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**Supporting Information  
for**

**Cinchona alkaloid thiourea-catalyzed one-pot  
synthesis and bioselective activities of  $\beta$ -amino acid  
ester derivatives containing a pyrimidine moiety**

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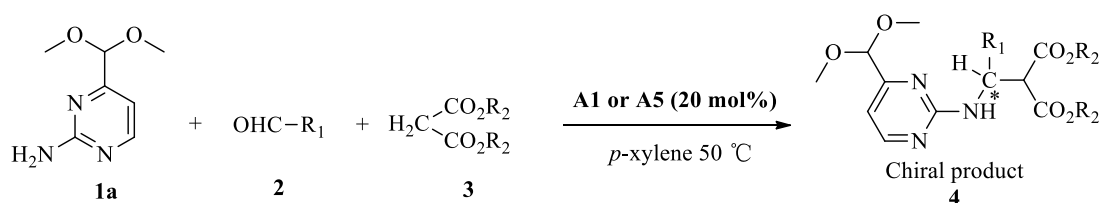
## Experimental and analytical data

### 1. Instruments and Materials.

All reactions were carried out in oven-dried glassware with magnetic stirring. Unless otherwise stated, the reagents were from Aladdin Chemicals Co. (Aladdin, Shanghai, China) and Daicel Chiral Technologies China Co., (Daicel, Shanghai, China). All solvents were distilled from appropriate drying agents prior to use. Silica gel GF254-coated glass plates (Branch Qingdao Haiyang Chemical Co., Qingdao, China) were used for TLC under detection at 254 nm. Silica gel 200–300 mesh (Branch Qingdao Haiyang Chemical Co., Qingdao, China) was applied in column chromatography. Infrared (IR) spectra were recorded on a Bruker VECTOR 22 spectrometer (Bruker, Karlsruhe, Germany) with KBr disks. NMR spectra were recorded on a Bruker 400 NMR (Bruker, Karlsruhe, Germany). HRMS data were measured on a Shimadzu Scientific LCMS-IT-TOF (Shimadzu, Kyoto, Japan). Elemental analysis was performed on an Elementar Vario-III CHN analyzer (Elementar, Frankfurt, Germany). HPLC analysis was conducted by using a Fuli Analytical Technologies LC5090 series system (Fuli analytical instrument Co., China), Chiralpak IA column (Daicel, Shanghai, China). Optical rotation values were measured by a Wzz-2s polarimeter (Shanghai Yue Feng Instrument and Meter Co., China).

### 2. Experimental section

#### General experimental procedure to prepare 4



Reactions were performed with 0.30 mmol of 4-(dimethoxymethyl)pyrimidin-2-amine (**1a**), 0.30 mmol of aldehyde **2**, 0.30 mmol of malonate **3** in 3.0 mL of *p*-xylene in the presence of 20 mol% catalyst **A1** or **A5** at 50°C and stirred for 48–60 h. After completion of the reaction (as observed by TLC), the crude product was purified by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1), which yielded the target product. Their structures were determined by <sup>1</sup>H NMR and <sup>13</sup>C NMR.

**diethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(phenyl)methyl)malonate (4a)**

light-yellow oil; yield 78%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.29 (d,  $J = 4.9$  Hz, 1H), 7.41 (d,  $J = 7.7$  Hz, 2H), 7.29 (t,  $J = 7.8$  Hz, 2H), 7.22 (t,  $J = 7.2$  Hz, 1H), 6.75 (d,  $J = 4.9$  Hz, 1H), 6.68 (d,  $J = 9.6$  Hz, 1H), 6.06 (dd,  $J = 9.5, 5.9$  Hz, 1H), 5.06 (s, 1H), 4.15–4.09 (m, 4H), 3.99 (d,  $J = 5.7$  Hz, 1H), 3.39 (s, 3H), 3.32 (s, 3H), 1.14 (t,  $J = 8.6$  Hz, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  167.81, 167.09, 166.05, 161.52, 158.70, 139.83, 128.44, 127.47, 126.72, 108.17, 103.00, 61.74, 61.52, 60.39, 57.38, 53.79, 53.64, 14.20, 13.88; IR (KBr):  $\nu$ 3220, 3011, 2951, 2923, 1654, 1582, 1525, 1498, 1369, 1244, 1027, 757  $\text{cm}^{-1}$ ; Anal. Calcd for  $\text{C}_{21}\text{H}_{27}\text{N}_3\text{O}_6$ : C, 60.42; H, 6.52; N, 10.07; found C, 60.35; H, 6.59; N, 10.00. HR-MS (ESI $^+$ )  $m/z$  Calcd for  $\text{C}_{21}\text{H}_{27}\text{N}_3\text{O}_6$   $[\text{M} + \text{H}]^+$  418.1973; found 418.1983.

**(–)diethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(phenyl)methyl)malonate**

(–) (**4a**), this product was obtained as a light-yellow oil from a reaction catalyzed by A1 (20 mol%) at 50°C for 48 h; yield 90% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 89% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0  $\text{mL} \cdot \text{min}^{-1}$ ,  $\lambda = 220$  nm,  $t_r$  (major) = 13.87 min,  $t_r$  (minor) = 9.35 min];  $[\alpha]_{\text{D}}^{25} = -41.2$  ( $c = 0.52$ ,  $\text{CHCl}_3$ );

**(+)diethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(phenyl)methyl)malonate**

(+) (**4a**), this product was obtained as a light-yellow oil from a reaction catalyzed by A5 (20 mol%) at 50°C for 48 h; yield 88% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 95% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0  $\text{mL} \cdot \text{min}^{-1}$ ,  $\lambda = 220$  nm,  $t_r$  (major) = 9.19 min,  $t_r$  (minor) = 13.89 min];  $[\alpha]_{\text{D}}^{25} = +80.2$  ( $c = 0.85$ ,  $\text{CHCl}_3$ );

**diethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(4-methoxyphenyl)methyl)malonate**

**(4b)**

light-yellow oil; yield 74%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.29 (d,  $J = 4.9$  Hz, 1H), 7.33 (d,  $J = 8.1$  Hz, 2H), 6.83 (d,  $J = 8.0$  Hz, 2H), 6.75 (d,  $J = 4.9$  Hz, 1H), 6.57 (d,  $J = 9.5$  Hz, 1H), 6.01–5.97 (m, 1H), 5.06 (s, 1H), 4.15–4.08 (m, 4H), 3.95 (d,  $J = 5.9$  Hz, 1H), 3.76 (s, 3H), 3.38 (s, 3H), 3.33 (s, 3H), 1.16–1.10 (m, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  167.90, 167.14, 166.02, 161.52, 158.90, 158.74, 131.91, 127.91, 113.82, 108.14, 61.72, 61.52, 57.54, 55.24, 53.68, 53.31, 14.21, 13.93, 13.89; IR (KBr):  $\nu$ 3225, 3005, 2953, 2923, 1621, 1586, 1497, 1451, 1363, 1234, 1031, 760  $\text{cm}^{-1}$ ;

Anal. Calcd for  $C_{22}H_{29}N_3O_7$ : C, 59.05; H, 6.53; N, 9.39; found C, 59.11; H, 6.47; N, 9.42; HR-MS (ESI<sup>+</sup>)  $m/z$  Calcd for  $C_{22}H_{29}N_3O_7$  [M + H]<sup>+</sup> 448.2087 found 448.2078.

**(–)diethyl2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(4-methoxyphenyl)methyl)malonate**

(–) (**4b**), this product was obtained as a light-yellow oil from a reaction catalyzed by A1 (20 mol%) at 50°C for 48 h; yield 93% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 95% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>–1</sup>,  $\lambda$  = 220 nm, tr (major) = 14.78 min, tr (minor) = 9.45 min];  $[\alpha]_D^{25} = -77.6$  (c = 1.10, CHCl<sub>3</sub>);

**(+)diethyl2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(4-methoxyphenyl)methyl)malonate**

(+) (**4b**), this product was obtained as a light-yellow oil from a reaction catalyzed by A5 (20 mol%) at 50°C for 48 h; yield 88% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 93% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>–1</sup>,  $\lambda$  = 220 nm, tr (major) = 9.49 min, tr (minor) = 14.85 min];  $[\alpha]_D^{25} = +81.6$  (c = 0.99, CHCl<sub>3</sub>);

**diethyl 2-(cyclohexyl((4-(dimethoxymethyl)pyrimidin-2-yl)amino)methyl)malonate (4c)**

light-yellow oil; yield 72%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.30 (s, 1H), 6.70 (d,  $J$  = 4.8 Hz, 1H), 6.06 (s, 1H), 5.06 (s, 1H), 4.76 (s, 1H), 4.24–4.21 (m, 2H), 4.05 (d,  $J$  = 10.4 Hz, 2H), 3.78 (d,  $J$  = 4.6 Hz, 1H), 3.38 (d,  $J$  = 5.2 Hz, 6H), 2.05 (s, 1H), 1.85–1.56 (m, 6H), 1.24 (s, 4H), 1.10–1.06 (m, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  168.47, 168.28, 165.89, 162.51, 158.28, 107.40, 102.85, 61.45, 61.29, 54.72, 53.63, 53.25, 41.65, 30.19, 29.35, 26.11, 26.02, 25.92, 14.02, 13.80. IR (KBr):  $\nu$  3203, 3003, 2983, 2912, 1651, 1544, 1493, 1251, 1230, 1172, 1094, 826 cm<sup>–1</sup>; Anal. Calcd for  $C_{21}H_{33}N_3O_6$ : C, 59.56; H, 7.85; N, 9.92; found C, 59.50; H, 7.89; N, 9.96; HR-MS (ESI<sup>+</sup>)  $m/z$  Calcd for  $C_{21}H_{33}N_3O_6$  [M + H]<sup>+</sup> 424.2442; found 424.2441

**(–)diethyl 2-(cyclohexyl((4-(dimethoxymethyl)pyrimidin-2-yl)amino)methyl)malonate**

(–) (**4c**), this product was obtained as a light-yellow oil from a reaction catalyzed by A1 (20 mol%) at 50°C for 60 h; yield 92% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 93%

ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>-1</sup>, λ = 220 nm, tr (major) = 9.78 min, tr (minor) = 7.04 min]; [α]<sub>D</sub><sup>25</sup> = -103.1 (c = 0.81, CHCl<sub>3</sub>);

**(+) diethyl 2-(cyclohexyl((4-(dimethoxymethyl)pyrimidin-2-yl)amino)methyl)malonate**

(+) (**4c**), this product was obtained as a light-yellow oil from a reaction catalyzed by A5 (20 mol%) at 50°C for 60 h; yield 93% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 97% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>-1</sup>, λ = 220 nm, tr (major) = 6.91 min, tr (minor) = 9.84 min]; [α]<sub>D</sub><sup>25</sup> = +52.6 (c = 0.43, CHCl<sub>3</sub>);

**dimethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(phenyl)methyl)malonate (**4d**)**

light-yellow oil; yield 75%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.29 (d, *J* = 5.0 Hz, 1H), 7.40 (d, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 6.76 (d, *J* = 5.0 Hz, 1H), 6.69 (d, *J* = 9.5 Hz, 1H), 6.06 (dd, *J* = 9.5, 5.9 Hz, 1H), 5.06 (s, 1H), 4.01 (d, *J* = 5.8 Hz, 1H), 3.65 (s, 6H), 3.32 (d, *J* = 26.5 Hz, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 168.18, 167.45, 166.10, 161.45, 158.69, 139.71, 128.52, 127.59, 126.65, 108.29, 102.98, 57.14, 53.90, 53.69, 52.73, 52.53; IR (KBr): ν<sub>3226</sub>, 3002, 2953, 2927, 1654, 1581, 1527, 1494, 1365, 1243, 1026, 750 cm<sup>-1</sup>; Anal. Calcd for C<sub>19</sub>H<sub>23</sub>N<sub>3</sub>O<sub>6</sub>: C, 58.60; H, 5.95; N, 10.79; found C, 58.65; H, 5.91; N, 10.74; HR-MS (ESI<sup>+</sup>) *m/z* Calcd for C<sub>19</sub>H<sub>23</sub>N<sub>3</sub>O<sub>6</sub> [M + H]<sup>+</sup> 390.1660; found 390.1671.

**(-)dimethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(phenyl)methyl)malonate**

(-) (**4d**), this product was obtained as a light-yellow oil from a reaction catalyzed by A1 (20 mol%) at 50°C for 48 h; yield 85% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 93% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>-1</sup>, λ = 220 nm, tr (major) = 14.39 min, tr (minor) = 10.71 min]; [α]<sub>D</sub><sup>25</sup> = -35.6 (c = 0.69, CHCl<sub>3</sub>);

**(+)dimethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(phenyl)methyl)malonate**

(+) (**4d**), this product was obtained as a light-yellow oil from a reaction catalyzed by A5 (20 mol%) at 50°C for 48 h; yield 90% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 97% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>-1</sup>, λ = 220 nm, tr (major) = 10.59 min, tr (minor) = 14.36 min]; [α]<sub>D</sub><sup>25</sup> = +52.6 (c = 0.82, CHCl<sub>3</sub>);

**dimethyl 2-((4-chlorophenyl)((4-(dimethoxymethyl)pyrimidin-2-yl)amino)methyl)malonate (4e)**

light-yellow oil; yield 71%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.29 (d,  $J = 5.0$  Hz, 1H), 7.35 (d,  $J = 8.3$  Hz, 2H), 7.28 (d,  $J = 8.1$  Hz, 2H), 6.78 (d,  $J = 5.0$  Hz, 1H), 6.68 (d,  $J = 9.3$  Hz, 1H), 5.99 (dd,  $J = 9.3, 5.8$  Hz, 1H), 5.06 (s, 1H), 3.97 (d,  $J = 5.6$  Hz, 1H), 3.66 (s, 6H), 3.39 (d,  $J = 23.8$  Hz, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  168.03, 167.24, 166.17, 161.26, 158.69, 138.34, 133.41, 128.69, 128.17, 108.55, 102.87, 56.88, 53.67, 53.44, 52.85, 52.66. IR (KBr):  $\nu$  3223, 3006, 2952, 2929, 1623, 1587, 1494, 1455, 1360, 1235, 1035, 768  $\text{cm}^{-1}$ ; Anal. Calcd for  $\text{C}_{19}\text{H}_{22}\text{ClN}_3\text{O}_6$ : C, 53.84; H, 5.23; N, 9.91; found C, 53.80; H, 5.19; N, 9.86; HR-MS ( $\text{ESI}^+$ )  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{22}\text{ClN}_3\text{O}_6$   $[\text{M} + \text{H}]^+$  424.1270; found 424.1270.

**(-)-2-((4-chlorophenyl)((4-(dimethoxymethyl)pyrimidin-2-yl)amino)methyl)malonate**

(-) (**4e**), this product was obtained as a light-yellow oil from a reaction catalyzed by A1 (20 mol%) at 50°C for 48 h; yield 82% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 93% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0  $\text{mL} \cdot \text{min}^{-1}$ ,  $\lambda = 220$  nm,  $t_r$  (major) = 11.85 min,  $t_r$  (minor) = 8.48 min];  $[\alpha]_{\text{D}}^{25} = -80.1$  ( $c = 0.62$ ,  $\text{CHCl}_3$ );

**(+)-2-((4-chlorophenyl)((4-(dimethoxymethyl)pyrimidin-2-yl)amino)methyl)malonate**

(+) (**4e**), this product was obtained as a light-yellow oil from a reaction catalyzed by A5 (20 mol%) at 50°C for 48 h; yield 89% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 95% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0  $\text{mL} \cdot \text{min}^{-1}$ ,  $\lambda = 220$  nm,  $t_r$  (major) = 8.42 min,  $t_r$  (minor) = 11.87 min];  $[\alpha]_{\text{D}}^{25} = +91.5$  ( $c = 0.75$ ,  $\text{CHCl}_3$ );

**dimethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(p-tolyl)methyl)malonate (4f)**

light-yellow oil; yield 77%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.28 (d,  $J = 4.9$  Hz, 1H), 7.28 (d,  $J = 7.6$  Hz, 2H), 7.11 (d,  $J = 7.7$  Hz, 2H), 6.75 (d,  $J = 5.0$  Hz, 1H), 6.65 (d,  $J = 9.6$  Hz, 1H), 6.01 (dd,  $J = 9.5, 5.9$  Hz, 1H), 5.06 (s, 1H), 3.99 (d,  $J = 5.8$  Hz, 1H), 3.65 (s, 6H), 3.38 (d,  $J = 19.8$  Hz, 6H), 2.29 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  168.23, 167.50, 166.08, 161.45, 158.66, 137.23, 136.68, 129.22, 126.54, 108.21, 57.20, 53.73, 53.65, 52.70, 52.51, 21.05. IR (KBr):  $\nu$  3205, 3001, 2982, 2915, 1657, 1548, 1499, 1255, 1233, 1171, 1090, 825  $\text{cm}^{-1}$ ; Anal. Calcd for  $\text{C}_{20}\text{H}_{25}\text{N}_3\text{O}_6$ : C, 60.84; H, 6.12; N, 10.04; found C, 60.80; H, 6.10; N, 10.02.

59.54; H, 6.25; N, 10.42; found C, 59.50; H, 6.21; N, 10.46; HR-MS (ESI<sup>+</sup>) *m/z* Calcd for C<sub>20</sub>H<sub>25</sub>N<sub>3</sub>O<sub>6</sub> [M + H]<sup>+</sup> 404.1816; found 404.1817.

**(–)dimethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(p-tolyl)methyl)malonate**

(–) (**4f**), this product was obtained as light-yellow oil from a reaction catalyzed by A1 (20 mol%) at 50°C for 60 h; yield 81% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 96% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>–1</sup>, λ = 220 nm, tr (major) = 11.02 min, tr (minor) = 7.72 min]; [α]<sub>D</sub><sup>25</sup> = –78.3 (c = 1.05, CHCl<sub>3</sub>);

**(+)dimethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(p-tolyl)methyl)malonate**

(+) (**4f**), this product was obtained as a light-yellow oil from a reaction catalyzed by A5 (20 mol%) at 50°C for 60 h; yield 87% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 95% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>–1</sup>, λ = 220 nm, tr (major) = 7.63 min, tr (minor) = 10.93 min]; [α]<sub>D</sub><sup>25</sup> = +41.8 (c = 0.56, CHCl<sub>3</sub>);

**dimethyl 2-(cyclohexyl((4-(dimethoxymethyl)pyrimidin-2-yl)amino)methyl)malonate (**4g**)**

light-yellow oil; yield 76%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.31 (s, 1H), 6.71 (d, *J* = 4.3 Hz, 1H), 6.03 (s, 1H), 5.07 (s, 1H), 4.76 (s, 1H), 3.82 (d, *J* = 3.7 Hz, 1H), 3.75 (s, 3H), 3.58 (s, 3H), 3.40 (s, 6H), 2.05 (s, 1H), 1.85–1.55 (m, 6H), 1.20–1.01 (m, 4H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 168.60, 165.92, 162.47, 158.33, 107.50, 102.77, 54.81, 53.69, 52.86, 52.37, 52.35, 41.47, 30.16, 29.32, 26.07, 25.97, 25.86; IR (KBr): ν 3223, 3002, 2958, 2921, 1658, 1584, 1529, 1491, 1364, 1243, 1023, 753 cm<sup>–1</sup>; Anal. Calcd for C<sub>19</sub>H<sub>29</sub>N<sub>3</sub>O<sub>6</sub>: C, 57.71; H, 7.39; N, 10.63; found C, 57.76; H, 7.35; N, 10.61; HR-MS (ESI<sup>+</sup>) *m/z* Calcd for C<sub>19</sub>H<sub>29</sub>N<sub>3</sub>O<sub>6</sub> [M + H]<sup>+</sup> 396.2129; found 396.2131.

**(–)dimethyl 2-(cyclohexyl((4-(dimethoxymethyl)pyrimidin-2-yl)amino)methyl)malonate**

(–) (**4g**), this product was obtained as light-yellow oil from a reaction catalyzed by A1 (20 mol%) at 50°C for 60 h; yield 80% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 91% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>–1</sup>, λ = 220 nm, tr (major) = 10.92 min, tr (minor) = 7.27 min]; [α]<sub>D</sub><sup>25</sup> = –41.7 (c = 0.77, CHCl<sub>3</sub>);

**(+)dimethyl 2-(cyclohexyl((4-(dimethoxymethyl)pyrimidin-2-yl)amino)methyl)malonate**

(+) (**4g**), this product was obtained as a light-yellow oil from a reaction catalyzed by A5 (20 mol%) at 50°C for 60 h; yield 84% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 94% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>-1</sup>, λ = 220 nm, tr (major) = 7.40 min, tr (minor) = 10.98 min]; [α]<sub>D</sub><sup>25</sup> = -63.5 (c = 0.96, CHCl<sub>3</sub>);

**dimethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(furan-2-yl)methyl)malonate (4h)**

light-yellow oil; yield 79%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.35 (d, *J* = 4.8 Hz, 1H), 7.27 (d, *J* = 18.1 Hz, 1H), 6.82 (d, *J* = 4.9 Hz, 1H), 6.40 (d, *J* = 9.7 Hz, 1H), 6.27 (d, *J* = 6.3 Hz, 2H), 6.16 (d, *J* = 9.9 Hz, 1H), 5.09 (s, 1H), 4.15 (d, *J* = 5.4 Hz, 1H), 3.67 (d, *J* = 18.0 Hz, 6H), 3.39 (d, *J* = 6.6 Hz, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 168.00, 167.25, 166.25, 161.31, 158.70, 152.42, 142.06, 110.42, 108.62, 106.99, 54.52, 53.80, 52.77, 52.65, 48.56. IR (KBr): ν<sub>3228</sub>, 3002, 2953, 2924, 1622, 1587, 1495, 1458, 1362, 1232, 1030, 765 cm<sup>-1</sup>; Anal. Calcd for C<sub>17</sub>H<sub>21</sub>N<sub>3</sub>O<sub>7</sub>: C, 53.82; H, 5.58; N, 11.08; found C, 53.85; H, 5.57; N, 11.11; HR-MS (ESI<sup>+</sup>) *m/z* Calcd for C<sub>17</sub>H<sub>21</sub>N<sub>3</sub>O<sub>7</sub> [M + H]<sup>+</sup> 380.1452; found 380.1451.

**(-)dimethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(furan-2-yl)methyl)malonate**

(-) (**4h**), this product was obtained as a light-yellow oil from a reaction catalyzed by A1 (20 mol%) at 50°C for 60 h; yield 94% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); >99% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>-1</sup>, λ = 220 nm, tr (major) = 15.00 min, tr (minor) = 9.54 min]; [α]<sub>D</sub><sup>25</sup> = -80.1 (c = 0.60, CHCl<sub>3</sub>);

**(+)dimethyl 2-(((4-(dimethoxymethyl)pyrimidin-2-yl)amino)(furan-2-yl)methyl)malonate**

(+) (**4h**), this product was obtained as a light-yellow oil from a reaction catalyzed by A5 (20 mol%) at 50°C for 60 h; yield 92% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 98% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10, 1.0 mL·min<sup>-1</sup>, λ = 220 nm, tr (major) = 9.54 min, tr (minor) = 15.01 min]; [α]<sub>D</sub><sup>25</sup> = +107.2 (c = 0.89, CHCl<sub>3</sub>);

**diethyl 2-(((6-chloropyrimidin-4-yl)amino)(4-methoxyphenyl)methyl)malonate (4i)**

light-yellow oil; yield 78%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.33 (s, 1H), 7.25 (d, *J* = 8.7 Hz, 2H), 6.84 (s, 2H), 6.41 (s, 1H), 4.14 (ddtd, *J* = 14.3, 10.8, 7.3, 3.5 Hz, 4H), 3.91 (d, *J* = 4.9 Hz, 1H),



3.78 (s, 3H), 1.17 (td,  $J = 7.1, 5.3$  Hz, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.78, 162.58, 159.31, 158.46, 127.57, 114.21, 62.13, 61.90, 56.95, 55.26, 13.90; IR (KBr):  $\nu$  3210, 2998, 2924, 2901, 1647, 1572, 1481, 1443, 1357, 1240, 1022, 794  $\text{cm}^{-1}$ ; Anal. Calcd for  $\text{C}_{19}\text{H}_{22}\text{ClN}_3\text{O}_5$ : C, 55.95; H, 5.44; N, 10.30; found C, 55.93; H, 5.42; N, 10.31; MS(ESI):  $m/z = 408([\text{M}+\text{H}]^+)$ ,  $430([\text{M}+\text{Na}]^+)$ .

