

Supplementary Information

Rapid Amide Ligation Between α -halo Acylsilanes and Amines Under Aqueous Conditions

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1: General information

Commercial reagents were purchased from TCI, Accela, J&K, Biomedical, Macklin, bide, or Adamas and used without further purification. The anhydrous solvents used in the experiments were all purchased and used directly. All reactions were carried out with oven-dried glassware. Analytical thin layer chromatography (TLC) was performed on 0.20 mm silica gel HSGF-254 plates (Huanghai, China). Column chromatography was performed on 200-300 mesh silica gel or 300-400 mesh silica gel (General-Reagent, China).

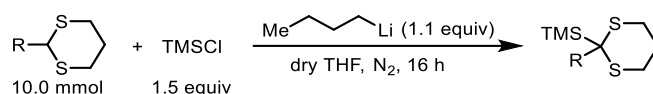
^1H NMR (400 MHz or 600 MHz), ^{13}C NMR (100 MHz or 150 MHz) and ^{19}F NMR (376 MHz or 565 MHz) were recorded on an NMR spectrometer with CDCl_3 or $\text{DMSO}-d_6$ as the solvent. Chemical shifts of ^1H , ^{13}C and ^{19}F NMR-spectra are reported in parts per million (ppm). The residual solvent signals were used as references and the chemical shifts were converted to the TMS scale (CDCl_3 : $\delta \text{H} = 7.26$ ppm, $\delta \text{C} = 77.16$ ppm, DMSO : $\delta \text{H} = 2.50$ ppm, $\delta \text{C} = 40.76$ ppm). All coupling constants (J values) were reported in Hertz (Hz). High resolution mass spectrometry data of new compounds were recorded on an LTQ Orbitrap Elite LC/MS (ESI). GPC for polymer molecular weight analysis was carried out with Waters 1515 equipped with a refractive index detector (RID), using polystyrene as standards and DMF was used as the eluent in a flow rate of 1.0 mL/min at 50 °C.

ESI-MS in proteins modification section was performed on a quadrupole time-of-flight mass spectrometer (Waters acquity UPLC I-CLASS/Synapt G2-Si). The mass spectrometry results had not been deconvoluted, the number of added ions had been marked in the figure. Lysozyme, from egg white was purchased from Amresco. Ribonuclease A, from bovine pancreas was purchased from MedChemExpress (MCE). Chymotrypsinogen A and myoglobin were purchased from Aladdin, and used without further purification.

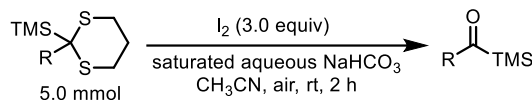
2: Preparation of the α -bromo-acylsilanes



Acylsilanes were prepared according to the literature.¹ Under an ambient atmosphere, aldehyde (10.0 mmol, 1.0 equiv), 1,3-dimercaptopropane (12.0 mmol, 1.2 equiv) and DCM (40.0 mL) were added to a round-bottom flask (100.0 mL). The reaction mixture was cooled to 0 °C and stirred for 5 min. Then, boron trifluoride diethyl etherate (3.0 mmol, 30 mol%) was added dropwise to the reaction mixture and stirred at 25 °C for 16 h. After water (60.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with DCM (3 × 30.0 mL). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure to afford the thioacetal quantitatively, which was used directly without further purification for the next step.

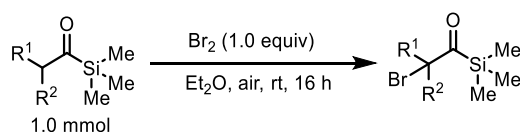


Under a nitrogen atmosphere, thioacetal (10.0 mmol, 1.0 equiv) and dry THF (20.0 mL) were added to a Schlenk tube (50.0 mL). The reaction mixture was cooled to -40 °C and stirred for 5 min. After, *n*-butyllithium (11.0 mmol, 1.1 equiv) was added dropwise to the reaction mixture and stirred for 4 h. Then, TMSCl (15.0 mmol, 1.5 equiv) was added. After 1 h the reaction was warmed to 25 °C for 11 h and then quenched with 30.0 mL of saturated aqueous NH₄Cl. The aqueous layer was extracted with DCM (3 × 30.0 mL). After that, the organic layer was dried over Na₂SO₄, filtered, and the filtrate was concentrated under reduced pressure to dryness. The residue was purified by chromatography on silica gel to afford the pure silyldithiane.



Under an ambient atmosphere, pure silyldithiane (5.0 mmol, 1.0 equiv), CH₃CN (40.0 mL) and saturated aqueous NaHCO₃ (10.0 mL) were added to a round-bottom flask (100.0 mL). After, I₂ (15.0 mmol, 3.0 equiv) was added to the reaction mixture and stirred at 25 °C for 2 h. Then quenched with 20.0 mL of saturated aqueous sodium thiosulfate. The aqueous layer was extracted with DCM (3 × 40.0 mL). After that, the organic layer was dried over Na₂SO₄, filtered, and the filtrate was concentrated under reduced pressure to dryness. The residue was purified by chromatography on silica gel to afford the acylsilanes.

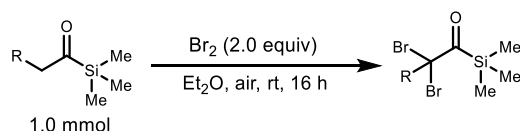
General Procedure I



Under an ambient atmosphere, acylsilanes (1.0 mmol, 1.0 equiv), ethyl ether (4.0 mL) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) were added to an oven-dried round

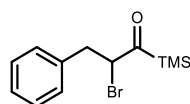
bottom flask (10.0 mL). The reaction was stirred at 25 °C for 16 h. The ethyl ether was evaporated and the crude solid was dissolved in ethyl acetate and loaded onto silica. The residue was purified by chromatography on silica gel to afford α -bromo-acylsilanes.

General Procedure II



Under an ambient atmosphere, acylsilanes (1.0 mmol, 1.0 equiv), ethyl ether (8.0 mL) and bromine (319.6 mg, 2.0 mmol, 2.0 equiv) were added to an oven-dried round bottom flask (25.0 mL). The reaction was stirred at 25 °C for 16 h. The ethyl ether was evaporated and the crude solid was dissolved in ethyl acetate and loaded onto silica. The residue was purified by chromatography on silica gel to afford α -bromo-acylsilanes.

2-Bromo-3-phenyl-1-(trimethylsilyl)propan-1-one 1a



Prepared via **General Procedure I** starting from 3-phenyl-1-(trimethylsilyl)propan-1-one (206.1 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1a** as a yellow oil.

Yield 187.4 mg (66%).

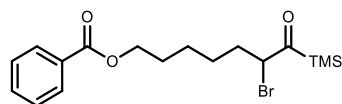
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.32-7.28 (m, 2H), 7.26-7.17 (m, 3H), 4.73-4.69 (m, 1H), 3.48-3.43 (m, 1H), 3.10-3.04 (m, 1H), 0.24 (s, 9H).

¹³C NMR (CDCl₃, 150 MHz) δ 234.1, 137.7, 129.5, 128.7, 127.1, 57.3, 37.5, -2.2.

HRMS (ESI) m/z : [M - Br]⁺ Calcd for C₁₂H₁₇OSi⁺: 205.1043; Found 205.1042.

6-Bromo-7-oxo-7-(trimethylsilyl)heptyl benzoate 1b



Prepared via **General Procedure I** starting from 7-oxo-7-(trimethylsilyl)heptyl benzoate (306.2 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1b** as a yellow oil.

Yield 193.6 mg (50%).

