aldehyde condensation reaction.

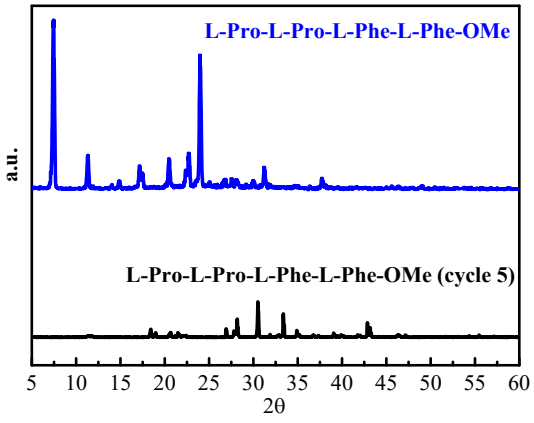



**Figure S2** XRD spectra of L-Pro-L-Pro-L-Phe-L-Phe-OMe (cycle 5).

**Table S4** Effect of temperature and catalyst dosage on reaction time.[a]

| Entry | Catalyst | Temperature (°C) | Time (d) | Yield (%)[b] | *ee* (%)[c] | syn/anti[c] |
|---|---|---|---|---|---|---|
| 1 | L-Pro-L-Pro-L-Phe-L-Phe-OMe (12.0 mg) | 25 | 7 | 95 | 99 (2R, 1'R) | 99/1 |
| 2 | L-Pro-L-Pro-L-Phe-L-Phe-OMe (16.0 mg) | 25 | 6.5 | 95 | 99 (2R, 1'R) | 991 |
| 3 | L-Pro-L-Pro-L-Phe-L-Phe-OMe (20.0 mg) | 25 | 6 | 95 | 98 (2R, 1'R) | 99/1 |
| 4 | L-Pro-L-Pro-L-Phe-L-Phe-OMe (24.0 mg) | 25 | 6 | 95 | 99 (2R, 1'R) | 99/1 |
| 5 | L-Pro-L-Pro-L-Phe-L-Phe-OMe (20.0 mg) | 30 | 6 | 95 | 99 (2R, 1'R) | 99/1 |
| 6 | L-Pro-L-Pro-L-Phe-L-Phe-OMe (20.0 mg) | 35 | 5.5 | 95 | 98 (2R, 1'R) | 99/1 |
| 7 | L-Pro-L-Pro-L-Phe-L-Phe-OMe (20.0 mg) | 40 | 5 | 95 | 92 (2R, 1'R) | 97/3 |
| 8 | L-Pro-L-Pro-L-Phe-L-Phe-OMe (20.0 mg) | 45 | 5 | 95 | 85 (2R, 1'R) | 96/4 |

[a] The reaction was performed with cyclohexanone (0.6 mmol), paranitroanisole (0.5 mmol), and MeOH (1mL). [b] Isolated yields. [C] For R enantiomer, determined by chiral HPLC analysis (Chiralpak AD-H) with hexane/isopropanol (90/10, v/v) as the eluent.

**Table S5** Some comparison data between proline catalyst and the peptide catalyst.

| references | Catalyst | reported ee and yield | this experiment |
|---|---|---|---|
| [47] Asymmetric catalysis with short-chain peptides | Polypeptide | ee 90-97%<br>yield 82-90% | ee 95-99%<br>yield 91-95% |
| [31] Recent efforts directed to the development of more sustainable asymmetric organocatalysis | Proline derivatives | ee 68-96%<br>yield 60-90% | |
| [40] Improving the Catalytic Performance of (S)-Proline as Organocatalyst in Asymmetric Aldol Reactions in the Presence of Solvate Ionic Liquids: Involvement of a Supramolecular Aggregate | Proline derivatives | ee 92-94%<br>yield 62-92% | |
| [46] Organocatalytic activity of a,a-dipeptide derivatives of (S)-proline in the asymmetric aldol reaction in absence of solvent. Evidence for non-covalent p–p interactions in the transition state | Polypeptide | ee 94-98%<br>yield 79-89% | |