**(-)-diethyl 2-(((6-chloropyrimidin-4-yl)amino)(4-methoxyphenyl)methyl)malonate**

(-) (**4i**), this product was obtained as a light-yellow oil from a reaction catalyzed by A1 (20 mol%) at  $50^\circ\text{C}$  for 48 h; yield 91% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 99% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10,  $1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 220 \text{ nm}$ , tr (major) = 15.67 min, tr (minor) = 9.57 min];  $[\alpha]_{\text{D}}^{25} = -36.2$  ( $c = 0.55$ ,  $\text{CHCl}_3$ );

**(+)-diethyl 2-(((6-chloropyrimidin-4-yl)amino)(4-methoxyphenyl)methyl)malonate**

(+) (**4i**), this product was obtained as a light-yellow oil from a reaction catalyzed by A5 (20 mol%) at  $50^\circ\text{C}$  for 48 h; yield 93% by preparative TLC (GF254 silica gel: hexane/ethyl ether = 5/1); 99% ee as determined by HPLC [Daicel Chiralpak IA, hexane/IPA = 90/10,  $1.0 \text{ mL}\cdot\text{min}^{-1}$ ,  $\lambda = 220 \text{ nm}$ , tr (major) = 9.55 min, tr (minor) = 15.77 min];  $[\alpha]_{\text{D}}^{25} = +40.3$  ( $c = 0.48$ ,  $\text{CHCl}_3$ );

Catalysts A1, A2, A3, A4 and A5 were prepared according to procedures previously reported, and their data were identical to those reported in the literature <sup>1</sup>.

### 3. Bioassay

The curative, protective and inactivation activities against TMV were evaluated based on the half-leaf blight spot method. The test methods as described in the literature <sup>2</sup>.

**Purification of TMV:** Using Gooding's method, the upper leaves of *N. tabacum* cv. K326 inoculated with TMV were selected, ground in phosphate buffer, and then filtered through a double-layer pledet. The filtrate was centrifuged at 10000 g, Treated twice with PEG, and then centrifuged again. The entire experiment was conducted at  $4^\circ\text{C}$ . Absorbance values were estimated at 260 nm using an ultraviolet spectrophotometer.

Virus concentration (mg/mL) =  $(A_{260} \times \text{dilution ratio})/E^{0.1\%}_{1 \text{ cm}}^{260 \text{ nm}}$

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**Curative effects of the compounds against TMV *in vivo*:** Growing 5–6-leaf stage *Nicotiana tabacum* L. tobaccos were selected. TMV (concentration of  $6 \times 10^{-3}$  mg/mL) was dipped and inoculated using a brush on the whole leaves, which were previously then dried. The compound solution was smeared on the left side of the leaves, scattered with silicon carbide. The leaves were then washed with water after inoculation for 0.5 h and the solvent was smeared on the right side for control. All plants were cultivated in an incubator at a temperature of  $23 \pm 1$  °C and an illumination of 10000 Lux. The number of local lesions was counted and recorded 3 to 4 days after inoculation. Three repetitions were conducted for each compound.

**Protection effects of the compounds against TMV *in vivo*:** The compound solution was seared on the left side, whereas the solvent was smeared on the right side of *Nicotiana tabacum* L. leaves of the same age to serve as the control. The leaves were inoculated with the virus after 12 h. A brush was dipped in  $6 \times 10^{-3}$  mg/mL TMV to inoculate the leaves which were previously scattered with silicon carbide. Subsequently, the leaves were washed with water and rubbed softly along the nervature once or twice. All plants were cultivated in an incubator at a temperature of  $23 \pm 1$  °C and an illumination of 10000 Lux. The number of local lesions was counted and recorded 3 to 4 days after inoculation. Three repetitions were conducted for each compound.

**Inactivation effects of the compounds against TMV *in vivo*:** The virus was inhibited by mixing with the compound solution at the same volume for 30 min. The mixture was then inoculated on *Nicotiana tabacum* L. leaves, and the right side of the leaves was inoculated with solvent and virus mixture for control. All of the leaves were previously scattered with silicon carbide. All plants were cultivated in an incubator at a temperature of  $23 \pm 1$  °C and an illumination of 10000 Lux. The number of local lesions was counted and record 3 to 4 days after inoculation. Three repetitions were conducted for each compound.

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The inhibitory rate of the compounds was calculated according to the following formula ("av" denotes average):

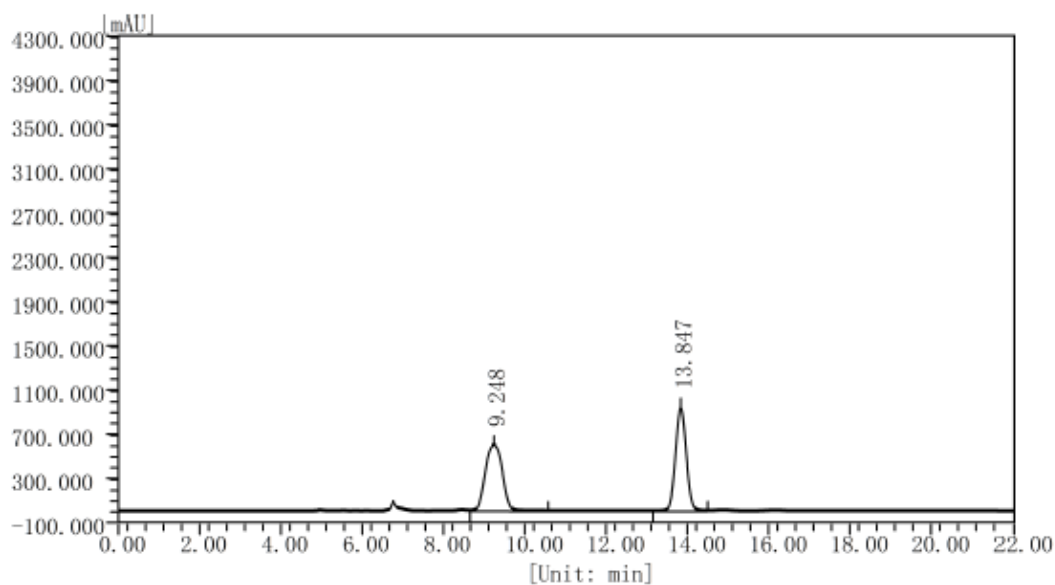
Inhibition rate (%) = [(av local lesion no. of control (not treated with compd) – av local lesion no. smeared with drugs) / av local lesion no. of control (not treated with compd)] × 100%

#### 4. References

1. (a) B. Vakulya, S. Varga, A. Csampai, and T. Soos, *Org. Lett.*, 2005, **7**, 1967; (b) S. Bai, X. Liang, B. A. Song, P. S. Bhadury, D. Hu, and S. Yang, *Tetrahedron: Asymmetry*, 2011, **42**, 518; (c) W. Li, B. A. Song, P. S. Bhadury, L. Liang, Z. Wang, X. Zhang, D. Hu, Z. Chen, Y. Zhang, S. Bai, J. Wu, and S. Yang, *Chirality*, 2012, **24**, 223.
2. (a) Z. Wan, D. Hu, P. Li, D. Xie, and X. Gan, *Molecules*, 2015, **20**, 11861; (b) B. A. Song, H. Zhang, H. Wang, S. Yang, L. Jin, D. Hu, L. Pang, and W. Xue, *J. Agric. Food Chem.*, 2005, **53**, 7886.

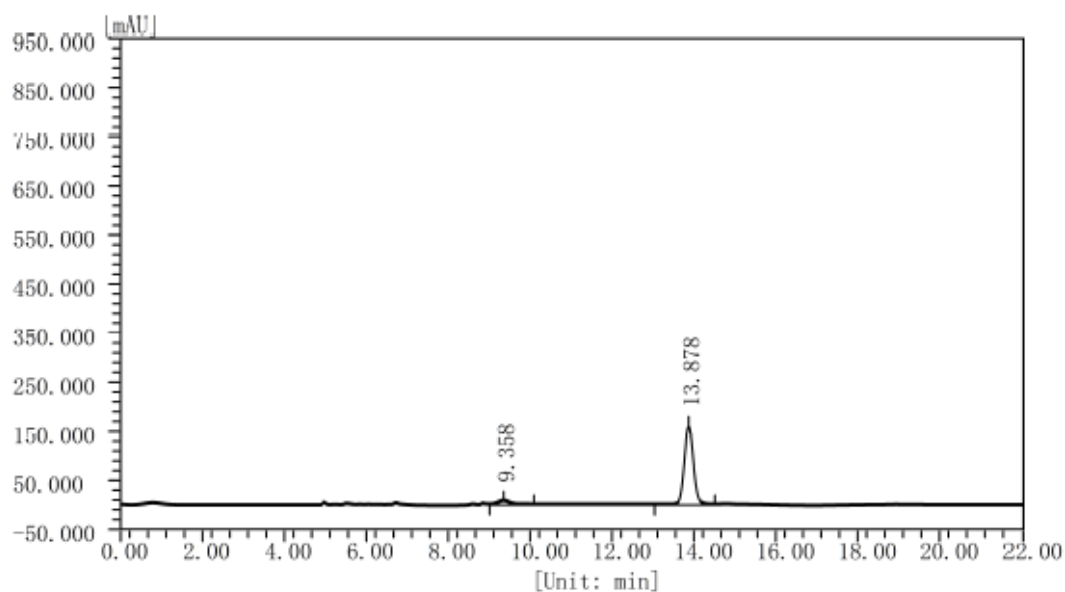
## 5. HPLC chromatograms

### Racemic **4a**



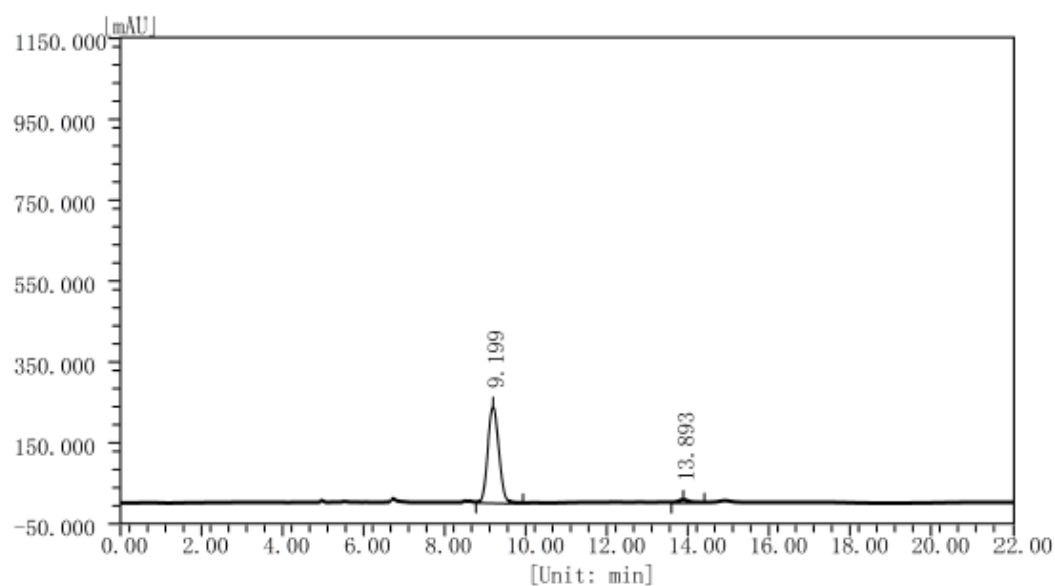
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	9.248	0.477	593065.2	17373543.1	50.0535	BB
2	13.847	0.288	935702.1	17336380.0	49.9465	BB
总计:			1528767.3	34709923.1	100.0000	

### (-)-**4a**, 89.9% ee Product of A1 catalyzed reaction



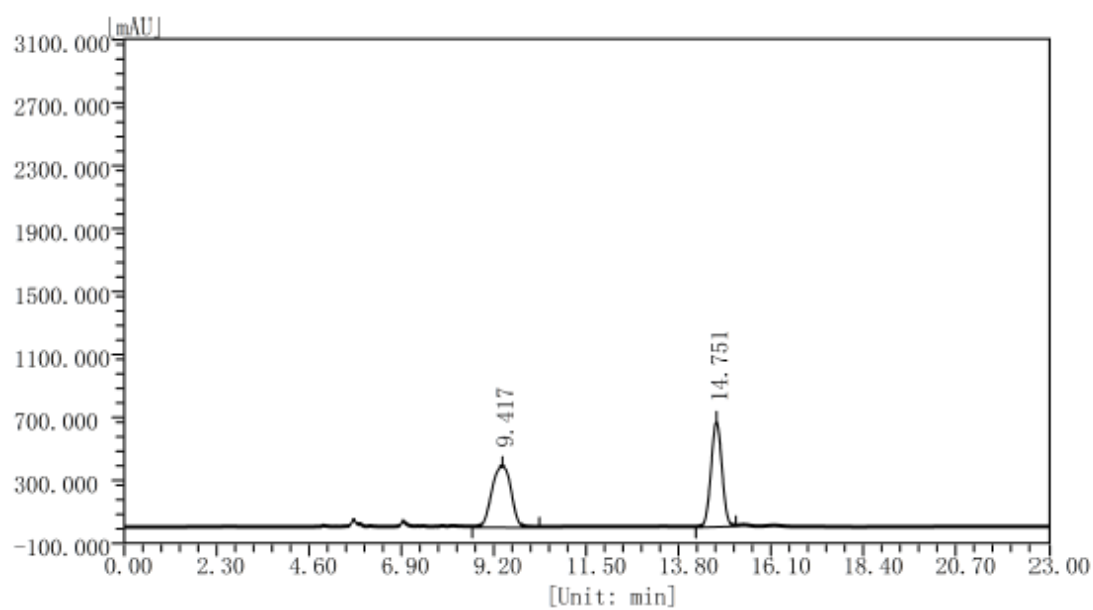
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	9.358	0.282	7349.3	131518.2	5.0120	BB
2	13.878	0.239	160335.3	2492526.9	94.9880	BB
总计:			167684.5	2624045.1	100.0000	

(+)-**4a**, 95.8% ee Product of **A5** catalyzed reaction



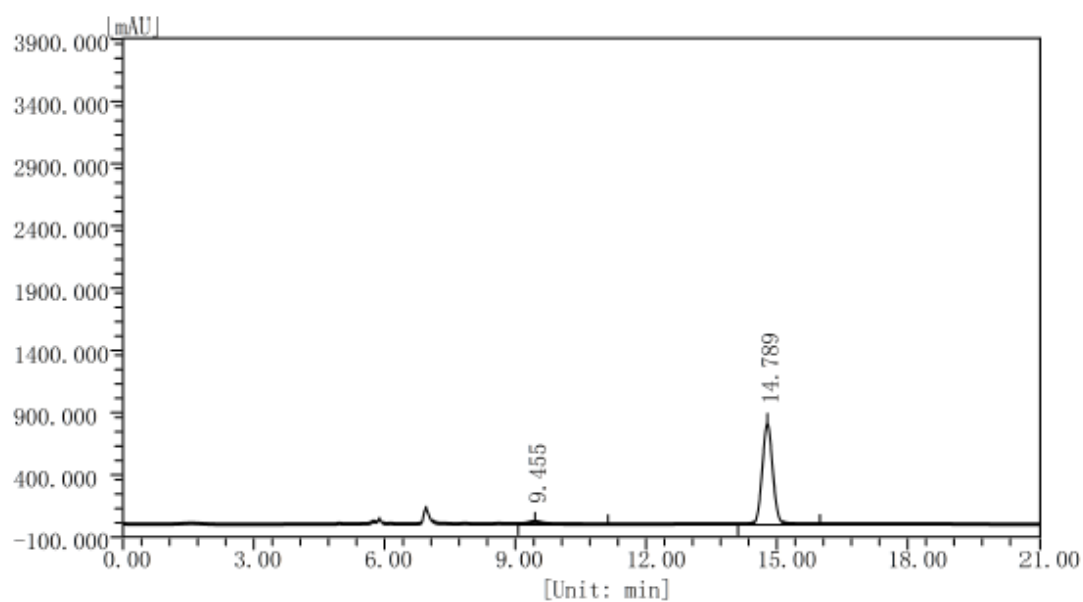
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	9.199	0.298	237644.6	4508909.9	97.9414	BB
2	13.893	0.231	6341.3	94770.8	2.0586	BB
总计:			243985.9	4603680.7	100.0000	

### Racemic **4b**



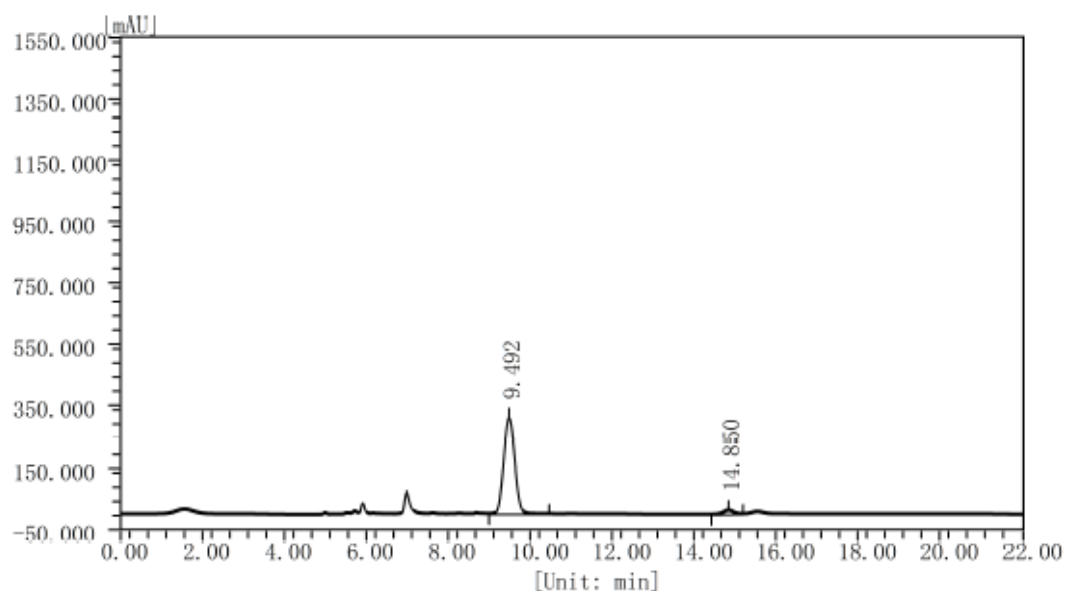
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	9.417	0.549	384248.0	12893463.1	50.4840	BB
2	14.751	0.296	667529.2	12646255.2	49.5160	BB
总计:			1051777.1	25539719.2	100.0000	

(-)-**4b**, 94.1% ee Product of **A1** catalyzed reaction



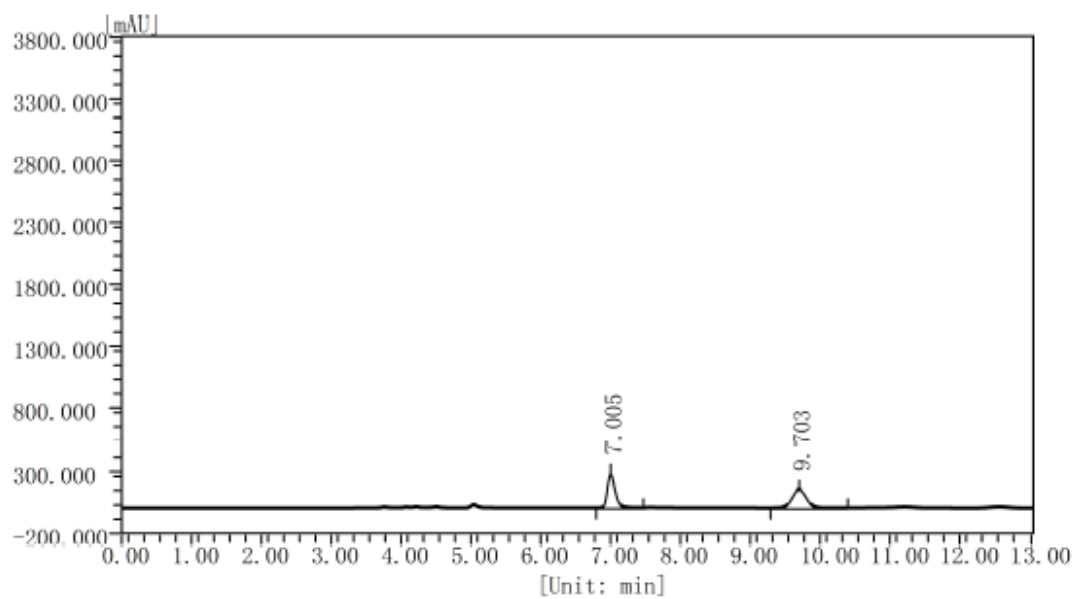
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	9.455	0.288	17829.8	355231.9	2.5345	BB
2	14.789	0.260	812505.5	13660902.1	97.4656	BB
总计:			830335.3	14016134.0	100.0000	

(+)-**4b**, 92.9% ee Product of A**5** catalyzed reaction



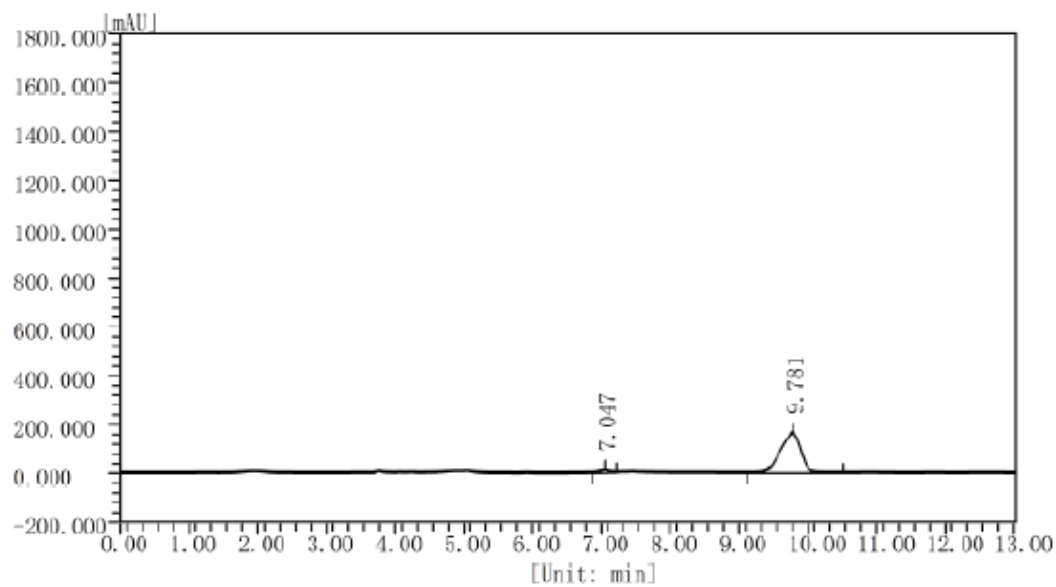
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	9.492	0.300	307957.9	5853624.6	96.4847	BB
2	14.850	0.260	12856.1	213268.4	3.5153	BB
总计:			320814.0	6066893.0	100.0000	

### Racemic **4c**



峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	7.005	0.118	278827.9	2206853.0	50.1382	BB
2	9.703	0.229	149827.4	2194691.2	49.8618	BB
总计:			428655.3	4401544.2	100.0000	