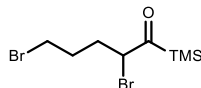
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.03 (d, J = 7.5 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 4.49-4.44 (m, 1H), 4.31 (t, J = 6.6 Hz, 2H), 2.06-1.97 (m, 1H), 1.93-1.84 (m, 1H), 1.82-1.75 (m, 2H), 1.59-1.36 (m, 4H), 0.29 (s, 9H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 234.2, 166.7, 133.0, 130.5, 129.6, 128.5, 64.8, 59.0, 31.2, 28.6, 27.1, 25.8, -1.9.

HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{26}\text{BrO}_3\text{Si}^+$: 385.0829; Found 385.0827.

2,5-Dibromo-1-(trimethylsilyl)pentan-1-one **1c**



Prepared via **General Procedure I** starting from 5-bromo-1-(trimethylsilyl)pentan-1-one (236.0 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1c** as a yellow oil.

Yield 144.1 mg (46%).

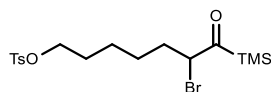
NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 4.53-4.50 (m, 1H), 3.43 (t, J = 6.2 Hz, 2H), 2.21-1.87 (m, 4H), 0.31 (s, 9H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 233.7, 57.9, 32.7, 30.4, 29.8, -1.9.

HRMS (ESI) m/z : $[\text{M} - \text{Br}]^+$ Calcd for $\text{C}_8\text{H}_{16}\text{BrOSi}^+$: 235.0148; Found 235.0147.

6-Bromo-7-oxo-7-(trimethylsilyl)heptyl 4-methylbenzenesulfonate **1d**



Prepared via **General Procedure I** starting from 7-oxo-7-(trimethylsilyl)heptyl 4-methylbenzenesulfonate (356.1 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1d** as a yellow oil.

Yield 259.6 mg (60%).

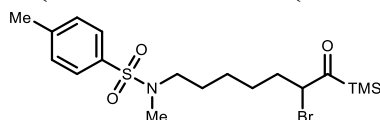
NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 7.77 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 4.43-4.40 (m, 1H), 4.00 (t, J = 6.3 Hz, 2H), 2.44 (s, 3H), 1.94-1.86 (m, 1H), 1.82-1.73 (m, 1H), 1.70-1.60 (m, 2H), 1.43-1.24 (m, 4H), 0.28 (s, 9H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 234.1, 144.8, 133.2, 129.9, 127.9, 70.3, 58.8, 30.9, 28.6, 26.7, 25.0, 21.7, -1.9.

HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{28}\text{BrO}_4\text{SSi}^+$: 435.0656; Found 435.0650.

N-(6-Bromo-7-oxo-7-(trimethylsilyl)heptyl)-*N*,4-dimethylbenzenesulfonamide **1e**



Prepared via **General Procedure I** starting from *N*,4-dimethyl-*N*-(7-oxo-7-(trimethylsilyl)heptyl)benzenesulfonamide (369.2 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1e** as a yellow oil.

Yield 280.1 mg (63%).

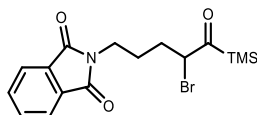
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.65 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 4.48-4.45 (m, 1H), 2.96 (t, J = 7.1 Hz, 2H), 2.68 (s, 3H), 2.42 (s, 3H), 2.01-1.92 (m, 1H), 1.87-1.78 (m, 1H), 1.54-1.46 (m, 3H), 1.40-1.31 (m, 3H), 0.29 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 234.2, 143.4, 134.5, 129.8, 127.5, 59.1, 49.9, 34.7, 31.1, 27.4, 27.0, 26.1, 21.6, -1.8.

HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₈H₃₁BrNO₃SSi⁺: 448.0972; Found 448.0967.

2-(4-Bromo-5-oxo-5-(trimethylsilyl)pentyl)isoindoline-1,3-dione 1f



Prepared via **General Procedure I** starting from 2-(5-oxo-5-(trimethylsilyl)pentyl)isoindoline-1,3-dione (303.1 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1f** as a yellow oil.

Yield 301.0 mg (79%).

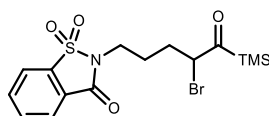
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.84-7.80 (m, 2H), 7.72-7.68 (m, 2H), 4.58-4.55 (m, 1H), 3.71 (t, J = 6.7 Hz, 2H), 2.02-1.85 (m, 3H), 1.79-1.70 (m, 1H), 0.28 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 233.7, 168.4, 134.1, 132.1, 123.4, 57.7, 37.1, 28.1, 26.4, -2.0.

HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₆H₂₁BrNO₃Si⁺: 382.0469; Found 382.0470.

2-(4-Bromo-5-oxo-5-(trimethylsilyl)pentyl)benzo[d]isothiazol-3(2H)-one 1,1-dioxide 1g



Prepared via **General Procedure I** starting from 2-(5-oxo-5-(trimethylsilyl)pentyl)benzo[d]isothiazol-3(2H)-one 1,1-dioxide (339.1 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1g** as a yellow oil.

Yield 331.6 mg (80%).

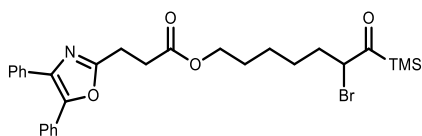
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.06-8.04 (m, 1H), 7.93-7.89 (m, 1H), 7.87-7.83 (m, 2H), 4.59-4.56 (m, 1H), 3.82 (t, J = 6.4 Hz, 2H), 2.09-2.03 (m, 2H), 2.01-1.89 (m, 2H), 0.29 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 233.6, 159.1, 137.7, 135.0, 134.5, 127.4, 125.4, 121.1, 57.5, 38.5, 28.0, 26.3, -1.9.

HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₅H₂₁BrNO₄SSi⁺: 418.0138; Found 418.0134.

6-Bromo-7-oxo-7-(trimethylsilyl)heptyl 3-(4,5-diphenyloxazol-2-yl)propanoate **1h**



Prepared via **General Procedure I** starting from 7-oxo-7-(trimethylsilyl)heptyl 3-(4,5-diphenyloxazol-2-yl)propanoate (477.2 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1h** as a yellow oil.

Yield 412.0 mg (74%).

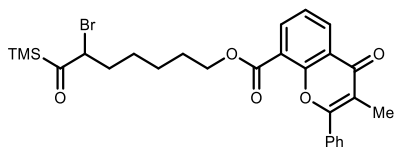
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.63 (d, J = 7.4 Hz, 2H), 7.57 (d, J = 7.4 Hz, 2H), 7.38-7.29 (m, 6H), 4.45-4.41 (m, 1H), 4.12 (t, J = 6.5 Hz, 2H), 3.18 (t, J = 7.5 Hz, 2H), 2.91 (t, J = 7.5 Hz, 2H), 1.98-1.90 (m, 1H), 1.87-1.79 (m, 1H), 1.67-1.60 (m, 2H), 1.50-1.25 (m, 4H), 0.29 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 234.2, 172.1, 161.9, 145.5, 135.1, 132.4, 129.0, 128.7, 128.65, 128.6, 128.2, 128.0, 126.5, 64.7, 59.0, 31.2, 31.1, 28.5, 27.1, 25.6, 23.6, -1.9.

HRMS (ESI) m/z : $[M + H]^+$ Calcd for C₂₈H₃₅BrNO₄Si⁺: 556.1513; Found 556.1509.

6-Bromo-7-oxo-7-(trimethylsilyl)heptyl 3-methyl-4-oxo-2-phenyl-4H-chromene-8-carboxylate **1i**



Prepared via **General Procedure I** starting from 7-oxo-7-(trimethylsilyl)heptyl 3-methyl-4-oxo-2-phenyl-4H-chromene-5-carboxylate (464.2 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1i** as a yellow oil.

Yield 356.5 mg (66%).

