# Optically active helical polymers bearing cinchona alkaloid pendants: an efficient chiral organocatalyst for asymmetric Henry reaction

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## Measurements

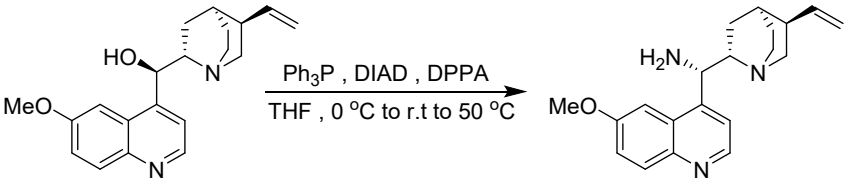
The NMR spectra were recorded using a Bruker 600 MHz spectrometer {H}. Size exclusion chromatography (SEC) was performed on Waters 1515 pump and Waters 2414 differential refractive index (RI) detector (set at 40 °C) using a series of two linear TSK gel GMHHR-H columns. Molecular weight ($M_n$) and its dispersity ($M_w/M_n$) were 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 FTIR system using KBr pellets. Circular dichroism (CD) spectra were obtained in a 1.0 or 0.1 cm quartz cell using a JASCO J1500 spectropolarimeter. High performance liquid chromatography (HPLC) with UV-vis detector was carried out on a JASCO Pu-418 pump with JASCO UV-4070 detectors, using *n*-hexane/*i*-PrOH as fluent on chiral column.

## 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. The Pd(II) catalyst was prepared according to the procedures reported by our group previously, and the structure was confirmed by $^1$H NMR.[1]

## Synthetic procedures

***Scheme S1.*** Synthesis of compound **2**

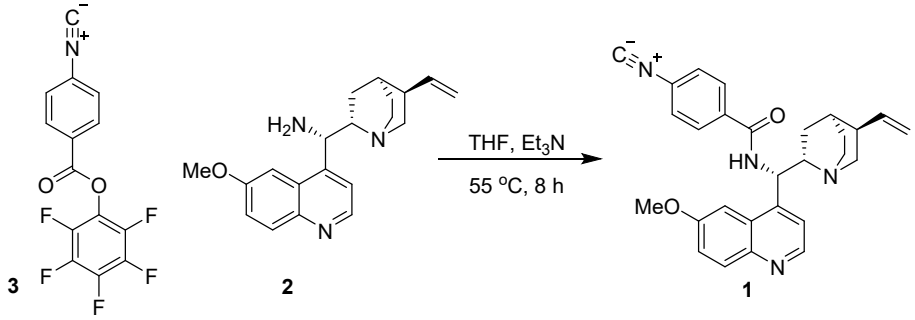



**2**

***Synthesis of compound 2***: Compound **2** was synthesis outlined in Scheme S1 according to the literature with slight modification.[2] Quinine (2.0 g, 6.33 mmol), $Ph_3P$ (2.2 g, 8.43 mmol) and anhydrous tetrahydrofuran (THF, 30 mL) were added in a 100 mL round-bottom flask under $N_2$ atmosphere, and the reaction mixture was cooled to 0 °C. Diisopropyl azodicarboxylic acid (DIAD) (1.55 mL,7.87 mmol) was added, followed by diphenylphos azide (DPPA) (1.65 mL, 7.66 mmol) in anhydrous THF (13.0 mL). The mixture was then heated to room temperature and stirred for 16 h, at which point the mixture was heated at 50 °C for another 2 h.

Then $Ph_3P$ (2.4 g, 8.96 mmol) was added and the mixture was continued stirring at 50 °C for 2 h. After cooling the solution to room temperature, $H_2O$ (0.7 mL) was added and the mixture was stirred for another 3 h. The mixture was then concentrated in vacuum, the coarse residue oil was redissolved in $CH_2Cl_2$ (30 mL), diluted with 2 M HCl (30 mL), and the aqueous phase was washed with $CH_2Cl_2$ (2 × 30 mL). Excess concentrated ammonia was added to the aqueous phase, then extracted with $CH_2Cl_2$ (3 × 30 mL), the combined organic phase was dried on $Na_2SO_4$, filtered and vacuum-concentrated. The residue was purified by column chromatography (95:5:0 ~ 9:1:0.1 $CH_2Cl_2$ : MeOH : $Et_3N$) and afforded compound **2** as a white solid (1.9 g, 93%). $^1$H NMR (600 MHz, $CDCl_3$) $\delta$: 8.70 (1H, d, $J$ = 4.2 Hz), 7.98 (1H, d, $J$ = 12.0 Hz), 7.60 (1H, br s), 7.41 (1H, br s), 7.33 (1H, dd, $J_1$ = 12.0 Hz, $J_2$ = 6.0 Hz), 5.75 (1H, ddd, $J_1$ = 12.0 Hz, $J_2$ = 6.0 Hz, $J_3$ = 6.0 Hz, CH=$CH_2$), 4.97–4.92 (2H, m, CH=$CH_2$), 4.55 (1H, br s), 3.91 (3H, s, $OCH_3$), 3.23 (1H, dd, $J_1$ = 12.0 Hz, $J_2$ = 6.0 Hz), 3.20–3.15 (1H, m), 3.05 (1H, br s), 2.79–2.73 (2H, m), 2.24–2.14 (3H, br m), 1.58–1.21 (5H, m).

***Scheme S2.*** Synthesis of monomer **1**

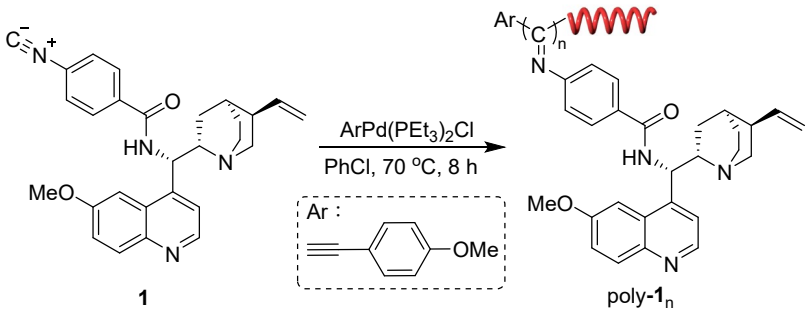



**3** **2** **1**

***Synthesis of monomer 1:*** The monomer **1** was synthesized according to Scheme S2. Pentafluorophenyl (PFP) ester-functionalized phenyl isocyanide (**3**) 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 monomer **3** (2.3 g, 7.4 mmol), compound

**2** (2.0 g, 6.2 mmol), and triethylamine (3.5 mL, 24.7 mmol) in dry THF (30 mL) was stirred at 25 °C for 8 h under $N_2$ atmosphere. Then the solvent was removed by evaporation under reduced pressure. The residue was re-dissolved in $CH_2Cl_2$ (25 mL) and washed with water (50 mL × 2) and aqueous solution of sodium bicarbonate (50 mL × 2). The organic layer was dried over magnesium sulfate ($MgSO_4$) and purified by flash column chromatography using dichloromethane and methanol as eluents (v/v = 9/1) to afford monomer **1** as a colorless oil (2.0 g, 72% yield).$^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 8.75 (d, $J$ = 12.0 Hz, 1H, ArH), 8.04 (d, $J$ = 12.0 Hz, 1H, ArH), 7.85 (d, $J$ = 6.0 Hz, 2H, ArH), 7.71 (d, $J$ = 6.0 Hz, 1H, ArH), 7.46 (d, $J$ = 6.0 Hz ,1H, ArH), 7.40 (q, $J_1$ = 6.0 Hz , $J_2$ = 6.0 Hz ,1H, ArH), 7.33 (d, $J$ = 6.0 Hz, 2H, ArH), 5.72 (ddd, $J_1$ = 12.0 Hz, $J_2$ = 6.0 Hz, $J_3$ = 6.0 Hz, 1H, CH), 5.07–5.05 (m, 2H, $CH_2$), 4.10 (dd, $J_1$ = 12.0 Hz, $J_2$ = 6.0 Hz ,1H, NHCH), 4.00 (s, 3H, $OCH_3$), 3.64 (br s, 1H, CH), 3.48–3.46 (m, 2H, $CH_2$), 2.98–2.87 (m, 2H, $CH_2$), 2.52–2.48 (m, 1H, CH), 2.03 (s, 1H, CH), 1.87–1.83 (m, 3H, CH,$CH_2$), 1.67–1.64 (m, 1H, CH). $^{13}$C NMR (150 MHz, $CDCl_3$, 25 °C) δ 172.9, 167.2, 165.6, 158.3, 147.0, 142.8, 138.9, 134.1, 132.6, 128.6, 126.3, 120.8, 115.6, 101.6, 60.4, 55.8, 54.8, 43.7, 38.0, 26.9, 26.3, 25.4, 21.0, 14.2. FT-IR (KBr, cm$^{-1}$): 3260 ($\nu_{NH}$), 3069, 2939, 2870 ($\nu_{C\text{-}H}$), 2122 ($\nu_{C\equiv N}$), 1620 ($\nu_{C=O}$). HRMS: $C_{28}H_{28}N_4O_2$ for $[M+H]^+$, calculated 453.2212, found 453.2289. Anal. Calcd (%) for $C_{28}H_{28}N_4O_2$: C, 74.31; H, 6.24; N, 12.38; Found: C, 74.24%; H, 6.19%; N, 12.31%.

***Scheme S3.*** Synthesis of poly-$\mathbf{1}_n$s



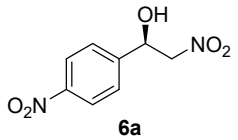

***Synthesis of poly-$1_n$s***: Taking poly-$\mathbf{1}_{150}$ as an example. Monomer **1** (100 mg, 0.22 mmol), Pd(II) catalyst (0.75 mg, $1.46\times10^{-3}$ mmol) and PhCl (0.4 mL) were added to a 10 mL reaction tube with magnetic stirring bar under $N_2$ atmosphere. The reaction flask was then immersed into an oil bath at 70 °C and stirred for 8 h. After cooled to room temperature, the polymerization solution was precipitated into a large amount of ethyl ether, and collected by centrifugation. After dried in vacuum at room temperature overnight, poly-$\mathbf{1}_{150}$ was obtained as a yellow solid (92.7 mg, 92% yield). SEC: $M_n$ = 66.9 kDa, $M_w/M_n$ = 1.22. $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 8.93–7.30 (br, 9H, ArH), 5.58–3.82 (br, 4H, CH and $CH_2$), 3.56 (br, 3H, $OCH_3$), 3.48–1.46 (br, 11H, $CH_2$ and $CH_3$). FT-IR (KBr, cm$^{-1}$): 3306 ($\nu_{NH}$), 2930, 2860 ($\nu_{C\text{-}H}$), 1621 ($\nu_{C=O}$), 1590 ($\nu_{C=N}$).

***General procedure for Henry reaction***

In a glass-reactor, a mixture of 20% loading (with respective to repeating units) poly-$\mathbf{1}_{150}$ and substrate **4** (0.20 mmol) in toluene (0.5 mL) and $(CF_3)_3COH$ (80 μL) was stirred for 30 min at a specific temperature indicated in Table 2 in the main text. Then

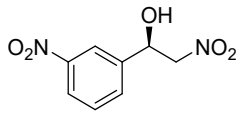
nitromethane (**5**) (2.0 mmol) was added to the reaction mixture. After the reaction was accomplished, diethyl ether was added to the solution which caused the polymer catalyst precipitated. After centrifugation to remove the solid, the solution was concentrated under reduced pressure and the crude product was purified by preparative thin layer chromatography (TLC) on silica gel using petroleum ether and ethyl acetate as an eluent to afford the product. Taking the reaction of *p*-nitrobenzaldehyde (**4a**) with nitromethane (**5**) as an example. Poly-$\mathbf{1}_{150}$ (18.0 mg, 0.04 mmol, with respective to repeating units) was added to the stirring solution of **4a** (30.2 mg, 0.20 mmol) in toluene (0.5 mL) and $(CF_3)_3COH$ (80 μL). The mixture was stirred for 30 min at –20 °C. Then nitromethane (**5**) (108 μL, 2.0 mmol) was added to this solution via a microsyringe. The resulting solution was stirred at –20 °C and monitored by TLC. After the reaction was accomplished, diethyl ether was added to the solution which caused the polymer catalyst precipitated. After centrifugation to remove the solid, the solution was concentrated under reduced pressure and the crude product was purified by preparative TLC on silica gel using petroleum ether and ethyl acetate as an eluent (petroleum ether /EtOAc = 4/1, v/v) to afford the product **6a** (33.9 mg, 80%).

***Characterization data for products of Henry reaction***



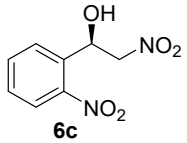

**6a**

2-nitro-1-(4-nitrophenyl)ethan-1-ol (**6a**): $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 8.28 (d, $J$ = 12.0 Hz, 2H), 7.63 (d, $J$ = 6.0 Hz, 2H), 5.61 (dd, 1H, $J_1$ = 12.0 Hz, $J_2$ = 6.0 Hz), 5.33 (m, 1H), 4.61–4.55 (m, 2H).The enantiomeric excess (*ee*): 75% was determined by chiral HPLC with a Chiralpack OD-H column at 254 nm (*n*-hexane/2-propanol = 90/10, v/v), at an eluent rate of 1.00 mL/min; $t_R$ = 41.6 min, $t_S$ = 54.7 min.




**6b**

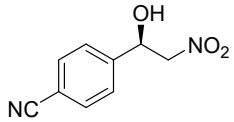
2-nitro-1-(3-nitrophenyl)ethan-1-ol (**6b**): $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 8.32 (t, $J$ = 6.0 Hz, 1H), 8.22 (d, $J$ = 6.0 Hz, 1H), 7.77 (d, $J$ = 6.0 Hz, 1H), 7.61 (t, $J$ = 6.0 Hz, 1H), 5.61 (dd, $J_1$ = 6.0 Hz , $J_2$ = 6.0 Hz, 1H), 5.40–5.34 (m, 1H), 4.65–4.57 (m, 2H).The *ee*: 40% was determined by chiral HPLC with a Chiralpack OD-H column at 215 nm (*n*-hexane/2-propanol = 90/10, v/v), at an eluent rate of 0.70 mL/min; $t_R$ = 47.9 min, $t_S$ = 55.5 min.




