Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

L-proline Modified Chiral Porous Hyper-crosslinked L-Phenylalanine Dipeptide — the Increased Reaction Rate and Selectivity in Asymmetric Catalysis

Yaodong Wang,[1] Lijia Liu,[1,2] Yudan Wang,[1*] Kexiao Sang,[1] Chunhong Zhang[1,2], Toshifumi Satoh[3]*

[1] Key Laboratory of Superlight Materials & Surface Technology, Ministry of Education, College of Materials Science and Chemical Engineering, Harbin Engineering University, Harbin, 150001, China;

[2] Yantai Research Institute of Harbin Engineering University, Yantai, 264006, China.

[3]Faculty of Engineering, Hokkaido University, Sapporo 060-8628, Japan

Corresponding authors: liulijia@hrbeu.edu.cn (L. Liu) and yudanwang@hrbeu.edu.cn (Y. Wang)

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, Boc-L-proline, N,N'-dicyclohexylcarbodiimide, 4, 4-bis (chloromethyl)-1, 1-biphenyl, 4-vinyl pyridine, 4-vinylbenzylchloride, styrene, trans-β-Nitrostyrene, 4-methoxystyrene, 1-hexene, 4-fluorostyrene, cyclohexanone, 4'-methylacetophenone, 4'-(trifluoromethoxy)-acetophenone, 2-acetonaphthone were purchased from Sahn Chemical Technology Co., Ltd. *p*-methoxylaniline, aniline, 4-fluoroaniline, hexylamine,

p-nitrobenzaldehyde, acetone, *p*-tolualdehyde, 4-bromo-2-hydroxybenzaldehyde, 4-bromobenzaldehyde, hydroxyacetone, acetophenone, 4-fluoroacetophenone, ninhydrin hydrate 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 structure in the catalyst was characterized by high-resolution transmission electron microscopy (Talos F200X G2, USA, HRTEM). The specific surface area was measured by nitrogen adsorption desorption experiment (ASAP 2020 Plus HD88, BET). Element content was analyzed using X-ray photoelectron spectroscopy (Thermo ESCALAB 250XI, USA, XPS), Organic element analyzer (Thermo Scientific Flash 2000, USA, EA) and Inductive Coupled Plasma Emission Spectrometer (ICAP 7400, Germany, ICP). The content of proline was determined by ninhydrin method (Ultraviolet and visible spectrophotometer, UV, Shimazu UV3600). 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)

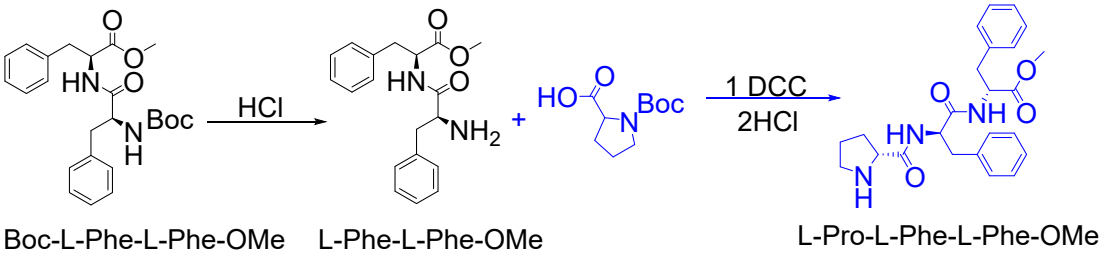
S 1.3 Synthesis of tripeptide catalyst

(1) Boc-L-Phe-L-Phe-OMe (10 mmol) was dissolved in ethyl acetate (EtOAc, 100 mL), HCl (37%, 5 mL) were added into the mixture and stirred at 298 K for additional 24 h to remove the Boc protective group, adjust pH to neutral，and the white solid product (L-Phe-L-Phe-OMe) was obtained by recrystallization ($CHCl_3$–CH_3OH). Yield: 57%–75%.

(2) Boc-L-proline (0.6 mmol), N,N'-dicyclohexyl carbon diimine (DCC, 1.5 mmol), L-Phe-L-Phe-OMe (0.5 mmol), and DCM were charged into a 100 mL three-necked flask, and stirred vigorously for 7 d under N_2

atmosphere. After the reaction, the white powdery product Boc-L-Pro-L-Phe-L-Phe-OMe was obtained by atmospheric pressure filtration.

(3) The white product (L-Pro-L-Phe-L-Phe-OMe) can be obtained by removing the Boc protection group according to the scheme in (1). Yield: 57%–60 %。



Scheme S1 Synthesis of L-Pro-L-Phe-L-Phe-OMe.

L-Phe-L-Phe-OMe, ^{1}H NMR (500 MHz, DMSO, δ): 2.50 (m, 4H, CH_2), 3.27(s, 3H, CH_3), 3.92(m, 2H, CH), 7.00-7.31 (m, 10H, Ar-H), 7.91 (s, 2H, NH_2).

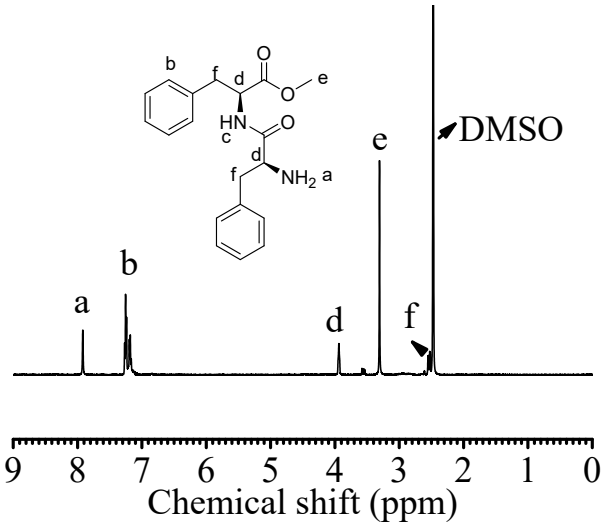


Figure S1 ^{1}H NMR spectra of L-Phe-L-Phe-OMe.

L-Pro-L-Phe-L-Phe-OMe, ^{1}H NMR (500 MHz, DMSO, δ): 2.20 (m, 4H, CH_2), 2.57 (m, 6H, CH_2), 3.31(m, 4H, CH_3, CH), 3.95(m, 2H, CH), 7.09-7.35 (m, 10H, Ar-H), 7.93 (s, 1H, NH).

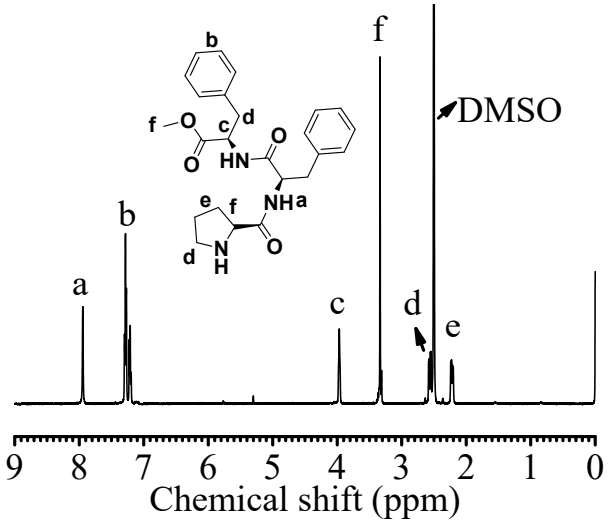


Figure S2 ^{1}H NMR spectra of L-Pro-L-Phe-L-Phe-OMe.

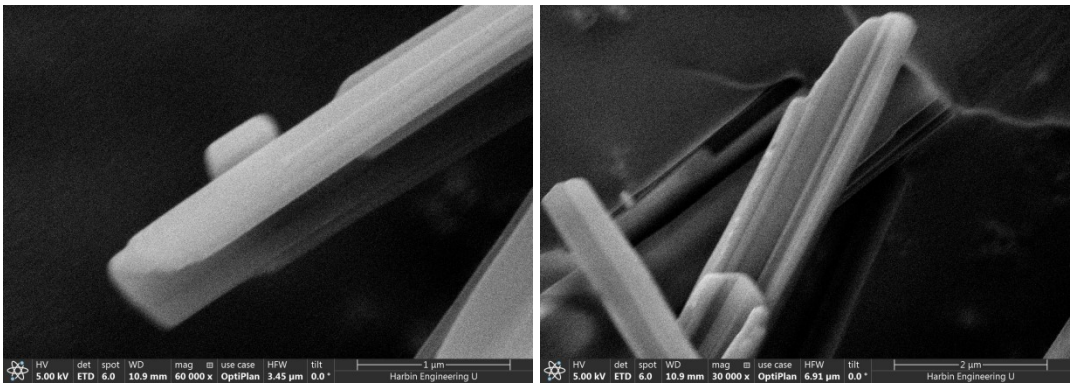


Figure S3 SEM images of L-Pro-L-Phe-L-Phe-OMe.

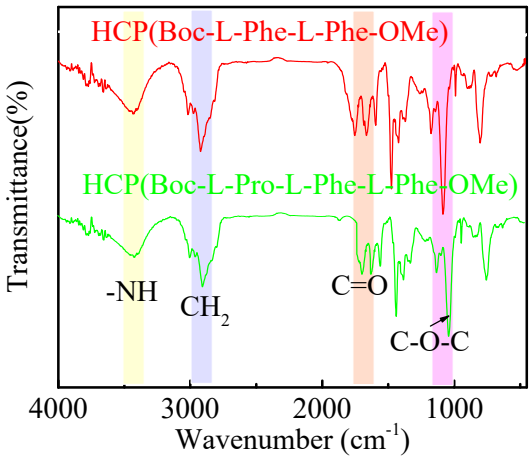


Figure S4 FT-IR spectra of HCP(Boc-L-Phe-L-Phe-OMe) (red line) and HCP(Boc-L-Pro-L-Phe-L-Phe-OMe) (green line).

Table S1 Elemental composition of the catalyst.

