Supporting Information

Significant Improvement on Enantioselectivity and Diastereoselectivity of Organocatalyzed Asymmetric Aldol Reaction Using Helical Polyisocyanides Bearing Proline Pendants

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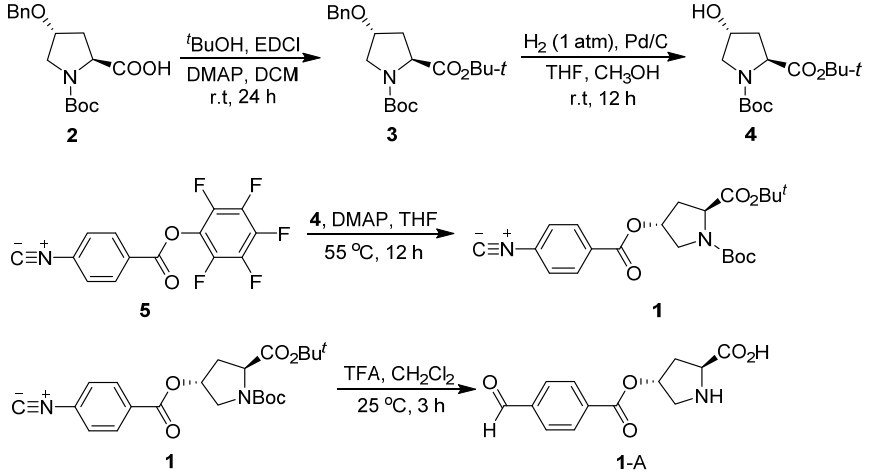
Measurements.

The ^{1}H and ^{13}C NMR spectra were recorded using a Bruker 600 MHz spectrometer {H}. Size exclusion chromatography (SEC) was performed on Waters 1515 pump and Waters 2414 differential refractive index (RI) detector (set at 40 °C) using a series of two linear TSK gel GMH_{HR}-H columns. Molecular weight (M_n) and its polydispersity (M_w/M_n) data are reported relative to polystyrene standards. The eluent was tetrahydrofuran (THF) at a flow rate of 0.8 mL/min. FT-IR spectra were recorded on Perkin-Elmer Spectrum BX FT-IR system using KBr pellets. Circular dichroism (CD) spectra were obtained in a 1.0 cm quartz cell using a JASCO J1500 spectropolarimeter. The polymer concentration was calculated on the basis of the monomer units and was 0.2 mg/mL. The UV-vis absorption spectra were recorded on a UNICO 4802 UV/vis double beam spectrophotometer. The optical rotations were measured in $CHCl_3$, THF and CH_3OH with vol. 1% of TFA at room temperature using a 10.0 cm quartz cell on a WZZ-2B polarimeter. Analytical high performance liquid chromatography (HPLC) was carried out on UltiMate 3000 and SHIMADZU LC-20AT equipment using chiral columns.

Materials.

All solvents were obtained from Sinopharm. Co. Ltd., and were purified by the standard procedures before use. All chemicals were purchased from Aladdin, Sinopharm, and Sigma-Aldrich Chemical Co. Ltd., and were used as received without further purification otherwise denoted. Methoxy phenylethynyl Pd(II) complex was prepared according to the procedures reported by our group previously, and the structure was confirmed by ^{1}H NMR spectra.[1]

Scheme S1. Synthesis of monomer **1** and **1**-A



Compound **3**. This compound was prepared according to the reported literature with slight modification.[2] Boc-Hyp(Bzl)-OH (**2**, 12.53 g, 38.98 mmol) was dissolved in dry CH_2Cl_2 (80 mL) at 0 °C. 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI, 8.23 g, 42.87 mmol), 4-dimethylaminopyridine (DMAP, 2.38 g, 19.49 mmol) and *tert*-butanol (11.55 g, 155.90 mmol) were added to this solution at 0 °C. After 2 h, the solution was warmed up to room temperature and stirred overnight. Then, the solvent was evaporated under reduced pressure. The residue was re-dissolved in ethyl acetate (EtOAc, 25 mL) and washed with water (50 mL × 2) and an aqueous solution of sodium bicarbonate ($NaHCO_3$, 50 mL × 2). The organic layer was dried over magnesium sulfate ($MgSO_4$) and purified by flash column chromatography using petroleum ether and EtOAc as eluent (v/v = 1/1) to afford **3** as a colorless oil (12.75 g, 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28–7.35 (m, 5H, ArH), 4.47–4.54 (m, 2H, CH_2), 4.23–4.30 (m, 1H, CH), 4.14–4.18 (m, 1H, CH), 3.51–3.69 (m, 2H, CH_2), 2.02–2.39 (m, 2H, CH_2), 1.44 (s, 9H, $(CH_3)_3$), 1.45 (s, 9H, CH_3).

Compound **4**. This compound was prepared followed the reported literature with slight modification.[2] 10% Pd/C (1.28 g) was first heated to 140 °C under vacuum overnight. Then, a degassed solution of **3** (12.75 g, 33.78 mmol) in THF (20 mL) and methanol (40 mL) was added to the activated Pd/C. The mixed solution was stirred at room temperature under an atmosphere of hydrogen for 12 h. The Pd/C was removed from the solution *via* filtration through celite. The filtrate was concentrated and the crude product was purified by flash column chromatography using petroleum ether and EtOAc as eluent (v/v = 3/1) to afford **4** as a colorless oil (7.75 g, 82% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.45–4.47 (t, 2H, CH), 4.10–4.32 (m, 1H, CH), 3.40–3.62 (m, 2H, CH_2), 2.02–2.30 (m, 2H, CH_2), 2.04 (s, 1H, OH), 1.46 (s, 9H, CH_3), 1.43 (s, 9H, CH_3).

Monomer **1**. Compound **5** was first prepared followed the procedure reported by our group previously and the structure was confirmed by ^{1}H NMR.[3] A mixed solution of **4** (2.31 g, 8.03 mmol), **5** (3.76 g, 12.01 mmol), DMAP (0.49 g, 4.01 mmol) in dry THF (20 mL) was stirred at 55 °C for 12 h under nitrogen. The solvent was removed by evaporation under reduced pressure, the residue was purified by silica gel chromatography using petroleum ether and EtOAc as eluent (v/v = 8/1) to afford **1** as a white solid (2.93 g, 88% yield).[4] m.p.: 216–218 °C; $[\alpha]_D^{20}$ = – 57.0 (*c* = 0.33, $CHCl_3$), ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ 8.04–8.05 (m, 2H, ArH), 7.45–7.46 (m, 2H, ArH), 5.49–5.51 (t, 1H, CH), 4.30–4.38 (m, 1H, CH), 3.64–3.85 (m, 2H, CH_2), 2.29–2.56 (m, 2H, CH_2), 1.49 (s, 9H, CH_3), 1.46 (s, 9H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ 174.10, 170.07, 167.00, 156.50, 133.59, 133.16, 129.16, 84.24, 83.17, 75.92, 61.10, 54.61, 39.35, 38.24, 30.96, 30.66. FT-IR (KBr,

cm^{-1}): 2984 ($\nu_{C\text{-}H}$), 2937 ($\nu_{C\text{-}H}$), 2128 ($\nu_{C\equiv N}$), 1746 ($\nu_{C=O}$), 1715 ($\nu_{C=O}$). MS m/z calcd for $C_{22}H_{28}N_2O_6$ $[M]^+$: 416.1947; Found: 416.1976. Anal. Calcd (%) for $C_{22}H_{28}N_2O_6$: C, 63.45; H, 6.78; N, 6.73. Found (%): C, 63.42; H, 6.79; N, 6.75.

Compound **1**-A. Monomer **1** (1.09 g, 2.62 mmol) was dissolved in dry CH_2Cl_2 (10 mL), trifluoroacetic acid (TFA, 1 mL) was slowly added to the stirring solution under an ice bath. The resulting solution was stirred for 3 h at room temperature. After the solvent was removed by evaporation under reduced pressure, the afforded residues was dissolved in 1 mL water and pH was adjusted to 6.4 by added ammonium hydroxide. After concentrated to dryness, the residue was purified by silica gel chromatography using CH_2Cl_2 and CH_3OH as eluent (v/v = 1/1) to afford **1**-A as a white solid (0.61 g, 83% yield).[2] m.p.: 68–69 °C; $[\alpha]_D^{20}$ = – 59.5 (*c* = 0.33, CH_3OH), ^1H NMR (600 MHz, CD_3OD, 25 °C): δ 8.95 (s, 0.23H, CHO), 8.36 (s, 0.77H, CHO), 8.06 (d, *J* = 8.4 Hz, 2H, ArH), 7.74 (d, *J* = 8.4 Hz, 2H, ArH), 7.32 (d, *J* = 6.0 Hz, 1H, NH), 5.63–5.64 (t, 1H, CH), 4.26–4.29 (m, 1H, CH), 3.54–3.74 (m, 2H, CH_2), 2.37–2.70 (m, 2H, CH_2). ^{13}C NMR (150 MHz, CD_3OD): δ 167.82, 163.08, 145.08, 133.19, 127.51, 121.47, 119.31, 63.11, 56.02, 53.61, 38.48. FT-IR (KBr, cm^{-1}): 3480 ($\nu_{N\text{-}H}$), 3001 ($\nu_{C\text{-}H}$), 2995 ($\nu_{C\text{-}H}$), 1714 ($\nu_{C=O}$), 1676 ($\nu_{C=O}$), 1600 ($\nu_{C\equiv N}$). MS m/z calcd for $C_{13}H_{15}N_2O_5$ $[M + H]^+$: 279.0981; Found: 279.1019. Anal. Calcd (%) for $C_{13}H_{14}N_2O_5$: C, 56.10; H, 5.08; N, 10.06. Found: C, 56.15%; H, 5.09%; N, 10.04%.