**6c**

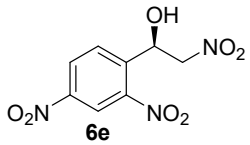
2-nitro-1-(2-nitrophenyl)ethan-1-ol (**6c**):$^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 8.08 (d, $J$ = 12.0 Hz ,1H), 7.96 (d, $J$ = 6.0 Hz, 1H), 7.75 (t, $J$ = 6.0 Hz, 1H), 7.56 (t, $J$ = 6.0 Hz, 1H), 6.06 (dd, $J_1$ = 12.0 Hz , $J_2$ = 6.0 Hz, 1H), 5.35–5.32 (m, 1H), 4.88 (dd, $J_1$ =

12.0 Hz , $J_2$ = 12.0 Hz, 1H), 4.56 (q, $J_1$ = 12.0 Hz , $J_2$ = 6.0 Hz, 1H). The *ee*: 37% was determined by chiral HPLC with a Chiralpack OD-H column at 215 nm (*n*-hexane/2-propanol = 90/10, v/v), at an eluent rate of 0.30 mL/min; $t_R$ = 57.1 min, $t_S$ = 63.5 min.



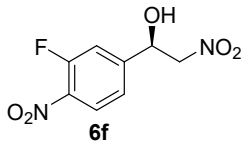
**6d**

4-(1-hydroxy-2-nitroethyl)benzonitrile (**6d**): $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 7.72 (t, $J$ = 6.0 Hz, 2H), 7.56 (t, $J$ = 6.0 Hz, 2H), 5.55 (s, 1H), 4.60–4.53 (m, 2H), 3.08 (s, 1H). The *ee*: 65% was determined by chiral HPLC with a Chiralpack OD-H column at 230 nm (n-hexane/2-propanol = 85/15, v/v), at an eluent rate of 0.80 mL/min; $t_R$ = 39.2 min, $t_S$ = 46.5 min.



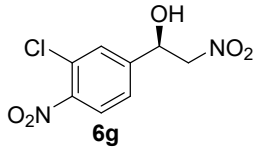
**6e**

1-(2,4-dinitrophenyl)-2-nitroethan-1-ol (**6e**): $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 8.95 (s, 1H), 8.58 (d, $J$ = 6.0 Hz, 1H), 8.25 (d, $J$ = 6.0 Hz, 1H), 6.17 (d, $J$ = 6.0 Hz, 1H), 5.36–5.33 (m, 1H), 4.88 (d, $J$ = 15.0 Hz, 1H), 4.59–4.55 (m, 1H).The *ee*: 50% was determined by chiral HPLC with a Chiralpack OD-H column at 230 nm (*n*-hexane/2-propanol = 90/10, v/v), at an eluent rate of 1.0 mL/min; $t_R$ = 24.1 min, $t_S$ = 30.5 min.



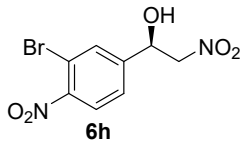
**6f**

1-(3-fluoro-4-nitrophenyl)-2-nitroethan-1-ol (**6f**): $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 8.11 (t, $J$ = 12.0 Hz, 1H), 7.45 (dd, $J_1$ = 12.0 Hz, $J_2$ = 6.0 Hz, 1H), 7.35 (d, $J$ = 6.0 Hz, 1H), 5.57 (t, $J$ = 6.0, Hz 1H), 5.35–5.32 (m, 1H), 4.58–4.57 (m, 2H). The *ee*: 69% was determined by chiral HPLC with a Chiralpack OD-H column at 230 nm (n-hexane/2-propanol = 80/20, v/v), at an eluent rate of 1.0 mL/min; $t_R$ = 16.4 min, $t_S$ = 19.5min.



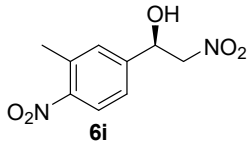
**6g**

1-(3-chloro-4-nitrophenyl)-2-nitroethan-1-ol (**6g**): $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 7.93 (d, $J$ = 6.0 Hz, 1H), 7.67 (s, 1H), 7.47 (d, $J$ = 6.0 Hz, 1H), 5.55 (q, $J_1$ = 12.0 Hz, $J_2$ = 6.0 Hz,1H), 5.36–5.32 (m, 1H), 4.61–4.54 (m, 2H). The *ee*: 57% was determined by chiral HPLC with a Chiralpack OD-H column at 230 nm (*n*-hexane/2-propanol = 80/20, v/v), at an eluent rate of 1.0 mL/min; $t_R$ = 18.1 min, $t_S$ = 24.1 min.



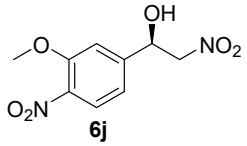
**6h**

1-(3-bromo-4-nitrophenyl)-2-nitroethan-1-ol (**6h**): $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 7.89 (d, $J$ = 6.0 Hz, 1H), 7.85 (d, $J$ = 6.0 Hz, 1H), 7.52 (dd, $J_1$ = 12.0 Hz , $J_2$ = 6.0 Hz, 1H), 5.54 (q, $J_1$ = 12.0 Hz , $J_2$ = 6.0 Hz, 1H), 5.36–5.34 (m, 1H), 4.58–4.56 (m, 2H).The *ee*: 45% was determined by chiral HPLC with a Chiralpack OD-H column at 230 nm (*n*-hexane/2-propanol = 85/15, v/v), at an eluent rate of 1.0 mL/min; $t_R$ = 34.5 min, $t_S$ = 39.8 min.



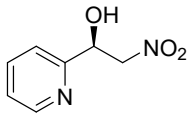

**6i**

1-(3-methyl-4-nitrophenyl)-2-nitroethan-1-ol (**6i**): $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 8.01 (d, $J$ = 6.0 Hz, 1H), 7.41 (t, 3H), 5.54 (dd, $J_1$ = 6.0 Hz , $J_2$ = 6.0 Hz, 1H), 5.36–5.34 (m, 1H), 4.61-4.53 (m, 2H), 2.62 (s, 3H). The *ee*: 57% was determined by chiral HPLC with a Chiralpack OD-H column at 254 nm (*n*-hexane/2-propanol = 90/10, v/v), at an eluent rate of 0.9 mL/min; $t_R$ = 27.4min, $t_S$ = 32.2min.




**6j**

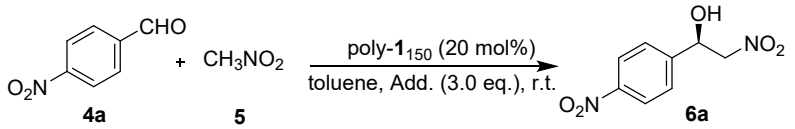
1-(3-methoxy-4-nitrophenyl)-2-nitroethan-1-ol (**6j**): $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 7.88 (d, $J$ = 6.0 Hz, 1H), 7.23 (s, 1H), 7.03 (d, $J$ = 6.0 Hz, 1H), 5.55 (q, $J_1$ = 12.0 Hz , $J_2$ = 6.0 Hz, 1H), 5.36-5.33 (m, 1H), 4.59-4.56 (m, 2H), 4.00(s, 3H).The *ee*: 47% was determined by chiral HPLC with a Chiralpack OD-H column at 254 nm (*n*-hexane/2-propanol = 90/10, v/v), at an eluent rate of 0.9 mL/min; $t_R$ = 27.7 min, $t_S$ = 35.3min.




**6k**

2-nitro-1-(pyridin-2-yl)ethan-1-ol (**6k**): $^1$H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta$ 8.60 (d,$J$ = 6.0 Hz ,1H), 7.84 (t, $J$ = 6.0 Hz , 1H), 7.50 (d, $J$ = 6.0 Hz ,1H), 7.36 (t , $J$ = 6.0 Hz ,1H), 5.52 (q, $J_1$ = 6.0 Hz , $J_2$ = 6.0 Hz,1H), 5.36-5.34 (m, 1H), 4.82 (dd, $J_1$ = 12.0 Hz, $J_2$ = 6.0 Hz ,1H), 4.72-4.68 (m, 1H).The *ee*: 50% was determined by chiral HPLC with a Chiralpack OD-H column at 215 nm (*n*-hexane/2-propanol = 90/10, v/v), at an eluent rate of 0.4 mL/min; $t_R$ = 27.6 min, $t_S$ = 35.4min.

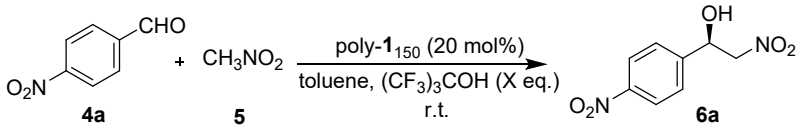
**Table S1.** The results for Henry reaction with different additives[a].




| run | Additive | Yield[c] (%) | *ee*[d] (%) |
|---|---|---|---|
| 1 | MeOH | 75 | 29 |
| 2 | $CF_3SO_3H$ | /[e] | /[e] |
| 3 | $CF_3CH_2OH/H_2O$[b] | 88 | 40 |
| 4 | $C_6H_5CH_2OH$ | 84 | 33 |
| 5 | phenol | 72 | 38 |
| 6 | *o*-nitrobenzoic acid | /[e] | /[e] |

[a]Unless otherwise denoted, all reactions were carried out with **4a** (0.20 mmol), **5** (2.0 mmol) in toluene (0.5 mL). [b]$H_2O$ (1.0 eq.) was added additionally. [c]Isolated yield. [d]The *ee* values were determined by HPLC analysis using a chiral stationary phase. [e]No product was detected.

**Table S2.** The results for Henry reaction with different equivalents of $(CF_3)_3COH$[a].




| run | X (eq.) | Yield[b] (%) | *ee*[c] (%) |
|---|---|---|---|
| 1 | 10.0 | 84 | 44 |
| 2 | 5.0 | 86 | 49 |
| 3 | 3.0 | 87 | 57 |
| 4 | 1.0 | 87 | 48 |
| 5 | 0.5 | 85 | 40 |
| 6 | 0.2 | 84 | 36 |

[a]Unless otherwise denoted, all reactions were carried out with **4a** (0.20 mmol), **5** (2.0 mmol) in toluene (0.5 mL) and $(CF_3)_3COH$ (X eq.). [b]Isolated yield. [c]The *ee* values were determined by HPLC analysis using a chiral stationary phase.

