

Supporting Information for

Continuous asymmetric Michael additions of ketones to β -nitroolefins over (1R, 2R)-(+)-1,2-DPEN modified sulfonic acid resin

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General Methods

Sulfonyl chloride resin (2.35 mmol/g substitution) was purchased from Tianjin Nankai Hecheng Science & Technology Co., LTD. (1R, 2R)-(+)-1, 2-DPEN was obtained from Lian Yungang Chiral Chemical (China) Co., LTD. Other commercial reagents were obtained from Tianjin Jiangtian Chemical Technology Co., Ltd and used without further purification except for otherwise explanation. Temperature-gravity property of the catalyst was measured with an STA 409PC thermo gravimetric (TG) analysis. The catalyst was heated from room temperature to 800 °C at a rate of 10 °C/min in a stream of N₂ (40 mL/min). Elemental analysis was carried out on a Vario Micro cube element analyzer. FTIR spectra were recorded on a Nicolet AVATAR 370 FTIR spectrometer.

Preparation of the catalyst

The catalyst was prepared as follows: 5.0 g sulfonyl chloride resins were dispersed in 50 mL dry dichloromethane with stirring at room temperature. 10.0 g (1R, 2R)-(+)-1, 2-DPEN was dissolved in 150 mL dry dichloromethane and added to the solution under vigorous stirring. The reaction mixture was stirred for 24 h and the solid catalyst was obtained by filtration. It was washed with DMF, ethanol and DCM for five times respectively. Then the catalyst was dried at 50 °C for 6 h.

Catalytic reaction

The asymmetric Michael addition of aldehydes or ketones to nitroolefins was carried out in a tubular, fixed-bed reactor with an inner diameter of 7 mm and a length of 275 mm, which was charged with 3.31 g (249 mm) catalysts. 1.33 mmol aldehydes or ketones and 0.133 mmol nitroolefins were added into 20 mL toluene. The solution

1 was dosed into the reactor by a micro-injector with 0.6 mL/h. The reaction mixture
2 was analyzed by high performance liquid chromatography (HPLC) with AS-H
3 column and ultraviolet detector.

4 **The preparation of nitroolefins**

5 Nitrostyrene was synthesized as follows. 25 mL 10 mol/L NaOH solution was
6 dropwise added to the solution of 15.0 g nitromethane and 26.5 g benzaldehyde in 100
7 mL methanol with stirring at 10 - 15 °C. Then 50 mL concentrated hydrochloric acid
8 was diluted with 75 mL water. Subsequently, it was dropwise added into the reaction
9 mixture. The obtained pale yellow solid was filtered and washed with water. The
10 crude nitrostyrene was purified by recrystallization in ethanol. The other nitroolefins
11 were similarly prepared.

12 **β -Nitrostyrene.** (Pale yellow needles), ^1H NMR (CDCl_3) & 7.35 -7.57 (m, 5H) ,
13 7.60 (d, $J = 13.5$ Hz, 1H), 8.00 (d, $J = 13.5$ Hz, 1H).

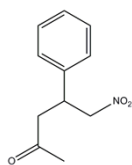
14 **4'-Methoxy- β -nitrostyrene.** (Yellow needles), ^1H NMR (CDCl_3) & 3.87 (s, 3H),
15 6.97 (d, $J = 8.5$ Hz, 2H), 7.50 (d, $J = 13.7$ Hz, 2H), 7.55 (d, $J = 9.0$ Hz, 1H), 7.98 (d, J
16 = 13.7 Hz, 1H).

17 **4'-Chloro- β -nitrostyrene.** (Yellow powder), ^1H NMR (CDCl_3) & 7.32-7.42 (m, 4H),
18 7.58 (d, $J = 13.7$ Hz, 1H), 7.95 (d, $J = 13.7$ Hz, 1H).

19 **2'-Chloro- β -nitrostyrene.** (Yellow powder), ^1H NMR (CDCl_3) & 7.37-7.46 (m, 2H),
20 7.53 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.0$ Hz, 1H), 7.62 (dd, $J_1 = 7.7$ Hz, $J_2 = 1.7$ Hz, 1H), 7.63 (d,
21 $J = 13.7$ Hz, 1H), 8.44 (d, $J = 13.7$ Hz, 1H).

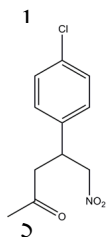
22 **The preparation of the racemic adducts**

23 To a solution of (DL)-proline (0.1 mmol) in 50.0 mL MeOH was added 10 mmol
24 aldehydes or ketones and 1 mmol nitroolefins. The reaction mixture was refluxed with
25 stirring for 12 h and then concentrated. The residue was purified by column
26 chromatography (the volume ration of petroleum ether and ethyl acetate is 10:1).