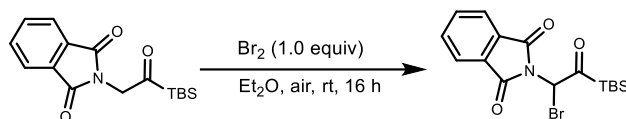
NMR Spectroscopy:

¹H NMR (CDCl₃, 600 MHz) δ 8.45 (d, J = 7.7 Hz, 1H), 8.25 (d, J = 7.4 Hz, 1H), 7.77-7.76 (m, 2H), 7.55-7.50 (m, 3H), 7.44 (t, J = 7.7 Hz, 1H), 4.43-4.41 (m, 1H), 4.33 (t, J = 6.6 Hz, 2H), 2.22 (s, 3H), 1.94-1.88 (m, 1H), 1.82-1.75 (m, 1H), 1.74-1.70 (m, 2H), 1.46-1.28 (m, 4H), 0.28 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 234.1, 178.4, 164.6, 161.3, 154.5, 136.3, 133.1, 130.9, 130.6, 129.4, 128.6, 124.2, 123.3, 120.9, 117.8, 65.5, 58.9, 31.1, 28.5, 27.1, 25.7, 11.9, -1.9.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for C₂₇H₃₁BrO₅SiNa⁺: 565.1016; Found 565.1016.

2-(1-Bromo-2-(*tert*-butyldimethylsilyl)-2-oxoethyl)isoindoline-1,3-dione **1j**



Under an ambient atmosphere, 2-(2-(*tert*-butyldimethylsilyl)-2-oxoethyl)isoindoline-1,3-dione (303.1 mg, 1.0 mmol, 1.0 equiv), ethyl ether (8.0 mL) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (10.0 mL). The reaction was stirred at 25 °C for 16 h. The ethyl ether was evaporated and the crude solid was dissolved in ethyl acetate and loaded onto silica. The residue was purified by chromatography on silica gel to afford **1j** as a white solid.

Yield 282.6 mg (74%).

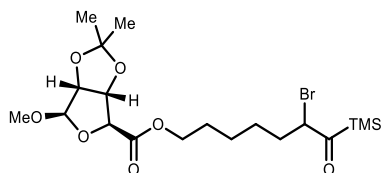
NMR Spectroscopy:

¹H NMR (CDCl₃, 600 MHz) δ 7.94-7.93 (m, 2H), 7.82-7.80 (m, 2H), 6.58 (s, 1H), 0.94 (s, 9H), 0.26 (s, 3H), 0.21 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz) δ 224.7, 165.9, 135.2, 131.9, 124.5, 60.8, 26.6, 17.4, -5.3, -5.5.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₆H₂₀BrNO₃SiNa⁺: 404.0288; Found 404.0294.

6-Bromo-7-oxo-7-(trimethylsilyl)heptyl (3*aS*,4*S*,6*R*,6*aR*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylate **1k**



Prepared via **General Procedure I** starting from 7-oxo-7-(trimethylsilyl)heptyl (3*aS*,4*S*,6*R*,6*aR*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylate (402.2 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1k** as a yellow oil.

Yield 185.0 mg (39%).

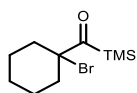
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 5.20-5.18 (m, 1H), 5.02 (s, 1H), 4.59-4.52 (m, 2H), 4.47-4.43 (m, 1H), 4.17-4.07 (m, 2H), 3.38 (s, 3H), 2.00-1.93 (m, 1H), 1.89-1.81 (m, 1H), 1.70-1.64 (m, 2H), 1.50-1.47 (m, 4H), 1.41-1.36 (m, 2H), 1.36-1.32 (m, 4H), 0.29 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 234.2, 170.3, 112.9, 109.5, 84.5, 83.9, 82.3, 65.3, 58.9, 55.6, 31.1, 28.4, 27.1, 26.5, 25.6, 25.3, -1.8.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₉H₃₃BrO₇SiNa⁺: 503.1071; Found 503.1076.

(1-Bromocyclohexyl)(trimethylsilyl)methanone **1l**



Prepared via **General Procedure I** starting from cyclohexyl(trimethylsilyl)methanone (184.1 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1l** as a yellow oil.

Yield 183.4 mg (70%).

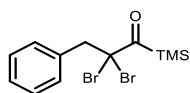
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 2.11-2.05 (m, 2H), 1.92-1.86 (m, 2H), 1.82-1.72 (m, 2H), 1.59-1.54 (m, 3H), 1.35-1.24 (m, 1H), 0.31 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 233.9, 79.5, 34.9, 25.3, 23.2, -0.3.

HRMS (ESI) m/z : [M + Na]⁺ Calcd for C₁₀H₁₉BrOSiNa⁺: 285.0280; Found 285.0281.

2,2-Dibromo-3-phenyl-1-(trimethylsilyl)propan-1-one **1m**



Prepared via **General Procedure II** starting from 3-phenyl-1-(trimethylsilyl)propan-1-one (206.1 mg, 1.0 mmol, 1.0 equiv) and bromine (319.6 mg, 2.0 mmol, 2.0 equiv) to give **1m** as a white solid.

Yield 319.1 mg (88%).

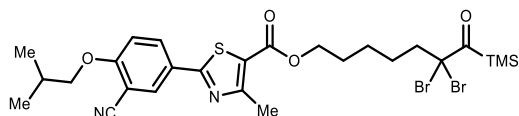
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.39-7.32 (m, 5H), 3.72 (s, 2H), 0.44 (s, 9H).

¹³C NMR (CDCl₃, 150 MHz) δ 223.0, 135.5, 131.7, 128.1, 127.7, 78.5, 47.6, -0.1.

HRMS (ESI) m/z : [M - Br]⁺ Calcd for C₁₂H₁₆BrOSi⁺: 283.0148; Found 283.0142.

6,6-Dibromo-7-oxo-7-(trimethylsilyl)heptyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate **1n**



Prepared via **General Procedure II** starting from 7-oxo-7-(trimethylsilyl)heptyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate (500.2 mg, 1.0 mmol, 1.0 equiv) and bromine (319.6 mg, 2.0 mmol, 2.0 equiv) to give **1n** as a white solid.

Yield 153.0 mg (23%).

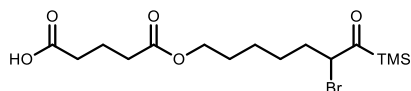
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.16 (s, 1H), 8.08 (d, J = 8.5 Hz, 1H), 7.00 (d, J = 8.8 Hz, 1H), 4.30 (t, J = 6.5 Hz, 2H), 3.88 (d, J = 6.5 Hz, 2H), 2.75 (s, 3H), 2.42-2.38 (m, 2H), 2.24-2.14 (m, 1H), 1.83-1.76 (m, 2H), 1.75-1.67 (m, 2H), 1.54 (q, J = 7.8 Hz, 2H), 1.07 (d, J = 6.7 Hz, 6H), 0.41 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 222.6, 167.3, 162.6, 162.1, 161.2, 132.7, 132.2, 126.0, 121.9, 115.5, 112.7, 103.1, 79.7, 75.8, 65.3, 42.8, 28.5, 28.3, 27.0, 25.7, 19.2, 17.6, -0.2.

HRMS (ESI) m/z: [M + H]⁺ Calcd for C₂₆H₃₅Br₂N₂O₄SSi⁺: 657.0448; Found 657.0448.

5-((6-bromo-7-oxo-7-(trimethylsilyl)heptyl)oxy)-5-oxopentanoic acid **1o**



Prepared via **General Procedure I** starting from 5-oxo-5-((7-oxo-7-(trimethylsilyl)heptyl)oxy)pentanoic acid (316.2 mg, 1.0 mmol, 1.0 equiv) and bromine (319.6 mg, 2.0 mmol, 2.0 equiv) to give **1o** as a white solid.