**S2 High performance liquid chromatography of the product**

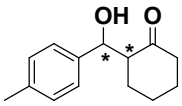
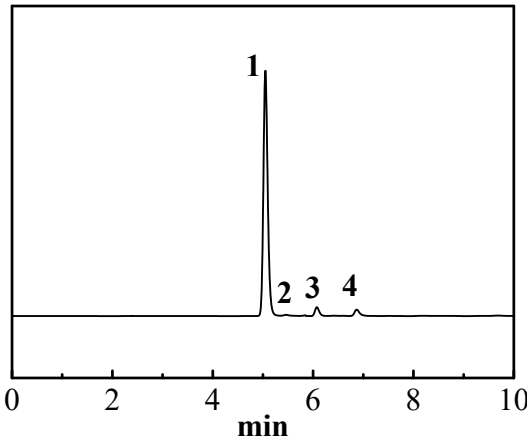
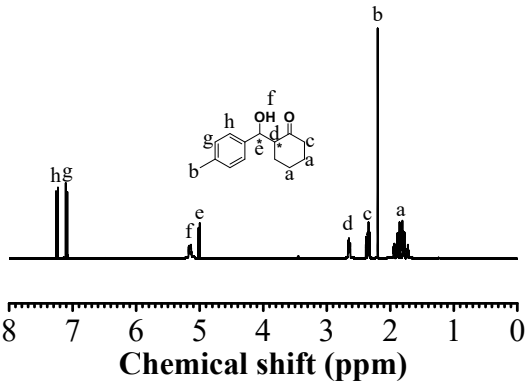



**Table 1, 3a (2R, 1'S).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 10 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) =5.050 min, $tR_2$ =5.458 min, $tR_3$ =6.095 min, $tR_4$ =6.870 min. $^1$H NMR (500 MHz, $CDCl_3$, δ): 1.68-1.99 (m, 6H, $CH_2$), 2.19 (s, 3H, $CH_3$), 2.33 (m,2H, $CH_2$), 2.63 (m, 1H, CH), 5.01 (m, 1H, CH), 5.14 (s, 1H, OH), 7.10 (m, 2H, Ar-H), 7.23 (m, 2H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 5.050 | 93.711 |
| 2 | 5.458 | 0.298 |
| 3 | 6.095 | 3.316 |
| 4 | 6.870 | 2.624 |



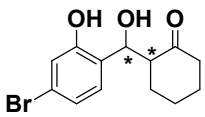
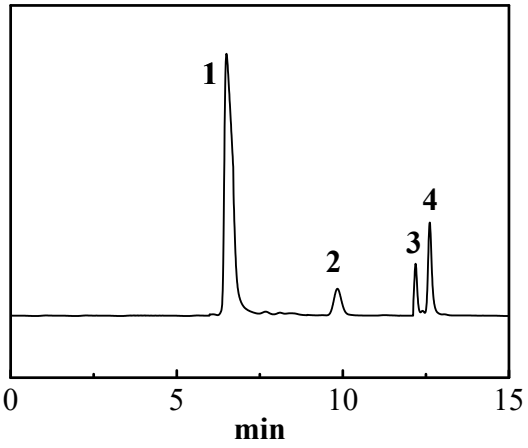
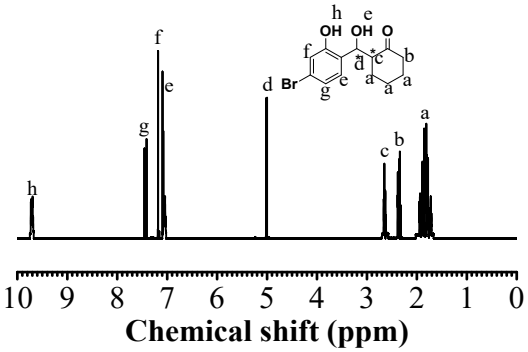



**Table 1, 3b (2R, 1'S).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 15 min, enantiomeric excess: 87%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) =6.500 min, $tR_2$ =9.842 min, $tR_3$ = 12.174 min, $tR_4$ = 12.610 min. $^1$H NMR (500 MHz, $CDCl_3$, δ): 1.64-2.00 (m, 6H, $CH_2$), 2.31 (m, 2H, $CH_2$), 2.65 (m,1H, CH), 4.99 (s, 1H, CH), 7.04 (s, 1H, OH), 7.07 (m, 1H, Ar-H), 7.18 (s, 1H, Ar-H), 7.41 (m, 1H, Ar-H), 9.69 (s, 1H, OH).




| | time/min | area% |
|---|---|---|
| 1 | 6.500 | 80.661 |
| 2 | 9.842 | 5.772 |
| 3 | 12.174 | 3.991 |
| 4 | 12.610 | 9.576 |



