

Supporting Information:

# Co-Crystal Structure-Guided Optimization of Dual-Functional Small Molecules for Improving the Peroxygenase Activity of Cytochrome P450BM3

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## **Product analysis**

### **Gas Chromatography (GC)**

The analytical condition for styrene epoxidation was as follows: splitting ratio: 1/9, temperature program: injector 280°C, detector 280°C, 100°C oven for 1 min, then 15°C /min gradient to 200°C, 60°C /min gradient to 280°C and then 280°C for 8 min (total 17.0 min).

The analytical conditions for 3-hexanol, 2-hexanol and 1-hexanol were as follows: splitting ratio: 1/9, temperature program: injector 260°C, detector 260°C, 80°C oven, then 10°C/min gradient to 160°C, 60°C/min gradient to 240°C and then 240°C for 2 min (total 11.33 min).

The analytical conditions for 1-phenylethanol and 2-phenylethanol were as follows: splitting ratio: 1/9, temperature program: injector 280°C, detector 280°C, 100°C oven for 1 min, then 25°C /min gradient to 180°C, 5°C /min gradient to 220°C, 30°C /min gradient to 280°C and then 280°C for 5 min (total 19.2 min).

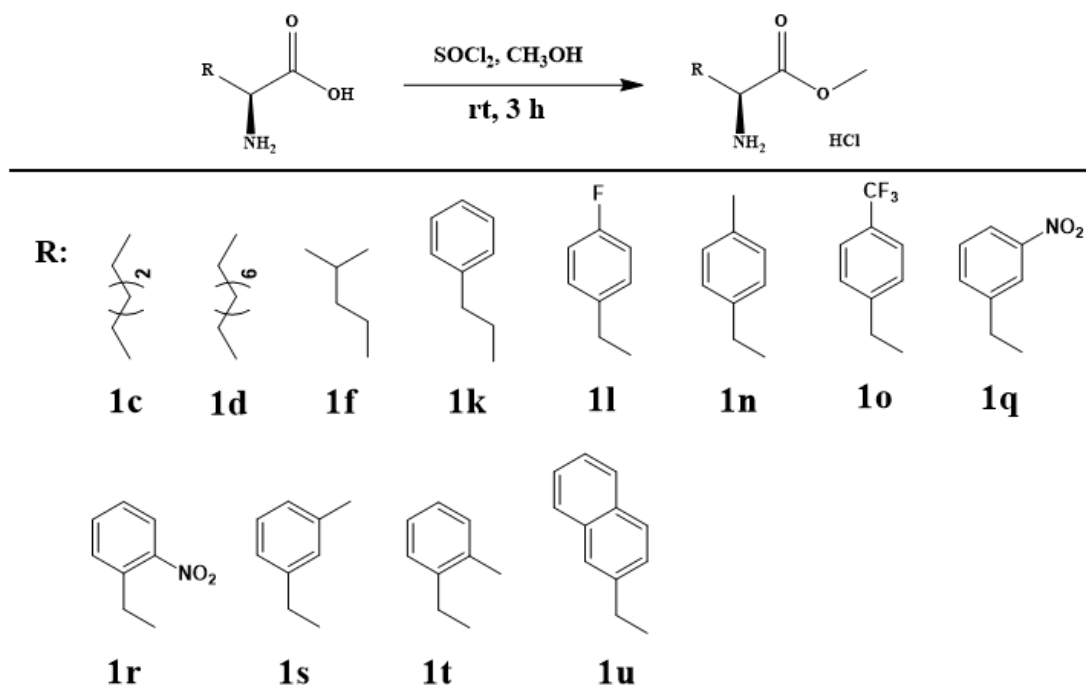
The analytical condition for naphthalene hydroxylation was as follows: splitting ratio: 1/9, temperature program: injector 280°C, detector 300°C, 100°C oven for 1 min, then 15°C /min gradient to 200°C, 60°C /min gradient to 280°C and then 280°C for 4 min (total 13.0 min).

### **Chiral Gas Chromatography**

The analytical condition of styrene epoxidation was as follows: splitting ratio: 1/9, temperature program: injector 200°C, detector 200°C, 80°C oven for 3 min, then 10°C/min gradient to 100°C for 5 min, 5°C /min gradient to 105°C for 7 min, 60°C/min gradient to 170°C for 3 min (total 19.08 min).

The analytical condition of ethylbenzene hydroxylation was as follows: splitting ratio: 1/9, temperature program: injector 250°C, detector 250°C, the initial temperature is 80°C, then 10°C/min gradient to 125°C for 8 min, 60°C /min gradient to 190°C for 5 min (total 18.6 min).

# synthesis



Scheme S1. Synthesis of amino acid hydrochloride.

Synthesis of **1c**: To a suspension of (S)-2-Aminooctanoic acid (1.0 g, 6.28 mmol) in MeOH (15mL) at 0 °C (ice bath) was added dropwise with stirring SOCl<sub>2</sub> (6.5 mL, 9.4 mmol) over 1 h. The flask was fitted with a reflux condenser and heated to 60 °C for 3 h then cooled to room temperature. After removed the solvent in a rotary evaporator, washed twice with ether to obtain produce colorless soild (95% yield), <sup>1</sup>H-NMR (600 MHz, DMSO-d<sub>6</sub>) δ 8.71(s, 3H), 3.96-3.94 (t, *J* = 12 Hz, 1H), 3.74 (s, 3H), 1.82-1.78 (m, 2H), 1.29-1.25 (m, 8H), 0.87-0.85 (t, *J* = 12 Hz, 3H).

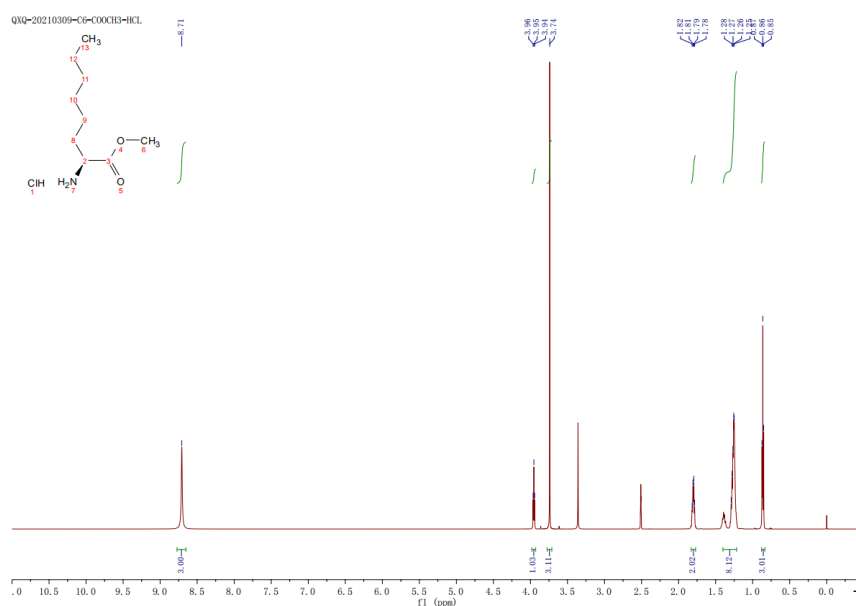
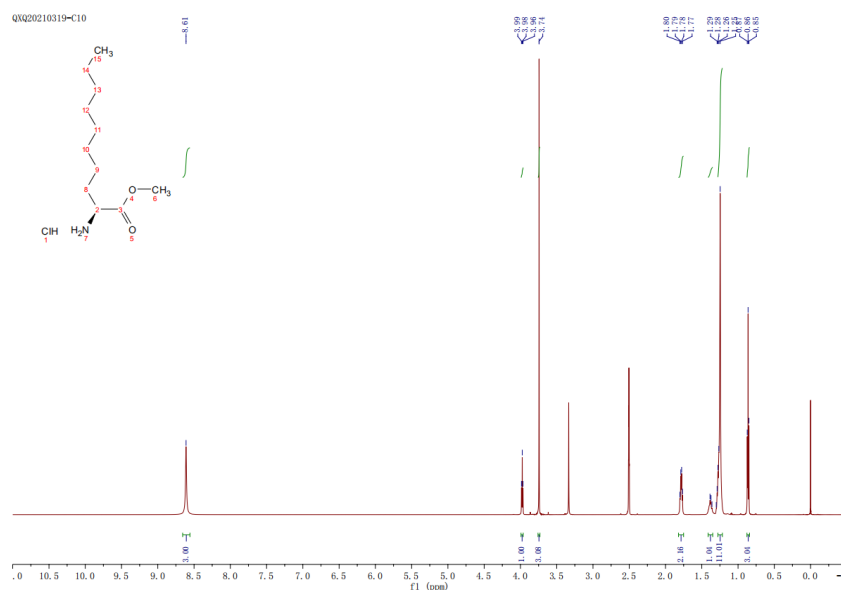


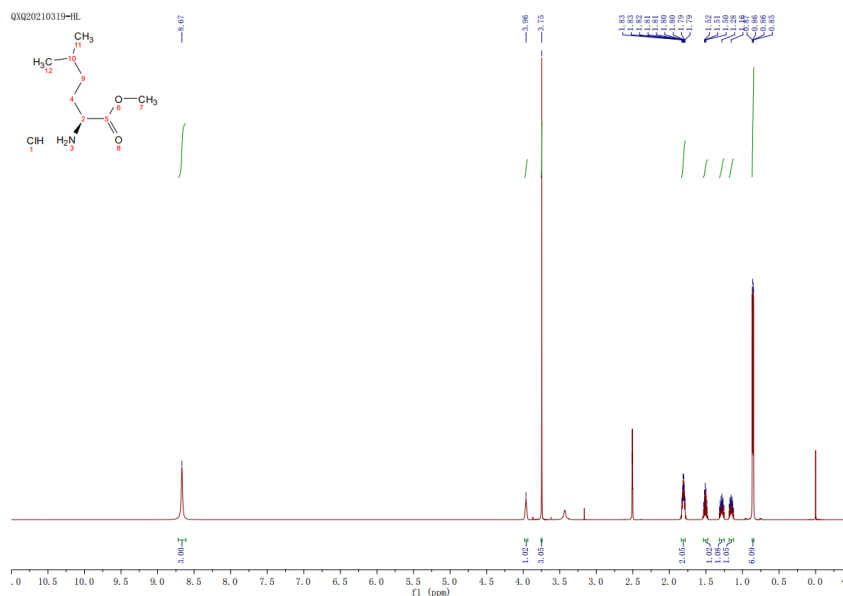
Figure S1. <sup>1</sup>H-NMR spectra of **1c**.

**1d**: Colorless solid (96% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.67 (s, 3H), 3.99-3.96 (t,  $J$  = 18 Hz, 1H), 3.74 (s, 3H), 1.80-1.77 (m, 2H), 1.39-1.36 (m, 1H), 1.30-1.25 (m, 1H), 0.87-0.85 (t,  $J$  = 12 Hz, 3H).



**Figure S2.**  $^1\text{H}$ -NMR spectra of **1d**.

**1e**: Colorless solid (94% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.67 (s, 3H), 3.99-3.96 (t,  $J$  = 18 Hz, 1H), 3.75 (s, 1H), 1.83-1.79 (m, 2H), 1.53-1.49 (m, 1H), 1.32-1.25 (m, 1H), 1.18-1.12 (m, 1H), 0.87-0.85 (m, 6H).



**Figure S3.**  $^1\text{H}$ -NMR spectra of **1e**.

**1k**: Colorless solid (97% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$  8.87 (s, 3H), 7.32-7.29 (m, 2H), 7.25-7.20 (m, 2H), 4.00-3.98 (t,  $J = 12$  Hz, 1H), 3.73 (s, 3H), 2.81-2.76 (m, 1H), 2.67-2.62 (m, 1H), 2.15-2.11 (m, 2H).

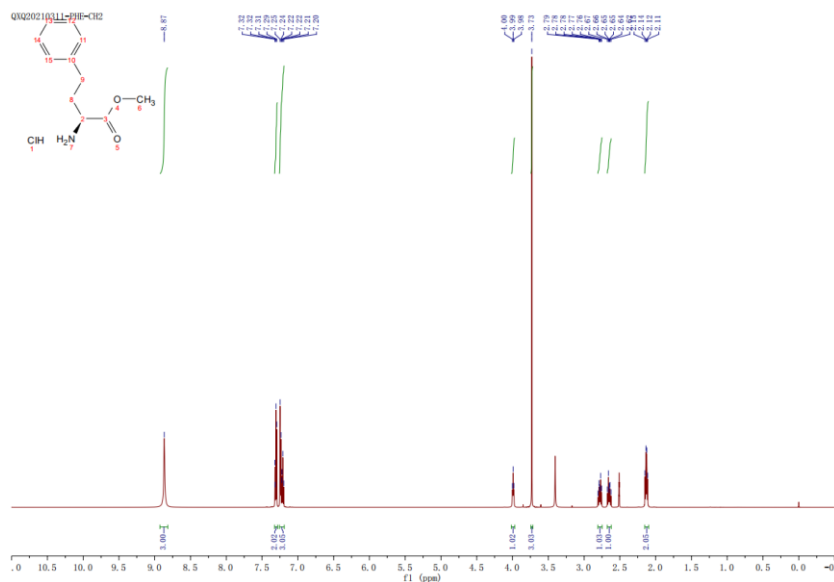


Figure S4.  $^1\text{H}$ -NMR spectra of **1k**.

**1l**: Colorless solid (96% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$  7.15 (s, 3H), 7.32-7.29 (m, 2H), 7.18-7.15 (t,  $J = 18$  Hz, 2H), 4.25-4.23 (t,  $J = 12$  Hz, 1H), 3.67 (s, 3H), 3.23-3.20 (m, 1H), 3.15-3.11 (m, 1H).

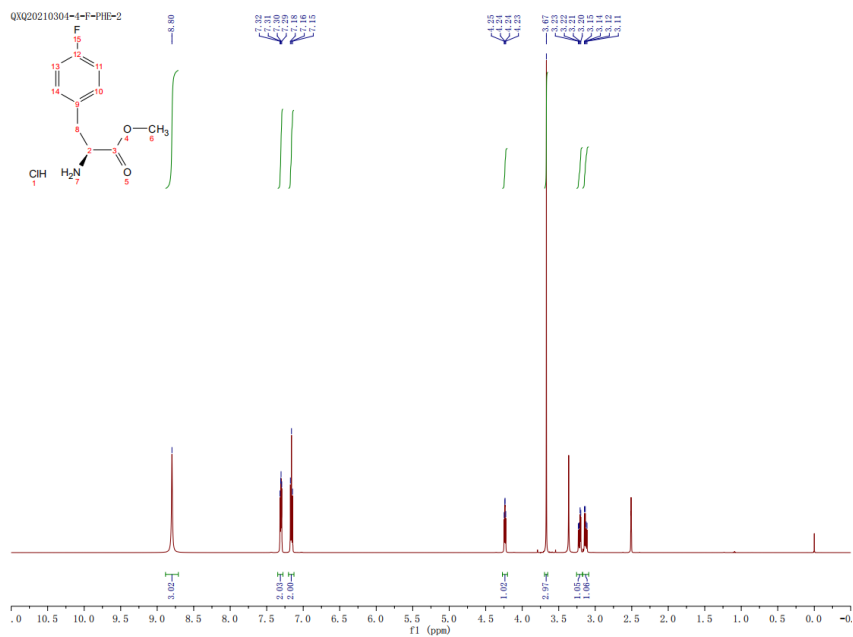


Figure S5.  $^1\text{H}$ -NMR spectra of **1l**.

**1n**: Colorless solid (92% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.80 (s, 3H), 7.14-7.11 (m, 4H), 4.19-4.17 (t,  $J = 12$  Hz, 1H), 3.65 (s, 3H), 3.20-3.17 (m, 1H), 3.09-3.06 (m, 1H), 2.28 (s, 3H).

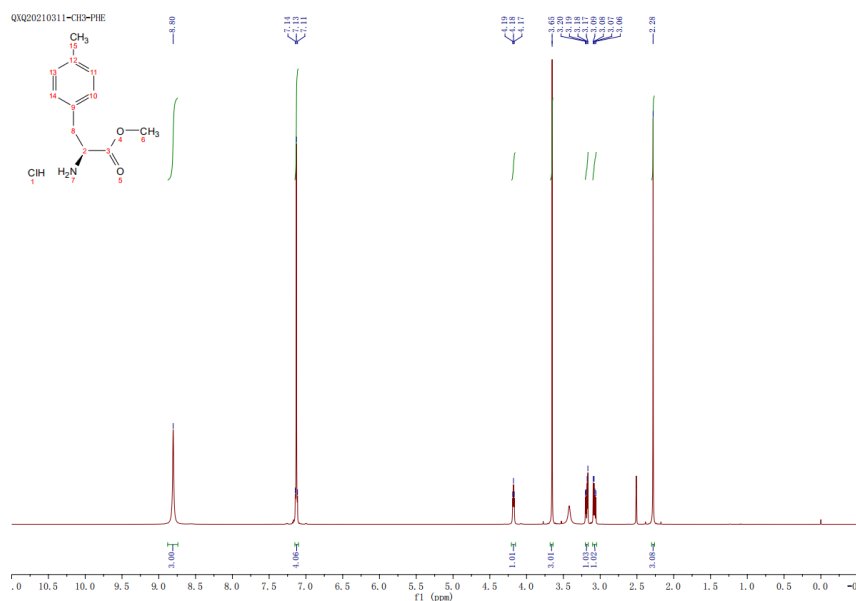


Figure S6.  $^1\text{H}$ -NMR spectra of **1n**.

**1o**: Colorless solid (94% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.85 (s, 3H), 7.71-7.70 (d,  $J = 6$  Hz, 2H), 7.52-7.51 (d,  $J = 6$  Hz, 2H), 4.35-4.33 (t,  $J = 12$  Hz, 1H), 3.69 (s, 3H), 3.34-3.31 (m, 1H), 3.27-3.23 (m, 1H).

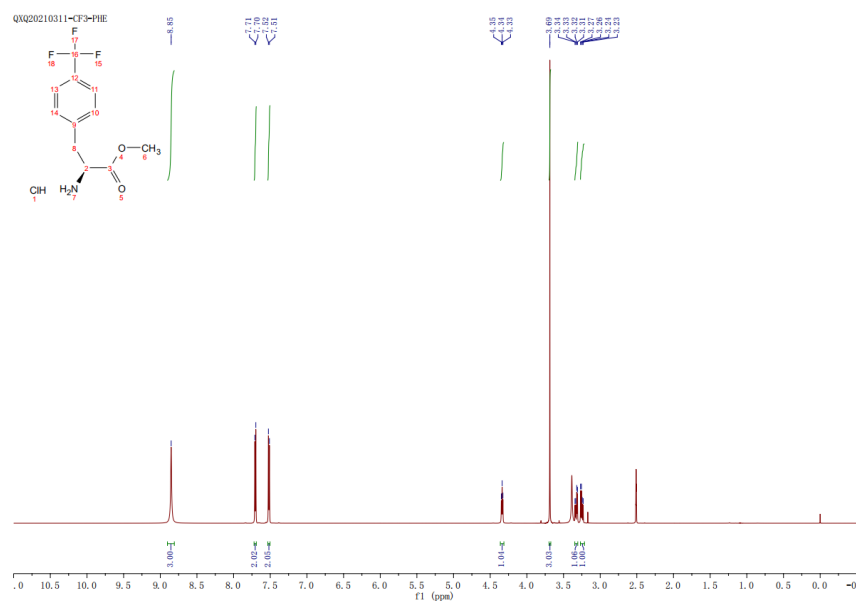


Figure S7.  $^1\text{H}$ -NMR spectra of **1o**.

**1q**: Light yellow solid (93% yield),  $^1\text{H}$ -NMR (600 MHz, DMSO- $d_6$ )  $\delta$  9.00 (s, 3H), 8.06-8.05 (m, 1H), 7.76-7.74 (m, 1H), 7.68-7.67 (m, 1H), 6.61-7.58 (m, 1H), 4.25-4.22 (t,  $J$  = 18 Hz, 1H), 3.58 (s, 3H), 3.52-3.39 (m, 2H).

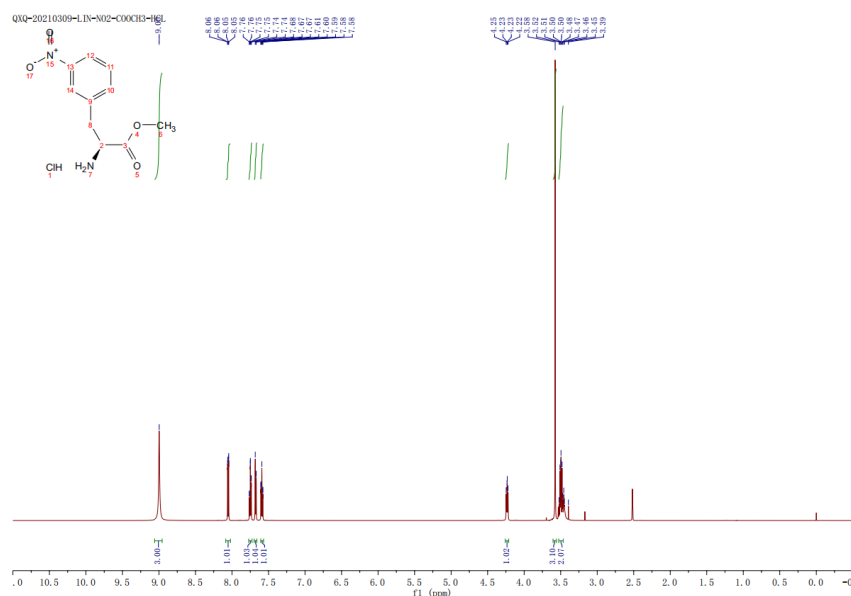


Figure S8.  $^1\text{H}$ -NMR spectra of **1q**.