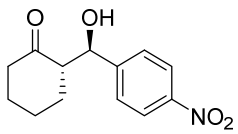
*Typical polymerization procedure for poly-**1**$_m$s:* Typical procedure for the polymerization of poly-**1**$_{150}$ is given below as an example. A 10 mL oven-dried flask was charged with monomer **1** (0.20 g, 0.48 mmol), the methoxy phenylethynyl Pd(II) catalyst (1.63 mg, 3.20

$\times 10^{-3}$ mmol), dry PhCl (2.40 mL) and a stir bar. The concentrations of monomer **1** and the Pd(II) complex were 0.2 and 0.0013 M, respectively ($[\mathbf{1}]_0/[Pd]_0 = 150$). The reaction flask was then immersed into an oil bath at 80 °C and stirred for 5 h. After cooled to room temperature, the polymerization solution was precipitated into a large amount of *n*-hexane, collected by centrifugation, and dried in vacuum at room temperature overnight to afford poly-$\mathbf{1}_{150}$ as a yellow solid (0.17 mg, 85% yield). SEC: M_n = 24.1 kDa, M_w/M_n = 1.07. ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ 7.33–7.60 (br, 2H, ArH), 5.65 (br, 2H, ArH), 4.96 (br, 1H, CH), 4.18 (br, 1H, CH), 3.51 (br, 2H, CH_2), 1.42–1.46 (br, 18H, CH_3). FT-IR (KBr, cm^{-1}): 2978 (ν_{C-H}), 2932 (ν_{C-H}), 2885 (ν_{C-H}), 1704 ($\nu_{C=O}$), 1600 ($\nu_{C=N}$).

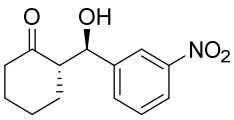
Typical procedure for poly-$\mathbf{1}_m$s-A: Typical experimental procedures for the preparation of poly-$\mathbf{1}_{150}$-A is given below as an example. Poly-$\mathbf{1}_{150}$ (0.17 g) was dissolved in dry CH_2Cl_2 (5 mL), TFA (0.5 mL) was slowly added to the stirred solution under an ice bath. The resulting solution was stirred for 10 h at room temperature. Excess acid was removed from the reaction by a flow of N_2 gas at the end of the reaction. The resulting residues were dissolved in a DMF/water (2 mL, v/v = 1/1) and dialyzed exhaustively against nanopure water (18.2 Ω) (MWCO = 3.5 kDa) and lyophilized to give deprotected poly-$\mathbf{1}_{150}$-A, or alternatively dissolved in DMF and precipitated out of solution via the addition of water. The precipitate was then filtered, washed with water and dried in the vacuum at 40 °C overnight (0.085 g, 80% yield).[2] SEC: M_n = 16.1 kDa, M_w/M_n = 1.19. ^{1}H NMR (600 MHz, DMSO-d^6, 25 °C): δ 7.22–7.56 (br, 2H, ArH), 5.72 (br, 2H, ArH), 4.09–5.11 (br, 6H, CH, CH_2). FT-IR (KBr, cm^{-1}): 3431 (ν_{N-H}), 2925 (ν_{C-H}), 2853(ν_{C-H}), 1716 ($\nu_{C=O}$), 1676 ($\nu_{C=O}$),

1600 ($\nu_{C=N}$).

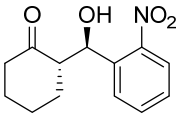
General procedure for Aldol reaction: Polymer catalyst with 20% (with respective to repeating units) loading was added to expected solvent, cyclohexanone (4.0 eq) was added to the stirring solution. After 1 h, aromatic aldehyde (1.0 eq) was added, and the resulting solution was stirred for the time indicated in Table S1 and Table 2, 3 in the main text at a specific temperature. Then, *n*-hexane was added, and the mixture was centrifuged. The solution was concentrated under reduced pressure and the crude product was purified by preparative thin layer chromatography (TLC) on silica gel using petroleum ether and EtOAc as eluent to afford the product. Characterization data for Aldol reaction products are shown below.



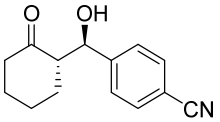
(2S 1'R,)-2-(Hydroxyl-(*p*-nitrophenyl)methyl)cyclohexan-1-one:[5] ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ 8.22 (d, 2H, J = 6.0 Hz, ArH), 7.51 (d, 2H, J = 6.0 Hz, ArH), 5.49 (s, 0.14H, *syn* CH), 4.89–4.91 (dd, J_1 = 6.0 Hz, J_2 = 3.0 Hz, 0.85H, *anti* CH), 4.07 (d, 1H, J = 3.0, OH), 1.37–2.43 (m, 9H, -$CHCH_2CH_2CH_2CH_2$-). Enantiomeric excess (*ee*): 81%, diastereomeric ratio (*dr*): 86/14, determined by HPLC analysis, Chiralpak AD-H; *n*-hexane/*i*-PrOH = 85/15 (v/v); 0.5 mL min^{-1}; 254 nm; 25 °C; t_{R1} (*syn.*) = 25.01 min, t_{R2} (*syn.*) = 27.32 min, t_{R1} (*anti.*) = 30.34 min, t_{R2} (*anti.*) = 39.60 min.



(2S, 1'R)-2-(Hydroxyl-(*m*-nitrophenyl)methyl)cyclohexan-1-one:[5] ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ 8.12–8.21 (m, 2H, ArH), 7.66–7.68 (m, 1H, ArH), 7.51–7.54 (m, 1H, ArH), 5.35 (s, 0.16H, *syn* CH), 4.89–4.90 (dd, J_1 = 3.0 Hz, J_2 = 3.0 Hz, 0.82H, *anti* CH), 4.12 (d, 1H, J = 3.0 Hz, OH), 1.28–2.64 (m, 9H, -$CHCH_2CH_2CH_2CH_2$-). *ee*: 82%, *dr*: 75/25, determined by HPLC analysis, Chiralpak IA; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.5 mL min^{-1}, 230 nm; 25 °C; t_{R1} (*syn.*) = 28.69 min, t_{R2} (*syn.*) = 33.37 min, t_{R1} (*anti.*) = 36.57 min, t_{R2} (*anti.*) = 45.09 min.

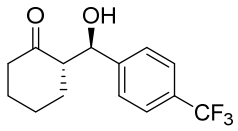


(2S, 1'R)-2-(Hydroxyl-(*o*-nitrophenyl)methyl)cyclohexan-1-one:[5] ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ 7.86 (d, J = 6.0 Hz, 1H, ArH), 7.78 (d, J = 6.0 Hz, 1H, ArH), 7.63–7.65 (t, 1H, ArH), 7.42–7.45 (t, 1H, ArH), 5.45 (d, J = 6.0 Hz, 1H, CH), 4.19 (s, 1H, OH), 1.26–2.78 (m, 9H, -$CHCH_2CH_2CH_2CH_2$-). *ee*: 90%, *dr*: >20/1, determined by HPLC analysis, Chiralpak AD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.5 mL min^{-1}; 254 nm; 25 °C; t_{R1} (*syn.*) = 18.60 min, t_{R1} (*anti.*) = 37.38 min, t_{R2} (*anti.*) = 40.29 min.

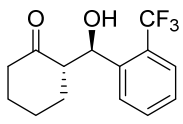


(2S, 1'R)-2-(Hydroxyl-(*p*-cyanophenyl)methyl)cyclohexan-1-one:[5] ^{1}H NMR (600 MHz,

$CDCl_3$, 25 °C): δ 7.41 (d, J = 6.0 Hz, 1H, ArH), 7.37 (d, J = 12.0 Hz, 1H, ArH), 7.08 (d, J = 12.0 Hz, 1H, ArH), 6.98 (d, J = 12.0 Hz, 1H, ArH), 5.61–5.63 (t, 0.23H, *syn* CH), 5.33 (d, J = 6.0 Hz, 0.76H, *anti* CH), 4.46 (d, J = 6.0 Hz, 1H, OH), 1.28–3.40 (m, 9H, -$CHCH_2CH_2CH_2CH_2$-). *ee*: 77%, *dr*: 77/23, determined by HPLC analysis, Chiralpak AD-H; *n*-hexane/*i*-PrOH = 85/15 (v/v); 0.5 mL min^{-1}; 230 nm; 25 °C; t_{R1} (*syn.*) = 20.66 min, t_{R2} (*syn.*) = 26.21 min, t_{R1} (*anti.*) = 23.29 min, t_{R2} (*anti.*) = 32.23 min.



(2S, 1'R)-2-(Hydroxyl-(*p*-trifluoromethylphenyl)methyl)cyclohexan-1-one:[6] ^1H NMR (600 MHz, $CDCl_3$, 25 °C): 7.59–7.61 (m, 2H, ArH), 7.42–7.45 (m, 2H, ArH), 5.44 (s, 0.22H, *syn* CH), 4.83–4.85 (dd, J_1 = 3.0 Hz, J_2 = 6.0 Hz, 0.72H, *trans* CH), 4.03 (d, 2H, J = 3.0 Hz, OH), 1.25–3.10 (m, 9H, -$CH_2CH_2CH_2CH_2$-). *ee*: 87%, *dr*: 88/12, determined by HPLC analysis, Chiralpak AD-H; *n*-hexane/*i*-PrOH = 95/5 (v/v); 0.8 mL min^{-1}; 210 nm; 25 °C; t_{R1} (*syn.*) = 11.44 min, t_{R2} (*syn.*) = 13.75 min, t_{R1} (*anti.*) = 19.43 min, t_{R2} (*anti.*) = 24.39 min.



