Electronic Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Supporting Information for:

Proline-based reduced dipeptides as recyclable and highly enantioselective organocatalysts for asymmetric Michael addition

*Xiaohui Cao, Ge Wang, Richeng Zhang, Yingying Wei, Wei Wang ,Huichao Sun, and Ligong Chen**

School of Chemical Engineering and Technology, Tianjin University, Tianjin, China

lgchen@tju.edu.cn

General Methods. ^{1}H and ^{13}C NMR were recorded on Varian-500 instruments. Chemical shifts were reported in ppm down field from internal Me_4Si. All the multiplet patterns assigned the first-order splitting patterns. Mass spectra were recorded using electrospray ionization (ESI) on LCQ Advanted MAX Mass instruments. Optical rotations were tested on a WZZ-3 polarimeter using 10mL cell with a 1 dm path length and Autopol II polarimete using 1mL cell with a 1 dm path length. HPLC analysis was measured using ChiralPak AS-H column.

Materials: Commercial reagents were used without purification except for otherwise explanation. Analytical thin layer chromatography was performed on 0.20 mm silica gel plates and silica gel (200-300 mesh) was used for flash chromatography both purchased from Qingdao Haiyang Chem. Company, Ltd..

Preparation of catalysts:

1. Preparation of (S)-3-phenyl-2-((S)-pyrrolidin-2-ylmethylamino)propanoic acid (4a)

To a stirred solution of N-Boc-L-prolinol **8**[3] (20.1 g, 0.1mol) in dry CH_2Cl_2 (300 mL) were added pyridinium chlorochromate (30.0 g, 0.14mol) and 4 Å molecular sieves (30.0 g). Stirring was continued at room temperature until TLC (EtOAc : Petroleum ether 1:4) showed that 8 had disappeared. Et_2O (300 mL) was added, the mixture was filtered through a Silica Gel G pad and concentrated to a residue that was The residue was chromatographed to afford pure **9**[4] (15.2 g, 76%), 1HNMR(500 MHz, $CDCl_3$) δ: 1.37(5H, s), 1.42(4H, s), 1.76-2.15(4H, m), 3.44(2H, m)，4.00-4.15(1H, m), 9.41(0.6H, d), 9.50(0.4H, br).

To a solution of **9** (2.0g,10.0mmol) in 20mL MeOH was added L-Phenylalanine methyl ester 2.2g,12.1mmol) and 4 Å molecular sieves (2.0 g).After stirred 0.5hours, the Pd/C (wet,5%,0.2g) was added and the complex stirring was continued at room temperature under 1atm H_2.TLC (EtOAc: Petroleum ether 1:1) showed that **9** had disappeared and intermediate **10** had generated[5]. The mixture was filtered to remove the catalyst, then concentrated *in vacuo*. The residue was purified by chromatograph to afford product **10.** (3.4g, 80%), 1HNMR(500 MHz，$CDCl_3$) δ: 1.42 (9H, s), 1.71-1.78 (4H, m), 2.52-2.55 (3H, m), 2.89-2.93 (2H, m), 3.19-3.21 (1H, m), 3.24-3.29 (2H, m), 3.46- 3.51(1 H, m), 3.60 (3H, s), 7.22-7.29 (5H, m),

10 (3.4g, 9mmol) was dissolved in MeOH 20mL and NaOH aqueous solution (1M, 12mL) was added, the mixture stirred until TLC showed no remaining starting material. After removed the organic solvent in vacuo, the residue was dissolved in 5mL H_2O. Then the aqueous solution was acidified to pH= 6 with 1M HCl, the compound **11** was precipitated. (2.8g, 90%), ^{1}HNMR(500 MHz, CD_3OD) δ: 1.37 (9H, s), 1.62-1.67 (1H, m), 1.75-1.87 (2H, m), 2.08-2.13 (1H, m), 2.87 -2.91(1H, m), 3.04-3.09 (1H, m), 3.39-3.44 (1H, m), 3.73-3.75 (1H, m), 3.92-3.94 (1H, m), 7.26-7.34(5H, m). ^{13}CNMR (125MHz, CD_3OD) δ: 23.50, 27.43, 30.26, 37.05, 52.79, 55.43, 64.49, 81.14, 127.456, 128.90, 129.37, 135.45, 157.29, 171.48.

11(2.8g,8mmol) was added to 20mL CH_2Cl_2 and the slurry chilled to 5℃, then was added 10mL TFA. The mixture stirred until TLC showed the starting material disappeared. After removed the solvent in vacuo, the residue was dissolved in 30mL H2O. The aqueous solution was neutralized with NaHCO3 (PH=6), then poured into a column with cation exchange resin (30g). The target compound **4a** was washed off by 2N aqueous ammonia then purified by chromatograph. (1.3g , 64%).

$[\alpha]_D^{rt}$= -50.1° (c=1.0, MeOH)

^{1}HNMR(500 MHz, CD_3OD) δ: 1.60-1.67(1H, m), 1.84-1.89(2H, m), 1.96-2.00(2H, m), 2.72-2.79(3H, m), 3.06-3.11(2H, m), 3.15-3.23(1H, m), 3.39-3.42(1H, m), 3.50-3.55(1H, m), 7.17-7.25(5H,m).

^{13}CNMR (125MHz, CD_3OD) δ: 24.62, 27.66, 39.81, 45.26, 47.29, 59.82, 65.07, 126.23, 128.22, 129.22, 139.21, 180.57.

IR (KBr): 3312, 2934, 2394, 1670, 1582, 1392, 1120, 867, 750, 525 cm^{-1}.

HRMS (ESI) calcd for $[M+H]^+$: $C_{14}H_{21}N_2O_2$, m/z 249.1608, found 249.1603

2. Preparation of (R)-3-phenyl-2-((S)-pyrrolidin-2-ylmethylamino)propanoic acid (4b)

The catalyst **4b** was synthesized from L-Phenylalanine methyl ester utilizing the similar procedure of **4a.**

$[\alpha]_D^{rt}$= +61.4° (c=1.0, MeOH)

^{1}HNMR(500 MHz, CD_3OD) δ: 1.53-1.60(1H, m), 1.91-1.99(3H, m), 2.32-2.37(1H, m), 2.69(1H, dd, J_1=14.0Hz, J_2=9.5Hz), 2.88(1H, dd, J_1=9.0Hz, J_2=4.5Hz), 3.13-3.23(3H, m), 3.44-3.46(1H, dd, J_1=14.5Hz, J_2=4.0Hz), 3.51-3.56(1H, m), 7.18-7.30(5H,m).

^{13}CNMR(125 MHz, CD_3OD) δ: 24.31, 27.37, 39.95, 44.63, 48.79, 60.36, 65.03, 126.35, 128.38, 129.06, 139.09, 180.49.

IR (KBr): 3320, 2927, 2389, 1586, 1532, 1400, 1020, 858, 723, 675, 543 cm^{-1}.

HRMS (ESI) calcd for $[M+H]^+$: $C_{14}H_{21}N_2O_2$, m/z 249.1608, found 249.1605

3. Preparation of (S)-3-methyl-2-((S)-pyrrolidin-2-ylmethylamino)butanoic acid (5)

The catalyst **5** was synthesized from L-Phenylalanine methyl ester utilizing the similar procedure of **4a.**

$[\alpha]_D^{rt}$= -11.4° (c=1.0, MeOH)

^{1}HNMR(500 MHz, CD_3OD) δ: 0.95(3H, d, J=7.0Hz), 0.99 (3H, d, J=7.0Hz), 1.75-1.79(1H, m), 1.92-1.98 (2H, m), 2.06-2.11 (2H, m), 2.79 (2H, qd, J_1=13.5Hz, J_2=6.0Hz), 2.92 (1H, d, J=5.0Hz), 3.19-3.29 (2H, m), 3.57-3.62 (1H, m).

^{13}CNMR(125 MHz, CD_3OD) δ: 17.83, 19.10, 24.50, 27.76, 31.65, 45.44, 48.35, 59.99, 70.08, 180.76.

IR (KBr): 3380, 2937, 2479, 1676, 1390, 1220,798, 743, 645, 583 cm^{-1}.

HRMS (ESI) calcd for $[M+H]^+$: $C_{10}H_{21}N_2O_2$, m/z 201.1603, found 201.1597

4. Preparation of (S)-3-hydroxy-2-((S)-pyrrolidin-2-ylmethylamino)propanoic acid (6)

The catalyst **6** was synthesized from L-Phenylalanine methyl ester utilizing the similar procedure of **4a.**

$[\alpha]_D^{rt}$= -17.4^o (1.0, MeOH)

^{1}HNMR(500 MHz，CD_3OD) δ：1.72-1.80 (1H, m), 1.88-2.00(1H, m), 2.05-2.11 (2H, m), 2.85-2.87 (2H, m), 3.24-3.29 (3H, m), 3.51 (1H, dd, J_1= 10.5Hz, J_2= 8.5Hz), 3.60-3.65 (1H, m), 3.86 (1H, dd, J_1= 11.0Hz, J_2= 4.0Hz).

^{13}CNMR(125 MHz，CD_3OD) δ：24.37, 27.98, 45.17, 48.86, 59.72, 63.34, 65.73, 178.45.

IR(KBr): 3350, 2930, 1589, 1398, 1022, 776, 658cm^{-1}.

HRMS (ESI) calcd for $[M+H]^+$: $C_8H_{17}N_2O_3$, m/z 189.1234, found 189.1229

5. Preparation of (S)-2-(pyrrolidin-2-ylmethylamino)acetic acid (7)

The catalyst **7** was synthesized from L-Phenylalanine methyl ester utilizing the similar procedure of **4a.**

$[\alpha]_D^{rt}$= 16.7^o (0.9, MeOH)

^{1}HNMR(500 MHz，CD_3OD) δ：1.65-1.72 (1H, m), 1.94-1.98(1H, m), 2.00-2.11 (2H, m), 2.73(1H, dd, J_1=13.5Hz, J_2=8.5Hz), 2.94 (1H, dd, J_1= 14.0Hz, J_2= 9.0Hz), 3.24 (2H, t, J=7.0Hz), 3.28 (1H, s), 3.60-3.66(1H, m).

^{13}CNMR(125 MHz，CD_3OD) δ：24.40, 27.71, 45.09, 49.87, 52.02, 59.75, 178.17.

IR(KBr): 3357, 3030, 1619, 1378, 948, 814, 724, 598cm^{-1}.

HRMS (ESI) calcd for $[M+H]^+$: $C_7H_{15}N_2O_2$, m/z 159.1128, found 159.1224

General experimental procedure for the Michael addition of cyclohexanone to nitroalkene by chiral catalyst 1, 2 and 3.

To a solution of the amide catalyst (0.1 mmol), TFA (0.1mmol) and the nitroalkene (0.5 mmol) in Solvent (1 ml) was added cyclohexanone (5 mmol), and the solution was stirred at ambient temperature until TLC showed the nitroalkene disappeared. Ethyl acetate (10 volumes)was added and the solution was washed with water, 1N HCl, dried (Na_2SO_4) and concentrated to give the crude product which was purified by flash chromatography on silica gel.

Relative and absolute configurations of the products were determined by comparison with the known 1H NMR, chiral HPLC analysis, and optical rotation values.

General experimental procedure for the Michael addition of cyclohexanone to nitroalkene by chiral catalyst 4a, 4b, 5, 6 and 7.

To a solution of the catalyst (0.075mmol) in MeOH(0.5mL)was added cyclohexanone (2.5mmol) and the nitroalkene(0.5mmol), and the solution was stirred ambient temperature until TLC showed the nitroalkene disappeared. The mixture was concentrated and the residue diluted by 1mL mixture solvent (ethyl acetate-petroleum ether 1:1) to precipitate the catalyst. The catalyst was recovered by filter and washed with petroleum ether. The filtrate was concentrated to give crude product which was purified by chromatography on silica gel. Compounds **14a-k** reported in Table 2 (entries 1-10) are known in literature and our spectroscopic data are in agreement with published data [5-8].

NMR data and HPLC data for Michael addition products

14a

^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.10-1.23 (1H, m), 1.43-1.73 (4H, m), 1.97-2.05 (1H, m), 2.26-2.45 (2H, m), 2.57-2.66 (1H, m), 3.65-3.73 (1H, m), 4.56 (1H, dd, *J* 12.5, 9.9 Hz), 4.87 (1H, dd, *J* 12.5, 4.5 Hz), 7.07-7.28 (5H, m);

^{13}C NMR (125MHz, $CDCl_3$) δ: 25.1, 28.4, 33.3, 42.7, 44.0, 52.3, 79.0, 127.7, 128.3, 129.0, 137.6, 210.1

MS (ESI, m/z): 248.1 ($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 90:10), 0.7 ml/min; t_r= 24.1min (minor), 36.8 min (major).

14b

^{1}H NMR (500 MHz, $CDCl_3$) δ : 1.20-1.28 (1H, m), 1.57-1.81 (4H, m), 2.03-2.11 (1H, m), 2.32 (3H, s), 2.36-2.42 (1H, m), 2.46-2.50 (1H, m), 2.64-2.70 (1H, m), 3.70-3.75 (1H, m), 4.59-4.63 (1H, m), 4.90-4.94 (1H, m) , 7.04 (2H, d, J=8.0 Hz) , 7.12 (2H, d, J=8.0 Hz).

^{13}C NMR (125MHz, CDCl3) δ: 20.9, 24.9, 28.4, 33.0, 42.6, 43.4, 52.4, 78.9, 127.9, 129.4, 134.5, 137.2, 211.9

MS (ESI, m/z): 266.3 ($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 90:10), 0.7 ml/min; t_r= 14.0min (minor), 27.7 min (major).

14c

^{1}H NMR (500 MHz, $CDCl_3$) δ : 1.19-1.28 (1H, m), 1.57-1.82 (4H, m), 2.05-2.11 (1H, m), 2.36-2.42 (1H, m), 2.46-2.50 (1H, m), 2.62-2.68 (1H, m), 3.69-3.74 (1H, m), 3.79 (3H, s), 4.57-4.61 (1H, m), 4.90-4.93 (1H, m) , 6.84 (2H, d, J=8.5 Hz) , 7.06 (2H, d, J=8.5 Hz).

^{13}C NMR (125MHz, $CDCl_3$) δ: 24.8, 28.4, 33.0, 42.5, 43.0, 52.5, 55.0, 78.9, 114.1, 129.0, 129.4, 158.8, 211.9.

MS (ESI, m/z): 278.1 ($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 90:10), 0.7 ml/min; t_r= 42.2min (minor), 68.6 min (major).

14d

^{1}H NMR (500 MHz, $CDCl_3$) δ : 1.19-1.28 (1H, m), 1.57-1.83 (4H, m), 2.08-2.13 (1H, m), 2.35-2.42 (1H, m), 2.46-2.51 (1H, m), 2.63-2.68 (1H, m), 3.74-3.79 (1H, m), 4.59-4.63 (1H, m), 4.92-4.96 (1H, m) , 7.11-7.14 (2H, m) , 7.29-7.32 (2H, m).

^{13}C NMR (125MHz, $CDCl_3$) δ: 211.6, 136.2, 133.6, 129.5, 129.1, 78.5, 52.3, 43.5, 42.7, 33.2, 28.5, 25.1.

MS (ESI, m/z): 282.0($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 90:10), 0.7 ml/min; t_r=22.7min (minor),37.9 min (major).

14e

^{1}H NMR (500 MHz, $CDCl_3$) δ : 1.30-1.38 (1H, m), 1.59-1.85 (4H, m), 2.09-2.14 (1H, m), 2.37-2.43 (1H, m), 2.47-2.51 (1H, m), 2.90-2.97 (1H, m), 4.27-4.31 (1H, m), 4.87-4.94 (2H, m), 7.20-7.25 (3H, m) , 7.38-7.39 (1H, m).

^{13}C NMR (125MHz, $CDCl_3$) δ: 25.3, 28.5, 33.0, 41.0, 42.8, 51.7, 77.3, 128.9, 130.4,134.6, 135.5, 211.7,

MS (ESI, m/z): 282.1($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 90:10), 0.7 ml/min; t_r= 20.6min (minor), 28.6 min (major).

14f

^{1}H NMR (500 MHz, $CDCl_3$) δ : 1.30-1.38 (1H, m), 1.60-1.86 (4H, m), 2.10-2.15 (1H, m), 2.35-2.42 (1H, m), 2.46-2.51 (1H, m), 2.84-2.92 (1H, m), 4.11-4.24 (1H, m), 4.86-4.92 (2H, m) , 7.17 (1H, d, J=8.0 Hz) , 7.23 (1H, dd, J_1=8.0 Hz, J_2=2.0 Hz), 7.41 (1H, d, J=2.0 Hz).

^{13}C NMR (125MHz, $CDCl_3$) δ: 25.2, 27.0, 28.4, 32.9, 40.5, 42.7, 51.6, 77.4, 127.7, 130.0, 133.9, 134.2, 135.2, 211.3.

MS (ESI, m/z): 316.2($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 90:10), 0.7 ml/min; t_r=16.4min (minor), 25.0min (major).