**1r**: Light yellow solid (91% yield),  $^1\text{H}$ -NMR (600 MHz, DMSO- $d_6$ )  $\delta$  8.87 (s, 3H), 8.21-8.20 (m, 1H), 8.17-8.15 (m, 1H), 7.77-7.75 (d,  $J$  = 12 Hz, 1H), 7.66-7.63 (t,  $J$  = 18 Hz, 1H), 4.41-4.39 (t,  $J$  = 12 Hz, 1H), 3.70 (s, 3H), 3.37-3.34 (m, 2H).

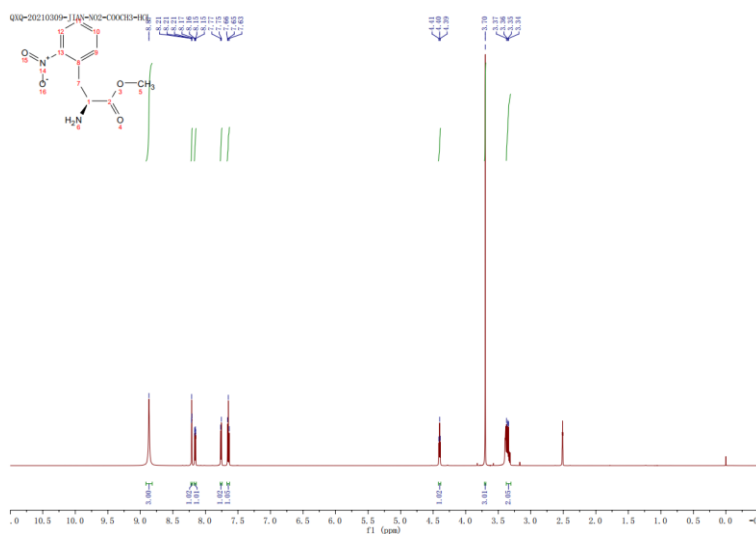


Figure S9.  $^1\text{H}$ -NMR spectra of **1r**.

**1s:** Light yellow solid (96% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$  8.89 (s, 3H), 7.18-7.13 (m, 4H), 4.08-4.06 (t,  $J = 18$  Hz, 1H), 3.51 (s, 3H), 3.28-3.03 (m, 1H), 3.06-3.03 (m, 1H), 2.29 (s, 3H).

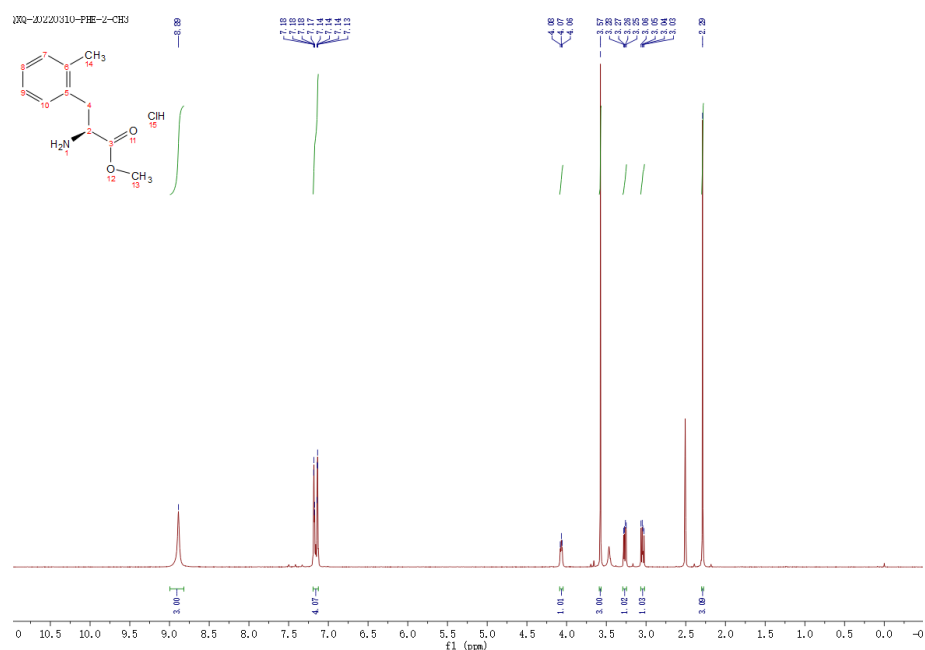


Figure S10.  $^1\text{H}$ -NMR spectra of **1s**.

**1t:** Light yellow solid (95% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$  8.74 (s, 3H), 7.23-7.20 (t,  $J = 18$  Hz, 1H), 7.10-7.09 (d,  $J = 6$  Hz, 1H), 7.05 (s, 1H), 7.10-7.09 (d,  $J = 6$  Hz, 1H), 4.23-4.21 (t,  $J = 12$  Hz, 1H), 3.66 (s, 3H), 3.18-3.14 (m, 1H), 3.08-3.04 (m, 1H), 2.29 (s, 3H).

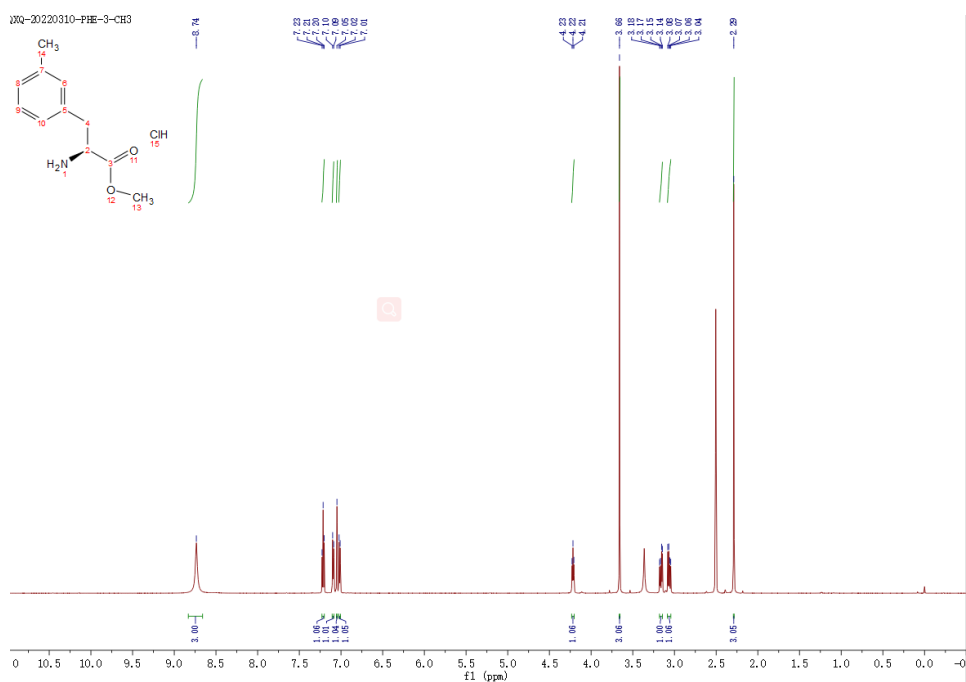
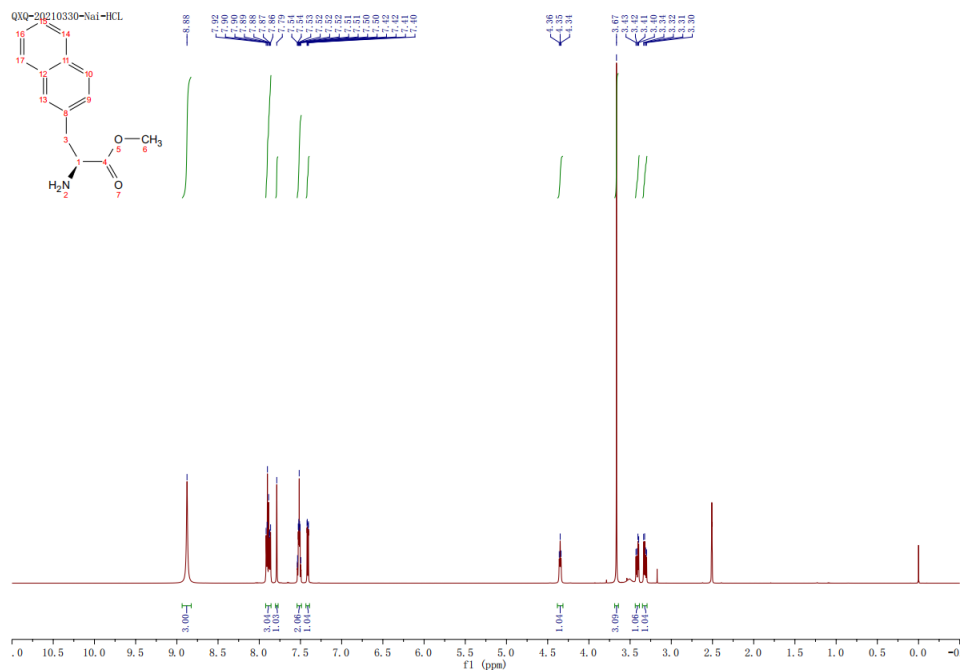


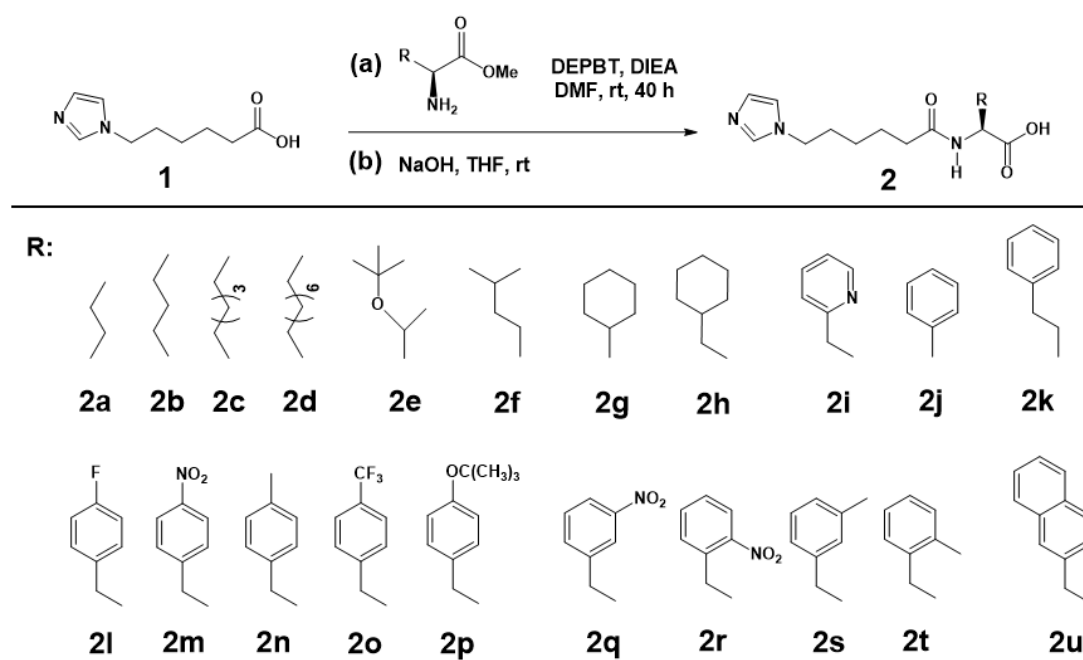
Figure S11.  $^1\text{H}$ -NMR spectra of **1t**.



**1u**: Colorless solid (94% yield),  $^1\text{H}$ -NMR (600 MHz, DMSO- $d_6$ )  $\delta$  8.88 (s, 3H), 7.92-7.86 (m, 3H), 7.79 (s, 1H), 7.54-7.50 (m, 2H), 7.42-7.40 (m, 1H), 3.36-3.34 (t, 1H), 3.67 (s, 3H), 3.43-3.40 (m, 1H), 3.34-3.30 (m, 1H).

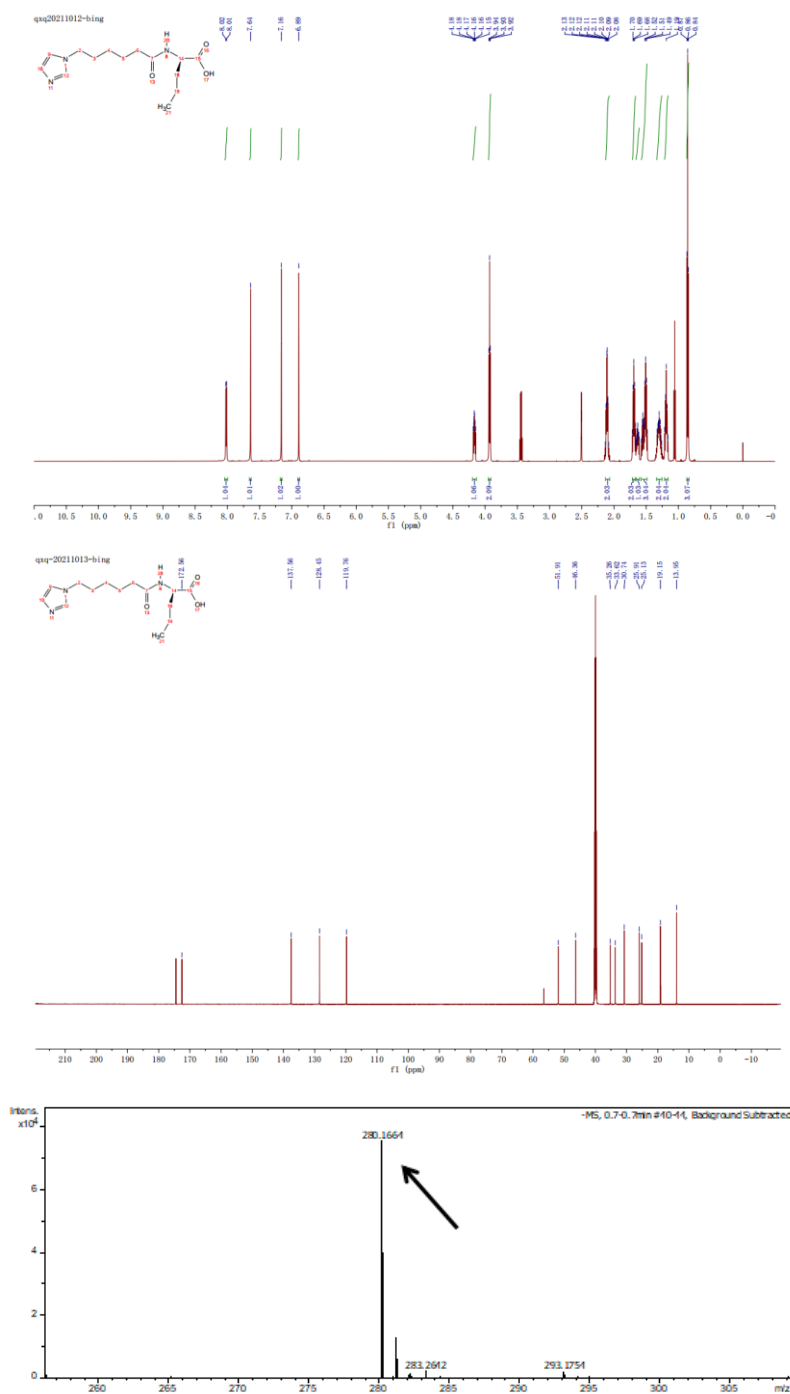


**Figure S12.**  $^1\text{H}$ -NMR spectra of **1u**.



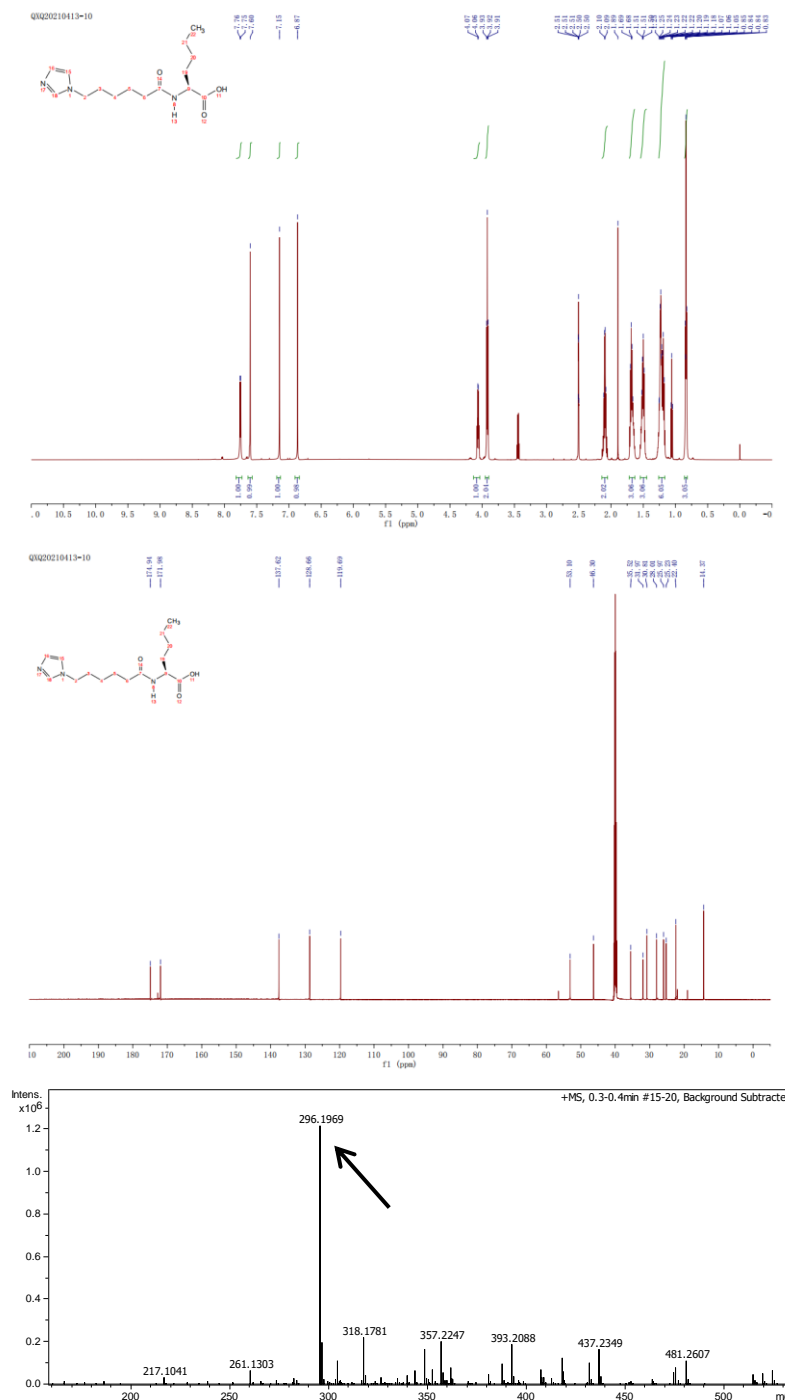
Scheme S2. Synthesis of DFSMs.

**2a:** Colorless oil (42% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$  8.02-8.01 (d,  $J$  = 6 Hz, 1H), 7.64 (s, 1H), 7.16 (s, 1H), 6.89 (m, 1H), 4.18-4.15 (m, 1H), 3.94-3.92 (t,  $J$  = 12 Hz, 2H), 2.13-2.08 (m, 2H), 1.72-1.67 (m, 3H), 1.66-1.61 (m, 1H), 1.58-1.48 (m, 3H), 1.33-1.26 (m, 2H), 1.21-1.16 (m, 2H), 0.87-0.84 (t,  $J$  = 18 Hz, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO-d}_6$ )  $\delta$  172.56, 137.56, 128.45, 119.76, 51.91, 46.36, 35.26, 33.62, 30.74, 25.91, 25.13, 19.15, 13.95. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{15}\text{H}_{26}\text{N}_3\text{O}_3$ : 280.1667; found: 280.1664.