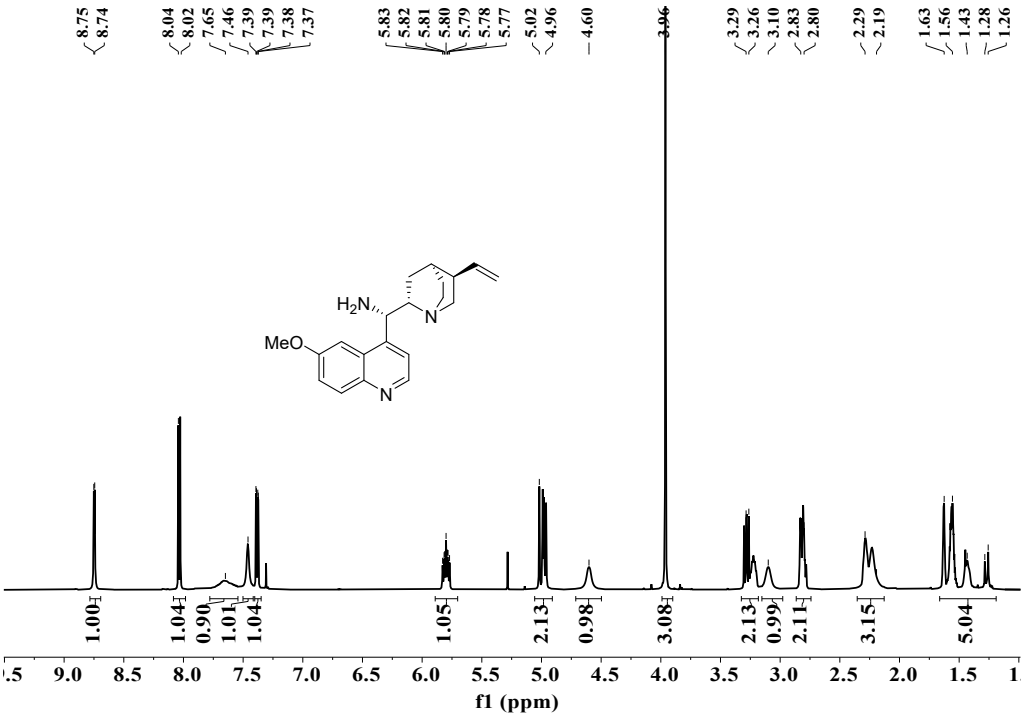



**Figure S1.** $^{1}$H NMR (600 MHz) spectrum of compound **2** measured in $CDCl_3$ at 25 °C.

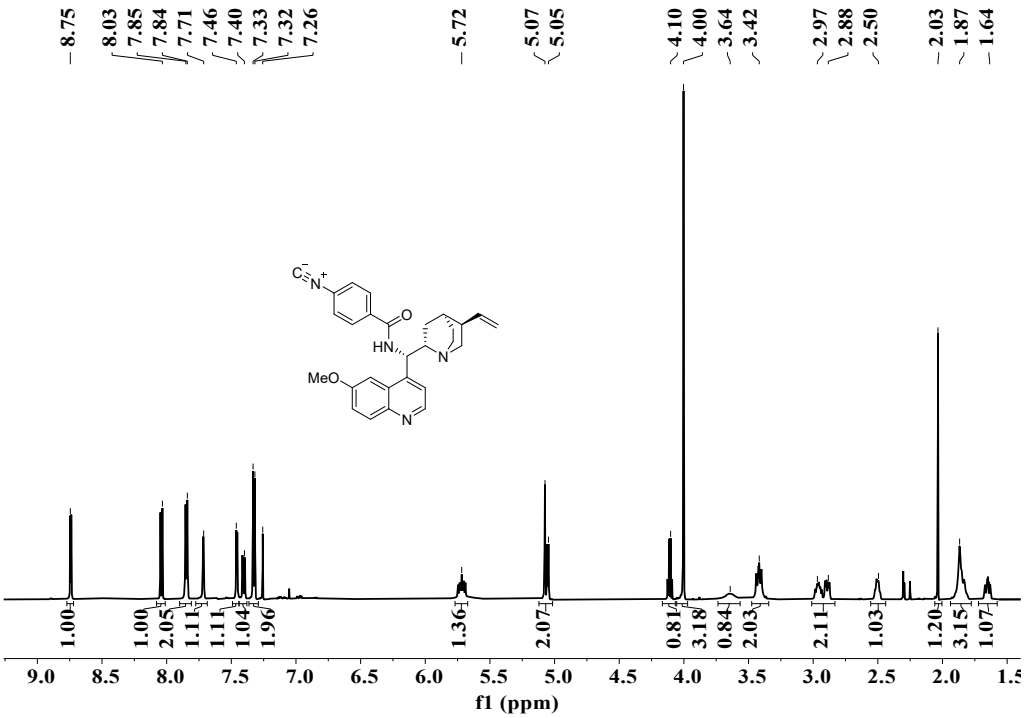



**Figure S2.** $^{1}$H NMR (600 MHz) spectrum of monomer **1** measured in $CDCl_3$ at 25 °C.

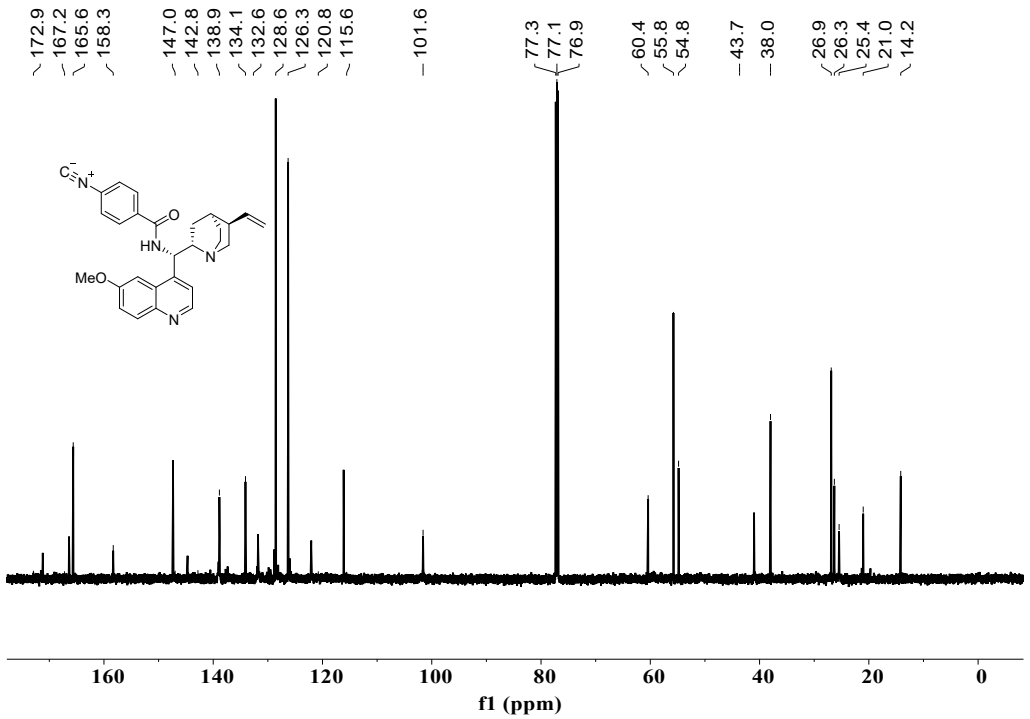



**Figure S3.** $^{13}C$ NMR (150 MHz) spectrum of monomer **1** measured in $CDCl_3$ at 25 °C.

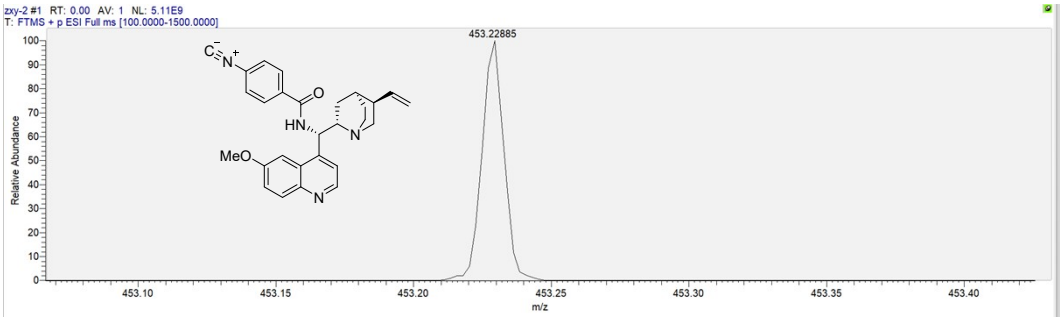



**Figure S4.** HRMS spectrum of monomer **1** for $[M+H]^+$.

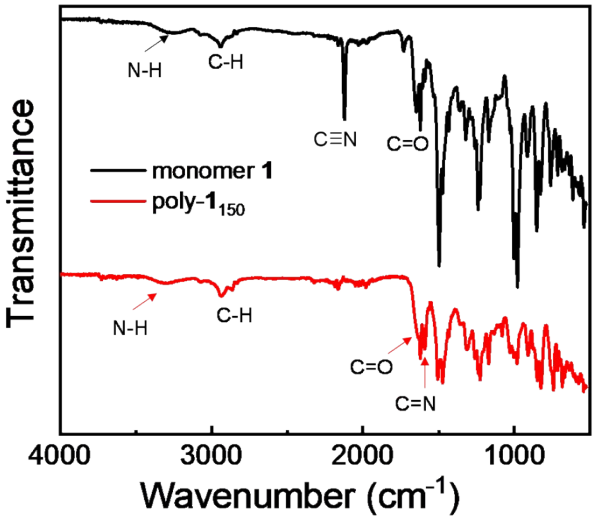



**Figure S5.** FT-IR spectrum of monomer **1** and poly-$\mathbf{1}_{150}$ measured at 25 °C using KBr pellets.

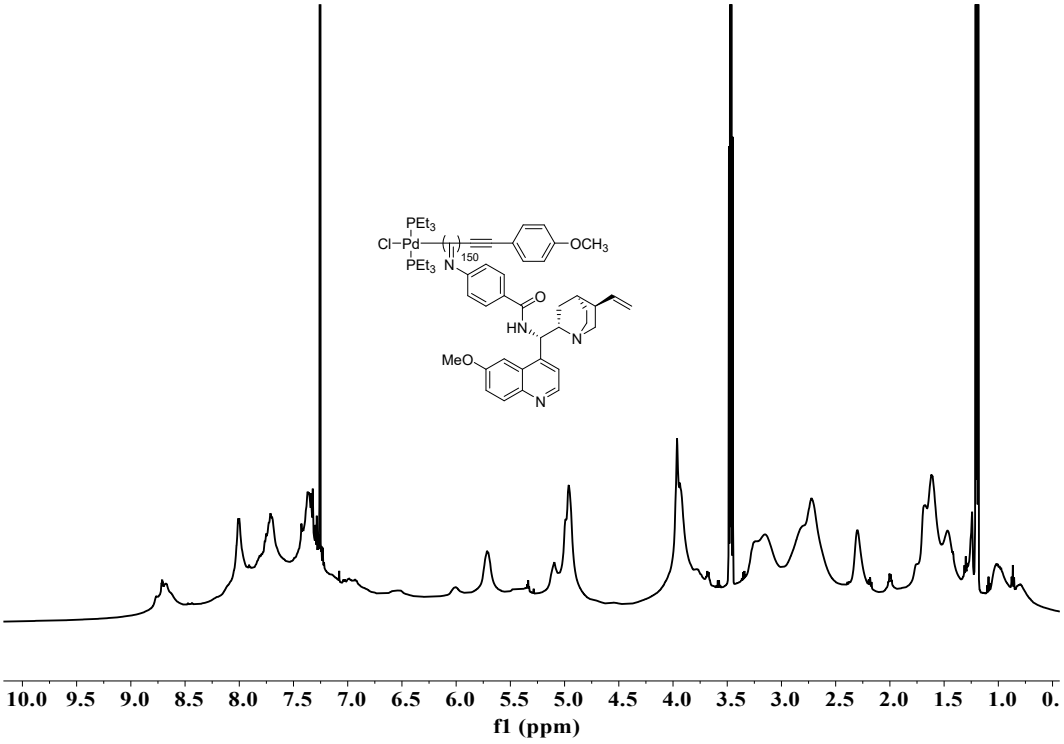



**Figure S6.** $^{1}$H NMR (600 MHz) spectrum of poly-$\mathbf{1}_{150}$ measured in $CDCl_3$ at 25 °C.

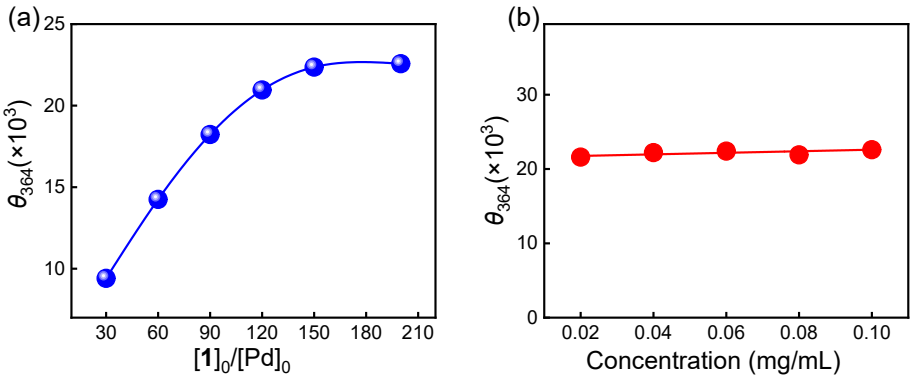



**Figure S7.** (a) The relationship between the molar ellipticity at 364 nm and $M_n$s of poly-**1**$_n$s measured in THF at 25 °C ($c$ = 0.2 mg/mL). (b) The molar ellipticity at 364 nm of poly-**1**$_{150}$ at different concentrations measured in THF at 25 °C.

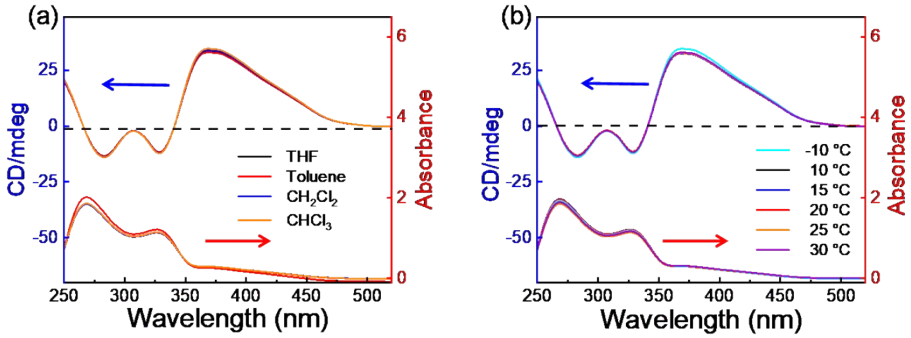



**Figure S8.** CD and UV-vis spectra of poly-**1**$_{150}$ measured in different solvents at 25 °C in THF (a) and in different temperatures (b). ($c$ = 0.2 mg/mL)