(2S, 1'R)-2-(Hydroxyl-(*o*-trifluoromethyl)methyl) cyclohexan-1-one:[7] ^1H NMR (600 MHz, $CDCl_3$, 25 °C): 7.71 (d, J = 6.0 Hz, 1H, ArH), 7.59–7.65 (m, 2H, ArH), 7.39–7.42

(t, 1H, ArH), 5.30 (d, J = 12.0 Hz, 1H), 4.00 (s, 1H), 1.25–2.76 (m, 9H, -$CH_2CH_2CH_2CH_2$-). *ee*: 95%, *dr*: >20/1, determined by HPLC analysis, Chiralpak AD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.5 mL min^{-1}; 254 nm; 25 °C; t_{R1} (*anti.*) = 24.55 min, t_{R2} (*anti.*) = 25.92 min.

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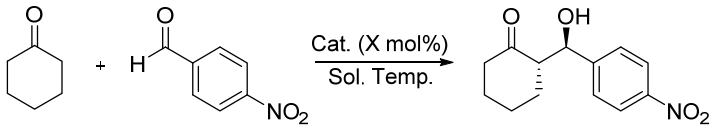
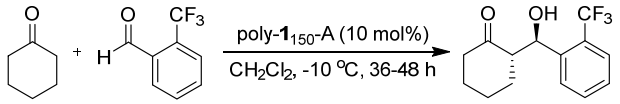
Table S1. Optimization of the reaction conditions for Aldol reaction of 4-nitrobenzaldehyde with cyclohexanone catalyzed by **1**-A and poly-**1**$_m$-A.[a]



Run	Solvent	Temp.	Cat.	X	*t* (h)	Yield[b]	anti./syn[c]	*ee*[c]
1	THF	r.t.	**1-A**	20	10	85	75/25	17
2	DMF	r.t.	**1-A**	20	10	86	85/15	14
3	CH_2Cl_2	r.t.	poly-**1**$_{50}$-A	20	12	80	83/17	57
4	CH_2Cl_2	r.t.	poly-**1**$_{75}$-A	20	12	79	83/17	66
5	CH_2Cl_2	r.t.	poly-**1**$_{100}$-A	20	12	81	85/15	71
6	CH_2Cl_2	r.t.	poly-**1**$_{150}$-A	20	12	80	84/16	72
7	CH_2Cl_2	r.t.	poly-**1**$_{200}$-A	20	12	81	82/18	71
8	CH_2Cl_2	r.t.	poly-**1**$_{150}$-A	30	12	83	85/15	72
9	CH_3OBu-*t*	r.t.	poly-**1**$_{150}$-**A**	20	12	67	60/40	71
10	PhCl	r.t.	poly-**1**$_{150}$-**A**	20	12	70	75/25	61
11	EtOAc	r.t.	poly-**1**$_{150}$-**A**	20	12	73	72/28	62
12	glycol	r.t.	poly-**1**$_{150}$-**A**	20	48	n.d[d].	--	--
13	cyclohexanone	r.t.	poly-**1**$_{150}$-**A**	20	12	83	63/37	57

[a]Unless otherwise specified, all reactions were carried out with 4-nitrobenzaldehyde (0.2 mmol), cyclohexanone (0.8 mmol) in specific solvent (1.0 mL). [b]Yield of isolated products. [c]*ee* values are reffered to the major isomer determined by HPLC analysis using a chiral stationary phase. [d]Not detected.

Table S2. Yield and *ee* values of the reaction for 2-trifluoromethylbenzaldehyde and cyclohexanone catalyzed by recycled poly-**1**$_{150}$-A[a]



Cycle	Yield[b] (%)	anti./syn.[c]	*ee* (%)[c]	Recovery (%)
1	65	>20/1	95	92
2	63	>20/1	94	91
3	63	>20/1	94	90
4[d]	58	>20/1	92	88

[a]Unless otherwise denoted, all reactions were carried out with 2-trifluoromethylbenzaldehyde (0.2 mmol), cyclohexanone (0.8 mmol) in CH_2Cl_2 (1.0 mL). [b]Yield of isolated products. [c]The *ee* values are referred to the major isomer determined by HPLC analysis using a chiral stationary phase. [d]The reaction time of the forth recycle was 48 h.

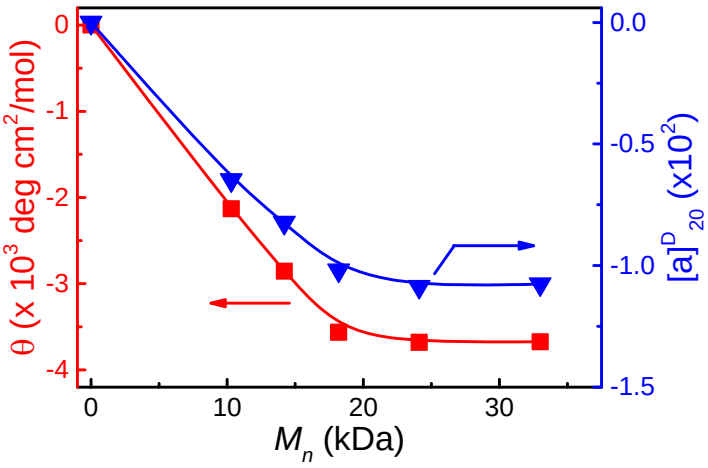


Figure S1. Plot of ellipticity and optical rotation values of poly-**1**$_m$s with the M_n.

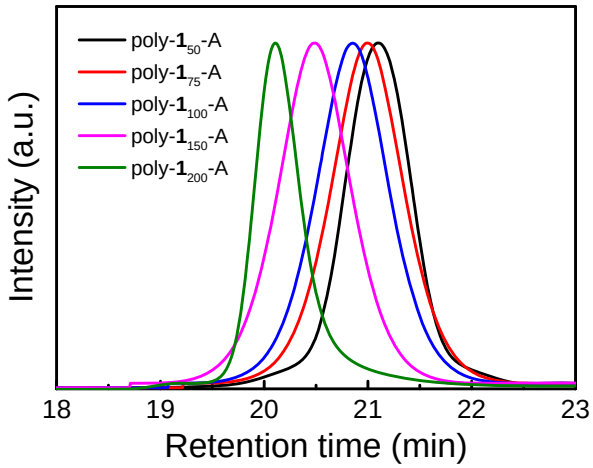


Figure S2. Size exclusion chromatograms of poly-**1**$_{50}$-A, poly-**1**$_{75}$-A, poly-**1**$_{100}$-A, poly-**1**$_{150}$-A, and poly-**1**$_{200}$-A . SEC condition: eluent = THF, temperature = 40 °C.

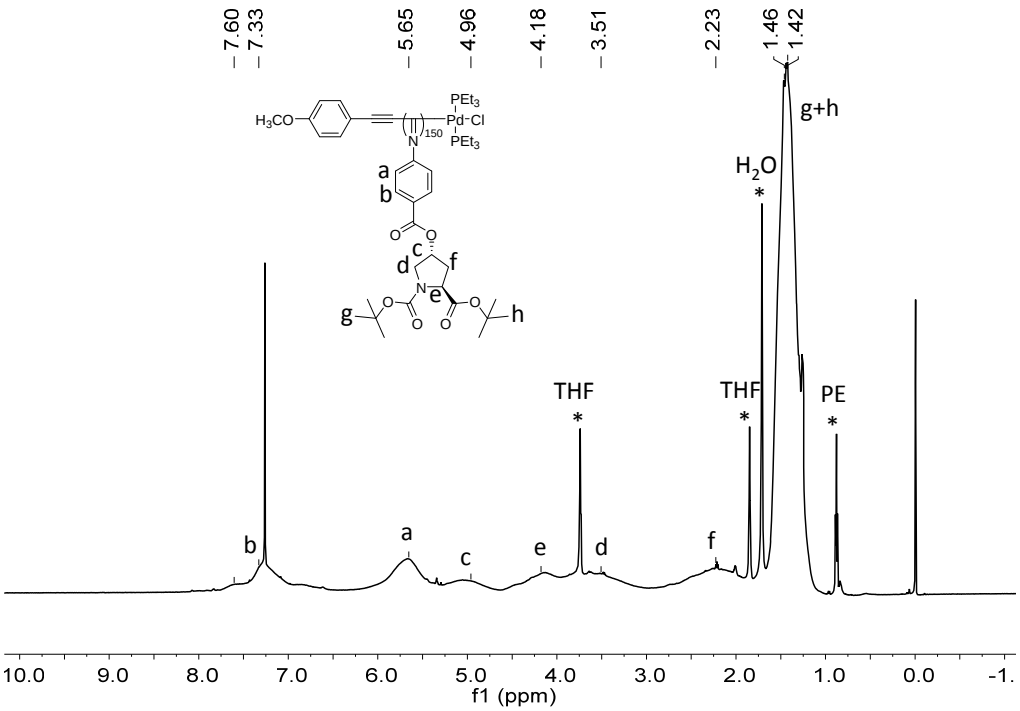


Figure S3. ^{1}H NMR (600 MHz) spectrum of poly-**1**$_{150}$ measured in $CDCl_3$ at 25 °C.