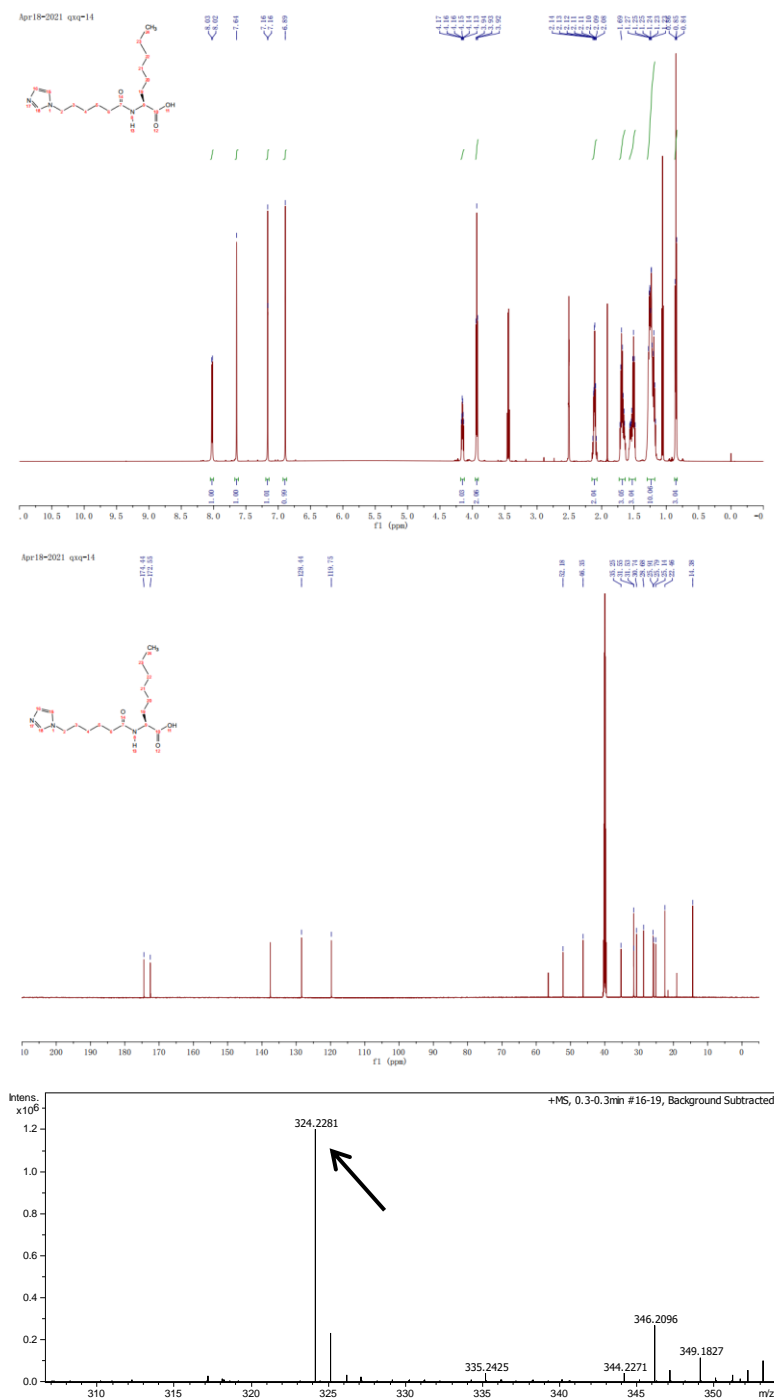
**Figure S13.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2a**.

**2b**: Colorless oil (52% yield),  $^1\text{H}$ -NMR (600 MHz, DMSO- $d_6$ )  $\delta$  7.76-7.75 (d,  $J$  = 6 Hz, 1H), 7.60 (s, 1H), 7.15 (s, 1H), 6.87 (m, 1H), 4.07-4.06 (m, 1H), 3.93 (t,  $J$  = 12 Hz, 2H), 2.11-2.08 (m, 3H), 1.70-1.66 (m, 3H), 1.52-1.49 (m, 3H), 1.25 – 1.19 (m, 6H), 0.85-0.83 (m, 3H).  $^{13}\text{C}$ -NMR (151 MHz, DMSO- $d_6$ )  $\delta$  174.94, 171.98, 137.62, 128.66, 119.69, 53.10, 46.30, 35.52, 31.97, 30.81, 28.01, 25.97, 25.23, 22.40, 14.37. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{15}\text{H}_{26}\text{N}_3\text{O}_3$ : 296.1969; found: 296.1969.



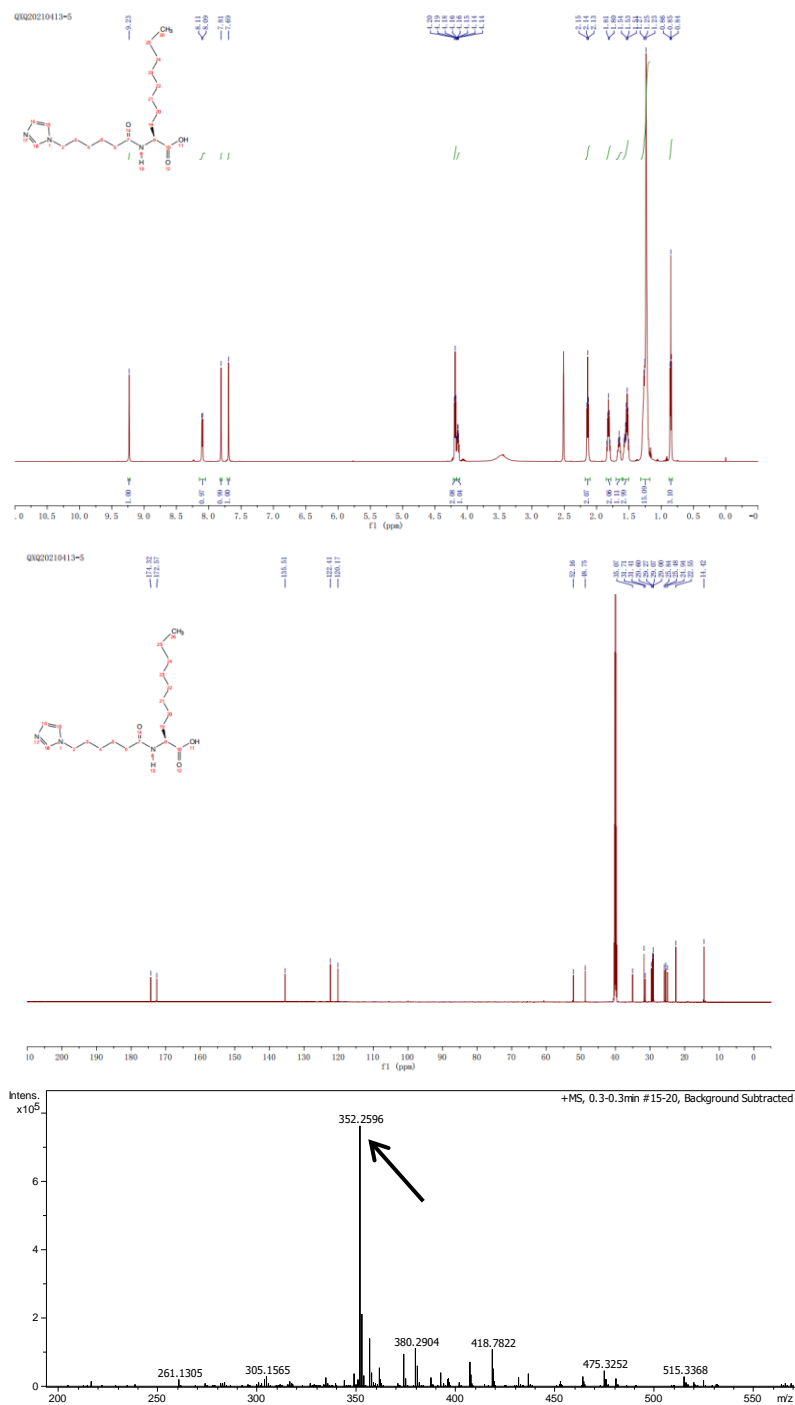
**Figure S14.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2b**.

**2c**: Colorless oil (63% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.03 (d,  $J = 6$  Hz, 1H), 7.64 (s, 1H), 7.16 (s, 1H), 6.89 (m, 1H), 4.17–4.13 (m, 1H), 3.94 (t,  $J = 12$  Hz, 2H), 2.14–2.08 (m, 3H), 1.71–1.66 (m, 3H), 1.53–1.49 (m, 3H), 1.27 – 1.23 (m, 6H), 0.86–0.84 (m, 3H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  174.44, 172.55, 119.75, 52.18, 46.35, 35.25, 31.55, 30.74, 28.68, 25.91, 25.79, 25.14, 22.46, 14.38. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{17}\text{H}_{30}\text{N}_3\text{O}_3$ : 324.2281; found: 324.2282.



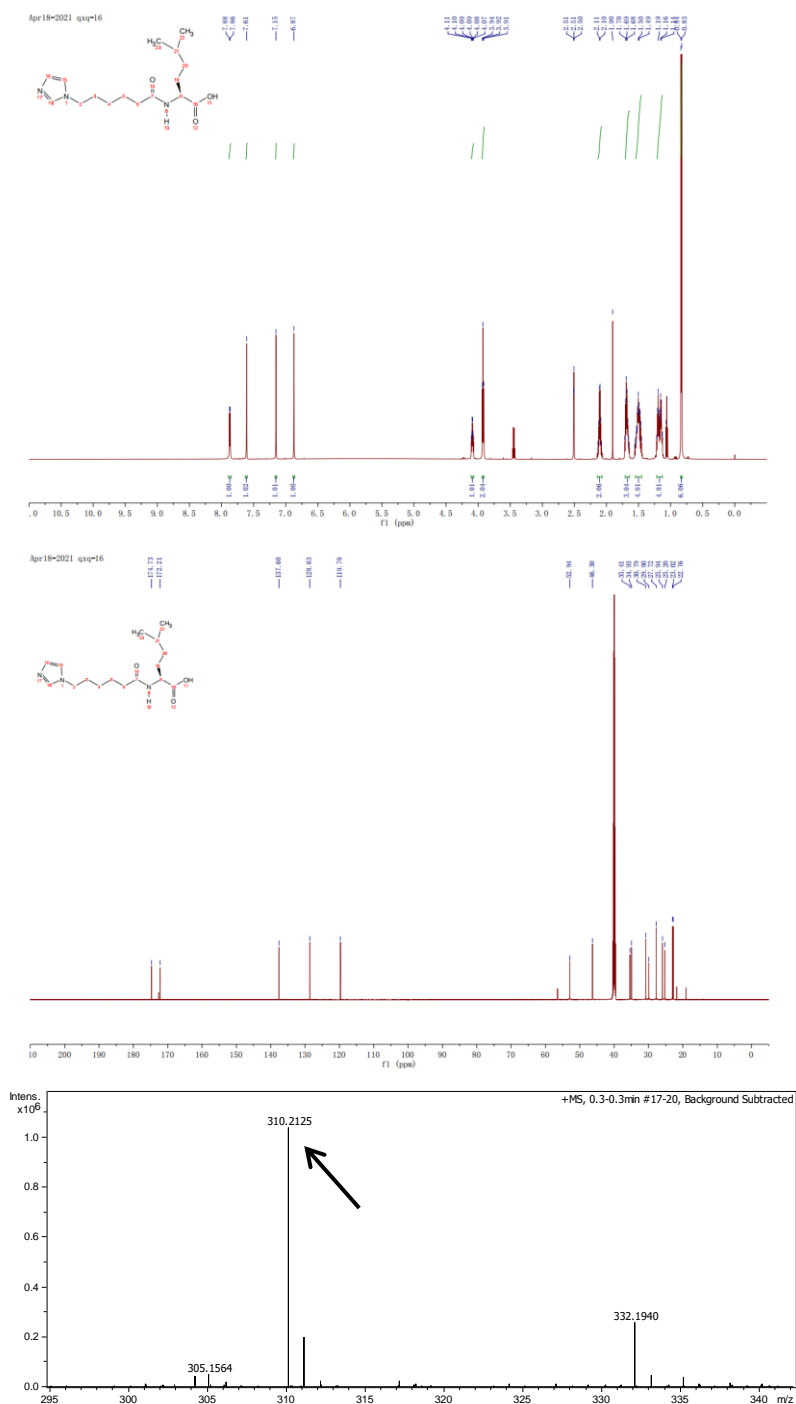
**Figure S15.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2c**.

**2d**: Colorless oil (71% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$  9.23 (s, 1H), 8.11 (d,  $J = 12$  Hz, 1H), 7.81 (s, 1H), 7.68 (m, 1H), 4.20-4.18 (t,  $J = 12$  Hz, 3H), 4.16-4.14 (m, 1H), 2.15-2.13 (t,  $J = 12$  Hz, 2H), 1.84-1.79 (m, 2H), 1.66-1.64 (m, 1H), 1.57-1.53 (m, 3H), 1.27-1.23 (m, 15H), 0.86-0.84 (m, 3H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO-d}_6$ )  $\delta$  174.32, 172.57, 135.51, 122.41, 120.17, 52.16, 48.75, 35.07, 31.71, 31.41, 29.60, 29.27, 29.07, 29.00, 25.84, 25.48, 24.94, 22.55, 14.42. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{19}\text{H}_{34}\text{N}_3\text{O}_3$ : 352.2596; found: 352.2595.



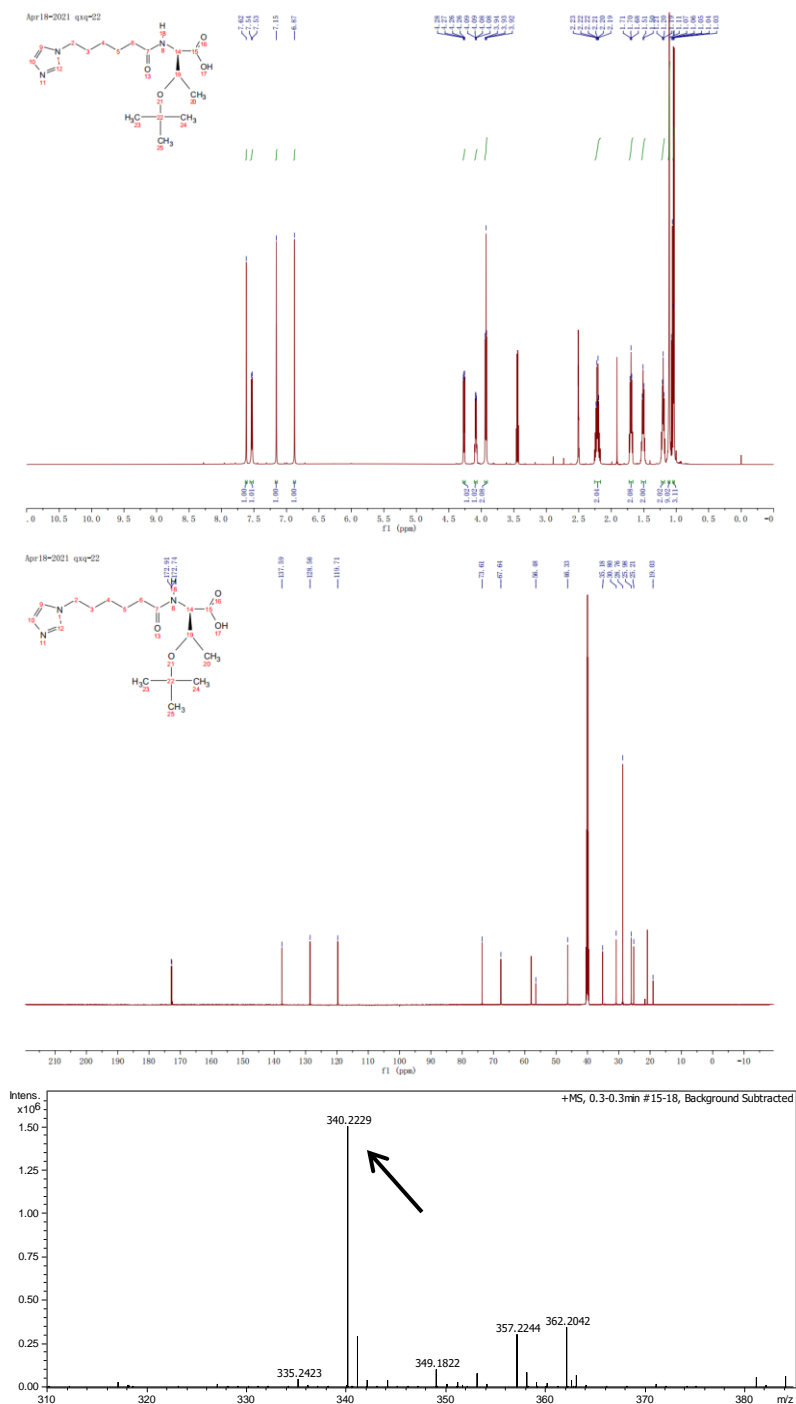
**Figure S16.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2d**.

**2e**: Colorless oil (58% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  7.88 (d,  $J$  = 12 Hz, 1H), 7.61 (s, 1H), 7.15 (s, 1H), 6.87 (m, 1H), 4.11–4.07 (m, 1H), 3.94–3.91 (t,  $J$  = 18 Hz, 2H), 2.13–2.08 (m, 2H), 1.71–1.65 (m, 2H), 1.52–1.47 (m, 4H), 1.20–1.107 (m, 4H), 0.84–0.83 (d,  $J$  = 6 Hz, 6H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  174.73, 172.21, 137.60, 128.63, 119.70, 52.94, 46.30, 35.41, 34.93, 30.79, 29.90, 27.72, 25.94, 25.20, 23.02, 22.76. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{16}\text{H}_{28}\text{N}_3\text{O}_3$ : 310.2125; found: 310.2125.



**Figure S17.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2e**.

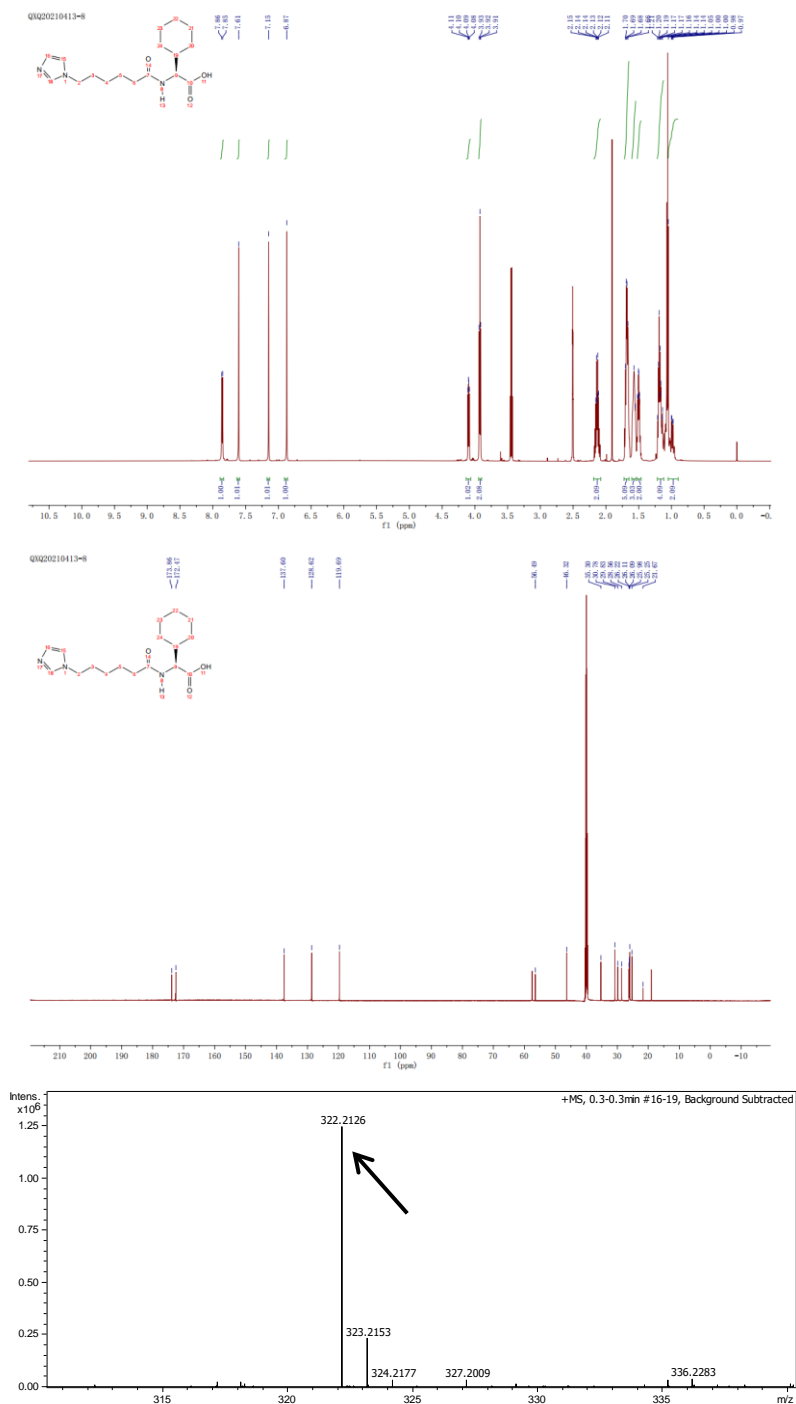
**2f**: Colorless oil (49% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  7.62 (s, 1H), 7.54 (d,  $J = 6$  Hz, 1H), 7.15 (s, 1H), 6.87 (m, 1H), 4.28-4.26 (q, 1H), 4.10-4.07 (m, 1H), 3.94-3.92 (t,  $J = 12$  Hz, 2H), 2.23-2.19 (m, 2H), 1.71-1.68 (m, 2H), 1.52-1.50 (m, 2H), 1.11 (s, 9H), 1.05-1.03 (d,  $J = 12$  Hz, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  172.91, 172.74, 137.59, 128.56, 119.71, 73.61, 67.64, 56.48, 46.33, 35.18, 30.80, 28.76, 25.98, 25.21, 19.03. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{18}\text{H}_{24}\text{N}_3\text{O}_3$ : 339.2210; found: 340.2229.