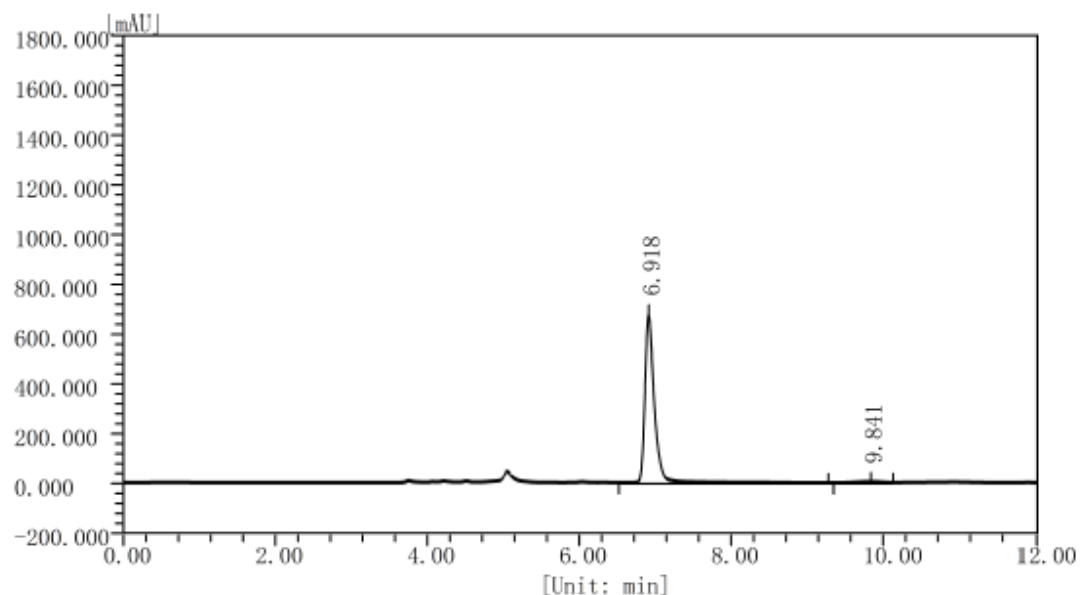
### (-)-**4c**, 93.8% ee Product of **A1** catalyzed reaction





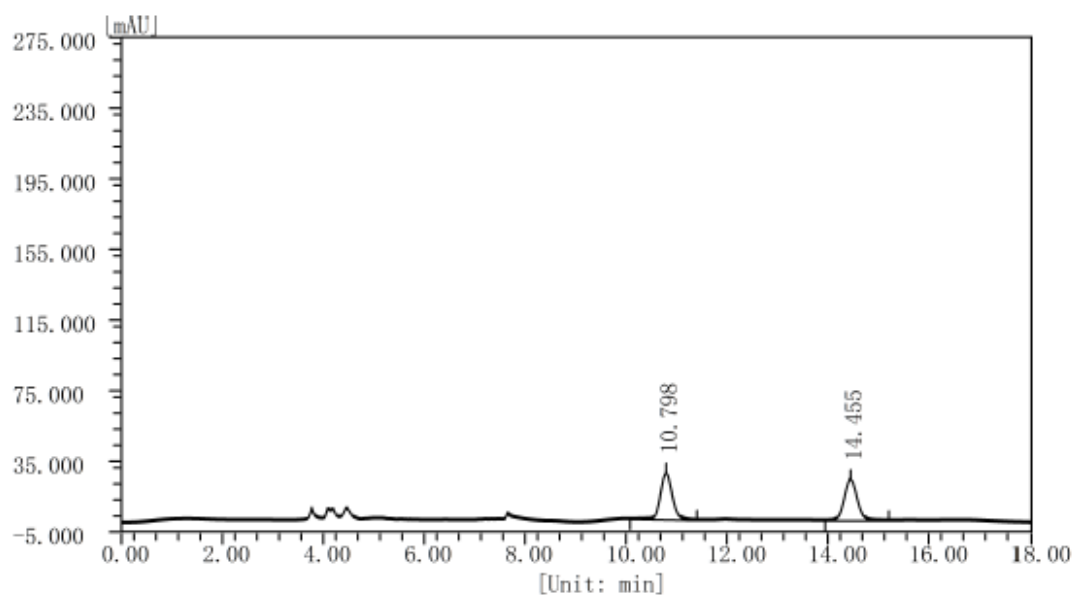
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	7.047	0.157	11592.8	111655.7	3.0887	BB
2	9.781	0.342	163957.9	3503305.7	96.9113	BB
总计:			175550.7	3614961.3	100.0000	

(+)-**4c**, 97.3% ee Product of **A5** catalyzed reaction



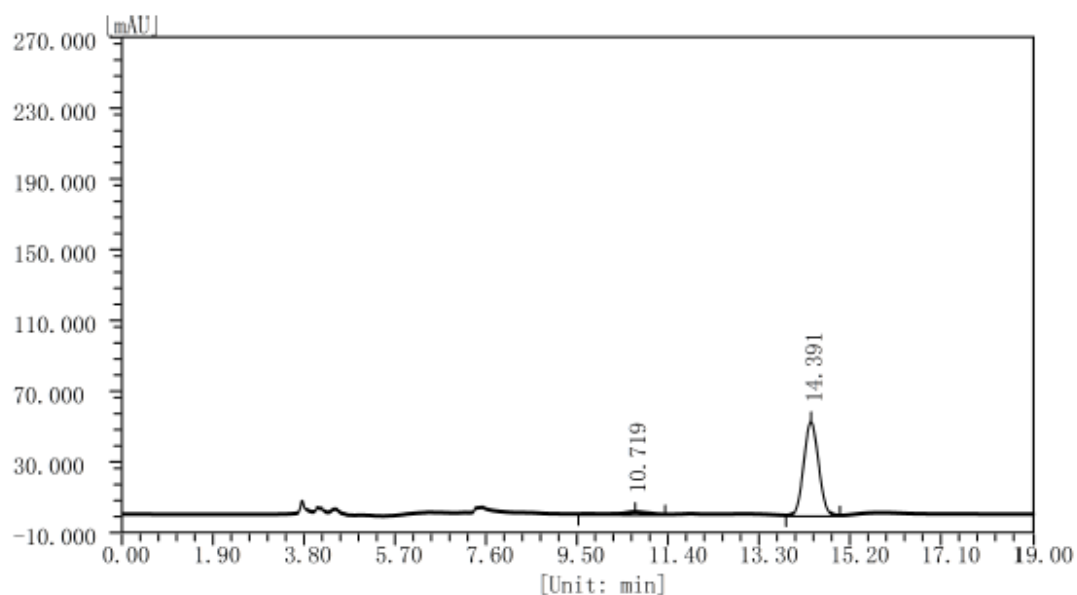
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	6.918	0.122	678063.9	5938698.1	98.6376	BB
2	9.841	0.326	3951.0	82025.8	1.3624	BB
总计:			682014.9	6020723.9	100.0000	

### Racemic **4d**



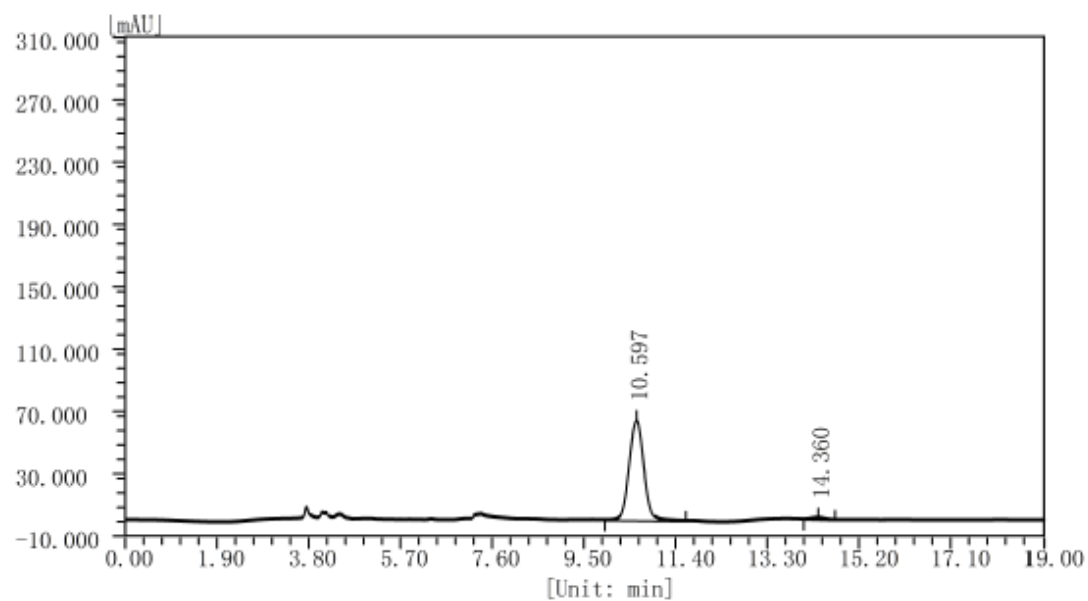
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	10.798	0.247	26411.6	431477.1	50.7848	BB
2	14.455	0.277	23206.3	418141.5	49.2152	BB
总计:			49617.9	849618.5	100.0000	

### (-)-**4d**, 93.5% ee Product of **A1** catalyzed reaction

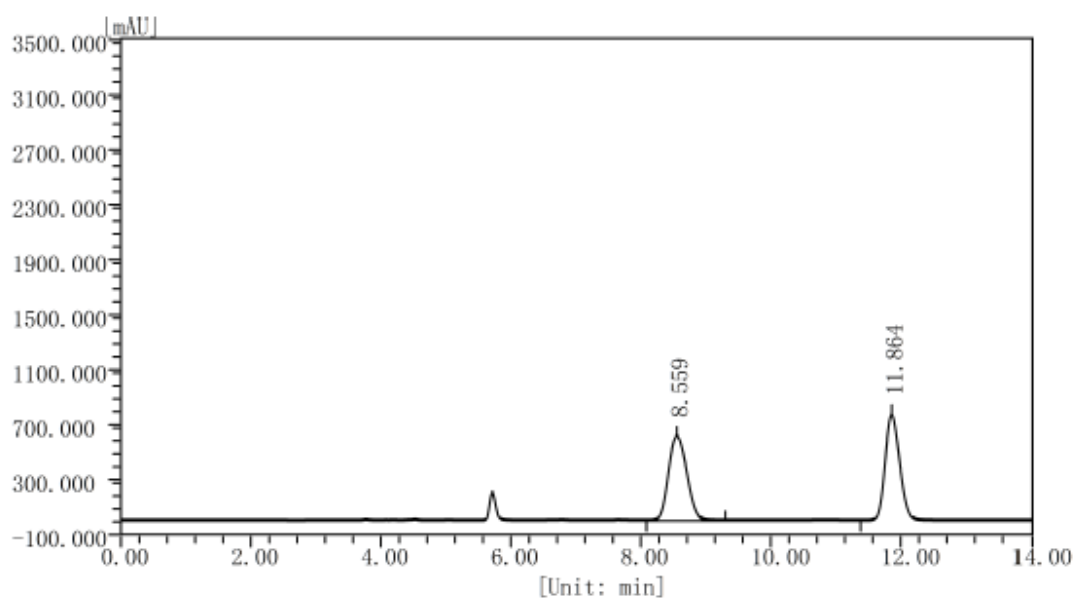


峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	10.719	0.452	1273.6	38792.7	3.2505	BB
2	14.391	0.340	53250.9	1154655.8	96.7495	BB
总计:			54524.5	1193448.5	100.0000	

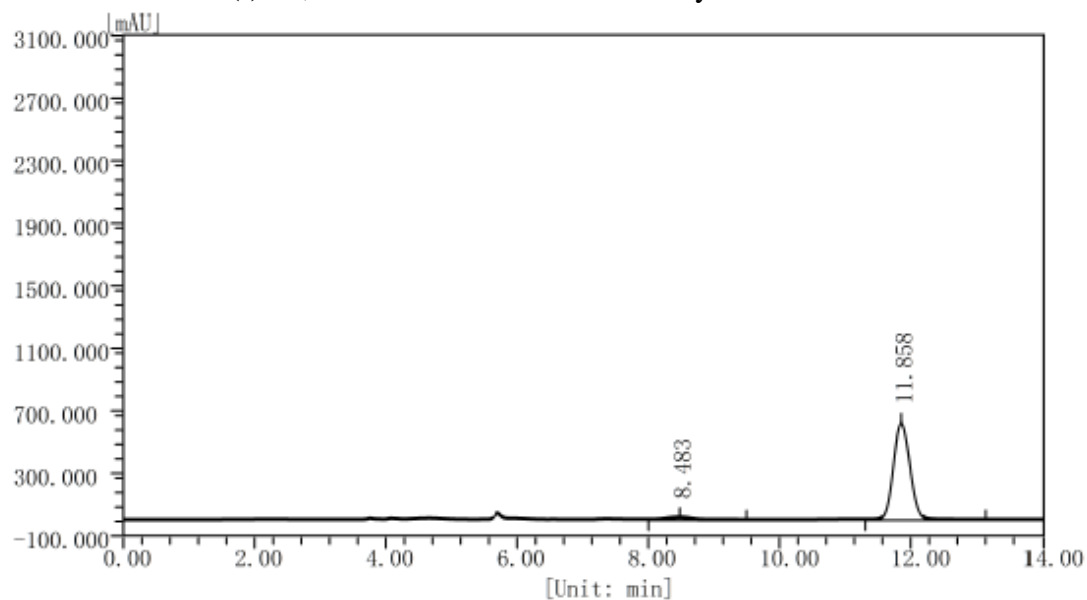
(+)-**4d**, 97.1% ee Product of **A5** catalyzed reaction



峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	10.597	0.327	64299.9	1366633.3	98.5898	BB
2	14.360	0.289	1114.4	19548.3	1.4102	BB
总计:			65414.3	1386181.6	100.0000	

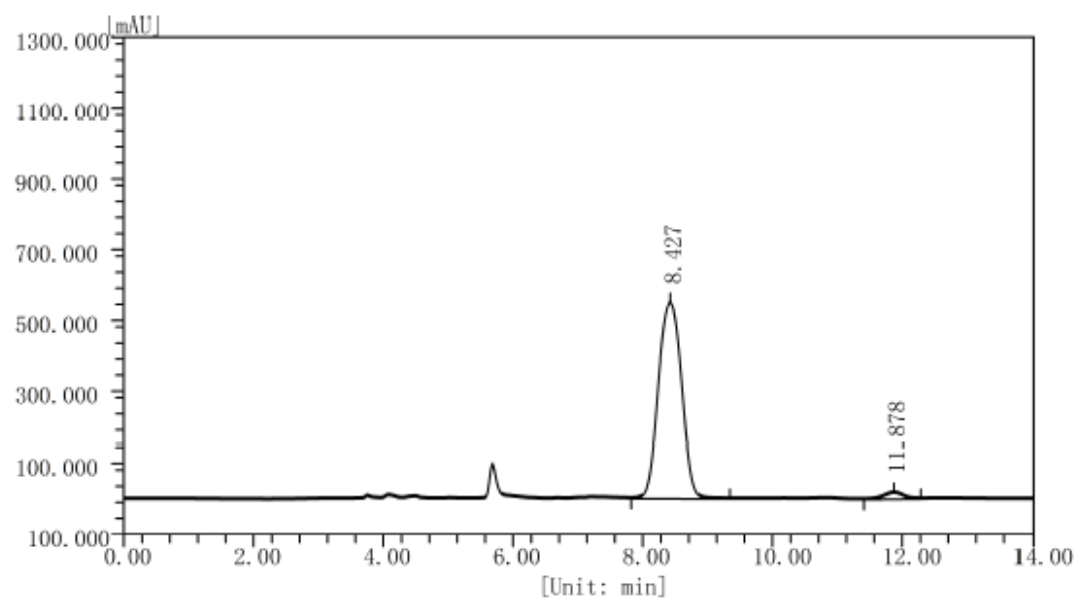
Racemic **4e**

峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	8.559	0.314	614311.3	12111650.4	50.0224	BB
2	11.864	0.242	773131.2	12100803.2	49.9776	BB
总计:			1387442.5	24212453.6	100.0000	

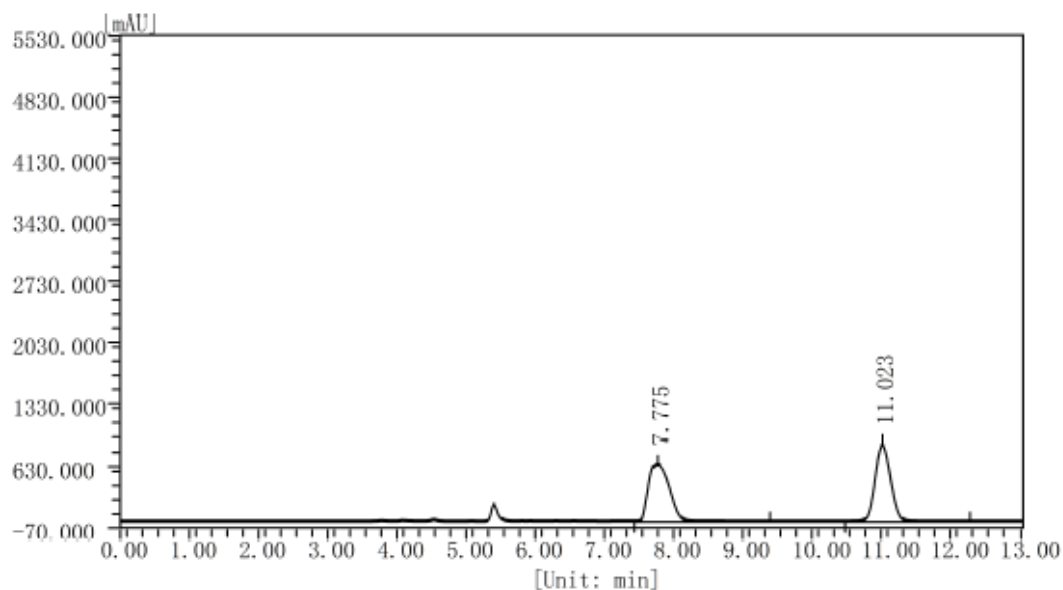
(-)-**4e**, 93.9% ee Product of A1 catalyzed reaction

峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	8.483	0.400	13729.7	338025.5	3.0201	BB
2	11.858	0.275	617450.1	10854403.4	96.9799	BB
总计:			631179.8	11192428.9	100.0000	

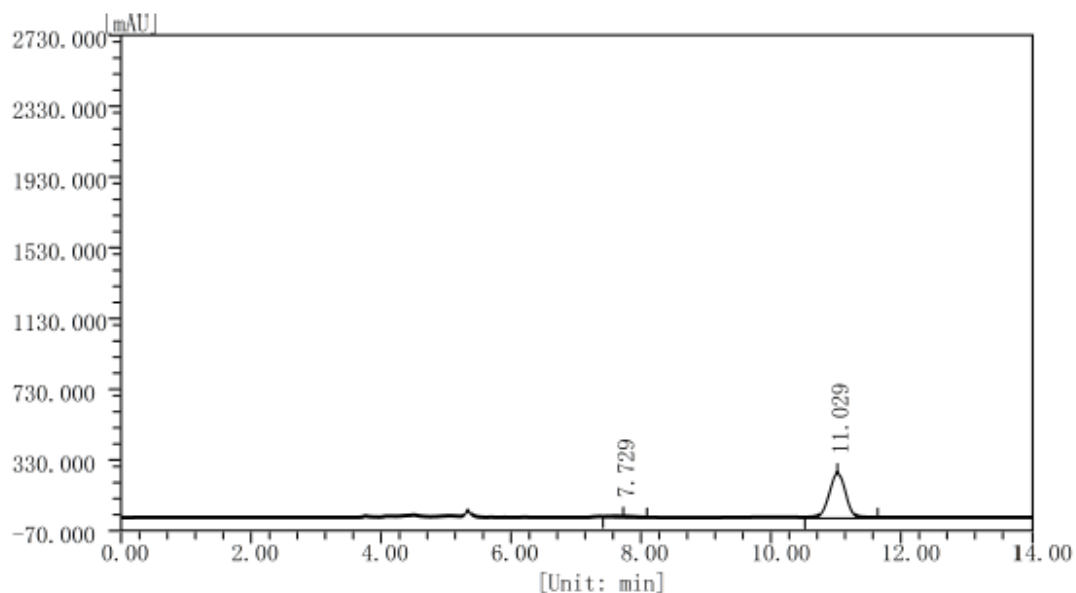
(+)-**4e**, 95.1% ee Product of A**5** catalyzed reaction



峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	8.427	0.401	547903.0	13590208.7	97.5359	BB
2	11.878	0.306	17645.2	343333.7	2.4641	BB
总计:			565548.2	13933542.5	100.0000	

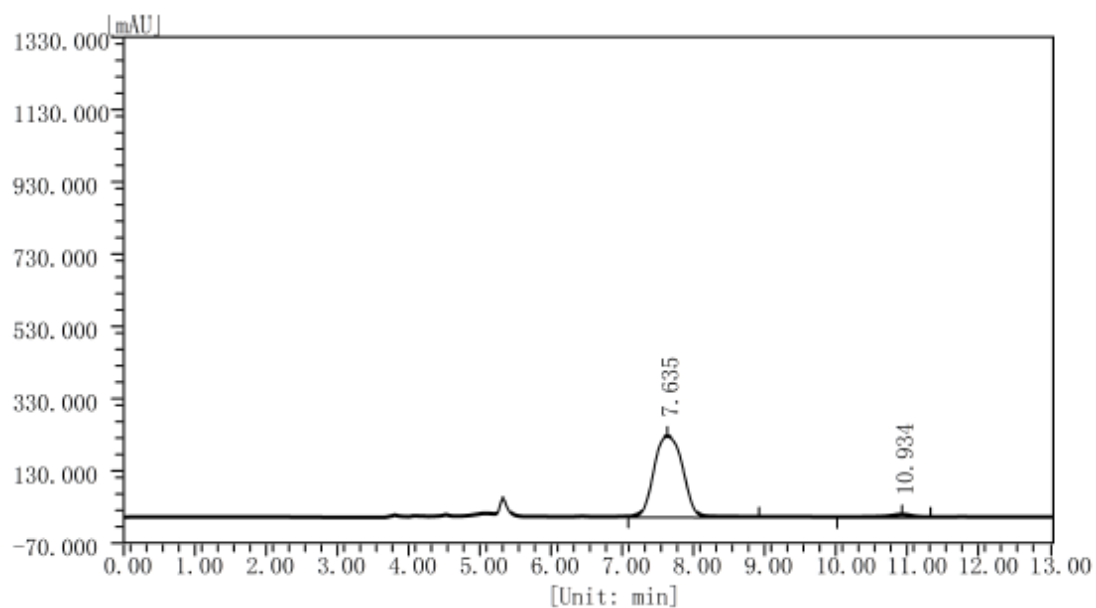
Racemic **4f**

峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	7.775	0.349	646034.5	13804638.1	50.2721	BB
2	11.023	0.246	865686.8	13655208.4	49.7279	BB
总计:			1511721.2	27459847.4	100.0000	

(-)-**4f**, 96.7% ee Product of **A1** catalyzed reaction

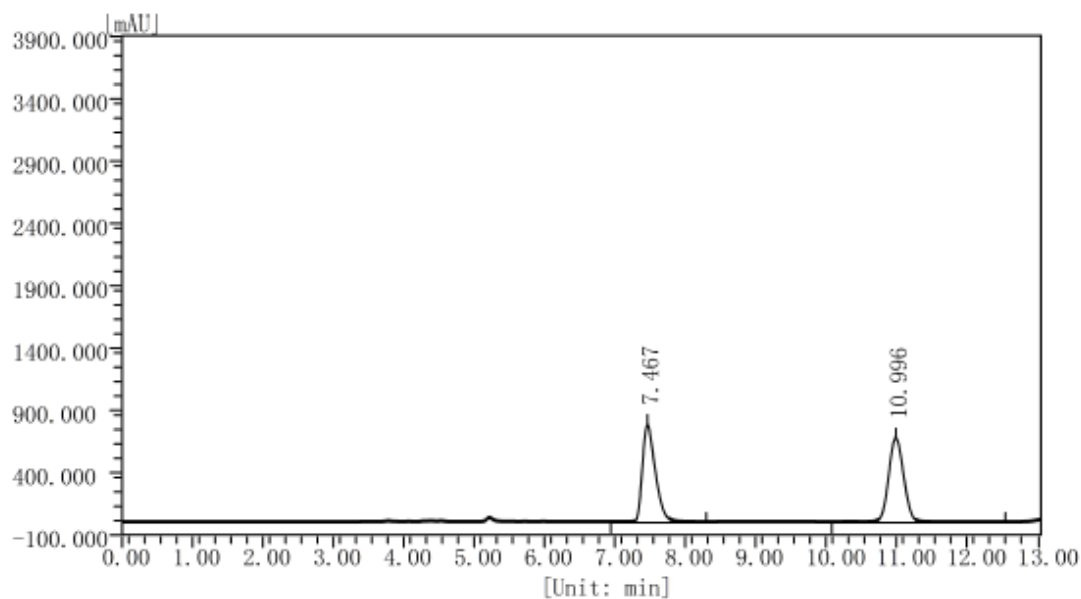
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	7.729	0.440	3189.3	76072.1	1.6777	BB
2	11.029	0.278	252005.6	4458320.6	98.3223	BB
总计:			255194.9	4534392.7	100.0000	