Entry	Catalyst	C 1s (%)	N 1s (%)	O 1s (%)	Cl 2p (%)
1	HCP(L-Pro-L-Phe-L-Phe-OMe)	87.43	1.59	10.98	0

Test condition: determined by X-ray photoelectron spectroscopy analysis

Table S2 ICP-MS test data of carrier and catalyst.

Entry	Catalyst	metallic element concentration (μg /L)[a]	metallic element mass (μg)[b]	mass percent[c] (‰)
1	HCP(L-Phe-L-Phe-OMe)	2.510(Fe)	0.0251	0.025
2	HCP(L-Pro-L-Phe-L-Phe-OMe)	2.134 (Fe)	0.0213	0.021

Test condition: 1mg of sample was weighed and dissolved in concentrated nitric acid with assistance of ultrasound. After complete dissolution, the solution was diluted to 10mL with deionization. The concentration of metal ions in the solution was determined by ICP-MS.
[b] metallic element mass in the samples = metallic element concentration x volume of solution.
[c] mass percent of metallic element in the materials = (metallic element mass / weight) x100%

Table S3 Proline content determination UV absorption data.

Entry	Content (μg/mL)	Abs.
1	1	0.04088
2	2	0.07828
3	3	0.1163
4	4	0.1529
5	5	0.1865
6	6	0.2228
7[a]	5.78	0.1371

Test condition: first, the stock solution was prepared by dissolving 25mg L-Pro in a 250 mL volumetric flask. Then, take six 50 mL volumetric flask and join stock solution 0.5, 1.0, 1.5, 2.0, 2.5, 3.0 mL, constant volume with distilled water to the scale, the concentration of L - Pro is 1，2，3，4，5，6 μg/mL. Take 7 test tubes, respectively add 2mL series of standard concentration of L-Pro solution and test solution,2mL glacial acetic acid,2mL acid ninhydrin solution, and heat with boiling water for 30min. Finally, after cooling, add 4 mL toluene solution, wait for the pigment to transfer to toluene solution, absorb the upper toluene solution and measure the absorbance at 520nm.
[a] 5 mg HCP(L-Pro-L-Phe-L-Phe-OMe) was added to 6mol/L hydrochloric acid and heated to reflux for 24h.

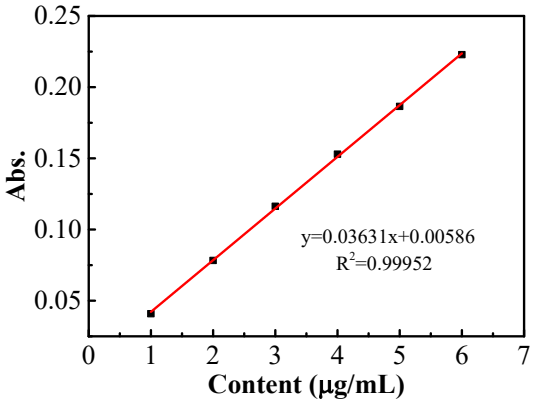


Figure S5 Standard curve for determination of proline content.

Table S4 Organic element analyzer test results.

Entry	Catalyst	N (μg/g)	C (μg/g)	H (μg/g)	O (μg/g)
1	HCP(L-Pro-L-Phe-L-Phe-OMe)	$2.0*10^{-3}$	$752.0*10^{-3}$	$59.7*10^{-3}$	$74.5*10^{-3}$

Test condition: pass the CNHS and O mode test of the organic element analyzer.

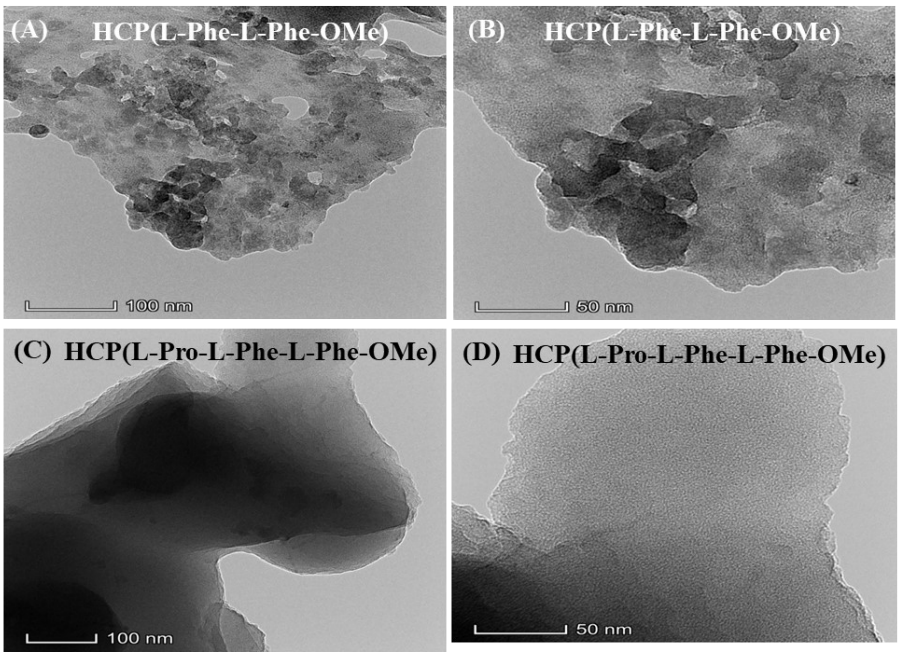
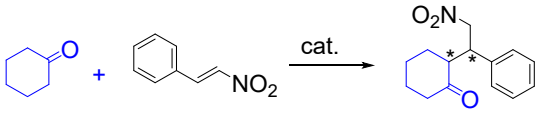


Figure S6 TEM images of (A–B) HCP(L-Phe-L-Phe-OMe), and (C–D) HCP(L-Pro-L-Phe-L-Phe-OMe).

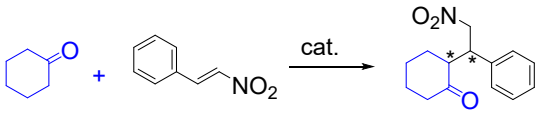
Table S5 Effect of time on catalytic effect of HCP(L-Pro-L-Phe-L-Phe-OMe) (Michael addition reaction).



Entry	Time (d)	Yield[a] (%)	ee[b] (%)	dr[c]
1	1	79	96	99/1
2	2	89	97	99/1
3	3	92	96	99/1
4	4	96	97	99/1
5	5	96	97	99/1
6	6	96	97	99/1
7	7	96	97	99/1

Reaction conditions: the reaction was performed with cyclohexanone (0.6 mmol), trans-β-nitrostyrene (0.5 mmol) (25 °C), the solvent was CH_3OH (1mL), and the catalyst dosage was 6 mg.
[a] Isolated yields.
[b] Chiral HPLC analysis (Chiralpak AD-H), with hexane/isopropanol (90/10, v/v) as the eluent.
[c] Diastereoisomer ratio (syn/anti)

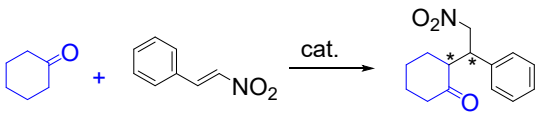
Table S6 Effect of time on catalytic effect of L-Pro-L-Phe-L-Phe-OMe (Michael addition reaction).



Entry	Time (d)	Yield[a] (%)	ee[b] (%)	dr[c]
1	1	20	70	99/1
2	2	59	71	99/1
3	3	69	69	99/1
4	4	75	70	99/1
5	5	81	71	99/1
6	6	92	71	99/1
7	7	96	71	99/1

Reaction conditions: the reaction was performed with cyclohexanone (0.6 mmol), trans-β-nitrostyrene (0.5 mmol) (25 °C), the solvent was CH_3OH (1mL), and the catalyst dosage was 6 mg.
[a] Isolated yields.
[b] Chiral HPLC analysis (Chiralpak AD-H), with hexane/isopropanol (90/10, v/v) as the eluent.
[c] Diastereoisomer ratio (syn/anti)

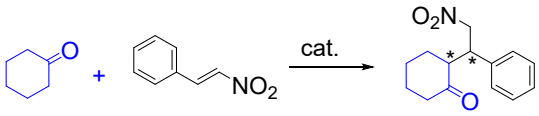
Table S7 Effect of solvent on catalytic effect of HCP(L-Pro-L-Phe-L-Phe-OMe) (Michael addition reaction).



Entry	Solvent	Yield[a] (%)	ee[b] (%)	dr[c]
1	none	92	97	99/1
2	CH_2Cl_2	95	96	99/1
3	$CHCl_3$	96	95	99/1
4	CH_3OH	96	96	99/1
5	DMF	93	94	99/1
6	Toluene	52	96	99/1

Reaction conditions: the reaction was performed with cyclohexanone (0.6 mmol), trans-β-nitrostyrene (0.5 mmol) (25 °C, 4 d), solvent volume was 1 mL, and the catalyst dosage was 6 mg.
[a] Isolated yields.
[b] Chiral HPLC analysis (Chiralpak AD-H), with hexane/isopropanol (90/10, v/v) as the eluent.
[c] Diastereoisomer ratio (syn/anti)

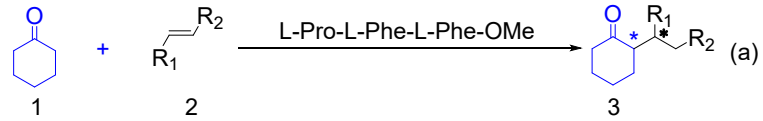
Table S8 Effect of catalyst dosage on catalytic effect of HCP(L-Pro-L-Phe-L-Phe-OMe) (Michael addition reaction).



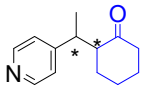
Entry	Catalyst dosage	Yield[a] (%)	ee[b] (%)	dr[c]
1	2 mg	90	96	99/1
2	4 mg	91	97	99/1
3	6 mg	96	97	99/1
4	8 mg	96	97	99/1

Reaction conditions: the reaction was performed with cyclohexanone (0.6 mmol), trans-β-nitrostyrene (0.5 mmol) (25 °C, 4 d), and the solvent was CH_3OH (1mL).
[a] Isolated yields.
[b] Chiral HPLC analysis (Chiralpak AD-H), with hexane/isopropanol (90/10, v/v) as the eluent.
[c] Diastereoisomer ratio (syn/anti)

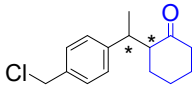
Table S9 Applicability of L-Pro-L-Phe-L-Phe-OMe for Michael addition reaction (different alkenes).