**Figure S18.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2f**.



**2g**: Colorless oil (67% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  7.86 (d,  $J$  = 6 Hz, 1H), 7.61 (s, 1H), 7.15 (s, 1H), 6.87 (m, 1H), 4.11-4.08 (m, 1H), 3.93-3.91 (t,  $J$  = 12 Hz, 2H), 2.15-2.11 (m, 2H), 1.70-1.66 (m, 5H), 1.57-1.49 (m, 5H), 1.21-1.14 (m, 4H), 1.00-0.97 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  173.86, 172.47, 137.60, 128.62, 119.69, 56.49, 46.32, 35.30, 30.78, 29.83, 26.22, 26.11, 26.09, 25.98, 25.25, 21.67. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{17}\text{H}_{28}\text{N}_3\text{O}_3$ : 322.2126; found: 322.2125.



**Figure S19.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2g**.

**2h**: Colorless oil (72% yield),  $^1\text{H}$ -NMR (600 MHz, DMSO- $d_6$ )  $\delta$  8.02 (d,  $J$  = 6 Hz, 1H), 7.61 (s, 1H), 7.15 (s, 1H), 6.88 (m, 1H), 4.24-4.23 (m, 1H), 3.94-3.91 (t,  $J$  = 18 Hz, 2H), 2.12-2.08 (m, 2H), 1.71-1.61 (m, 7H), 1.52-1.47 (m, 4H), 1.30-1.11 (m, 6H), 0.94-0.90 (m, 1H), 0.84-0.78 (m, 1H).  $^{13}\text{C}$ -NMR (151 MHz, DMSO- $d_6$ )  $\delta$  174.94, 172.49, 137.59, 128.63, 119.70, 49.89, 46.31, 35.29, 34.08, 33.61, 31.98, 30.75, 26.48, 26.27, 26.08, 25.87, 25.14. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{18}\text{H}_{23}\text{BrN}_3\text{O}_3$ : 408.0908; found: 408.0917.

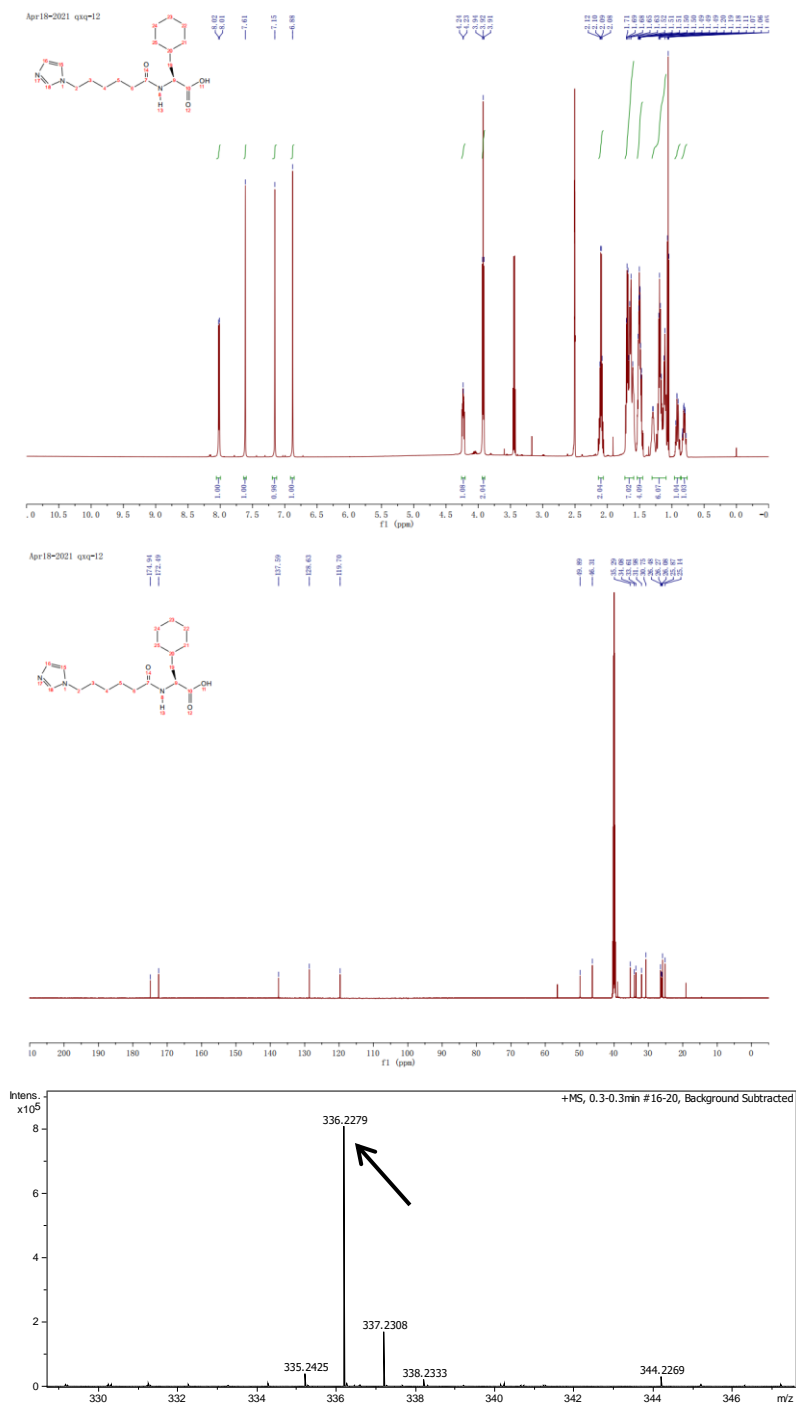
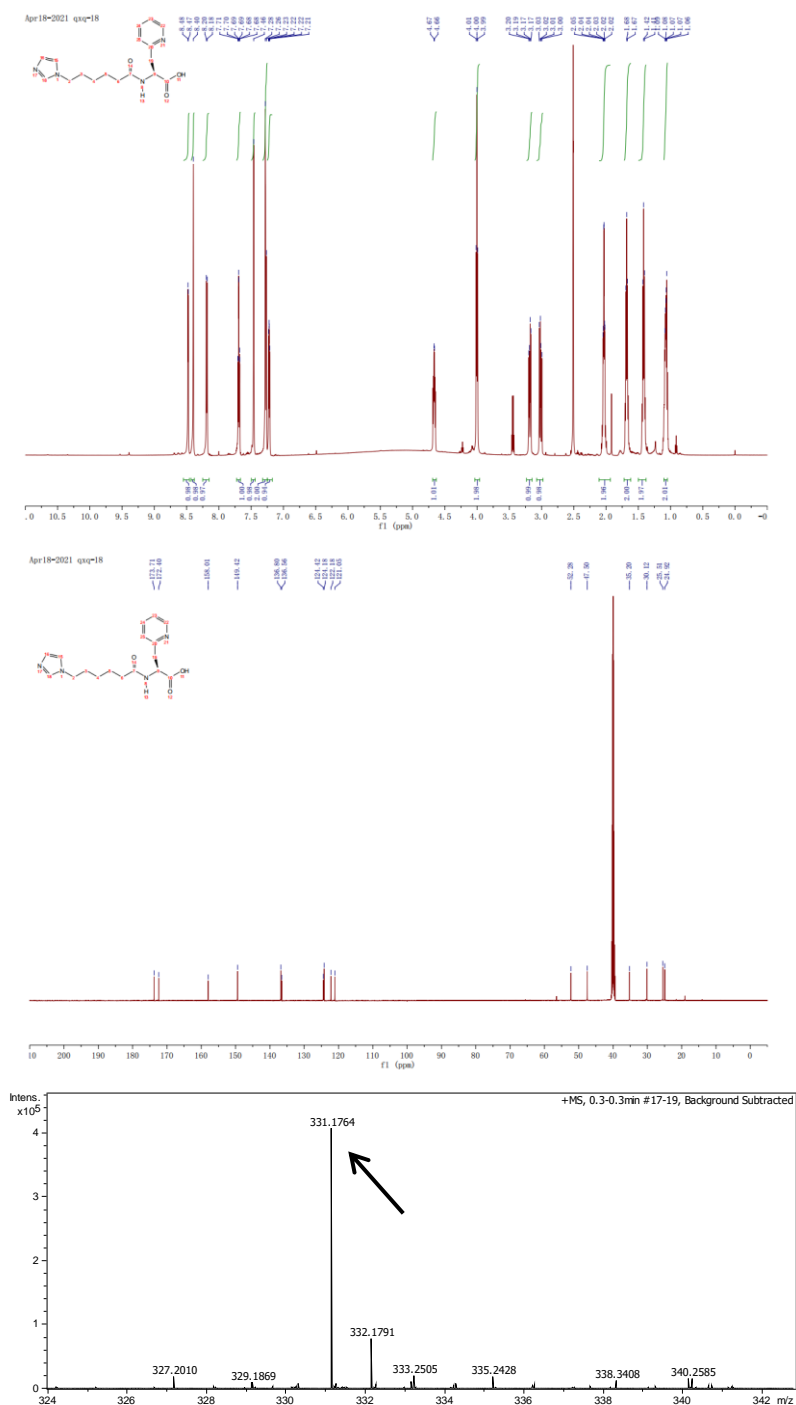


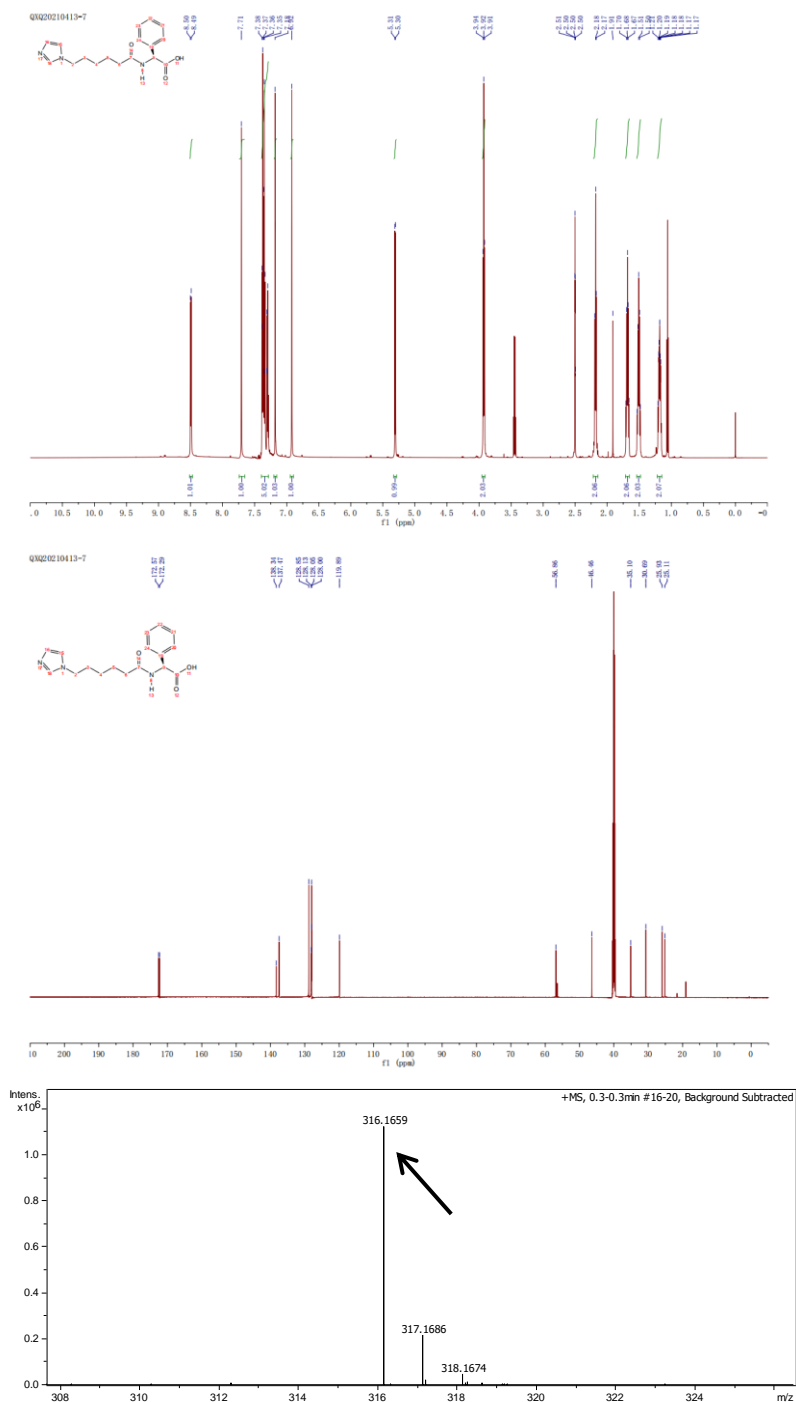
Figure S20.  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2h**.

**2i:** Colorless oil (61% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.48 (d,  $J = 6$  Hz, 1H), 8.40 (s, 1H), 8.20 (d,  $J = 12$  Hz, 1H), 7.71–7.68 (m, 1H), 7.46 (s, 1H), 7.28 (d,  $J = 12$  Hz, 2H), 7.23–7.21 (m, 1H), 4.67–4.66 (m, 1H), 4.01–3.99 (t,  $J = 12$  Hz, 2H), 3.20–3.17 (m, 1H), 3.03–3.00 (m, 1H), 2.05–2.02 (m, 2H), 1.69–1.67 (m, 2H), 1.43–1.41 (m, 2H), 1.09–1.06 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  173.71, 172.40, 158.01, 149.42, 136.80, 136.56, 124.42, 124.18, 122.18, 121.05, 52.28, 47.50, 35.20, 30.12, 25.51, 24.92. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{17}\text{H}_{23}\text{N}_4\text{O}_3$ : 331.1764; found: 331.1765.



**Figure S21.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2i**.

**2j**: Colorless oil (81% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.50 (d,  $J = 6$  Hz, 1H), 7.71 (s, 1H), 7.39–7.30 (m, 5H), 7.18 (s, 1H), 7.46 (s, 1H), 6.92 (s, 1H), 5.31–5.30 (d,  $J = 6$  Hz, 1H), 3.94–3.91 (t,  $J = 18$  Hz, 2H), 2.19–2.17 (m, 2H), 1.71–1.66 (m, 2H), 1.53–1.48 (m, 2H), 1.21–1.17 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  172.57, 172.29, 138.34, 128.85, 128.13, 128.05, 128.00, 119.89, 56.86, 46.46, 35.10, 30.69, 25.93, 25.11. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{17}\text{H}_{22}\text{N}_3\text{O}_3$ : 316.1659; found: 316.1656.



**Figure S22.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2j**.

**2k**: Colorless oil (76% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.21 (d,  $J = 6$  Hz, 1H), 8.10 (s, 1H), 7.35 (s, 1H), 7.30 (t,  $J = 18$  Hz, 2H), 7.20-7.18 (m, 3H), 7.12 (s, 1H), 4.16-4.12 (m, 1H), 4.02-4.00 (t,  $J = 12$  Hz, 2H), 2.64-2.57 (m, 2H), 2.18-2.14 (m, 2H), 1.97-1.95 (m, 1H), 1.88-1.85 (m, 1H), 1.76-1.72 (m, 2H), 1.56-1.52 (m, 2H), 1.26-1.22 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  174.22, 172.71, 141.55, 136.99, 128.82, 126.08, 120.54, 51.78, 47.06, 35.26, 33.31, 31.99, 30.43, 25.82, 25.08. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{19}\text{H}_{26}\text{N}_3\text{O}_3$ : 344.1968; found: 344.1969.

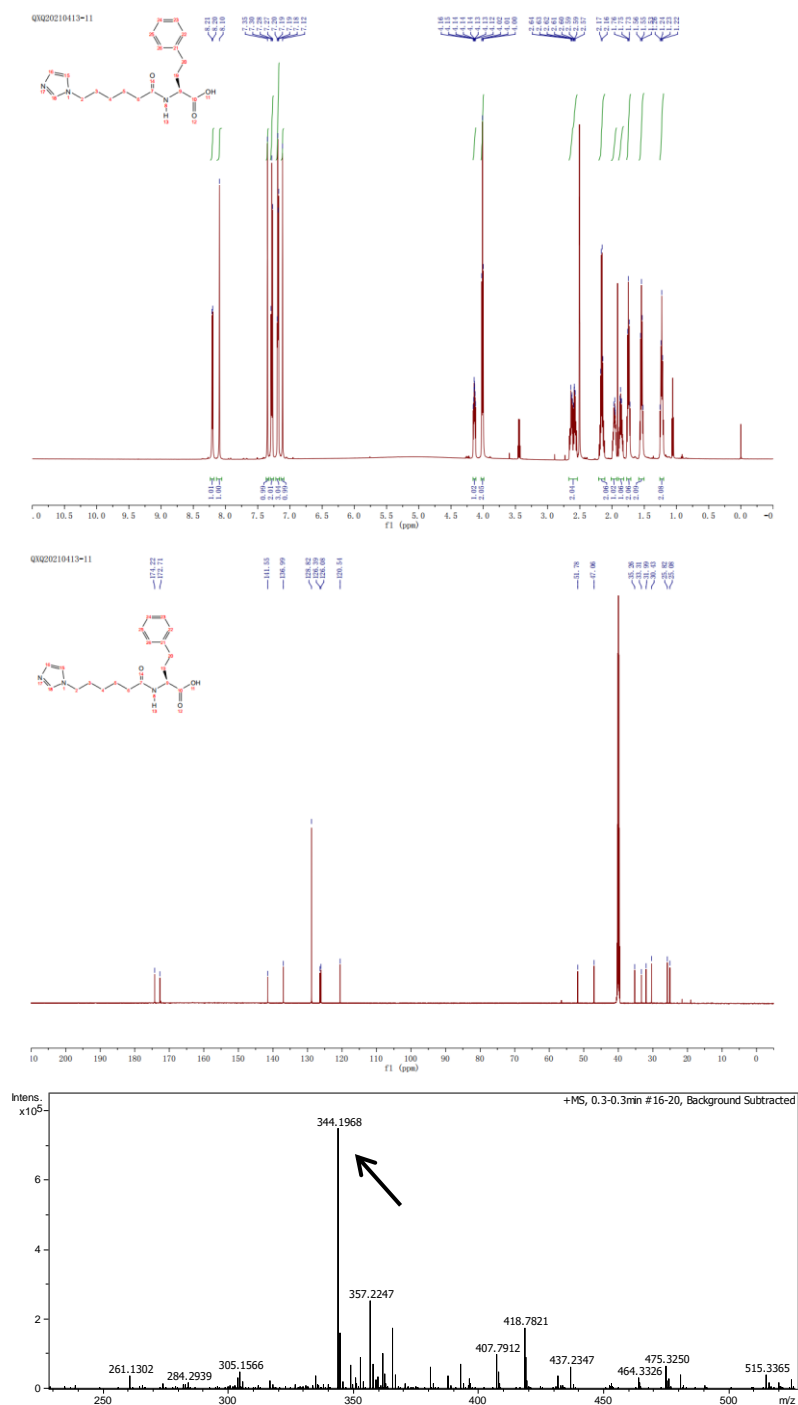
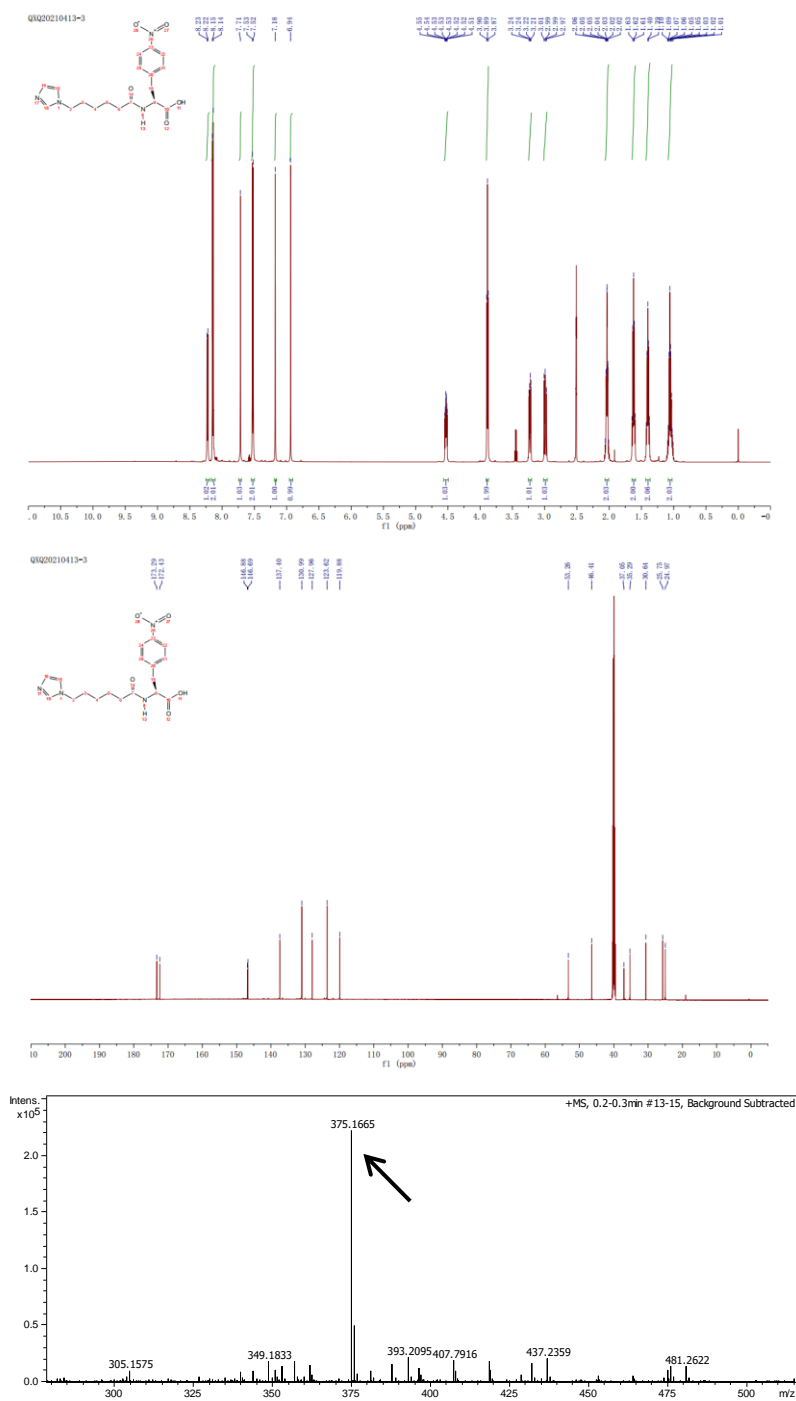


Figure S23.  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2k**.