Yield 248.2 mg (63%).

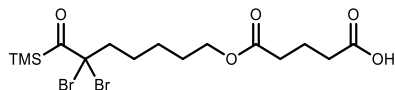
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.73 (s, 1H), 4.45 (t, *J* = 7.0 Hz, 1H), 4.07 (t, *J* = 6.5 Hz, 2H), 2.45-2.36 (m, 4H), 1.99-1.91 (m, 2H), 1.67-1.60 (m, 2H), 1.41-1.25 (m, 6H), 0.29 (s, 9H).

¹³C NMR (CDCl₃, 150 MHz) δ 234.2, 178.8, 173.0, 64.4, 59.0, 33.2, 33.1, 31.1, 28.4, 27.0, 25.6, 19.9, -1.9.

HRMS (ESI) m/z: [M + H]⁺ Calcd for C₁₅H₂₈BrO₅Si⁺: 395.0884; Found 395.0886.

5-((6,6-dibromo-7-oxo-7-(trimethylsilyl)heptyl)oxy)-5-oxopentanoic acid **1p**



Prepared via **General Procedure II** starting from 5-oxo-5-((7-oxo-7-(trimethylsilyl)heptyl)oxy)pentanoic acid (316.2 mg, 1.0 mmol, 1.0 equiv) and bromine (319.6 mg, 2.0 mmol, 2.0 equiv) to give **1p** as a white solid.

Yield 316.2 mg (67%).

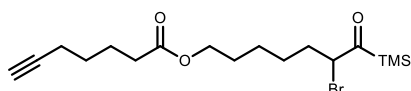
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 10.13 (s, 1H), 4.08 (t, *J* = 6.6 Hz, 2H), 2.44-2.35 (m, 6H), 1.98-1.91 (m, 2H), 1.71-1.61 (m, 4H), 1.48-1.41 (m, 2H), 0.41 (s, 9H).

¹³C NMR (CDCl₃, 150 MHz) δ 222.4, 178.8, 173.0, 79.7, 64.4, 42.7, 33.2, 33.0, 28.4, 26.9, 25.4, 19.9, -0.30.

HRMS (ESI) m/z: [M + Na]⁺ Calcd for C₁₅H₂₆Br₂O₅SiNa⁺: 494.9808; Found 494.9805.

6-Bromo-7-oxo-7-(trimethylsilyl)heptyl hept-6-ynoate **1q**



Prepared via **General Procedure I** starting from 7-oxo-7-(trimethylsilyl)heptyl hept-6-ynoate (310.2 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv)

to give **1q** as a white solid.

Yield 248.3 mg (66%).

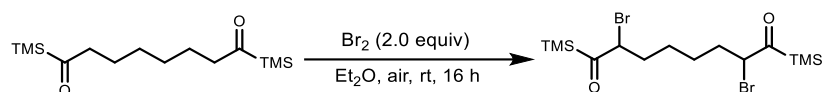
NMR Spectroscopy:

¹H NMR (CDCl₃, 600 MHz) δ 4.47-4.45 (m, 1H), 4.06 (t, *J* = 6.6 Hz, 2H), 2.32 (t, *J* = 7.5 Hz, 2H), 2.23-2.20 (m, 2H), 2.01-1.95 (m, 2H), 1.88-1.84 (m, 1H), 1.77-1.72 (m, 2H), 1.66-1.61 (m, 2H), 1.59-1.55 (m, 2H), 1.54-1.47 (m, 1H), 1.42-1.34 (m, 3H), 0.30 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 234.2, 173.5, 84.0, 68.6, 64.2, 58.9, 33.8, 31.1, 28.4, 27.9, 27.0, 25.6, 24.0, 18.1, -2.0.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₇H₂₉BrO₃SiNa⁺: 411.0962; Found 411.0963.

2,7-Dibromo-1,8-bis(trimethylsilyl)octane-1,8-dione **7**



Under an ambient atmosphere, 1,8-bis(trimethylsilyl)octane-1,8-dione (286.2 mg, 1.0 mmol, 1.0 equiv), ethyl ether (8.0 mL) and bromine (319.6 mg, 2.0 mmol, 2.0 equiv) were added to an oven-dried round bottom flask (25.0 mL). The reaction was stirred at 25 °C for 16 h. The ethyl ether was evaporated and the crude solid was dissolved in ethyl acetate and loaded onto silica. The residue was purified by chromatography on silica gel to afford **7** as a yellow oil.

Yield 194.5 mg (44%).

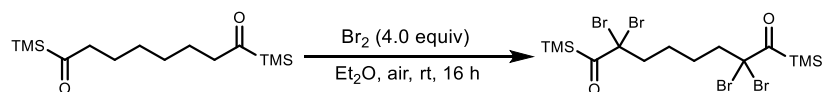
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 4.45 (t, *J* = 6.9 Hz, 2H), 2.02-1.94 (m, 2H), 1.90-1.82 (m, 2H), 1.54-1.45 (m, 2H), 1.36-1.26 (m, 2H), 0.29 (s, 18H).

¹³C NMR (CDCl₃, 100 MHz) δ 234.1, 58.7, 31.0, 26.9, -1.8.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₄H₂₈O₂Br₂Si₂Na⁺: 464.9887; Found 464.9879.

2,2,7,7-Tetrabromo-1,8-bis(trimethylsilyl)octane-1,8-dione **10**



Under an ambient atmosphere, 1,8-bis(trimethylsilyl)octane-1,8-dione (286.2 mg, 1.0 mmol, 1.0 equiv), ethyl ether (8.0 mL) and bromine (639.2 mg, 4.0 mmol, 4.0 equiv) were added to an oven-dried round bottom flask (25.0 mL). The reaction was stirred at 25 °C for 16 h. The ethyl ether was evaporated and the crude solid was dissolved in ethyl acetate and loaded onto silica. The residue was purified by chromatography on silica gel to afford **10** as a white solid.

Yield 526.8 mg (88%).

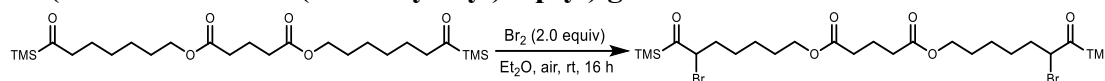
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 2.44-2.41 (m, 4H), 1.77-1.72 (m, 4H), 0.42 (s, 18H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 222.5, 79.5, 42.8, 26.9, -0.2.

HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{14}\text{H}_{26}\text{O}_2\text{Br}_4\text{Si}_2\text{Na}^+$: 620.8097; Found 620.8092.

Bis(6-bromo-7-oxo-7-(trimethylsilyl)heptyl) glutarate **12**



Under an ambient atmosphere, bis(7-oxo-7-(trimethylsilyl)heptyl) glutarate (500.3 mg, 1.0 mmol, 1.0 equiv), ethyl ether (8.0 mL) and bromine (319.6 mg, 2.0 mmol, 2.0 equiv) were added to an oven-dried round bottom flask (25.0 mL). The reaction was stirred at 25 °C for 16 h. The ethyl ether was evaporated and the crude solid was dissolved in ethyl acetate and loaded onto silica. The residue was purified by chromatography on silica gel to afford **12** as a yellow oil.

Yield 220.2 mg (34%).

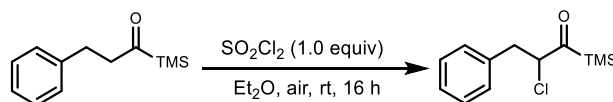
NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 4.47-4.43 (m, 2H), 4.05 (t, J = 6.6 Hz, 4H), 2.35 (t, J = 7.4 Hz, 4H), 2.00-1.82 (m, 6H), 1.66-1.59 (m, 4H), 1.53-1.45 (m, 2H), 1.42-1.32 (m, 6H), 0.29 (s, 18H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 234.2, 173.1, 64.4, 59.0, 33.4, 31.2, 28.5, 27.1, 25.6, 20.3, -1.8.

HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{25}\text{H}_{47}\text{O}_6\text{Br}_2\text{Si}_2^+$: 657.1272; Found 657.1275.

2-Chloro-3-phenyl-1-(trimethylsilyl)propan-1-one **1aa**



Under an ambient atmosphere, 3-phenyl-1-(trimethylsilyl)propan-1-one (206.1 mg, 1.0 mmol, 1.0 equiv), ethyl ether (8.0 mL) and sulfuryl chloride (73.1 mg, 1.0 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (10.0 mL). The reaction was stirred at 25 °C for 16 h. The ethyl ether was evaporated and the crude solid was dissolved in ethyl acetate and loaded onto silica. The residue was purified by chromatography on silica gel to afford **1aa** as a yellow oil.

Yield 98.6 mg (41%).

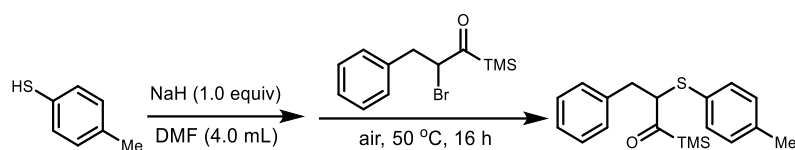
NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 7.34-7.30 (m, 2H), 7.28-7.26 (m, 1H), 7.22 (d, J = 7.5 Hz, 2H), 4.57-4.53 (m, 1H), 3.37-3.32 (m, 1H), 2.99-2.93 (m, 1H), 0.27 (s, 9H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 236.9, 136.9, 129.6, 128.7, 127.1, 67.2, 38.0, -2.2.

HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{12}\text{H}_{17}\text{OClSiNa}^+$: 263.0629; Found 263.0632.

3-Phenyl-2-(*p*-tolylthio)-1-(trimethylsilyl)propan-1-one **1ab**



Under an ambient atmosphere, 4-methylbenzenethiol (124.0 mg, 1.0 mmol, 1.0 equiv), dry *N,N*-dimethylformamide (4.0 mL) and NaH (60%, 40.0 mg, 1.0 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (10.0 mL). The reaction was stirred at 25 °C for 30 min. Then 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (284.0 mg, 1.0 mmol, 1.0 equiv) was added to the reaction mixture and stirred at 50 °C for 16 h. Then water (40.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 15.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **1ab** as a white solid.

Yield 285.4 mg (87%).

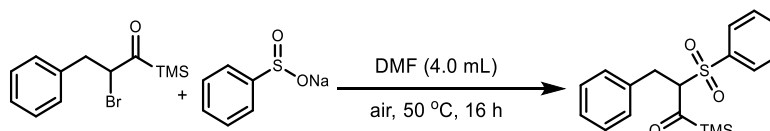
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.28-7.27 (m, 1H), 7.26-7.24 (m, 1H), 7.21-7.13 (m, 5H), 7.09 (d, *J* = 8.0 Hz, 2H), 4.12-4.08 (m, 1H), 3.22-3.16 (m, 1H), 2.90-2.85 (m, 1H), 2.33 (s, 3H), 0.17 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 235.9, 139.0, 138.5, 133.7, 129.9, 129.3, 128.5, 128.4, 126.5, 61.2, 34.7, 21.3, -2.2.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₉H₂₅OSSi⁺: 329.1390; Found 329.1392.

3-Phenyl-2-(phenylsulfonyl)-1-(trimethylsilyl)propan-1-one **1ac**



Under an ambient atmosphere, 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (284.0 mg, 1.0 mmol, 1.0 equiv), *N,N*-dimethylformamide (4.0 mL) and sodium benzenesulfonate (164.0 mg, 1.0 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (10.0 mL). The reaction was stirred at 50 °C for 16 h. Then water (40.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 15.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **1ac** as a white solid.

Yield 286.8 mg (83%).

NMR Spectroscopy:

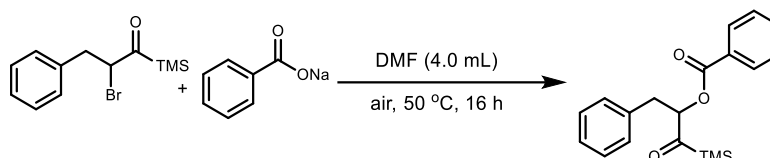
¹H NMR (CDCl₃, 400 MHz) δ 7.78-7.76 (m, 2H), 7.72-7.68 (m, 1H), 7.60-7.56 (m, 2H), 7.22-7.15 (m, 3H), 6.99-6.96 (m, 2H), 5.00-4.96 (m, 1H), 3.15-3.04 (m, 2H), -0.04 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 241.1, 137.2, 136.1, 134.4, 129.7, 129.2, 128.9,

127.1, 75.7, 32.9, -3.6.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{18}H_{22}SO_3SiNa^+$: 369.0951; Found 369.0952.

1-Oxo-3-phenyl-1-(trimethylsilyl)propan-2-yl benzoate **1ad**



Under an ambient atmosphere, 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (142.0 mg, 0.5 mmol, 1.0 equiv), *N,N*-dimethylformamide (4.0 mL) and sodium benzoate (79.2 mg, 0.55 mmol, 1.1 equiv) were added to an oven-dried round bottom flask (10.0 mL). The reaction was stirred at 50 °C for 16 h. Then water (40.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with EtOAc (3×15.0 mL). After that, the organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **1ad** as a white solid.

Yield 92.0 mg (56%).

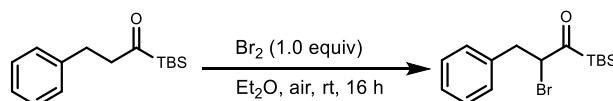
NMR Spectroscopy:

1H NMR ($CDCl_3$, 400 MHz) δ 8.04 (d, $J = 8.0$ Hz, 2H), 7.60-7.56 (m, 1H), 7.48-7.44 (m, 2H), 7.31-7.26 (m, 3H), 7.24-7.20 (m, 2H), 5.60-5.57 (m, 1H), 3.20-3.15 (m, 1H), 3.11-3.05 (m, 1H), 0.16 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 243.7, 166.0, 136.4, 133.4, 129.9, 129.7, 129.6, 128.6, 127.0, 83.7, 36.1, -2.7.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{19}H_{22}O_3SiNa^+$: 349.1230; Found 349.1233.

2-(1-Bromo-2-(*tert*-butyldimethylsilyl)-2-oxoethyl)isoindoline-1,3-dione **1ae**



Under an ambient atmosphere, 1-(*tert*-butyldimethylsilyl)-3-phenylpropan-1-one (248.1 mg, 1.0 mmol, 1.0 equiv), ethyl ether (8.0 mL) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (10.0 mL). The reaction was stirred at 25 °C for 16 h. The ethyl ether was evaporated and the crude solid was dissolved in ethyl acetate and loaded onto silica. The residue was purified by chromatography on silica gel to afford **1ae** as a yellow oil.

Yield 199.6 mg (61%).

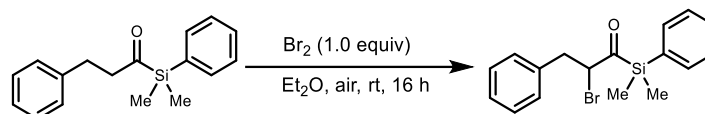
NMR Spectroscopy:

1H NMR ($CDCl_3$, 400 MHz) δ 7.30-7.26 (m, 2H), 7.23-7.18 (m, 3H), 4.74-4.70 (m, 1H), 3.48-3.43 (m, 1H), 3.08-3.03 (m, 1H), 0.82 (s, 9H), 0.21 (s, 3H), 0.19 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 233.6, 137.8, 129.7, 128.7, 127.1, 55.8, 37.4, 26.4, 17.0, -6.1, -6.2.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{15}H_{23}BrOSiNa^+$: 349.0594; Found 349.0587.