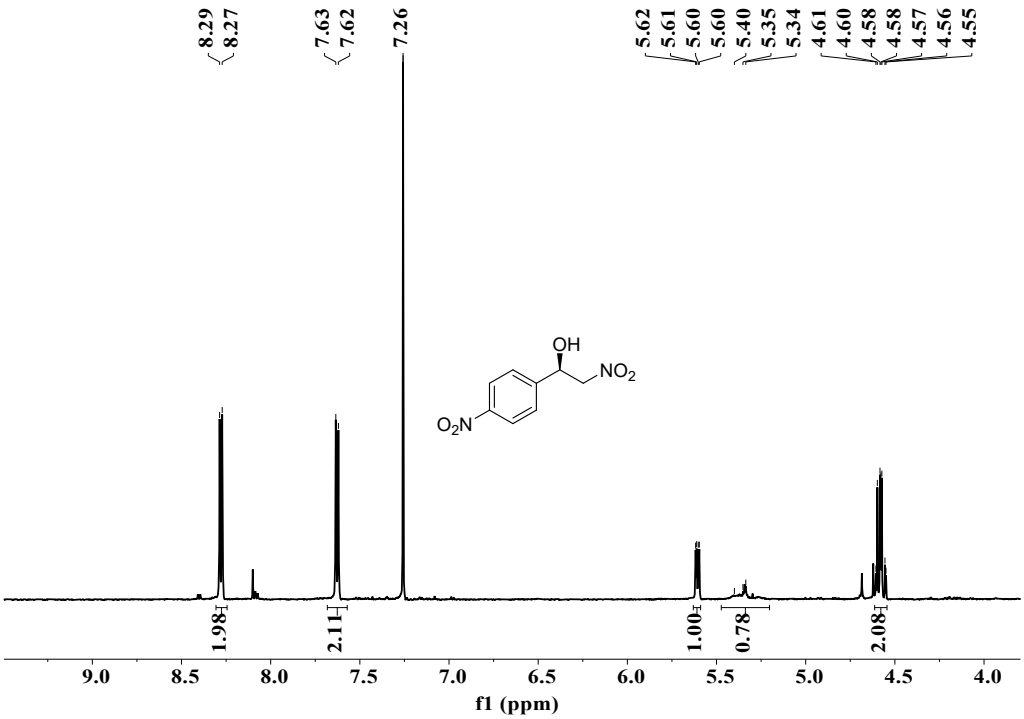



**Figure S9.** $^{1}$H NMR (600 MHz) spectrum of **6a** measured in $CDCl_3$ at 25 °C.

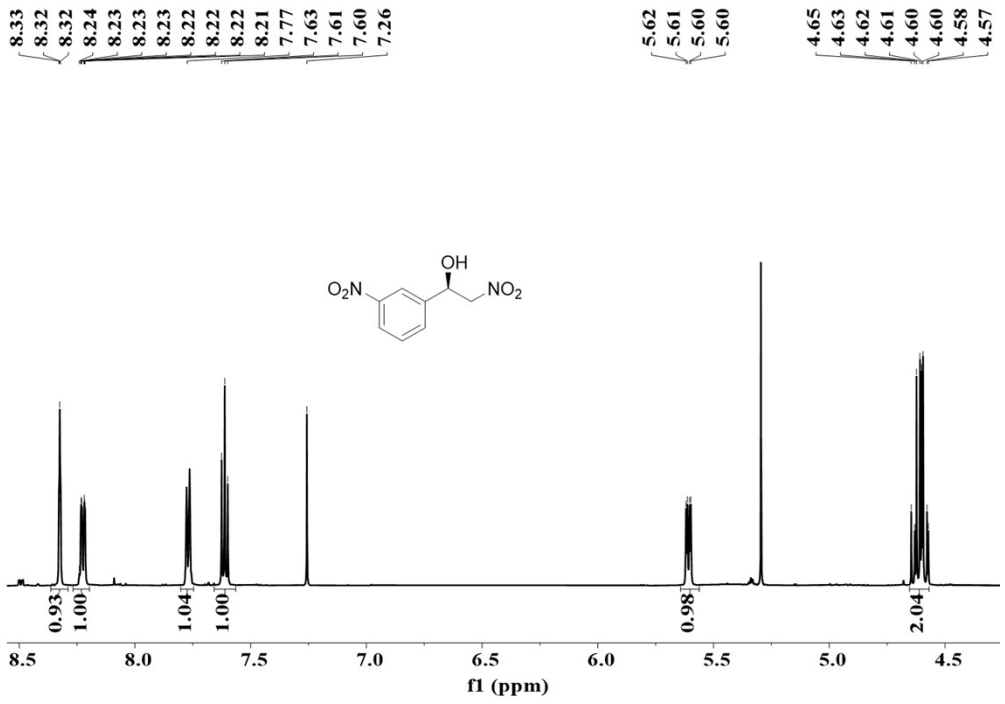



**Figure S10.** $^{1}$H NMR (600 MHz) spectrum of **6b** measured in $CDCl_3$ at 25 °C.

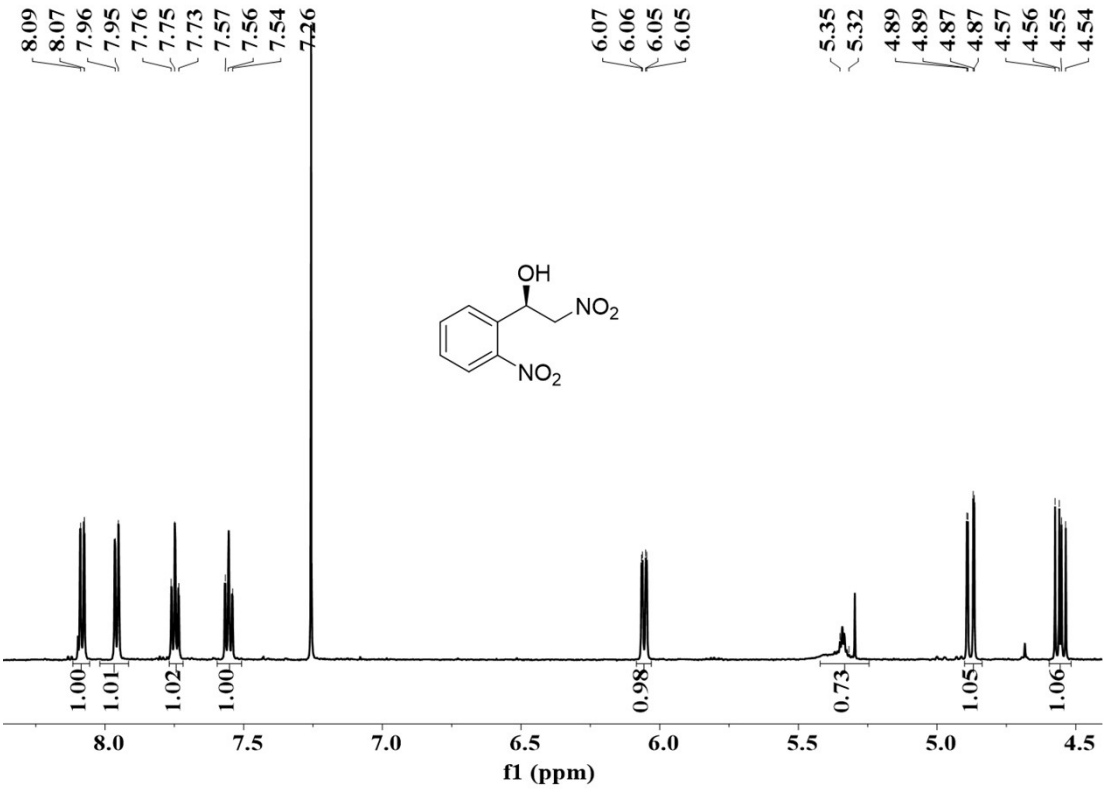



**Figure S11.** $^{1}$H NMR (600 MHz) spectrum of **6c** measured in $CDCl_3$ at 25 °C.

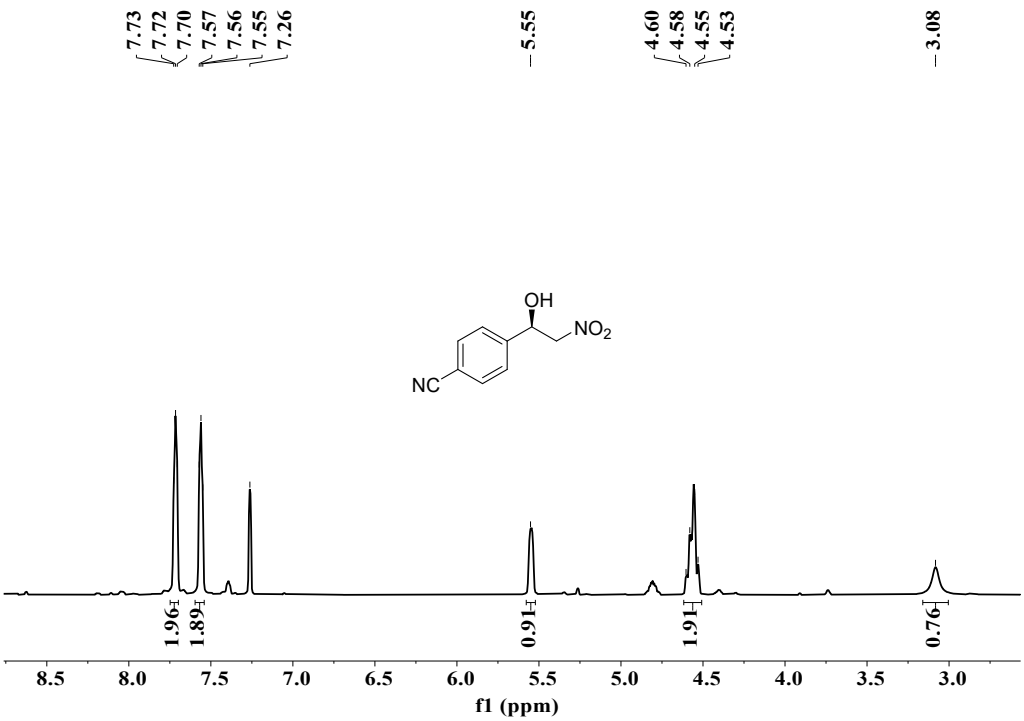



**Figure S12.** $^{1}$H NMR (600 MHz) spectrum of **6d** measured in $CDCl_3$ at 25 °C

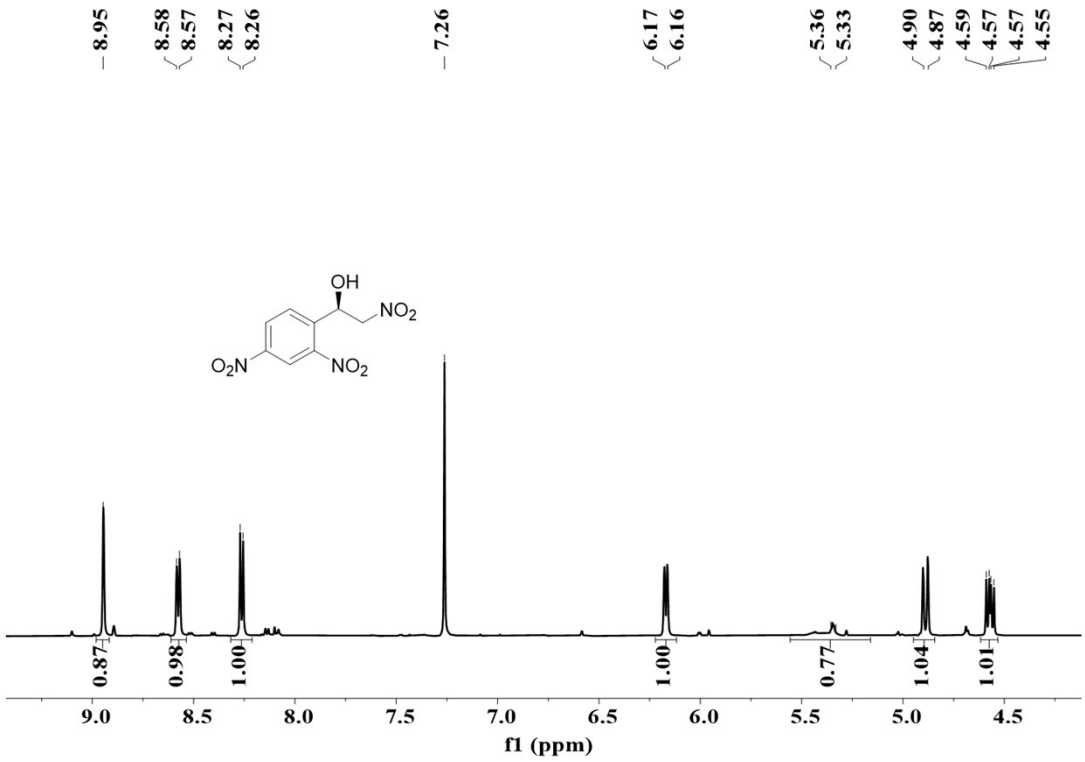



**Figure S13.** $^{1}$H NMR (600 MHz) spectrum of **6e** measured in $CDCl_3$ at 25 °C.

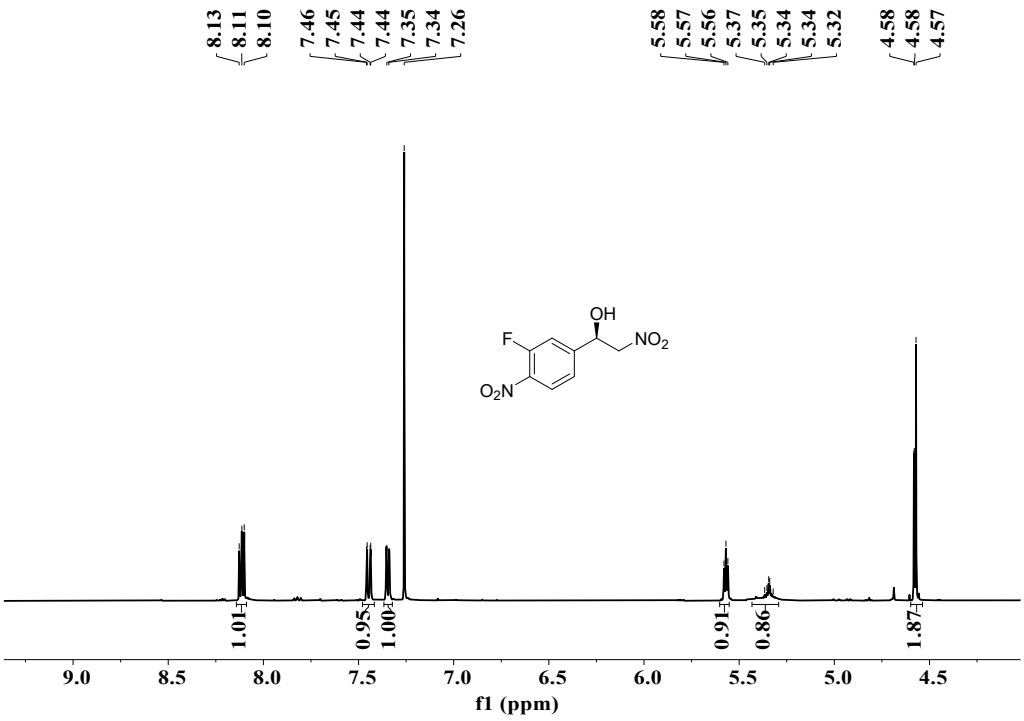



**Figure S14.** $^{1}$H NMR (600 MHz) spectrum of **6f** measured in $CDCl_3$ at 25 °C.

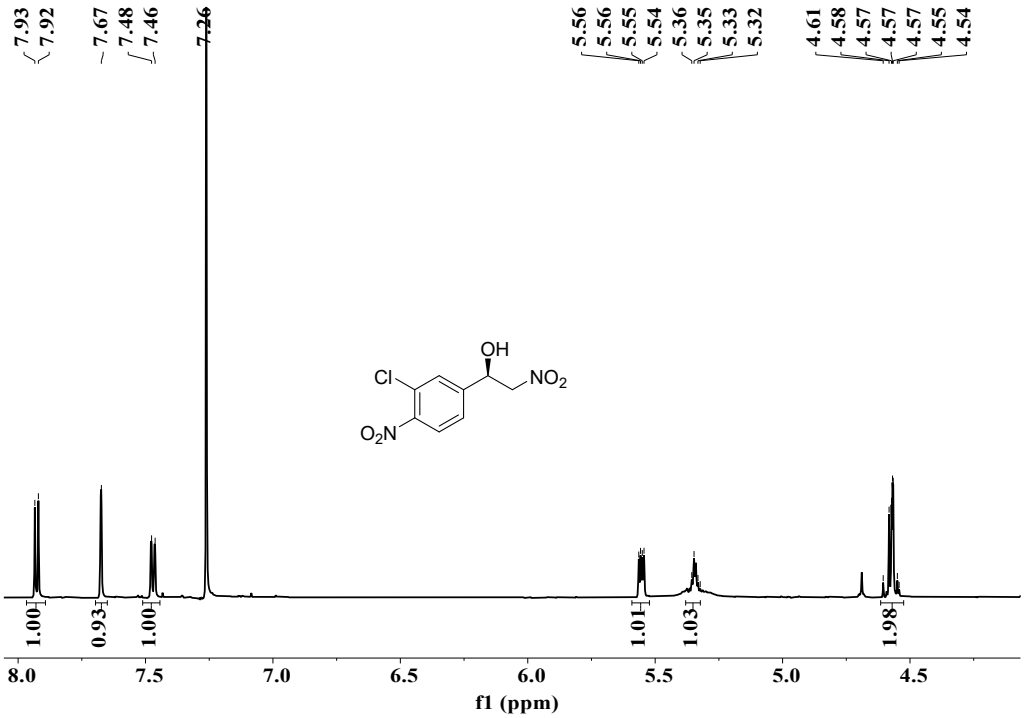



**Figure S15.** $^1$H NMR (600 MHz) spectrum of **6g** measured in $CDCl_3$ at 25 °C.

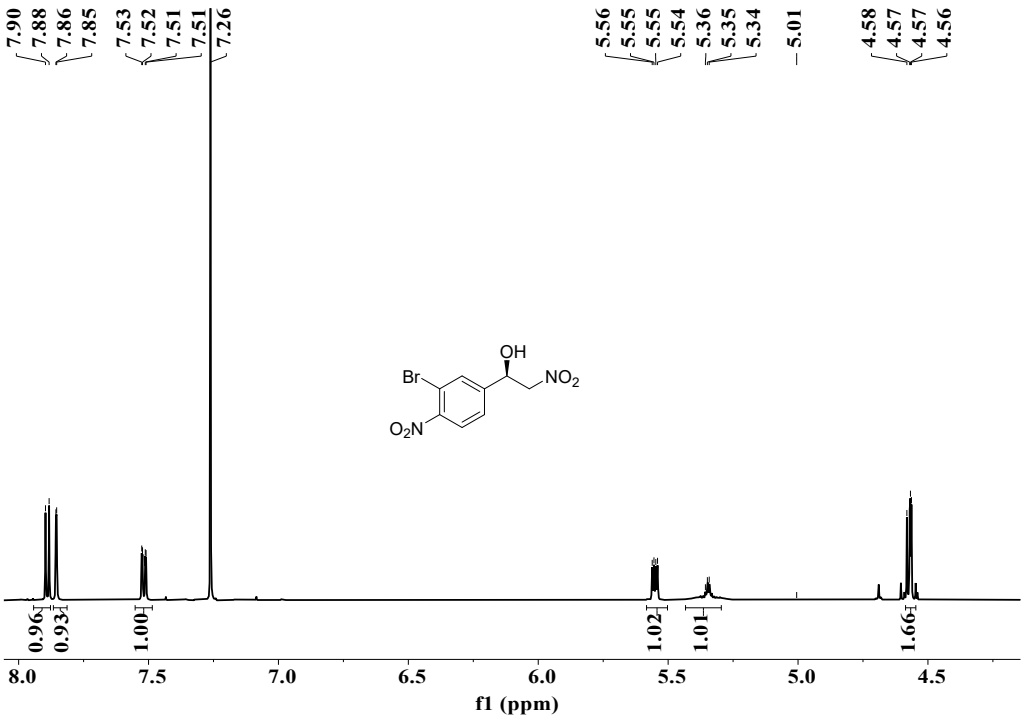