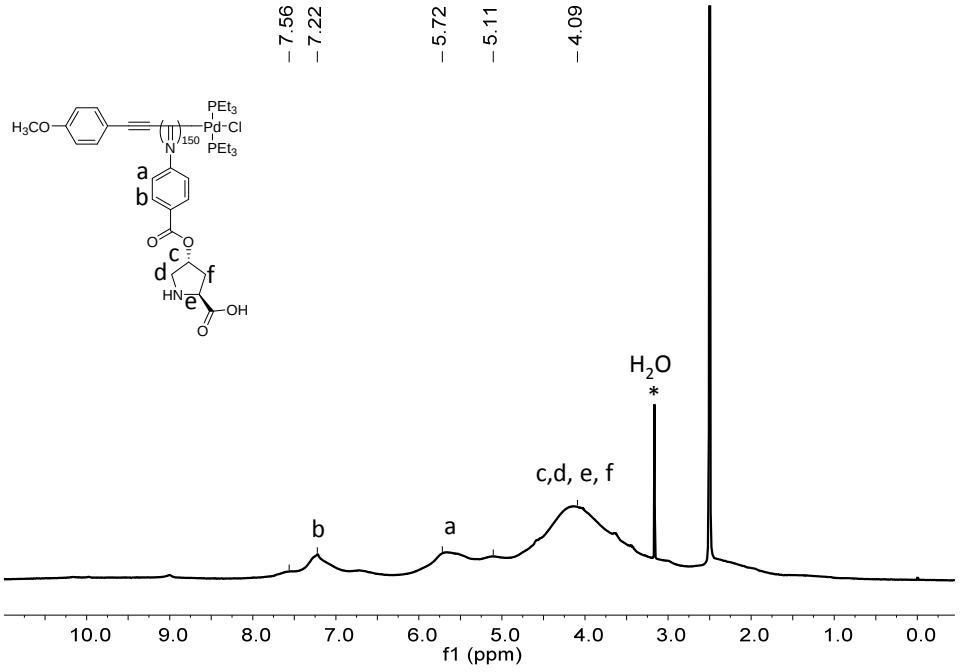


Figure S4. ^{1}H NMR (600 MHz) spectrum of poly-**1**$_{150}$-A measured in DMSO-d^6 at 25 °C.

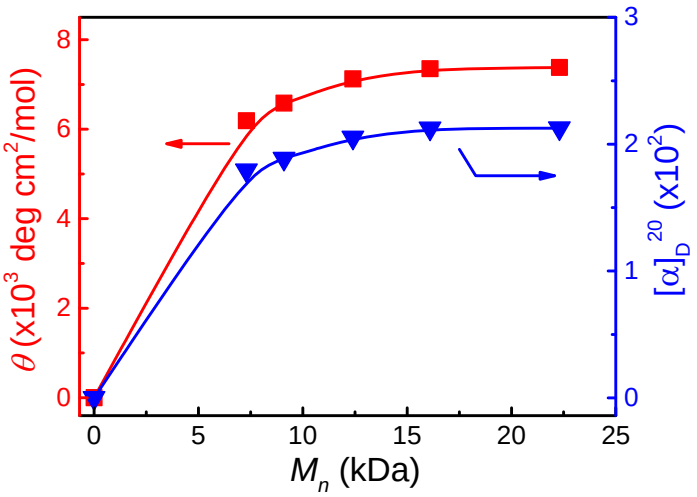


Figure S5. Plot of ellipticity and optical rotation values of poly-**1**$_m$-As with the M_n.

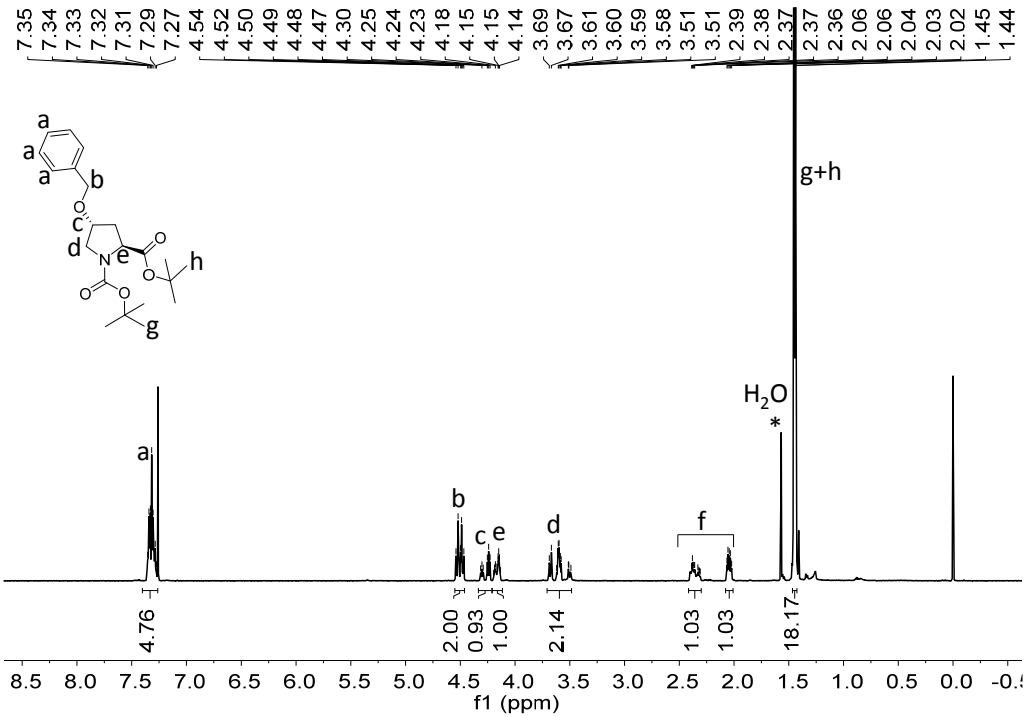


Figure S6 . ^{1}H NMR (600 MHz) spectrum of **3** measured in $CDCl_3$ at 25 °C.

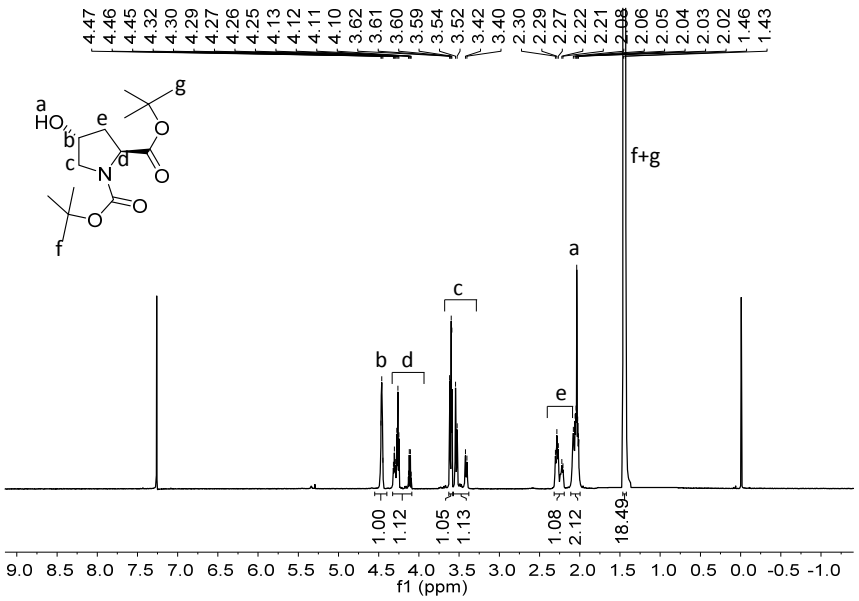


Figure S7 . ^{1}H NMR(600 MHz) spectrum of **4** measured in $CDCl_3$ at 25 °C.

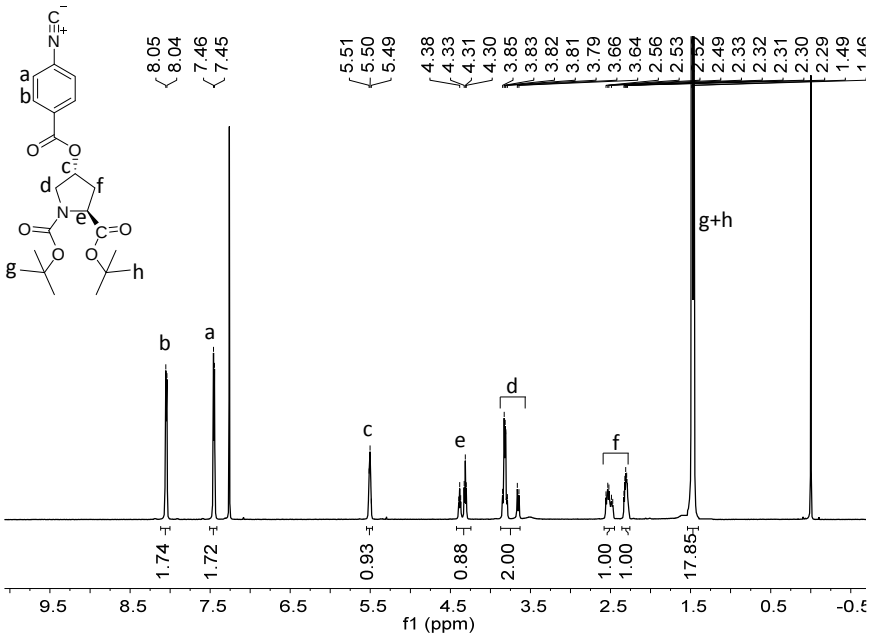


Figure S8 . ^{1}H NMR (600 MHz) spectrum of monomer **1** measured in $CDCl_3$ at 25 °C.