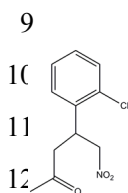


27 ^1H NMR (CDCl_3) & 7.20-7.35 (m, 5H), 4.69 (dd, $J_1=12.5$ Hz, $J_2=6.5$ Hz,
28 1H), 4.60 (dd, $J_1 = 12.5$ Hz, $J_2 = 8.0$ Hz, 1H), 3.97-4.03 (m, 1H), 2.92 (d, $J = 5$ Hz,
29 2H), 2.12 (s, 3H); The compound was analyzed by chiral HPLC with a Chiralpack
30 AS-H column under 1 mL/min at 213 nm (the n-hexane / 2-propanol volume ratio is
31 85:15); $t_r = 27.3$ min (major), 37.0 min (minor).

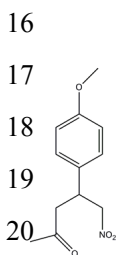
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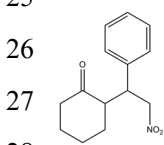
$^1\text{H NMR (CDCl}_3)$ & 7.30 (d, $J = 8.5$ Hz, 2H), 7.15 (d, $J = 8.5$ Hz, 2H), 4.68 (dd, $J_1 = 12.4$ Hz, $J_2 = 6.7$ Hz, 1H), 4.57 (dd, $J_1 = 12.4$ Hz, $J_2 = 7.9$ Hz, 1H), 3.97-4.03 (m, 1H), 2.89 (d, $J = 7.0$ Hz, 2H), 2.13 (s, 3H); The compound was analyzed by chiral HPLC with a Chiralpack AS-H column at 213 nm under 1 mL/min (the n-hexane / 2-propanol volume ratio is 85:15); $t_r = 21.5$ min (major), 34.0 min (minor).



$^1\text{H NMR (CDCl}_3)$ & 7.39 -7.41 (m, 1H), 7.19 -7.25 (m, 3H), 4.76 (m, 2H), 4.46 (m, 1H), 2.93-3.09 (m, 2H), 2.16 (s, 3H); The compound was analyzed by chiral HPLC with a Chiralpack AS-H column at 213 nm under 1 mL/min (the n-hexane / 2-propanol volume ratio is 90:10); $t_r = 19.3$ min(major), 22.6 min(minor).



$^1\text{H NMR (CDCl}_3)$ & 7.13 (d, $J = 9.4$ Hz, 2H), 6.84 (d, $J = 9.4$ Hz, 2H), 4.65 (dd, $J_1 = 12.2$ Hz, $J_2 = 6.9$ Hz, 1H), 4.55 (dd, $J_1 = 12.2$ Hz, $J_2 = 7.8$ Hz, 1H), 3.94-3.98 (m, 1H), 3.77 (s, 3H), 2.88 (d, $J = 7.1$ Hz, 2H), 2.10 (s, 3H); The compound was analyzed by chiral HPLC with a Chiralpack AS-H column at 213 nm under 1.4 mL/min (the n-hexane / 2-propanol volume ratio is 85:15); $t_r = 19.9$ min (major), 47.3 min (minor).



$^1\text{H NMR (CDCl}_3)$ & 7.07- 7.28 (m, 5H), 4.87 (dd, $J_1 = 12.5$ Hz, $J_2 = 4.5$ Hz, 1H), 4.56 (dd, $J_1 = 12.5$ Hz, $J_2 = 9.9$ Hz, 1H), 3.65-3.73 (m, 1H), 2.57-2.66 (m, 1H), 2.26-2.45 (m, 2H), 1.97-2.05 (m, 1H), 1.43-1.73 (m, 4H), 1.10-1.23 (m, 1H); The compound was analyzed by chiral HPLC with a Chiralpack AS-H column at 213 nm under 1.0 mL/min (the n-hexane / 2-propanol volume ratio is 90:10); $t_r = 15.2$ min(major), 24.5 min(minor).

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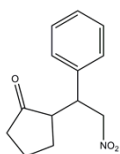
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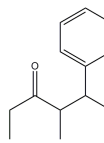
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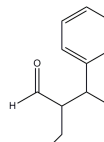
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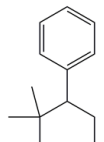
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$^1\text{H NMR (CDCl}_3)$ & 7.15- 7.37 (m, 5H), 5.01 (d, $J = 8.5$ Hz, 1H), 4.66-4.79 (m, 1H), 3.66-3.72 (m, 1H), 2.04-2.54 (m, 3H), 1.78-1.95 (m, 2H), 1.57-1.78 (m, 2H); The compound was analyzed by chiral HPLC with a Chiralpack AS-H column at 213 nm under 0.5 mL/min (the n-hexane / 2-propanol volume ratio is 80:20); $t_r = 22.4$ min (major), 29.8 min (minor).