14g

^{1}H NMR (500 MHz, $CDCl_3$) δ : 1.22–1.32 (1H, m), 1.56–1.77 (3H, m), 1.78–1.85 (1H, m), 2.16–2.08 (1H, m), 2.44–2.35 (1H, m), 2.52–2.45 (1H, m), 2.78–2.69(1H, m), 3.94 (1H, td, J_1 = 10.0 J_2=4.5 Hz,), 4.71 (1H, dd, J_1 = 13.0 J_2= 10.0 Hz,), 5.00 (1H, dd, J_1 =13.0 , J_2=4.5 Hz,), 7.41 (2H, d, J = 8.5 Hz), 8.15 (2H, d, J =8.5 Hz,).

^{13}C NMR (125MHz, $CDCl_3$) δ: 24.9, 28.1, 33.0, 42.5, 43.6, 52.0, 77.9, 123.9, 129.2, 145.5, 147.2, 210.8.

MS (ESI, m/z): 315.1($M+Na^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack OD-H column at 238nm (hexane:2-propanol 80:20), 0.9 ml/min; t_r=47.4min (minor), 58.6 min (major).

14h

^{1}H NMR (500 MHz, $CDCl_3$) δ : 1.19-1.28 (1H, m), 1.57-1.82 (4H, m), 2.05-2.11 (1H, m), 2.36-2.42 (1H, m), 2.46-2.50 (1H, m), 2.62-2.68 (1H, m), 3.69-3.74 (1H, m), 3.79 (3H, s), 4.57-4.61 (1H, m), 4.90-4.93 (1H, m) , 6.84 (2H, d, *J*=8.5 Hz) , 7.06 (2H, d, *J*=8.5 Hz).

^{13}C NMR (125MHz, $CDCl_3$) δ: 25.2, 28.2, 33.0, 41.8, 42.7, 52.1, 77.6, 124.7, 128.4, 129.0, 132.7, 133.0, 150.7, 211.0.

MS (ESI, m/z): 293.2($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 93:7), 0.7 ml/min; t_r=37.4min (minor), 78.6 min (major).

14i

^{1}H NMR (500 MHz, $CDCl_3$): δ2.51-2.57 (1H, m), 2.60-2.69 (1H, m), 2.85-2.91 (1H, m), 3.27 (dd, J_1 = 20.0Hz, J_2=8.5 Hz, 1H), 3.65-3.87 (3H, m), 4.10-4.18 (1H, m), 4.62-4.67 (1H, m), 4.94 (1H, dd, J_1 = 12.5, J_2=4.5 Hz,), 7.17-7.36 (5H, m).

^{13}C NMR (125MHz, $CDCl_3$) δ: 41.26, 42.91, 53.20, 68.92, 71.52, 78.64, 127.87, 128.23, 129.18, 136.21, 207.32.

MS (ESI, m/z): 250.1($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 90:10), 0.7 ml/min; t_r=35.6min (minor), 43.6 min (major).

14j

^{1}H NMR (500 MHz, $CDCl_3$,): δ: 2.48 (1H , dd, J_1=13.5 Hz,J_2=9.5,) , 2.62–2.66 (1H, m,), 2.82–2.95 (2H, m), 2.96–3.09 (3H, m), 4.03 (1H , dt, J_1=10.0 Hz, J_2= 4.4Hz,), 4.63 (1H, dd, J_1=12.5 Hz, J_2=10.0Hz,), 4.76 (dd, J_1= 12.5 Hz, J_2= 4.5Hz, 1H),7.22–7.42 (5H, m);

^{13}C NMR (125MHz, $CDCl_3$) δ: 31.6, 35.1, 44.5, 53.5, 55.0, 78.5, 128.1, 128.3, 129.3, 136.4, 209.5.

MS (ESI, m/z): 266.1($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 80:20), 0.9ml/min; t_r= 20.5 min (minor), 28.7min (major).

14k

^{1}H NMR ($CDCl_3$, 500 MHz): □ 1.57-1.78 (2H, m), 1.78-1.95 (2H, m), 2.04-2.54 (3H, m), 3.66–3.72 (1 H, m), 4.66–4.79 (1H, anti-isomer, m), 5.01 (1H, d, J = 8.5 Hz), 7.15-7.37 (5H, m). ^{13}C NMR ($CDCl_3$, 125 MHz): 20.15, 28.19, 38.56, 44.06, 50.37, 78.19, 127.76, 127.90, 128.36, 137.32, 218.48.

MS (ESI, m/z): 266.1($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at

238nm (hexane:2-propanol 80:20), 0.5ml/min; t_r= 18.6 min (minor), 32.3min (major).

14l

^{1}H NMR (500 MHz, CDCl3) δ: 0.95 (3H, d, J = 7.1 Hz,), 1.05 (3H, t, J = 7.3 Hz), 2.43−2.35 (m, 1H), 2.63–2.54 (m, 1H), 3.01-2.94 (m, 1H), 3.73−3.68 (m, 1H), 4.58 (1H, dd, J_1 = 12.5Hz, J_2= 4.5 Hz), 4.65 (1H, dd, J_1 = 12.5Hz, J_2=9.0 Hz), 7.33−7.25 (m, 3H), 7.15−7.14 (m, 2H).

^{13}C NMR (125MHz, $CDCl_3$) δ: 7.2, 14.3, 35.7, 45.8, 49.0, 77.5, 128.8, 138.0, 212.5.

MS (ESI, m/z): 236.2($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 90:10), 0.7 ml/min; t_r=13.0min (minor), 17.4 min (major).

14m

^{1}H NMR (500 MHz, $CDCl_3$) δ：2.13（3H, s），2.92（2H, d, J=5Hz），3.99-4.04（1H, m），4.59-4.63（1H, dd, J_1=12.5Hz, J_2=8.0Hz）4.68-4.72（1H, dd, J_1=12.5Hz, J_2=6.5Hz）, 7.21-7.53（5H, m）

^{13}C NMR (125MHz, $CDCl_3$) δ: 30.4, 39.0, 46.1, 55.5, 79.4, 127.3, 127.9, 129.0, 138.8, 205.4.

MS (ESI, m/z): 208.0($M+H^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 90:10), 0.7 ml/min; t_r=27.9min (minor), 34.9 min (major).

14n

^{1}H NMR (500 MHz, $CDCl_3$) δ : 0.97 (3H, d, J= 7.5Hz), 2.22 (3H, s), 2.94-3.00 (1H, m), 3.68 (1H, dt, J_1= 9.0Hz, J_2=5.0Hz), 4.60-4.68 (2H, m), 7.15-7.35 (5H, m).

^{13}C NMR (125MHz, $CDCl_3$) δ: 14.2, 29.4, 45.7, 49.7, 77.5, 127.8, 127.9, 128.9, 137.9, 209.8.

MS (ESI, m/z): 222.1(M+H$^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 90:10), 0.5 ml/min; t_r=30.8min (minor), 37.7 min (major).

14o

^{1}H NMR (500 MHz, $CDCl_3$) δ : 0.82-0.91 (3H, m), 1.48-1.55 (2H, m), 2.66-2.72 (1H, m),3.77-3.82 (1H, m), 4.61-4.75 (2H, m), 7.18-7.22 (2H, m), 7.29-7.37 (2H, m), 9.73 (1H, d, J=2.5 Hz).

^{13}C NMR (125MHz, $CDCl_3$) δ: 10.7. 20.4, 42.7, 55.0, 78.5, 128.0, 128.1, 129.1, 136.7, 203.2,

MS (ESI, m/z): 222.3(M+H$^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 99:1), 2.0 ml/min; t_r=28.6min (minor), 30.8 min (major).

14p

^{1}H NMR (500`MHz, CDCl3) δ : 0.99 (3H, d, J = 7.3 Hz) , 2.71-2.83 (1H, m), 3.78 (1H, td, J1 = , 5.5 Hz, J2= 9.5Hz), 4.65 (1H, dd, J1 =9.5Hz, J2= 12.5Hz), 4.76 (1H, dd, J1 = 13.0Hz, J2= 5.5 Hz), 7.16-7.35 (5H, m), 9.72 (1H, d, J = 1.8 Hz).

^{13}C NMR (125MHz, CDCl3) δ: 12.1, 44.0, 48.4, 78.1, 128.0, 128.1, 129.1, 136.5, 202.2.

MS (ESI, m/z): 208.2(M+H$^+$)

The enantiomeric excess was determined by chiral HPLC with a Chiralpack OD column at 238nm (hexane:2-propanol 80:20), 1.0 ml/min; t_r=23.6min (minor), 29.8 min (major).

14q

^{1}H NMR (500`MHz, CDCl3) δ : 1.01 (3H, s), 1.13(3H, s), 3.78(1H, dd, J_1=11.5Hz, J_2=4.5Hz), 4.69 (1H, dd, J_1=13.0Hz, J_2=4.5Hz), 4.85(1H, dd, J_1=13.0Hz, J_2=4.5Hz), 7.18-7.35(5H, m), 9.52 (1H, s).

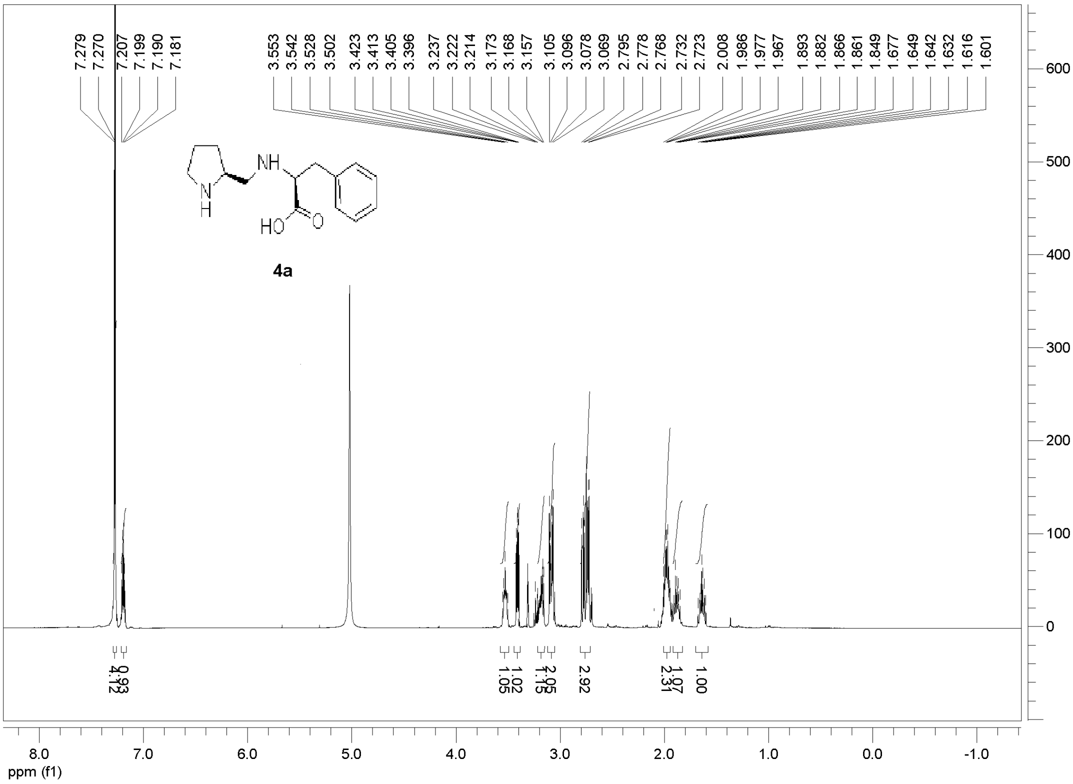
^{13}C NMR (125MHz, $CDCl_3$) δ: 204.4, 135.5, 129.3, 128.9, 128.4, 48.7, 48.4, 21.8, 19.1.

MS (ESI, m/z): 222.1($M+H^+$)

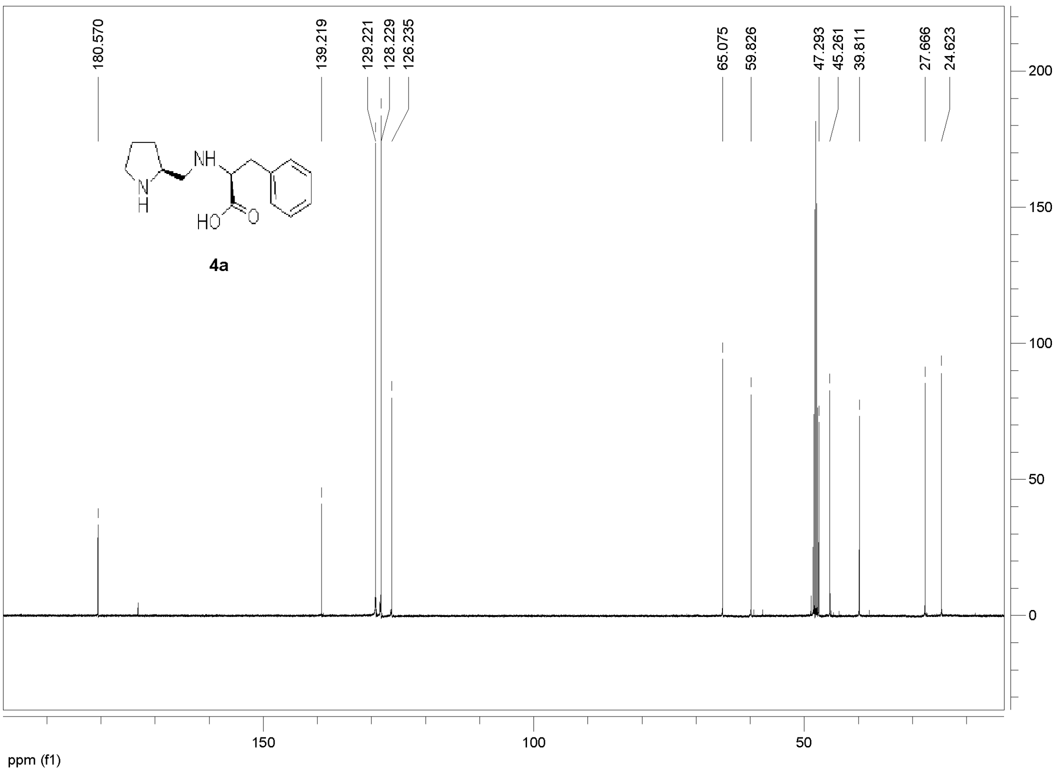
The enantiomeric excess was determined by chiral HPLC with a Chiralpack AS-H column at 238nm (hexane:2-propanol 80:20), 0.5 ml/min; t_r=36.2min (minor), 39.8 min (major).