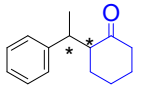
1 2 3


3a

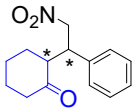
97% ee, 97/3 dr,74% yield


3b

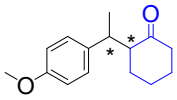
92% ee, 99/1 dr, 39% yield


3c

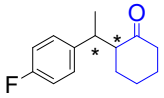
97% ee, 75/25 dr, 65% yield


3d

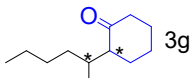
71% ee, 99/1 dr, 70% yield


3e

95% ee, 95/5 dr, 63% yield


3f

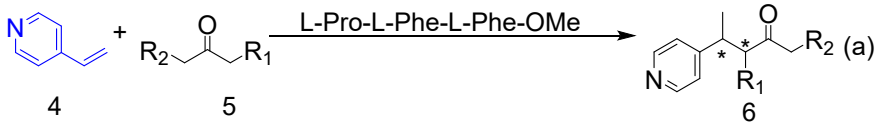
97% ee, 98/2 dr, 64% yield


3g

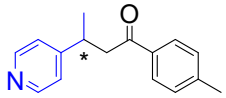
29% ee, 65/35 dr, 56% yield

Reaction conditions: The reaction was performed with cyclohexanone (0.6 mmol),olefin derivative (0.5 mmol), L-Pro-L-Phe-L-Phe-OMe (6 mg) and CH_3OH (1 mL) at 25 °C; The reaction time was 4 d. (a) Chiral HPLC analysis (Chiralpak AD-H) with hexane/isopropanol (90/10, v/v) as the eluent. Diastereoisomer ratio (syn/anti)

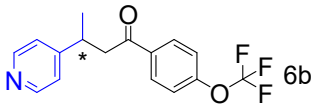
Table S10 Applicability of L-Pro-L-Phe-L-Phe-OMe for Michael addition reaction (different ketone).



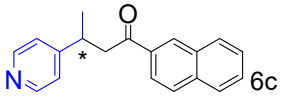
4 5 6


6a

51% ee, 12% yield


6b

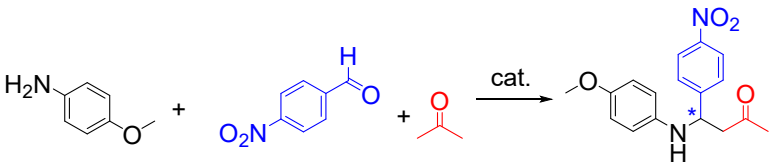
- ee, -% yield


6c

21% ee, 10% yield

Reaction conditions: the reaction was performed with 4-vinylpyridine (0.5 mmol), ketone derivative (0.6 mmol), L-Pro-L-Phe-L-Phe-OMe (6 mg) and CH_3OH (1 mL) at 25 °C. Reaction time was 4 d. (a) Chiral HPLC analysis (Chiralpak AD-H) with hexane/isopropanol (90/10, v/v) as the eluent.

Table S11 Effect of time on catalytic effect of HCP(L-Pro-L-Phe-L-Phe-OMe) (Mannich reaction).



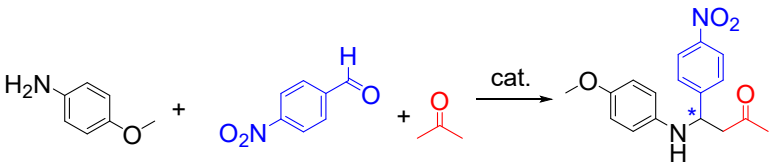
Entry	Time (s)	Yield[a] (%)	ee[b] (%)
1	10	85	89
2	20	90	89
3	30	93	89
4	40	95	91
5	50	94	91
6	60	95	92
7	120	95	91
8	180	95	88
9	240	95	91
10	300	95	90
11	360	95	90
12	450	95	90

Reaction conditions: the reaction was performed with *p*-methoxyaniline (0.6 mmol), *p*-nitrobenzaldehyde (0.5 mmol), acetone (0.5 mmol) (25 °C), solvent was$CHCl_3$ (1mL), and the catalyst dosage was 8 mg.

[a] Isolated yields.

[b] Chiral HPLC analysis (Chiralpak AD-H), with hexane/isopropanol (90/10, v/v) as the eluent.

Table S12 Effect of time on catalytic effect of L-Pro-L-Phe-L-Phe-OMe (Mannich Reaction).



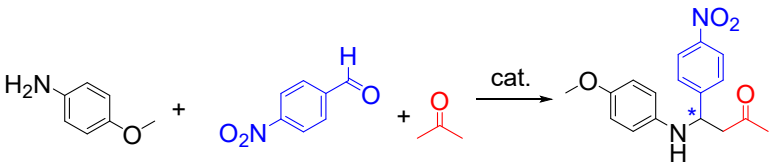
Entry	Time (s)	Yield[a] (%)	ee[b] (%)
1	10	0	0
2	20	12	72
3	30	20	74
4	40	41	77
5	50	60	78
6	60	87	75
7	120	90	79
8	180	90	79
9	240	91	78
10	300	93	79
11	360	94	77
12	450	94	79

Reaction conditions: the reaction was performed with *p*-methoxyaniline (0.6 mmol), *p*-nitrobenzaldehyde (0.5 mmol), acetone (0.5 mmol) (25 °C), solvent was$CHCl_3$ (1mL), and the catalyst dosage was 8 mg.

[a] Isolated yields.

[b] Chiral HPLC analysis (Chiralpak AD-H), with hexane/isopropanol (90/10, v/v) as the eluent.

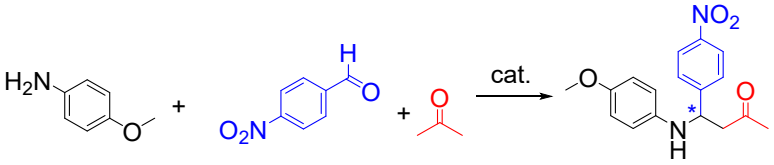
Table S13 Effect of solvent on catalytic effect of HCP(L-Pro-L-Phe-L-Phe-OMe) (Mannich Reaction).



Entry	Solvent	Yield[a] (%)	ee[b] (%)
1	none	50	89
2	CH_3OH	61	88
3	CH_2Cl_2	66	91
4	H_2O	91	89
5	DMF	96	91
6	Toluene	95	92
7	$CHCl_3$	95	91

Reaction conditions: the reaction was performed with *p*-methoxyaniline (0.6 mmol), *p*-nitrobenzaldehyde (0.5 mmol), acetone (0.5 mmol) (25 °C, 40 s), solvent volume (1mL), and the catalyst dosage was 8 mg.
[a] Isolated yields.
[b] Chiral HPLC analysis (Chiralpak AD-H), with hexane/isopropanol (90/10, v/v) as the eluent.

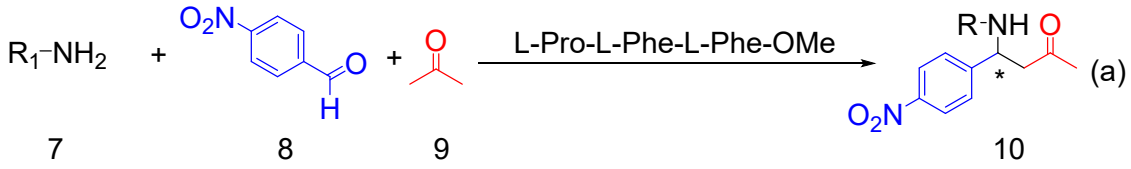
Table S14 Effect of catalyst dosage on catalytic effect of HCP(L-Pro-L-Phe-L-Phe-OMe) (Mannich Reaction).



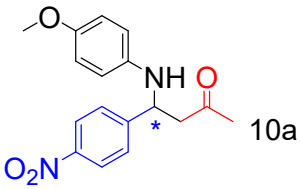
Entry	Catalyst dosage (mg)	Yield[a] (%)	ee[b] (%)
1	2	66	90
2	4	79	92
3	6	92	91
4	8	95	91
5	10	95	91

Reaction conditions: the reaction was performed with *p*-methoxyaniline (0.6 mmol), *p*-nitrobenzaldehyde (0.5 mmol), acetone (0.5 mmol) (25 °C, 40 s), solvent was $CHCl_3$ (1mL).
[a] Isolated yields.
[b] Chiral HPLC analysis (Chiralpak AD-H), with hexane/isopropanol (90/10, v/v) as the eluent.

Table S15 Applicability of L-Pro-L-Phe-L-Phe-OMe for Mannich reaction (different alkenes).

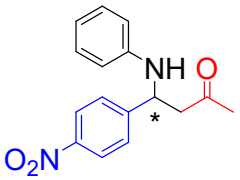


7 8 9 10



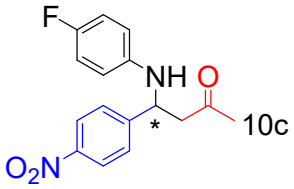
10a

79% ee, 63% yield



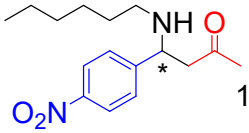
10b

80% ee, 50% yield



10c

-% ee, -% yield

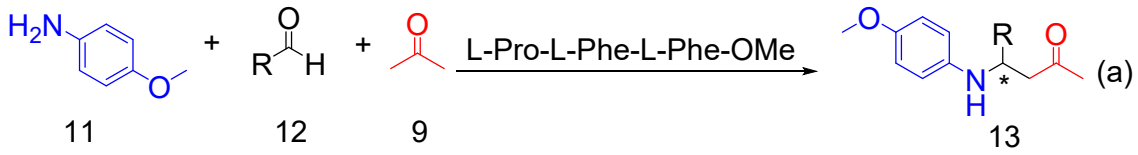


10d

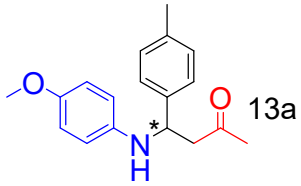
39% ee, 29% yield

Reaction conditions: the reaction was performed with amine derivatives (0.6 mmol), *p*-nitrobenzaldehyde (0.5 mmol), acetone (0.5 mmol), L-Pro-L-Phe-L-Phe-OMe (8 mg) and $CHCl_3$ (1 mL) at 25 °C. Reaction time was 40 s.
(a) Chiral HPLC analysis (Chiralpak AD-H) with hexane/isopropanol (90/10, v/v) as the eluent.