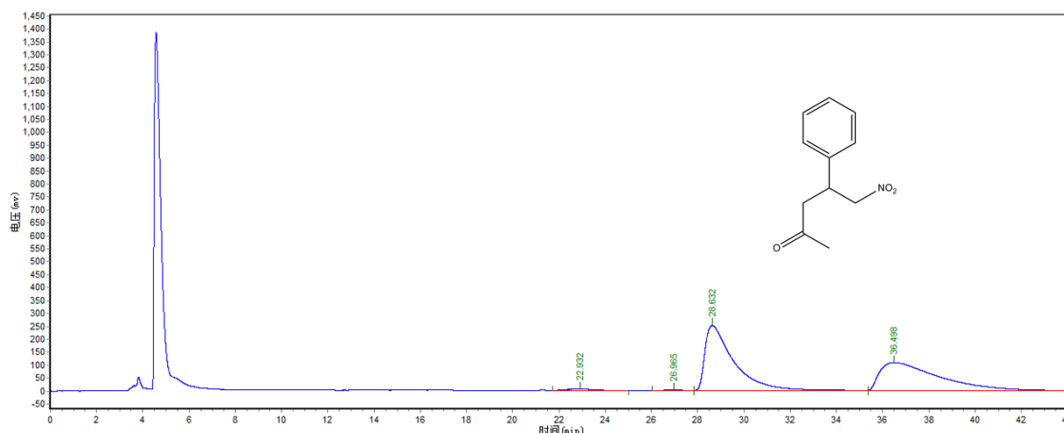
$^1\text{H NMR (CDCl}_3)$ & 7.33- 7.25 (m, 3H), 7.15-7.14 (m, 2H), 4.65 (dd, $J_1 = 12.5$ Hz, $J_2 = 9.0$ Hz, 1H), 4.58 (dd, $J_1 = 12.5$ Hz, $J_2 = 4.5$ Hz, 1H), 3.73-3.68 (m, 1H), 3.01-2.94 (m, 1H), 2.63-2.54 (m, 1H), 2.43-2.35 (m, 1H), 1.05 (t, $J = 7.3$ Hz, 3H), 0.95 (d, $J = 7.1$ Hz, 3H); The compound was analyzed by chiral HPLC with a Chiralpack AS-H column at 213 nm under 0.5 mL/min (the n-hexane / 2-propanol volume ratio is 90:10); $t_r = 13.9$ min (major), 17.9 min (minor).

$^1\text{H NMR (CDCl}_3)$ & 9.73 (d, $J = 2.5$ Hz, 1H), 7.29- 7.37 (m, 2H), 7.18-7.22 (m, 3H), 4.61-4.75 (m, 2H), 3.77-3.82 (m, 1H), 2.66-2.72 (m, 1H), 1.48-1.55 (m, 2H), 0.82-0.91 (m, 3H); The compound was analyzed by chiral HPLC with a Chiralpack AS-H column at 213 nm under 2 mL/min (the n-hexane / 2-propanol volume ratio is 99:1); $t_r = 26.6$ min (major).

$^1\text{H NMR (CDCl}_3)$ & 9.52 (s, 1H), 7.18- 7.35 (m, 5H), 4.85 (dd, $J_1 = 13.0$ Hz, $J_2 = 4.5$ Hz, 1H), 4.69 (dd, $J_1 = 13.0$ Hz, $J_2 = 4.5$ Hz, 1H), 3.78 (dd, $J_1 = 11.5$ Hz, $J_2 = 4.5$ Hz, 1H), 1.13 (s, 3H), 1.01 (s, 3H); The compound was analyzed by chiral HPLC with a Chiralpack AS-H column at 213 nm under 1 mL/min (the n-hexane / 2-propanol volume ratio is 80:20).

1 HPLC spectra for Michael addition

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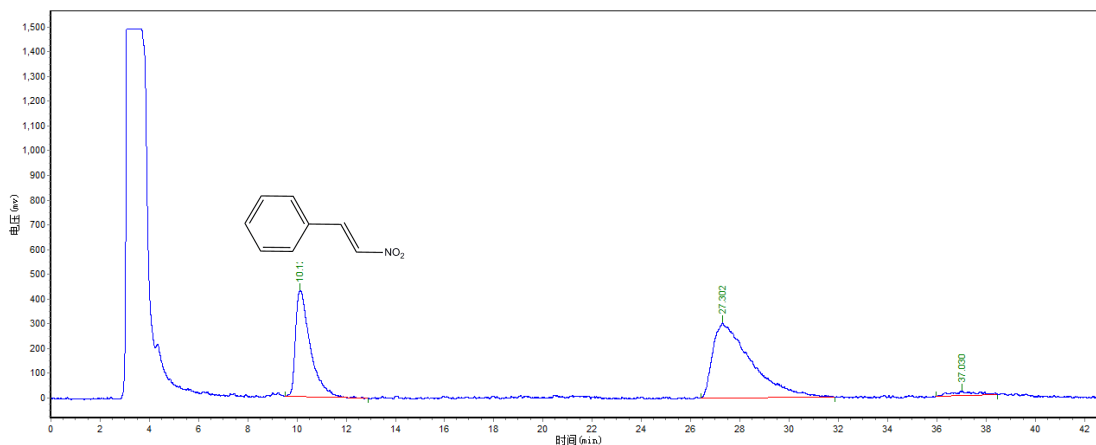