(+)-**4f**, 95.7% ee Product of A**5** catalyzed reaction



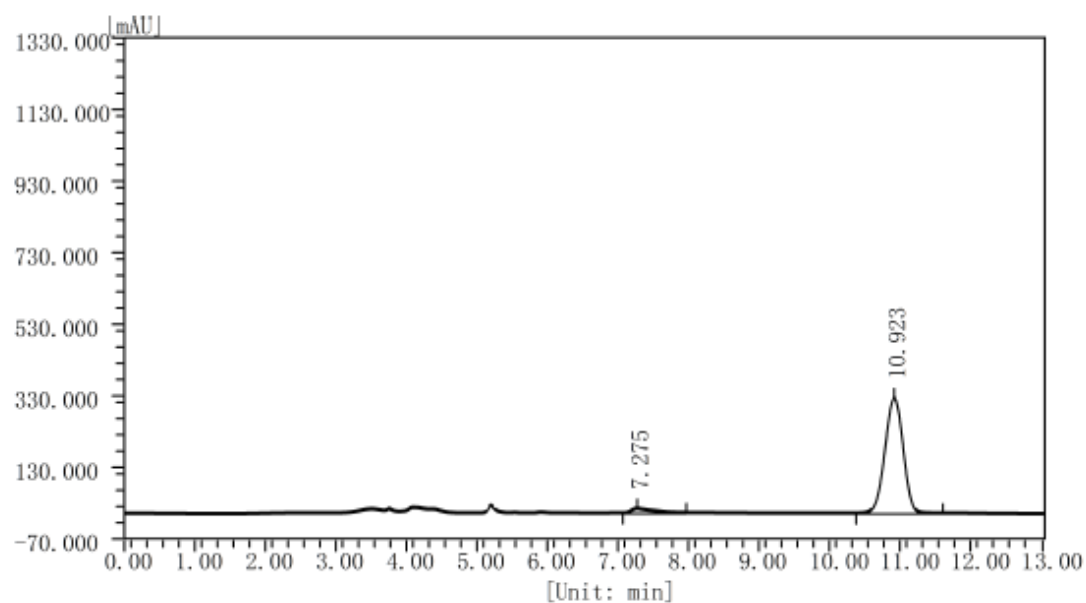
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	7.635	0.459	222305.3	6258674.0	97.8645	BB
2	10.934	0.293	6742.8	136567.4	2.1355	BB
总计:			229048.0	6395241.4	100.0000	

### Racemic **4g**



峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	7.467	0.197	785504.6	10093811.6	49.8827	BB
2	10.996	0.233	676696.3	10141270.8	50.1173	SVB
总计:			1462200.9	20235082.4	100.0000	

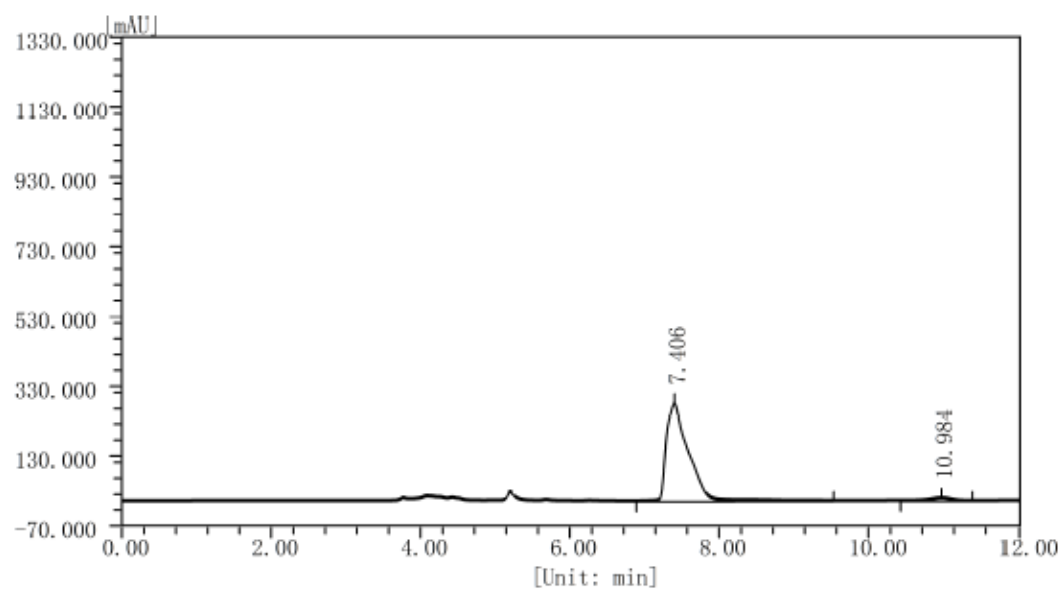
### (-)-**4g**, 89.9% ee Product of **A1** catalyzed reaction



峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	7.275	0.320	12248.2	243376.5	4.0072	BB
2	10.923	0.284	322251.2	5830144.5	95.9928	BB
总计:			334499.3	6073521.0	100.0000	

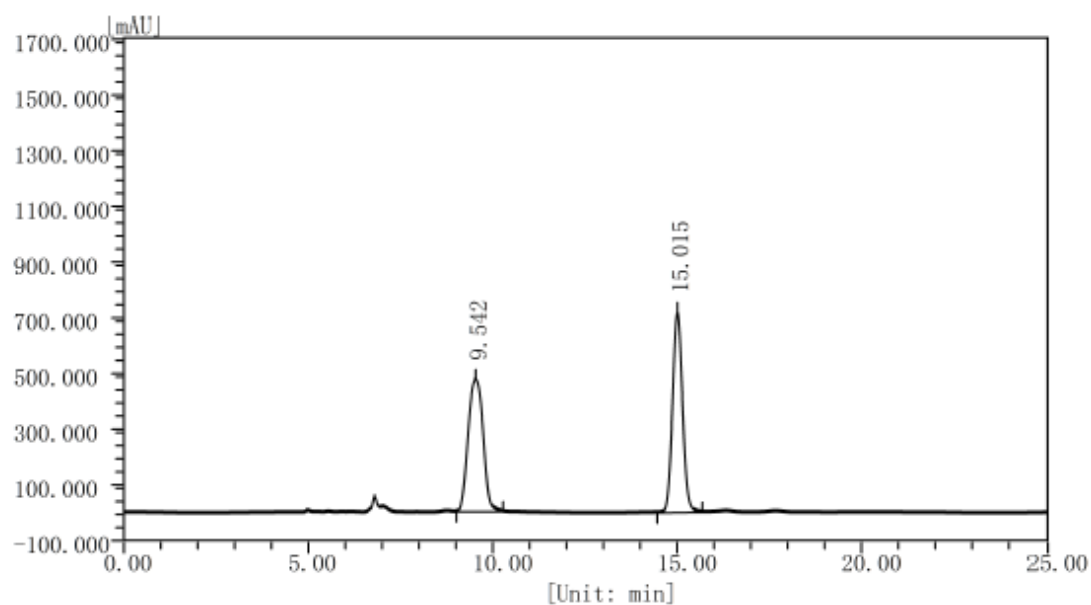


(+)-**4g**, 94.9% ee Product of **A5** catalyzed reaction



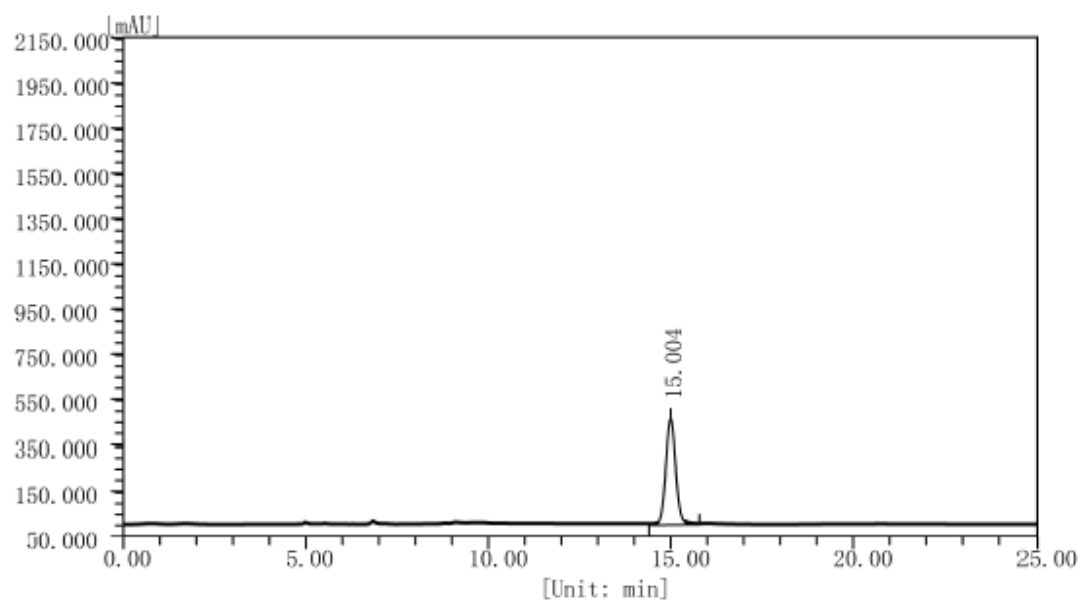
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	7.406	0.315	280375.9	5722805.8	97.4247	BB
2	10.984	0.291	8002.5	151273.5	2.5753	BB
总计:			288378.4	5874079.3	100.0000	

### Racemic **4h**



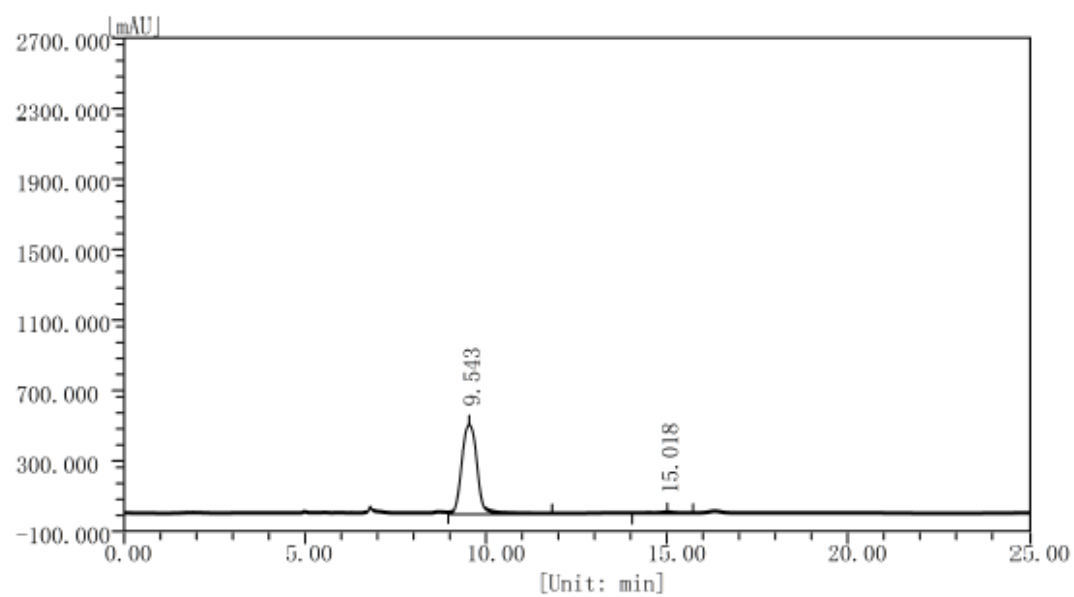
峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	9.542	0.460	473830.8	13431670.5	49.6782	BB
2	15.015	0.292	718649.0	13605682.1	50.3218	BB
总计:			1192479.7	27037353.5	100.0000	

### (-)-**4h**, >99% ee Product of **A1** catalyzed reaction

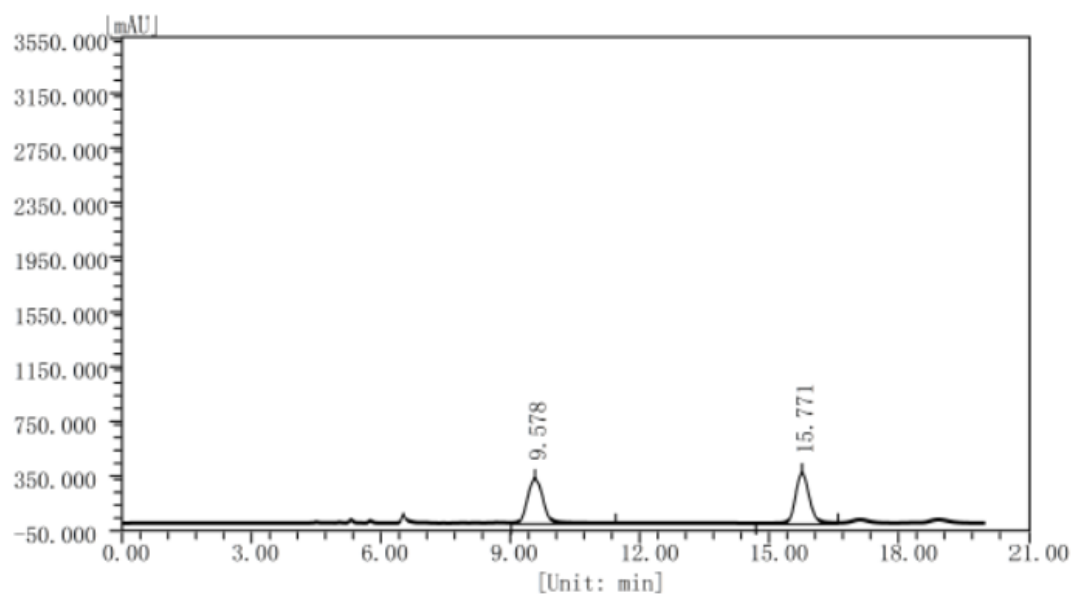


峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	15.004	0.292	461302.5	8795988.5	100.0000	SVB
总计:			461302.5	8795988.5	100.0000	

(+)-**4h**, 98.7% ee Product of **A5** catalyzed reaction

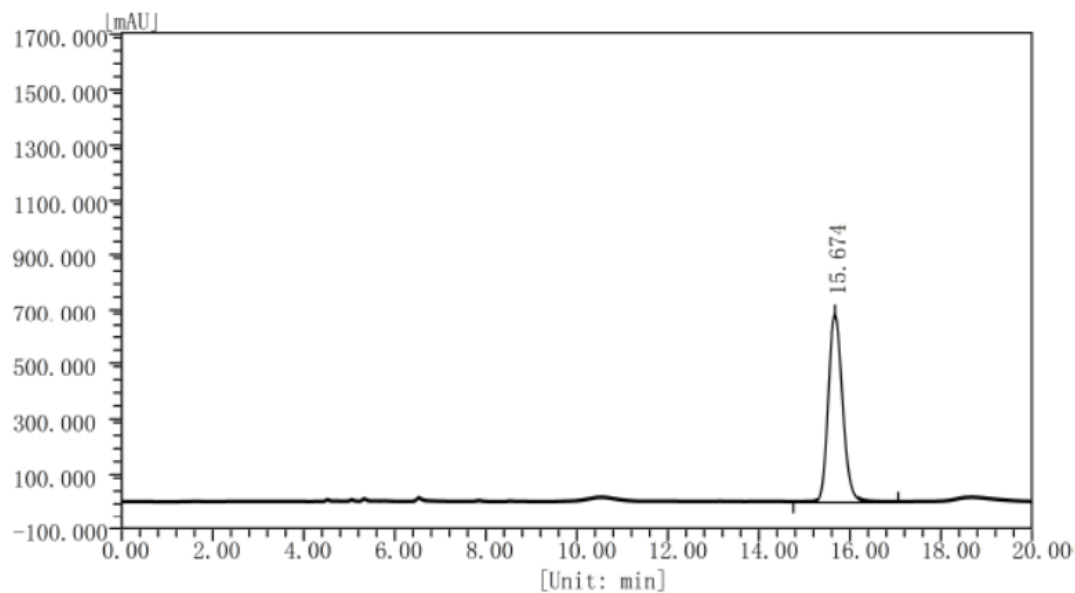


峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	9.543	0.464	504398.9	14765972.9	99.3453	VB
2	15.018	0.288	4511.9	97307.7	0.6547	VV
总计:			508910.8	14863280.6	100.0000	

Racemic **4i**

峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	9.578	0.397	323321.5	8287348.0	50.0657	VB
2	15.771	0.343	369752.7	8265584.1	49.9343	BV
总计:			693074.1	16552932.1	100.0000	

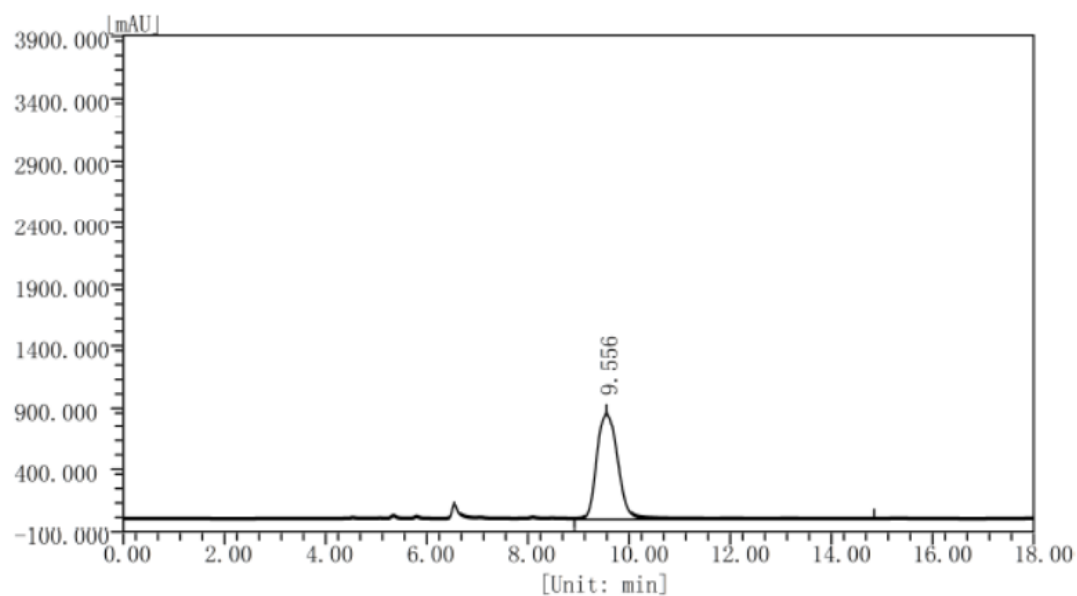
(-)-**4i**, >99% ee Product of **A1** catalyzed reaction



峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	15.674	0.337	682176.9	14918290.1	100.0000	BB
总计:			682176.9	14918290.1	100.0000	

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(+)-**4i**, >99% ee Product of A**5** catalyzed reaction

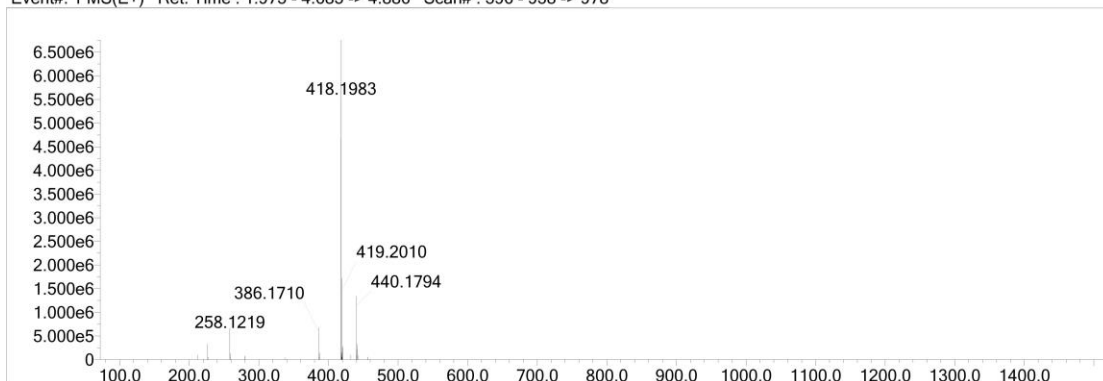


峰序	保留时间 [min]	半峰宽 [min]	峰高 [uV]	峰面积 [uV*s]	峰面积 [%]	峰类型
1	9.556	0.455	847464.3	24414127.8	100.0000	SBB
总计:			847464.3	24414127.8	100.0000	

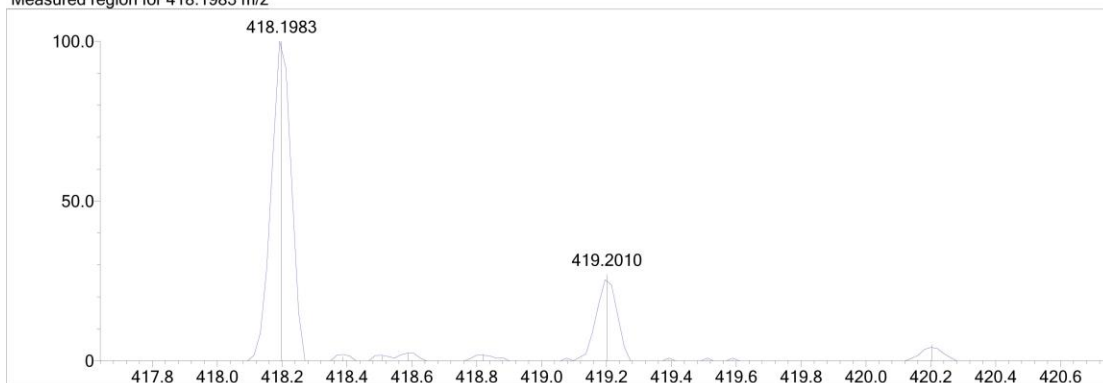
## 6. Mass spectra

### HR-MS of **4a**

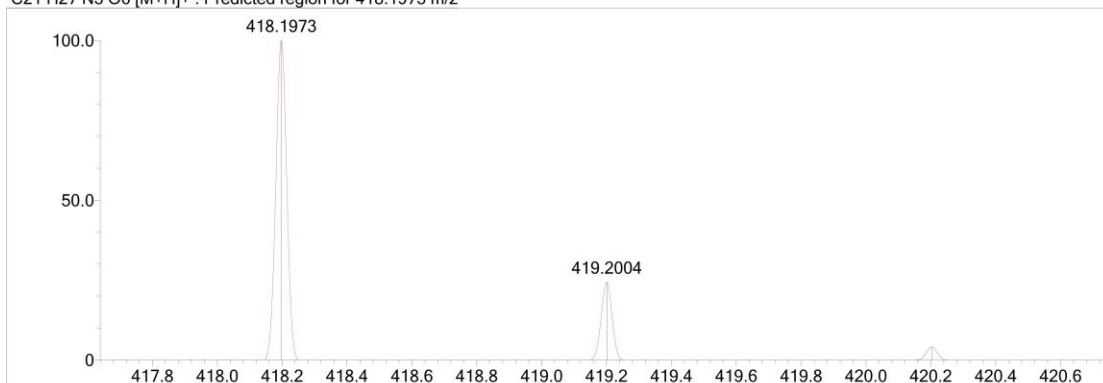
Event#: 1 MS(E+) Ret. Time : 1.975 - 4.685 -> 4.886 Scan#: 396 - 938 -> 978