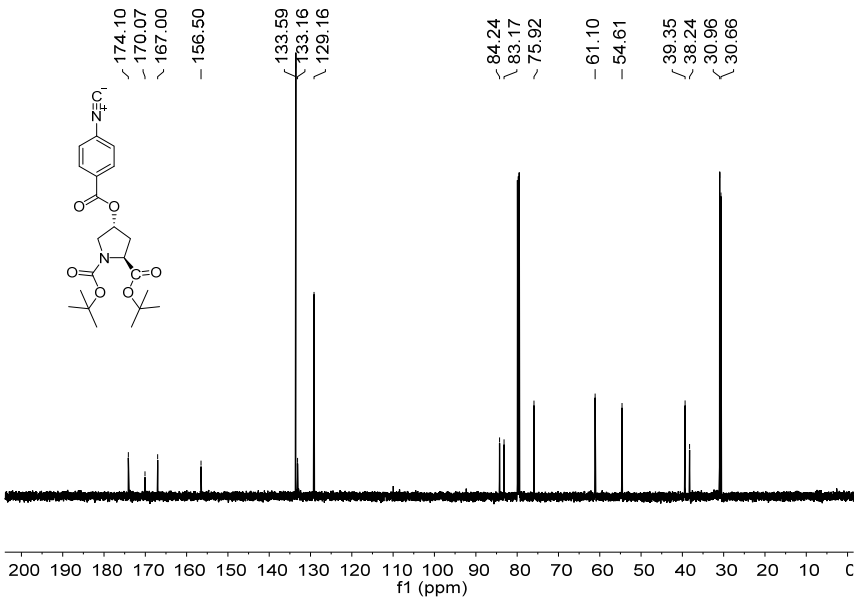


Figure S9 . ^{13}C NMR (150 MHz) spectrum of monomer **1** measured in $CDCl_3$ at 25 °C.

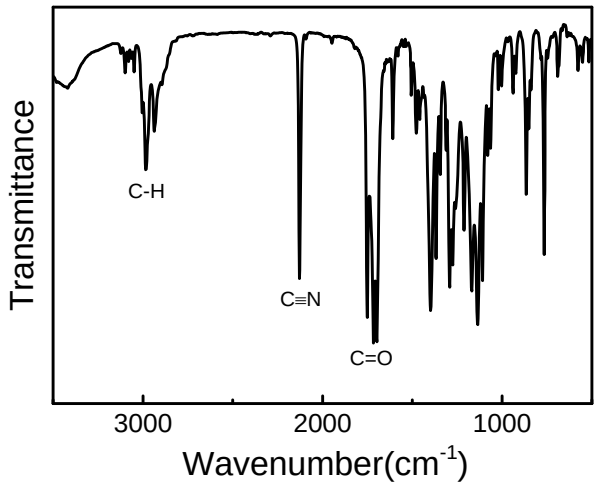


Figure S10 . FT-IR spectrum of monomer **1** measured at 25 °C using KBr pellets.

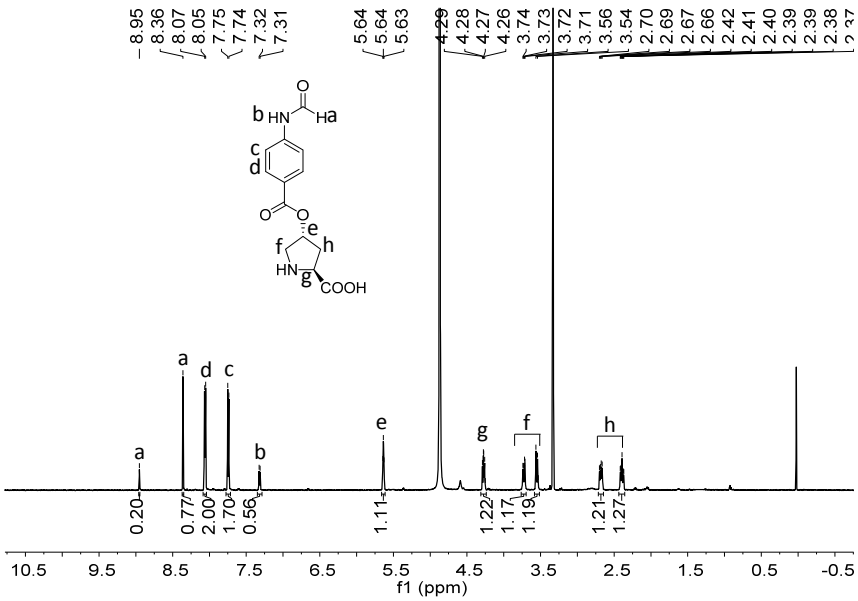


Figure S11. ^{1}H NMR (600 MHz) spectrum of **1-**A measured in $CDCl_3$ at 25 °C.

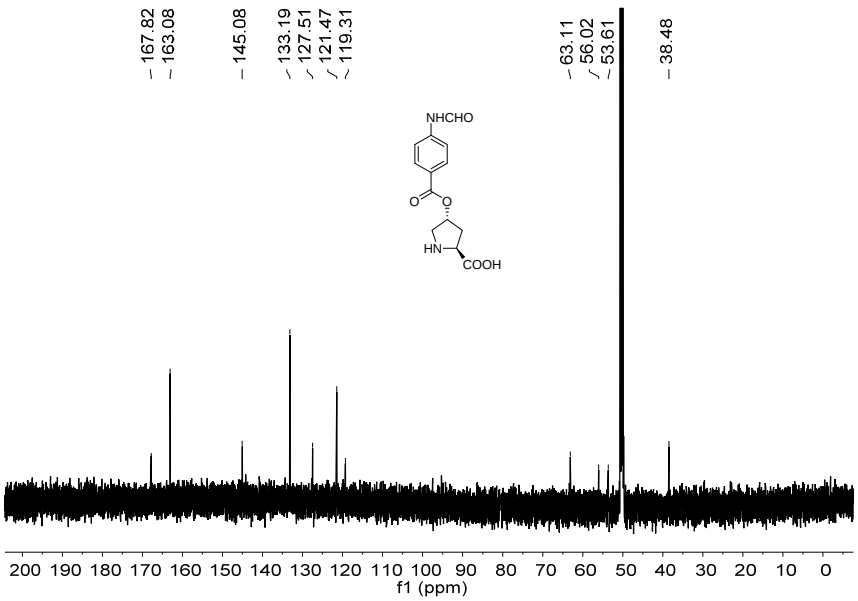


Figure S12. ^{13}C NMR (150 MHz) spectrum of **1-A** measured in CD_3OD at 25 °C.

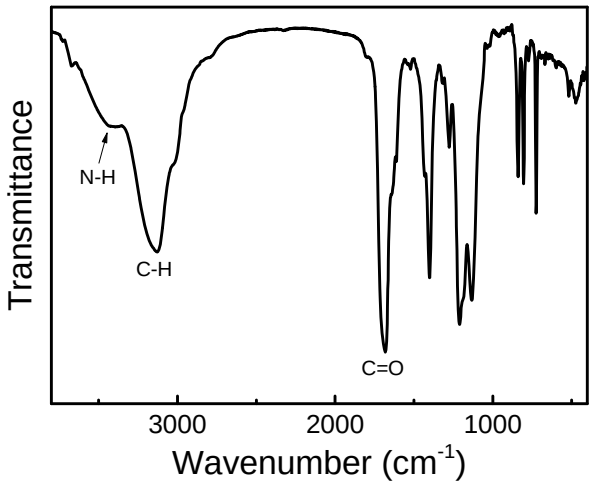


Figure S13. FT-IR spectrum of **1**-A measured at 25 °C using KBr pellets.

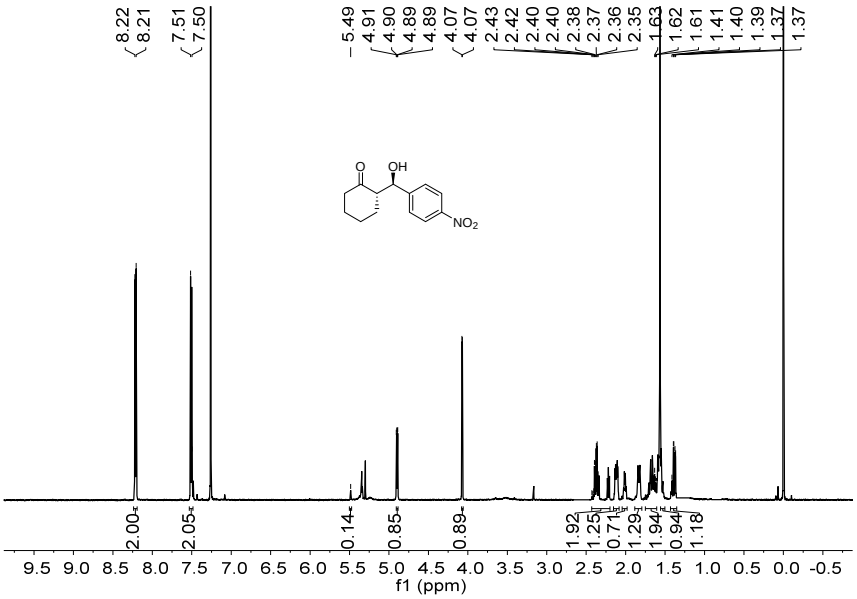


Figure S14. ^{1}H NMR (600 MHz) spectrum of (2S,1'R)-2-(hydroxyl-(*p*-nitrophenyl)methyl) cyclohexan-1-one measured in $CDCl_3$ at 25 °C.

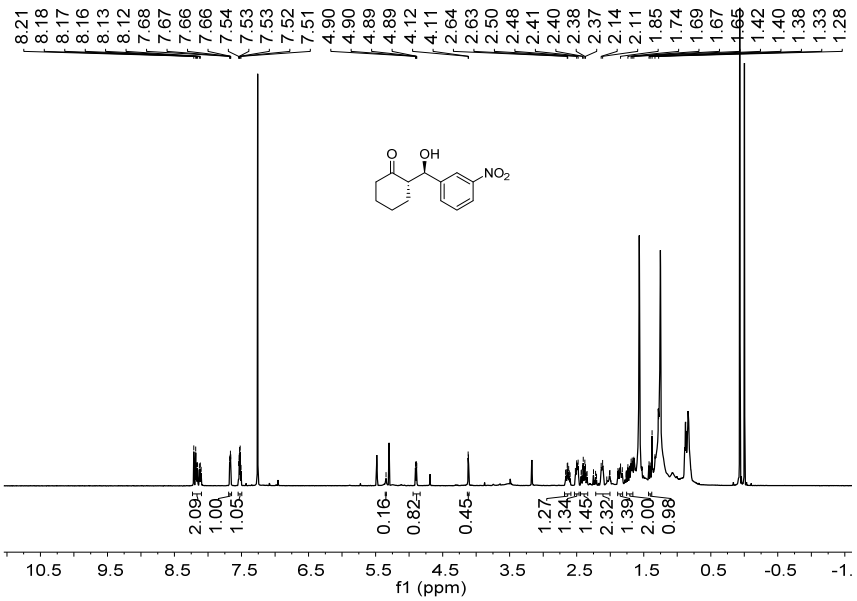


Figure S15. ^{1}H NMR (600 MHz) spectrum of (2S,1'R)-2-(hydroxyl-(*m*-nitrophenyl)methyl) cyclohexan-1-one measured in $CDCl_3$ at 25 °C.