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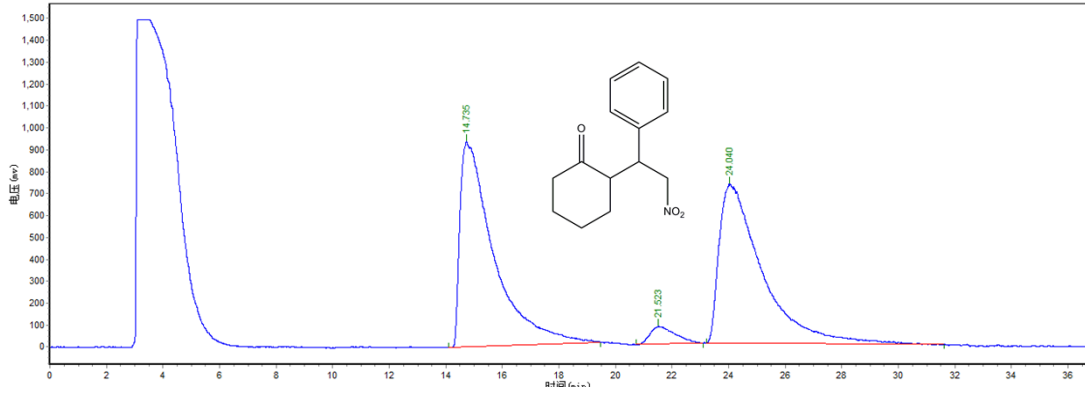