Table S16 Applicability of L-Pro-L-Phe-L-Phe-OMe for Mannich reaction (different aldehyde).

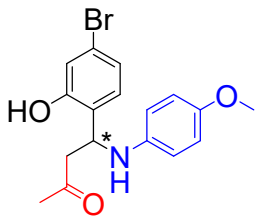


11 12 9 13



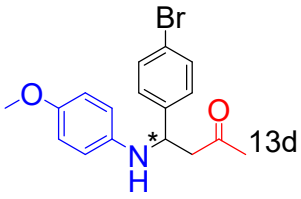
13a

83% ee, 21% yield



13b

59% ee, 36% yield

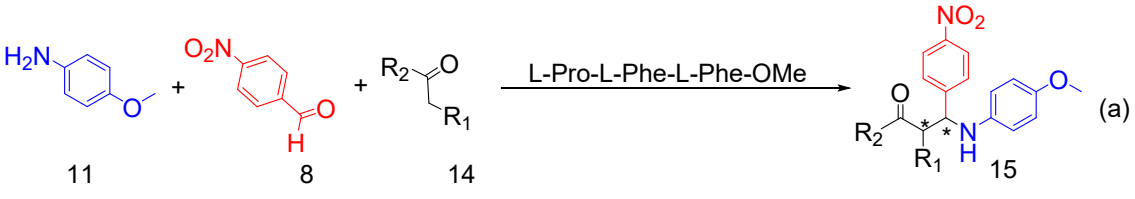


13d

-% ee, -% yield

Reaction conditions: the reaction was performed with Aldehyde derivative (0.5 mmol), *p*-methoxylaniline (0.6 mmol), acetone (0.5 mmol),L-Pro-L-Phe-L-Phe-OMe (8 mg) and $CHCl_3$ (1 mL) at 25 °C. Reaction time was 40 s.
(a) Cchiral HPLC analysis (Chiralpak AD-H) with hexane/isopropanol (90/10, v/v) as the eluent.

Table S17 Applicability of L-Pro-L-Phe-L-Phe-OMe for Mannich reaction (different ketone).



15a

- ee, - dr, -yield

15b

95% ee, 23% yield

15c

69% ee,39% yield

15d

79% ee, 41% yield

Reaction conditions: the reaction was performed with ketone derivatives (0.6 mmol), *p*-methoxylaniline (0.6 mmol), *p*-nitrobenzaldehyde (0.5 mmol), L-Pro-L-Phe-L-Phe-OMe (8 mg) and $CHCl_3$ (1 mL) at 25 °C. Reaction time was 40 s.
(a) Chiral HPLC analysis (Chiralpak AD-H) with hexane/isopropanol (90/10, v/v) as the eluent.

Table S18 Solubility test of L-Pro-L-Phe-L-Phe-OMe.

Entry	solvent	solubility
1	CH_2Cl_2	insoluble
2	$CHCl_3$	insoluble
3	DMF	insoluble
4	Toluene	insoluble
5	CH_3OH	insoluble
6	H_2O	insoluble
7	DMSO	slightly soluble

Test condition: Weigh 1 mg sample and stir to dissolve at room temperature.

S2 High performance liquid chromatography of the product

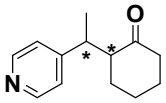
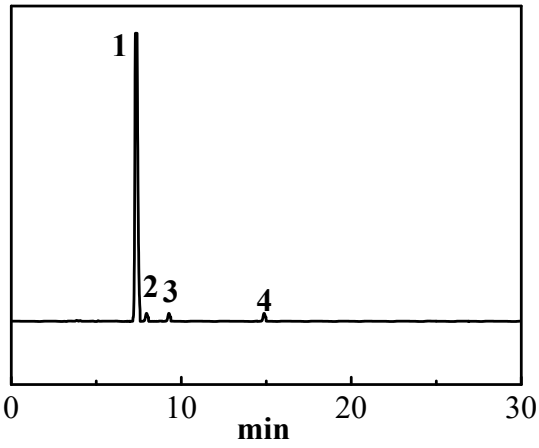


Table 2, 3a (2S, 1'R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 0.5 h, enantiomeric excess: 99% (2S, 1'R); Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 7.349 min, tR_2 = 7.857 min, tR_3 = 9.312 min, tR_4 = 14.830 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 1.18 (m, 3H, CH_3), 1.44-2.02 (m, 6H, CH_2), 2.22-2.52 (m, 3H, CH_2, CH), 3.00 (m, 1H,CH), 7.12 and 8.53 (m, 4H, Ar-H)



	time/min	area
1	7.349	98.727%
2	7.857	1.134%
3	9.312	0.052%
4	14.830	0.087%

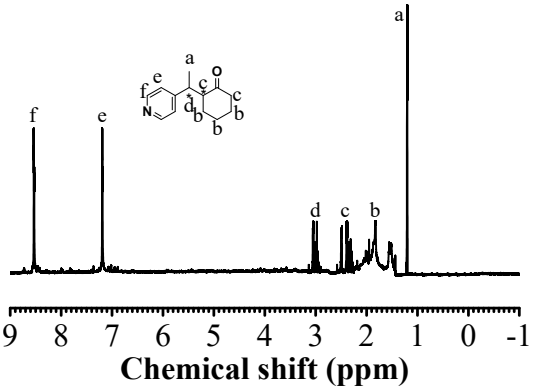
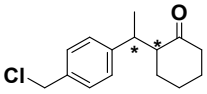
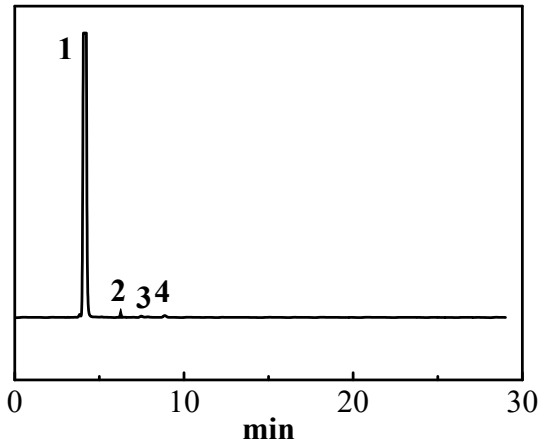


Table 2, 3b (2S, 1'R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction



time 0.5 h, enantiomeric excess: 98% (2S, 1'R); 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) = 4.120 min, tR_2 = 6.227 min, tR_3 = 7.568 min, tR_4 = 8.910 min. ^1H NMR (500 MHz, $CDCl_3$, δ): 1.19 (s, 3H, CH_3), 1.41-1.99 (m, 6H, CH_2), 2.27-2.51 (m, 3H, CH_2, CH), 3.01 (m, 1H,CH), 4.67 (s, 2H, CH_2), 7.14 -7.28 (m, 4H, Ar-H)



	time/min	area
1	4.120	99.153%
2	6.227	0.157%
3	7.568	0.256%
4	8.910	0.434%

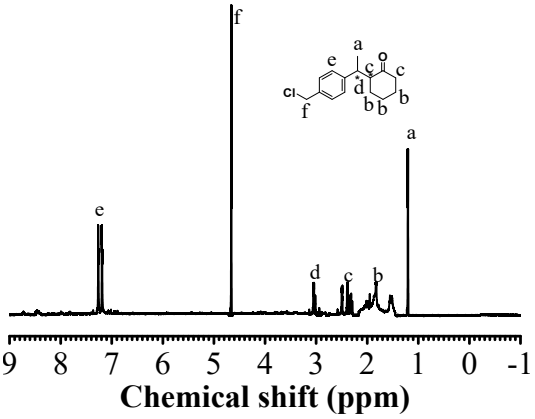
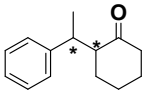
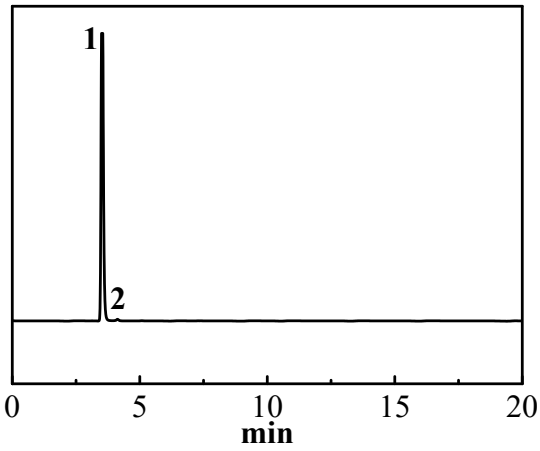
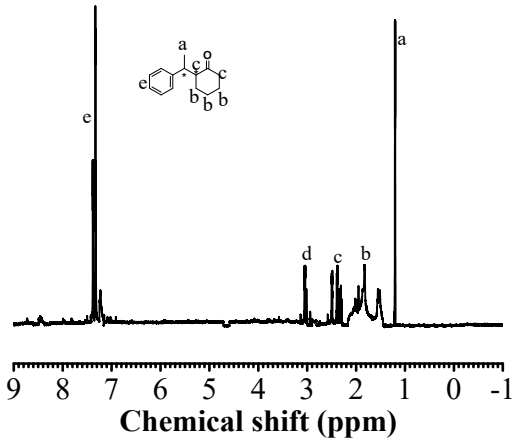