Chemical structure of compound 10: OC(=O)C1=CC=C(C=C1)C2=CC=CC=C2C3=CC=CC=C3C4=CC=CC=C4C5=CC=CC=C5C6=CC=CC=C6C7=CC=CC=C7C8=CC=CC=C8C9=CC=CC=C9C10=CC=CC=C10C11=CC=CC=C11C12=CC=CC=C12C13=CC=CC=C13C14=CC=CC=C14C15=CC=CC=C15C16=CC=CC=C16C17=CC=CC=C17C18=CC=CC=C18C19=CC=CC=C19C20=CC=CC=C20C21=CC=CC=C21C22=CC=CC=C22C23=CC=CC=C23C24=CC=CC=C24C25=CC=CC=C25C26=CC=CC=C26C27=CC=CC=C27C28=CC=CC=C28C29=CC=CC=C29C30=CC=CC=C30C31=CC=CC=C31C32=CC=CC=C32C33=CC=CC=C33C34=CC=CC=C34C35=CC=CC=C35C36=CC=CC=C36C37=CC=CC=C37C38=CC=CC=C38C39=CC=CC=C39C40=CC=CC=C40C41=CC=CC=C41C42=CC=CC=C42C43=CC=CC=C43C44=CC=CC=C44C45=CC=CC=C45C46=CC=CC=C46C47=CC=CC=C47C48=CC=CC=C48C49=CC=CC=C49C50=CC=CC=C50C51=CC=CC=C51C52=CC=CC=C52C53=CC=CC=C53C54=CC=CC=C54C55=CC=CC=C55C56=CC=CC=C56C57=CC=CC=C57C58=CC=CC=C58C59=CC=CC=C59C60=CC=CC=C60C61=CC=CC=C61C62=CC=CC=C62C63=CC=CC=C63C64=CC=CC=C64C65=CC=CC=C65C66=CC=CC=C66C67=CC=CC=C67C68=CC=CC=C68C69=CC=CC=C69C70=CC=CC=C70C71=CC=CC=C71C72=CC=CC=C72C73=CC=CC=C73C74=CC=CC=C74C75=CC=CC=C75C76=CC=CC=C76C77=CC=CC=C77C78=CC=CC=C78C79=CC=CC=C79C80=CC=CC=C80C81=CC=CC=C81C82=CC=CC=C82C83=CC=CC=C83C84=CC=CC=C84C85=CC=CC=C85C86=CC=CC=C86C87=CC=CC=C87C88=CC=CC=C88C89=CC=CC=C89C90=CC=CC=C90C91=CC=CC=C91C92=CC=CC=C92C93=CC=CC=C93C94=CC=CC=C94C95=CC=CC=C95C96=CC=CC=C96C97=CC=CC=C97C98=CC=CC=C98C99=CC=CC=C99C100=CC=CC=C100C101=CC=CC=C101C102=CC=CC=C102C103=CC=CC=C103C104=CC=CC=C104C105=CC=CC=C105C106=CC=CC=C106C107=CC=CC=C107C108=CC=CC=C108C109=CC=CC=C109C110=CC=CC=C110C111=CC=CC=C111C112=CC=CC=C112C113=CC=CC=C113C114=CC=CC=C114C115=CC=CC=C115C116=CC=CC=C116C117=CC=CC=C117C118=CC=CC=C118C119=CC=CC=C119C120=CC=CC=C120C121=CC=CC=C121C122=CC=CC=C122C123=CC=CC=C123C124=CC=CC=C124C125=CC=CC=C125C126=CC=CC=C126C127=CC=CC=C127C128=CC=CC=C128C129=CC=CC=C129C130=CC=CC=C130C131=CC=CC=C131C132=CC=CC=C132C133=CC=CC=C133C134=CC=CC=C134C135=CC=CC=C135C136=CC=CC=C136C137=CC=CC=C137C138=CC=CC=C138C139=CC=CC=C139C140=CC=CC=C140C141=CC=CC=C141C142=CC=CC=C142C143=CC=CC=C143C144=CC=CC=C144C145=CC=CC=C145C146=CC=CC=C146C147=CC=CC=C147C148=CC=CC=C148C149=CC=CC=C149C150=CC=CC=C150C151=CC=CC=C151C152=CC=CC=C152C153=CC=CC=C153C154=CC=CC=C154C155=CC=CC=C155C156=CC=CC=C156C157=CC=CC=C157C158=CC=CC=C158C159=CC=CC=C159C160=CC=CC=C160C161=CC=CC=C161C162=CC=CC=C162C163=CC=CC=C163C164=CC=CC=C164C165=CC=CC=C165C166=CC=CC=C166C167=CC=CC=C167C168=CC=CC=C168C169=CC=CC=C169C170=CC=CC=C170C171=CC=CC=C171C172=CC=CC=C172C173=CC=CC=C173C174=CC=CC=C174C175=CC=CC=C175C176=CC=CC=C176C177=CC=CC=C177C178=CC=CC=C178C179=CC=CC=C179C180=CC=CC=C180C181=CC=CC=C181C182=CC=CC=C182C183=CC=CC=C183C184=CC=CC=C184C185=CC=CC=C185C186=CC=CC=C186C187=CC=CC=C187C188=CC=CC=C188C189=CC=CC=C189C190=CC=CC=C190C191=CC=CC=C191C192=CC=CC=C192C193=CC=CC=C193C194=CC=CC=C194C195=CC=CC=C195C196=CC=CC=C196C197=CC=CC=C197C198=CC=CC=C198C199=CC=CC=C199C200=CC=CC=C200C201=CC=CC=C201C202=CC=CC=C202C203=CC=CC=C203C204=CC=CC=C204C205=CC=CC=C205C206=CC=CC=C206C207=CC=CC=C207C208=CC=CC=C208C209=CC=CC=C209C210=CC=CC=C210C211=CC=CC=C211C212=CC=CC=C212C213=CC=CC=C213C214=CC=CC=C214C215=CC=CC=C215C216=CC=CC=C216C217=CC=CC=C217C218=CC=CC=C218C219=CC=CC=C219C220=CC=CC=C220C221=CC=CC=C221C222=CC=CC=C222C223=CC=CC=C223C224=CC=CC=C224C225=CC=CC=C225C226=CC=CC=C226C227=CC=CC=C227C228=CC=CC=C228C229=CC=CC=C229C230=CC=CC=C230C231=CC=CC=C231C232=CC=CC=C232C233=CC=CC=C233C234=CC=CC=C234C235=CC=CC=C235C236=CC=CC=C236C237=CC=CC=C237C238=CC=CC=C238C239=CC=CC=C239C240=CC=CC=C240C241=CC=CC=C241C242=CC=CC=C242C243=CC=CC=C243C244=CC=CC=C244C245=CC=CC=C245C246=CC=CC=C246C247=CC=CC=C247C248=CC=CC=C248C249=CC=CC=C249C250=CC=CC=C250C251=CC=CC=C251C252=CC=CC=C252C253=CC=CC=C253C254=CC=CC=C254C255=CC=CC=C255C256=CC=CC=C256C257=CC=CC=C257C258=CC=CC=C258C259=CC=CC=C259C260=CC=CC=C260C261=CC=CC=C261C262=CC=CC=C262C263=CC=CC=C263C264=CC=CC=C264C265=CC=CC=C265C266=CC=CC=C266C267=CC=CC=C267C268=CC=CC=C268C269=CC=CC=C269C270=CC=CC=C270C271=CC=CC=C271C272=CC=CC=C272C273=CC=CC=C273C274=CC=CC=C274C275=CC=CC=C275C276=CC=CC=C276C277=CC=CC=C277C278=CC=CC=C278C279=CC=CC=C279C280=CC=CC=C280C281=CC=CC=C281C282=CC=CC=C282C283=CC=CC=C283C284=CC=CC=C284C285=CC=CC=C285C286=CC=CC=C286C287=CC=CC=C287C288=CC=CC=C288C289=CC=CC=C289C290=CC=CC=C290C291=CC=CC=C291C292=CC=CC=C292C293=CC=CC=C293C294=CC=CC=C294C295=CC=CC=C295C296=CC=CC=C296C297=CC=CC=C297C298=CC=CC=C298C299=CC=CC=C299C300=CC=CC=C300C301=CC=CC=C301C302=CC=CC=C302C303=CC=CC=C303C304=CC=CC=C304C305=CC=CC=C305C306=CC=CC=C306C307=CC=CC=C307C308=CC=CC=C308C309=CC=CC=C309C310=CC=CC=C310C311=CC=CC=C311C312=CC=CC=C312C313=CC=CC=C313C314=CC=CC=C314C315=CC=CC=C315C316=CC=CC=C316C317=CC=CC=C317C318=CC=CC=C318C319=CC=CC=C319C320=CC=CC=C320C321=CC=CC=C321C322=CC=CC=C322C323=CC=CC=C323C324=CC=CC=C324C325=CC=CC=C325C326=CC=CC=C326C327=CC=CC=C327C328=CC=CC=C328C329=CC=CC=C329C330=CC=CC=C330C331=CC=CC=C331C332=CC=CC=C332C333=CC=CC=C333C334=CC=CC=C334C335=CC=CC=C335C336=CC=CC=C336C337=CC=CC=C337C338=CC=CC=C338C339=CC=CC=C339C340=CC=CC=C340C341=CC=CC=C341C342=CC=CC=C342C343=CC=CC=C343C344=CC=CC=C344C345=CC=CC=C345C346=CC=CC=C346C347=CC=CC=C347C348=CC=CC=C348C349=CC

**Figure S24.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2l**.

**2m**: Colorless solid (88% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.23 (d,  $J = 6$  Hz, 1H), 8.15 (d,  $J = 6$  Hz, 2H), 7.71 (s, 1H), 7.53 (d,  $J = 6$  Hz, 2H), 7.18 (s, 1H), 6.94 (s, 1H), 4.55-4.51 (m, 1H), 3.90-3.87 (t,  $J = 18$  Hz, 2H), 3.24-3.21 (m, 1H), 3.01-2.97 (m, 1H), 2.06-2.01 (m, 2H), 1.65-1.60 (m, 2H), 1.43-1.38 (m, 2H), 1.10-1.01 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  173.29, 172.43, 146.88, 146.69, 137.40, 130.99, 127.96, 123.62, 119.88, 53.26, 46.41, 37.05, 35.29, 30.64, 25.75, 24.97. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{18}\text{H}_{23}\text{N}_4\text{O}_5$ : 375.1665; found: 375.1663.



**Figure S25.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2m**.

Chemical structure of compound 16: CC1=CC=C(C=C1)C(=O)N[C@@H](C(=O)OCCOC2=CC=CC=C2)C(=O)O

<sup>1</sup>H NMR spectrum (400 MHz, DMSO-d<sub>6</sub>) peaks (ppm): 8.04 (d, 1H), 7.44 (d, 1H), 7.34 (d, 1H), 7.24 (d, 1H), 4.34 (t, 1H), 3.94 (t, 1H), 3.04 (t, 1H), 2.94 (t, 1H), 2.84 (t, 1H), 2.74 (t, 1H), 2.64 (t, 1H), 2.54 (t, 1H), 2.44 (t, 1H), 2.34 (t, 1H), 2.24 (t, 1H), 2.14 (t, 1H), 2.04 (t, 1H), 1.94 (t, 1H), 1.84 (t, 1H), 1.74 (t, 1H), 1.64 (t, 1H), 1.54 (t, 1H), 1.44 (t, 1H), 1.34 (t, 1H), 1.24 (t, 1H), 1.14 (t, 1H), 1.04 (t, 1H), 0.94 (t, 1H), 0.84 (t, 1H), 0.74 (t, 1H), 0.64 (t, 1H), 0.54 (t, 1H), 0.44 (t, 1H), 0.34 (t, 1H), 0.24 (t, 1H), 0.14 (t, 1H), 0.04 (t, 1H).

<sup>13</sup>C NMR spectrum (100 MHz, DMSO-d<sub>6</sub>) peaks (ppm): 174.4, 173.4, 172.4, 171.4, 170.4, 169.4, 168.4, 167.4, 166.4, 165.4, 164.4, 163.4, 162.4, 161.4, 160.4, 159.4, 158.4, 157.4, 156.4, 155.4, 154.4, 153.4, 152.4, 151.4, 150.4, 149.4, 148.4, 147.4, 146.4, 145.4, 144.4, 143.4, 142.4, 141.4, 140.4, 139.4, 138.4, 137.4, 136.4, 135.4, 134.4, 133.4, 132.4, 131.4, 130.4, 129.4, 128.4, 127.4, 126.4, 125.4, 124.4, 123.4, 122.4, 121.4, 120.4, 119.4, 118.4, 117.4, 116.4, 115.4, 114.4, 113.4, 112.4, 111.4, 110.4, 109.4, 108.4, 107.4, 106.4, 105.4, 104.4, 103.4, 102.4, 101.4, 100.4, 99.4, 98.4, 97.4, 96.4, 95.4, 94.4, 93.4, 92.4, 91.4, 90.4, 89.4, 88.4, 87.4, 86.4, 85.4, 84.4, 83.4, 82.4, 81.4, 80.4, 79.4, 78.4, 77.4, 76.4, 75.4, 74.4, 73.4, 72.4, 71.4, 70.4, 69.4, 68.4, 67.4, 66.4, 65.4, 64.4, 63.4, 62.4, 61.4, 60.4, 59.4, 58.4, 57.4, 56.4, 55.4, 54.4, 53.4, 52.4, 51.4, 50.4, 49.4, 48.4, 47.4, 46.4, 45.4, 44.4, 43.4, 42.4, 41.4, 40.4, 39.4, 38.4, 37.4, 36.4, 35.4, 34.4, 33.4, 32.4, 31.4, 30.4, 29.4, 28.4, 27.4, 26.4, 25.4, 24.4, 23.4, 22.4, 21.4, 20.4, 19.4, 18.4, 17.4, 16.4, 15.4, 14.4, 13.4, 12.4, 11.4, 10.4, 9.4, 8.4, 7.4, 6.4, 5.4, 4.4, 3.4, 2.4, 1.4, 0.4.

MS spectrum (ESI+) peaks (m/z): 261.1304, 304.2605, 344.1969 (base peak), 366.1785, 381.2969, 407.7912, 418.7822, 437.2348, 464.3328.

**Figure S26.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2n**.



**2o**: Colorless oil (89% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.61 (s, 1H), 8.27 (d,  $J = 12$  Hz, 1H), 7.64 (d,  $J = 12$  Hz, 1H), 7.54 (s, 1H), 7.48 (d,  $J = 12$  Hz, 2H), 7.39 (s, 1H), 4.52-4.49 (m, 1H), 4.05-4.03 (t,  $J = 12$  Hz, 2H), 3.18-3.15 (m, 1H), 2.97-2.93 (m, 1H), 2.07-2.04 (m, 2H), 1.71-1.68 (m, 2H), 1.43-1.40 (m, 2H), 1.10-1.05 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  173.32, 172.48, 143.29, 136.26, 130.46, 125.38, 125.36, 123.27, 123.27, 121.40, 53.32, 47.77, 36.91, 35.14, 29.94, 25.46, 24.83. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{19}\text{H}_{23}\text{F}_3\text{N}_3\text{O}_3$ : 398.1681; found: 398.1686.

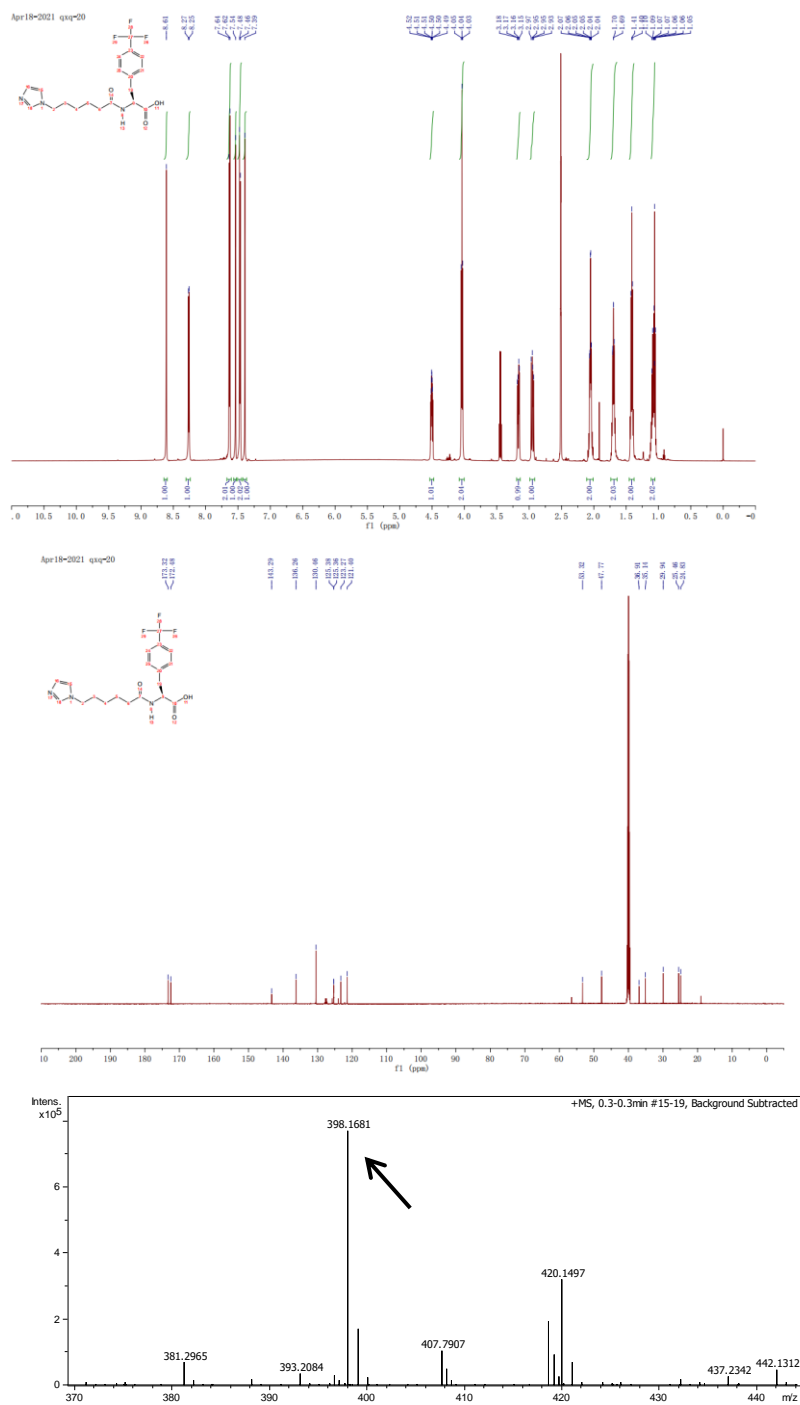


Figure S27.  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2o**.