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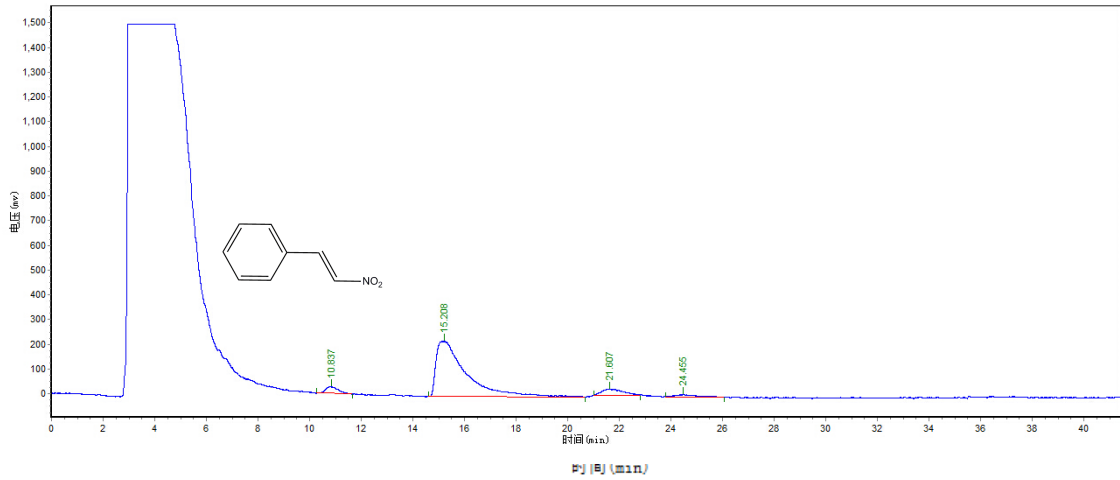
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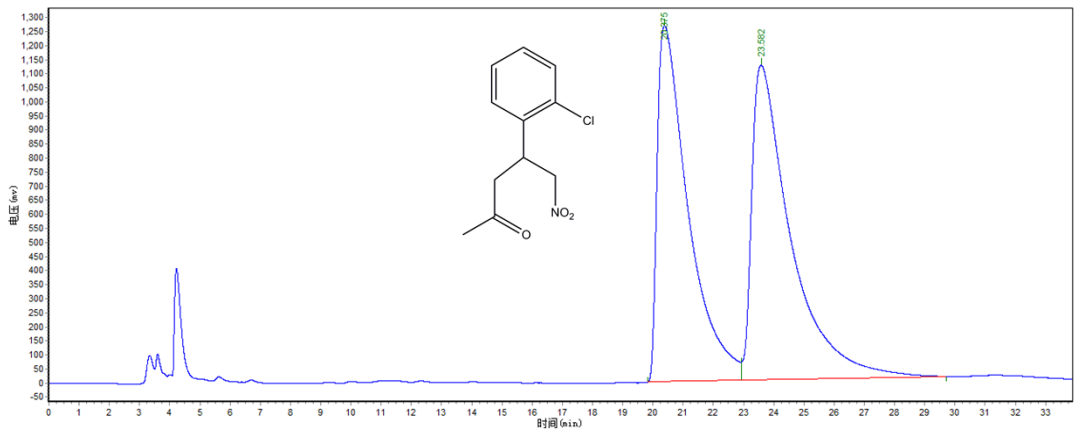
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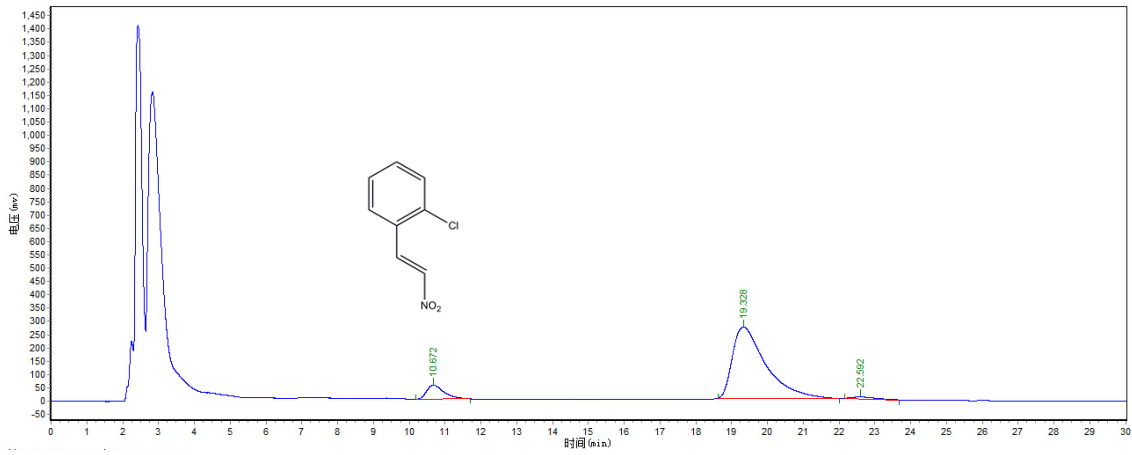
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| 2 | | 19.328 | 268123.469 | 17239874.000 | 89.3842 |
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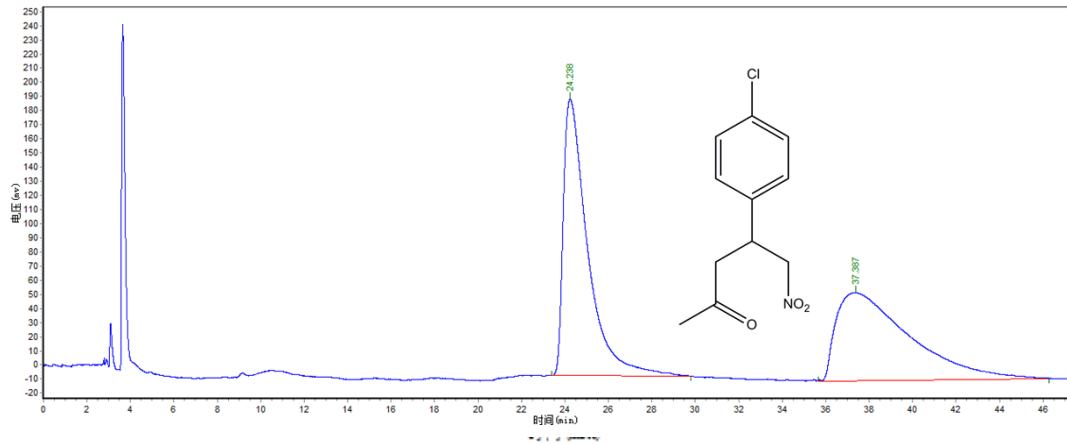
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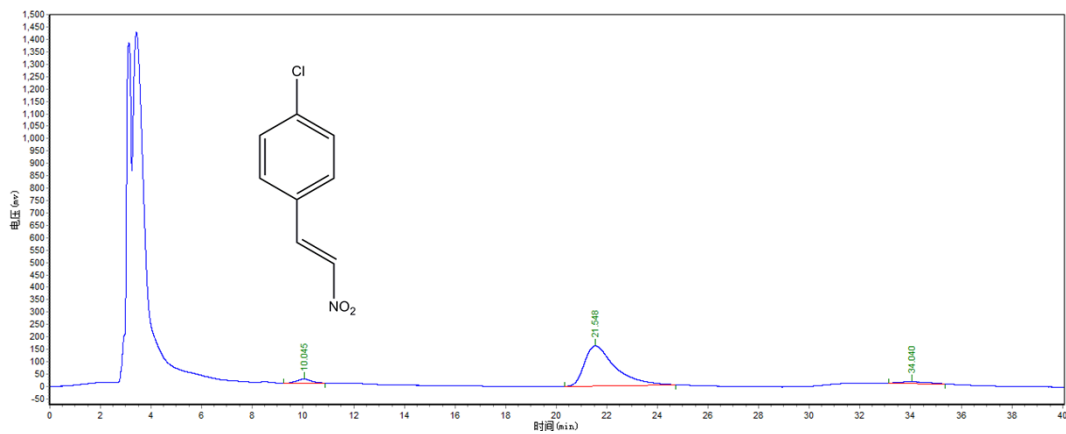