**Figure S16.** $^1$H NMR (600 MHz) spectrum of **6h** measured in $CDCl_3$ at 25 °C.

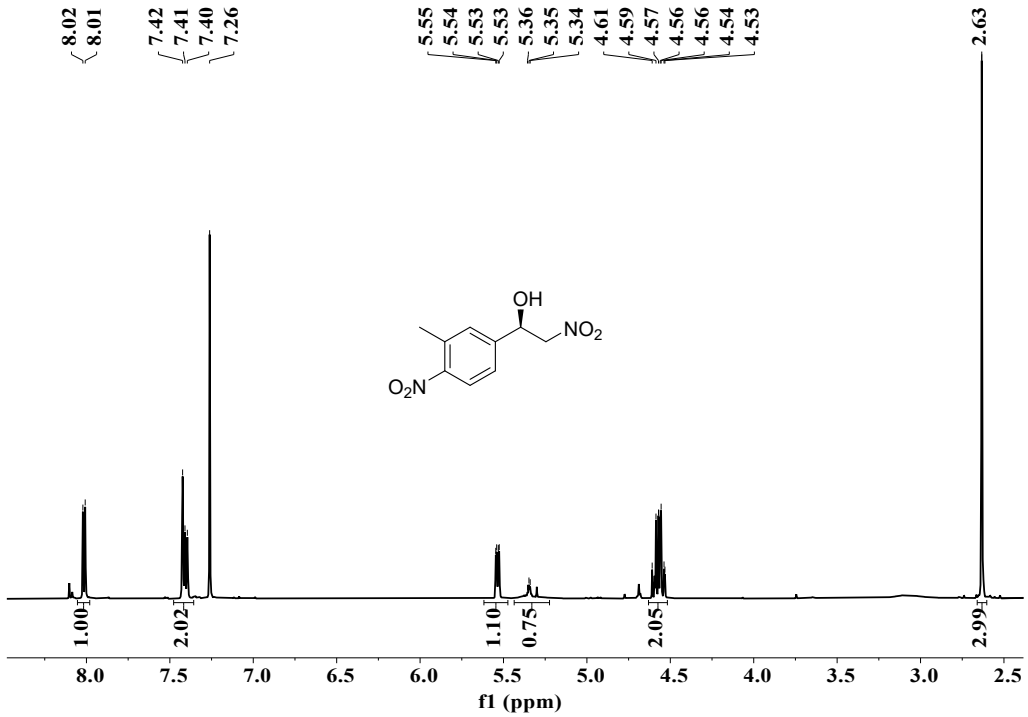



**Figure S17.** $^{1}$H NMR (600 MHz) spectrum of **6i** measured in $CDCl_3$ at 25 °C.

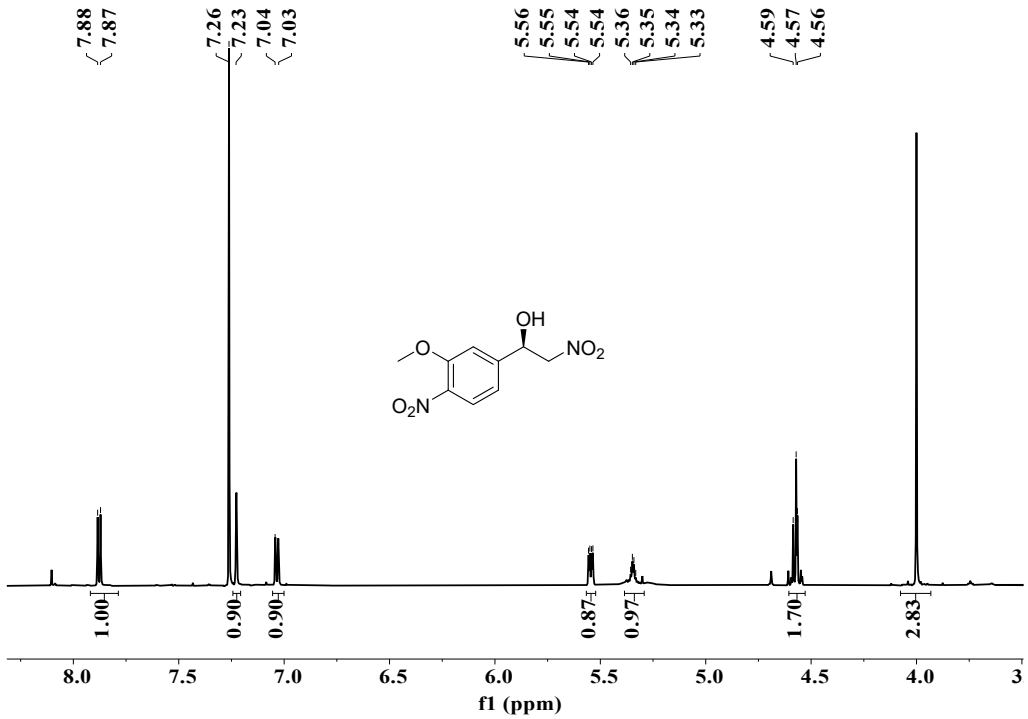



**Figure S18.** $^{1}$H NMR (600 MHz) spectrum of **6j** measured in $CDCl_3$ at 25 °C.

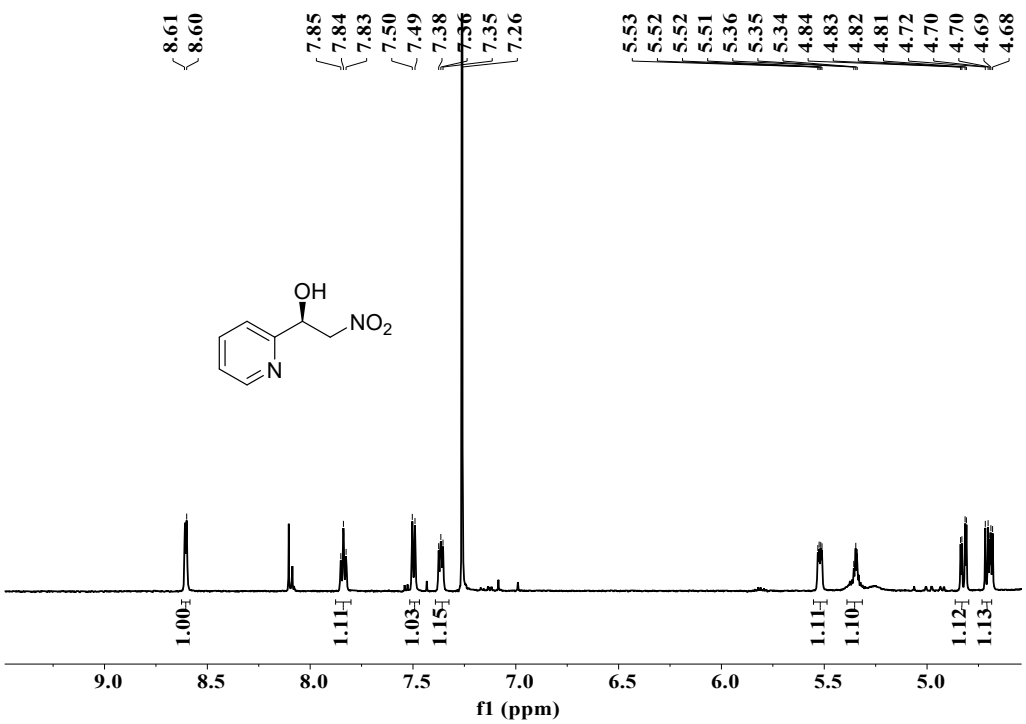
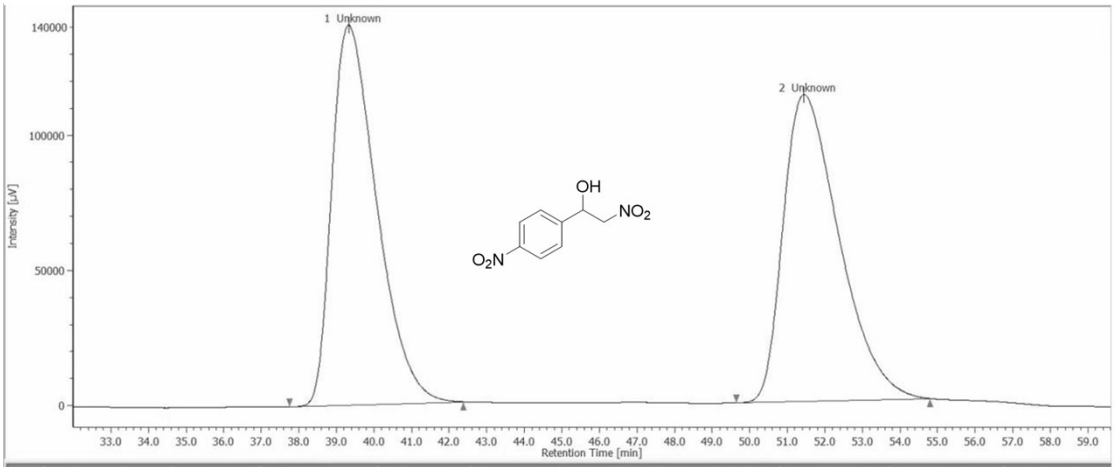
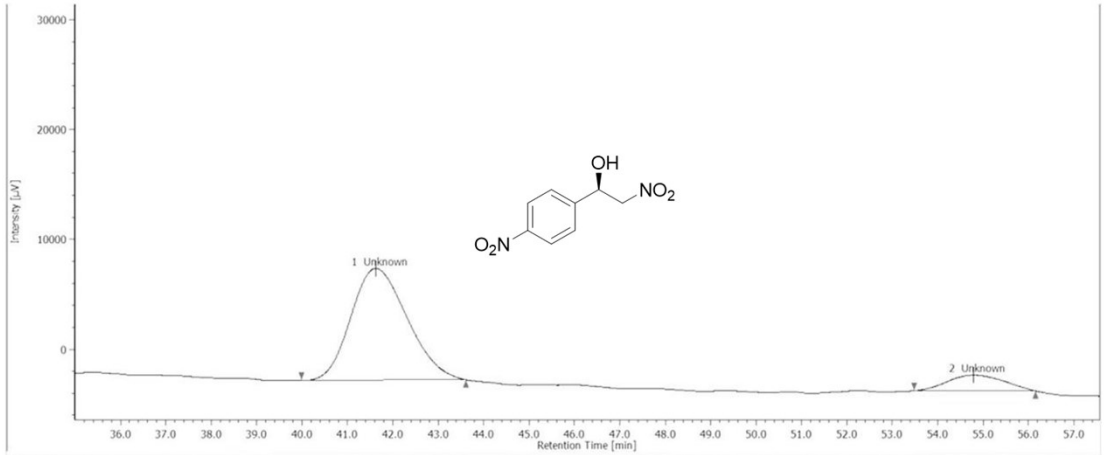



**Figure S19.** $^{1}$H NMR (600 MHz) spectrum of **6k** measured in $CDCl_3$ at 25 °C.



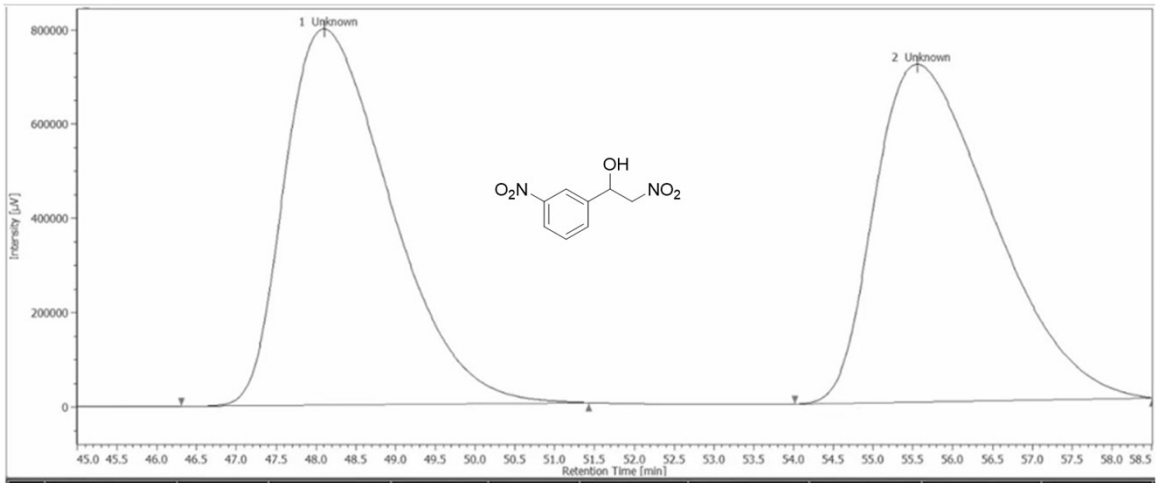

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 39.325 | 11650839 | 140389 | 49.817 | 55.320 | 37.750 | 42.375 | 37.750 | 42.375 |
| 2 | Unknown | 51.433 | 11736312 | 113389 | 50.183 | 44.680 | 49.633 | 54.783 | 49.633 | 54.783 |

**Figure S20**. HPLC curve of *rac*-**6a** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 1.00 mL/min; 254 nm; 25 °C).