2-Bromo-1-(dimethyl(phenyl)silyl)-3-phenylpropan-1-one **1af**



Under an ambient atmosphere, 1-(dimethyl(phenyl)silyl)-3-phenylpropan-1-one (268.1 mg, 1.0 mmol, 1.0 equiv), ethyl ether (8.0 mL) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (10.0 mL). The reaction was stirred at 25 °C for 16 h. The ethyl ether was evaporated and the crude solid was dissolved in ethyl acetate and loaded onto silica. The residue was purified by chromatography on silica gel to afford **1af** as a yellow oil.

Yield 263.2 mg (76%).

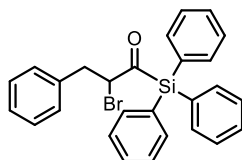
NMR Spectroscopy:

1H NMR ($CDCl_3$, 400 MHz) δ 7.51-7.48 (m, 2H), 7.44-7.40 (m, 1H), 7.38-7.34 (m, 2H), 7.25-7.19 (m, 3H), 7.09-7.05 (m, 2H), 4.69-4.65 (m, 1H), 3.42-3.36 (m, 1H), 3.02-2.97 (m, 1H), 0.60 (s, 3H), 0.51 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 232.3, 137.5, 134.3, 133.8, 130.2, 129.4, 128.6, 128.3, 127.0, 57.0, 37.4, -3.4, -3.9.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{17}H_{19}BrOSiNa^+$: 369.0281; Found 369.0282.

2-Bromo-3-phenyl-1-(triphenylsilyl)propan-1-one **1ag**



Prepared via **General Procedure I** starting from 3-phenyl-1-(triphenylsilyl)propan-1-one (392.2 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1ag** as a yellow oil.

Yield 280.2 mg (60%).

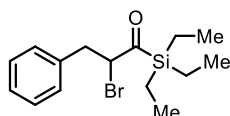
NMR Spectroscopy:

1H NMR ($CDCl_3$, 400 MHz) δ 7.53-7.51 (m, 6H), 7.49-7.44 (m, 3H), 7.39-7.35 (m, 6H), 7.25-7.21 (m, 3H), 7.06-7.04 (m, 2H), 4.83 (t, $J = 7.4$ Hz, 1H), 3.50-3.45 (m, 1H), 3.05-3.00 (m, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 229.9, 137.5, 136.3, 130.9, 130.6, 129.7, 128.7, 128.4, 127.0, 56.7, 37.5.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{27}H_{23}BrOSiNa^+$: 493.0594; Found 493.0589.

2-Bromo-3-phenyl-1-(triethylsilyl)propan-1-one **1ah**



Prepared via **General Procedure I** starting from 3-phenyl-1-(triethylsilyl)propan-1-one (248.2 mg, 1.0 mmol, 1.0 equiv) and bromine (159.8 mg, 1.0 mmol, 1.0 equiv) to give **1ah** as a yellow oil.

Yield 270.0 mg (83%).

NMR Spectroscopy:

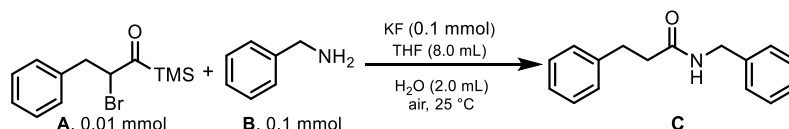
¹H NMR (CDCl₃, 400 MHz) δ 7.32-7.27 (m, 2H), 7.25-7.19 (m, 3H), 4.68 (t, *J* = 7.3 Hz, 1H), 3.50-3.45 (m, 1H), 3.09-3.03 (m, 1H), 0.92 (t, *J* = 7.7 Hz, 9H), 0.79-0.75 (m, 6H).

¹³C NMR (CDCl₃, 100 MHz) δ 233.6, 137.9, 129.6, 128.7, 127.0, 56.8, 37.3, 7.3, 2.8.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₅H₂₃BrOSiNa⁺: 349.0594; Found 349.0585.

3: Kinetic studies of the acylation of *N*-benzyl-3-phenylpropanamide ²

1.0 mM



Under an ambient atmosphere, benzylamine (10.7 mg, 0.1 mmol, 10.0 equiv), tetrahydrofuran (8.0 mL), H₂O (2.0 mL), KF (5.8 mg, 0.1 mmol, 10.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (2.8 mg, 0.01 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (25.0 mL) with a round-bottom flask. The reaction was monitored by GC-MS. The reactions were repeated 3 times.

Analysis

The reaction between benzylamine and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one is a bimolecular process that follows second-order kinetics. Reaction rates can be written as follows:

$$V = -\frac{d[A]}{dt} = k[A][B] = k_1[A]$$

$$[A] = [A_0] - [C]$$

$$\ln([A_0] - [C]) = -k_1t + c$$

Logarithmic scale concentrations of [A₀] - [C] versus time (sec) were plotted (**Figure S1**), and the slopes of their fitted curve were determined as *k*₁. From these, the second-order rate constant of this reaction was estimated from *k*₁, the second-order rate *k* = *k*₁/[B]; average *k* = 0.611 M⁻¹·s⁻¹.

Supplementary Table S1. Summary of pseudo-first-order kinetics at 1.0 mM

Trial	[B]	k_1 (s ⁻¹)	k (M ⁻¹ ·s ⁻¹)
1	10 mM	0.0061	0.61
2	10 mM	0.00531	0.531
3	10 mM	0.00693	0.691

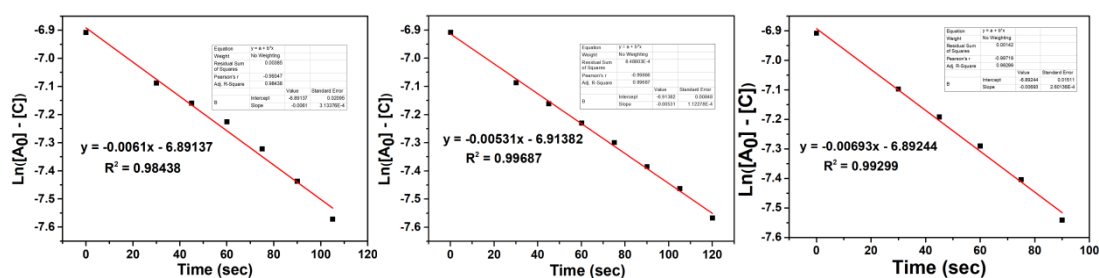


Figure S1. Pseudo-first order kinetics.

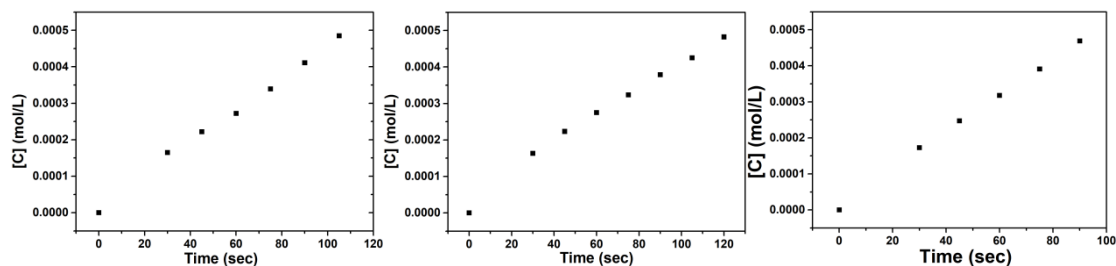
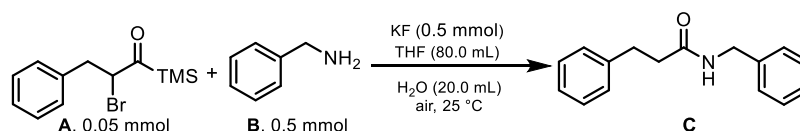


Figure S2. Product vs time (sec).