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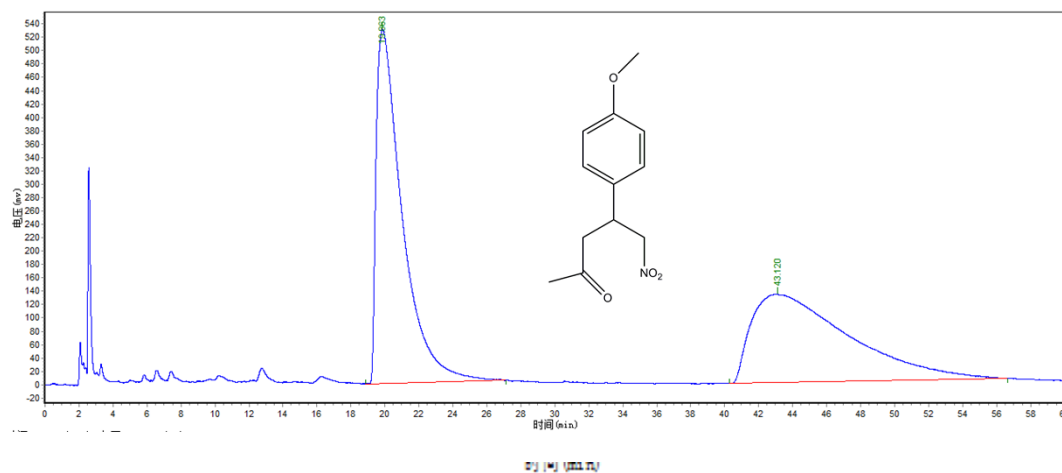
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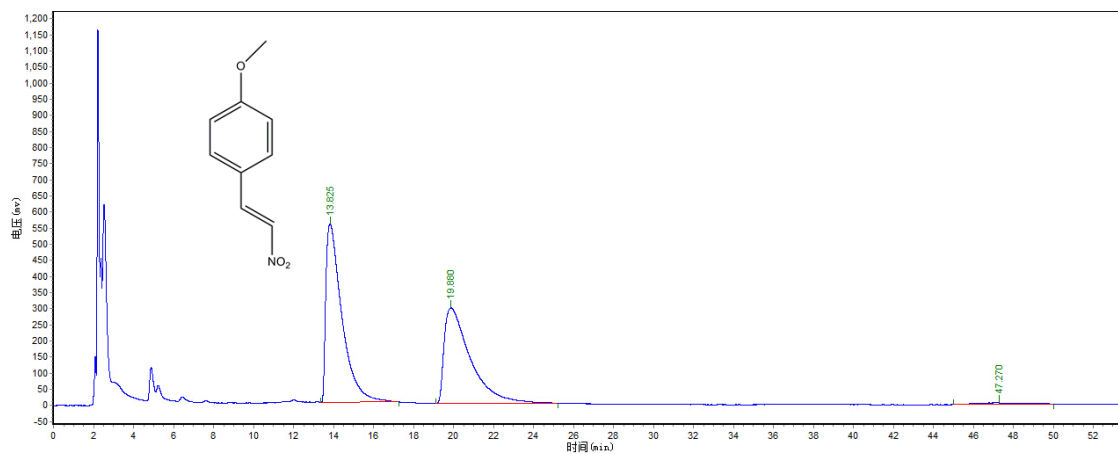


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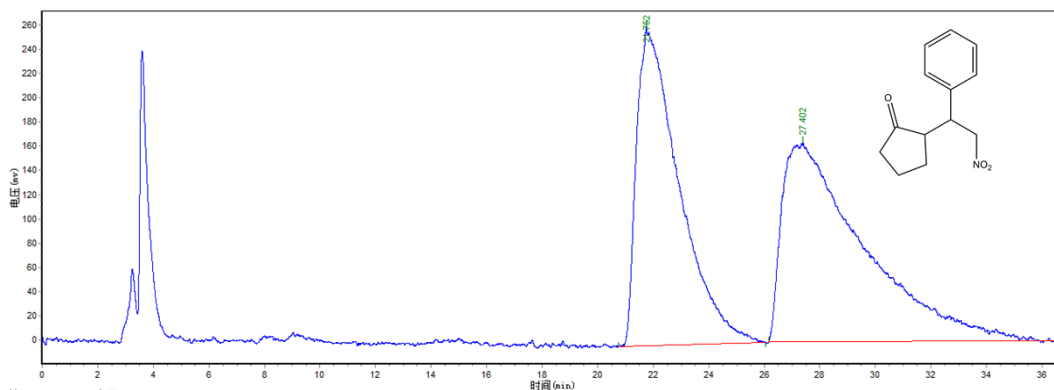
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| 3 | | 47.270 | 4745.064 | 714934.938 | 1.2213 |
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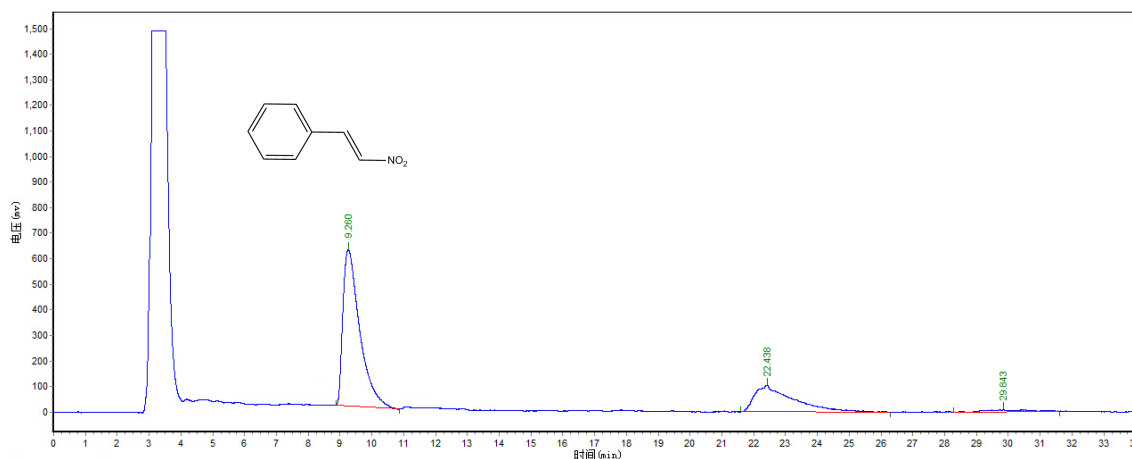