NMR Spectra for New Catalysts

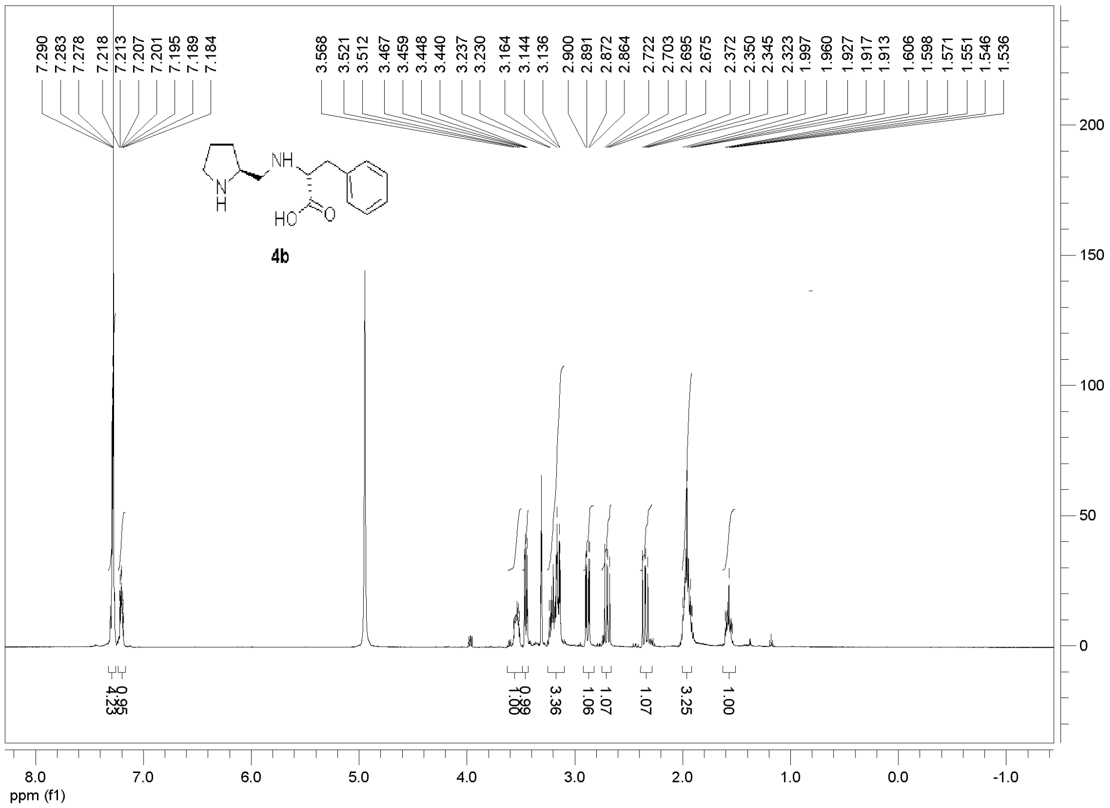
[1]HNMR of **4a**



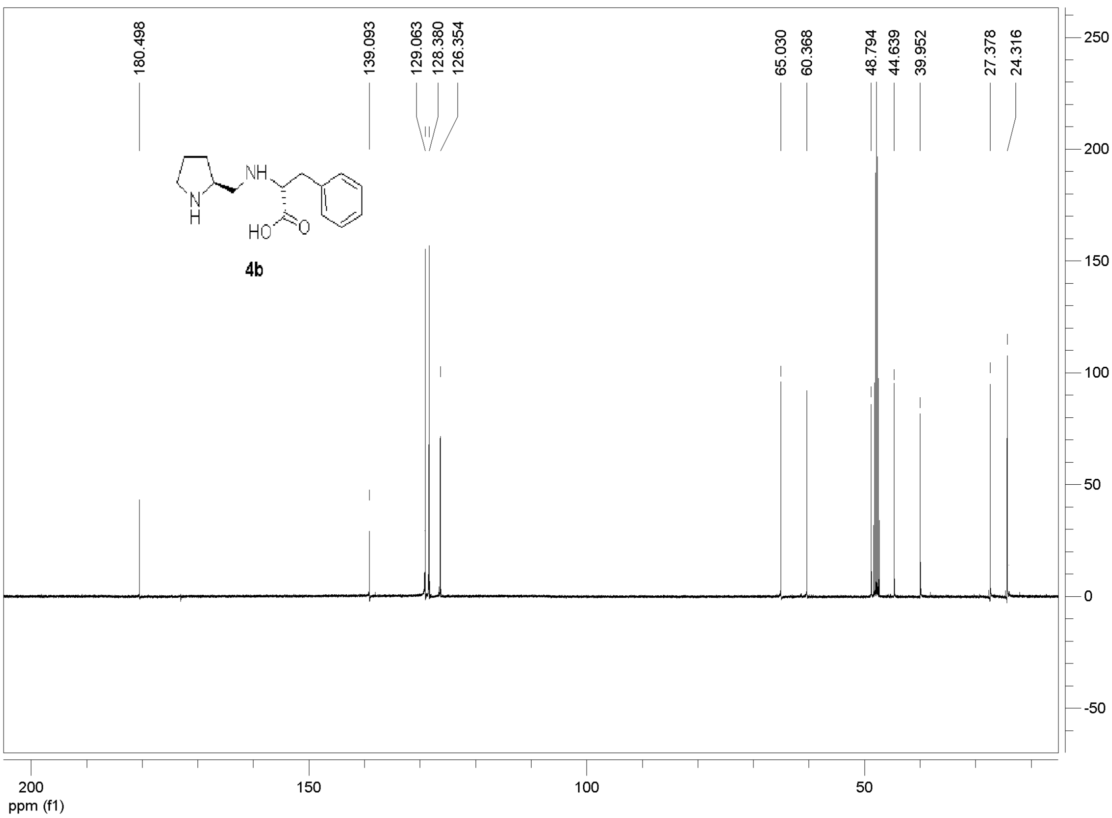
[13]CNMR of **4a**



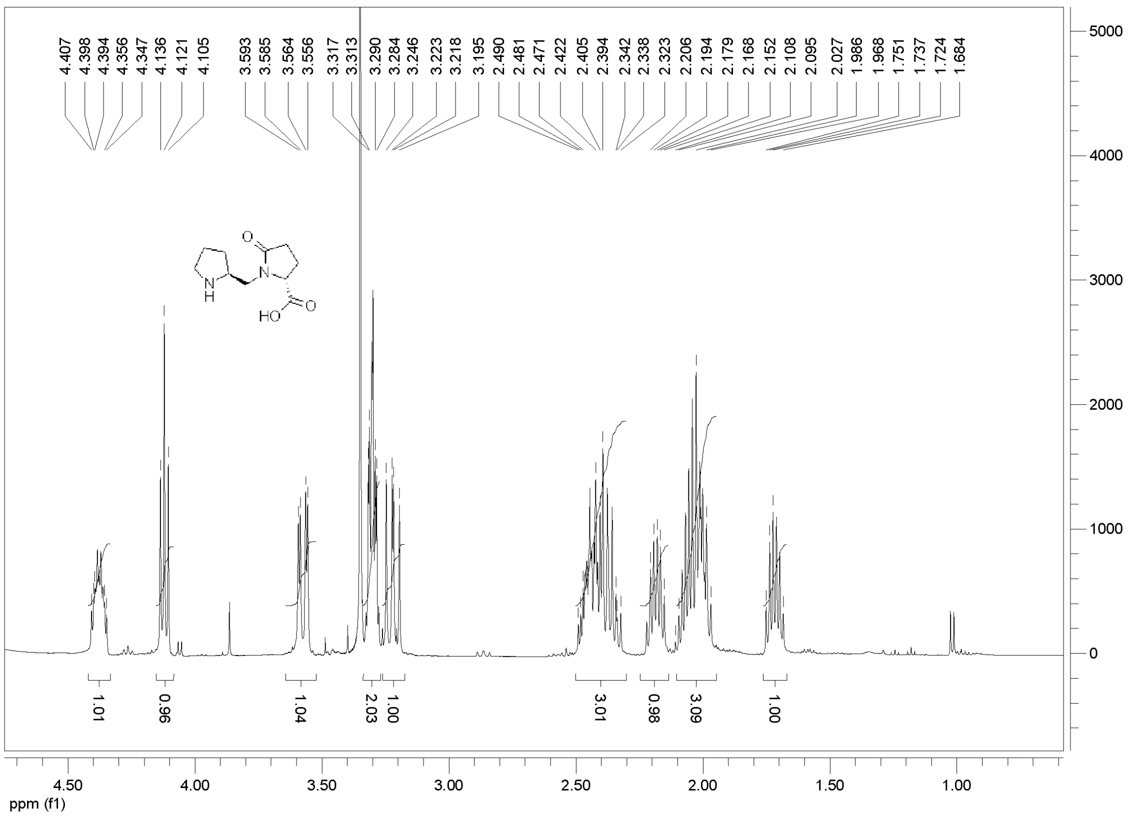
[1]HNMR of **4b**



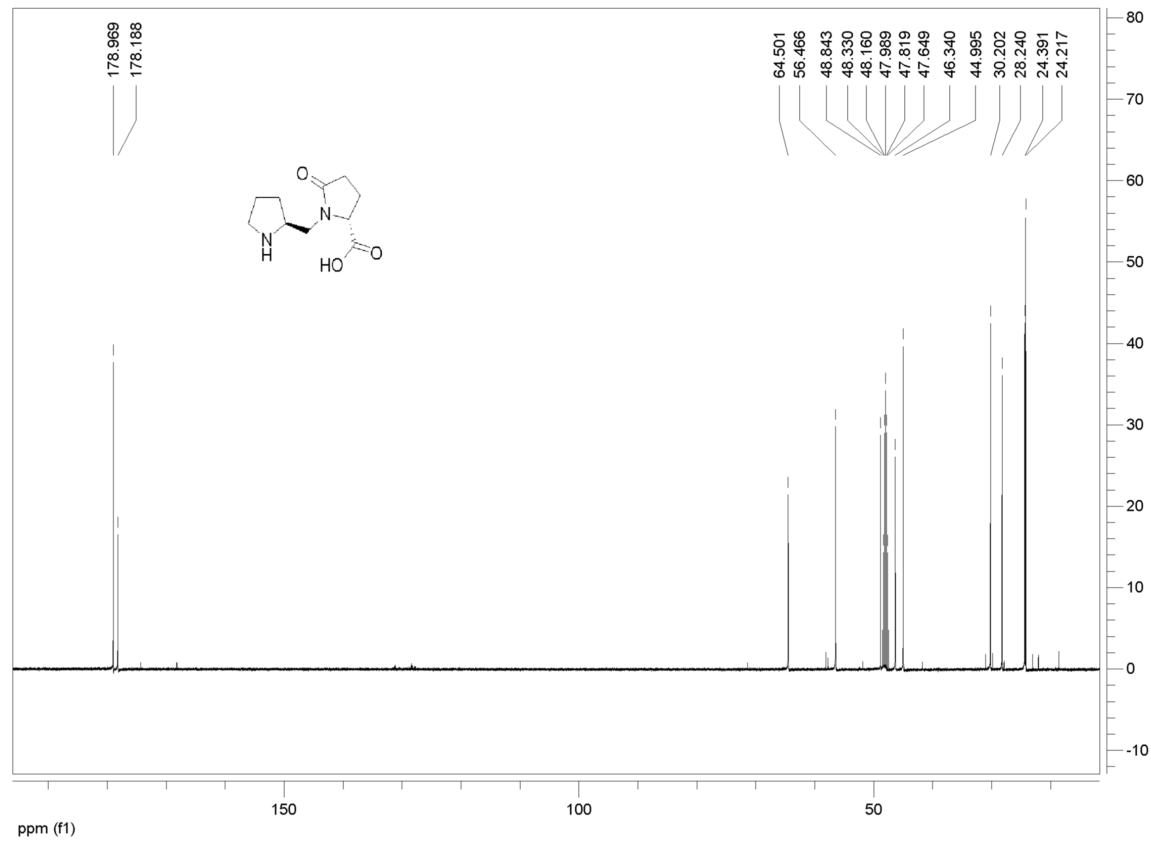
[13]CNMR of 4a



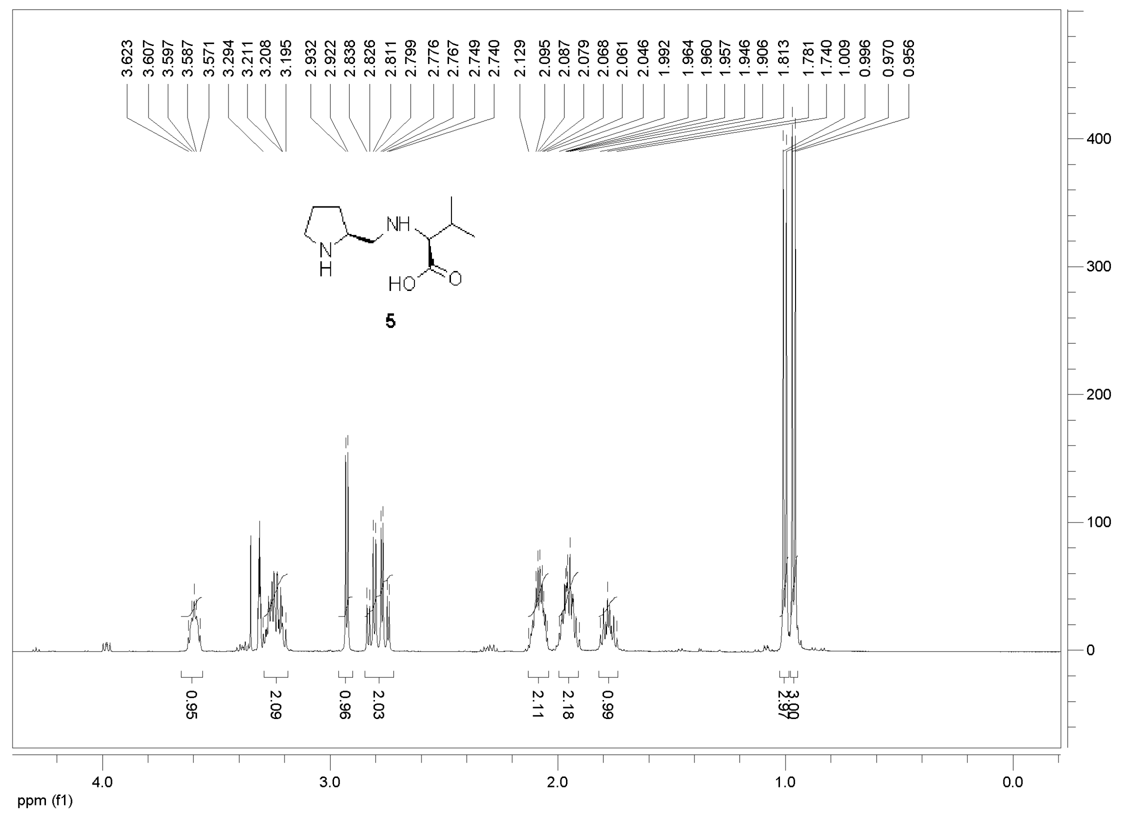
^{1}HNMR of **4b**



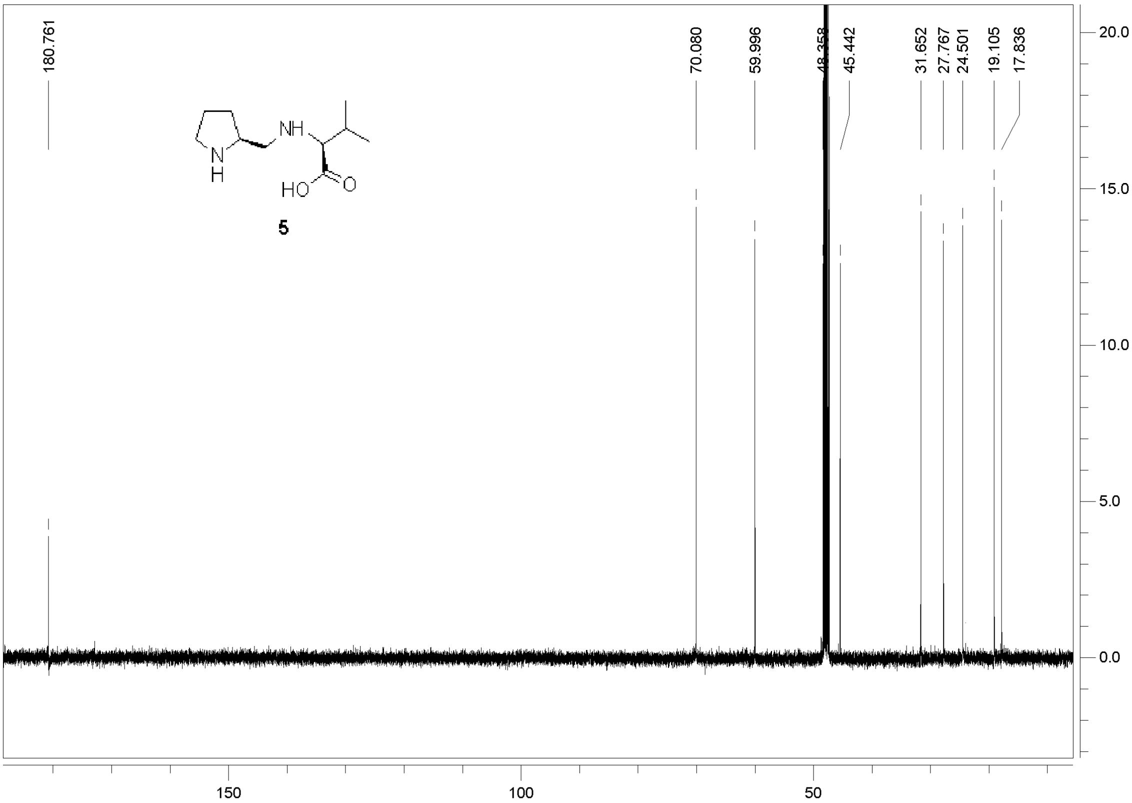
^{13}CNMR of **4b**


178.969
178.188
64.501
56.466
48.843
48.330
48.160
47.989
47.819
47.649
46.340
44.995
30.202
28.240
24.391
24.217
O
N
N
H
HO
O
150
100
50
ppm (f1)

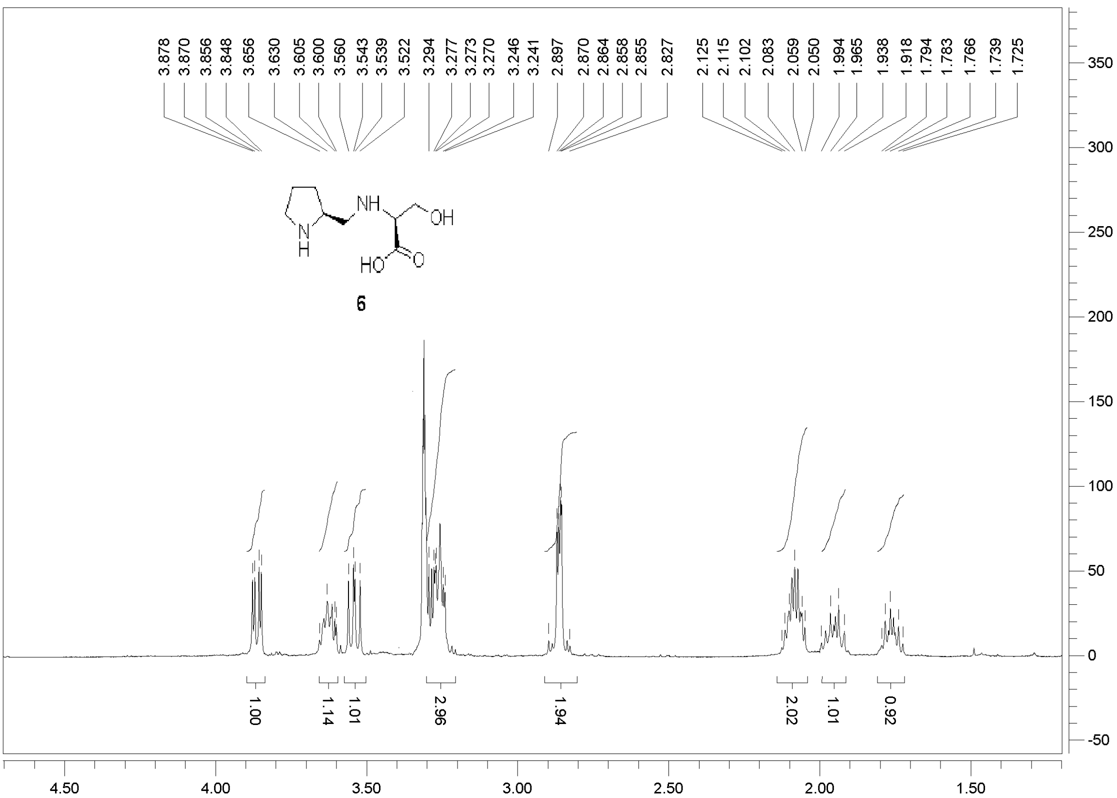
^{1}HNMR of **5**


3.623
3.607
3.597
3.587
3.571
3.294
3.211
3.208
3.195
2.932
2.922
2.838
2.826
2.811
2.799
2.776
2.767
2.749
2.740
2.129
2.095
2.087
2.079
2.068
2.061
2.046
1.992
1.964
1.960
1.957
1.946
1.906
1.813
1.781
1.740
1.009
0.996
0.970
0.956
NH
N
H
HO
O
5
0.95
2.09
0.96
2.03
2.11
2.18
0.99
3.00
2.97
4.0
3.0
2.0
1.0
0.0
ppm (f1)