**2p**: Colorless oil (74% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.61 (s, 1H), 8.27 (d,  $J = 12$  Hz, 1H), 7.64 (d,  $J = 12$  Hz, 1H), 7.54 (s, 1H), 7.48 (d,  $J = 12$  Hz, 2H), 7.39 (s, 1H), 4.52-4.49 (m, 1H), 4.05-4.03 (t,  $J = 12$  Hz, 2H), 3.18-3.15 (m, 1H), 2.97-2.93 (m, 1H), 2.07-2.04 (m, 2H), 1.71-1.68 (m, 2H), 1.43-1.40 (m, 2H), 1.10-1.05 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  173.32, 172.48, 143.29, 136.26, 130.46, 125.38, 125.36, 123.27, 123.27, 121.40, 53.32, 47.77, 36.91, 35.14, 29.94, 25.46, 24.83. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{22}\text{H}_{32}\text{N}_3\text{O}_4$ : 402.2382; found: 402.2387.

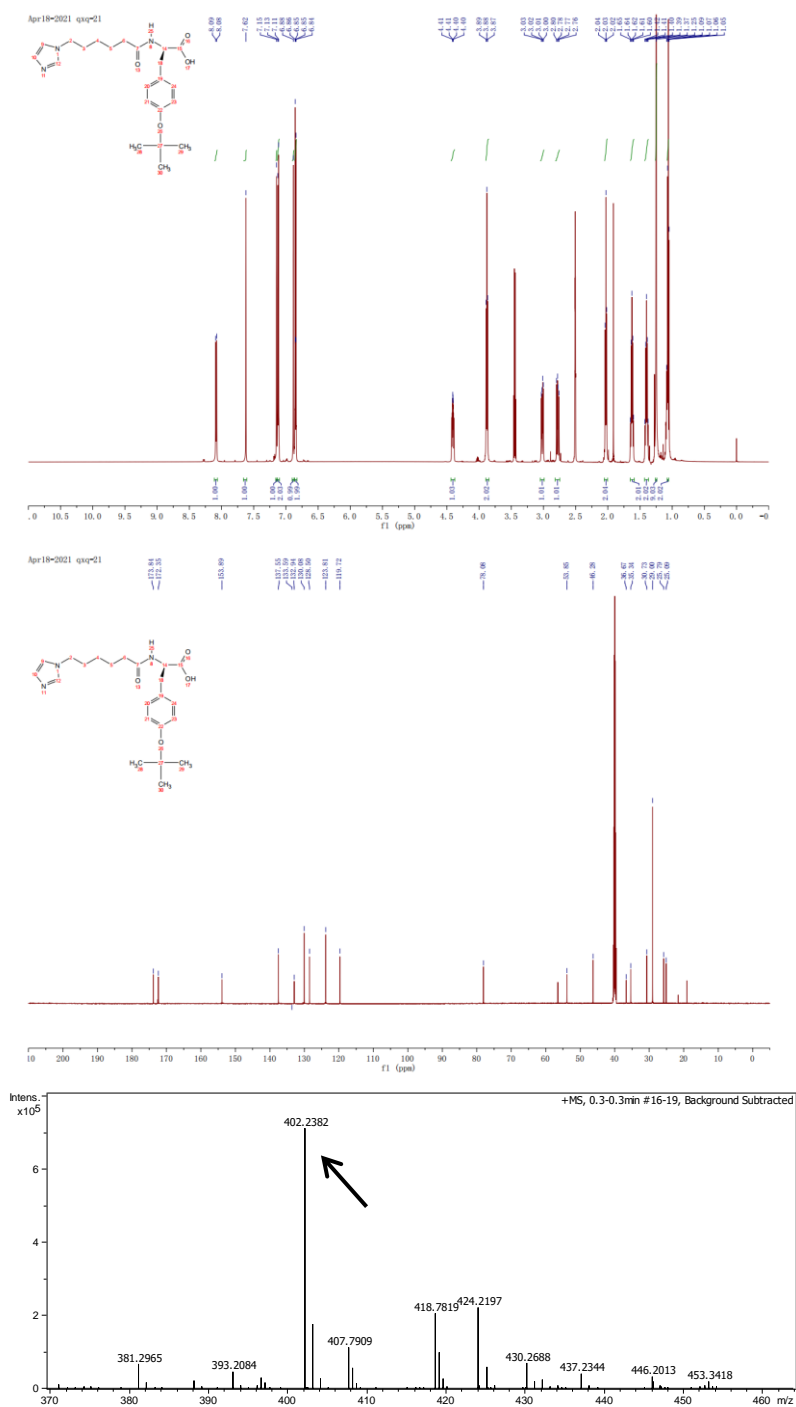
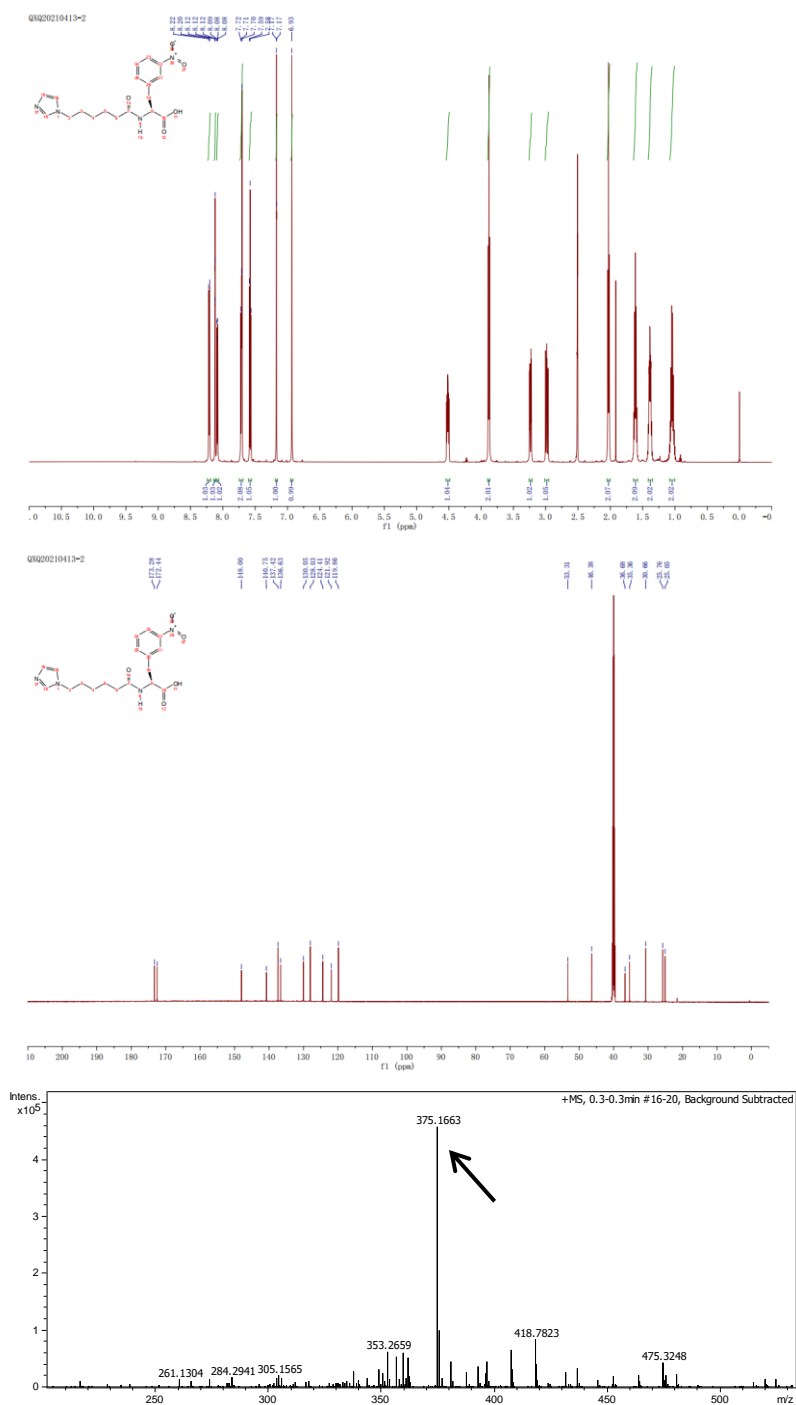


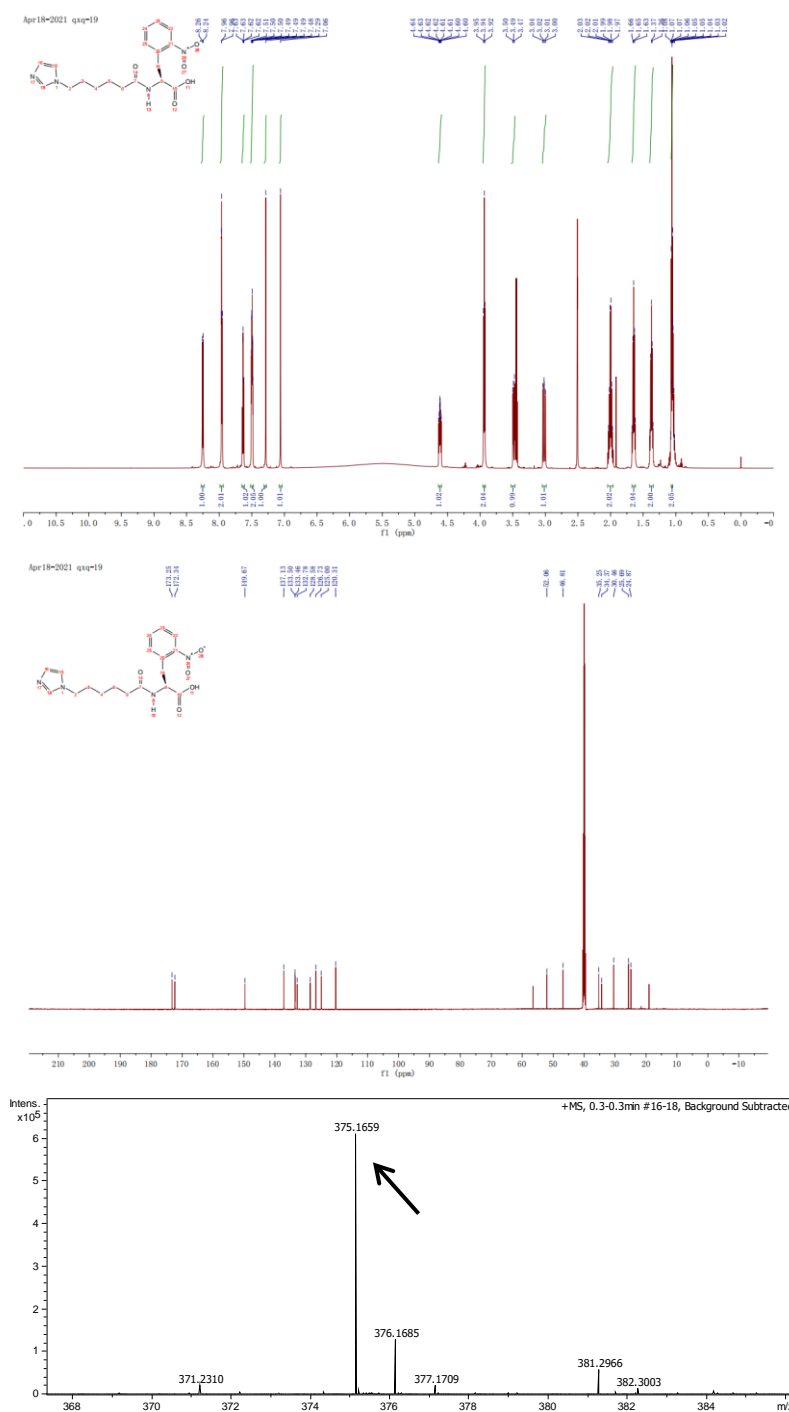
Figure S28.  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2p**.

**2q**: Colorless solid (86% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.22 (d,  $J = 6$  Hz, 1H), 8.12 (m, 2H), 8.09 (s, 1H), 7.72-7.70 (t,  $J = 12$  Hz, 2H), 7.59-7.56 (t,  $J = 18$  Hz, 1H), 7.17 (s, 1H), 6.93 (s, 1H), 4.54-4.50 (m, 1H), 3.89-3.87 (t,  $J = 12$  Hz, 2H), 3.24-3.22 (m, 1H), 3.00-2.96 (m, 1H), 2.04-2.02 (m, 2H), 1.62-1.60 (m, 2H), 1.40-1.37 (m, 2H), 1.06-1.02 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  173.28, 172.44, 148.00, 140.75, 137.42, 136.63, 130.05, 128.03, 124.41, 121.92, 119.86, 53.31, 46.38, 36.68, 35.36, 30.66, 25.76, 25.05. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{18}\text{H}_{23}\text{N}_4\text{O}_5$ : 375.1663; found: 375.1663.



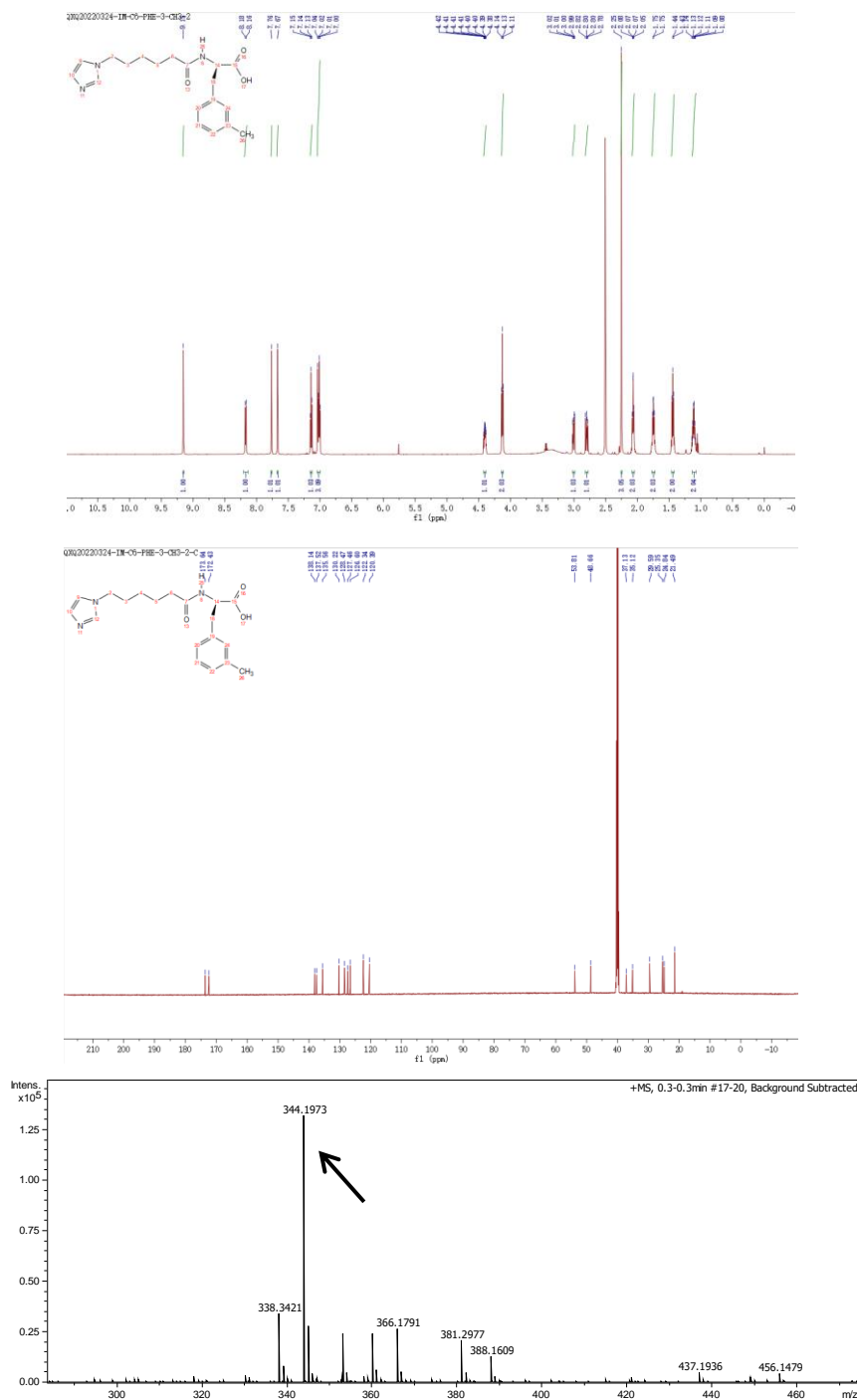
**Figure S29.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2q**.

**2r**: Colorless solid (79% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.26 (d,  $J = 6$  Hz, 1H), 7.97–7.95 (m, 2H), 7.63 (t,  $J = 6$  Hz, 1H), 7.51–7.48 (m, 2H), 7.29 (s, 1H), 7.06 (s, 1H), 4.63–4.60 (m, 1H), 3.94–3.92 (t,  $J = 12$  Hz, 2H), 3.50–3.47 (m, 1H), 3.04–3.00 (m, 1H), 2.03–1.97 (m, 2H), 1.67–1.62 (m, 2H), 1.40–1.35 (m, 2H), 1.08–1.02 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  173.25, 172.34, 149.67, 137.13, 133.50, 133.46, 132.78, 128.58, 126.73, 125.00, 120.31, 52.06, 46.81, 35.25, 34.37, 30.46, 25.69, 24.87. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{18}\text{H}_{23}\text{N}_4\text{O}_5$ : 375.1659; found: 375.1663.



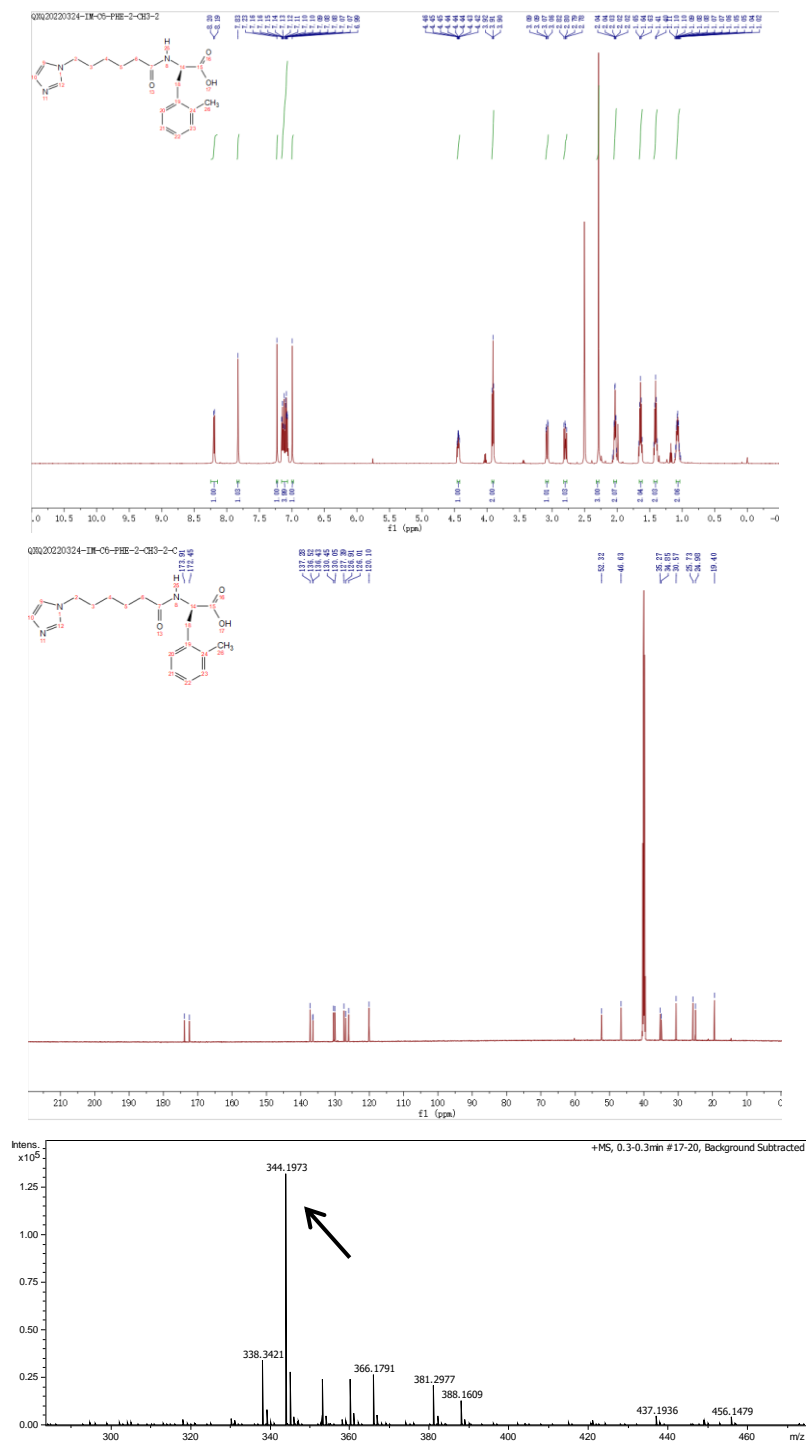
**Figure S30.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2r**.