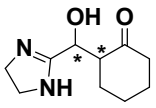
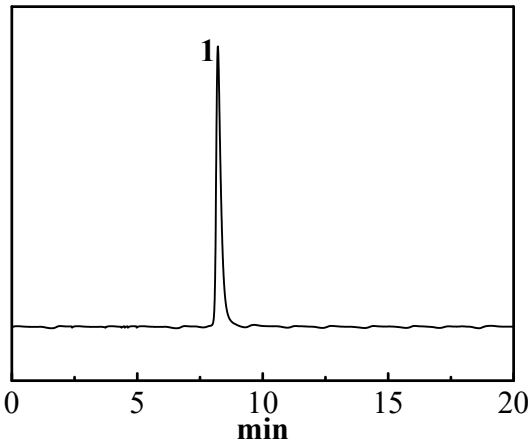
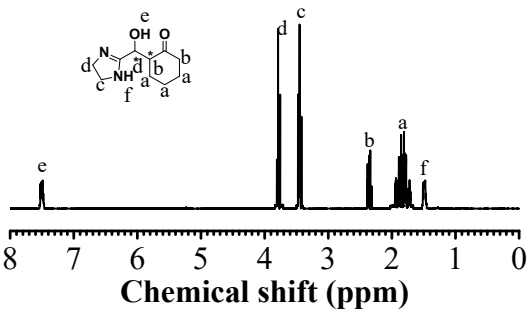



**Table 1, 3c (2R, 1'S).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 20 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 8.217 min. $^1H$ NMR (500 MHz, $CDCl_3$, δ): 1.49 (s, 1H, NH), 1.65-1.97 (m, 6H, $CH_2$), 2.33 (m, 2H, $CH_2$), 3.44 (m, 2H, $CH_2$), 3.81 (s, 3H, $CH_2$, CH), 7.49 (s, 1H, OH).




| | time/min | area% |
|---|---|---|
| 1 | 8.217 | >99 |



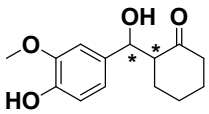
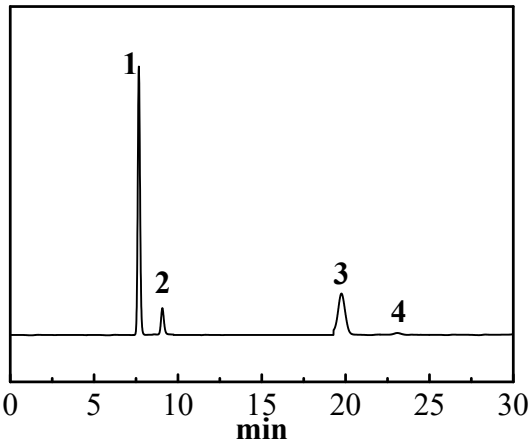
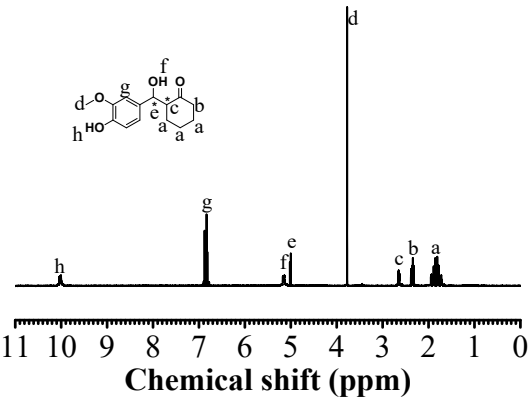



**Table 1, 3d (2R, 1'S).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe aicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 7.458 min, $tR_2$ = 8.017 min, $tR_3$ = 19.809 min, $tR_4$ = 23.189 min. $^1H$ NMR (500 MHz, $CDCl_3$, δ): 1.70-1.97 (m, 6H, $CH_2$), 2.38 (m, 2H, $CH_2$), 2.65 (m,1H, CH), 3.78 (s, 3H, $CH_3$), 4.98 (s, 1H, CH), 5.17 (s, 1H, OH), 6.82 (m, 3H, Ar-H), 10.02 (s, 1H, OH).




| | time/min | area% |
|---|---|---|
| 1 | 7.458 | 68.562 |
| 2 | 8.017 | 8.017 |
| 3 | 19.809 | 11.787 |
| 4 | 23.189 | 0.819 |