0.5 mM



Under an ambient atmosphere, benzylamine (53.5 mg, 0.5 mmol, 10.0 equiv), tetrahydrofuran (80.0 mL), H₂O (20.0 mL), KF (29.0 mg, 0.5 mmol, 10.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (14.2 mg, 0.05 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (250.0 mL) with a round-bottom flask. The reaction was monitored by GC-MS, using mesitylene as an internal standard. The reactions were repeated 3 times.

Analysis

The reaction between benzylamine and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one is a bimolecular process that follows second-order kinetics. Reaction rates can be written as follows:

$$V = -\frac{d[A]}{dt} = k[A][B] = k_1[A]$$

$$[A] = [A_0] - [C]$$

$$\ln([A_0] - [C]) = -k_1 t + c$$

Logarithmic scale concentrations of $[A_0] - [C]$ versus time (sec) were plotted (**Figure S1**), and the slopes of their fitted curve were determined as k_1 . From these, the second-order rate constant of this reaction was estimated from k_1 , the second-order rate $k = k_1/[B]$; average $k = 0.973 \text{ M}^{-1}\cdot\text{s}^{-1}$.

Supplementary Table S2. Summary of pseudo-first-order kinetics at 0.5 mM

Trial	[B]	$k_1 (\text{s}^{-1})$	$k (\text{M}^{-1}\cdot\text{s}^{-1})$
1	5 mM	0.00508	1.016
2	5 mM	0.00483	0.966
3	5 mM	0.00468	0.936

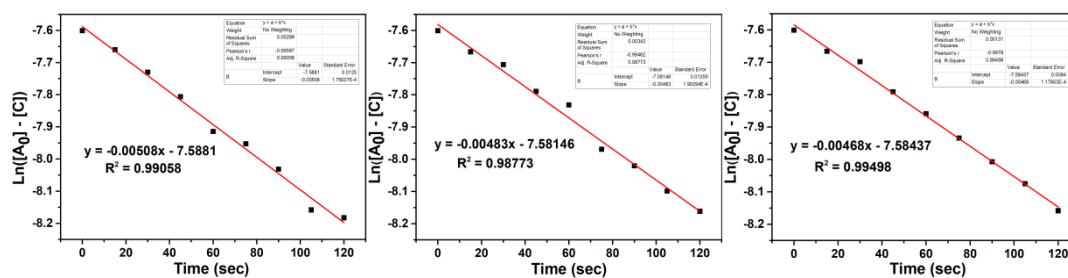


Figure S3. Pseudo-first order kinetics.

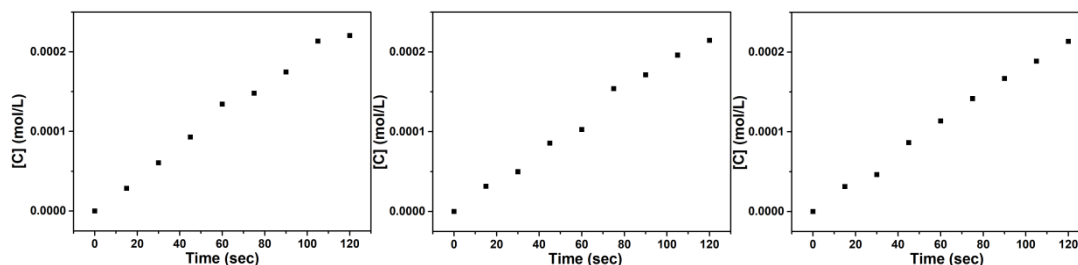
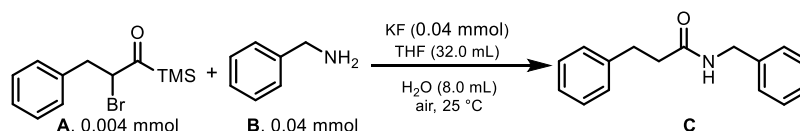


Figure S4. Product vs time (sec).

0.1 mM



Under an ambient atmosphere, benzylamine (1.0 M, 40.0 μL , 10.0 equiv), tetrahydrofuran (32.0 mL), H_2O (8.0 mL), KF (1.0 M, 40.0 μL , 10.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (0.1 M, 40.0 μL , 1.0 equiv) were added to an oven-dried round bottom flask (100.0 mL) with a round-bottom flask. The

reaction was monitored by GC-MS, using mesitylene as an internal standard. The reactions were repeated 3 times.

Analysis

The reaction between benzylamine and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one is a bimolecular process that follows second-order kinetics. Reaction rates can be written as follows:

$$V = -\frac{d[A]}{dt} = k[A][B] = k_1[A]$$

$$[A] = [A_0] - [C]$$

$$\ln([A_0] - [C]) = -k_1t + c$$

Logarithmic scale concentrations of $[A_0] - [C]$ versus time (sec) were plotted (**Figure S1**), and the slopes of their fitted curve were determined as k_1 . From these, the second-order rate constant of this reaction was estimated from k_1 , the second-order rate $k = k_1/[B]$; average $k = 0.861 \text{ M}^{-1}\cdot\text{s}^{-1}$.

Supplementary Table S3. Summary of pseudo-first-order kinetics at 0.1 mM

Trial	[B]	$k_1 \text{ (s}^{-1}\text{)}$	$k \text{ (M}^{-1}\cdot\text{s}^{-1}\text{)}$
1	1 mM	0.000985	0.985
2	1 mM	0.00750	0.750
3	1 mM	0.00847	0.847

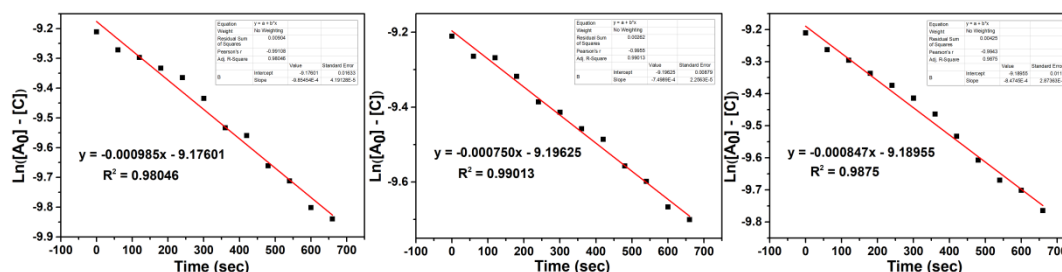


Figure S5. Pseudo-first order kinetics.

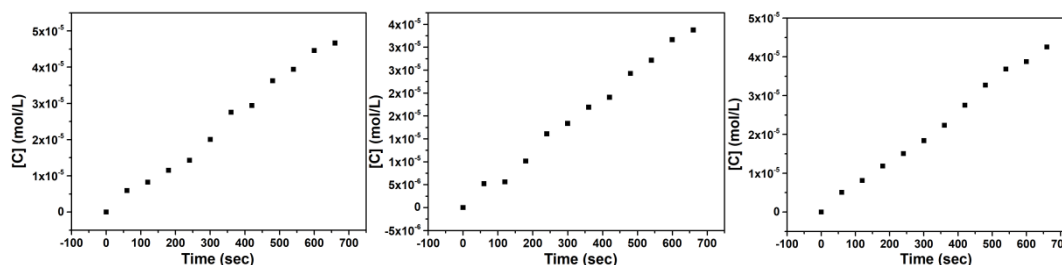
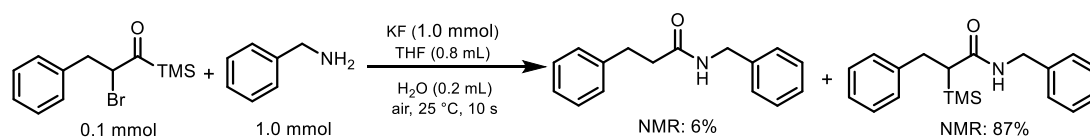


Figure S6. Product vs time (sec).