Measured region for 418.1983 m/z



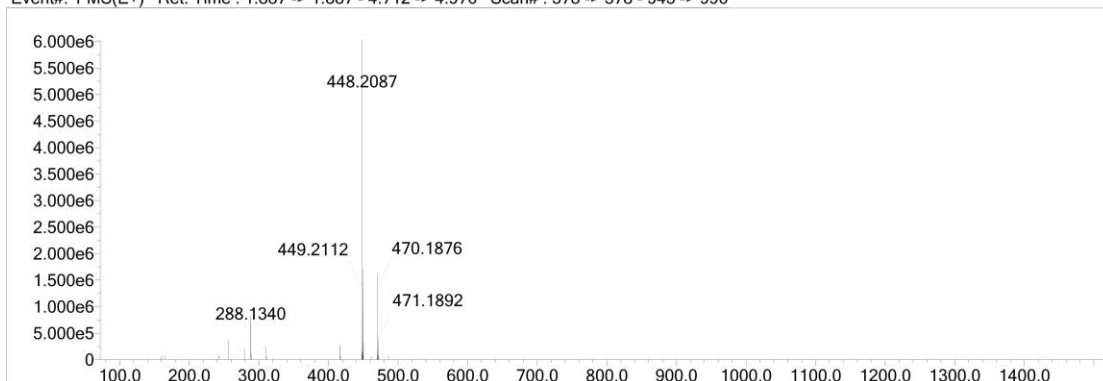
C21 H27 N3 O6 [M+H]<sup>+</sup> : Predicted region for 418.1973 m/z



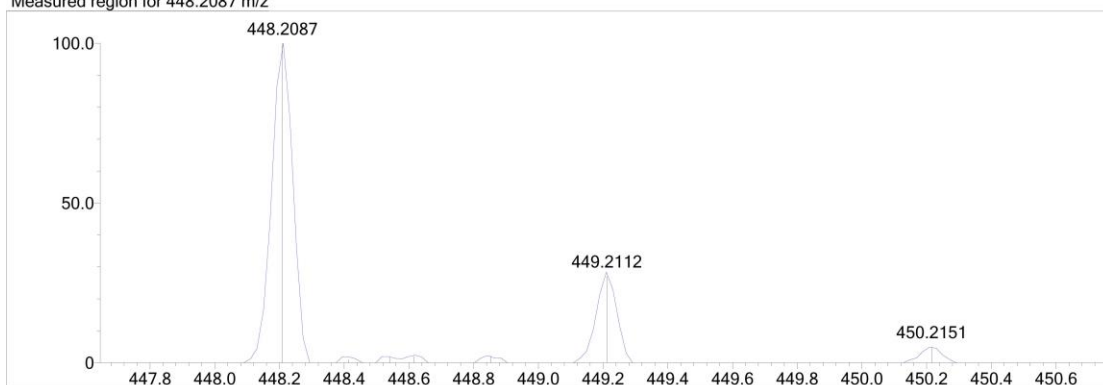
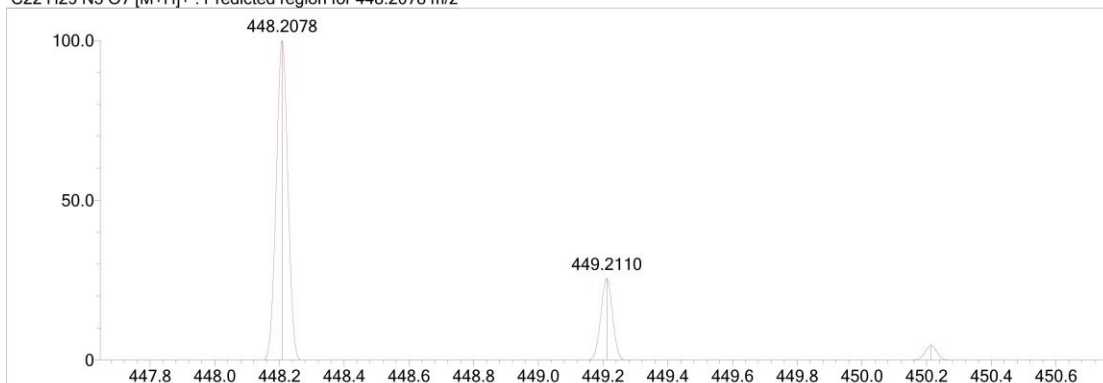
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	81.61	C21 H27 N3 O6	[M+H] <sup>+</sup>	418.1983	418.1973	1.0	2.39	84.55	10.0

HR-MS of **4b**

Event#: 1 MS(E+) Ret. Time : 1.887 -&gt; 1.887 -&gt; 4.712 -&gt; 4.976 Scan#: 378 -&gt; 378 - 943 -&gt; 996



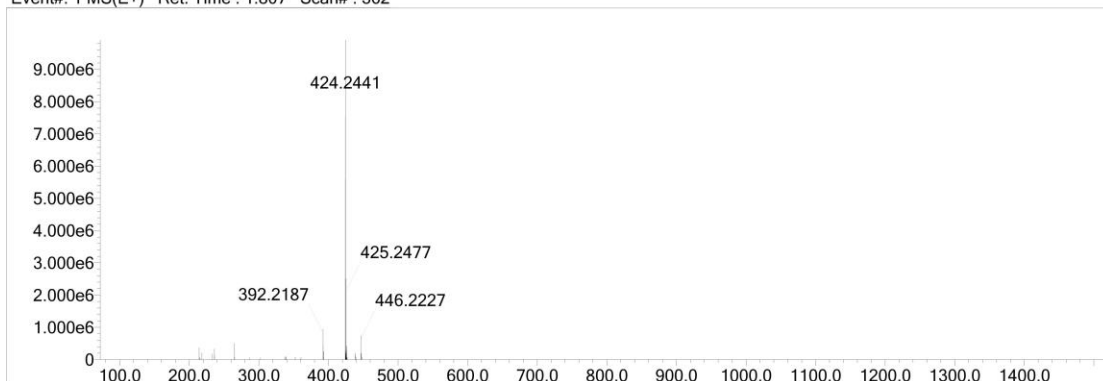
Measured region for 448.2087 m/z

C22 H29 N3 O7 [M+H]<sup>+</sup> : Predicted region for 448.2078 m/z

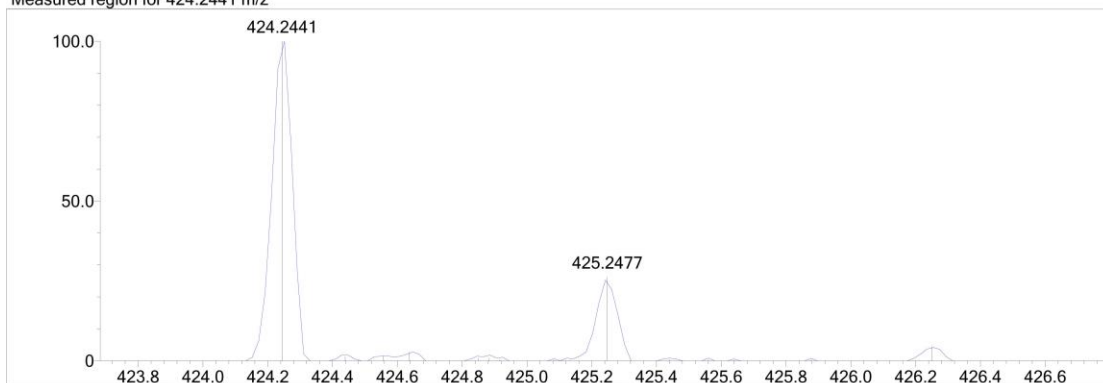
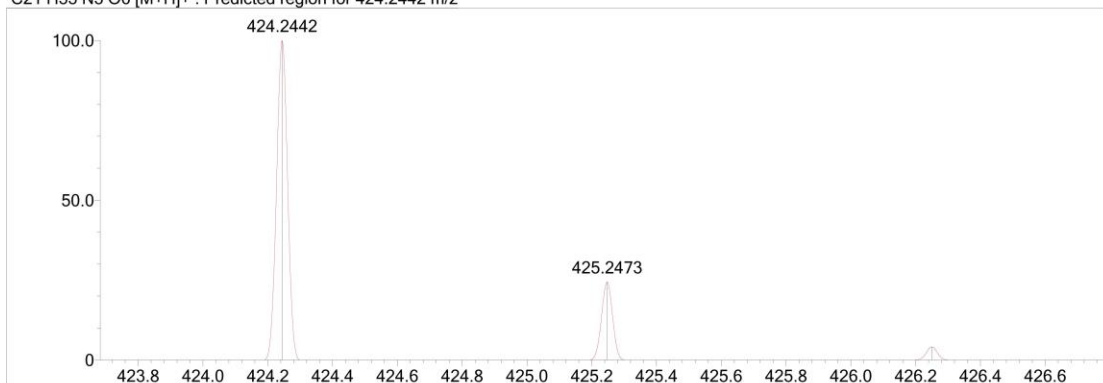
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
2	80.87	C22 H29 N3 O7	[M+H] <sup>+</sup>	448.2087	448.2078	0.9	2.01	82.97	10.0

HR-MS of **4c**

Event#: 1 MS(E+) Ret. Time : 1.807 Scan#: 362



Measured region for 424.2441 m/z

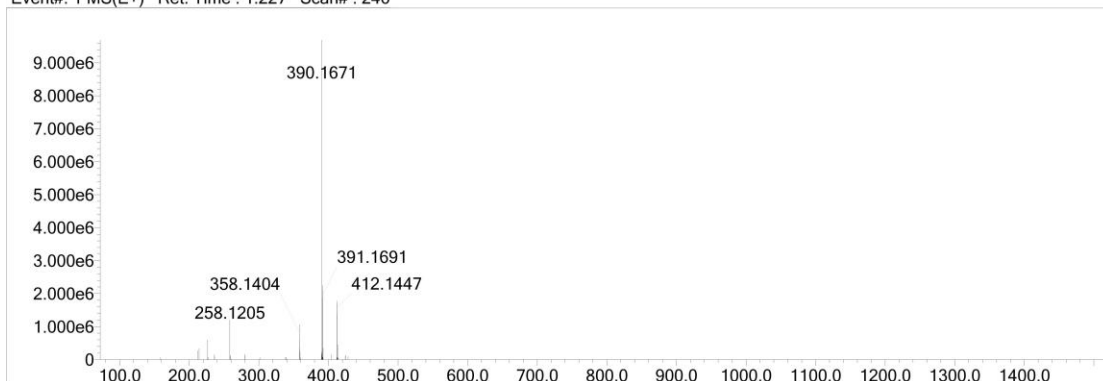
C21 H33 N3 O6 [M+H]<sup>+</sup> : Predicted region for 424.2442 m/z

Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	94.01	C21 H33 N3 O6	[M+H] <sup>+</sup>	424.2441	424.2442	-0.1	-0.24	94.01	7.0

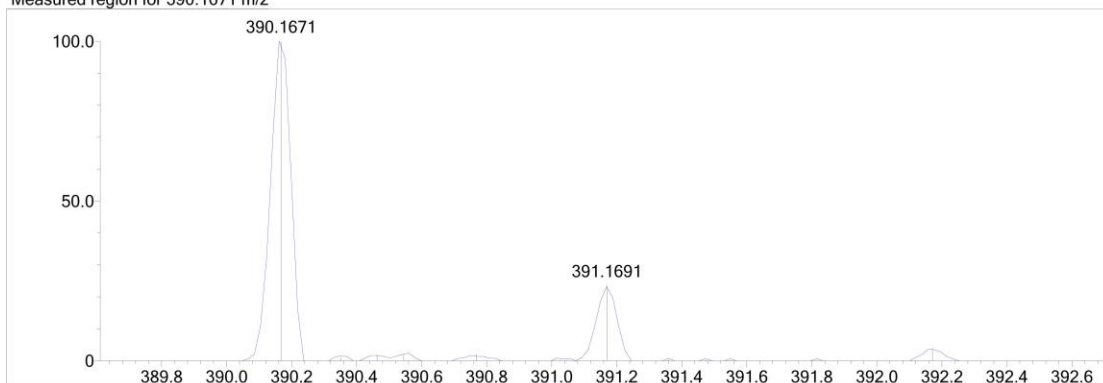
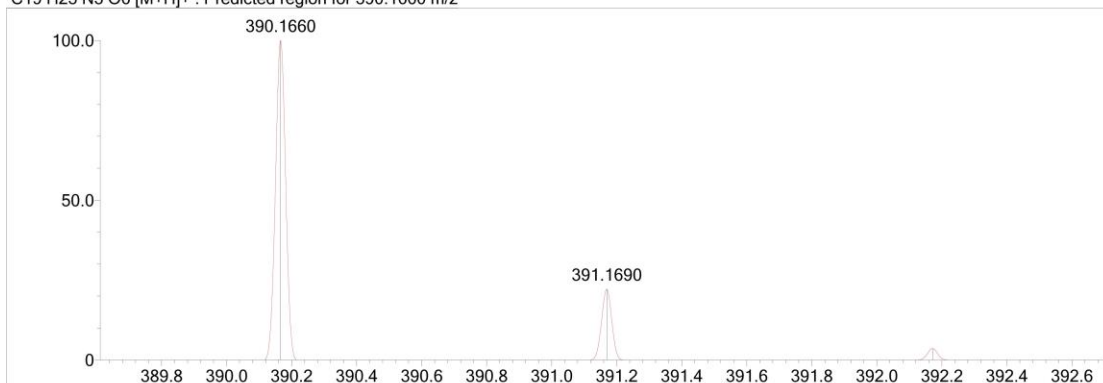


HR-MS of **4d**

Event#: 1 MS(E+) Ret. Time : 1.227 Scan#: 246



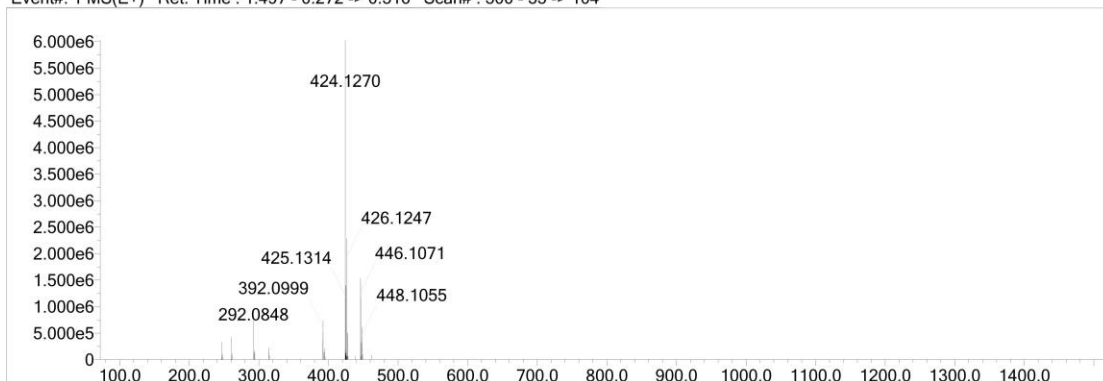
Measured region for 390.1671 m/z

C19 H23 N3 O6 [M+H]<sup>+</sup> : Predicted region for 390.1660 m/z

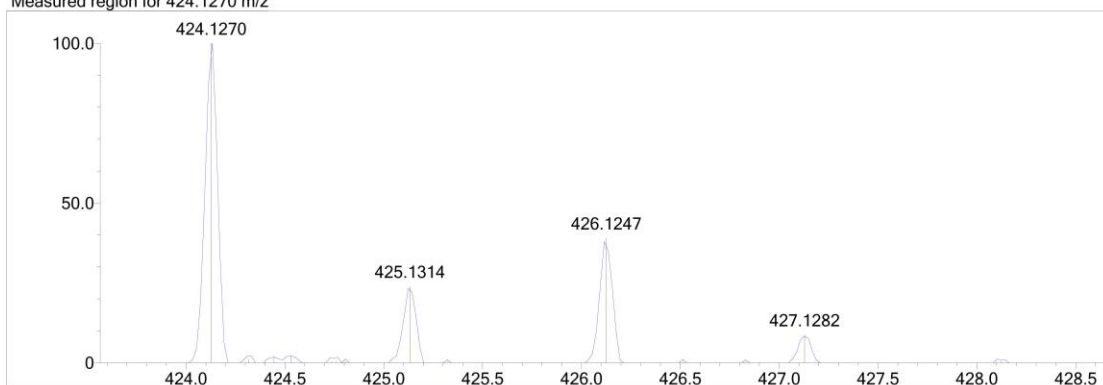
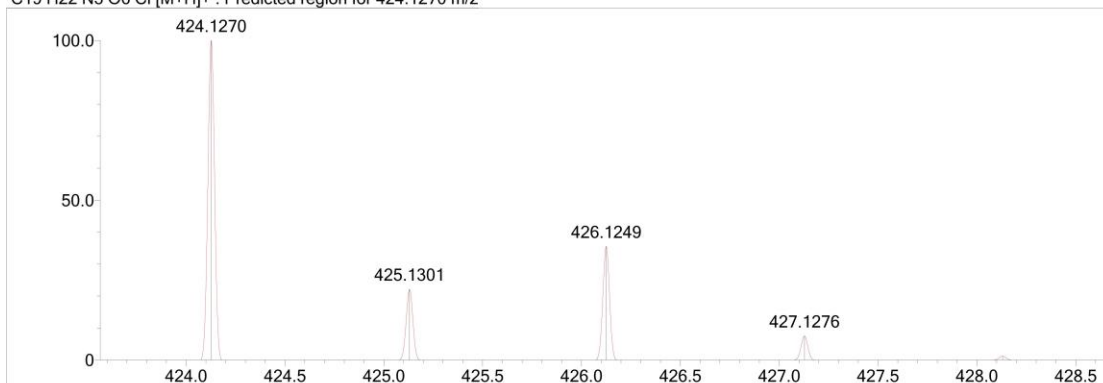
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	88.40	C19 H23 N3 O6	[M+H] <sup>+</sup>	390.1671	390.1660	1.1	2.82	92.61	10.0

HR-MS of **4e**

Event#: 1 MS(E+) Ret. Time : 1.497 - 0.272 -&gt; 0.516 Scan#: 300 - 55 -&gt; 104



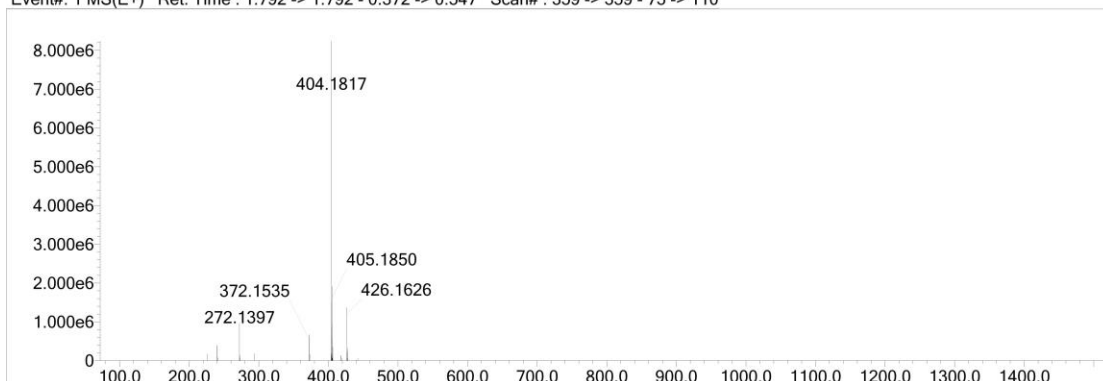
Measured region for 424.1270 m/z

C19 H22 N3 O6 Cl [M+H]<sup>+</sup> : Predicted region for 424.1270 m/z

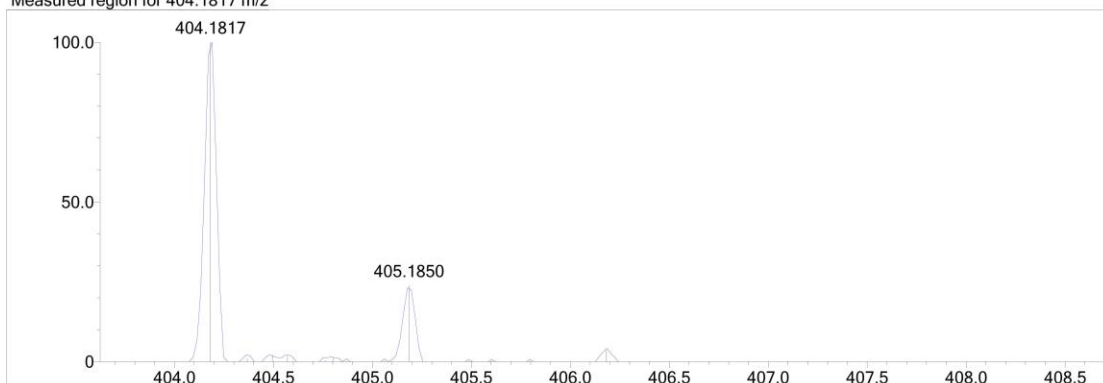
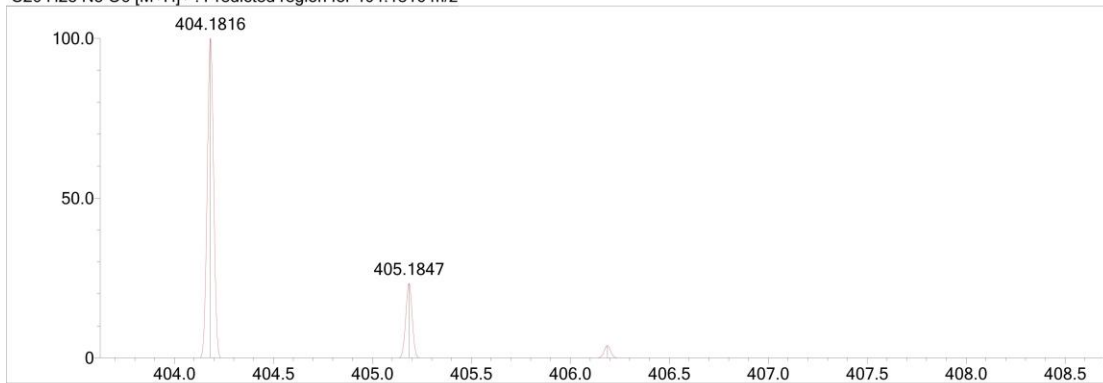
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	73.01	C19 H22 N3 O6 Cl	[M+H] <sup>+</sup>	424.1270	424.1270	0.0	0.00	73.01	10.0

HR-MS of **4f**

Event#: 1 MS(E+) Ret. Time : 1.792 -&gt; 1.792 -&gt; 0.372 -&gt; 0.547 Scan#: 359 -&gt; 359 - 75 -&gt; 110



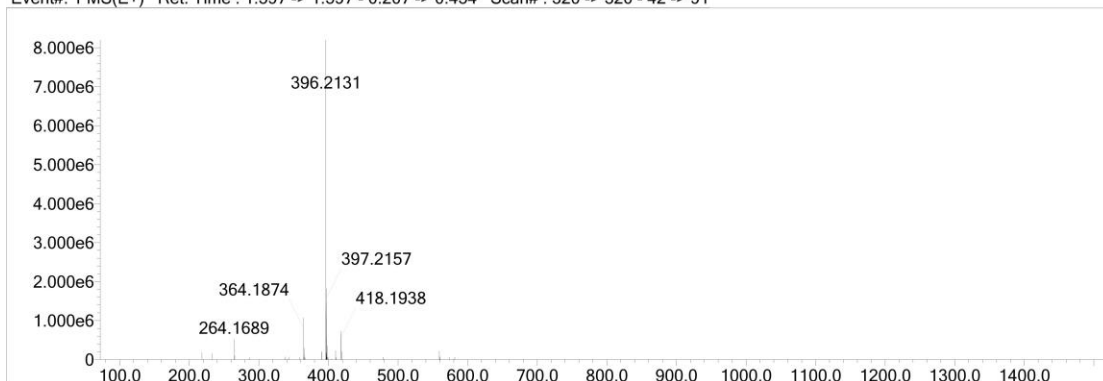
Measured region for 404.1817 m/z

C20 H25 N3 O6 [M+H]<sup>+</sup> : Predicted region for 404.1816 m/z

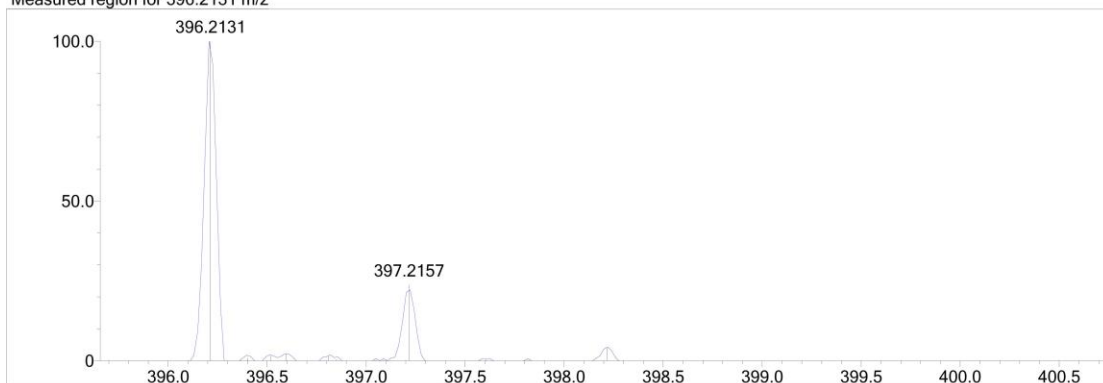
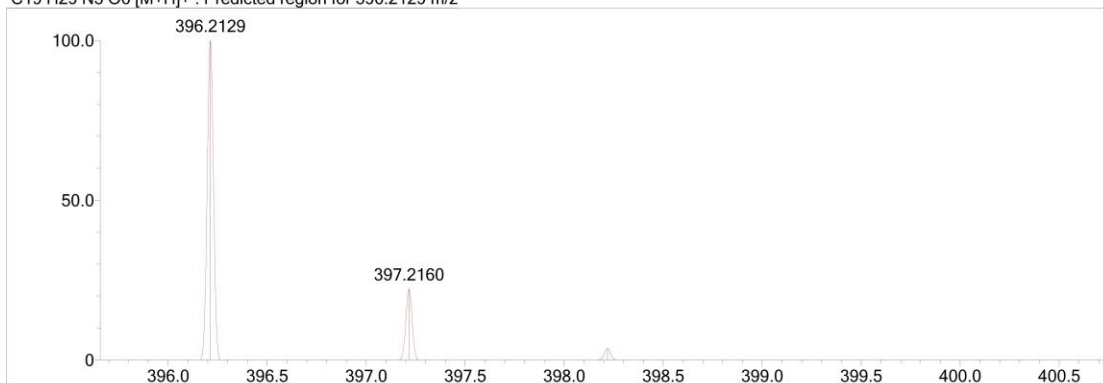
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	88.63	C20 H25 N3 O6	[M+H] <sup>+</sup>	404.1817	404.1816	0.1	0.25	88.63	10.0