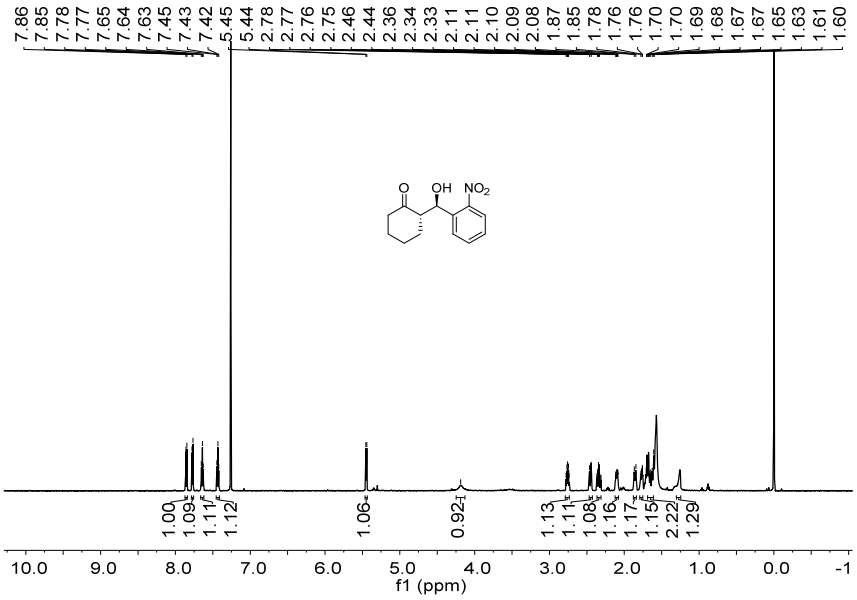


Figure S16. ^{1}H NMR (600 MHz) spectrum of (2S,1'R)-2-(hydroxyl-(*o*-nitrophenyl)methyl) cyclohexan-1-one measured in $CDCl_3$ at 25 °C.

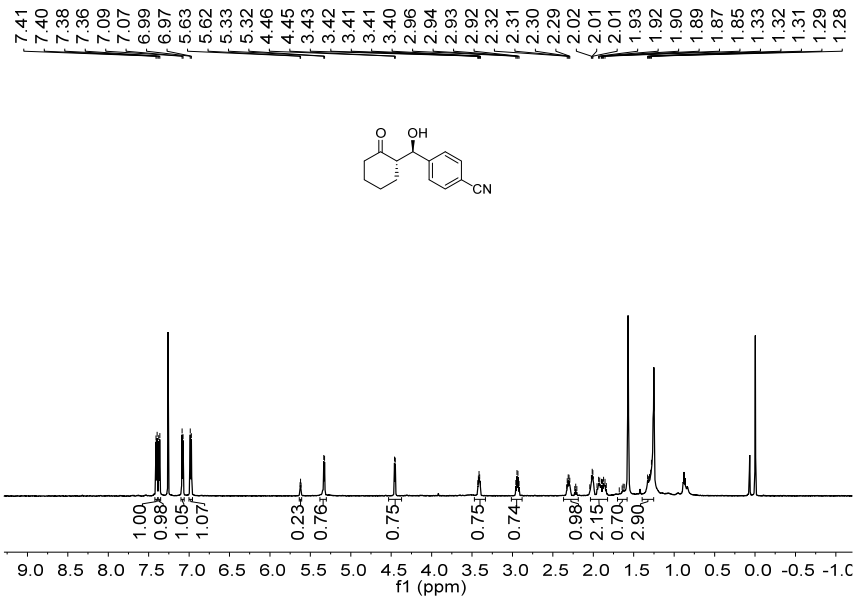


Figure S17. ^{1}H NMR (600 MHz) spectrum of (2S,1'R)-2-(hydroxyl-(*p*-cyanophenyl)methyl) cyclohexan-1-one measured in $CDCl_3$ at 25 °C.

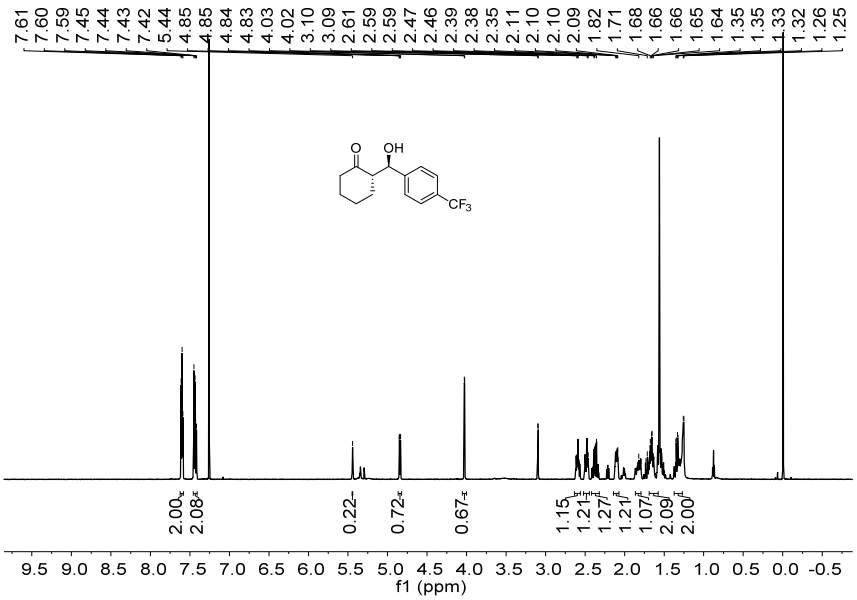


Figure S18. ^{1}H NMR (600 MHz) spectrum of (2S,1'R)-2-(hydroxyl-(*p*-trifluoromethylphenyl)methyl) cyclohexan-1-one measured in $CDCl_3$ at 25 °C.

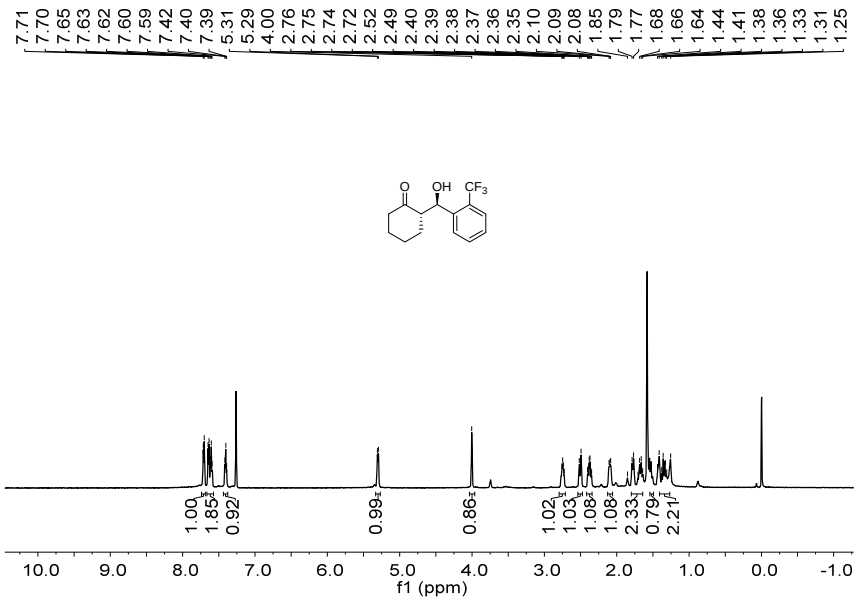
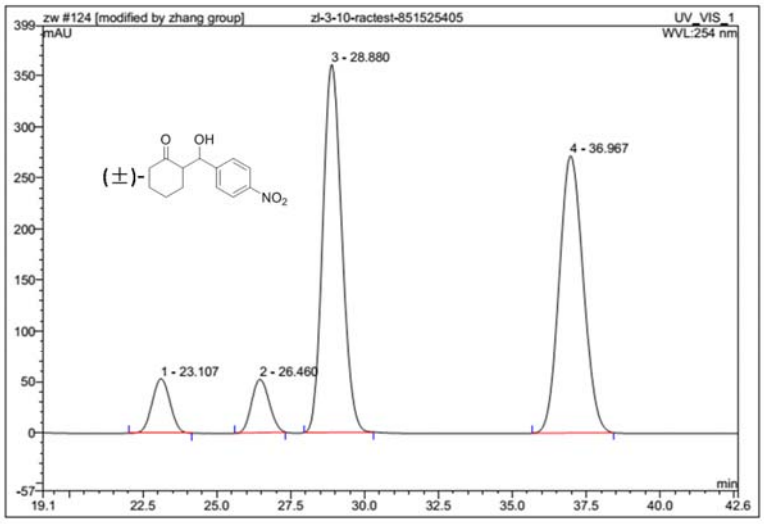
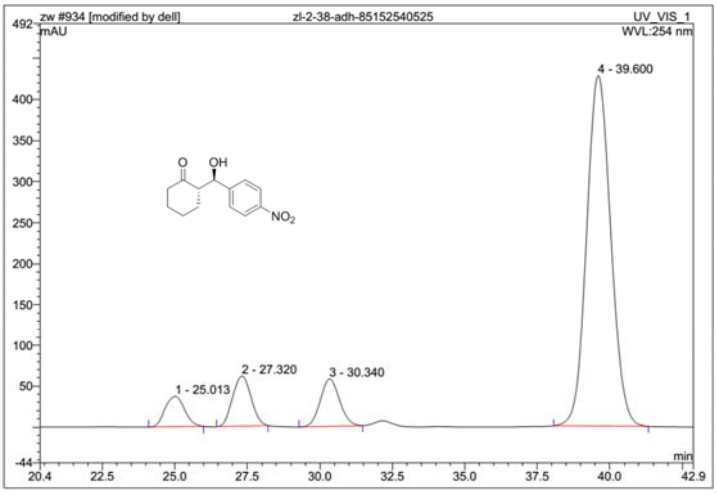


Figure S19. ^{1}H NMR (600 MHz) spectrum of (2S,1'R)-2-(hydroxyl-(*o*-trifluoromethylphenyl)methyl) cyclohexan-1-one measured in $CDCl_3$ at 25 °C.