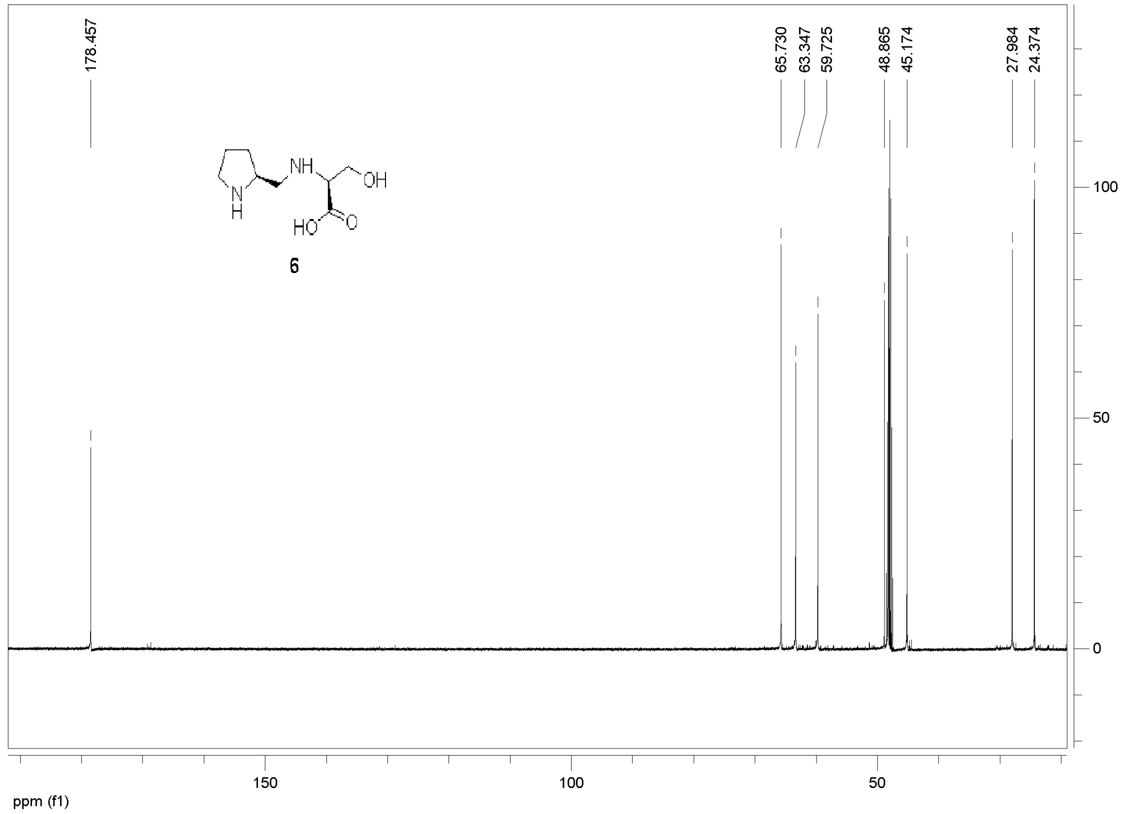
^{13}CNMR of **5**



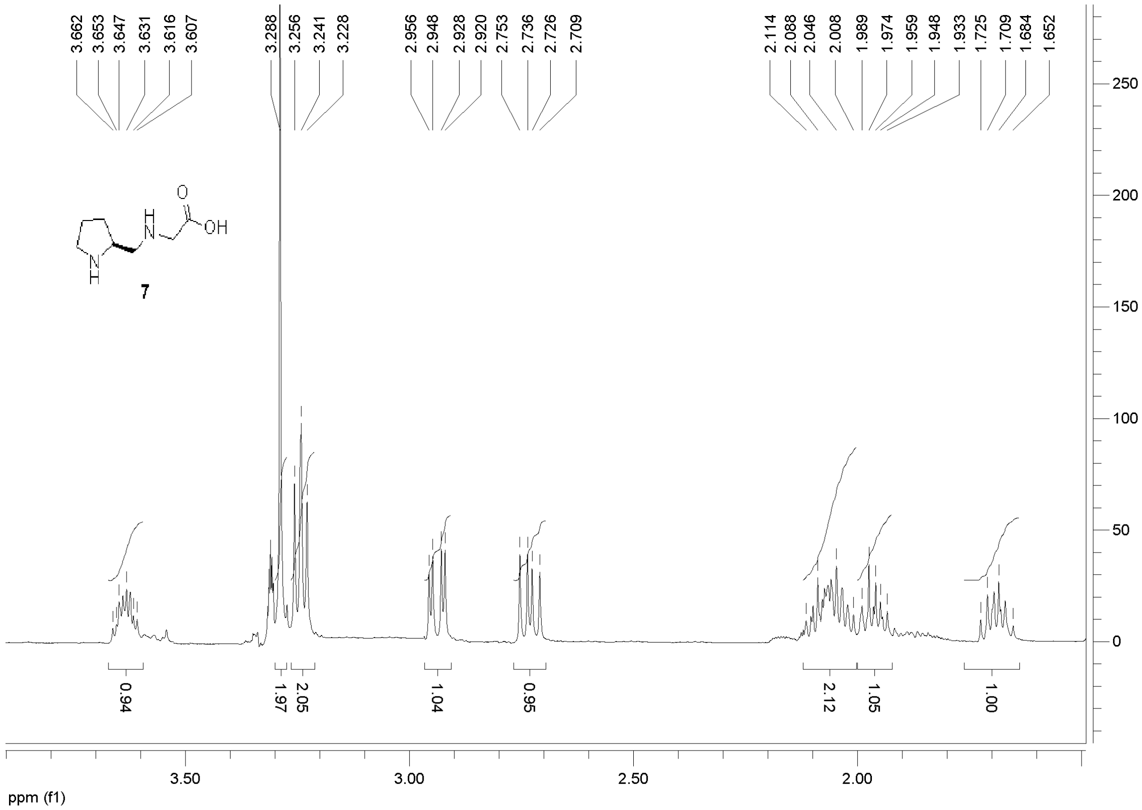
^{1}HNMR of **6**



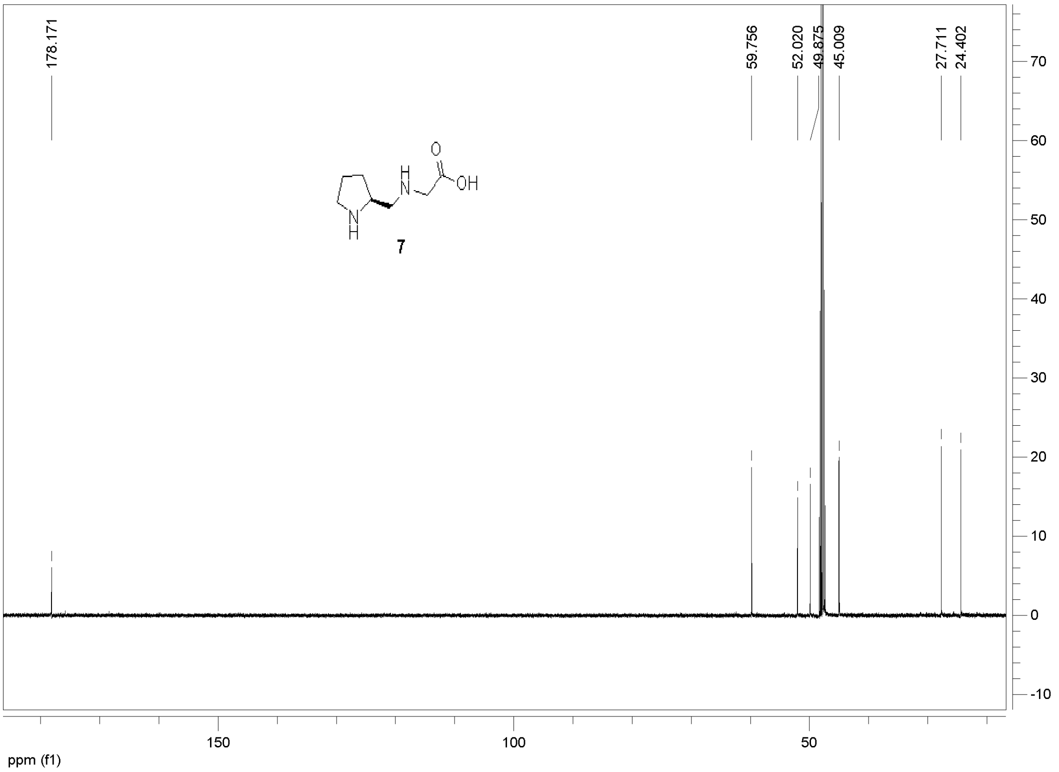
^{13}CNMR of **6**



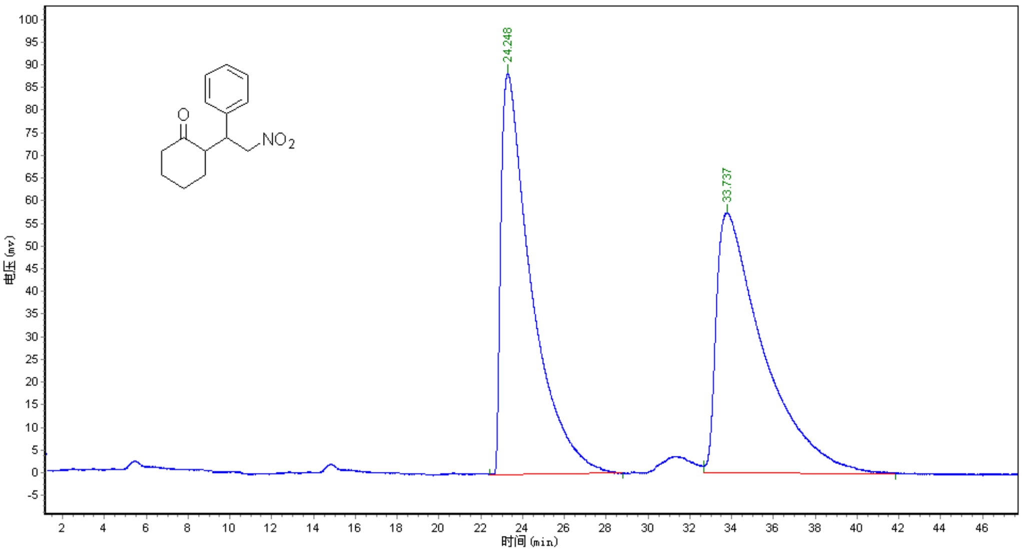
^{1}HNMR of **7**



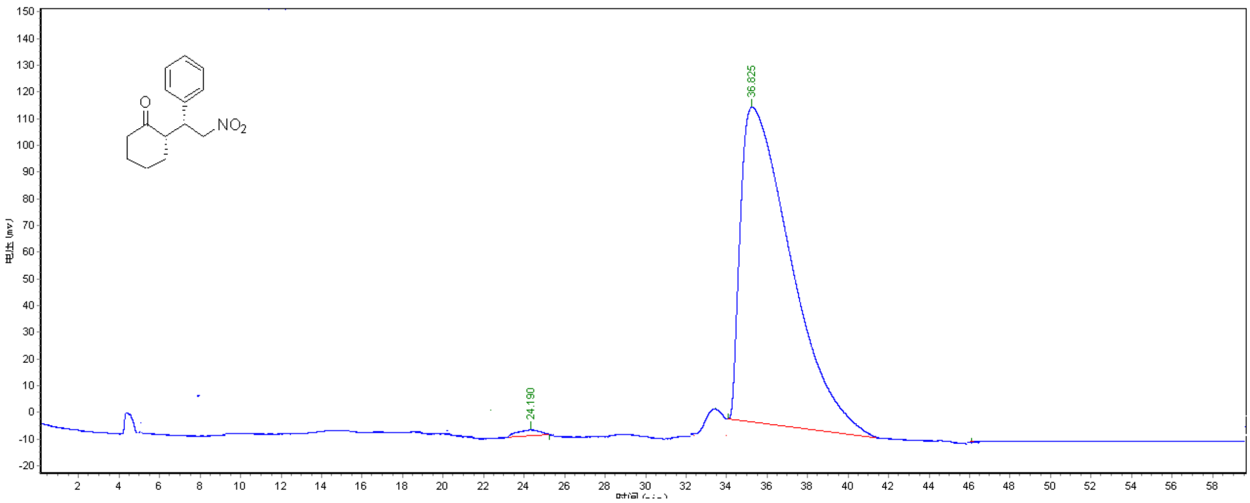
^{13}CNMR of **7**


178.171
59.756
52.020
49.875
45.009
27.711
24.402
OH
O
H
N
N
H
7
70
60
50
40
30
20
10
0
-10
150
100
50
ppm (f1)

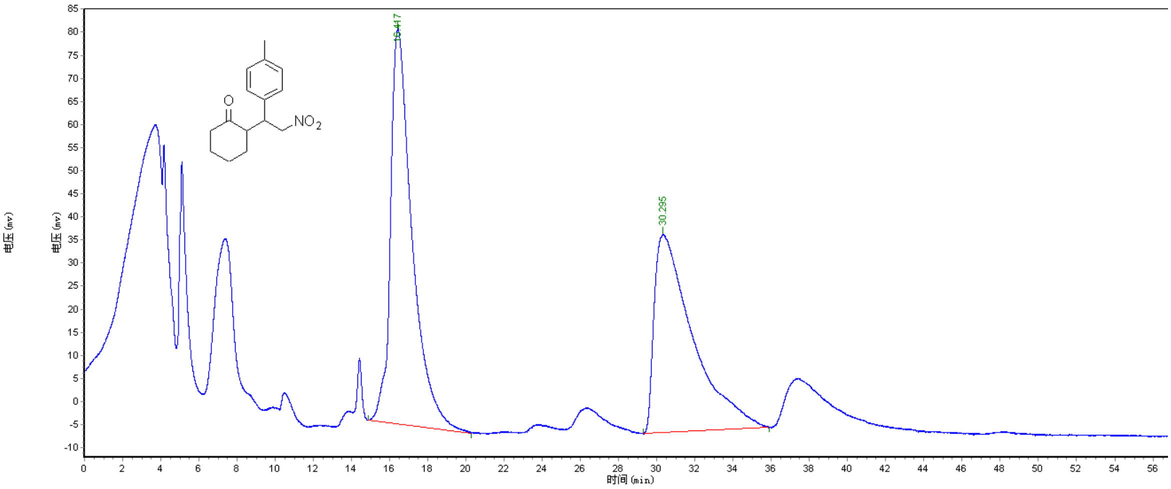
HPLC Spectra for Michael products



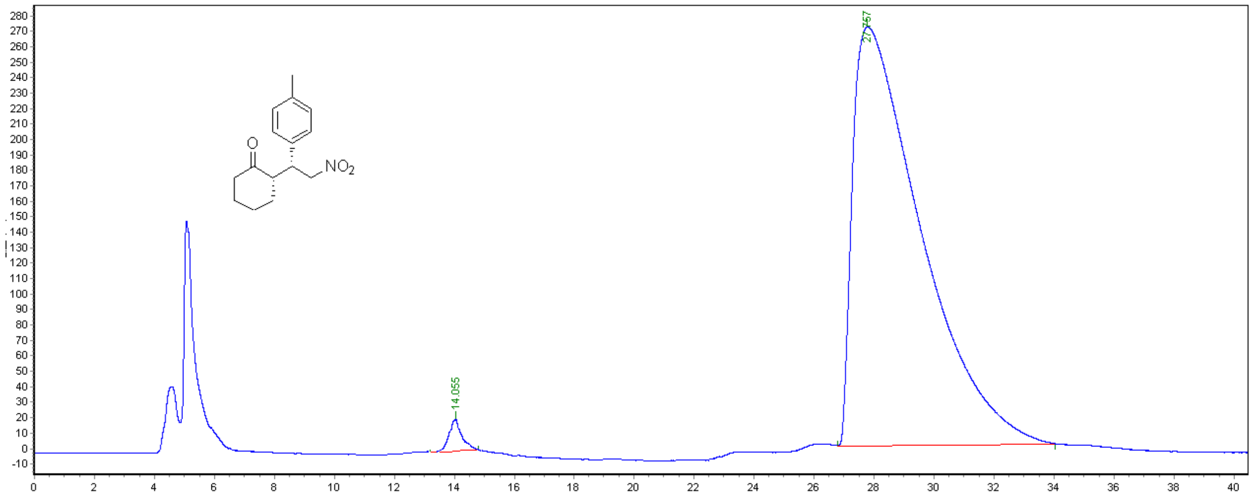
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	24.248	89797.089	9089520.500	49.8130
2	33.737	57520.215	9157790.052	50.1870
Total		830106.063	144420154.500	100.0000