HR-MS of **4g**

Event#: 1 MS(E+) Ret. Time : 1.597 -&gt; 1.597 - 0.207 -&gt; 0.454 Scan# : 320 -&gt; 320 - 42 -&gt; 91



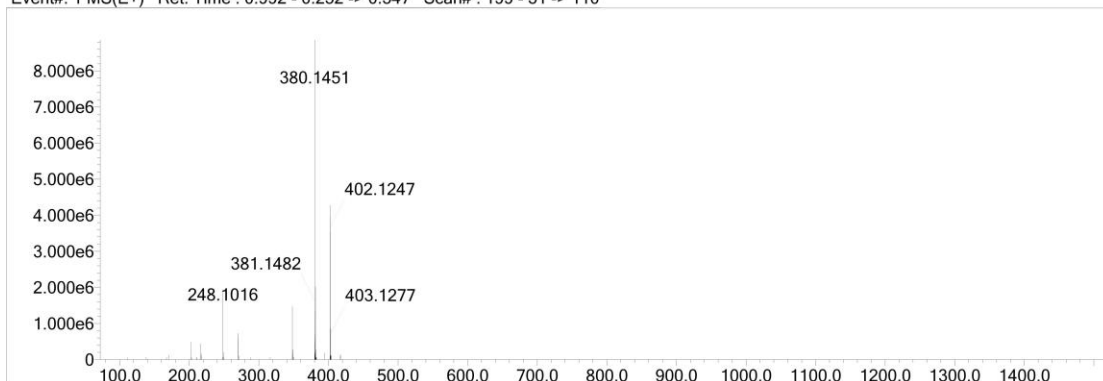
Measured region for 396.2131 m/z

C19 H29 N3 O6 [M+H]<sup>+</sup> : Predicted region for 396.2129 m/z

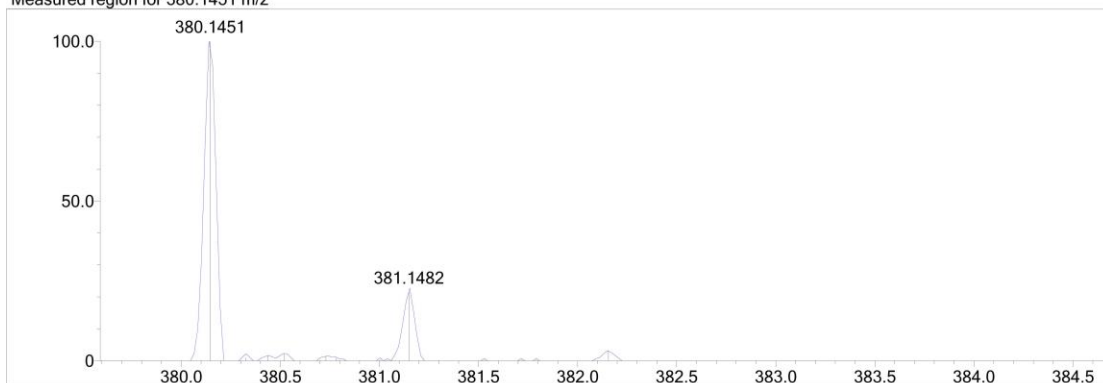
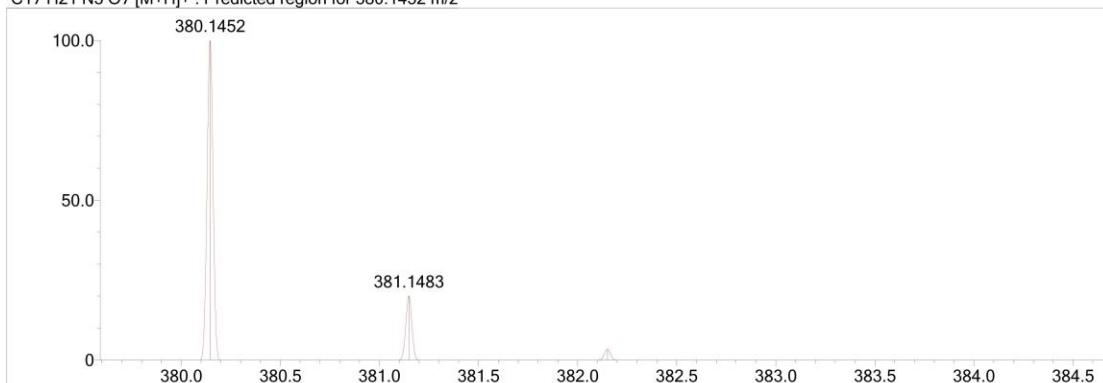
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	88.61	C19 H29 N3 O6	[M+H] <sup>+</sup>	396.2131	396.2129	0.2	0.50	88.61	7.0

HR-MS of **4h**

Event#: 1 MS(E+) Ret. Time : 0.992 - 0.252 -&gt; 0.547 Scan#: 199 - 51 -&gt; 110



Measured region for 380.1451 m/z

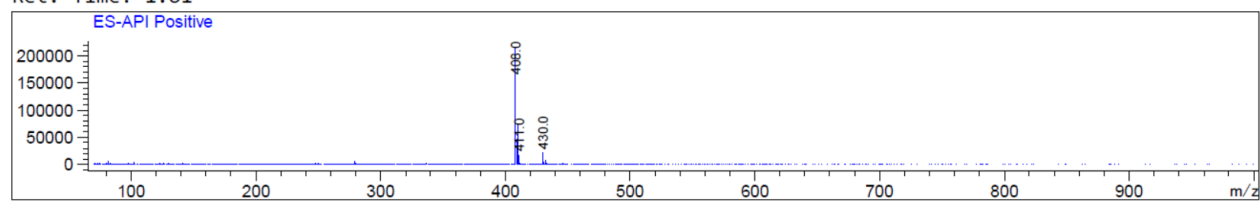
C17 H21 N3 O7 [M+H]<sup>+</sup> : Predicted region for 380.1452 m/z

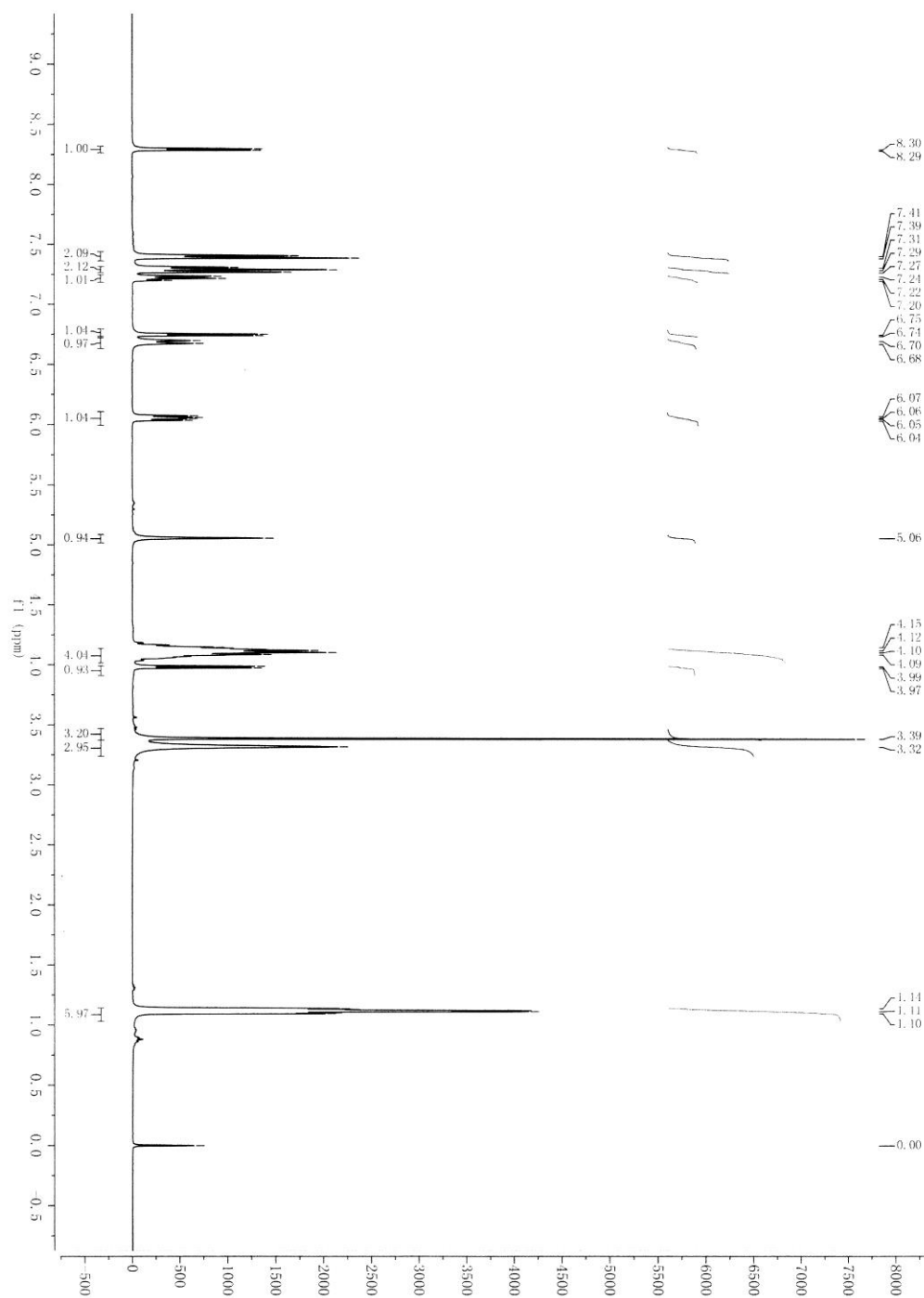
Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	83.91	C17 H21 N3 O7	[M+H] <sup>+</sup>	380.1451	380.1452	-0.1	-0.26	83.91	9.0

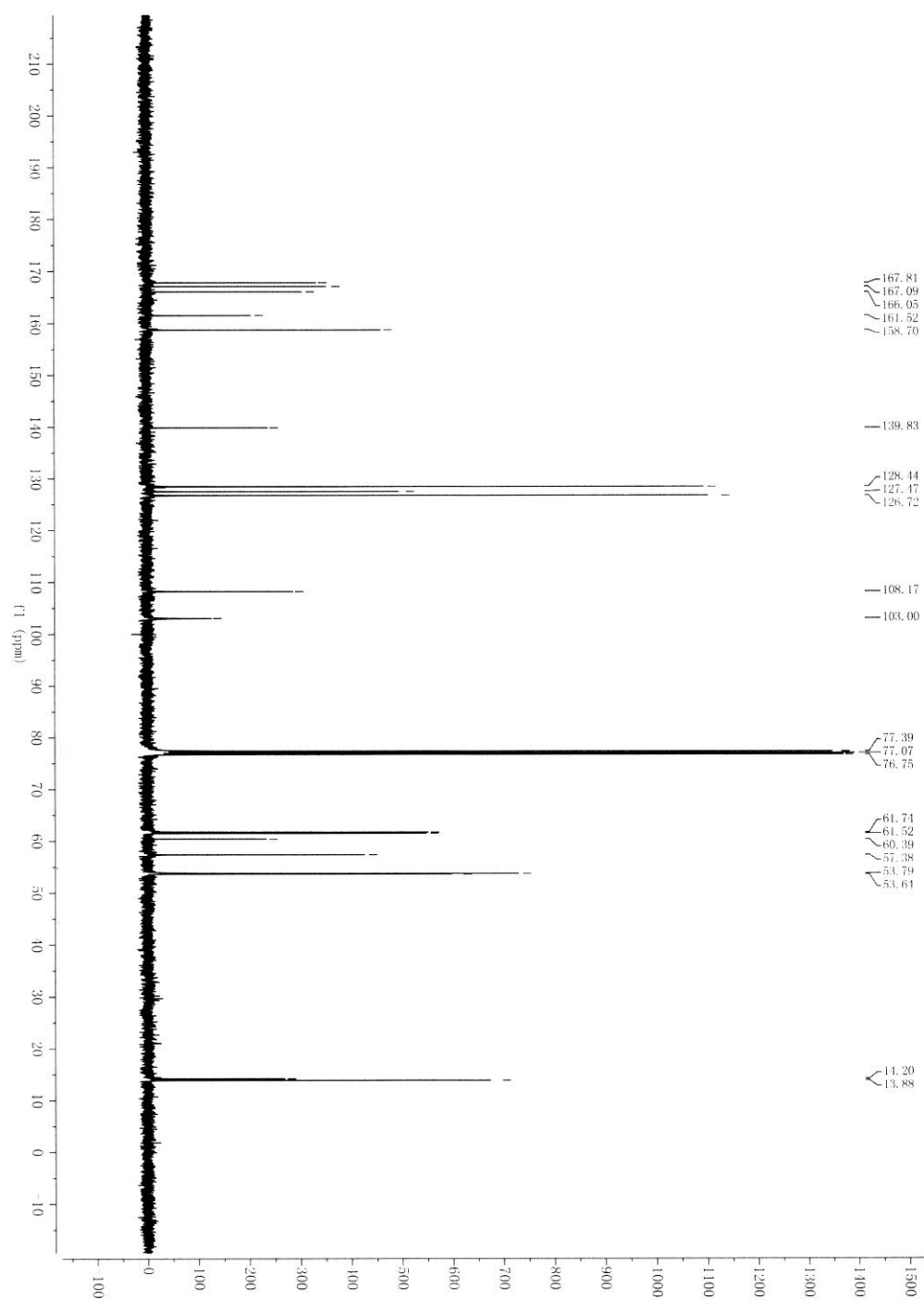
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**MS of 4i**

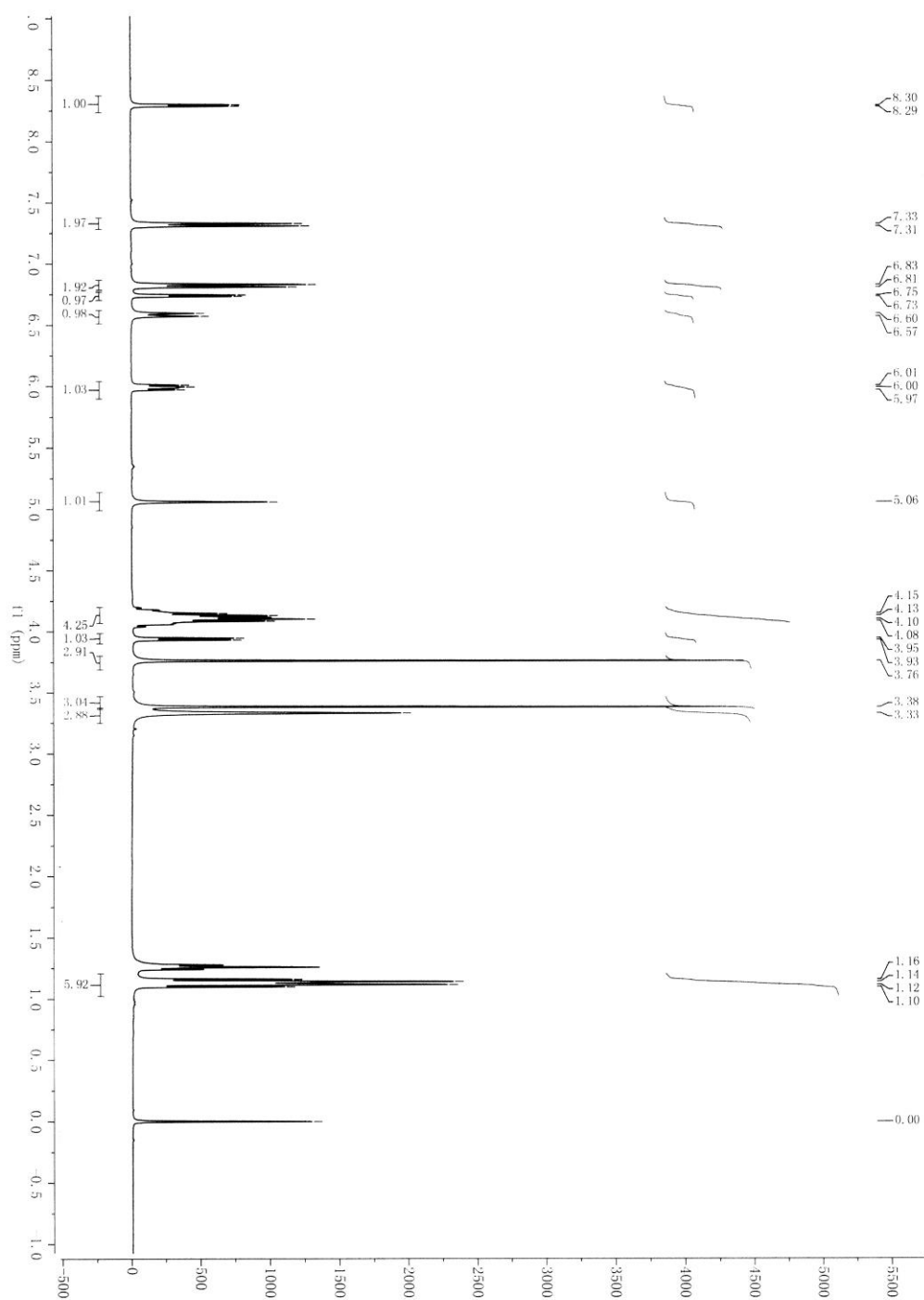
Ret. Time: 1.81

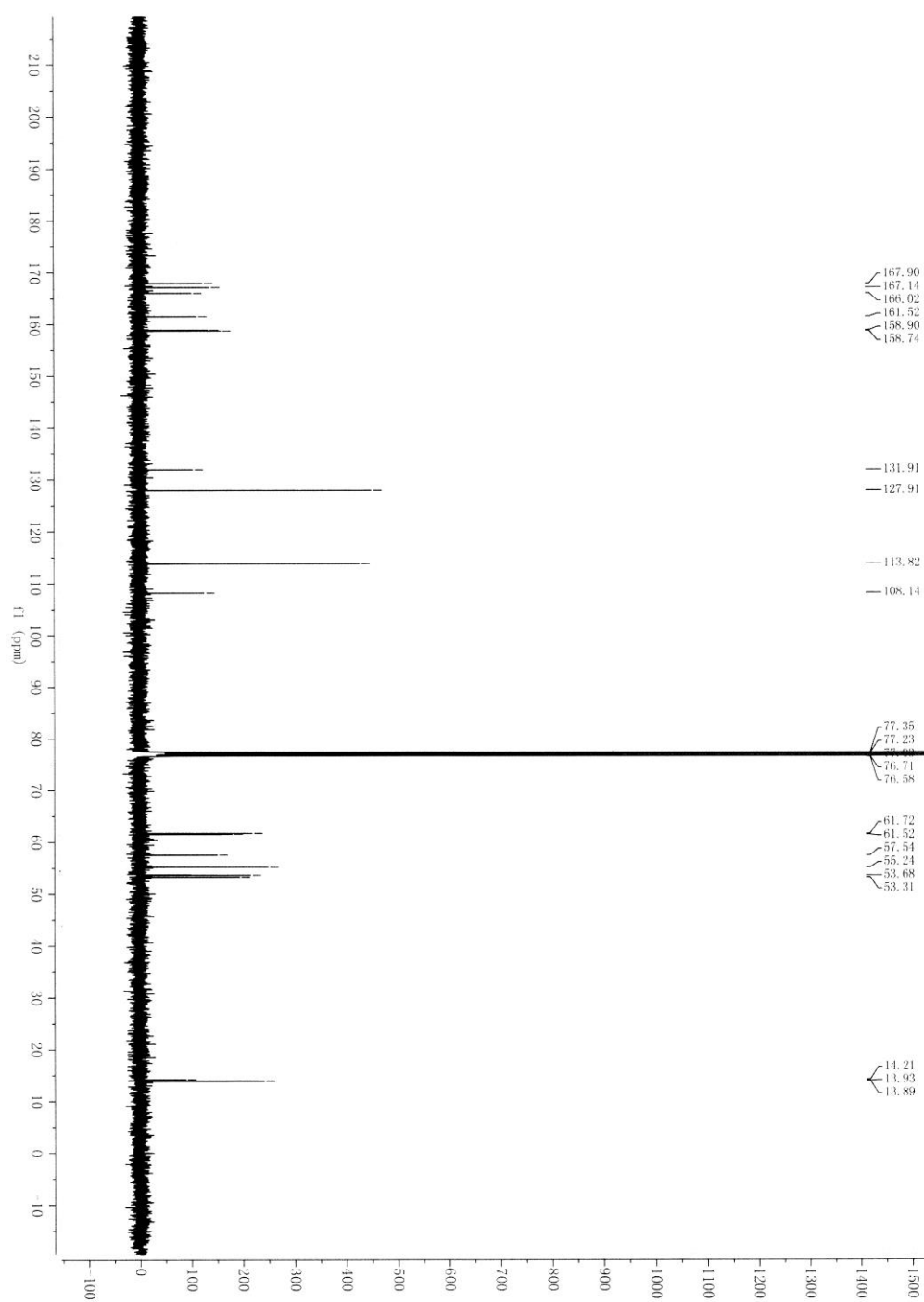


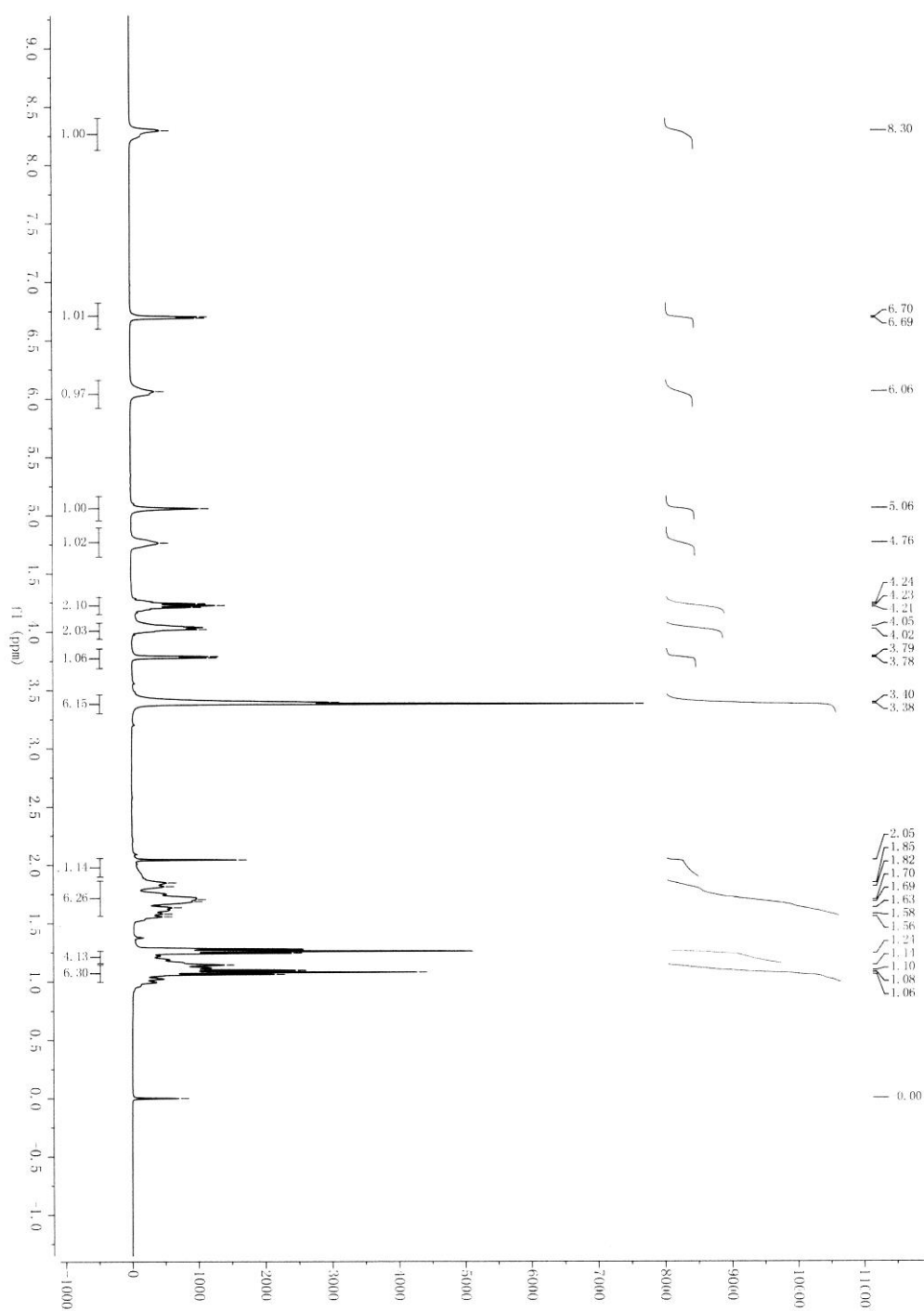
7.  $^1\text{H}$  &  $^{13}\text{C}$  NMR spectra $^1\text{H}$  NMR of 4a