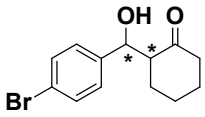
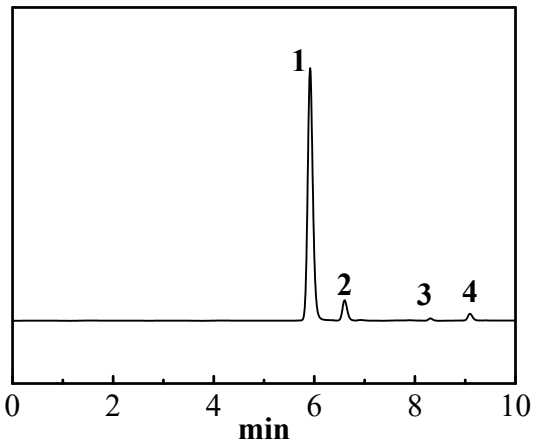
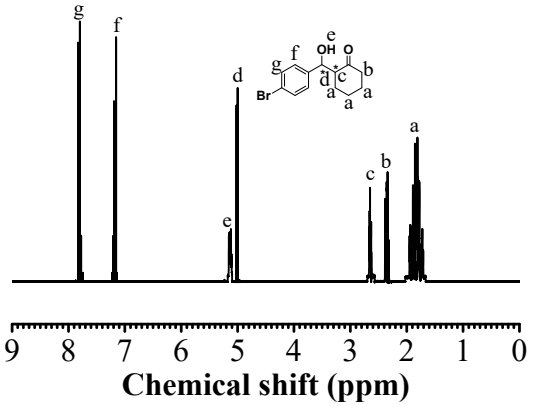



**Table 1, 3e (2R, 1'S).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 10 min, enantiomeric excess: 95%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 5.917 min, $tR_2$ = 6.603 min, $tR_3$ = 8.298 min, $tR_4$ = 9.108 min. $^1$H NMR (500 MHz, $CDCl_3$, δ): 1.62-1.82 (m, 6H, $CH_2$), 2.33 (m, 2H, $CH_2$), 2.65 (m,1H, CH), 4.99 (s, 1H, CH), 5.13 (s, 1H, OH), 7.14 (m, 2H, Ar-H), 7.79 (m, 2H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 5.917 | 96.460 |
| 2 | 6.603 | 2.366 |
| 3 | 8.298 | 0.120 |
| 4 | 9.108 | 1.054 |



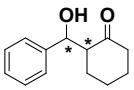
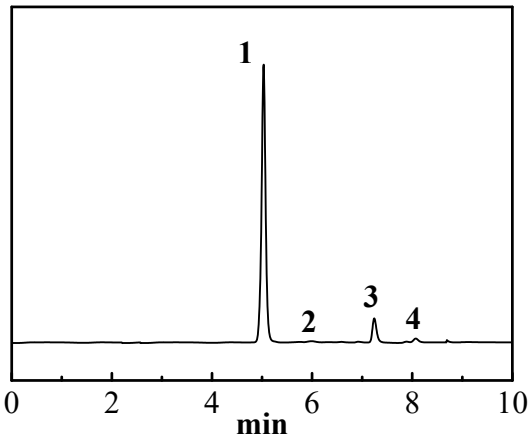
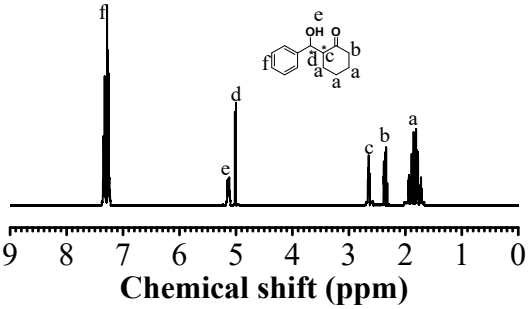


**Table 1, 3f (2R, 1'S).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 10 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 5.033 min, $tR_2$ = 5.992 min, $tR_3$ = 7.244 min, $tR_4$ = 8.081 min. $^1H$ NMR (500 MHz, $CDCl_3$, δ): 1.69-1.95 (m, 6H, $CH_2$), 2.33 (m, 2H, $CH_2$), 2.66 (m,1H, CH), 5.00 (s, 1H, CH), 5.12 (s, 1H, OH), 7.20-7.39 (m, 5H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 5.033 | 9.0667 |
| 2 | 5.992 | 0.755 |
| 3 | 7.244 | 7.940 |
| 4 | 8.081 | 1.258 |