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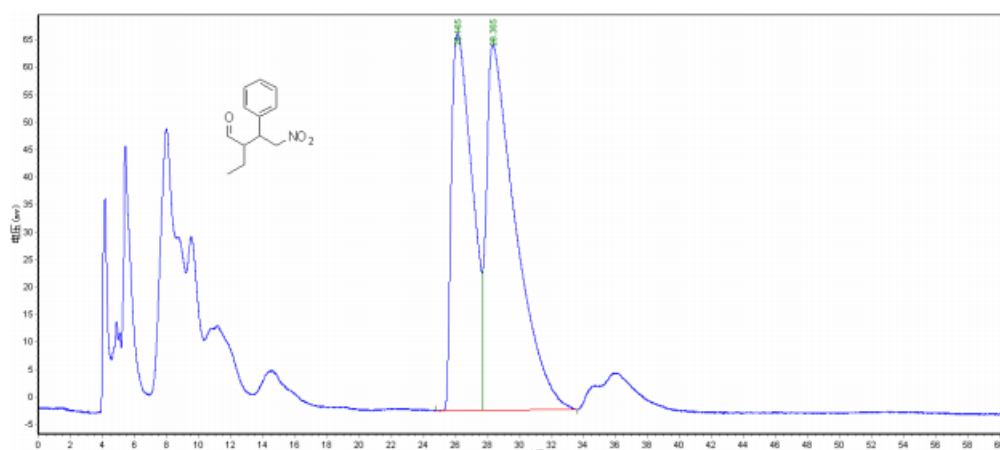


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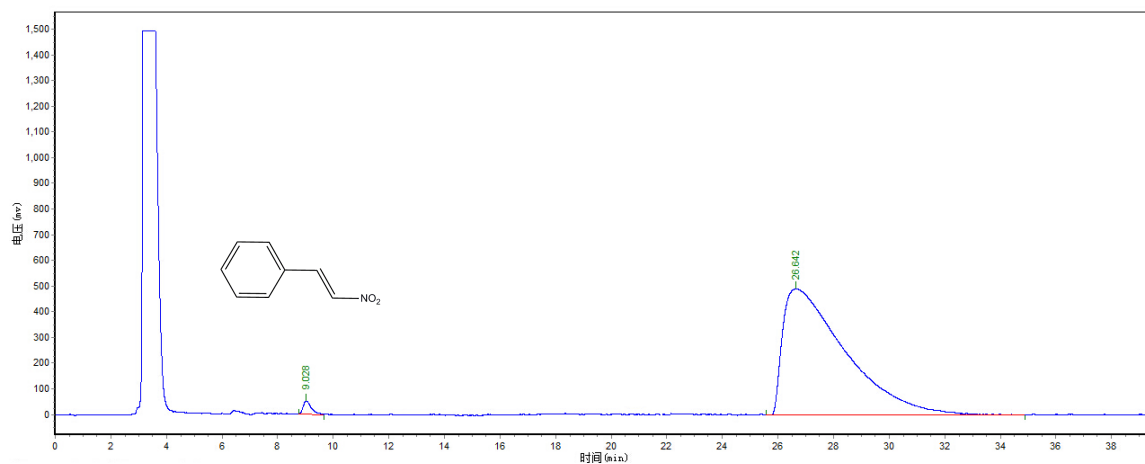
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| 3 | | 29.843 | 8457.284 | 714728.313 | 2.2419 |
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| Peak# | RT(min) | Height(μV) | Area (μV*Sec) | Area % |
|--------------|---------|------------|---------------|----------|
| 1 | 26.165 | 68524.813 | 6194734.000 | 42.0449 |
| 2 | 28.365 | 66588.875 | 8538897.000 | 57.9551 |
| Total | | 135113.688 | 14733631.000 | 100.0000 |