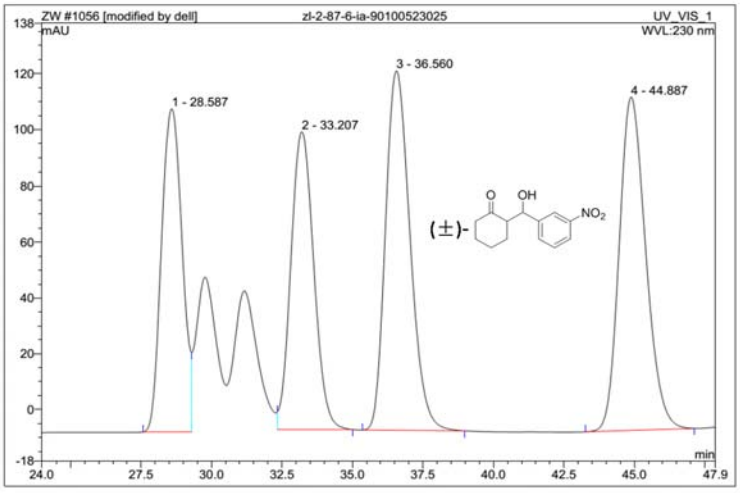
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	23.11	n.a.	53.326	37.468	6.26	n.a.	BMB*
2	26.46	n.a.	52.270	36.035	6.02	n.a.	BMB*
3	28.88	n.a.	360.898	268.796	44.94	n.a.	BMB*
4	36.97	n.a.	272.066	255.869	42.78	n.a.	BMB*
Total:			738.561	598.168	100.00	0.000	

Figure S20. HPLC curve of racemic 2-(hydroxyl-(*p*-nitrophenyl)methyl) cyclohexan-1-one (Chiralpak AD-H; *n*-hexane/*i*-PrOH = 85/15 (v/v); 0.5 mL min^{-1}; 254 nm; 25 °C).



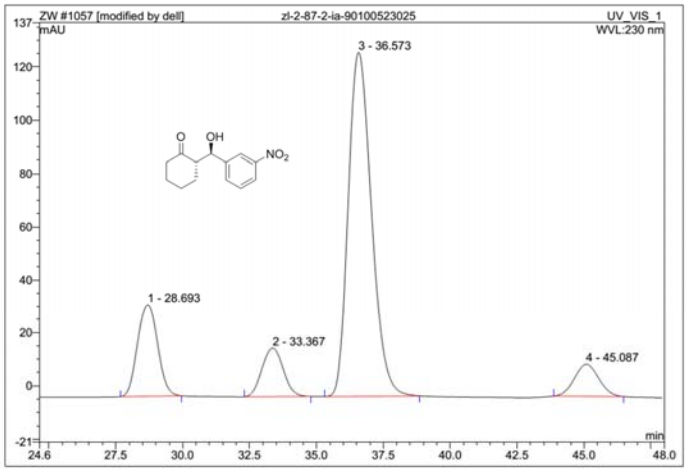
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	25.01	n.a.	36.903	28.704	5.41	n.a.	BMB*
2	27.32	n.a.	61.145	45.064	8.49	n.a.	BMB*
3	30.34	n.a.	57.835	44.412	8.37	n.a.	BMB*
4	39.60	n.a.	427.806	412.620	77.74	n.a.	BMB*
Total:			583.689	530.799	100.00	0.000	

Figure S21. HPLC curve of (2S,1'R)-2-(hydroxyl-(*p*-nitrophenyl)methyl) cyclohexan-1-one (Chiralpak AD-H; *n*-hexane/*i*-PrOH = 85/15 (v/v); 0.5 mL min^{-1}; 254 nm; 25 °C).



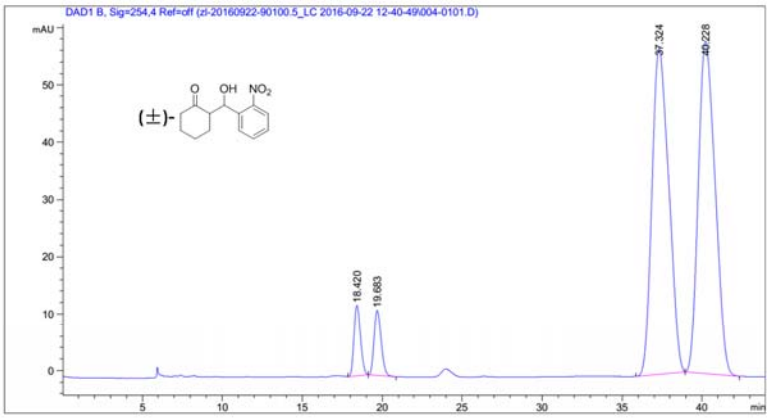
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	28.59	n.a.	115.466	97.972	21.42	n.a.	BM *
2	33.21	n.a.	106.317	100.116	21.89	n.a.	MB*
3	36.56	n.a.	128.350	129.411	28.30	n.a.	BMB*
4	44.89	n.a.	119.010	129.853	28.39	n.a.	BMB*
Total:			469.143	457.352	100.00	0.000	

Figure S22. HPLC curve of racemic 2-(hydroxyl-(*m*-nitrophenyl)methyl) cyclohexan-1-one (Chiralpak IA; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.5 mL min^{-1}; 230 nm; 25 °C).



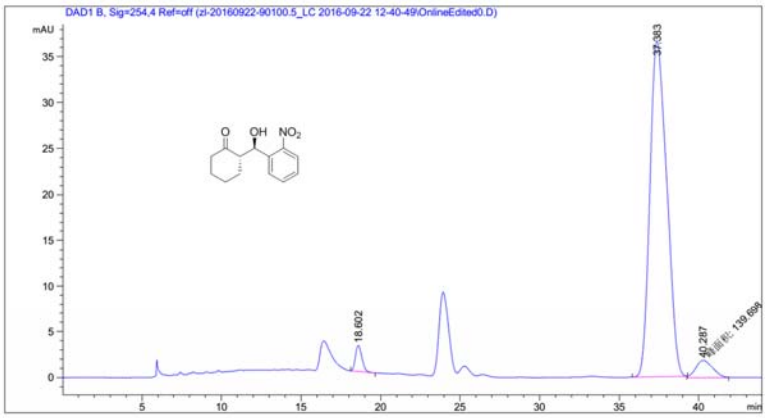
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	28.69	n.a.	34.586	29.987	15.80	n.a.	BMB*
2	33.37	n.a.	18.223	16.791	8.85	n.a.	BMB*
3	36.57	n.a.	129.405	130.279	68.65	n.a.	BMB*
4	45.09	n.a.	12.027	12.706	6.70	n.a.	BMB*
Total:			194.241	189.764	100.00	0.000	

Figure S23. HPLC curve of (2S,1'R)-2-(hydroxyl-(*m*-nitrophenyl)methyl) cyclohexan-1-one (Chiralpak IA; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.5 mL min^{-1}; 230 nm; 25 °C).



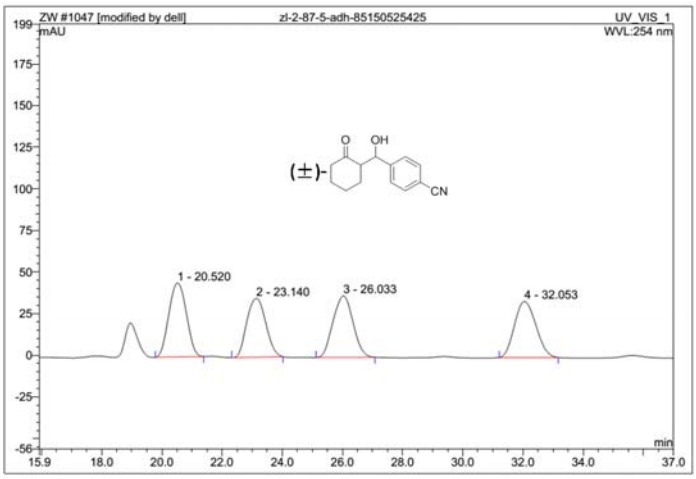
No.	Ret. Time min	Type	Width min	Area mAU*s	Height mAU	Rel. Area %
1	18.420	BB	0.4392	351.99307	12.39913	3.8651
2	19.683	BB	0.4751	352.78204	11.46119	3.8738
3	37.324	BB	1.0785	4156.01807	57.01313	45.6359
4	40.228	BB	1.0916	4246.10449	58.16722	46.6251
Total:				9106.89767	139.04067	

Figure S24. HPLC curve of racemic 2-(hydroxyl-(*o*-nitrophenyl)methyl) cyclohexan-1-one (Chiralpak AD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.5 mL min^{-1}; 254 nm; 25 °C).