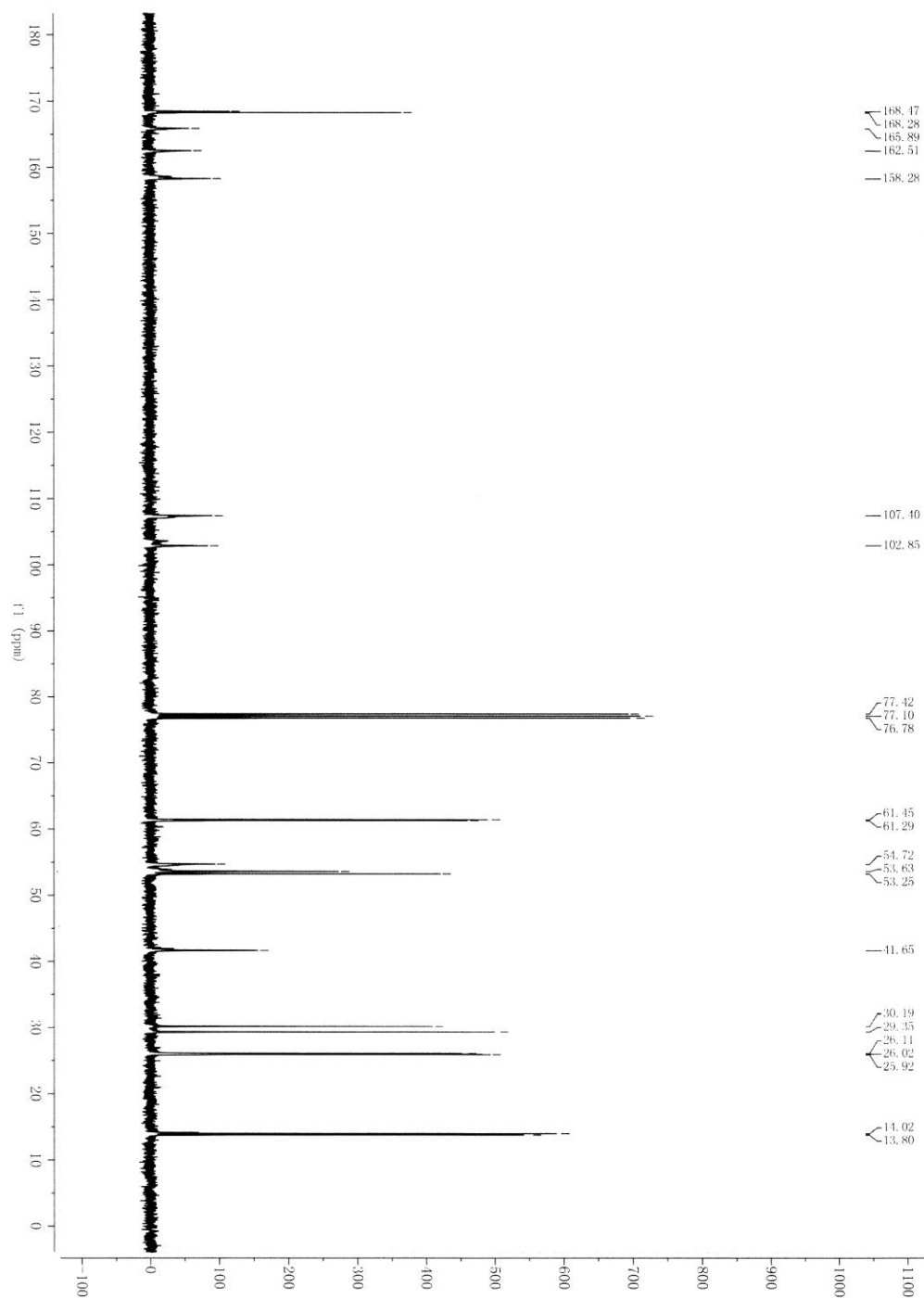
**$^{13}\text{C}$  NMR of 4a**

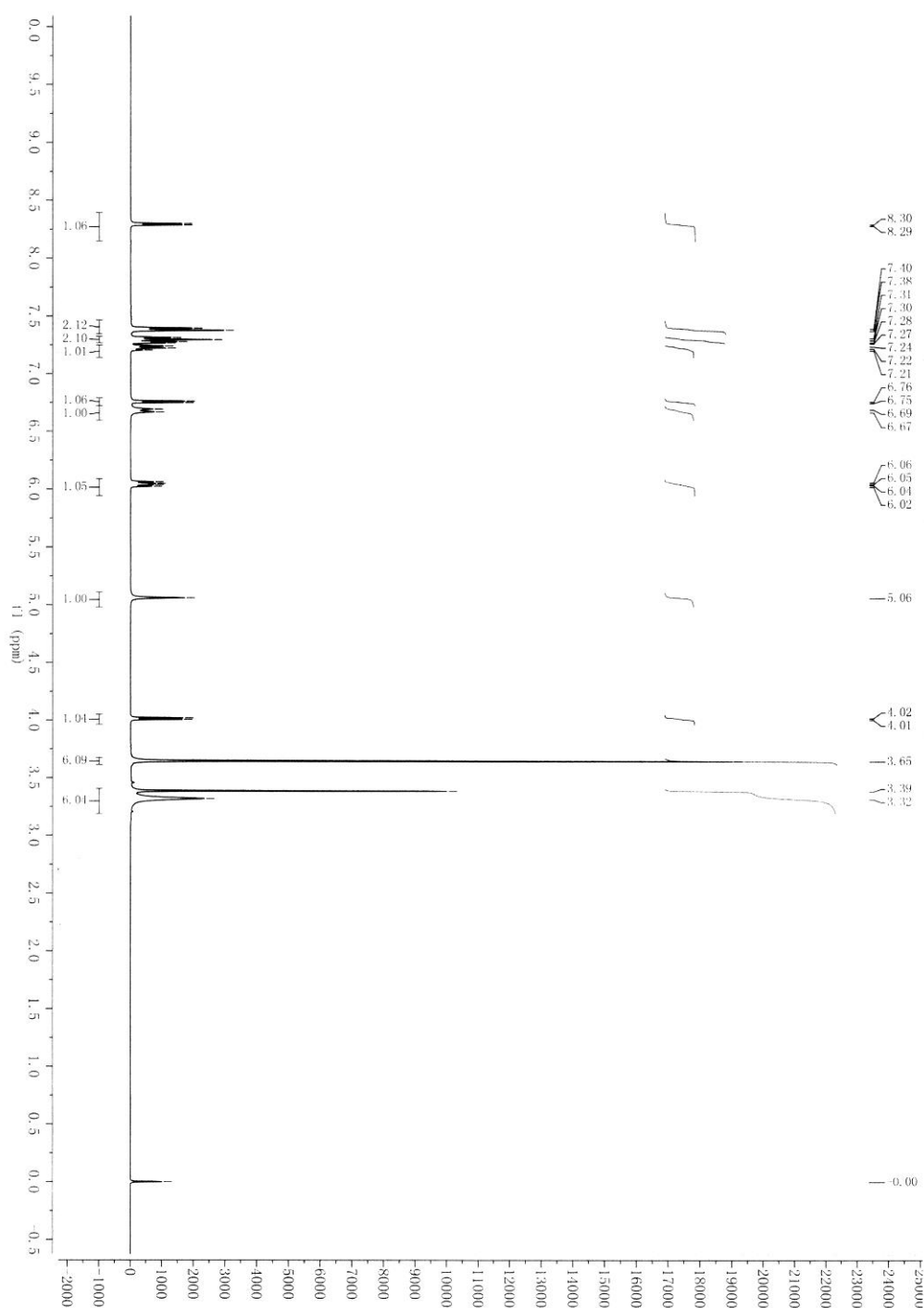


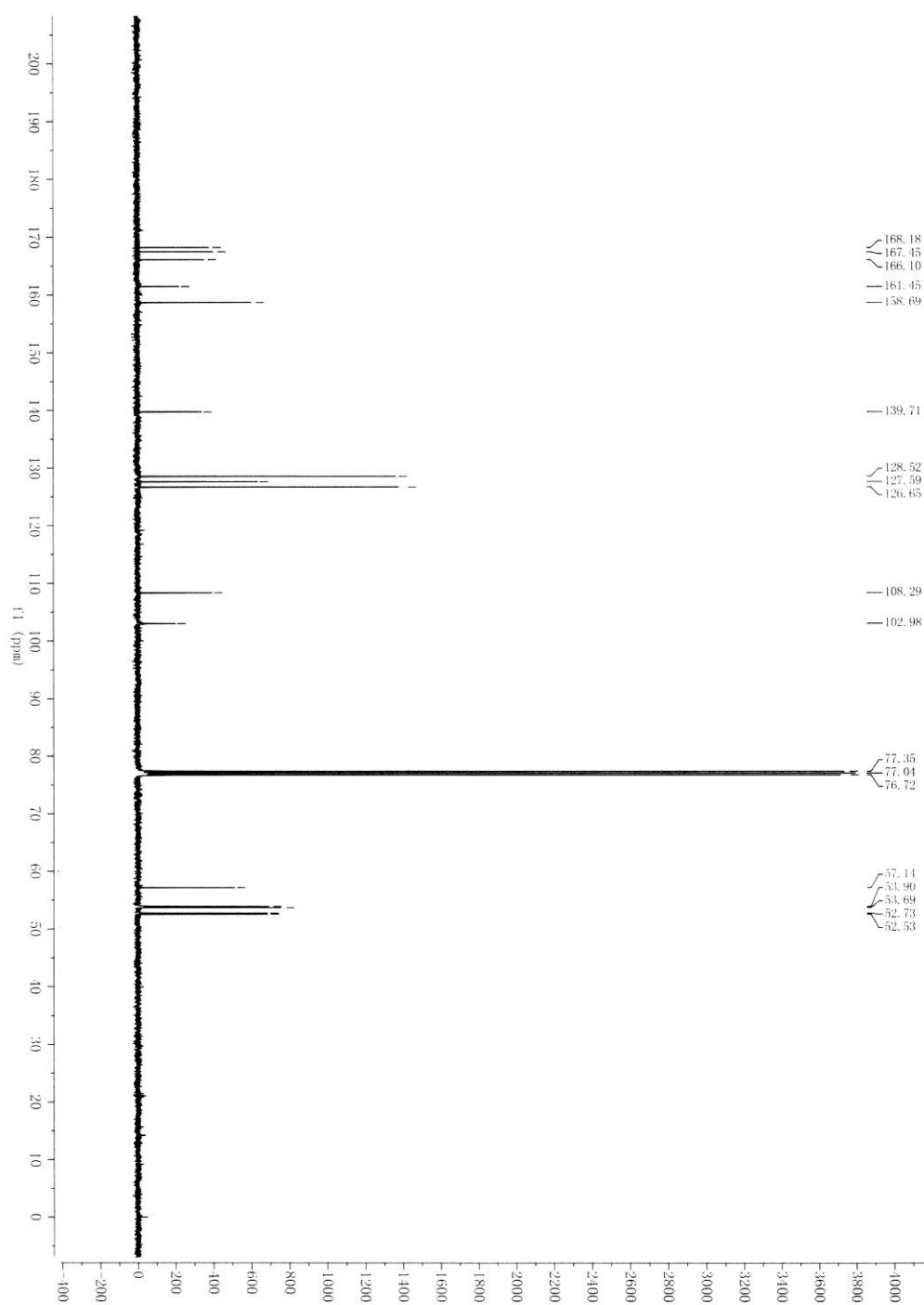
**$^1\text{H}$  NMR of 4b**

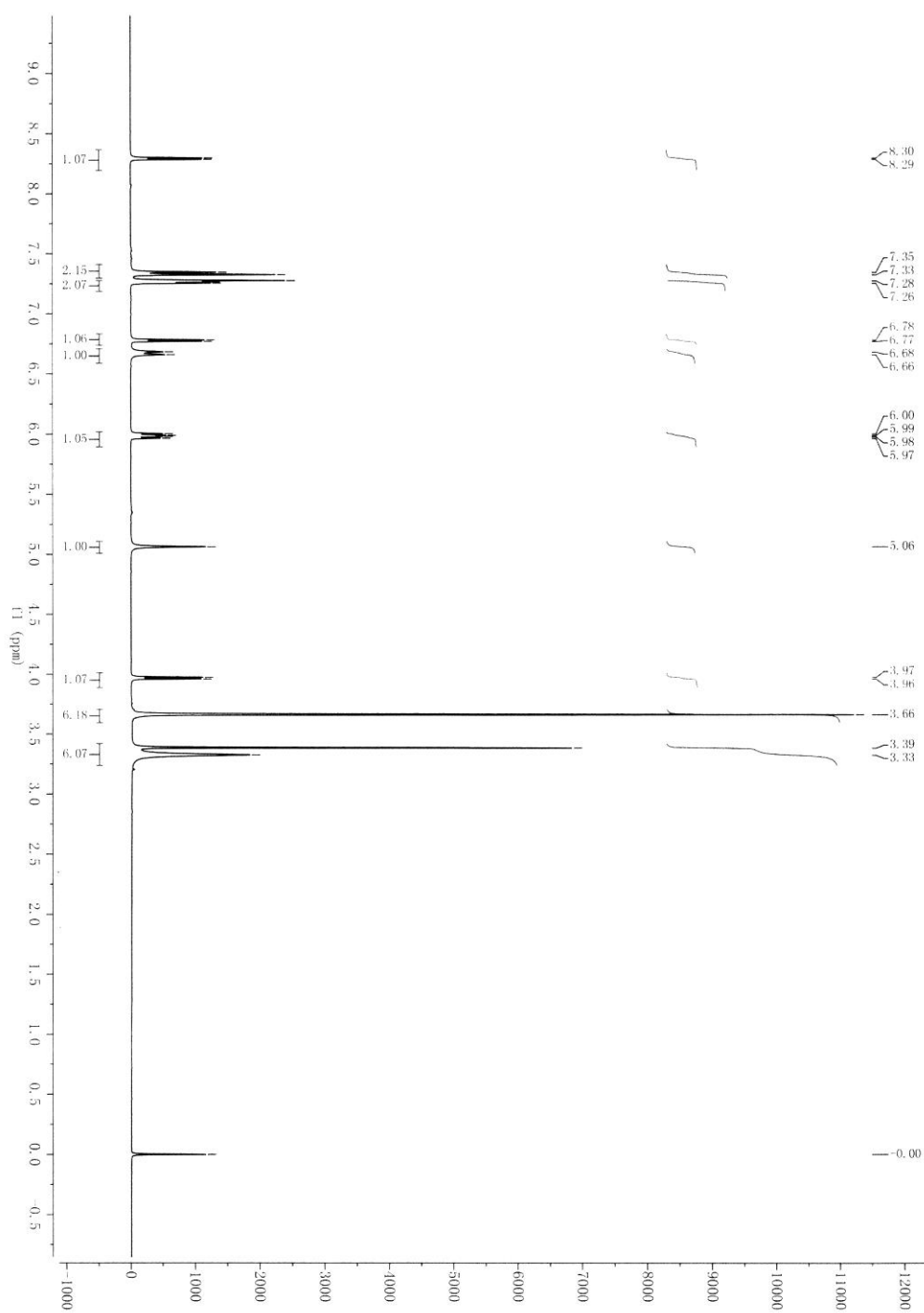
$^{13}\text{C}$  NMR of **4b**

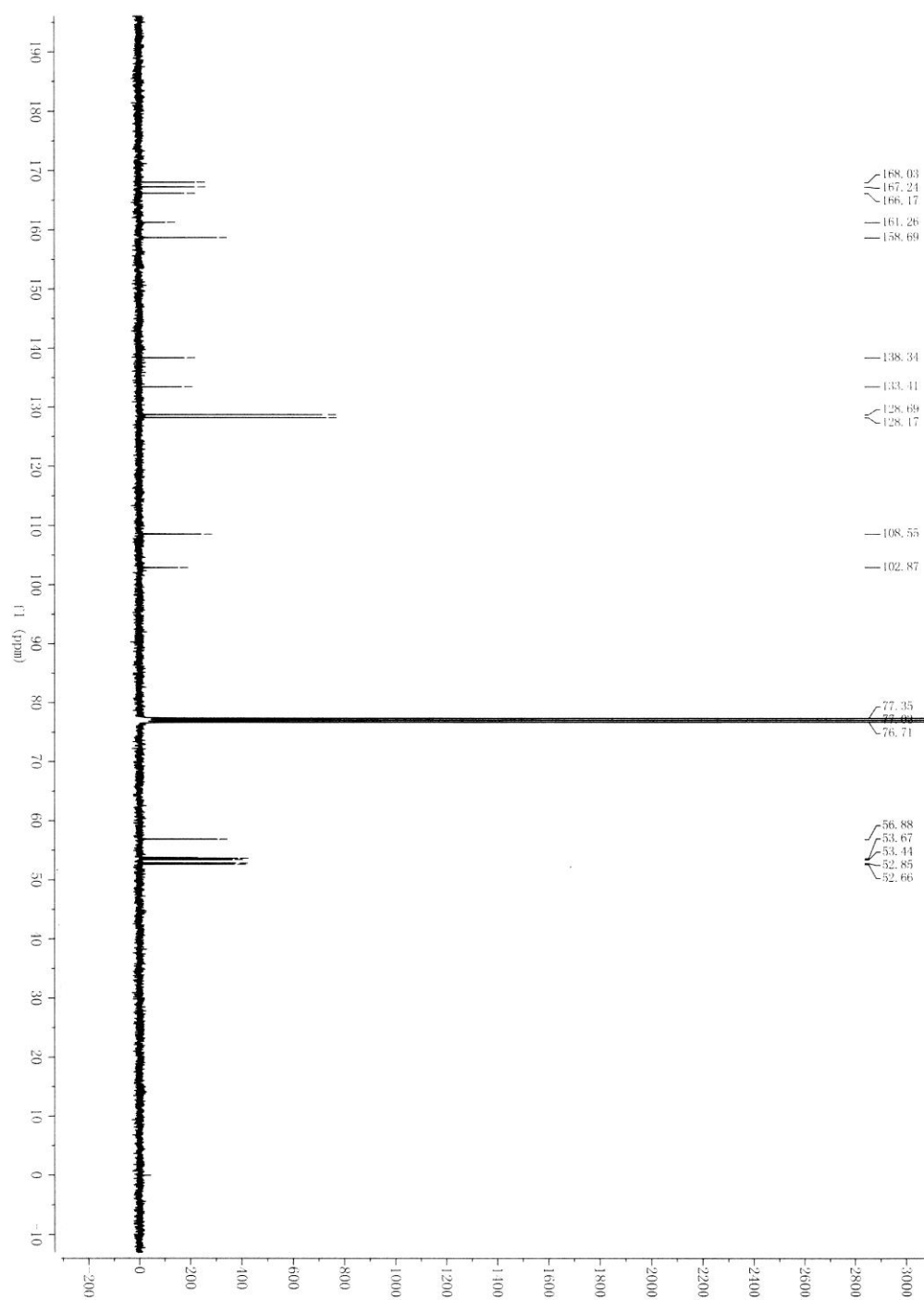
**$^1\text{H}$  NMR of 4c**

$^{13}\text{C}$  NMR of **4c**

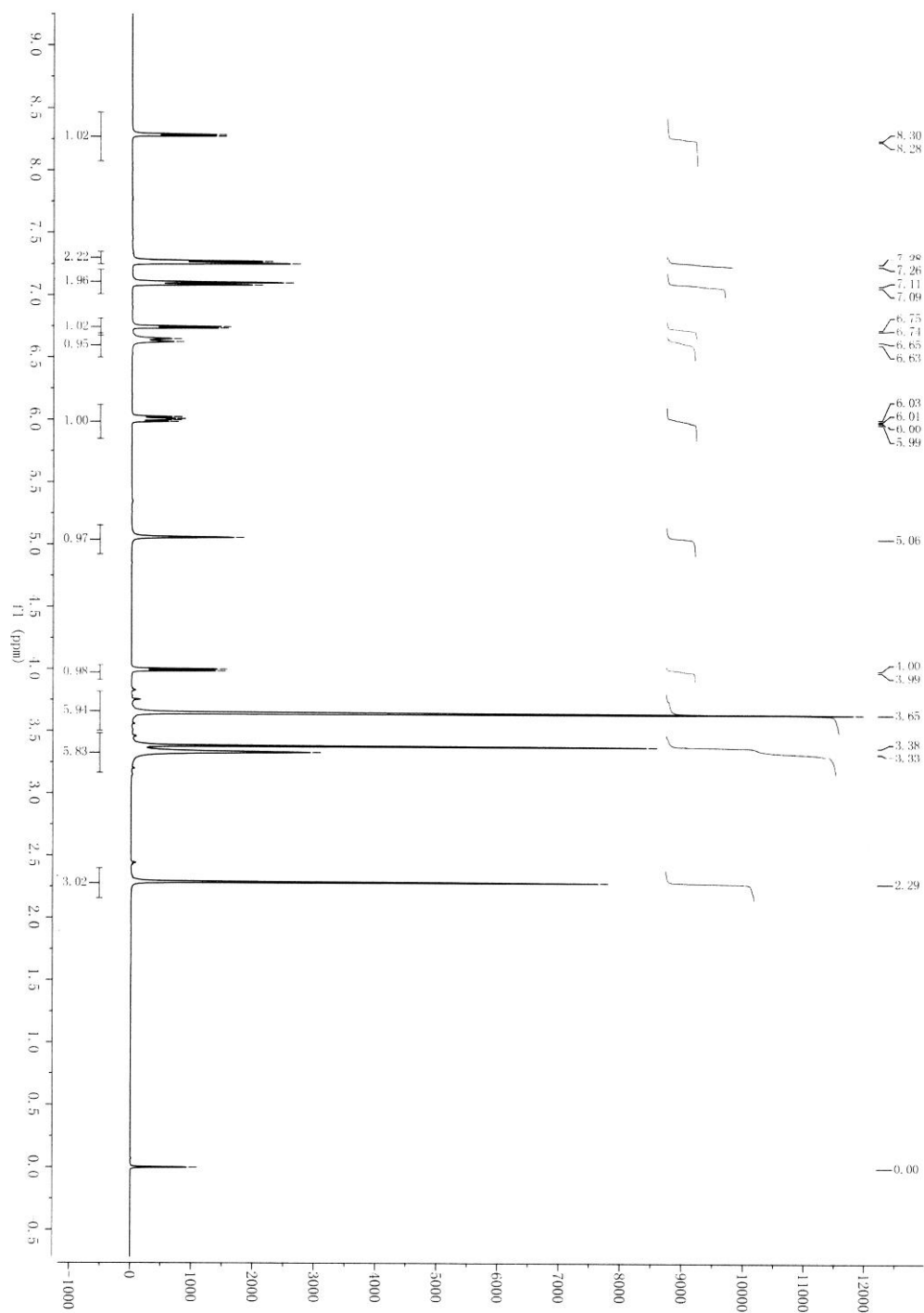
$^1\text{H}$  NMR of 4d

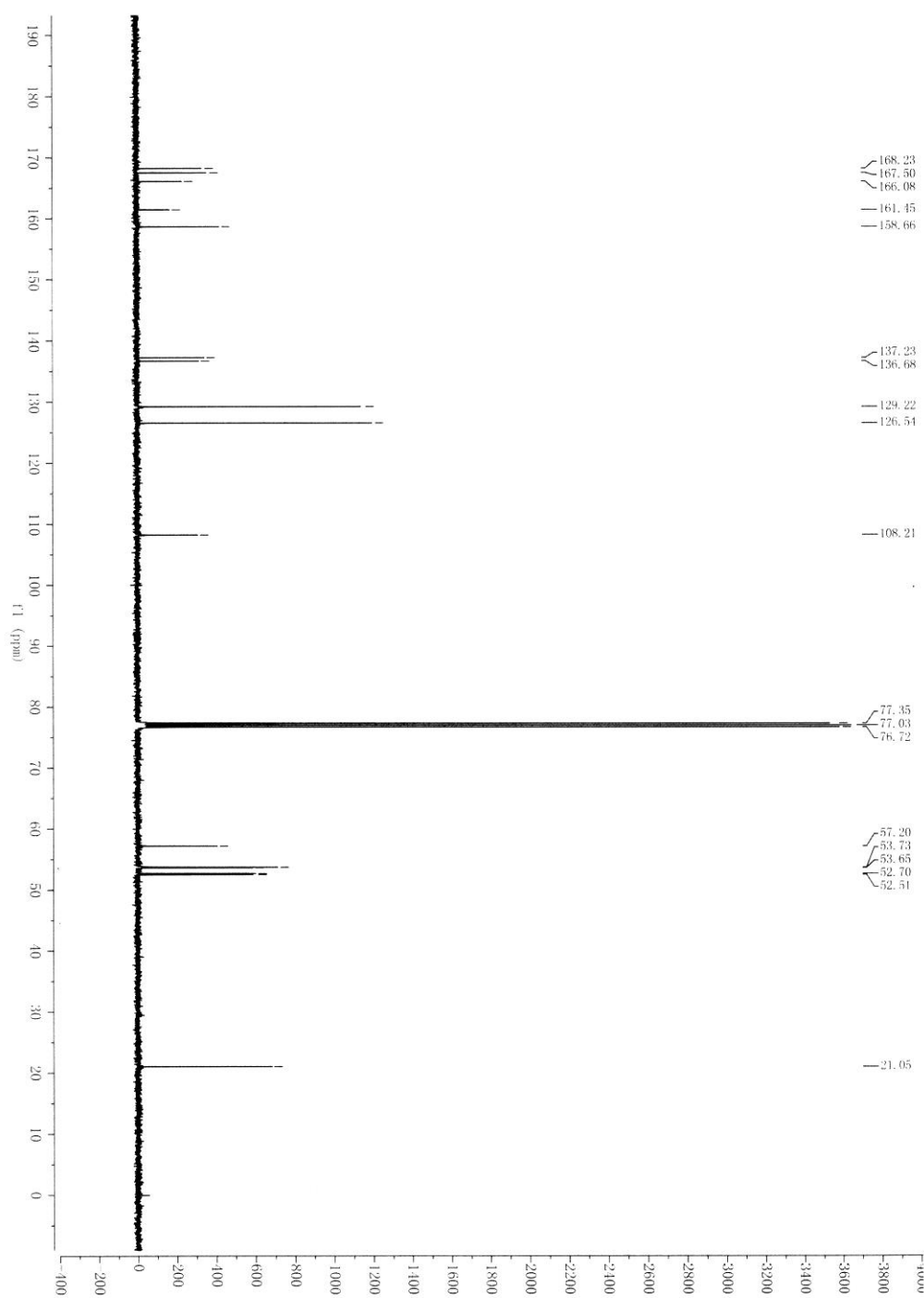
$^{13}\text{C}$  NMR of 4d

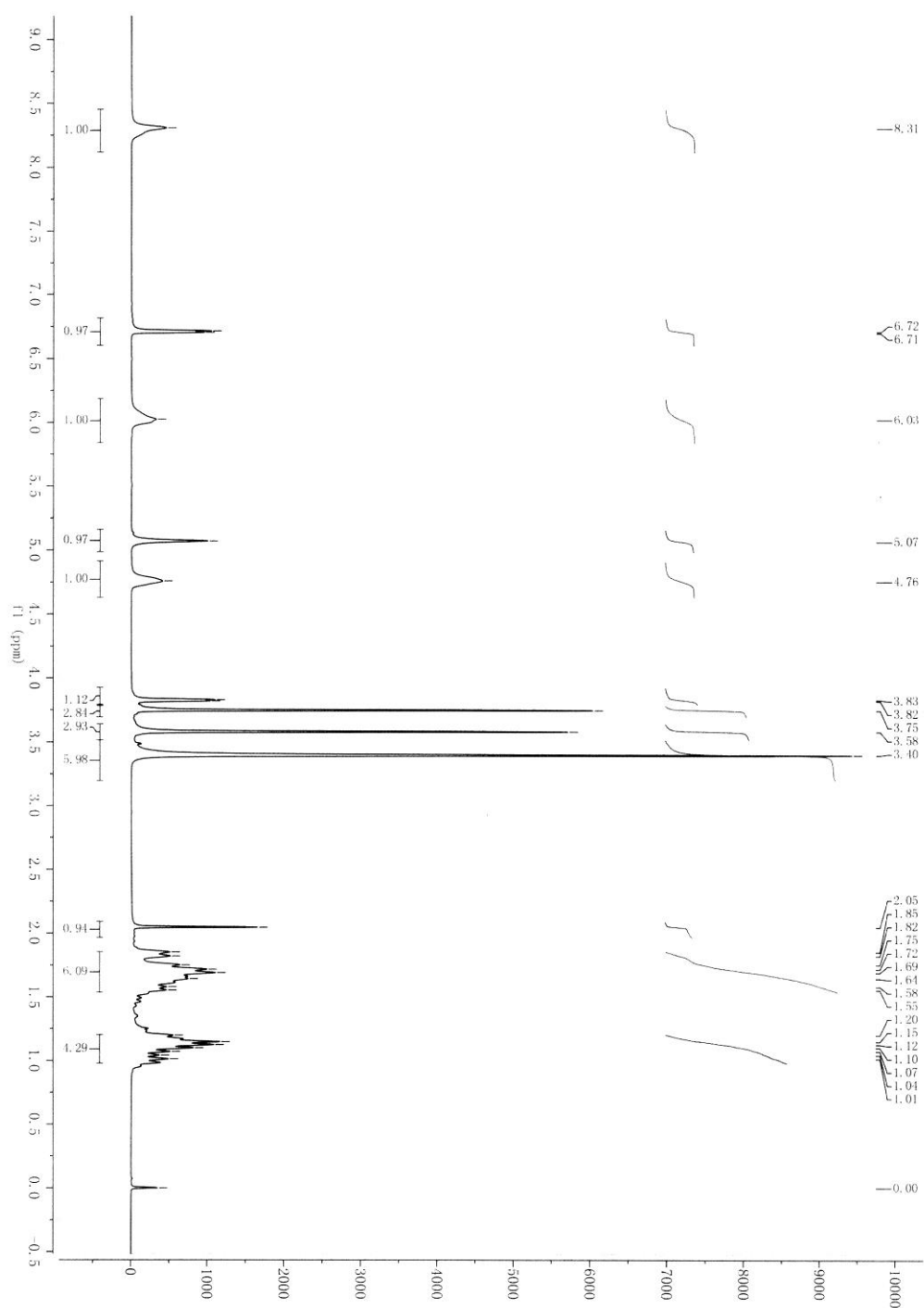