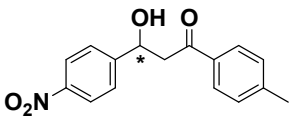
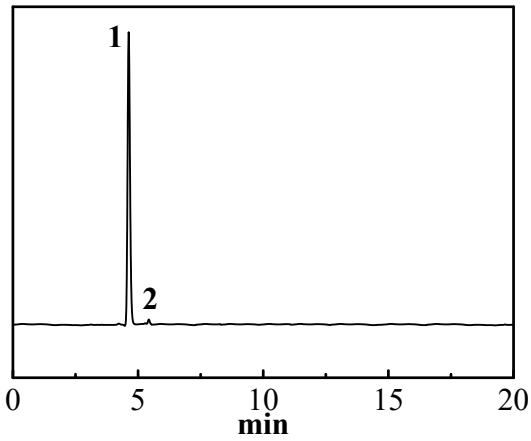
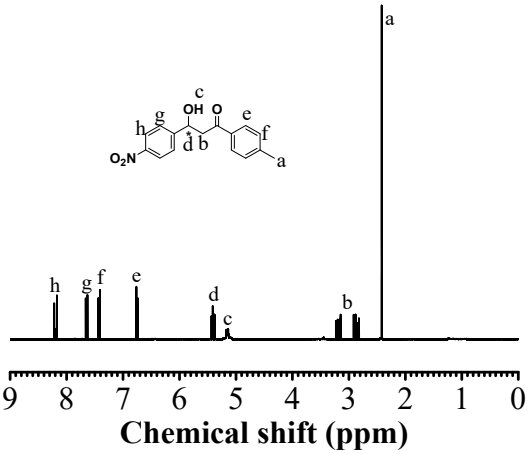



**Table 2, 6a (R).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 20 min, enantiomeric excess: 97%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 4.625 min, $tR_2$ = 5.425 min. $^1$H NMR (500 MHz, $CDCl_3$, δ): 2.41 (m, 3H, $CH_3$), 2.89 and 3.16 (m, 2H, $CH_2$), 5.14 (s, 1H, OH), 5.41 (m, 1H, CH), 6.75 (m, 2H, Ar-H), 7.40 (m, 2H, Ar-H), 7.65 (m, 2H, Ar-H), 8.17 (m, 2H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 4.625 | 98.961 |
| 2 | 5.425 | 1.039 |



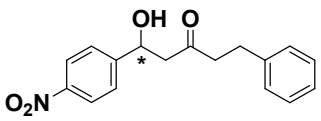
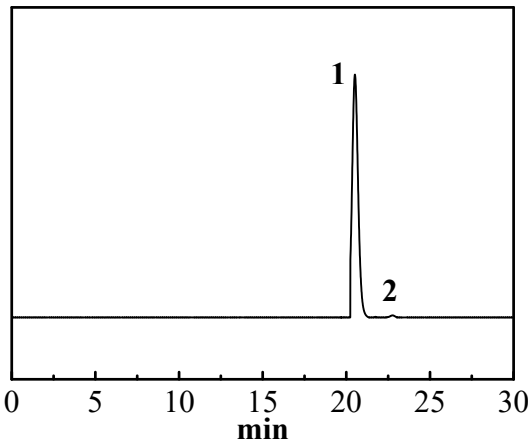
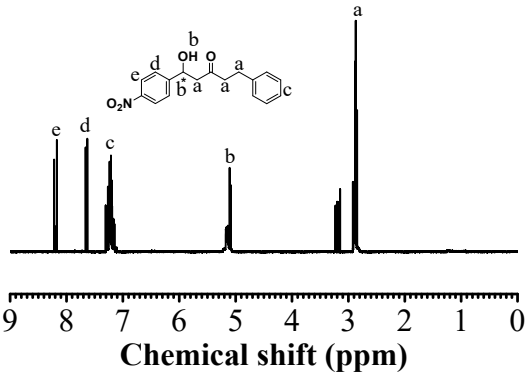



**Table 2, 6b (R).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 20 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 20.537 min, $tR_2$ = 22.788 min. $^1$H NMR (500 MHz, $CDCl_3$, δ): 2.78-3.25 (m, 6H, $CH_2$), 5.09 (m, 2H, CH, OH), 7.12-7.30 (m, 5H, Ar-H), 7.63 (m, 2H, Ar-H), 8.16 (m, 2H, Ar-H)




| | time/min | area% |
|---|---|---|
| 1 | 20.537 | 99.978 |
| 2 | 22.788 | 0.022 |