Table 2, 3c (2S, 1'R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the  catalyst. Reaction time 30 min, enantiomeric excess: 98% (2S, 1'R); Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 3.542 min, tR_2 = 4.125 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 1.19 (m, 3H, CH_3), 1.43-2.16 (m, 6H, CH_2), 2.25-2.62 (m, 3H, CH_2, CH), 3.04 (m, 1H,CH), 7.15 -7.40 (m, 5H, Ar-H)



	time/min	area
1	3.542	99.552%
2	4.125	0.448%



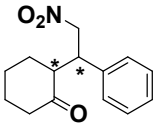
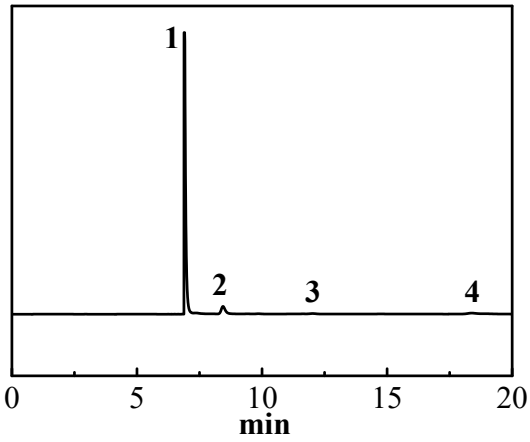
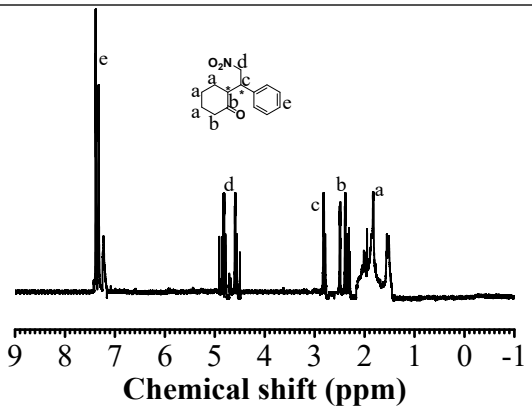


Table 2, 3d (2S, 1'R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 20 min, enantiomeric excess: 97% (2S, 1'R); Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 6.910 min, tR_2 = 8.436 min, tR_3 = 12.069 min, tR_4 = 18.461 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 1.46-2.19 (m, 6H, CH_2), 2.26-2.56 (m, 3H, CH_2, CH), 2.80 (m, 1H,CH), 4.55 and 4.83 (m, 2H, CH_2), 7.14-7.42 (m, 5H, Ar-H)



	time/min	area
1	6.910	98.110%
2	8.436	1.189%
3	12.069	0.232%
4	18.461	0.469%



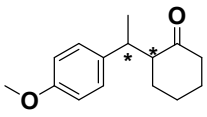
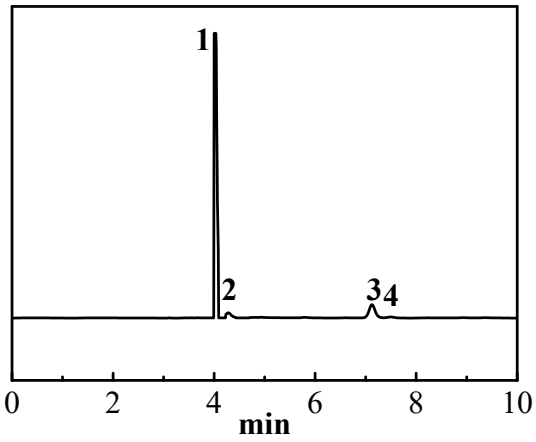
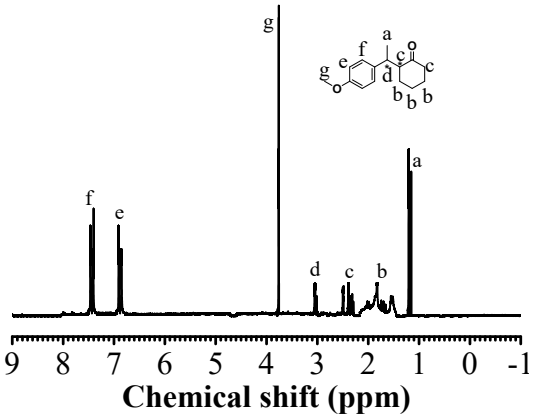


Table 2, 3e (2S, 1'R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 10 min, enantiomeric excess: 99% (2S, 1'R); Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 4.036 min, tR_2 = 4.278 min, tR_3 = 7.111 min, tR_4 = 7.474 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 1.19 (s, 3H, CH_3)1.45-2.17 (m, 6H, CH_2), 2.25-2.56 (m, 3H, CH_2, CH), 3.06 (m, 1H,CH), 3.76 (s, 3H, CH_3), 6.91 and 7.39 (m, 4H, Ar-H)



	time/min	area
1	4.036	96.757%
2	4.278	0.315%
3	7.111	2.797%
4	7.474	0.131%



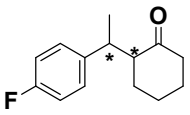
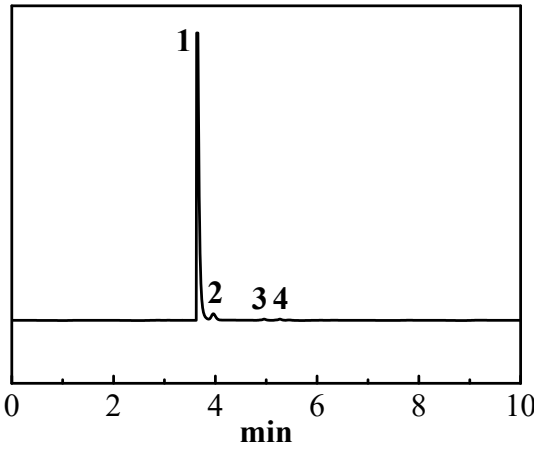
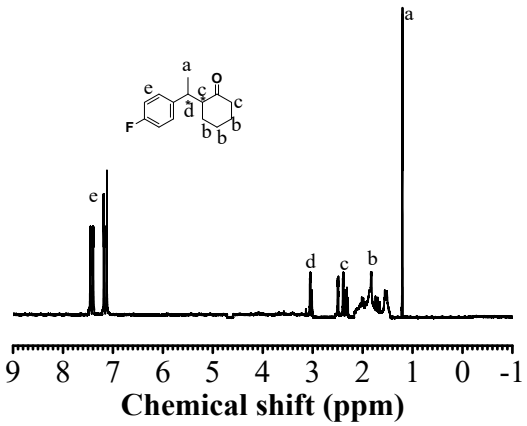


Table 2, 3f (2S, 1'R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 10 min, enantiomeric excess: 99% (2S, 1'R); Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 3.660 min, tR_2 = 3.950 min, tR_3 = 4.933 min, tR_4 = 5.259 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 1.18 (m, 3H, CH_3), 1.42-2.07 (m, 6H, CH_2), 2.38-2.84 (m, 3H, CH_2, CH), 3.02 (m, 1H,CH), 7.10 and 7.39 (m, 4H, Ar-H)



	time/min	area
1	3.660	98.860%
2	3.950	0.827%
3	4.933	0.228%
4	5.259	0.086%



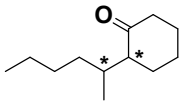
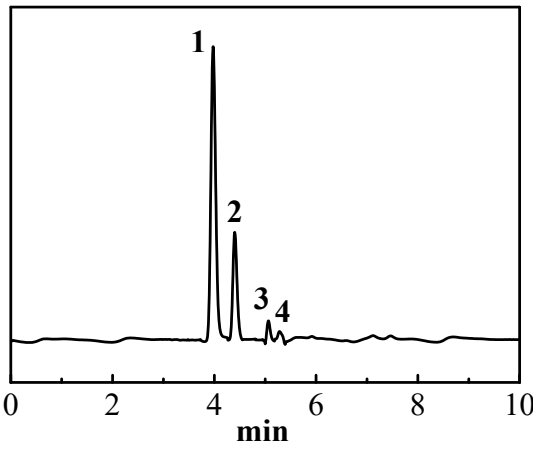
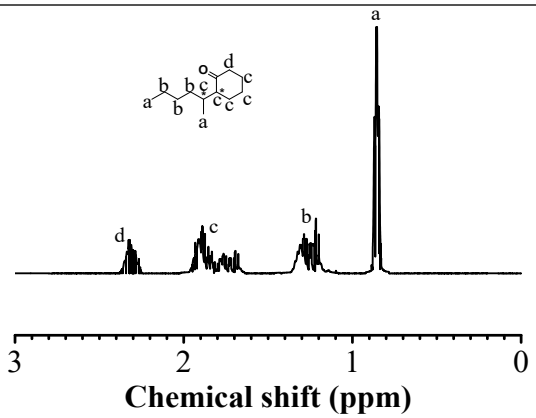


Table 2, 3g (2S, 1'R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 10 min, enantiomeric excess: 51% (2S, 1'R); Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 3.975 min, tR_2 = 4.400 min, tR_3 = 5.077min, tR_4 = 5.271 min. ^1H NMR (500 MHz, $CDCl_3$, δ): 0.82-0.88 (m, 6H, CH_3), 1.16-1.36 (m, 6H, CH_2), 1.64-1.95 (m, 8H, CH_2, CH), 2.25-2.36 (m, 2H, CH_2).



	time/min	area
1	3.975	71.547%
2	4.400	22.985%
3	5.077	4.112%
4	5.271	1.356%



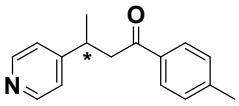
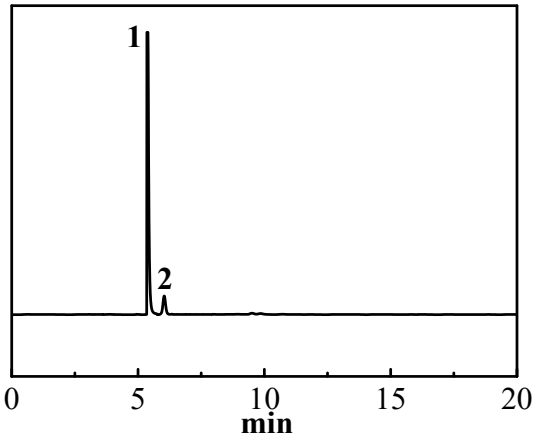
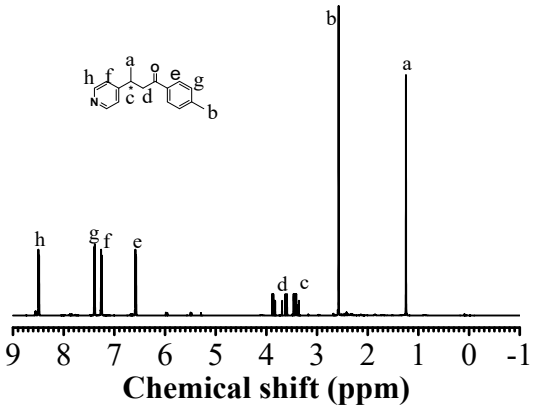