**2s:** Colorless solid (86% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  9.15 (s, 1H), 8.18-8.16 (d,  $J$  = 12 Hz, 1H), 7.76 (s, 1H), 7.67 (s, 1H), 7.15-7.13 (t,  $J$  = 18 Hz, 1H), 7.04-7.00 (m, 3H), 4.42-4.38 (m, 1H), 4.14-4.11 (t,  $J$  = 18 Hz, 2H), 3.02-2.99 (m, 1H), 2.82-2.78 (m, 1H), 2.25 (s, 3H), 2.08-2.05 (m, 2H), 1.76-1.73 (m, 2H), 1.46-1.43 (m, 2H), 1.14-1.08 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  173.64, 172.43, 138.14, 137.52, 135.56, 130.22, 128.47, 127.46, 126.60, 122.34, 120.39, 53.81, 48.66, 37.13, 35.12, 29.59, 25.35, 24.84, 21.49. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{22}\text{H}_{26}\text{N}_3\text{O}_3$ : 344.1973; found: 344.1969.



**Figure S31.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2s**.

**2t**: Colorless solid (86% yield),  $^1\text{H}$ -NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.20-8.19 (d,  $J = 6$  Hz, 1H), 7.83 (s, 1H), 7.23 (s, 1H), 7.16-7.07 (m, 4H), 6.99 (s, 1H), 4.46-4.42 (m, 1H), 3.92-3.90 (t,  $J = 12$  Hz, 2H), 3.09-3.06 (m, 1H), 2.82-2.78 (m, 1H), 2.29 (s, 3H), 2.07-2.01 (m, 2H), 1.67-1.62 (m, 2H), 1.43-1.39 (m, 2H), 1.11-1.02 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{DMSO}-d_6$ )  $\delta$  173.91, 172.45, 137.28, 136.52, 136.42, 130.45, 130.05, 127.39, 126.91, 126.01, 120.10, 52.32, 46.63, 35.27, 34.85, 30.57, 25.73, 24.98, 19.40. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{22}\text{H}_{26}\text{N}_3\text{O}_3$ : 344.1973; found: 344.1969.



**Figure S32.**  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2t**.

**2w**: Colorless solid (88% yield),  $^1\text{H}$ -NMR (600 MHz, DMSO- $d_6$ )  $\delta$  8.21 (d,  $J$  = 12 Hz, 1H), 7.87 (d,  $J$  = 6 Hz, 1H), 7.83-7.81 (m, 2H), 7.73 (s, 1H), 7.65 (s, 1H), 7.48-7.41 (m, 3H), 7.11 (s, 1H), 6.92 (s, 1H), 4.60-4.56 (m, 1H), 3.76 (t,  $J$  = 12 Hz, 2H), 3.26-3.23 (m, 1H), 3.04-3.00 (m, 1H), 2.04 (t,  $J$  = 12 Hz, 2H), 1.53-1.49 (m, 2H), 1.38-1.34 (m, 2H), 1.01-0.95 (m, 2H).  $^{13}\text{C}$ -NMR (151 MHz, DMSO- $d_6$ )  $\delta$  173.73, 172.49, 172.44, 137.37, 135.99, 133.41, 132.31, 128.14, 128.00, 127.92, 127.91, 127.86, 126.44, 125.91, 119.33, 53.72, 46.32, 37.49, 35.32, 30.58, 25.67, 25.02, 21.57. LCMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$ : calcd. for  $\text{C}_{22}\text{H}_{26}\text{N}_3\text{O}_3$ : 380.1972; found: 380.1969.

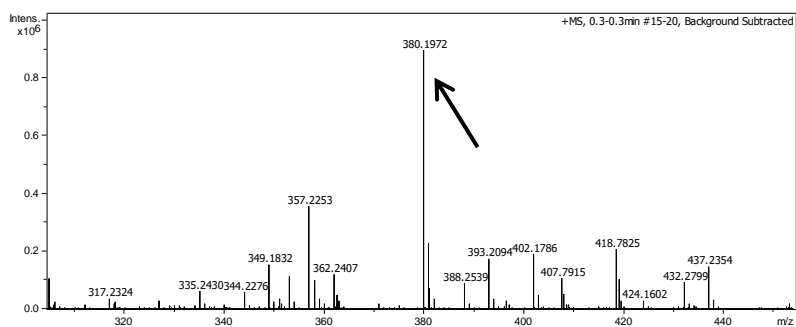
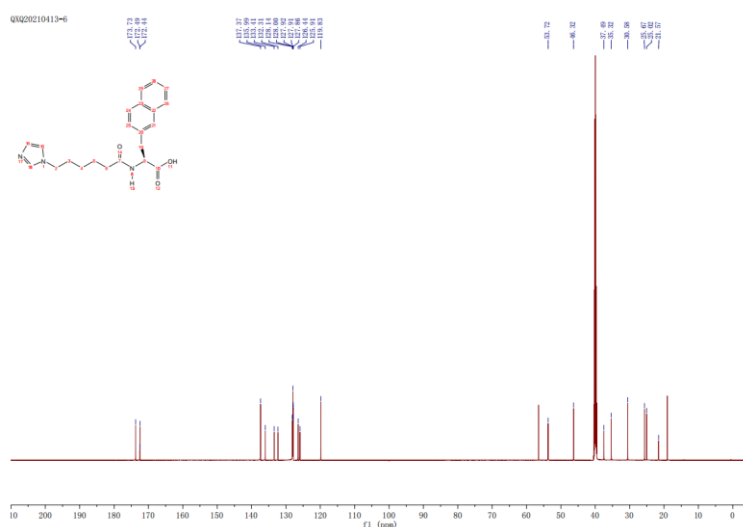
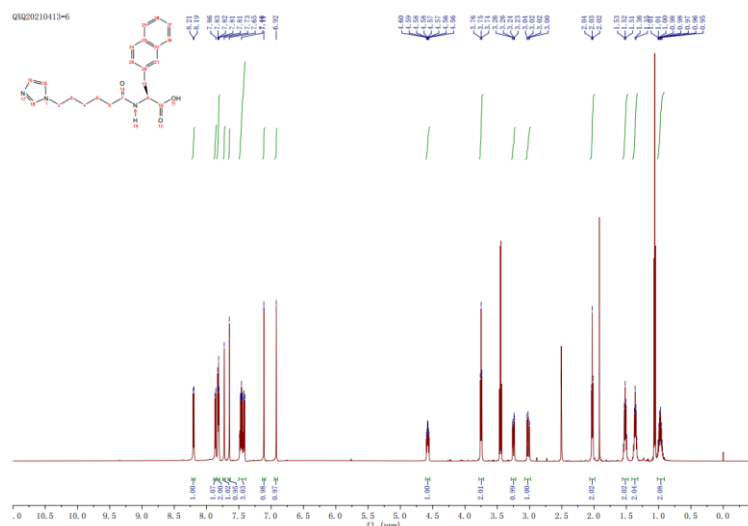
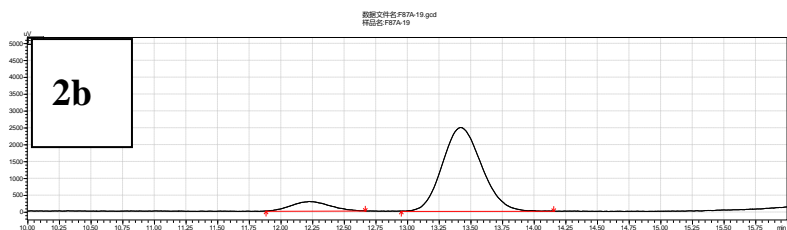
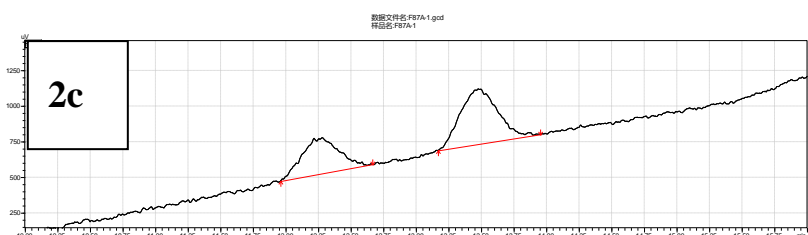


Figure S33.  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and LCMS spectra of **2u**.

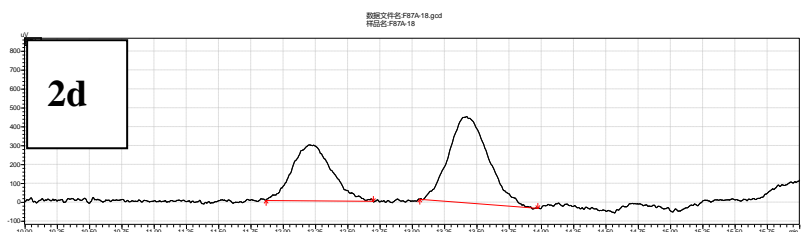
Typical chiral GC analyses for the epoxidation of styrene



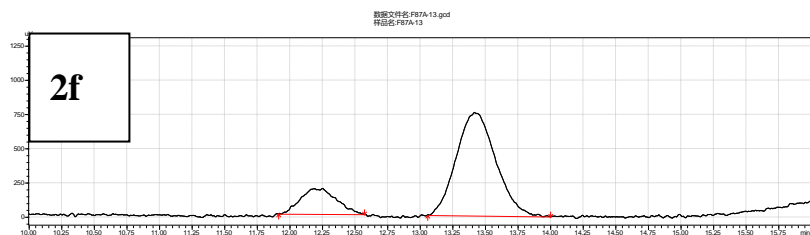
RT (min)	12.225 (S)	13.421 (R)
Area	4617	53226
ee % (R)	84	



RT (min)	12.28 (S)	13.478 (R)
Area	5009	7760
ee % (R)	22	

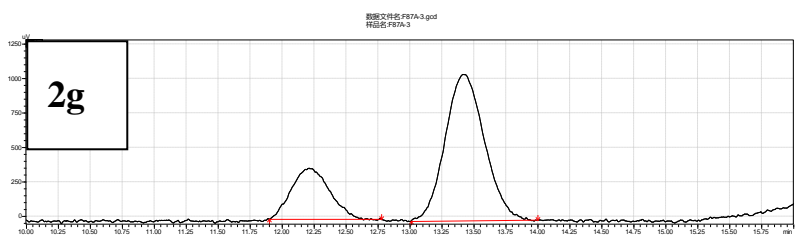


RT (min)	12.25 (S)	13.427 (R)
Area	4016	22419
ee % (R)	70	

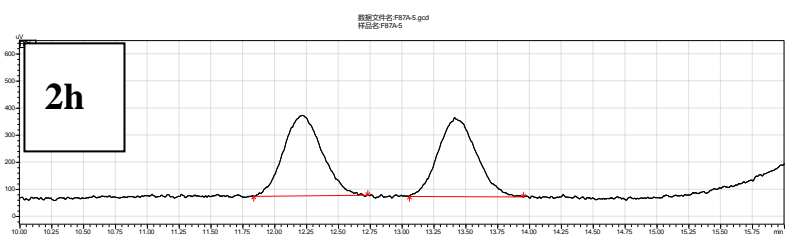


RT (min)	12.253 (S)	13.418 (R)
Area	3100	15857
ee % (R)	67	

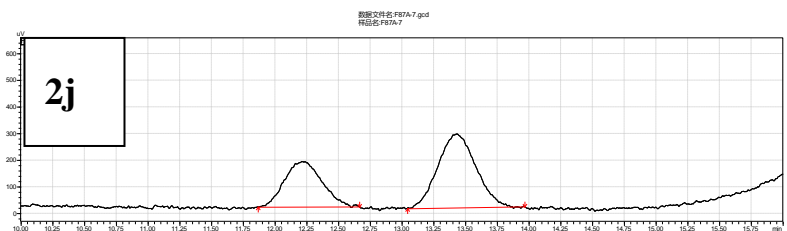




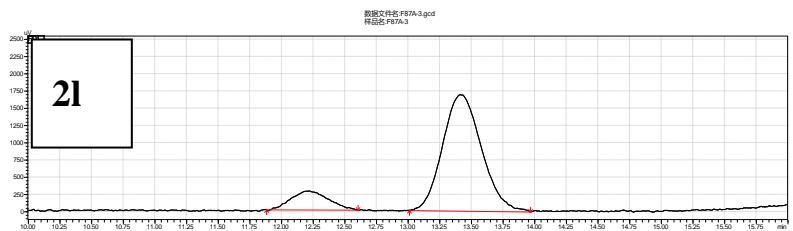
RT (min)	12.211 (S)	13.417 (R)
Area	7099	22643
ee % (R)	52	



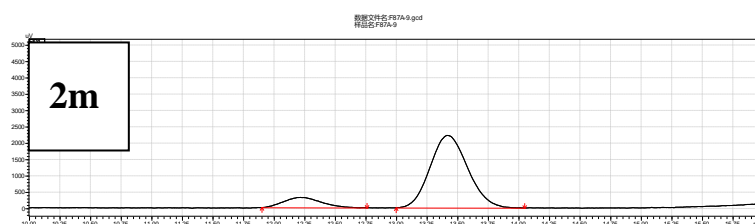
RT (min)	12.216 (S)	13.414 (R)
Area	5610	6046
ee % (R)	4	



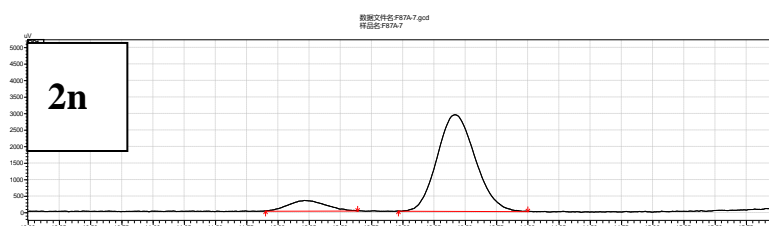
RT (min)	12.212 (S)	13.433 (R)
Area	3478	5730
ee % (R)	24	



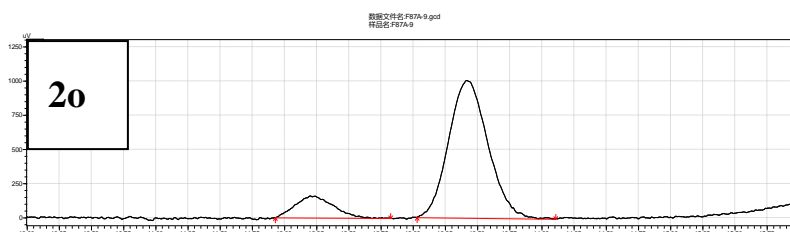
RT (min)	12.220 (S)	13.414 (R)
Area	4489	35874
ee % (R)	77	



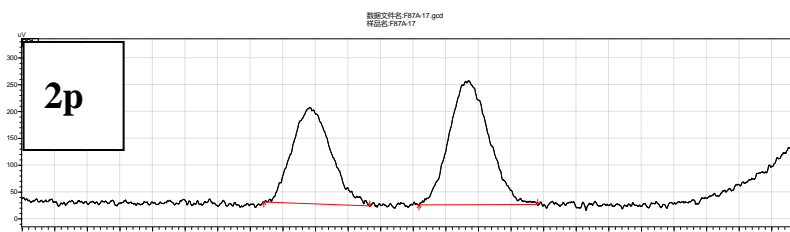
RT (min)	12.216 (S)	13.416 (R)
Area	4814	47323
ee % (R)	82	



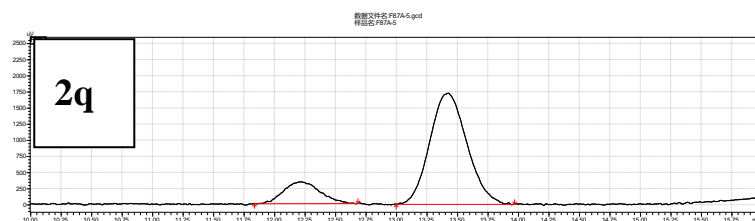
RT (min)	12.212 (S)	13.419 (R)
Area	5069	61687
ee % (R)	85	



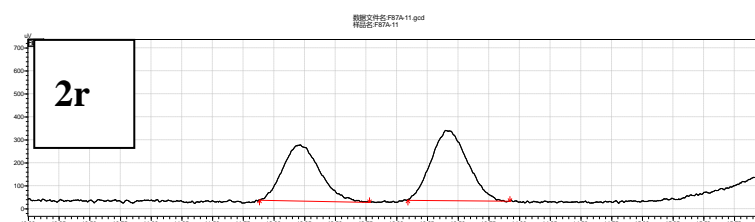
RT (min)	12.202 (S)	13.418 (R)
Area	2441	21358
ee % (R)	79	



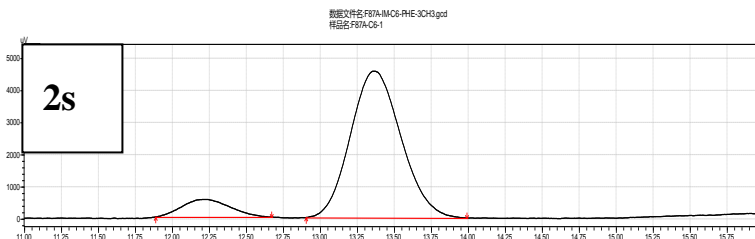
RT (min)	12.210 (S)	13.426 (R)
Area	3708	4902
ee % (R)	14	



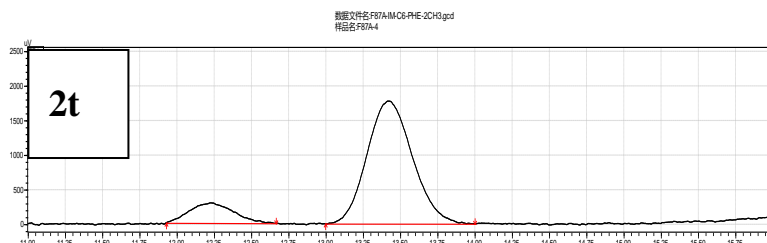
RT (min)	12.218 (S)	13.427 (R)
Area	5202	36358
ee % (R)	75	



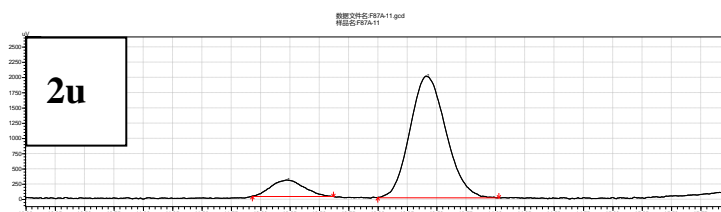
RT (min)	12.216 (S)	13.400 (R)
Area	5090	6254
ee % (R)	13	



RT (min)	12.216 (S)	13.400 (R)
Area	10395	108720
ee % (R)	83	

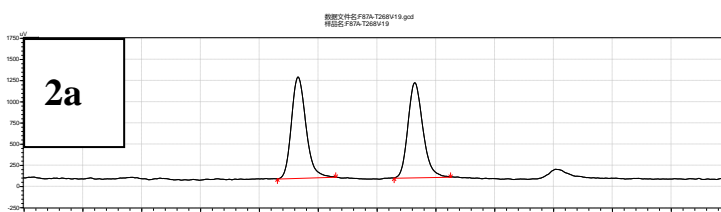


RT (min)	12.216 (S)	13.400 (R)
Area	6024	36628
ee % (R)	71	

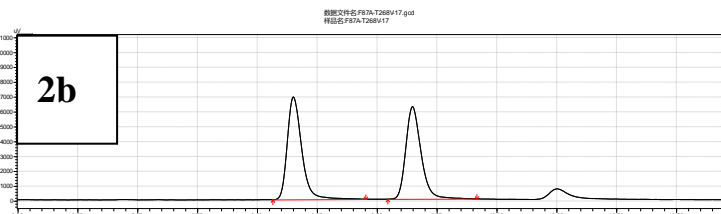


RT (min)	12.222 (S)	13.411 (R)
Area	3436	42291
ee % (R)	85	

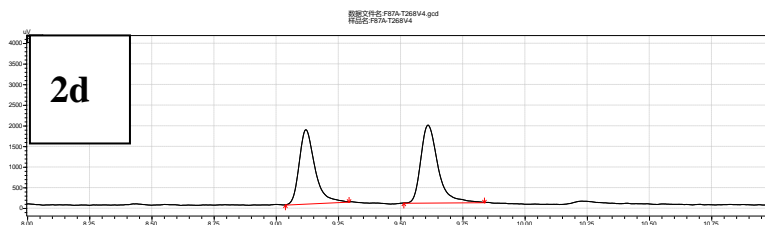
### Typical chiral GC analyses for the hydroxylation of ethylbenzene