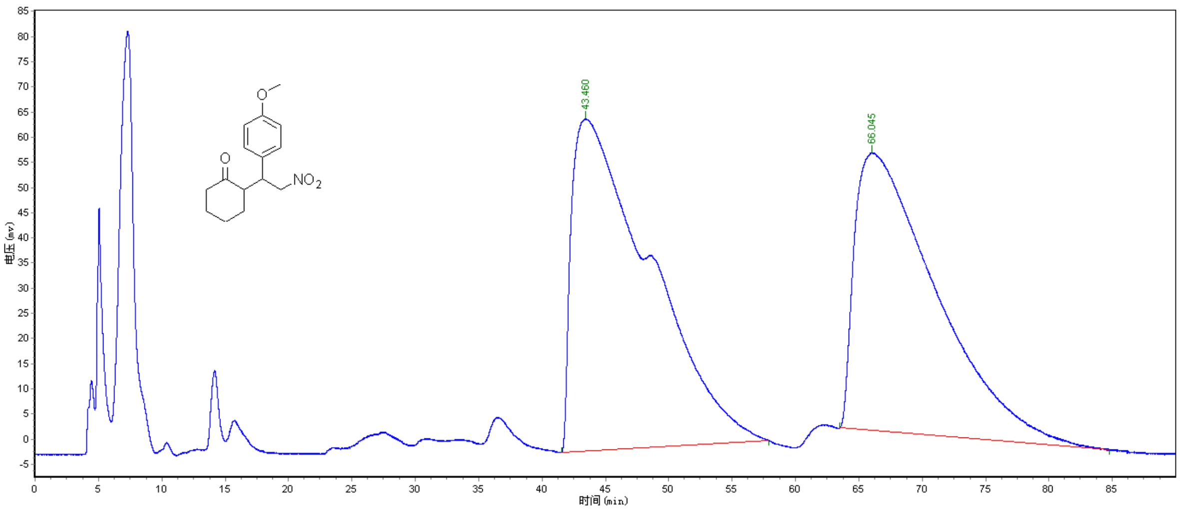
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	24.190	2353.120	174397.000	0.8497
2	36.825	117876.742	20351248.000	99.1503
Total		120229.862	20525645.000	100.0000



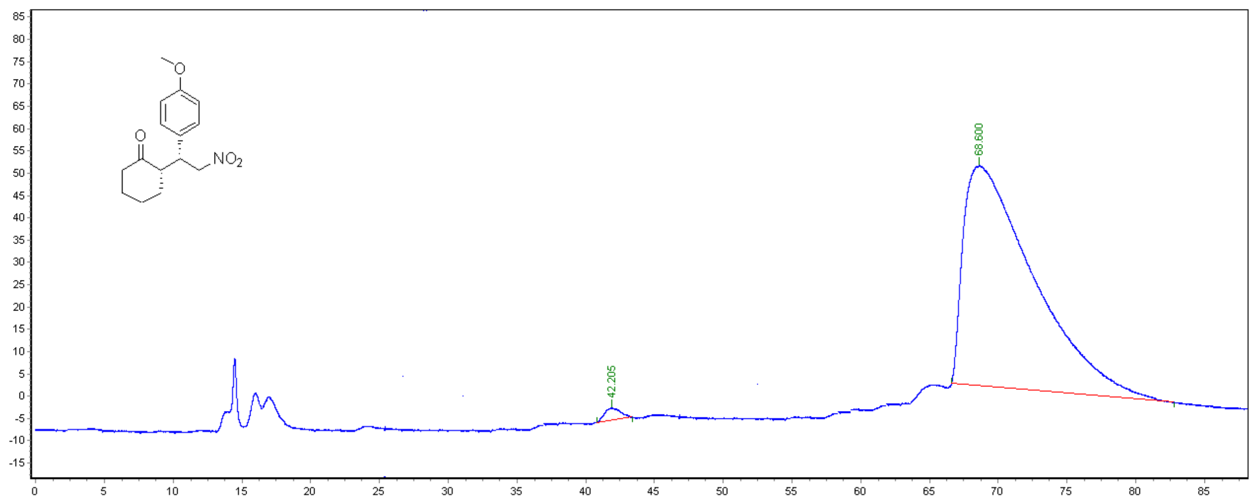
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	16.417	85547.992	6718509.500	52.8275
2	30.295	42918.449	5999309.500	47.1725
Total		128466.441	12717819.000	100.0000



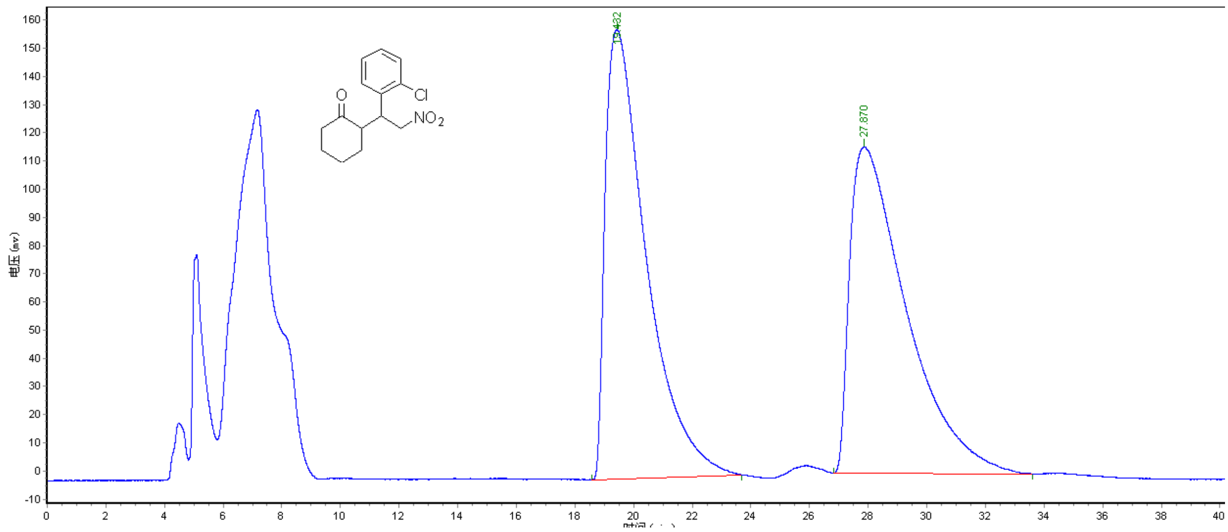
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	14.055	17764.008	408197.250	0.9448
2	27.757	270969.938	42797700.000	99.0552
Total		293733.945	43205897.250	100.0000



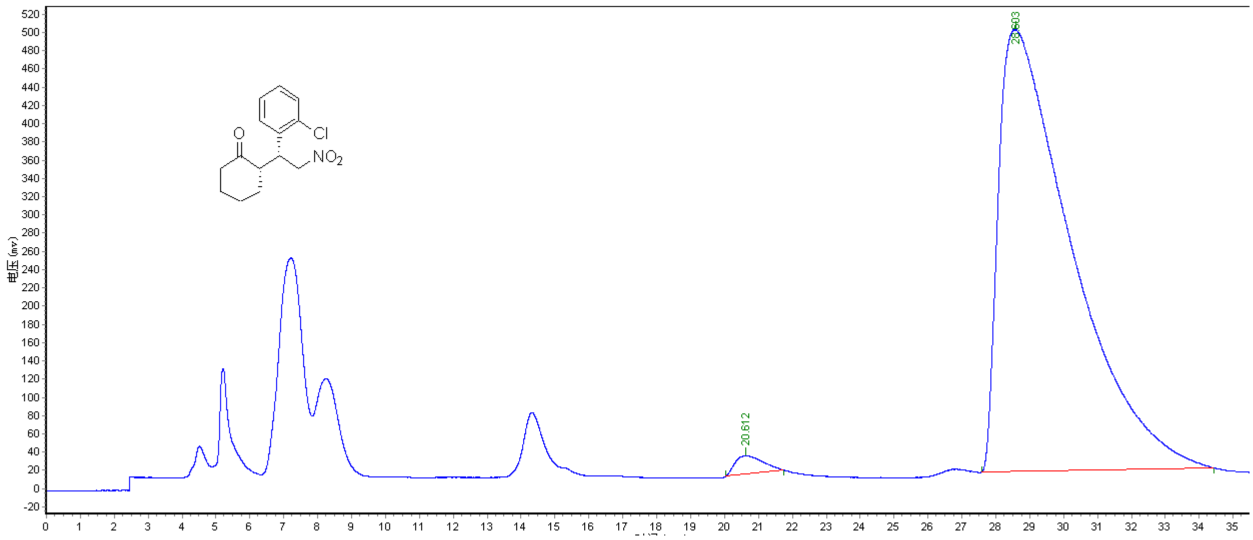
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	43.460	66073.688	29037792.000	54.0044
2	66.045	55026.984	24731528.000	45.9956
Total		121100.672	53769320.000	100.0000



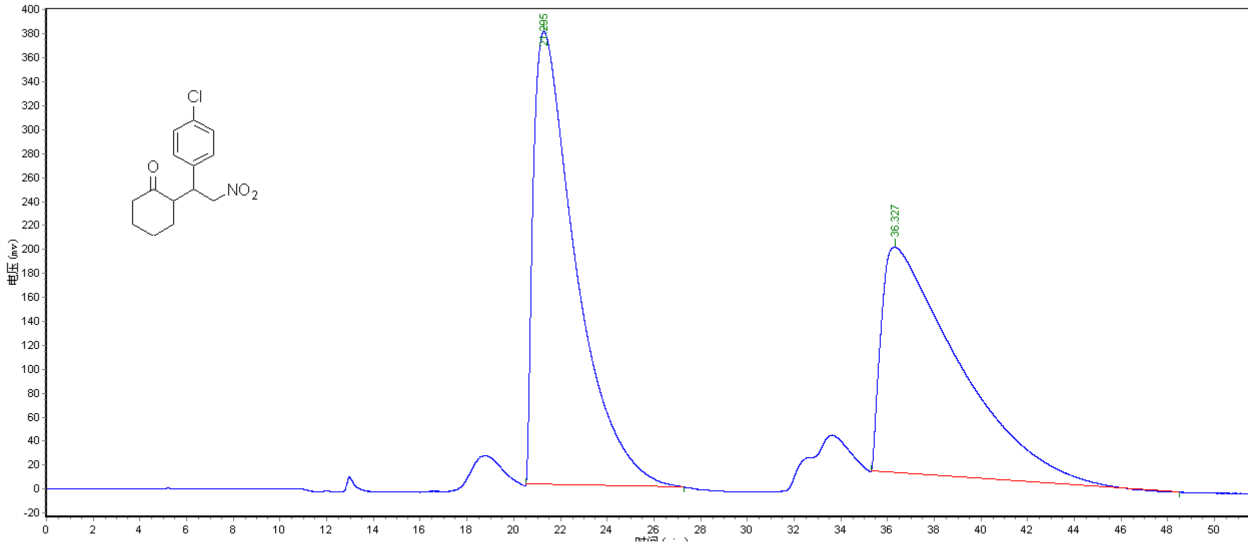
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	42.205	2643.760	212710.094	1.1989
2	68.600	49161.367	17529488.000	98.8011
Total		51805.127	17742198.094	100.0000



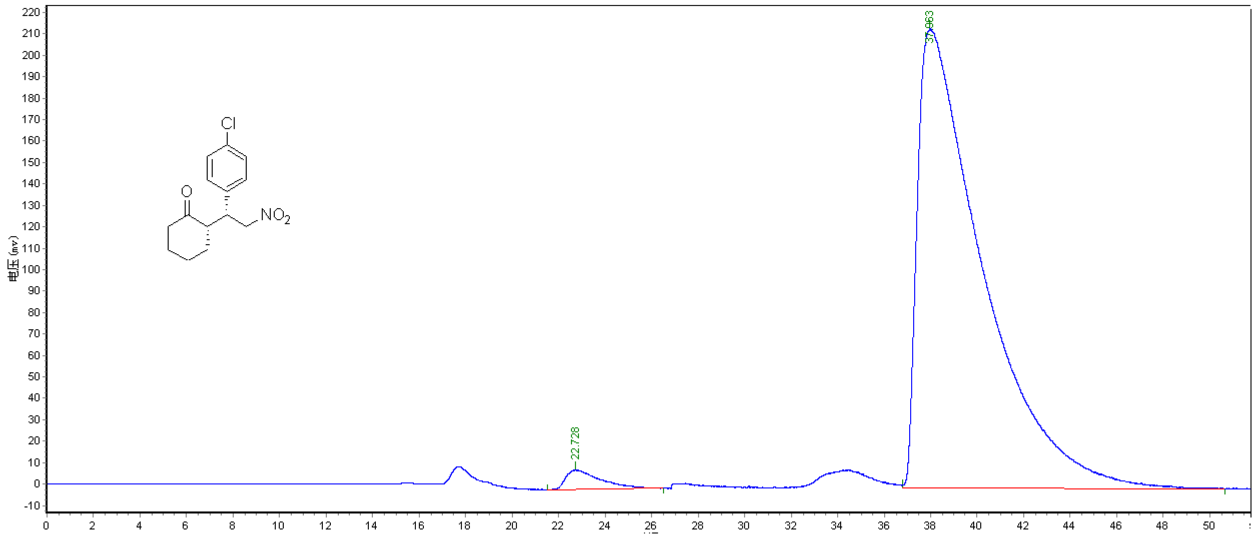
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	19.432	159320.328	15497548.000	49.9615
2	27.870	115760.672	15521430.000	50.0385
Total		275081.000	31018978.000	100.0000



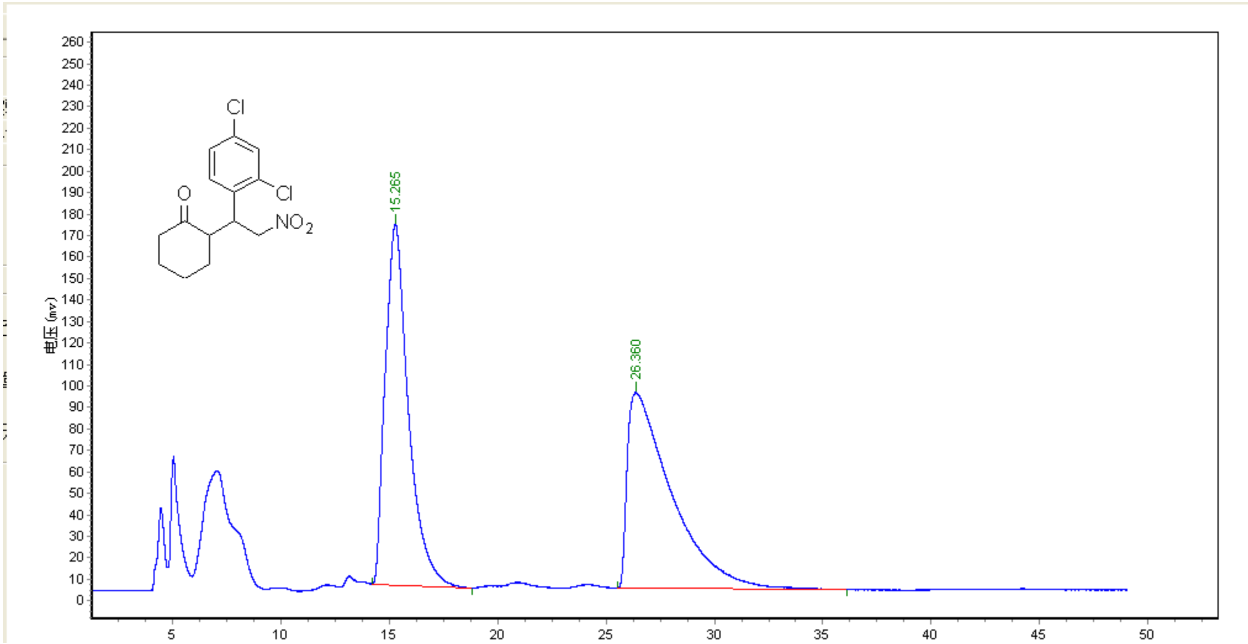
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	20.612	20169.227	1149273.875	1.5635
2	28.603	484251.531	72358728.000	98.4365
Total		504420.758	73508001.875	100.0000