Table 3, 6a (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 20 min, enantiomeric excess: 93%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 5.359 min, tR_2 = 5.990 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 1.25 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 3.37 (m, 1H, CH), 3.65 and 3.87 (m, 2H, CH_2), 6.57 (m, 2H, Ar-H), 7.22 (m, 2H, Ar-H), 7.39 (m, 2H, Ar-H), 8.51 (m, 2H, Ar-H).



	time/min	area
1	5.359	96.672%
2	5.990	3.328%



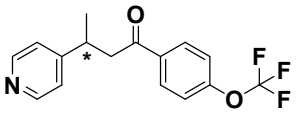
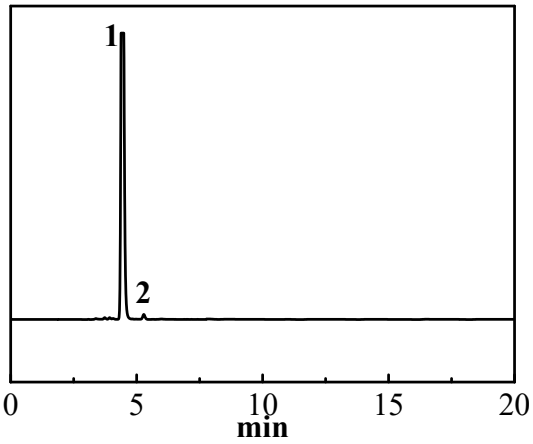
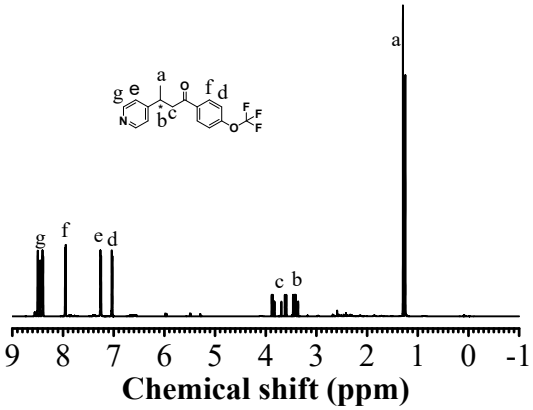


Table 3, 6b (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 20 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 4.467 min, tR_2 = 5.283 min. ^1H NMR (500 MHz, $CDCl_3$, δ): 1.27 (m, 3H, CH_3), 3.41 (m, 1H, CH), 3.65 and 3.83 (m, 2H, CH_2), 7.03 (m, 2H, Ar-H), 7.26 (m, 2H, Ar-H), 7.94 (m, 2H, Ar-H), 8.45 (m, 2H, Ar-H).



	time/min	area
1	4.467	99.001%
2	5.283	0.999%



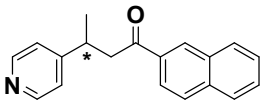
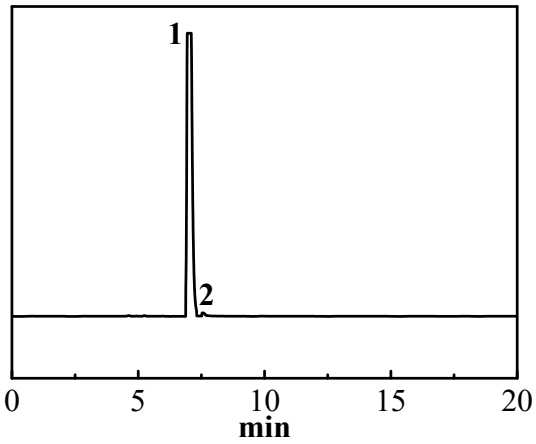
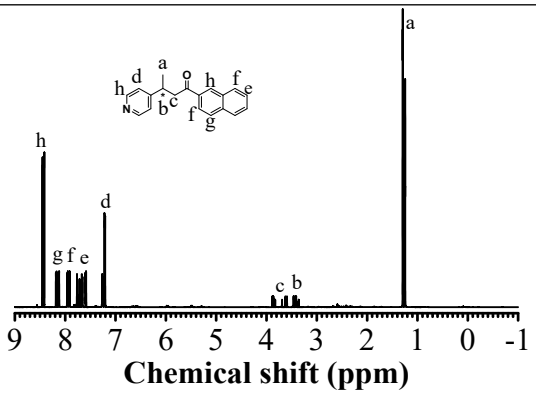


Table 3, 6c (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 20 min, enantiomeric excess: 99%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 7.006 min, tR_2 = 7.587 min. ^1H NMR (500 MHz, $CDCl_3$, δ): 1.25 (m, 3H, CH_3), 3.43 (m, 1H, CH), 3.67 and 3.87 (m, 2H, CH_2), 7.22 (m, 2H, Ar-H), 7.68 (m, 2H, Ar-H), 7.92 (m, 3H, Ar-H), 8.14 (m, 1H, Ar-H), 8.43 (m, 3H, Ar-H).



	time/min	area
1	7.006	99.981%
2	7.587	0.019%



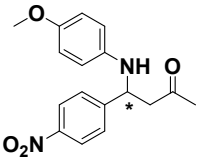
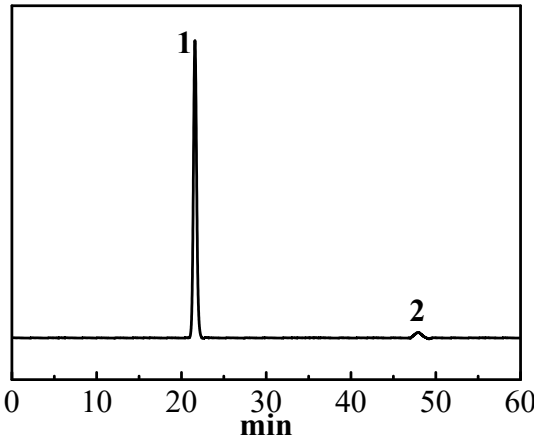
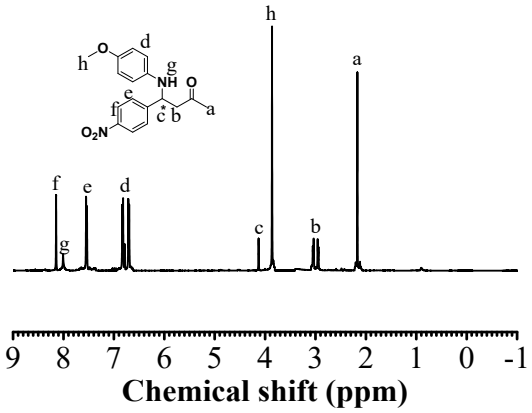


Table 4, 10a (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 60 min, enantiomeric excess: 91%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 21.592 min, tR_2 = 47.908 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 2.17 (s, 3H, CH_3), 2.90 and 3.05 (m, 2H, CH_2), 3.85 (s, 3H, CH_3), 4.11 (m, 1H, CH), 6.62-6.87 (m, 4H, Ar-H), 7.54 (m, 2H, Ar-H), 8.00 (m, 1H, NH), 8.13 (m, 2H, Ar-H).



	time/min	area
1	21.592	95.256%
2	47.908	4.744%



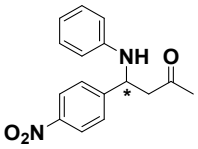
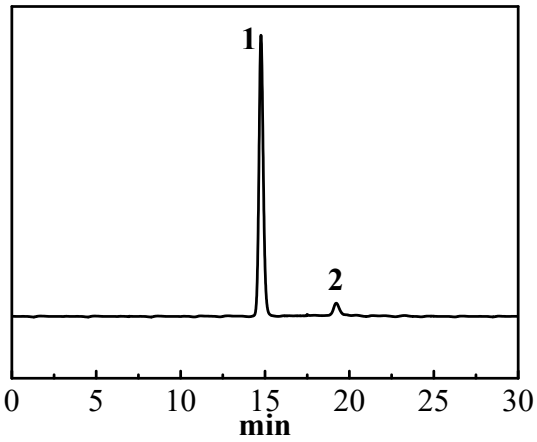
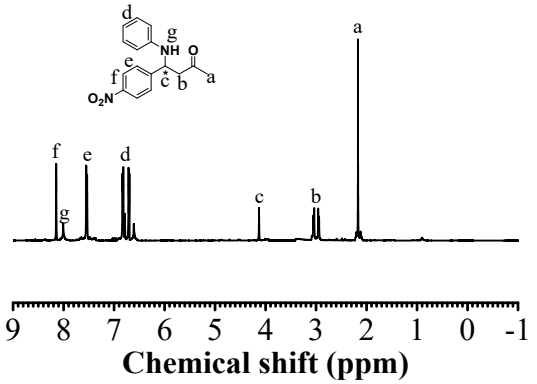


Table 4, 10b (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 30 min, enantiomeric excess: 89%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 14.758 min, tR_2 =19.217 min. ^1H NMR (500 MHz, $CDCl_3$, δ): 2.15 (s, 3H, CH_3), 2.94 and 3.06 (m, 2H, CH_2), 4.14 (m, 1H, CH), 6.53-6.87 (m, 5H, Ar-H), 7.54 (m, 2H, Ar-H), 8.01 (m, 1H, NH), 8.14 (m, 2H, Ar-H).