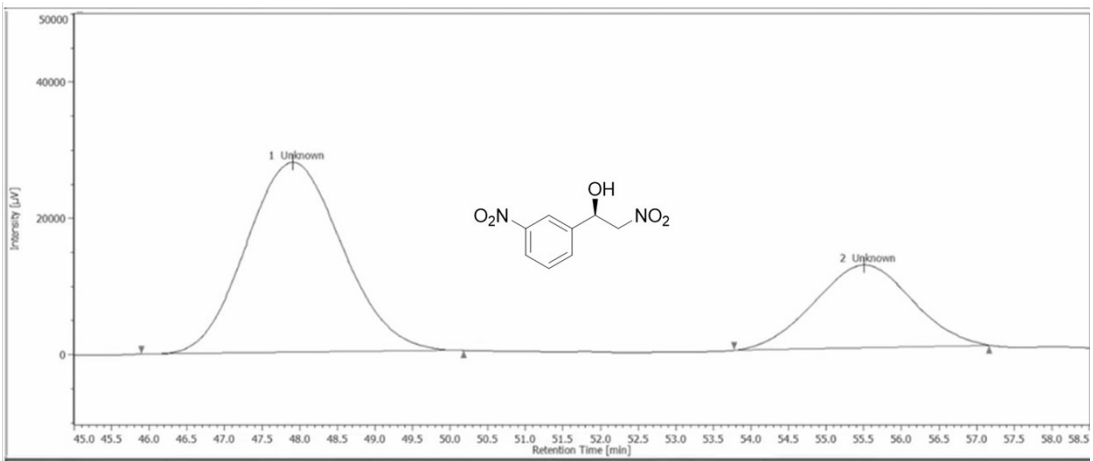

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 41.617 | 872917 | 10165 | 87.668 | 87.740 | 39.983 | 43.600 | 39.983 | 43.600 |
| 2 | Unknown | 54.783 | 122786 | 1420 | 12.332 | 12.260 | 53.475 | 56.142 | 53.475 | 56.142 |

**Figure S21**. HPLC curve of (*R*)-**6a** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 1.00 mL/min; 254 nm; 25 °C).



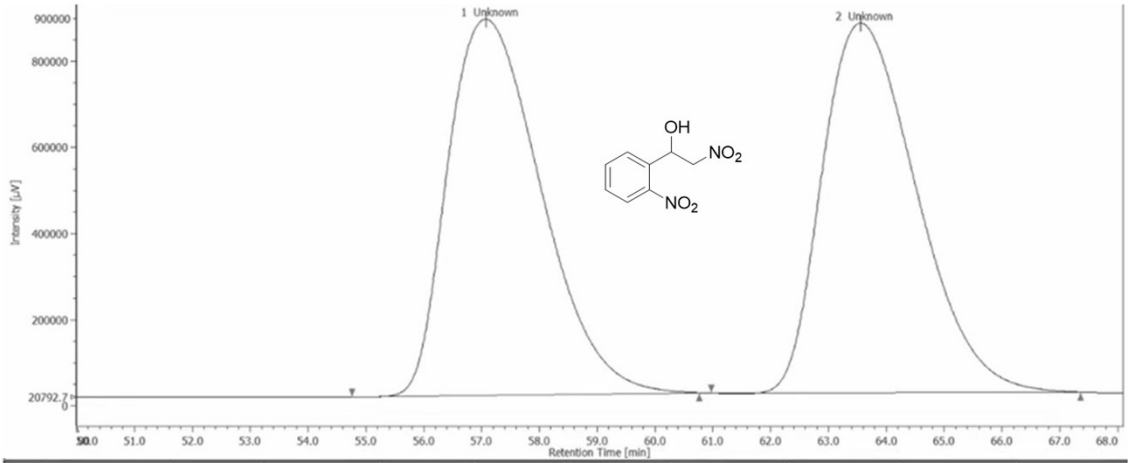

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 48.100 | 73556227 | 796687 | 49.867 | 52.704 | 46.308 | 51.425 | 46.308 | 51.425 |
| 2 | Unknown | 55.550 | 73948616 | 714938 | 50.133 | 47.296 | 54.008 | 58.500 | 54.008 | 58.500 |

**Figure S22**. HPLC curve of *rac*-**6b** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.7 mL/min; 215 nm; 25 °C).



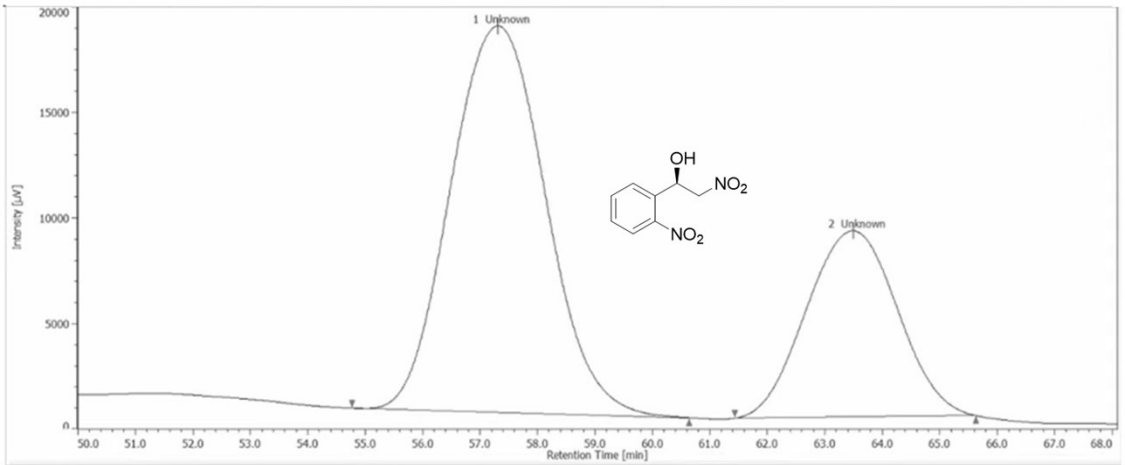

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 47.908 | 2473086 | 27850 | 69.281 | 69.658 | 45.892 | 50.175 | 45.892 | 50.175 |
| 2 | Unknown | 55.500 | 1096585 | 12131 | 30.719 | 30.342 | 53.767 | 57.158 | 53.767 | 57.158 |

**Figure S23**. HPLC curve of (*R*)-**6b** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.7 mL/min; 215 nm; 25 °C).



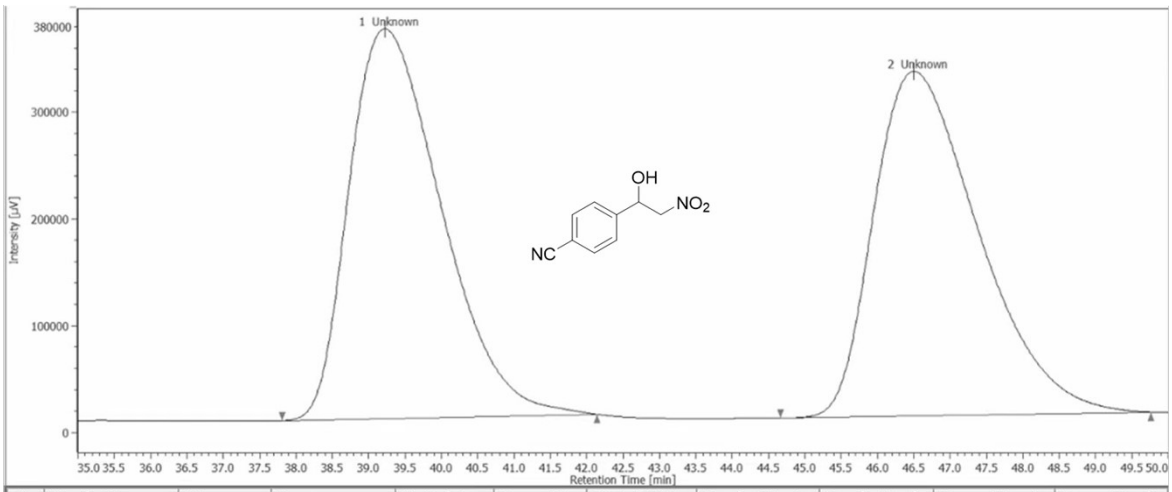

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 57.067 | 97963666 | 871609 | 50.156 | 50.434 | 54.758 | 60.758 | 54.758 | 60.758 |
| 2 | Unknown | 63.550 | 97353583 | 856605 | 49.844 | 49.566 | 60.967 | 67.350 | 60.967 | 67.350 |

**Figure S24**. HPLC curve of *rac*-**6c** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.3 mL/min; 215 nm; 25 °C).



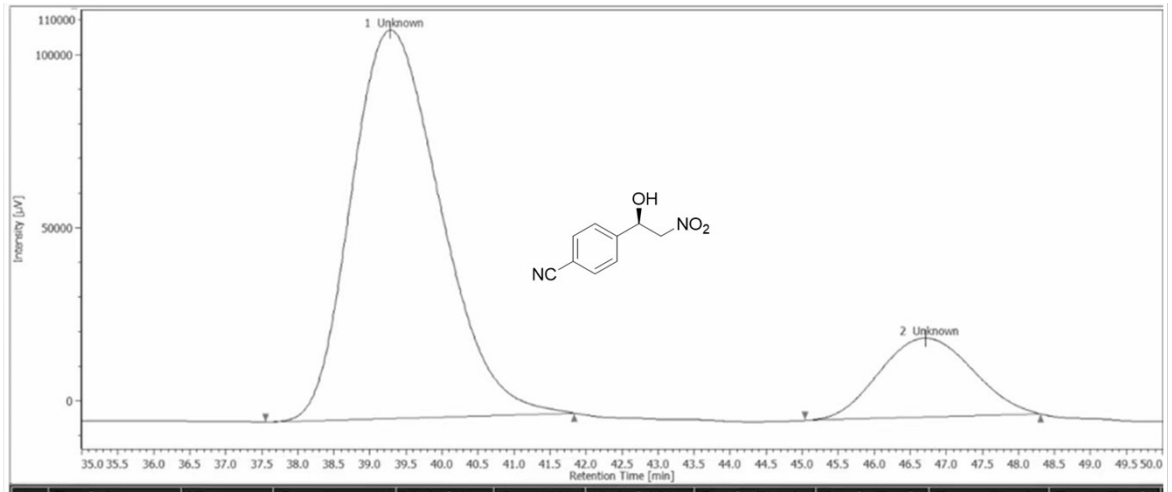

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 57.300 | 2099407 | 18263 | 68.395 | 67.476 | 54.767 | 60.633 | 54.767 | 60.633 |
| 2 | Unknown | 63.483 | 970113 | 8803 | 31.605 | 32.524 | 61.425 | 65.617 | 61.425 | 65.617 |

**Figure S25**. HPLC curve of (*R*)-**6c** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.3 mL/min; 215 nm; 25 °C).



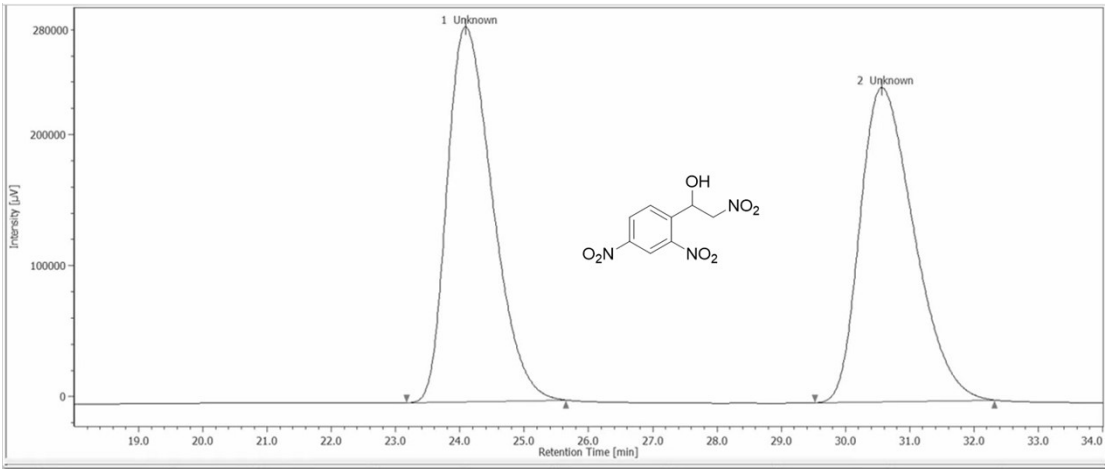

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 39.225 | 32184562 | 364360 | 49.920 | 53.074 | 37.808 | 42.133 | 37.808 | 42.133 |
| 2 | Unknown | 46.492 | 32287778 | 322159 | 50.080 | 46.926 | 44.658 | 49.750 | 44.658 | 49.750 |

**Figure S26**. HPLC curve of *rac*-**6d** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 85/15 (v/v); 0.8 mL/min; 230 nm; 25 °C).