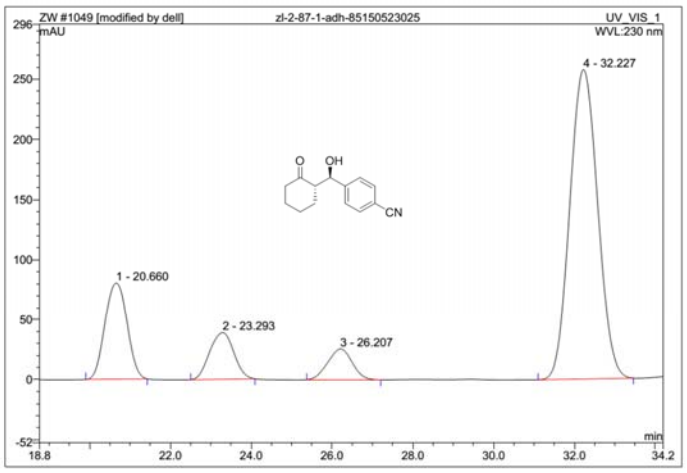
No.	Ret. Time min	Type	Width	Area mAU*s	Height mAU	Rel. Area %
1	18.602	BB	0.4315	80.31540	2.82678	2.7596
2	37.383	BB	1.0811	2690.40234	36.62058	92.4405
3	40.287	MM	1.2360	139.69821	1.88375	4.7999
Total:				2910.41595	41.33110	

Figure S25. HPLC curve of (2S,1'R)-2-(hydroxyl-(*o*-nitrophenyl)methyl) cyclohexan-1-one (Chiralpak AD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.5 mL min^{-1}; 254 nm; 25 °C).



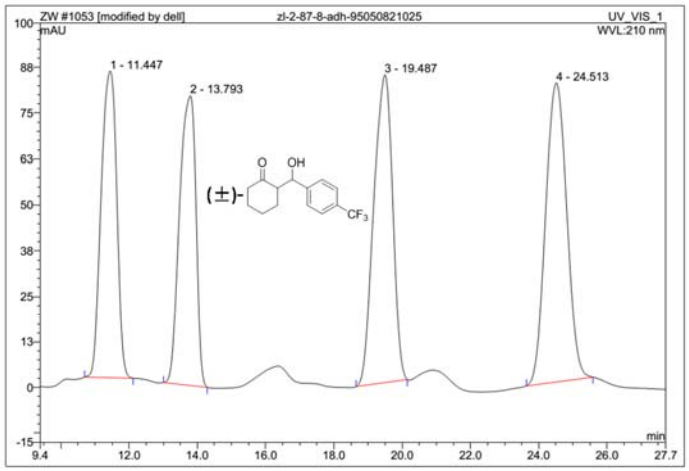
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	20.52	n.a.	44.518	30.024	26.81	n.a.	BMB*
2	23.14	n.a.	35.439	25.807	23.04	n.a.	BMB*
3	26.03	n.a.	37.068	28.432	25.39	n.a.	BMB*
4	32.05	n.a.	33.755	27.736	24.76	n.a.	BMB*
Total:			150.779	112.000	100.00	0.000	

Figure S26. HPLC curve of racemic 2-(hydroxyl-(*p*-cyanophenyl)methyl) cyclohexan-1-one (Chiralpak AD-H; *n*-hexane/*i*-PrOH = 85/15 (v/v); 0.5 mL min^{-1}; 230 nm; 25 °C).



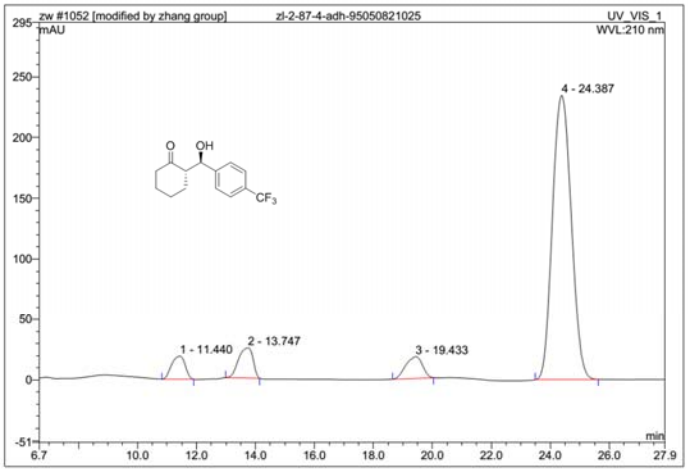
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	20.66	n.a.	80.522	50.928	16.89	n.a.	BMB*
2	23.29	n.a.	38.751	26.769	8.88	n.a.	BMB*
3	26.21	n.a.	25.676	17.947	5.95	n.a.	BMB*
4	32.23	n.a.	257.601	205.839	68.28	n.a.	BMB*
Total:			402.551	301.482	100.00	0.000	

Figure S27. HPLC curve of (2S,1'R)-2-(hydroxyl-(*p*-cyanophenyl)methyl) cyclohexan-1-one (Chiralpak AD-H; *n*-hexane/*i*-PrOH = 85/15 (v/v); 0.5 mL min^{-1}; 230 nm; 25 °C).



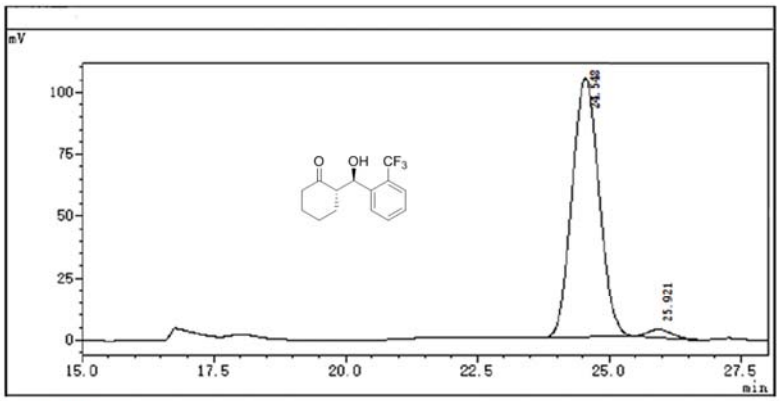
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.45	n.a.	83.761	44.311	22.11	n.a.	BMB*
2	13.79	n.a.	79.149	43.910	21.91	n.a.	BMB*
3	19.49	n.a.	84.069	53.702	26.79	n.a.	BMB*
4	24.51	n.a.	81.697	58.507	29.19	n.a.	BMB*
Total:			328.676	200.430	100.00	0.000	

Figure S28. HPLC curve of racemic 2-(hydroxyl-(*p*-trifluoromethylphenyl)methyl) cyclohexan-1-one (Chiralpak AD-H; *n*-hexane/*i*-PrOH = 95/5 (v/v); 0.8 mL min^{-1}; 210 nm; 25 °C).



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.44	n.a.	19.010	10.114	4.82	n.a.	BMB*
2	13.75	n.a.	24.798	14.063	6.70	n.a.	BMB*
3	19.43	n.a.	17.983	11.824	5.64	n.a.	BMB*
4	24.39	n.a.	234.537	173.751	82.84	n.a.	BMB*
Total:			296.328	209.751	100.00	0.000	

Figure S29. HPLC curve of (2S,1'R)-2-(hydroxyl-(*p*-trifluoromethylphenyl)methyl) cyclohexan-1-one (Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5 (v/v); 0.8 mL min^{-1}; 210 nm; 25 °C).

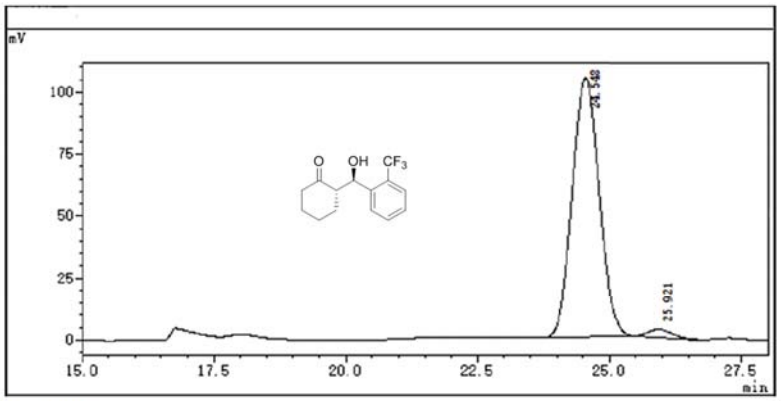


Peak table

Detector A 254 nm

No.	Ret. Time	Area	Height	Concentration	Concentration unit	Mark
1	24.548	3715592	104257	97.376		
2	25.921	100131	3207	2.624		V
Total		3815723	107464			

Figure S30. HPLC curve of racemic 2-(hydroxyl-(*o*-trifluoromethylphenyl)methyl) cyclohexan-1-one (Chiralpak AD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.5 mL min^{-1}; 254 nm; 25 °C).



Peak table

Detector A 254 nm

No.	Ret. Time	Area	Height	Concentration	Concentration unit	Mark
1	24.548	3715592	104257	97.376		
2	25.921	100131	3207	2.624		V
Total		3815723	107464			

Figure S32. HPLC curve of (2S,1'R)-2-(hydroxyl-(*o*-trifluoromethylphenyl)methyl) cyclohexan-1-one (Chiralpak AD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.5 mL min^{-1}; 254 nm; 25 °C).