	time/min	area
1	14.758	94.734%
2	19.217	5.266%



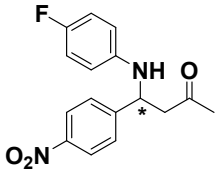
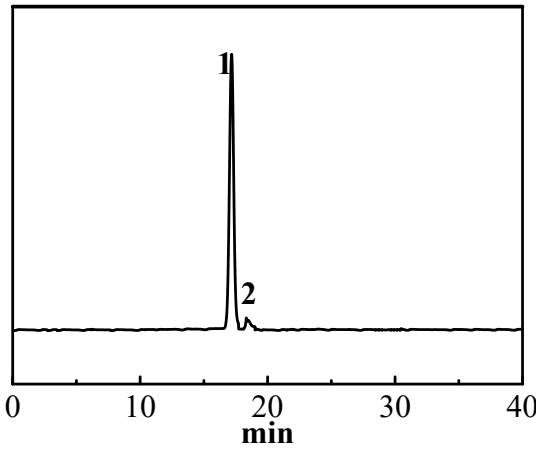
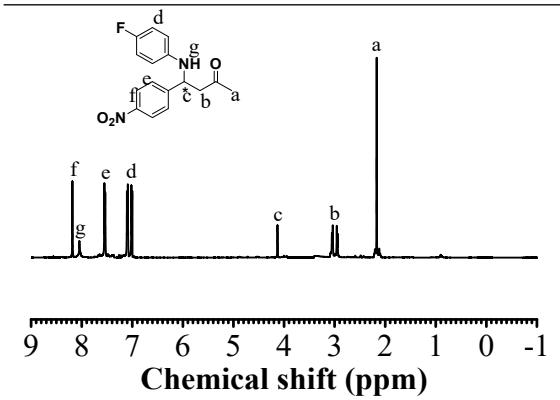


Table 4, 10c (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 40 min, enantiomeric excess: 85 %; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 17.191 min, tR_2 =18.441 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 2.16 (s, 3H, CH_3), 2.95 and 3.03 (m, 2H, CH_2), 4.11 (m, 1H, CH), 6.94-7.13 (m, 4H, Ar-H), 7.55 (m, 2H, Ar-H), 8.06 (m, 1H, NH), 8.20 (m, 2H, Ar-H).



	time/min	area
1	17.191	92.120%
2	18.441	7.880%



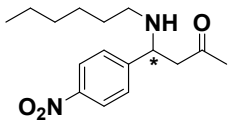
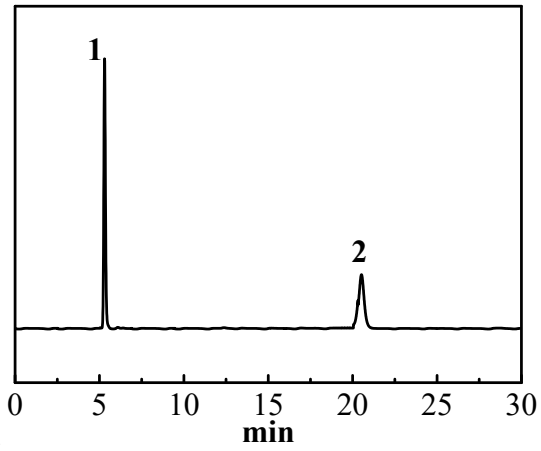
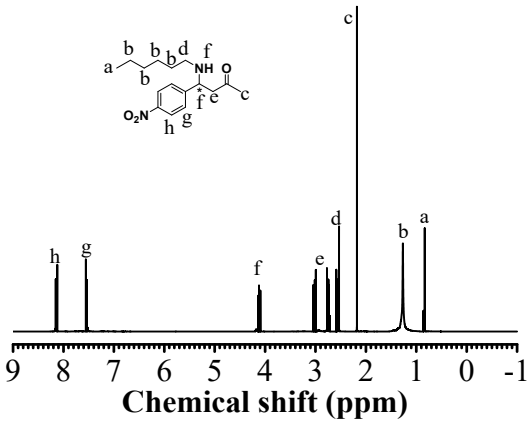


Table S15, 10d (R). The product is yellow liquid. L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 30 min, enantiomeric excess: 39%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 5.300 min, tR_2 =20.525 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.82 (m, 3H, CH_3), 1.27 (m, 8H, CH_2), 2.17 (s, 3H, CH_3), 2.54 (m, 2H, CH_2), 2.74 and 3.00 (m, 2H, CH_2), 4.11 (m, 2H, CH, NH), 7.56 (m, 2H, Ar-H), 8.14 (m, 2H, Ar-H).



	time/min	area
1	5.300	69.778%
2	20.525	30.222%



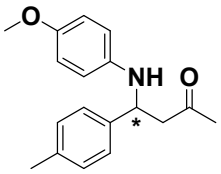
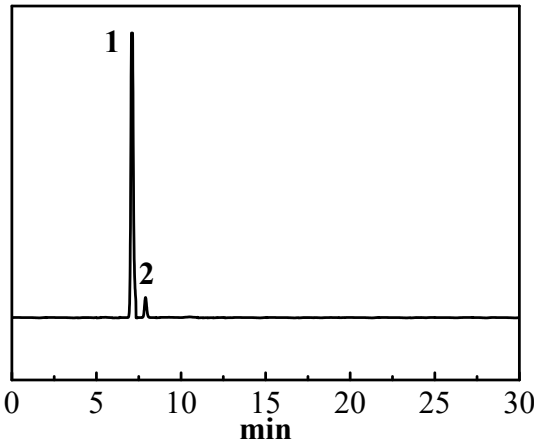
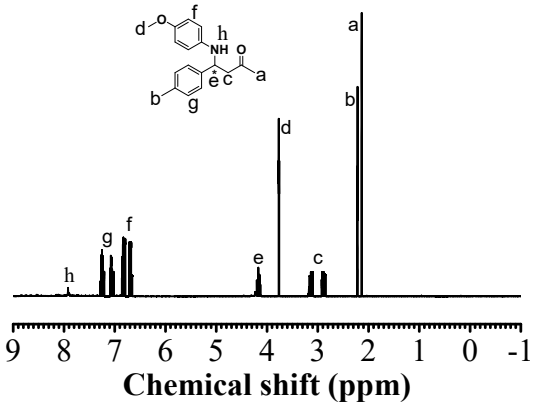


Table 5, 13a (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 30 min, enantiomeric excess: 89%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 7.100 min, tR_2 =7.895 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 2.14 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 2.88 and 3.13 (m, 2H, CH_2), 3.76 (s, 3H, CH_3), 4.14 (m, 1H, CH), 6.69 and 6.79 (m, 4H, Ar-H), 7.08 and 7.24 (m, 4H, Ar-H), 7.96 (m, 1H, NH).



	time/min	area
1	7.100	94.832%
2	7.895	5.168%



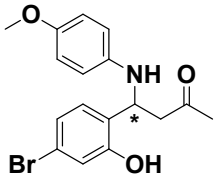
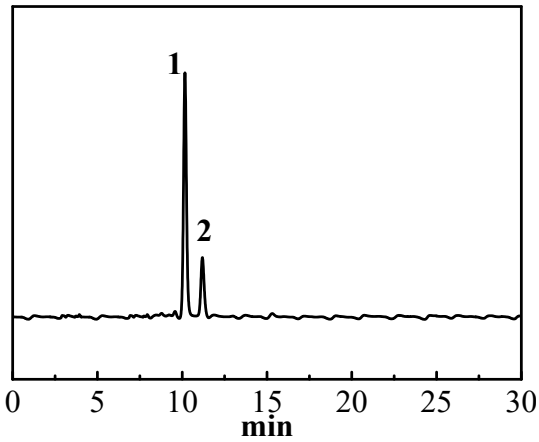
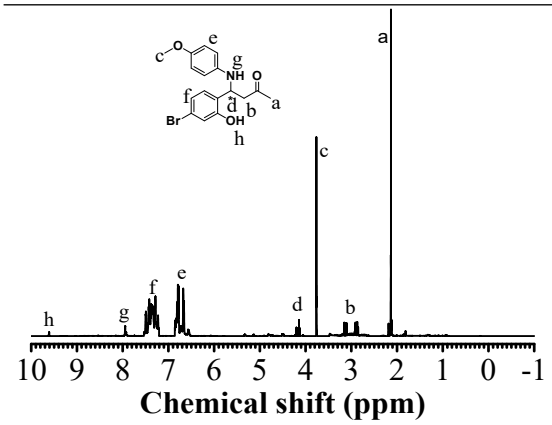


Table S16, 13b (R). The product is yellow liquid. L-Pro-L-Phe-L-Phe-OMe is the catalyst. Reaction time 30 min, enantiomeric excess: 59%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 10.158 min, tR_2 =11.192 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 2.13 (s, 3H, CH_3), 2.85 and 3.13 (m, 2H, CH_2), 3.76 (s, 3H, CH_3), 4.14 (m, 1H, CH), 6.53-6.89 (m, 4H, Ar-H), 7.18-7.55 (m, 3H, Ar-H), 7.94 (m, 1H, NH), 9.60 (m, 1H, OH).



	time/min	area
1	10.158	79.287%
2	11.192	20.713%



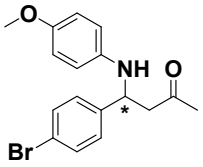
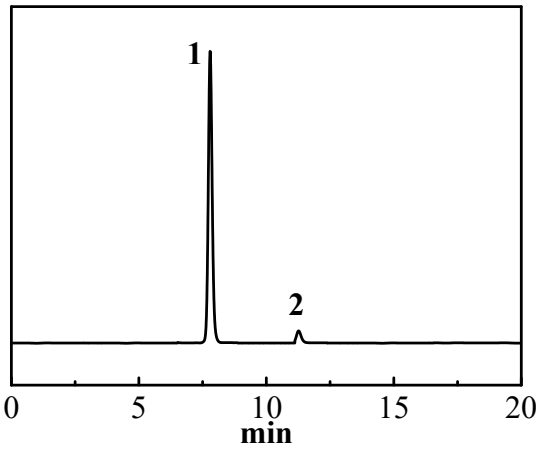
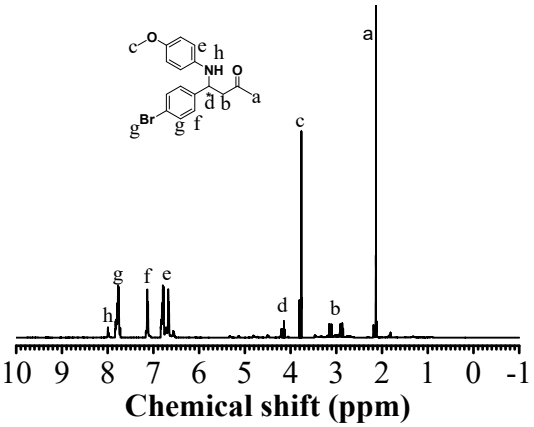