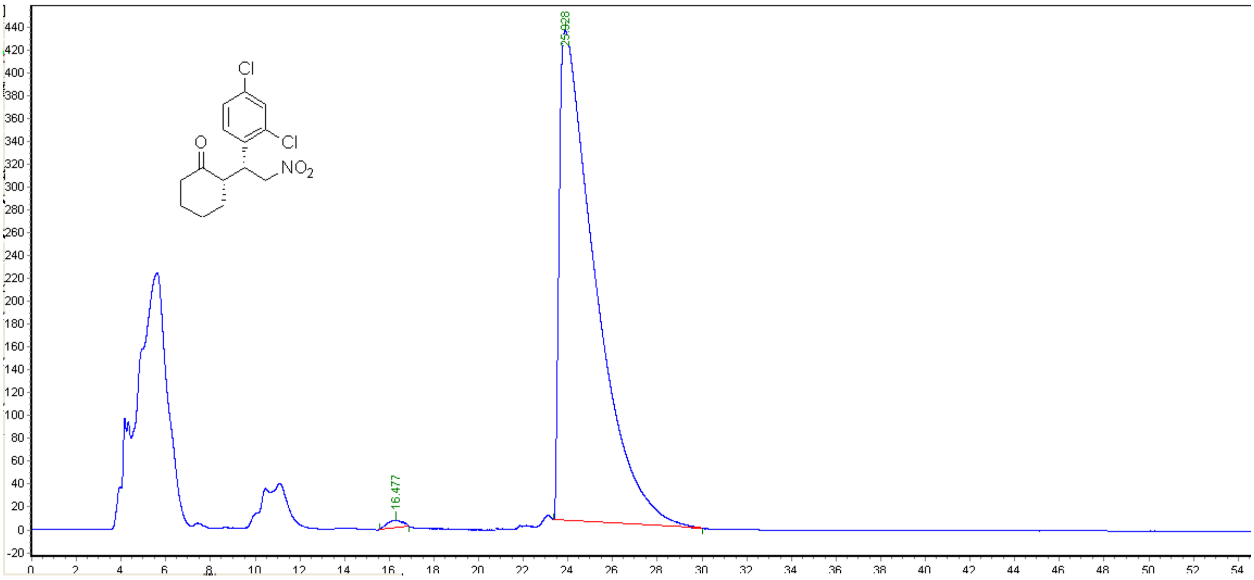
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	21.295	377983.656	47648892.000	52.4376
2	36.327	188112.688	43218880.000	47.5624
Total		566096.344	90867772.000	100.0000



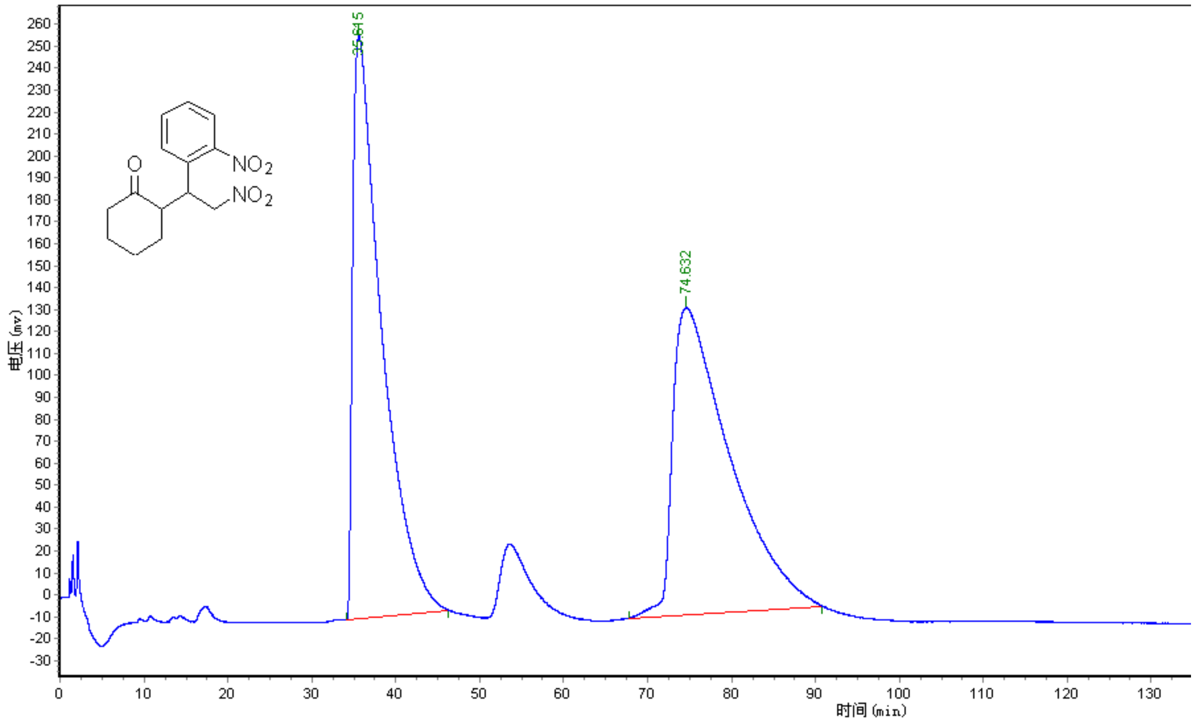
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	22.728	8987.304	928992.563	2.1762
2	37.963	214429.281	41758848.000	97.8238
Total		223416.585	42687840.563	100.0000



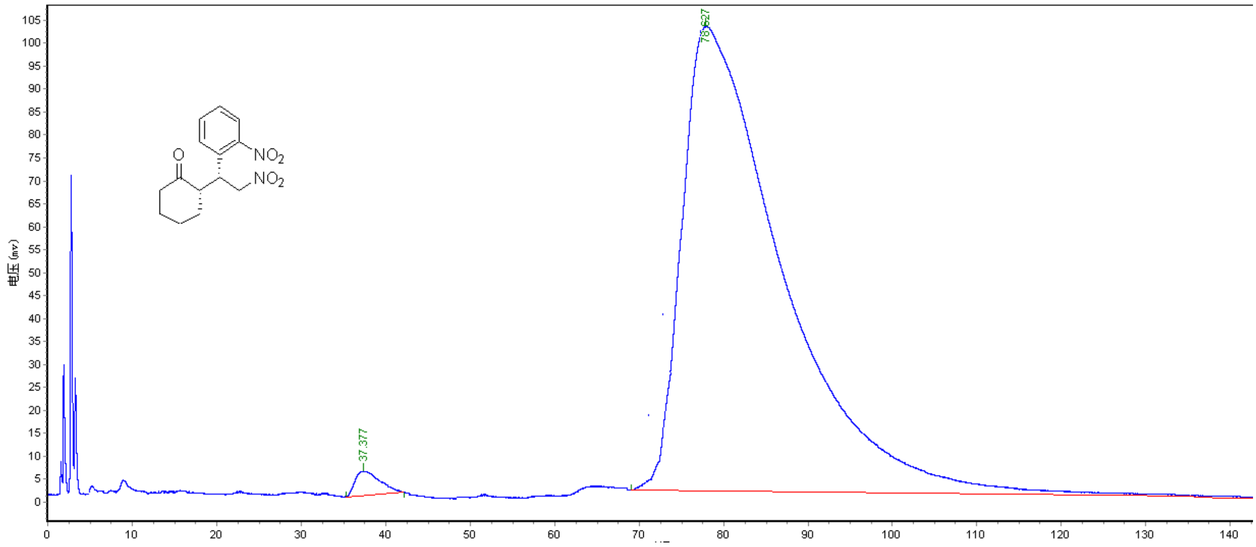
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	15.265	167943.172	12458516.000	48.9060
2	26.360	91165.672	13015885.000	51.0940
Total		2059208.844	25474401.000	100.0000



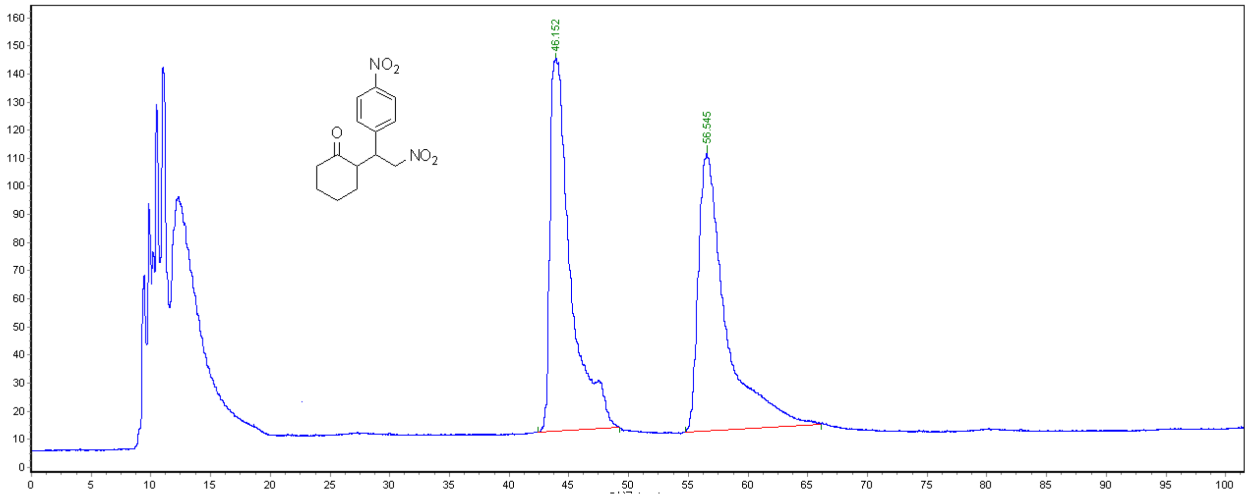
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	16.477	6413.407	298275.219	0.6210
2	25.032	428321.750	47736712.000	99.3790
Total		434735.157	48034987.219	100.0000



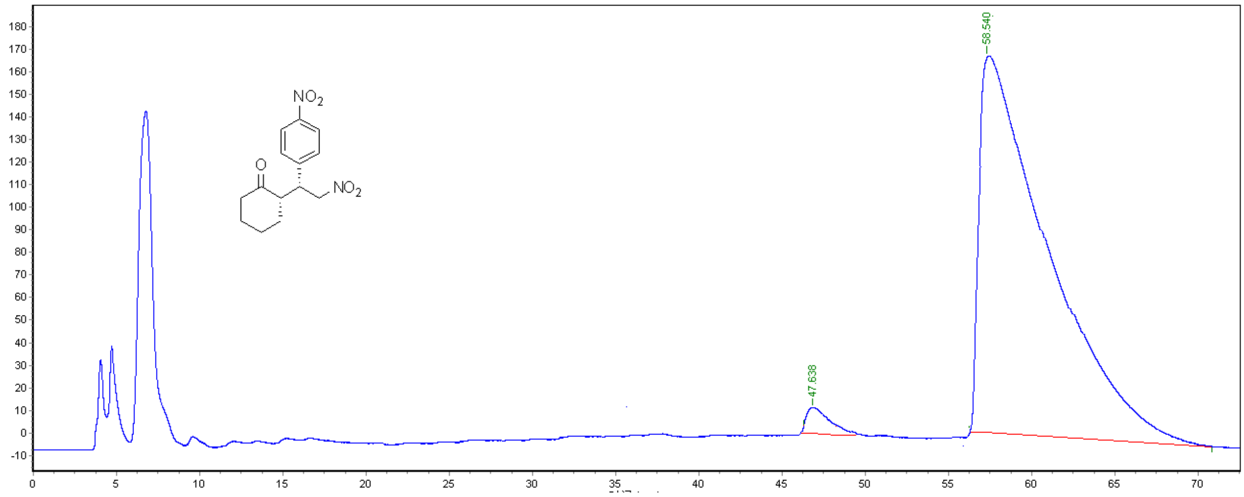
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	35.615	265755.875	64020672.000	49.1598
2	74.632	139921.578	66208928.000	50.8402
Total		405677.453	130229600.000	100.0000



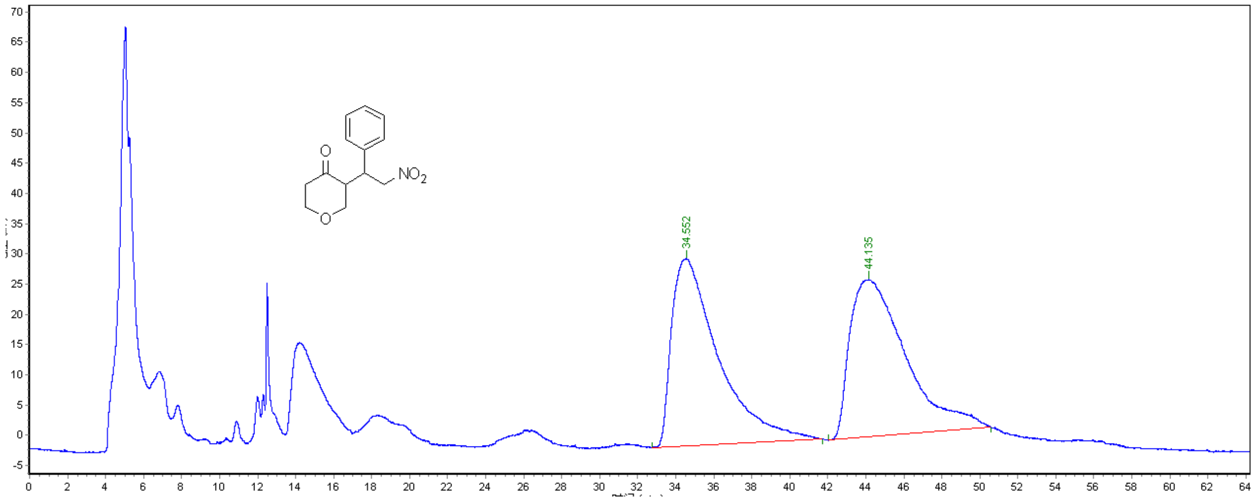
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	37.377	5249.968	1063619.500	1.1925
2	78.627	101172.086	88125744.000	98.8075
Total		106422.054	89189363.500	100.0000



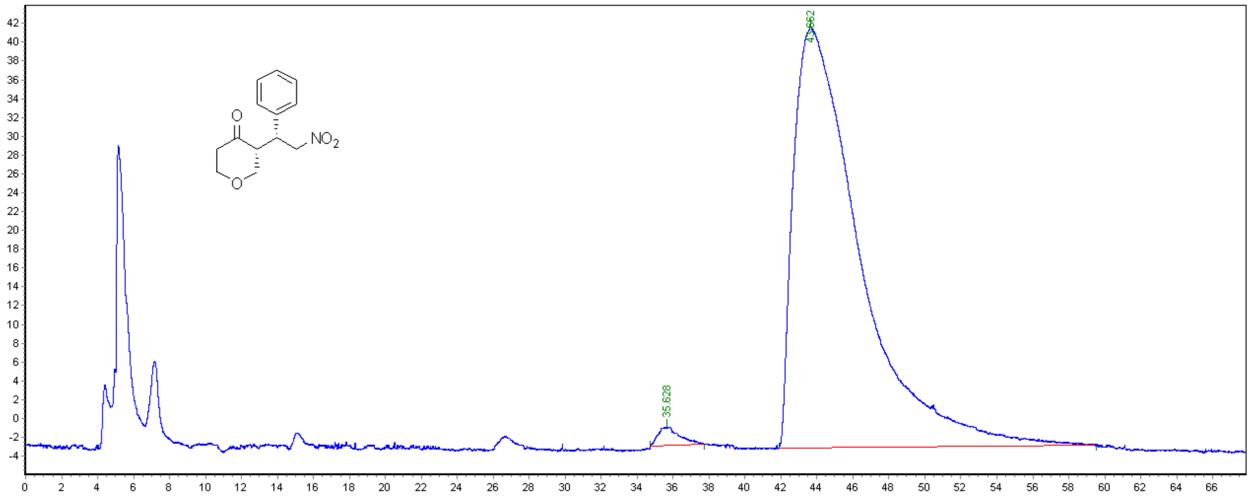
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	28.213	140589.344	16737876.000	52.2881
2	46.152	97862.648	15272974.000	47.7119
Total		238451.992	32010850.000	100.0000