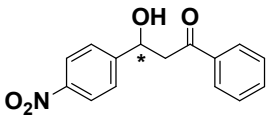
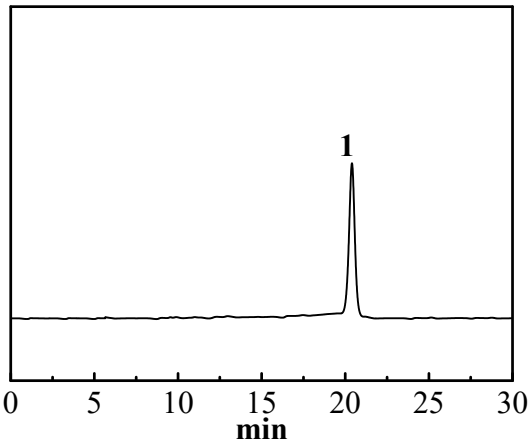
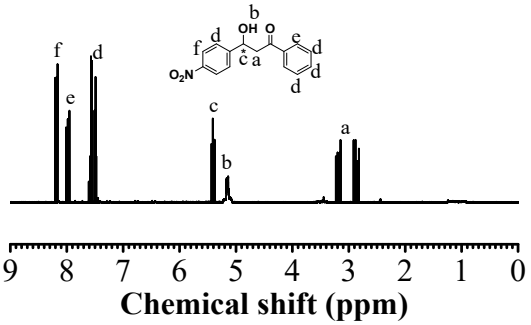



**Table 2, 6c (R).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 30 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 20.400 min. $^1H$ NMR (500 MHz, $CDCl_3$, δ): 2.87 and 3.14 (m, 2H, CH2), 5.11 (s, 1H, OH), 5.42 (m, 1H, CH), 7.42-7.63 (m, 5H, Ar-H), 7.98 (m, 2H, Ar-H), 8.16 (m, 2H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 20.400 | >99 |



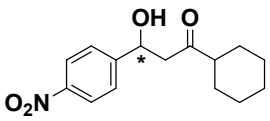
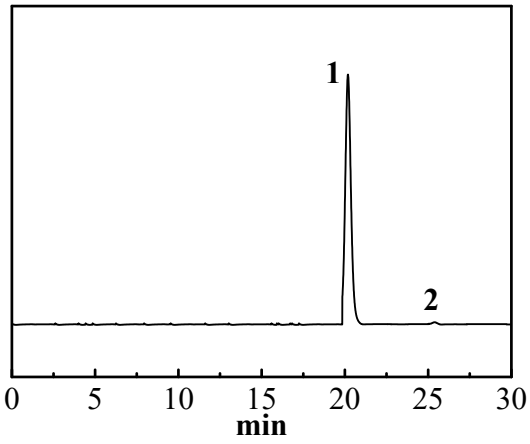
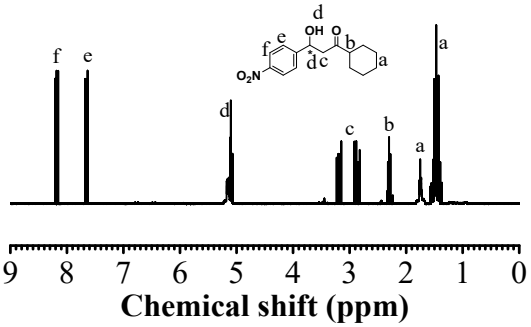



**Table 2, 6d (R).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 30 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 20.211 min, $tR_2$ = 25.403 min. $^1$H NMR (500 MHz, $CDCl_3$, δ): 1.33-1.82 (m, 10H, $CH_2$), 2.29 (m, 1H, CH), 2.89 and 3.16 (m, 2H, CH2), 5.10 (m, 2H, CH, OH), 7.62 (m, 2H, Ar-H), 8.17 (m, 2H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 20.211 | 99.971 |
| 2 | 25.403 | 0.029 |



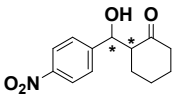
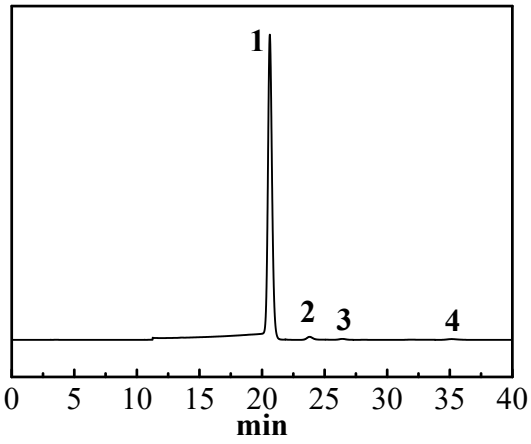
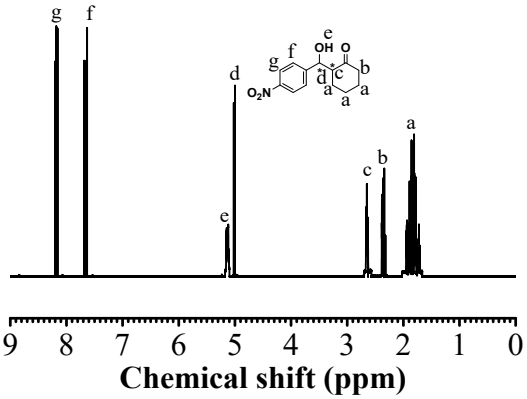