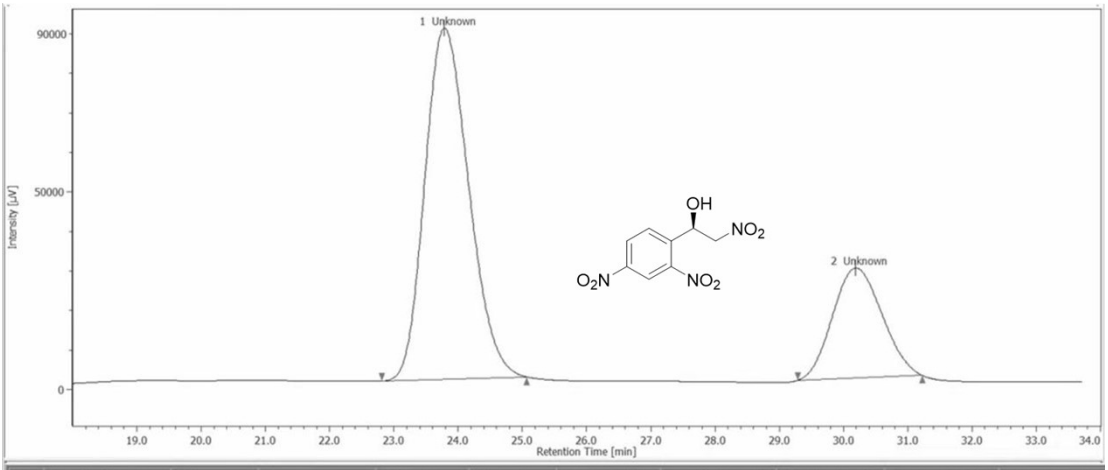

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 39.283 | 9626212 | 112003 | 82.451 | 83.107 | 37.550 | 41.833 | 37.550 | 41.833 |
| 2 | Unknown | 46.700 | 2048925 | 22766 | 17.549 | 16.893 | 45.033 | 48.300 | 45.033 | 48.300 |

**Figure S27**. HPLC curve of (*R*)-**6d** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 85/15 (v/v); 0.8 mL/min; 230 nm; 25 °C).



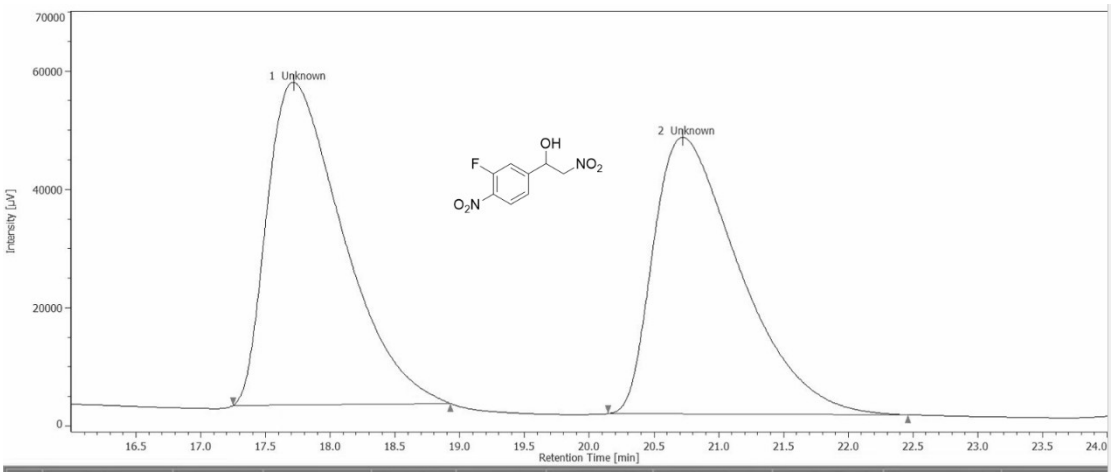

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 24.083 | 14031745 | 286007 | 50.073 | 54.412 | 23.167 | 25.642 | 23.167 | 25.642 |
| 2 | Unknown | 30.558 | 13990683 | 239622 | 49.927 | 45.588 | 29.517 | 32.308 | 29.517 | 32.308 |

**Figure S28**. HPLC curve of *rac*-**6e** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 1.0 mL/min; 230 nm; 25 °C).



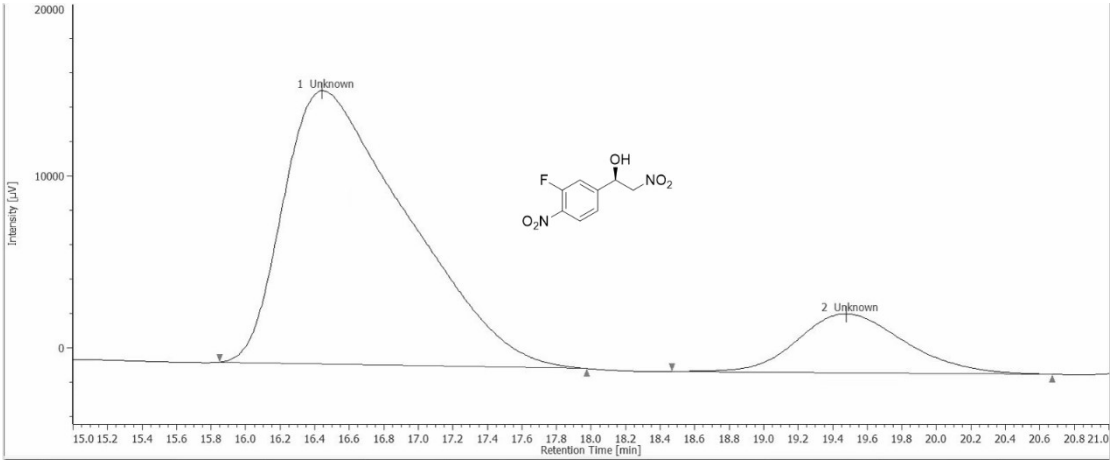

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 23.783 | 4221489 | 88754 | 74.021 | 76.159 | 22.808 | 25.058 | 22.808 | 25.058 |
| 2 | Unknown | 30.183 | 1481609 | 27784 | 25.979 | 23.841 | 29.283 | 31.217 | 29.283 | 31.217 |

**Figure S29**. HPLC curve of (*R*)-**6e** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 1.0 mL/min; 230 nm; 25 °C).



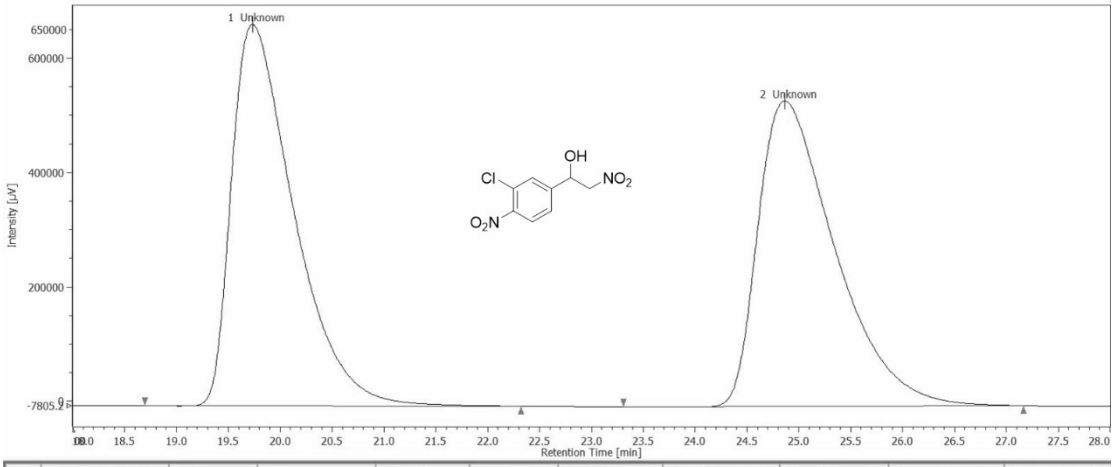

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 17.717 | 2219378 | 54403 | 50.524 | 53.814 | 17.250 | 18.925 | 17.250 | 18.925 |
| 2 | Unknown | 20.717 | 2173362 | 46691 | 49.476 | 46.186 | 20.142 | 22.458 | 20.142 | 22.458 |

**Figure S30**. HPLC curve of *rac*-**6f** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 80/20 (v/v); 1.0 mL/min; 230 nm; 25 °C).



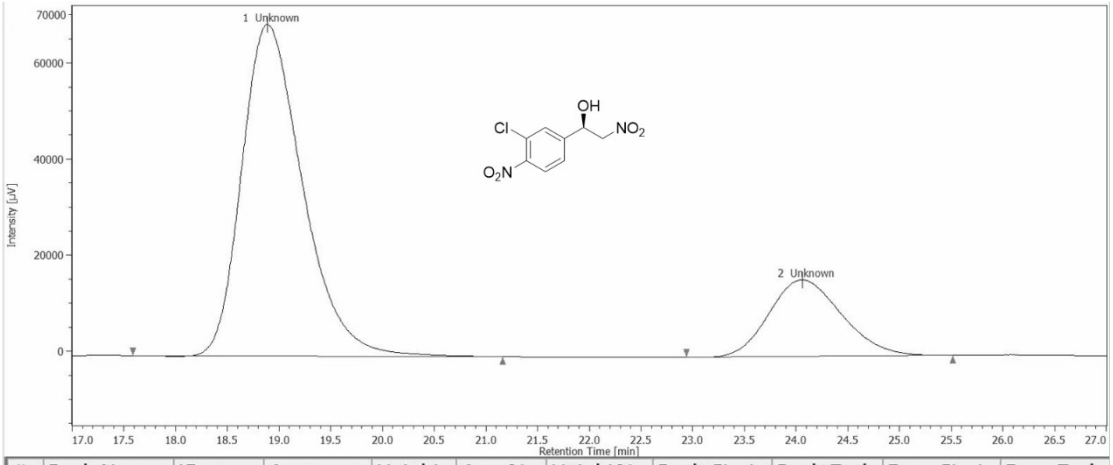

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 16.442 | 792928 | 15859 | 84.235 | 82.230 | 15.850 | 17.975 | 15.850 | 17.975 |
| 2 | Unknown | 19.475 | 148397 | 3427 | 15.765 | 17.770 | 18.467 | 20.667 | 18.467 | 20.667 |

**Figure S31**. HPLC curve of (*R*)-**6f** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 80/20 (v/v); 1.0 mL/min; 230 nm; 25 °C).



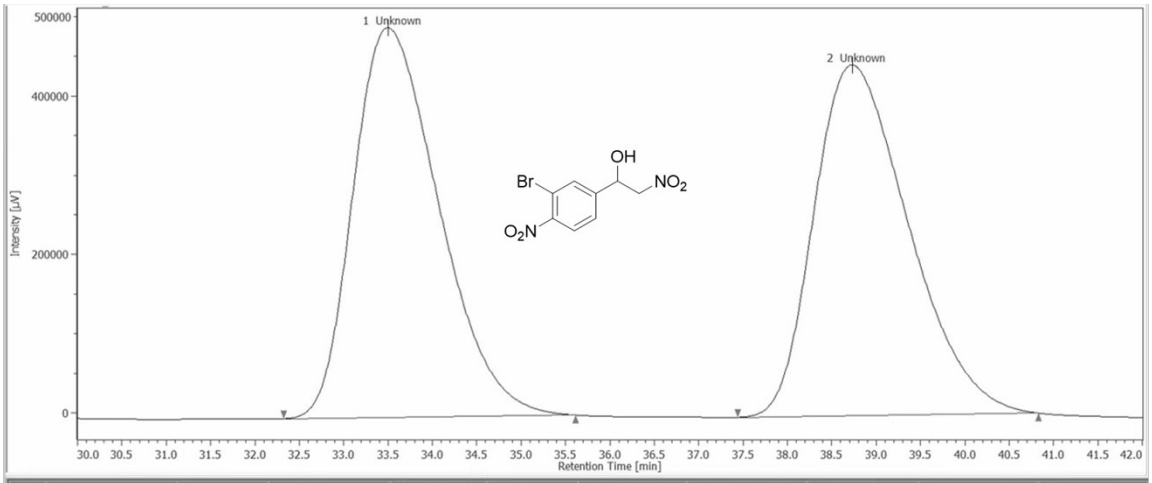

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 19.733 | 27804240 | 666490 | 50.296 | 55.541 | 18.692 | 22.317 | 18.692 | 22.317 |
| 2 | Unknown | 24.858 | 27476989 | 533502 | 49.704 | 44.459 | 23.308 | 27.158 | 23.308 | 27.158 |

**Figure S32**. HPLC curve of *rac*-**6g** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 80/20 (v/v); 1.0 mL/min; 230 nm; 25 °C).



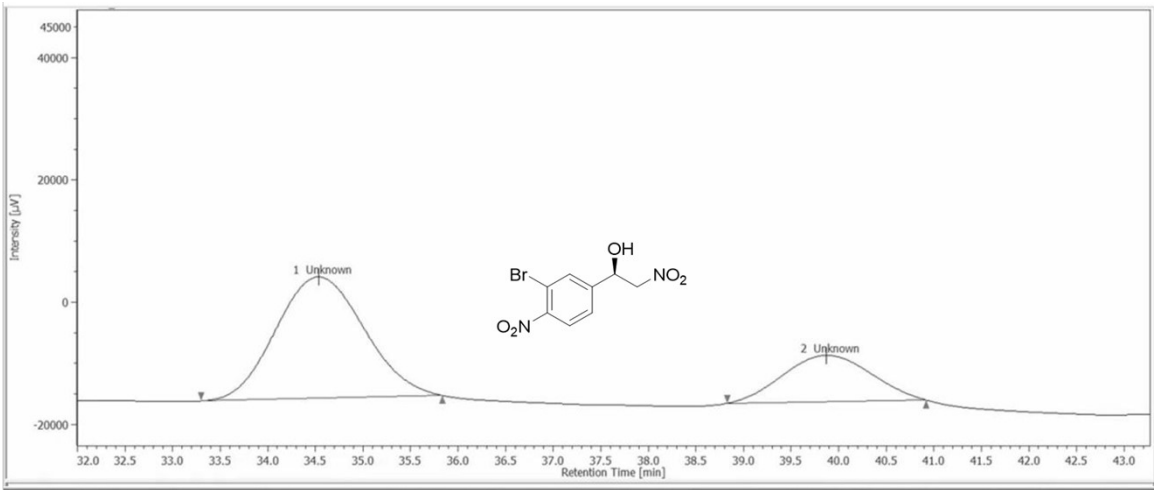

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 18.883 | 2818658 | 68858 | 78.435 | 81.243 | 17.583 | 21.158 | 17.583 | 21.158 |
| 2 | Unknown | 24.058 | 774962 | 15897 | 21.565 | 18.757 | 22.933 | 25.508 | 22.933 | 25.508 |

**Figure S33**. HPLC curve of (*R*)-**6g** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 80/20 (v/v); 1.0 mL/min; 230 nm; 25 °C).