**$^1\text{H}$  NMR of 4e**

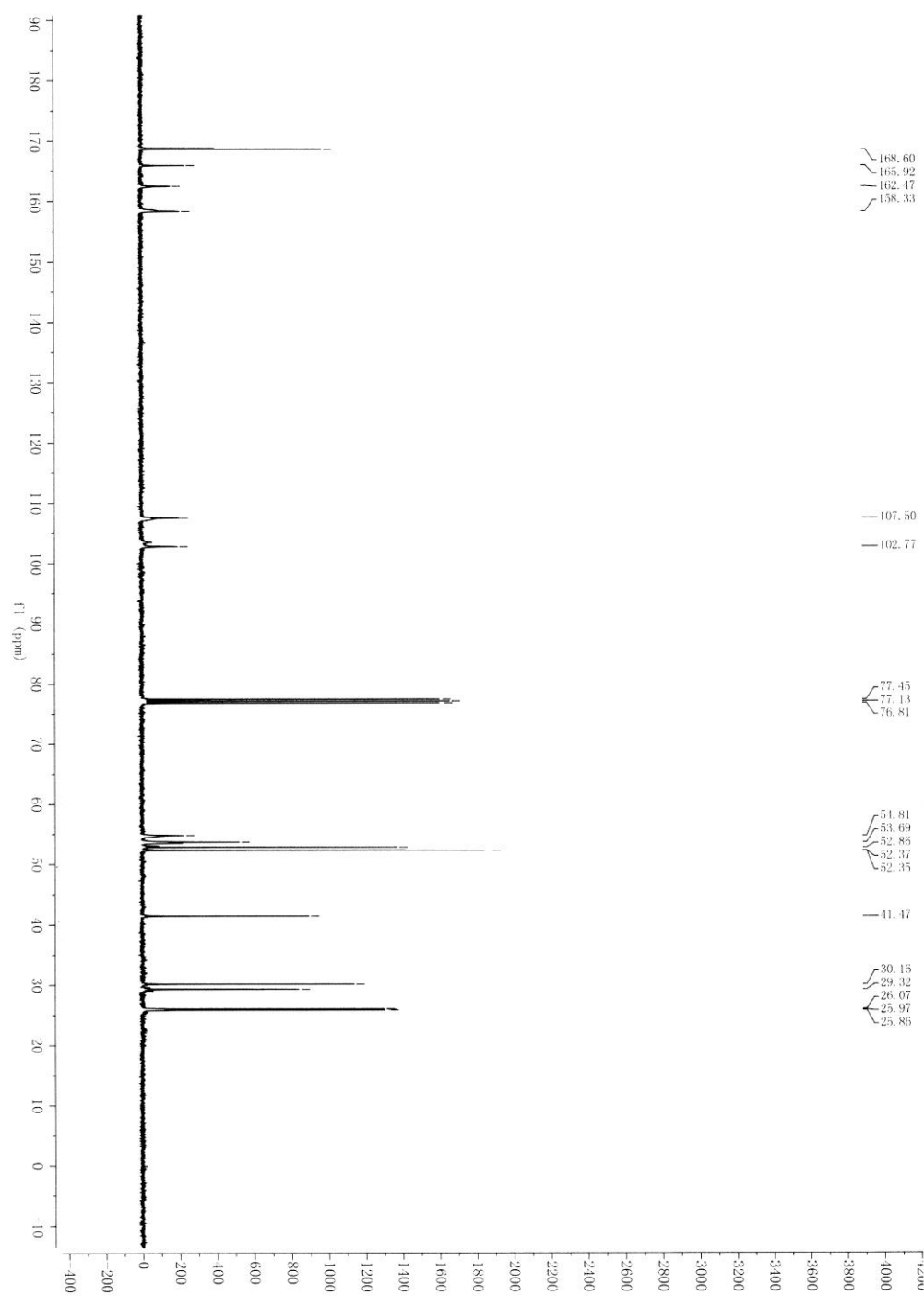
$^{13}\text{C}$  NMR of **4e**

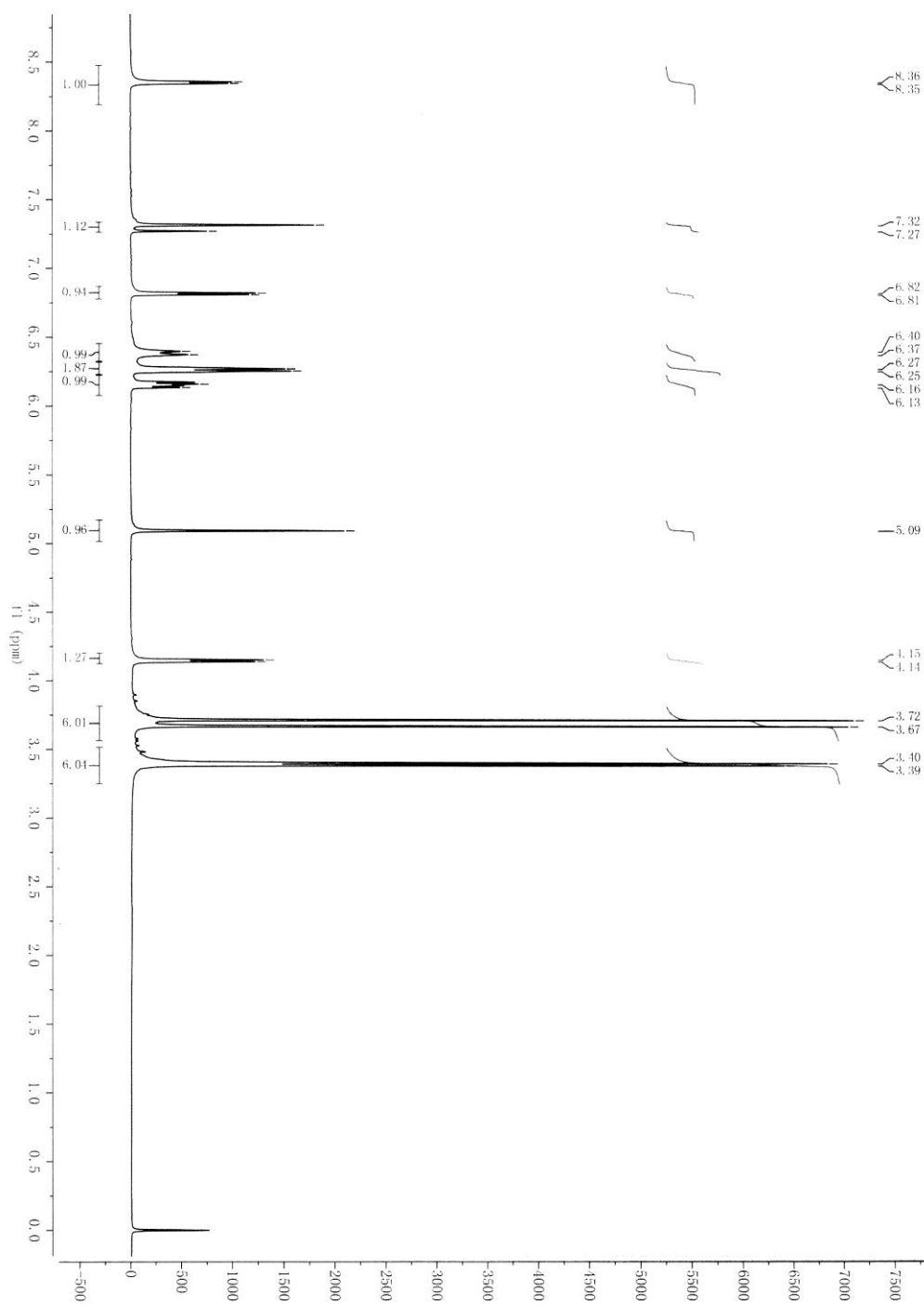


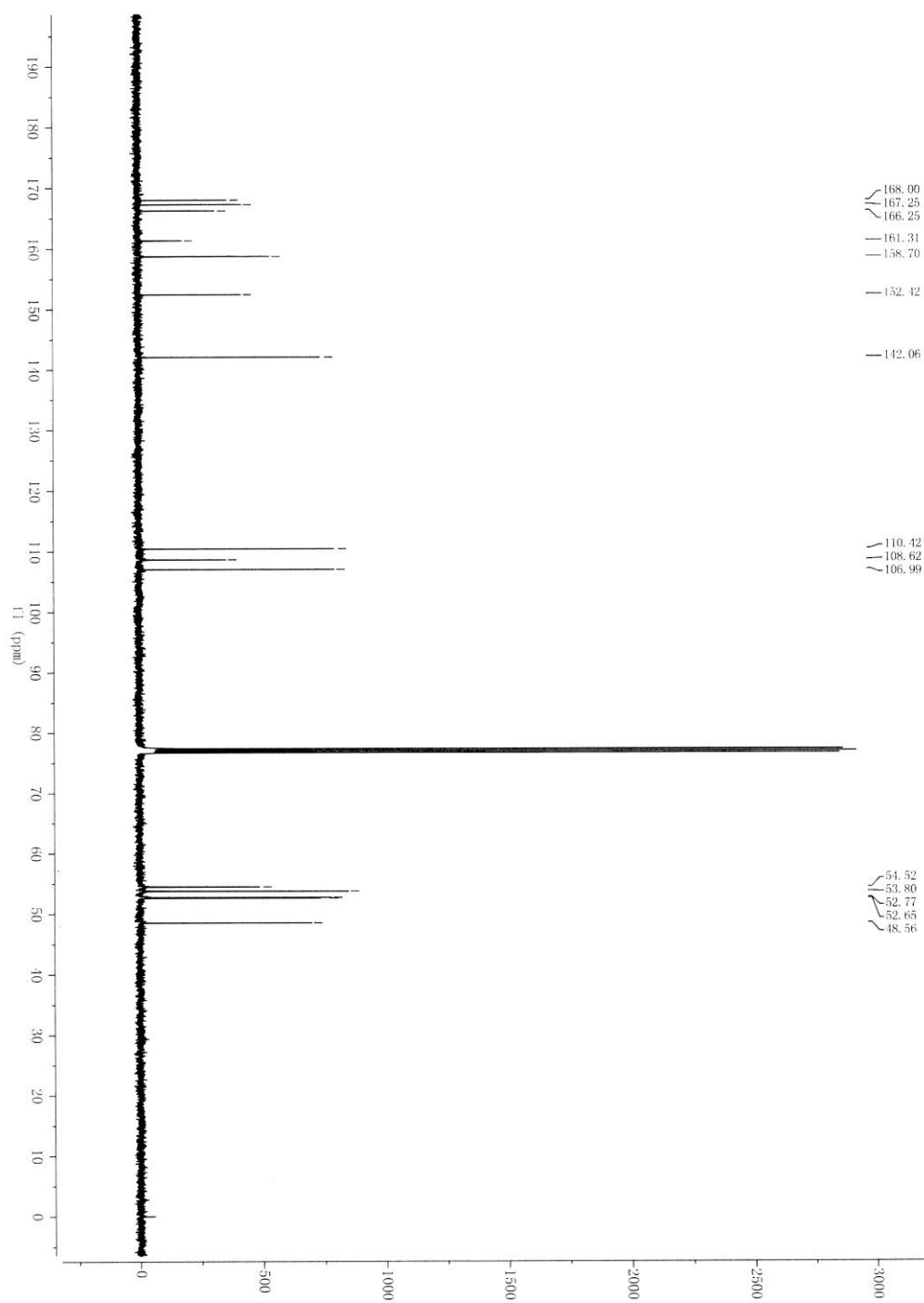
**$^1\text{H}$  NMR of 4f**

$^{13}\text{C}$  NMR of **4f**

**$^1\text{H}$  NMR of 4g**

$^{13}\text{C}$  NMR of **4g**

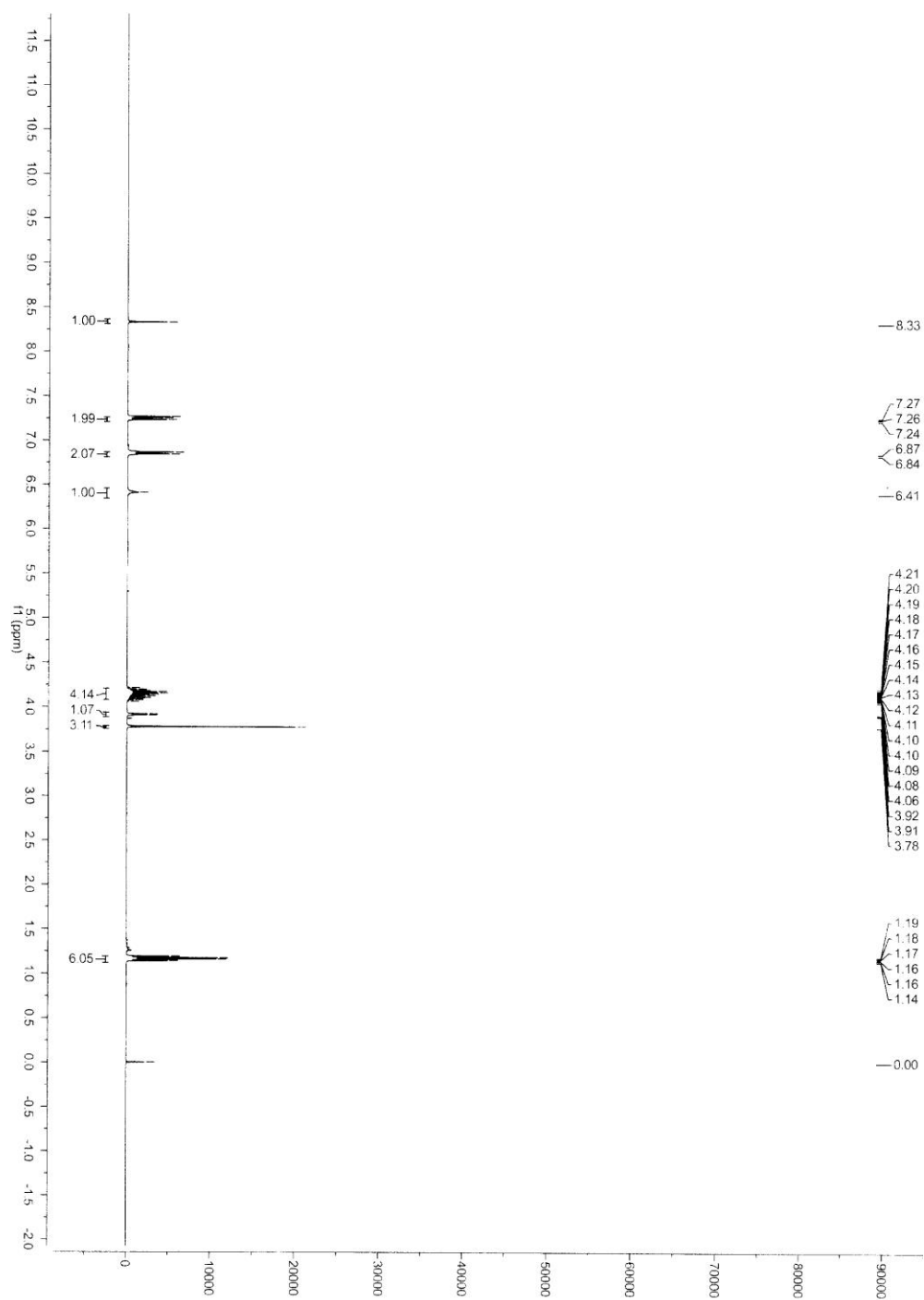
$^1\text{H}$  NMR of **4h**

$^{13}\text{C}$  NMR of **4h**

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 $^1\text{H}$  NMR of **4i**

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$^{13}\text{C}$  NMR of **4i**