**Table 2, 6e (2R, 1'S).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 40 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 20.702 min, $tR_2$ = 23.800 min, $tR_3$ = 26.433 min, $tR_4$ = 35.133 min. $^1$H NMR (500 MHz, $CDCl_3$, δ): 1.67-1.98 (m, 6H, $CH_2$), 2.33 (m, 2H, $CH_2$), 2.66 (m,1H, CH), 5.02 (s, 1H, CH), 5.17 (s, 1H, OH), 7.61 (m, 2H, Ar-H), 8.17 (m, 2H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 20.702 | 98.541 |
| 2 | 23.800 | 1.146 |
| 3 | 26.433 | 0.188 |
| 4 | 35.133 | 0.124 |



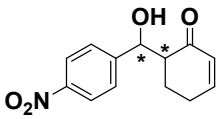
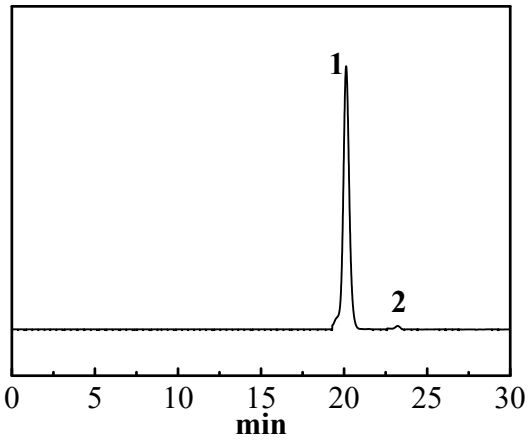
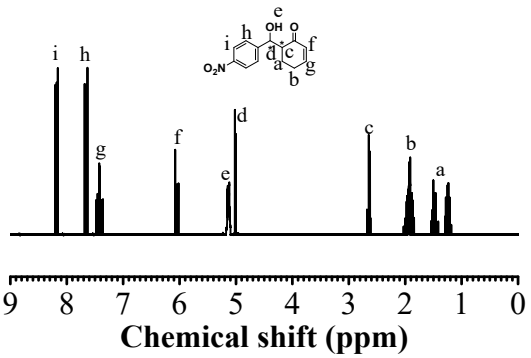



**Table 2, 6f (2R, 1'S).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 30 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 20.098 min, $tR_2$ = 23.189 min. $^1$H NMR (500 MHz, $CDCl_3$, δ): 1.22 and 1.49 (m, 2H, $CH_2$), 1.93 (m, 2H, $CH_2$), 2.61 (m, 1H, CH), 2.30 (m,1H, CH), 5.01 (m, 1H, CH), 5.13 (m, 1H, OH), 6.07 (m, 1H, CH), 7.42 (m, 1H, CH), 7.63 (m, 2H, Ar-H), 8.16 (m, 2H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 20.098 | 99.961 |
| 2 | 23.189 | 0.039 |



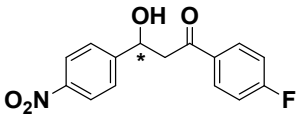
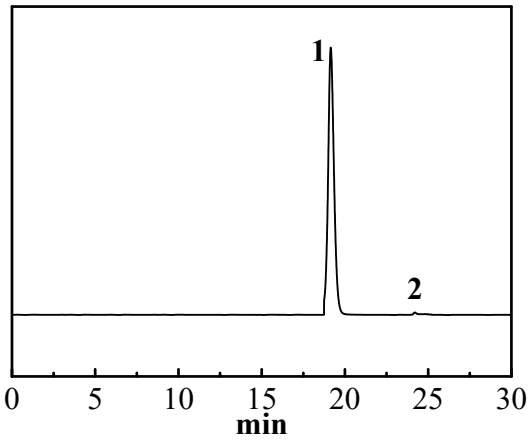
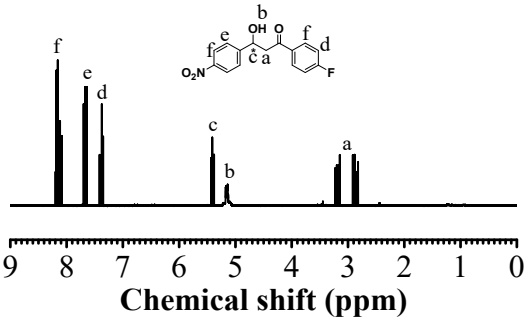