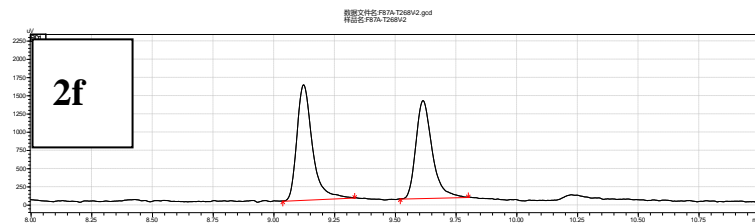
RT (min)	9.165 (R)	9.661 (S)
Area	5117	4942
ee % (R)	2	



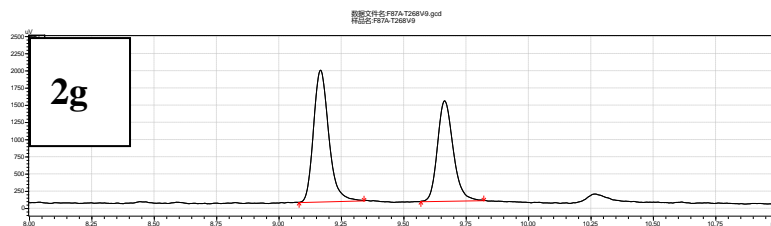
RT (min)	9.151 (R)	9.648 (S)
Area	28878	27453
ee % (R)	3	



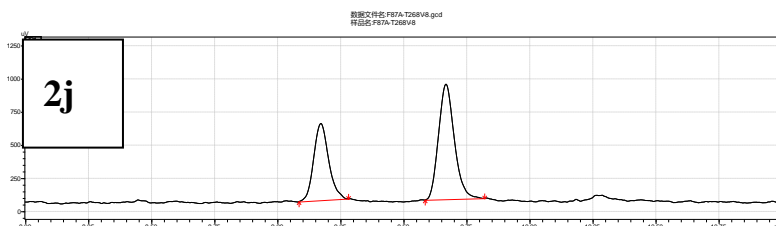
RT (min)	9.120 (R)	9.611 (S)
Area	7889	9027
ee % (R)	-7	



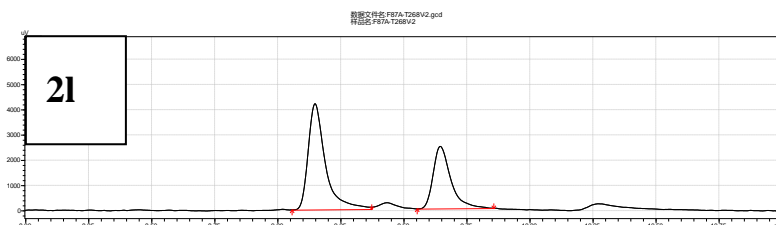
RT (min)	9.123 (R)	9.615 (S)
Area	6997	6235
ee % (R)	6	



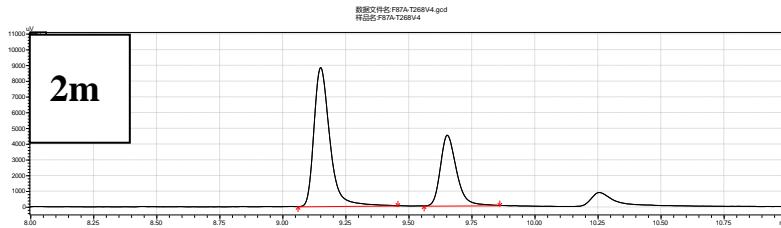
RT (min)	9.167 (R)	9.664 (S)
Area	8105	6378
ee % (R)	12	



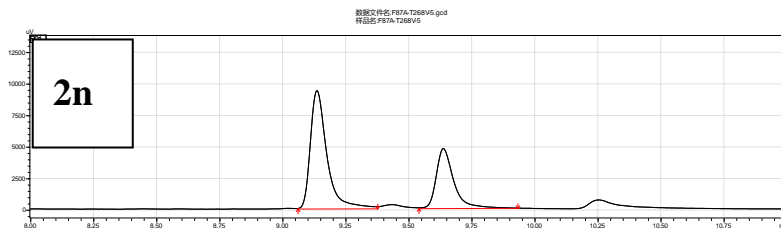
RT (min)	9.039 (R)	9.515 (S)
Area	1878	3382
ee % (R)	-29	



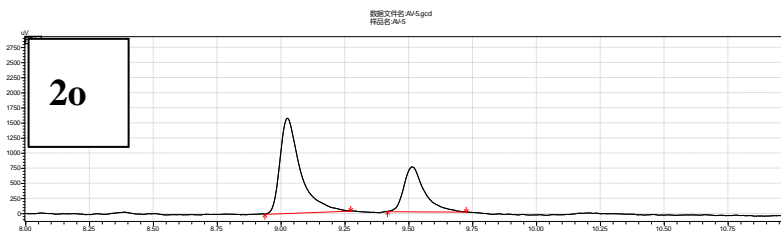
RT (min)	9.149 (R)	9.645 (S)
Area	19934	12004
ee % (R)	25	



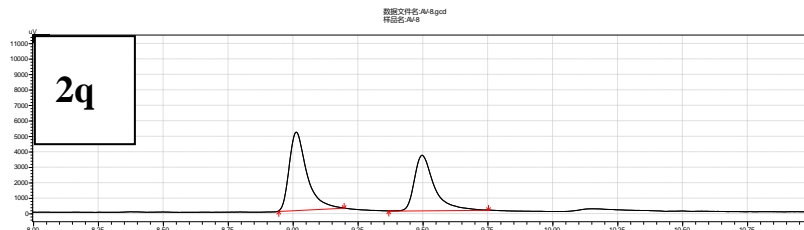
RT (min)	9.151 (R)	9.653 (S)
Area	38610	19817
ee % (R)	32	



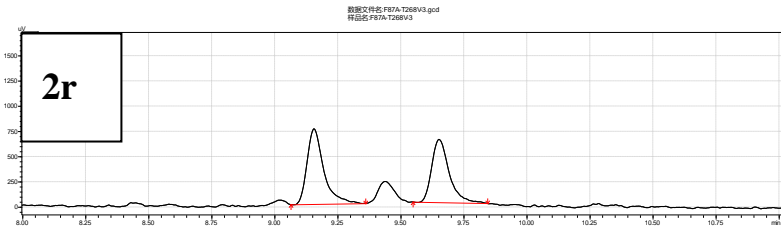
RT (min)	9.136 (R)	9.637 (S)
Area	42733	22681
ee % (R)	31	



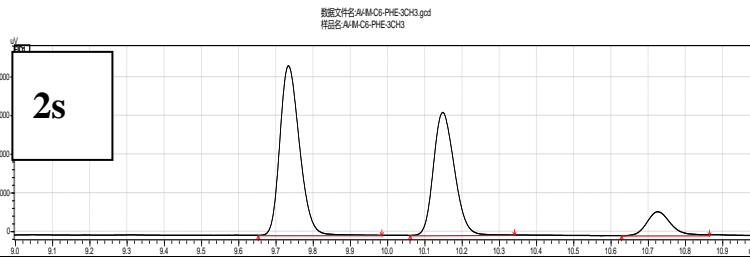
RT (min)	9.026 (R)	9.515 (S)
Area	8773	4129
ee % (R)	36	



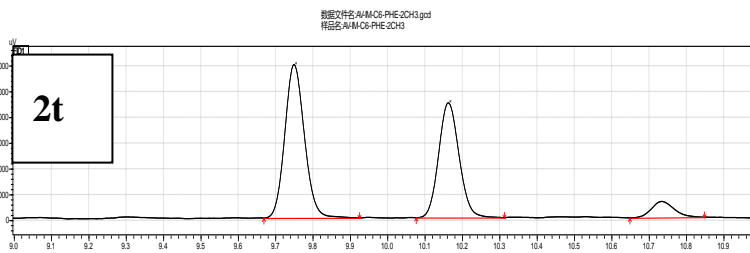
RT (min)	9.168 (R)	9.666 (S)
Area	16733	11166
ee % (R)	12	



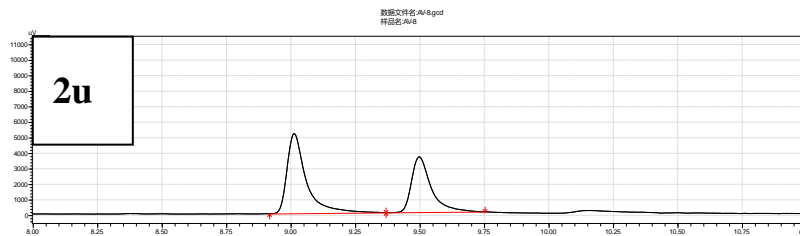
RT (min)	9.156 (R)	9.652 (S)
Area	3427	2992
ee % (R)	7	



RT (min)	9.734 (R)	10.149 (S)
Area	80224	62027
ee % (R)	13	



RT (min)	9.75 (R)	10.163 (S)
Area	21735	16923
ee % (R)	12	



RT (min)	9.013 (R)	9.498 (S)
Area	26703	18883
ee % (R)	17	

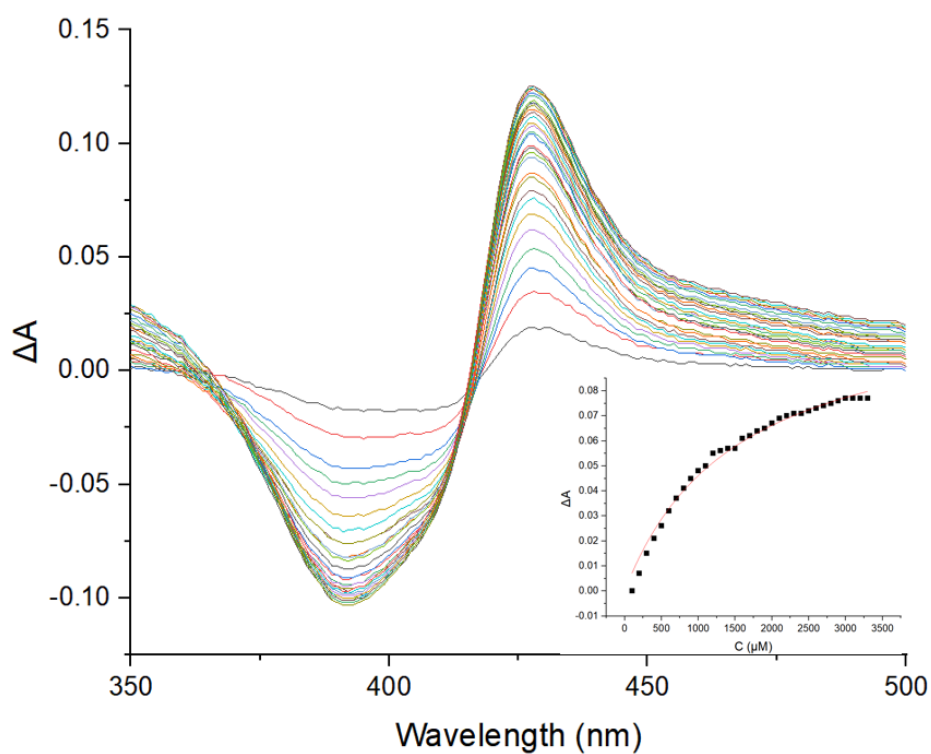


Figure S34. The UV-vis spectral change of F87A upon the addition of 2a (left) and the dissociation constants estimated by the titration experiment (inlet).

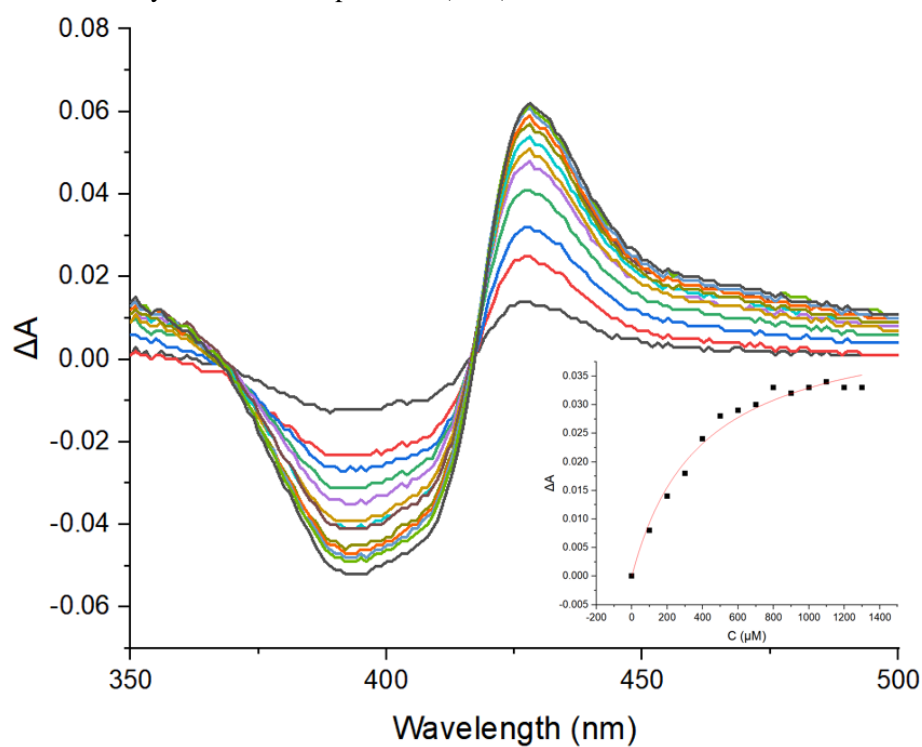


Figure S35. The UV-vis spectral change of F87A upon the addition of 2k (left) and the dissociation constants estimated by the titration experiment (inlet).



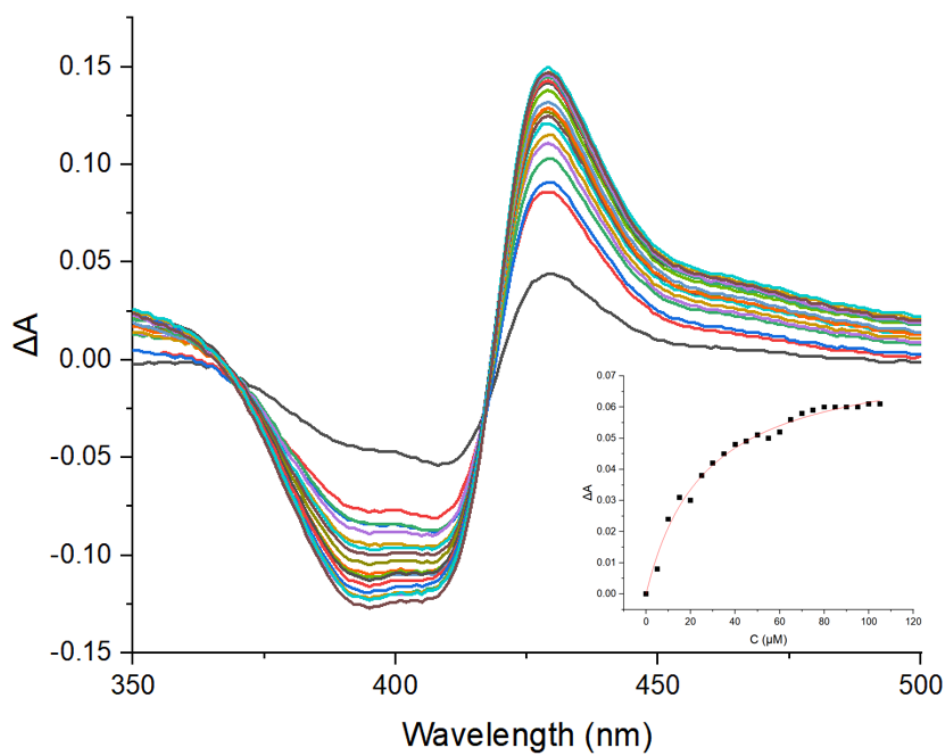


Figure S36. The UV-vis spectral change of F87A upon the addition of 2n (left) and the dissociation constants estimated by the titration experiment (inlet).

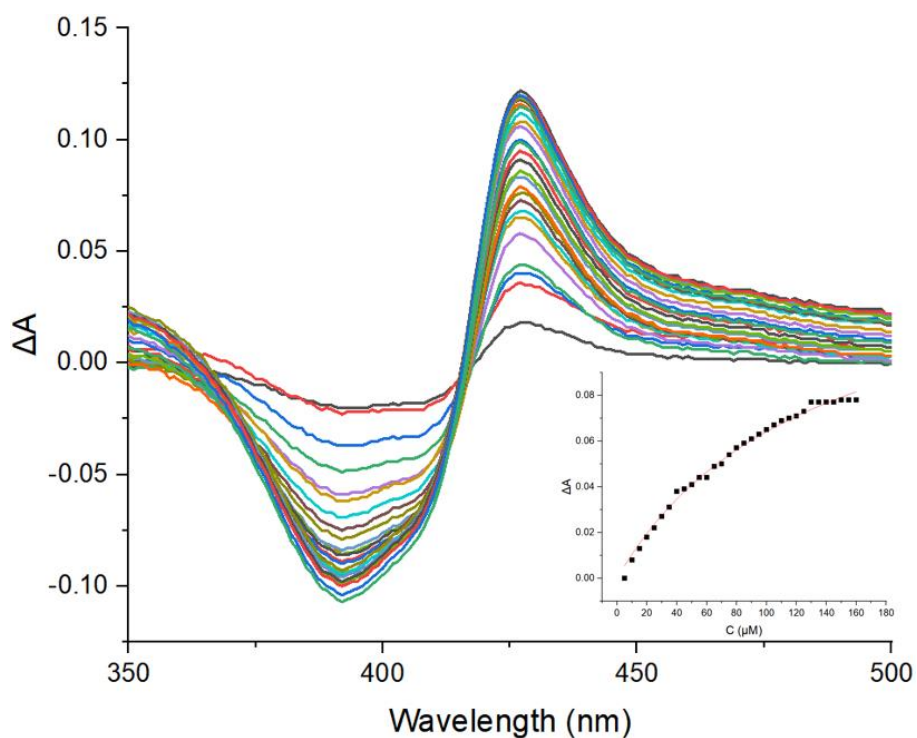


Figure S37. The UV-vis spectral change of F87A upon the addition of 2s (left) and the dissociation constants estimated by the titration experiment (inlet).

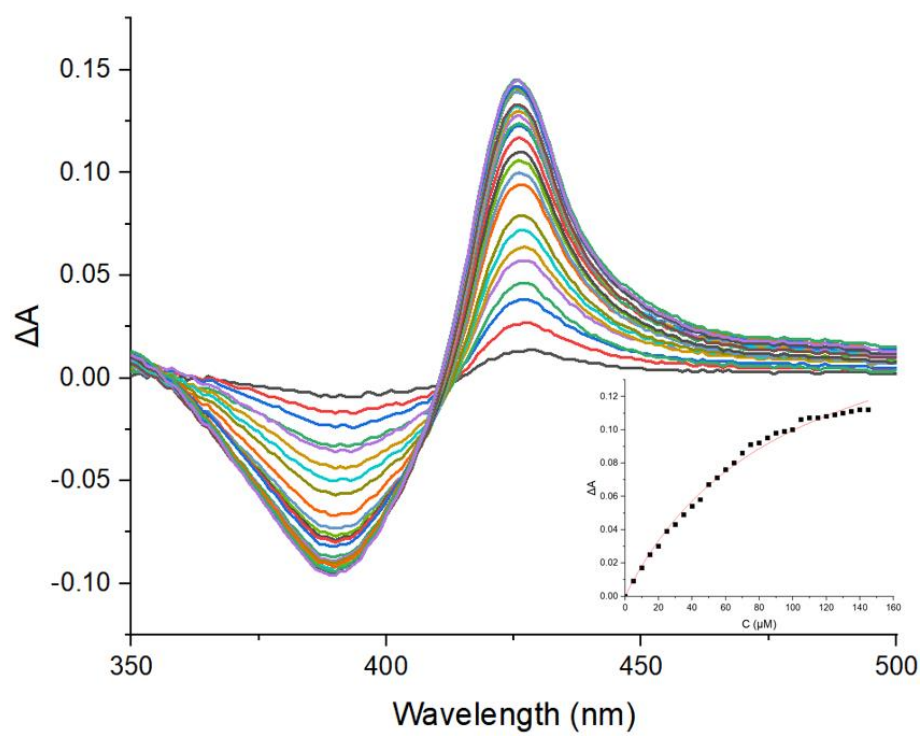


Figure S38. The UV-vis spectral change of F87A upon the addition of Im-C6-Phe (left) and the dissociation constants estimated by the titration experiment (inlet).