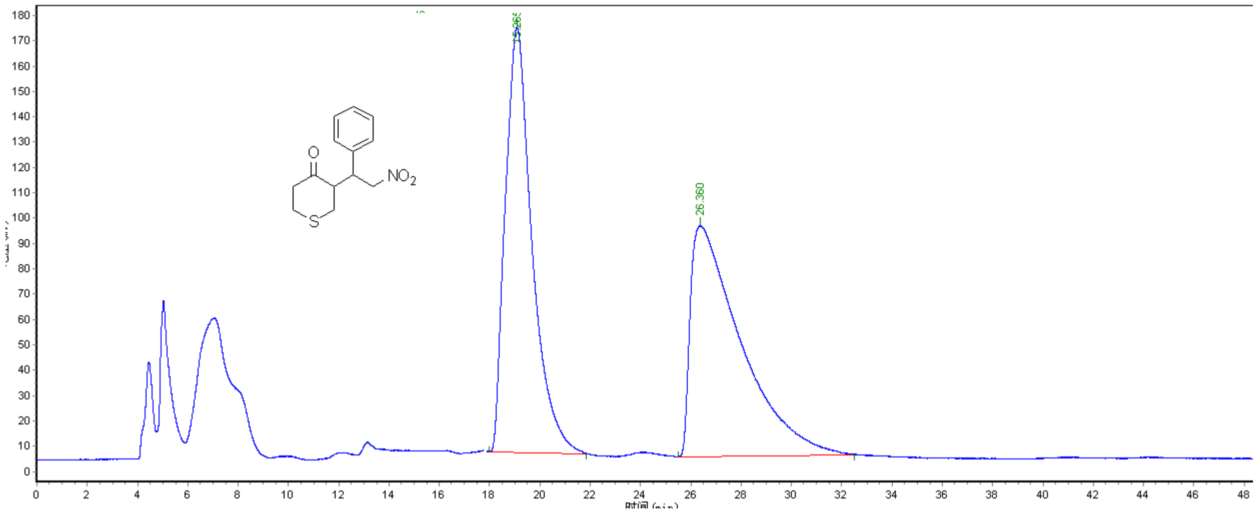
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	47.638	8138.460	577487.625	1.1249
2	58.540	178382.266	50761172.000	98.8751
Total		186520.726	51338659.625	100.0000



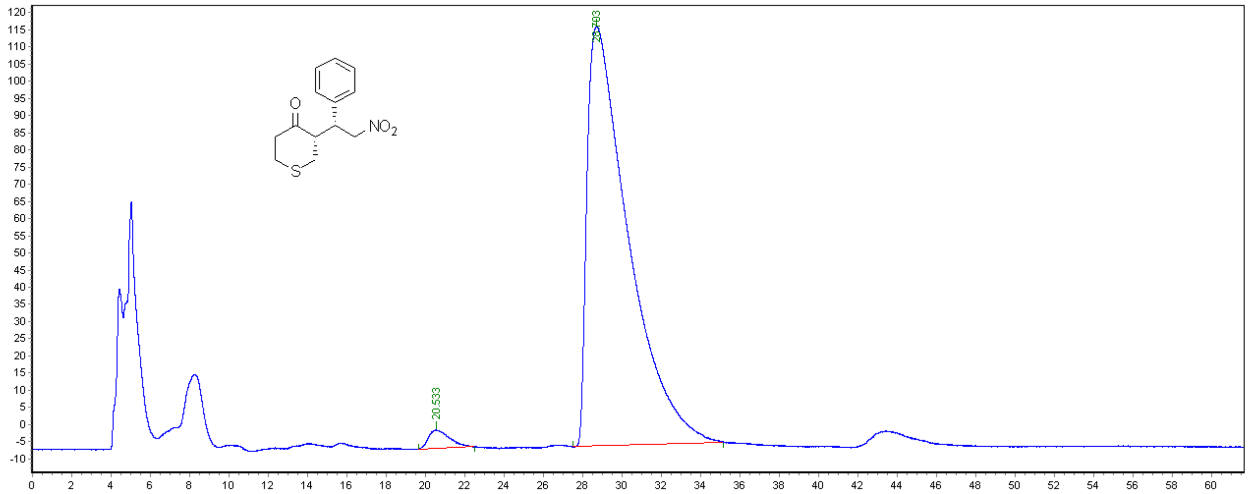
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	34.552	30859.949	5309957.000	49.4529
2	44.135	26093.508	5427454.000	50.5471
Total		56953.457	10737411.000	100.0000



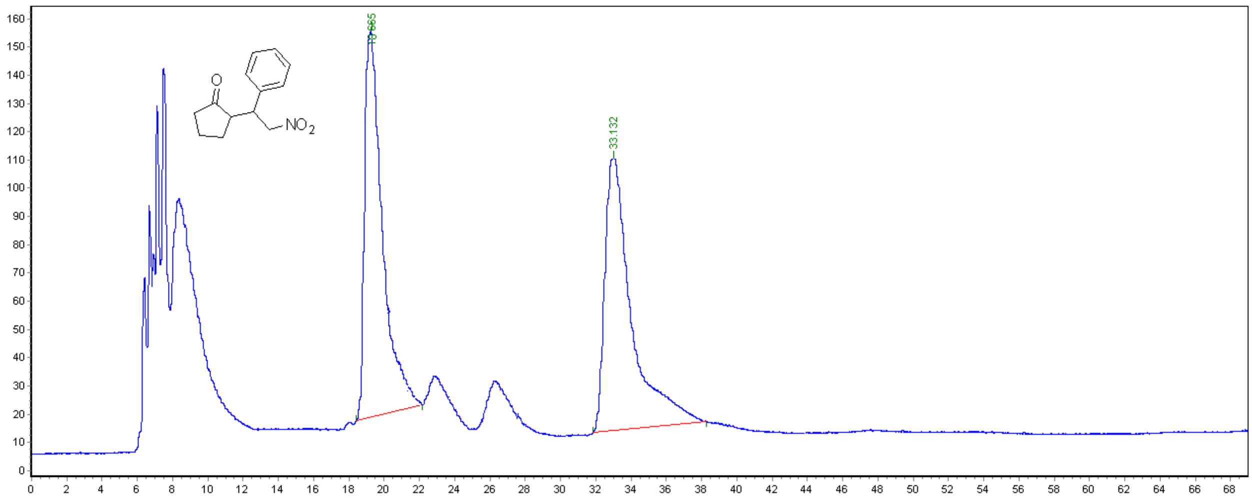
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	35.628	1934.743	158194.688	1.3662
2	43.662	44770.473	11420697.000	98.6338
Total		46705.216	11578891.688	100.0000



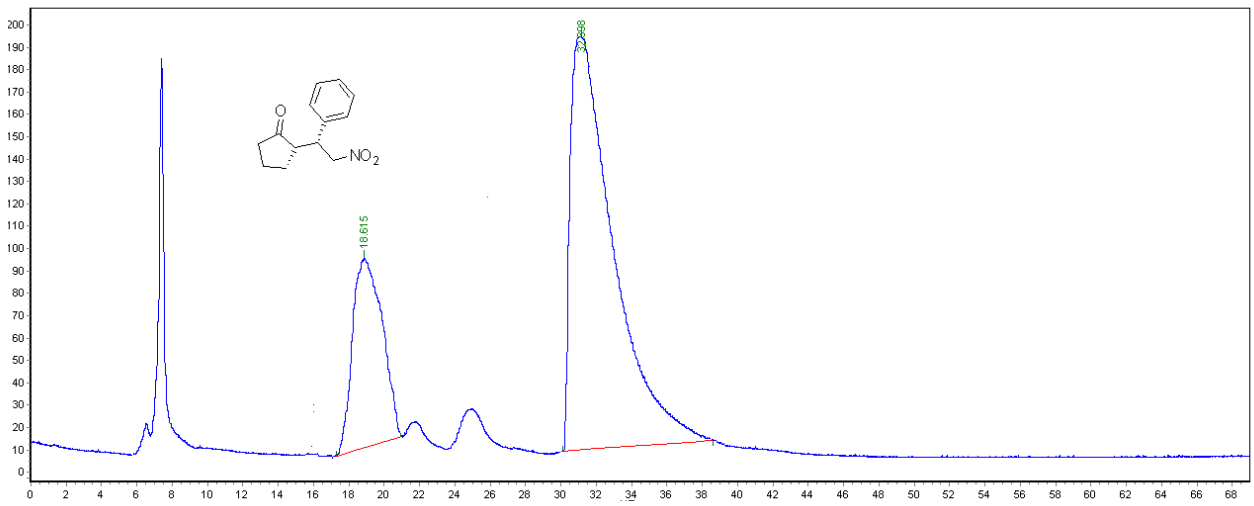
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	19.265	167720.672	12359834.000	49.3854
2	26.360	91078.211	12667453.000	50.6146
Total		258798.883	25027287.000	100.0000



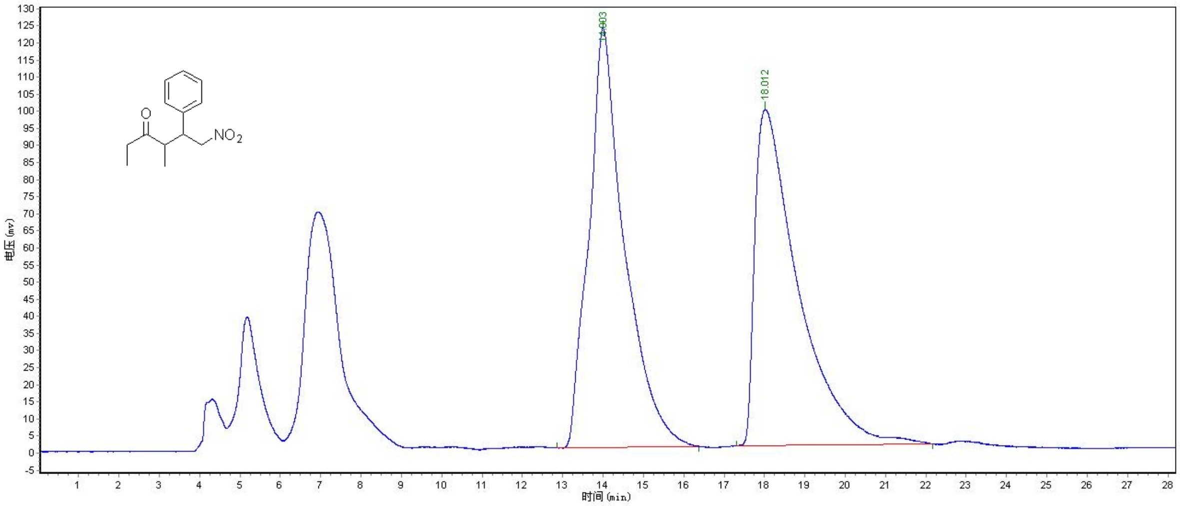
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	20.533	5327.267	388404.281	2.1327
2	28.703	122194.617	17823544.000	97.8673
Total		127521.884	18211948.281	100.0000



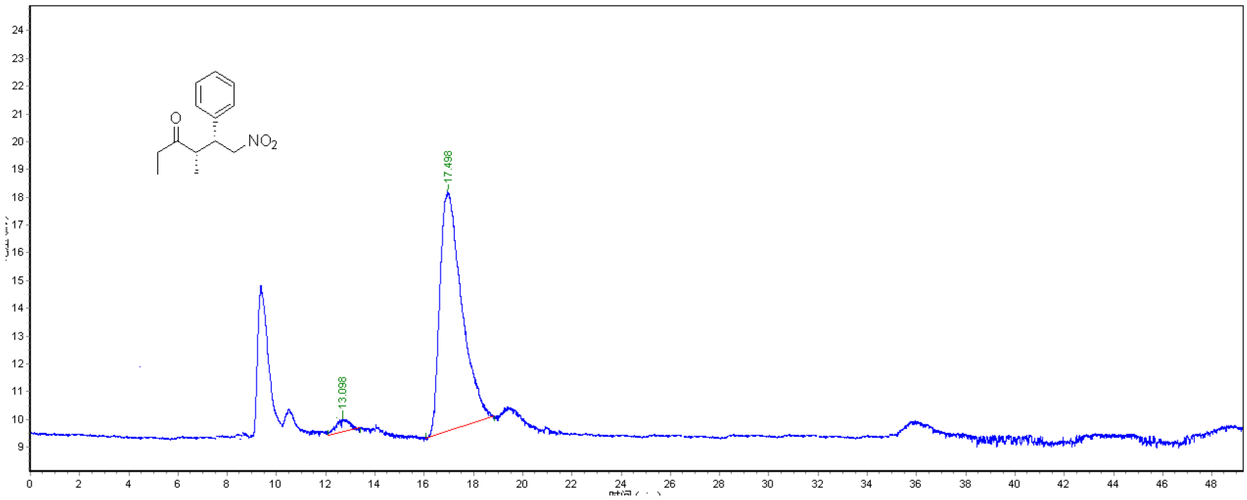
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	18.665	137788.734	14728761.000	49.6804
2	33.132	97324.453	14918269.000	50.3196
Total		235113.188	29647030.000	100.0000



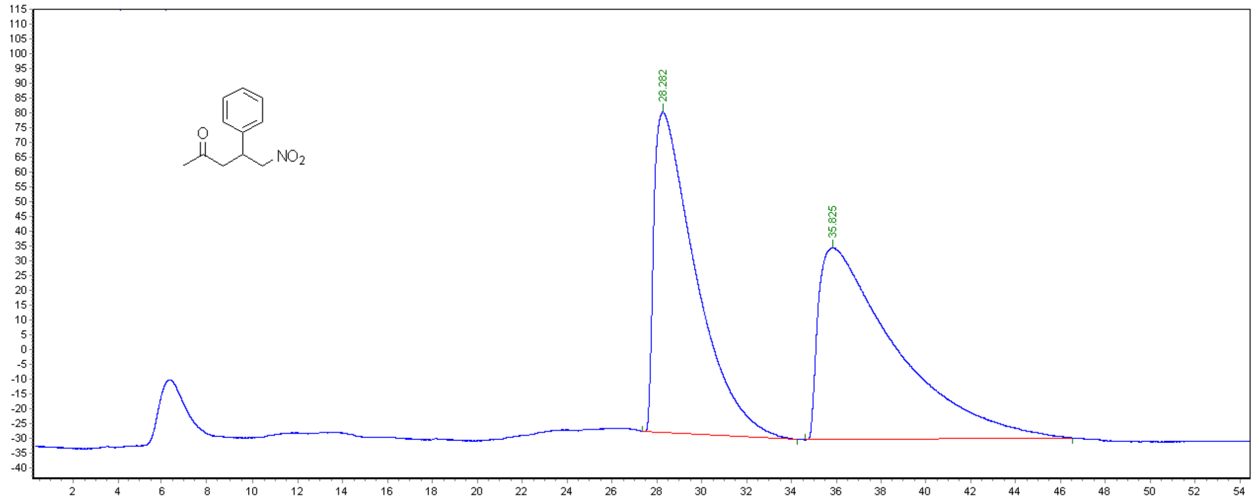
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	18.615	72633.414	18975470.000	20.1941
2	32.398	188471.125	74989952.000	79.8059
Total		261104.539	93965422.000	100.0000



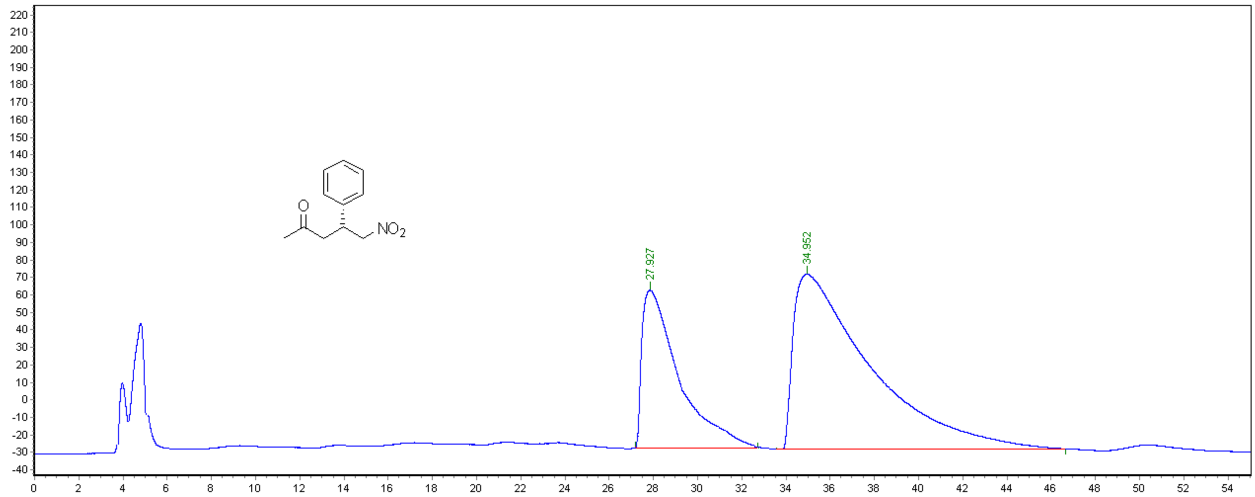
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	14.003	122658.617	7565940.500	50.8165
2	18.012	98356.328	7322801.500	49.1835
Total		221014.945	14888742.000	100.0000