Table 5, 13c (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 20 min, enantiomeric excess: 91%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 7.792 min, tR_2 =11.267 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 2.12 (s, 3H, CH_3), 2.89 and 3.11 (m, 2H, CH_2), 3.74 (s, 3H, CH_3), 4.18 (m, 1H, CH), 6.59-6.83 (m, 4H, Ar-H), 7.11 (m, 2H, Ar-H), 7.75 (m, 2H, Ar-H), 7.97 (m, 1H, NH).



	time/min	area
1	7.792	95.248%
2	11.267	4.752%



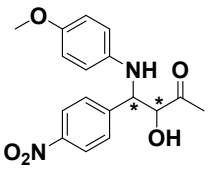
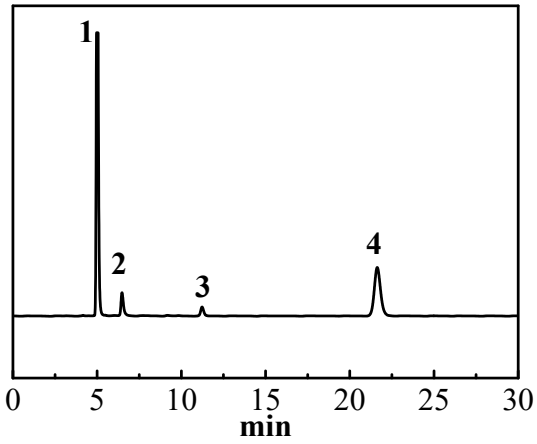
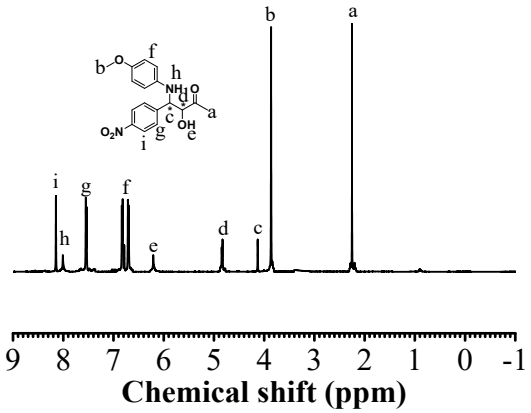


Table 6, 15a (3S, 4R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 30 min, enantiomeric excess: 85%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 5.042 min, tR_2 =6.475 min，tR_3 = 11.233 min, tR_4 =21.633 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 2.25 (s, 3H, CH_3), 3.85 (s, 3H, CH_3), 4.12 (m, 1H, CH), 4.83 (m, 1H, CH), 6.21 (m, 1H, OH), 6.57-6.85 (m, 4H, Ar-H), 7.54 (m, 2H, Ar-H), 8.00 (m, 1H, NH), 8.14 (m, 2H, Ar-H).



	time/min	area
1	5.042	64.375%
2	6.475	4.927%
3	11.233	2.606%
4	21.633	28.092%



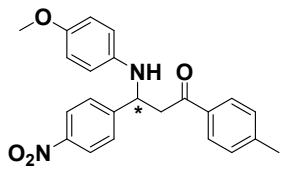
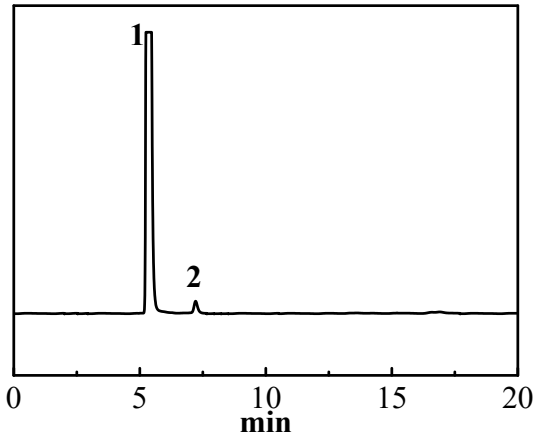
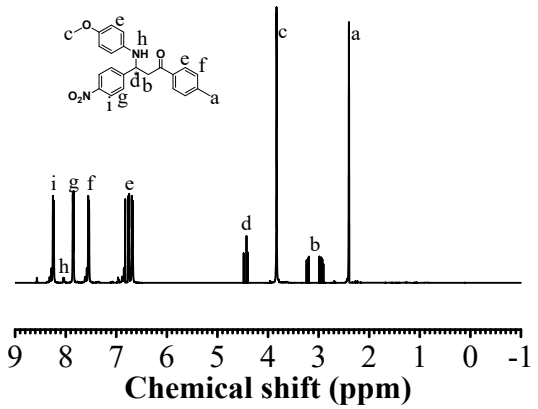


Table 6, 15b (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 20 min, enantiomeric excess: 95%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 5.450 min, tR_2 = 7.217 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 2.39 (s, 3H, CH_3) 2.94 and 3.21 (m, 2H, CH_2), 3.81 (s, 3H, CH_3), 4.43 (m, 1H, CH), 6.60-6.88 (m, 6H, Ar-H), 7.54 (m, 2H, Ar-H), 7.84 (m, 2H, Ar-H), 8.05 (m, 1H, NH), 8.25 (m, 2H, Ar-H).



	time/min	area
1	5.450	97.574%
2	7.217	2.462%



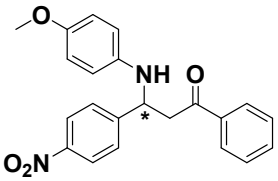
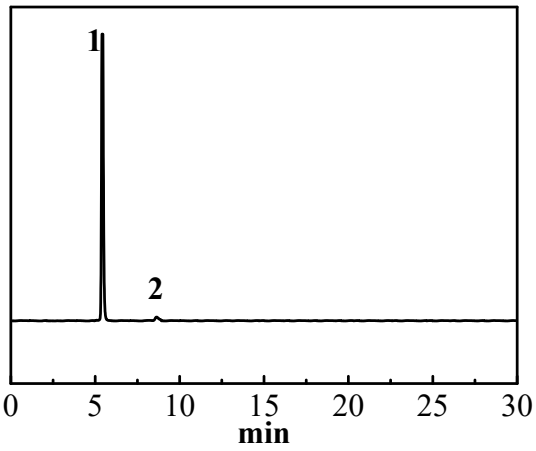
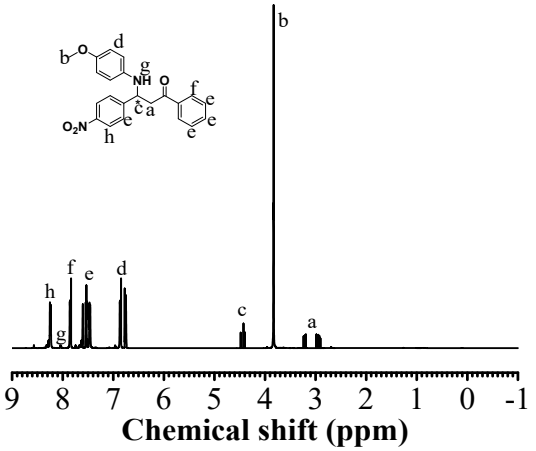


Table 6, 15c (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 30 min, enantiomeric excess: 97%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 5.425 min, tR_2 = 8.633 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 2.95 and 3.20 (m, 2H, CH_2), 3.83 (s, 3H, CH_3), 4.40 (m, 1H, CH), 6.70-6.88 (m, 4H, Ar-H), 7.40-7.65 (m, 5H, Ar-H), 7.84 (m, 2H, Ar-H), 8.05 (m, 1H, NH), 8.24 (m, 2H, Ar-H).



	time/min	area
1	5.425	98.045%
2	8.633	1.955%



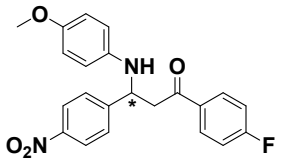
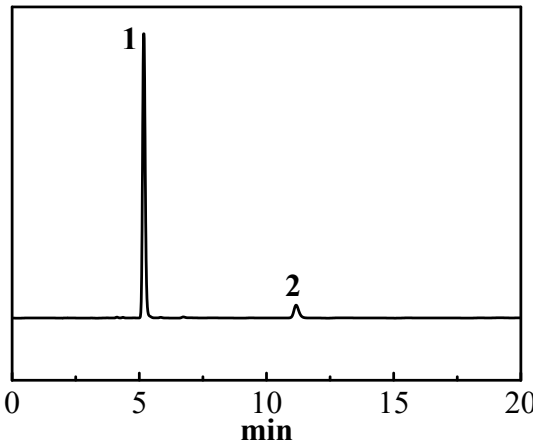


Table 6, 15d (R). The product is yellow liquid. HCP(L-Pro-L-Phe-L-Phe-OMe) is the catalyst. Reaction time 20 min, enantiomeric excess: 85%; Chiral HPLC analysis: Daicel Chiralpak AD-H, hexane/iso-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, retention time: tR_1 (major) = 5.175 min, tR_2 = 11.167 min. ^{1}H NMR (500 MHz, $CDCl_3$, δ): 2.94 and 3.20 (m, 2H, CH_2), 3.83 (s, 3H, CH_3), 4.43 (m, 1H, CH), 6.70-6.91 (m, 4H, Ar-H), 7.30 (m, 2H, Ar-H), 7.61 (m, 2H, Ar-H), 8.05 (m, 1H, OH), 8.13-8.38 (m, 4H, Ar-H).



	time/min	area
1	5.175	92.395%
2	11.167	7.605%