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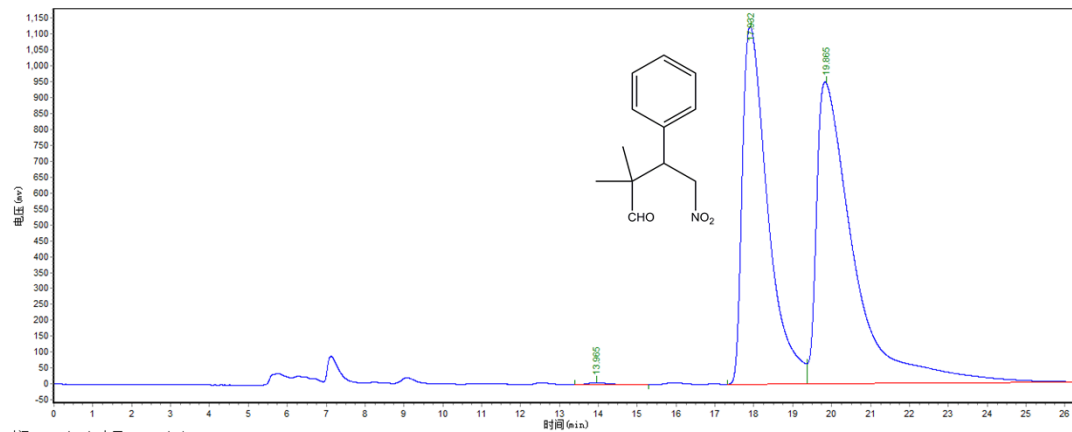


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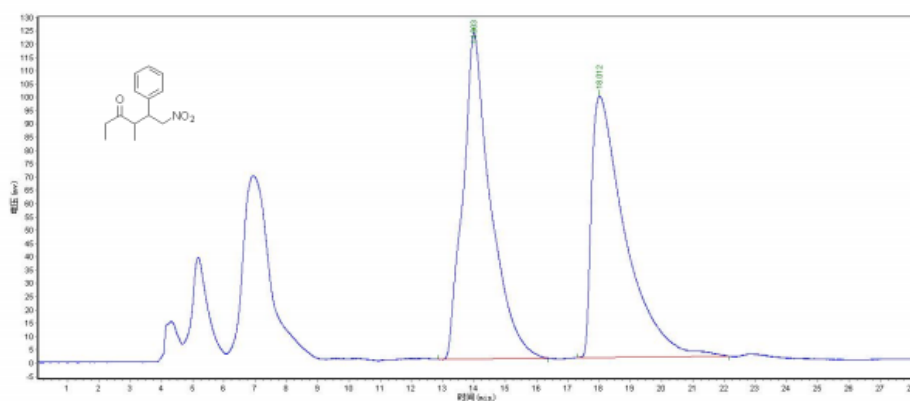
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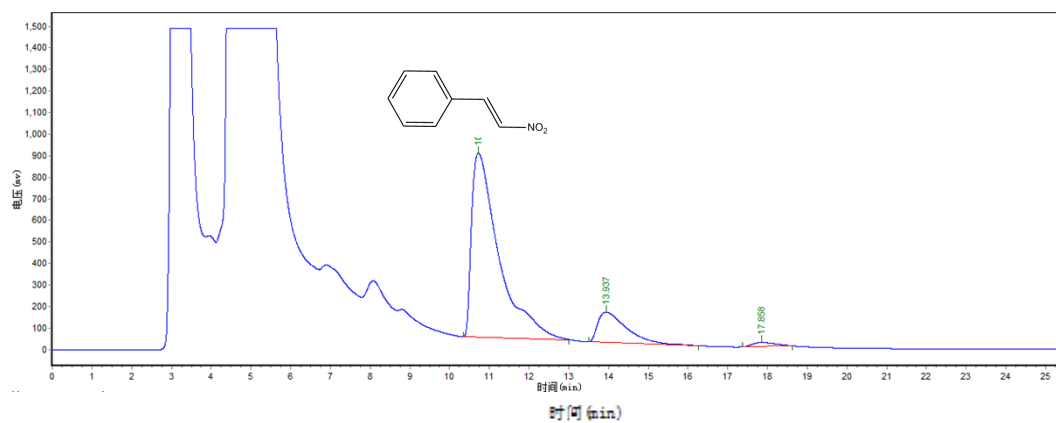
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| Peak# | RT(min) | Height(μV) | Area (μV*Sec) | Area % |
|--------------|---------|------------|---------------|----------|
| 1 | 14.003 | 122658.617 | 7565940.500 | 50.8165 |
| 2 | 18.012 | 98356.328 | 7322801.500 | 49.1835 |
| Total | | 221014.945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

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| 峰号 | 峰名 | 保留时间 | 峰高 | 峰面积 | 含量 |
|-----------|----|--------|-------------|--------------|----------|
| 1 | | 10.728 | 854840.250 | 40429528.000 | 83.7005 |
| 2 | | 13.937 | 141180.953 | 7136096.500 | 14.7737 |
| 3 | | 17.858 | 18272.529 | 736973.000 | 1.5257 |
| 总计 | | | 1014293.732 | 48302597.500 | 100.0000 |

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