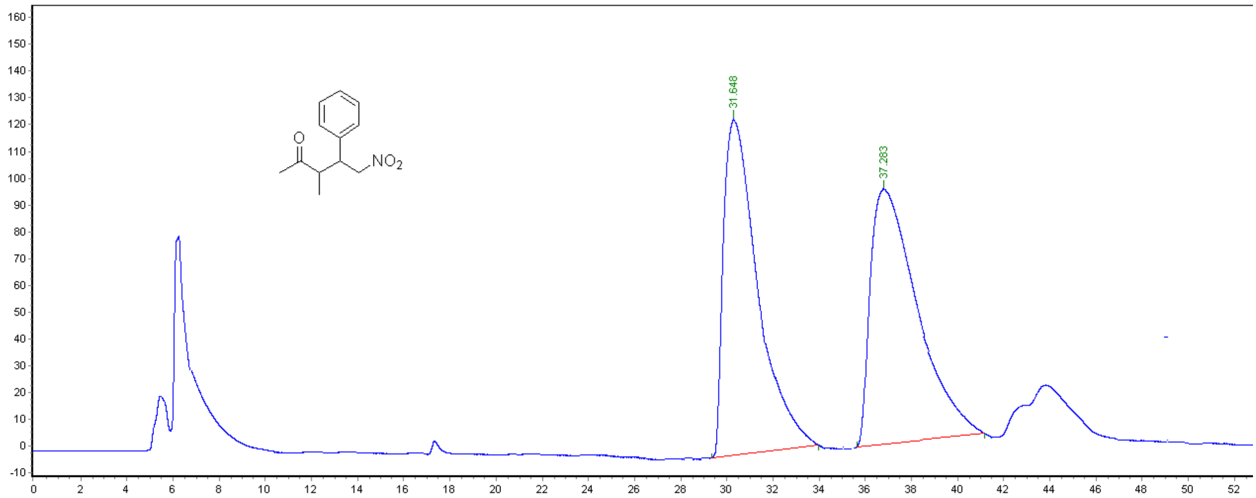
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	13.075	444.475	16435.248	2.9766
2	17.482	8638.579	535705.625	97.0234
Total		9083.054	552140.873	100.0000



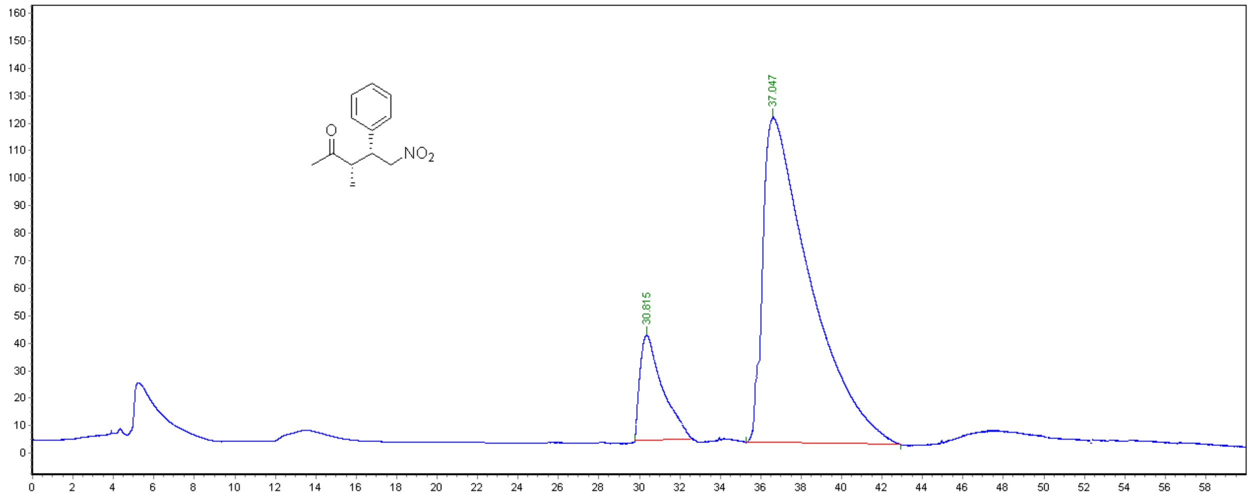
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	28.282	108260.148	13971850.000	47.3759
2	35.825	64890.875	15519637.000	52.6241
Total		173151.023	29491487.000	100.0000



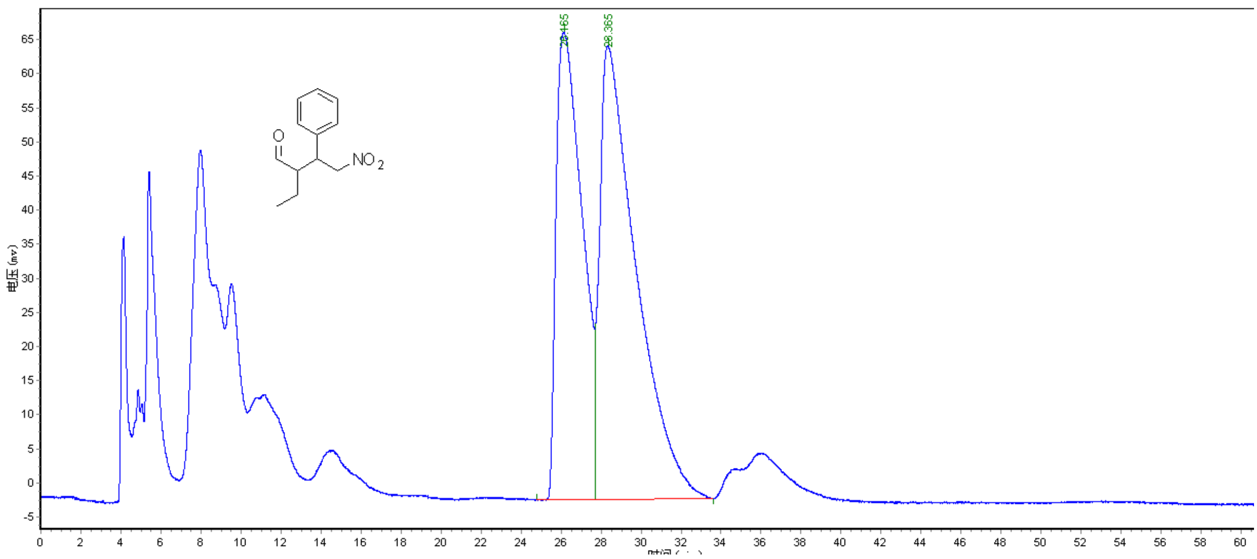
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	27.927	79805.508	7904004.500	24.6569
2	34.952	99905.281	24151960.000	75.3431
Total		179710.789	32055964.500	100.0000



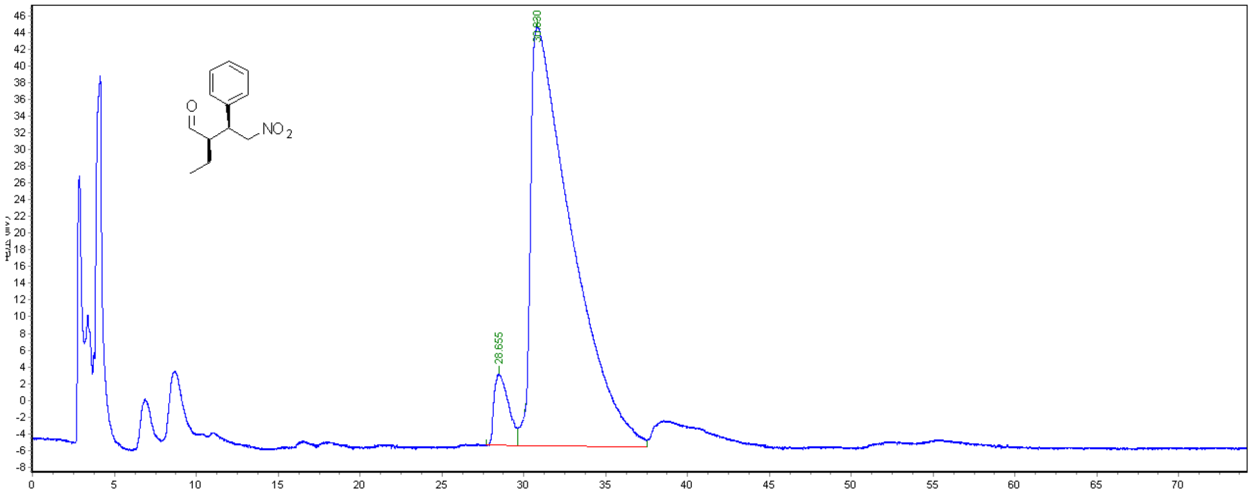
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	31.837	139953.484	10892872.000	50.7712
2	37.703	99988.469	10561964.000	49.2288
Total		239941.953	21454836.000	100.0000



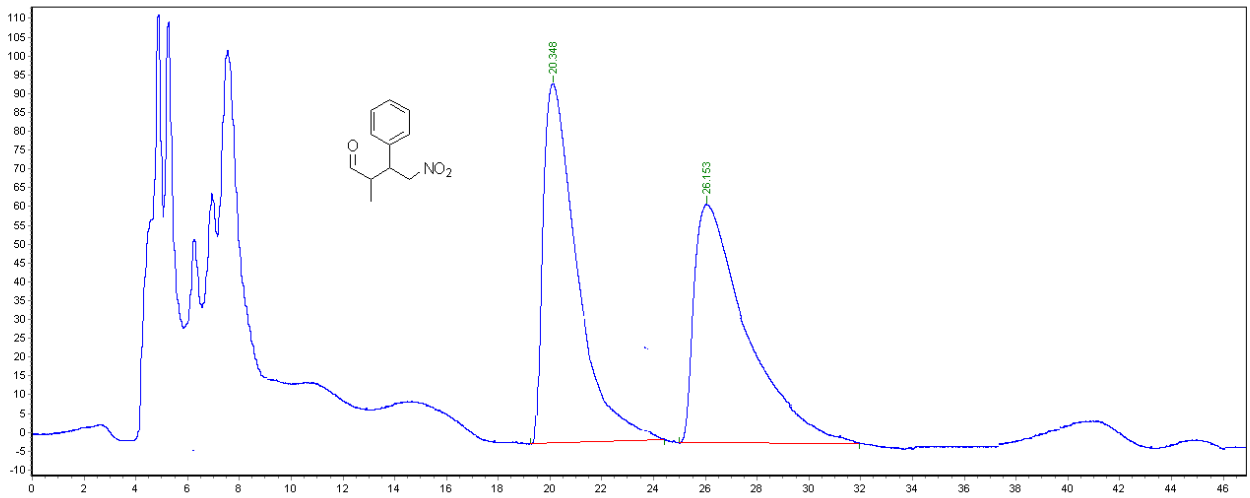
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	30.815	40159.480	3142607.000	13.0705
2	37.047	117705.906	20900938.000	86.9295
Total		157865.387	24043545.000	100.0000



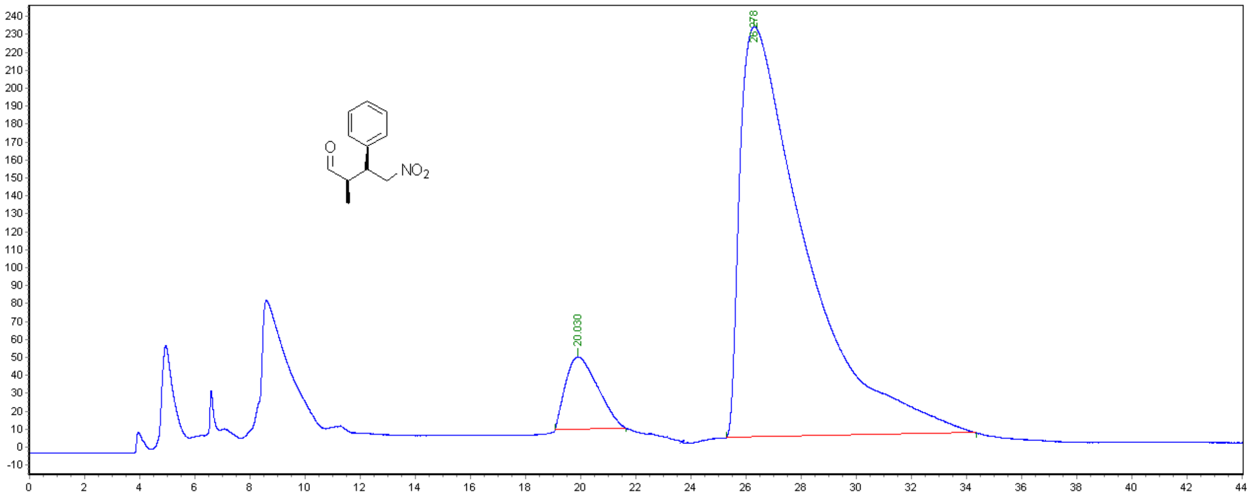
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	26.165	68524.813	6194734.000	42.0449
2	28.365	66588.875	8538897.000	57.9551
Total		135113.688	14733631.000	100.0000



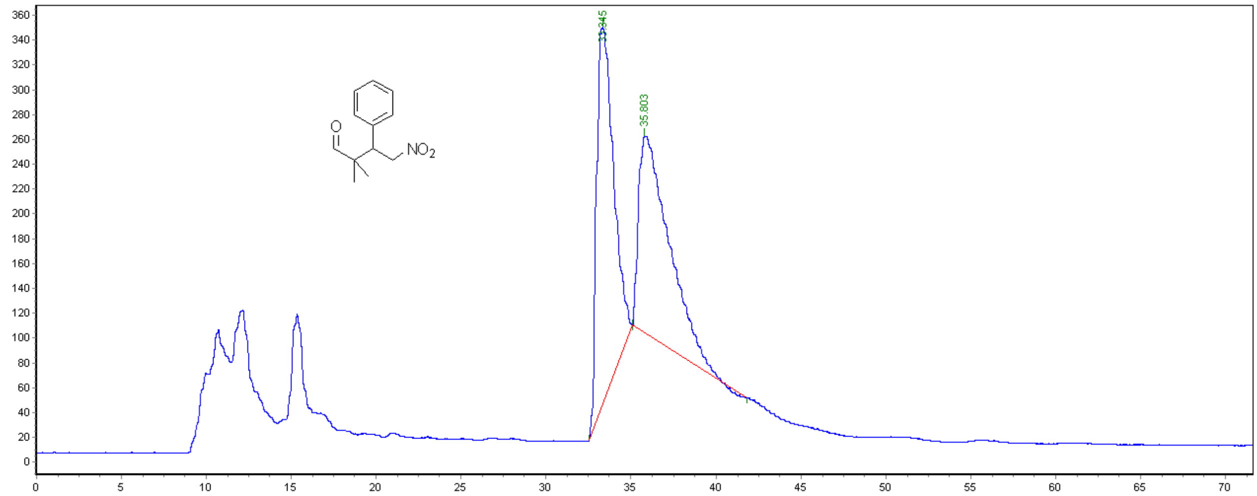
Peak#	RT(min)	Height(μV)	Area (μV*Sec)	Area %
1	28.655	7874.764	432506.344	4.7583
2	30.830	50137.391	8657014.000	95.2417
Total		58012.155	9089520.344	100.0000



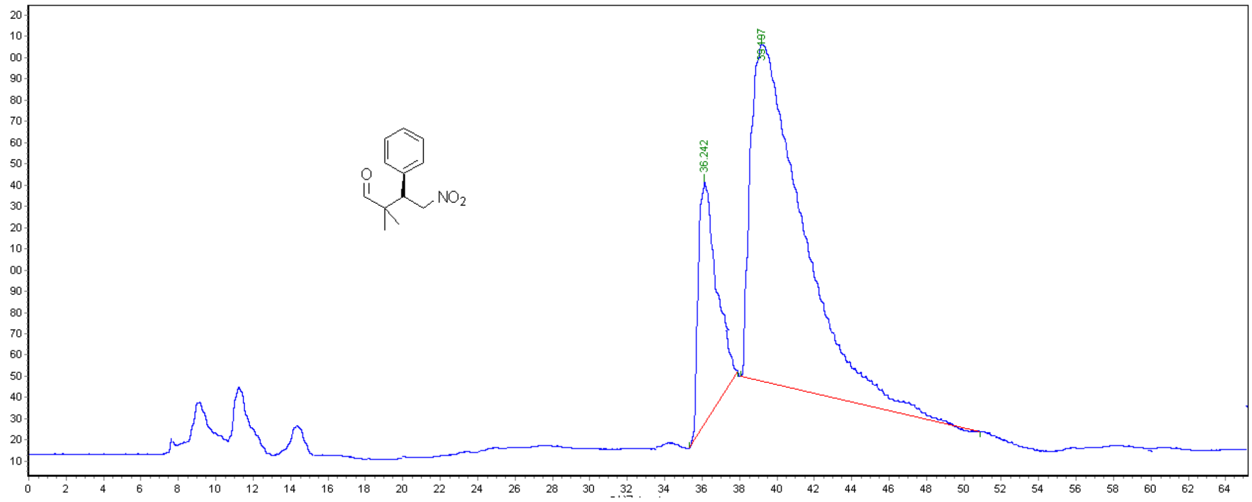
Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	20.348	100167.289	11416691.000	50.9358
2	26.153	69950.875	10997206.000	49.0642
Total		183118.164	22413897.000	100.0000



Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	20.030	40044.746	3242451.250	7.9104
2	26.278	228416.859	37747436.000	92.0896
Total		268461.605	40989887.250	100.0000



Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	33.345	303781.125	20989056.000	51.1411
2	35.803	158088.969	20052418.000	48.8589
Total		461870.094	41041474.000	100.0000



Peak#	RT(min)	Height(µV)	Area (µV*Sec)	Area %
1	36.242	103018.508	6281926.000	18.5676
2	39.197	156818.922	27550860.000	81.4324
Total		259837.430	33832786.000	100.0000