**Table 2, 6g (R).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 30 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 19.150 min, $tR_2$ = 24.05 min. $^1$H NMR (500 MHz, $CDCl_3$, δ): 2.85 and 3.16 (m, 2H, CH2), 5.16 (s, 1H, OH), 5.42 (m, 1H, CH), 7.35 (m, 2H, Ar-H), 7.65 (m, 2H, Ar-H), 8.16 (m, 4H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 19.150 | 99.931 |
| 2 | 24.205 | 0.069 |



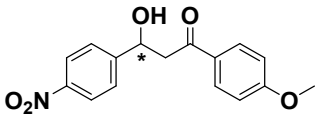
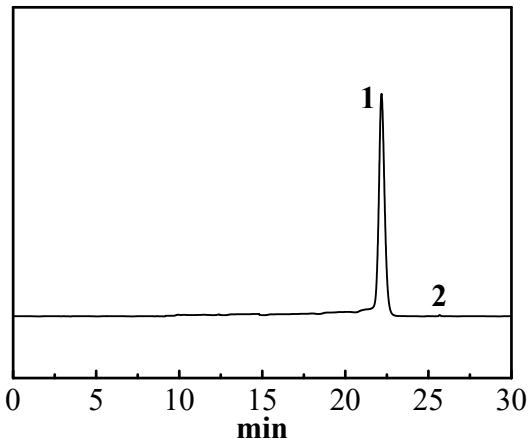
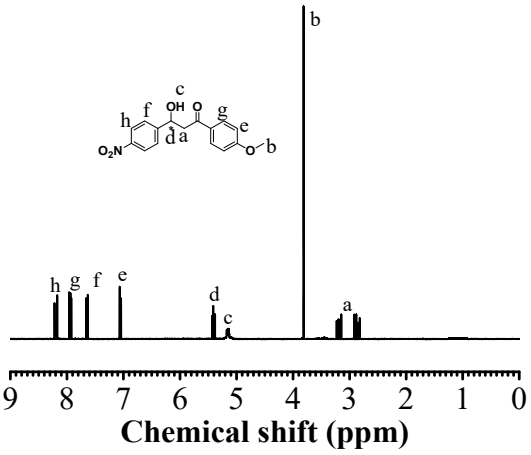



**Table 2, 6h (R).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 30 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) = 22.205 min, $tR_2$ =25.660 min. $^1H$ NMR (500 MHz, $CDCl_3$, δ): 2.84 and 3.19 (m, 2H, CH2), 3.80 (s, 3H, $CH_3$), 5.12 (s, 1H, OH), 5.40 (m, 1H, CH), 7.07 (m, 2H, Ar-H), 7.64 (m, 2H, Ar-H), 7

95 (m, 2H, Ar-H), 8.19 (m, 2H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 22.205 | 99.954 |
| 2 | 25.660 | 0.056 |



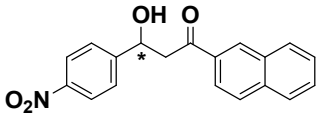
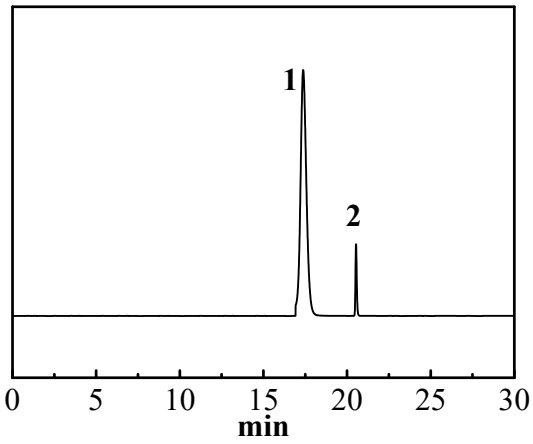



**Table 2, 6i (R).** The product is yellow liquid. L-Pro-L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 30 min, enantiomeric excess: 87%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol =90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $tR_1$ (major) =17.414 min, $tR_2$ =20.537 min. $^1$H NMR (500 MHz, $CDCl_3$, δ): 2.89 and 3.19 (m, 2H, CH2), 5.14 (s, 1H, OH), 5.40 (m, 1H, CH), 7.55-7.86 (m, 5H, Ar-H), 8.04 (m, 2H, Ar-H), 8.21 (m, 3H, Ar-H), 8.55 (s, 1H, Ar-H).




| | time/min | area% |
|---|---|---|
| 1 | 17.414 | 93.603 |
| 2 | 20.537 | 6.397 |