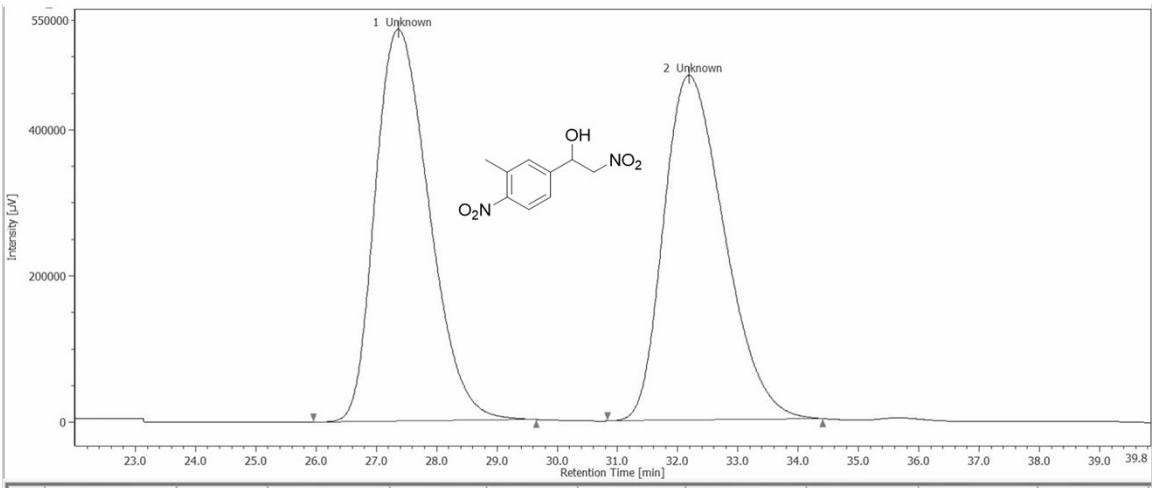

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 33.500 | 32995194 | 490665 | 50.217 | 52.625 | 32.325 | 35.608 | 32.325 | 35.608 |
| 2 | Unknown | 38.725 | 32710634 | 441715 | 49.783 | 47.375 | 37.433 | 40.825 | 37.433 | 40.825 |

**Figure S34**. HPLC curve of *rac*-**6h** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 85/15 (v/v); 1.0 mL/min; 230 nm; 25 °C).



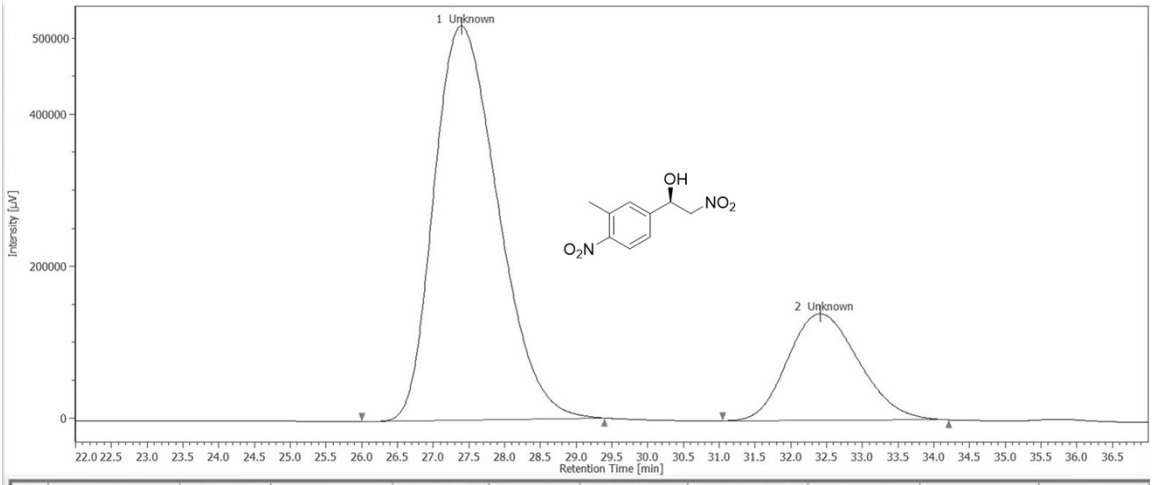

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 34.533 | 1278546 | 19827 | 72.403 | 72.400 | 33.300 | 35.833 | 33.300 | 35.833 |
| 2 | Unknown | 39.867 | 487328 | 7559 | 27.597 | 27.600 | 38.825 | 40.917 | 38.825 | 40.917 |

**Figure S35**. HPLC curve of (*R*)-**6h** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 85/15 (v/v); 1.0 mL/min; 230 nm; 25 °C).



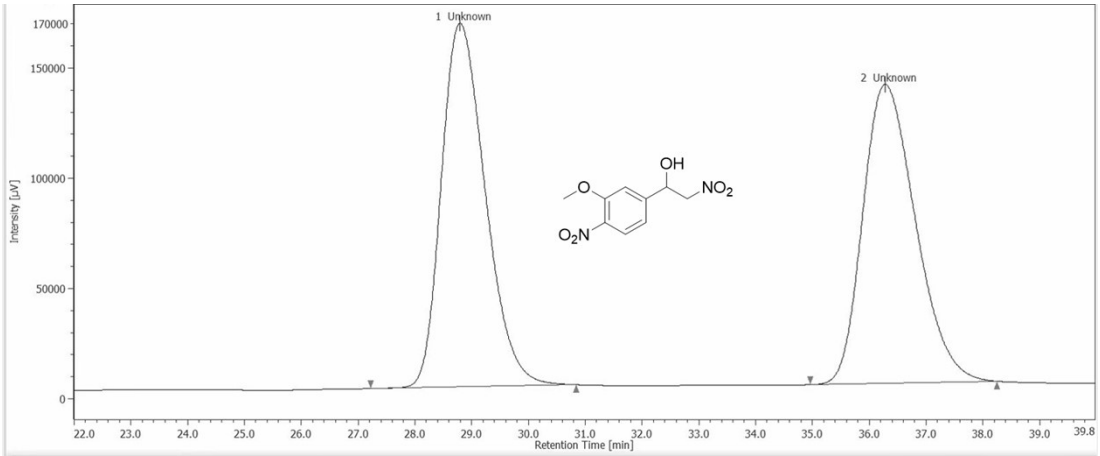

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 27.358 | 33237763 | 535303 | 50.164 | 53.195 | 25.958 | 29.650 | 25.958 | 29.650 |
| 2 | Unknown | 32.183 | 33020028 | 470994 | 49.836 | 46.805 | 30.833 | 34.400 | 30.833 | 34.400 |

**Figure S36**. HPLC curve of *rac*-**6i** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.9 mL/min; 254 nm; 25 °C).



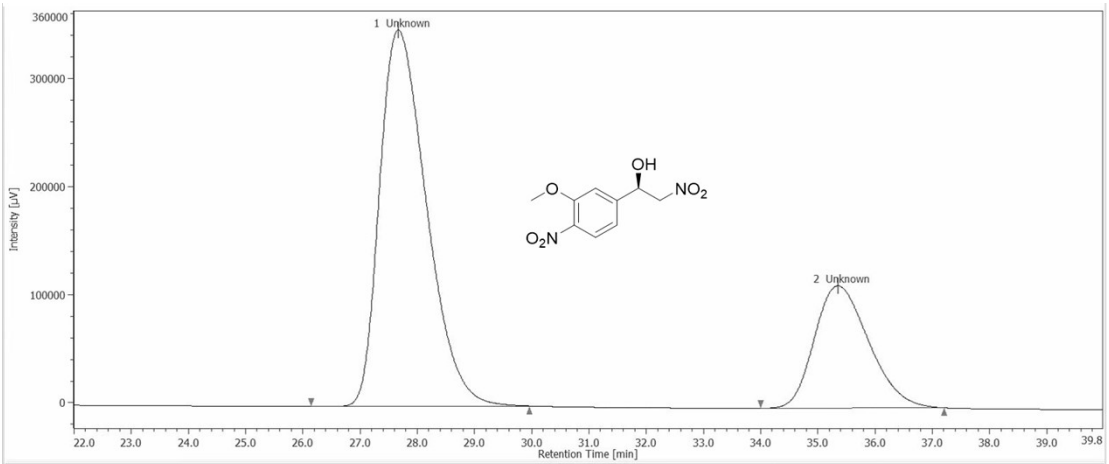

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 27.392 | 32225041 | 517712 | 76.935 | 78.711 | 26.000 | 29.392 | 26.000 | 29.392 |
| 2 | Unknown | 32.408 | 9660906 | 140028 | 23.065 | 21.289 | 31.042 | 34.200 | 31.042 | 34.200 |

**Figure S37**. HPLC curve of (*R*)-**6i** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.9 mL/min; 254 nm; 25 °C).



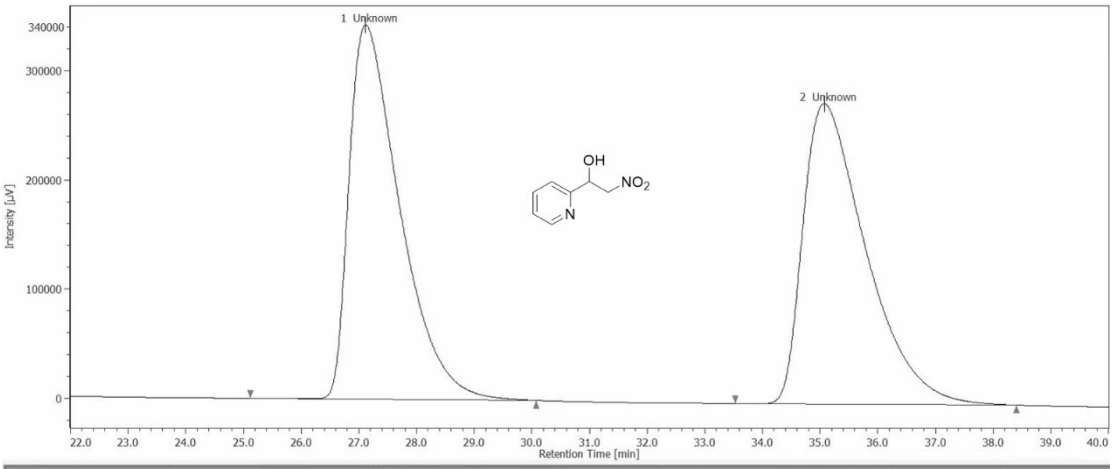

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 28.792 | 8842998 | 164761 | 50.334 | 54.885 | 27.217 | 30.833 | 27.217 | 30.833 |
| 2 | Unknown | 36.275 | 8725644 | 135432 | 49.666 | 45.115 | 34.958 | 38.242 | 34.958 | 38.242 |

**Figure S38**. HPLC curve of *rac*-**6j** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.9 mL/min; 254 nm; 25 °C).



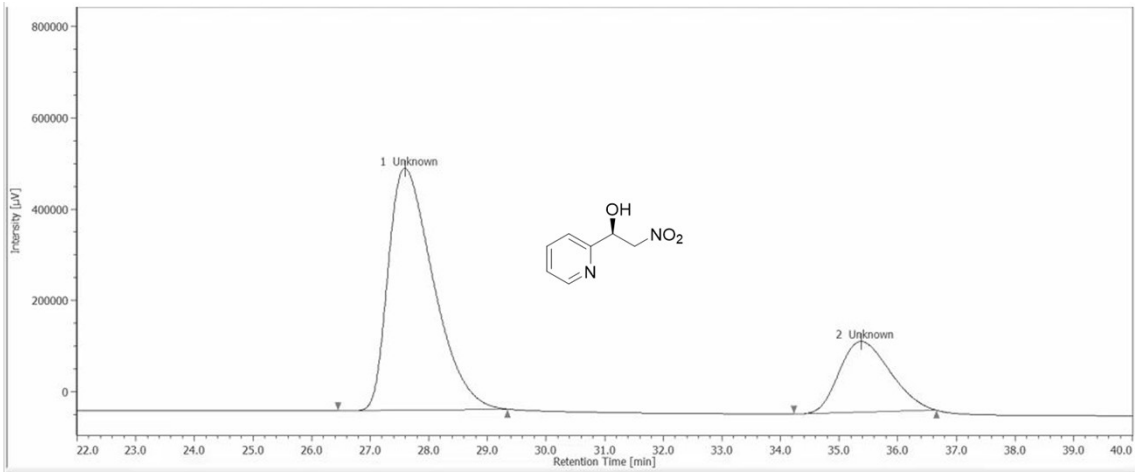

| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 27.667 | 19743961 | 347769 | 72.618 | 75.484 | 26.142 | 29.950 | 26.142 | 29.950 |
| 2 | Unknown | 35.342 | 7444681 | 112952 | 27.382 | 24.516 | 33.992 | 37.200 | 33.992 | 37.200 |

**Figure S39**. HPLC curve of (*R*)-**6j** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.9 mL/min; 254 nm; 25 °C).




| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 27.117 | 20872013 | 341739 | 50.054 | 55.476 | 25.117 | 30.075 | 25.117 | 30.075 |
| 2 | Unknown | 35.067 | 20826687 | 274269 | 49.946 | 44.524 | 33.525 | 38.392 | 33.525 | 38.392 |

**Figure S40**. HPLC curve of *rac*-**6k** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.4 mL/min; 215 nm; 25 °C).




| # | Peak Name | tR | Area | Height | Area% | Height% | Peak Start | Peak End | Base Start | Base End |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 27.592 | 28258351 | 528629 | 75.185 | 77.347 | 26.450 | 29.342 | 26.450 | 29.342 |
| 2 | Unknown | 35.367 | 9326673 | 154824 | 24.815 | 22.653 | 34.225 | 36.650 | 34.225 | 36.650 |

**Figure S41**. HPLC curve of (*R*)-**6k** (Chiralpak OD-H; *n*-hexane/*i*-PrOH = 90/10 (v/v); 0.4 mL/min; 215 nm; 25 °C).

## References


1. Y.-X. Xue, J.-L. Chen, Z.-Q. Jiang, Z. Yu, N. Liu, J. Yin, Z.-Q. Wu, *Polym. Chem.*, 2014, **5**, 6435.
2. S. Medina, M. Harper, E. Balmond, S. Miranda, G. Crisenza, D. Coe, M. Galan, *Org. Lett.*, 2016, **18**, 4222.
3. J. Yin, L. Xu, X. Han, L. Zhou, C.-L. Li, Z.-Q. Wu, *Polym. Chem.*, 2017, *8*, 545.
4. Z.-L. Tang, H. Iida, H.-Y. Hu, E.Yashima, *ACS Macro Lett.*, 2012, **1**, 261.