0.1 M (THF)



Under an ambient atmosphere, benzylamine (107.0 mg, 1.0 mmol, 10.0 equiv), THF (0.8 mL), H₂O (0.2 mL), KF (58.0 mg, 1.0 mmol, 10.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (28.4 mg, 0.1 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 10 s. The sample was analyzed by ¹H NMR. The percentage yield of the product was calculated by using 1,3,5-trimethoxybenzen (21.2 mg, 1.26 equiv) as an internal standard.

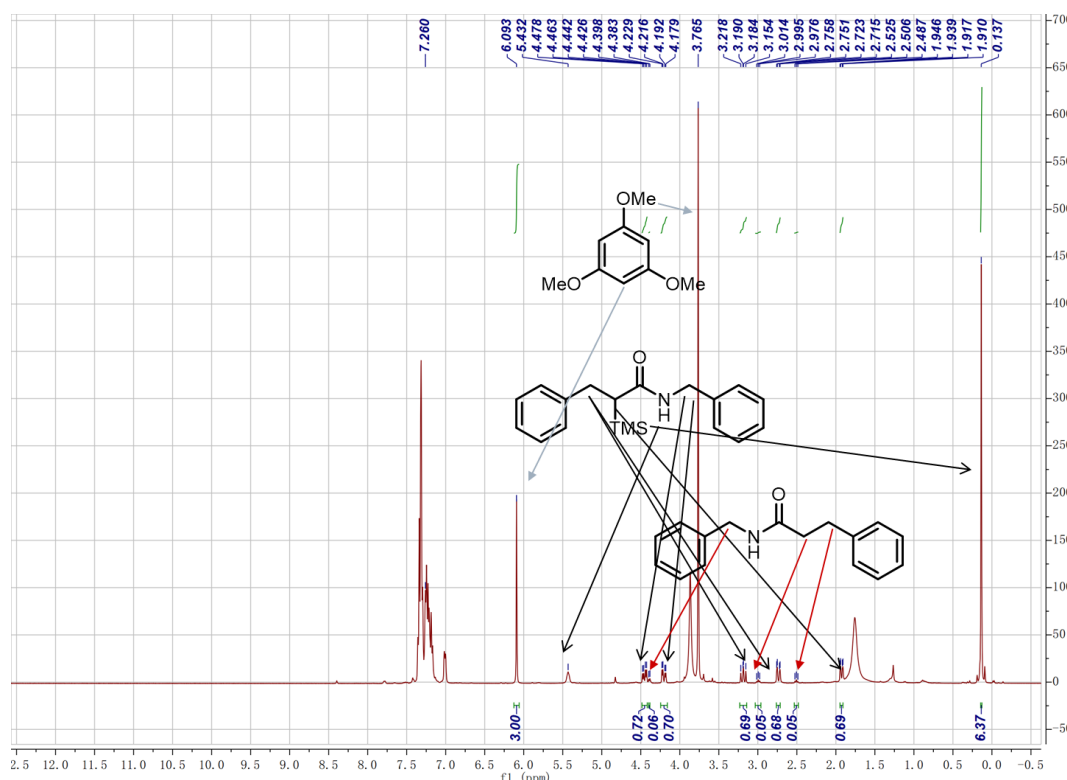
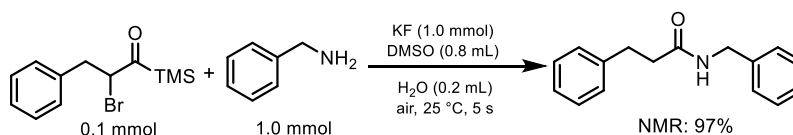


Figure S7. ¹H NMR (CDCl₃, 400 MHz, 298 K) of the resulting mixtures for **3a**, **3-Int** and 1,3,5-trimethoxybenzene (10 sec).

0.1 M (DMSO)



Under an ambient atmosphere, benzylamine (107.0 mg, 1.0 mmol, 10.0 equiv), DMSO (0.8 mL), H₂O (0.2 mL), KF (58.0 mg, 1.0 mmol, 10.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (28.4 mg, 0.1 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 5 sec. The sample was analyzed by ¹H NMR. The percentage yield of the product

was calculated by using 1,3,5-trimethoxybenzen (16.8 mg, 1.0 equiv) as an internal standard.

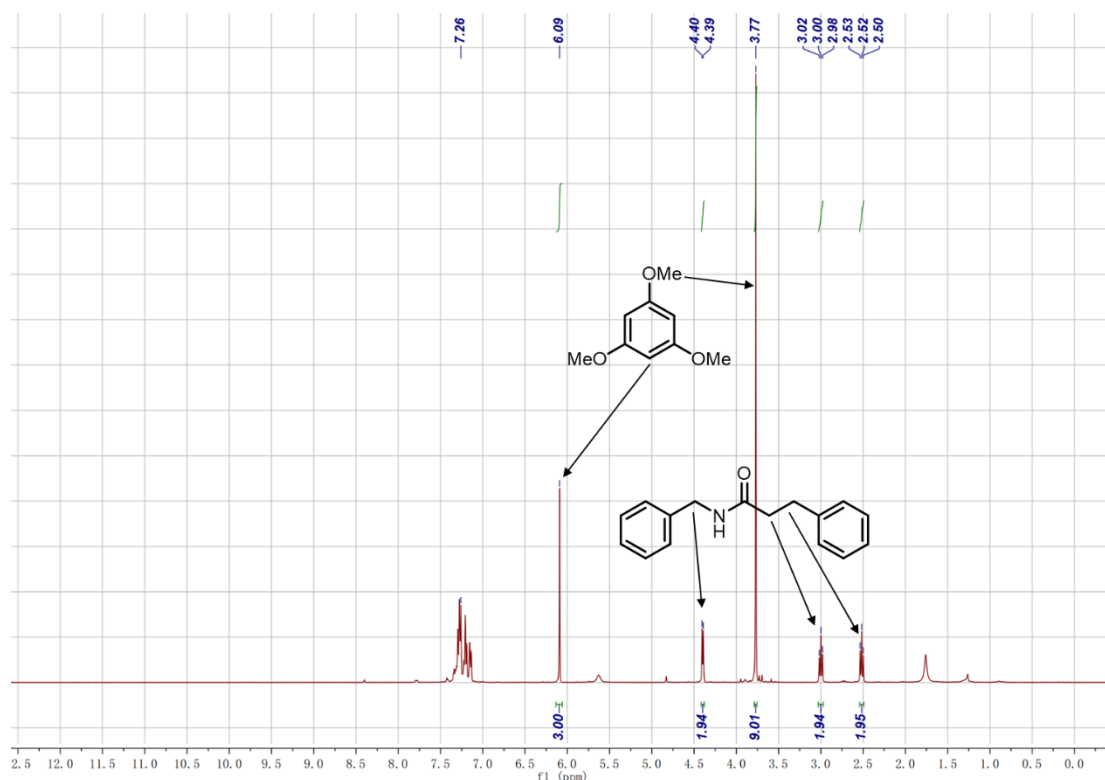
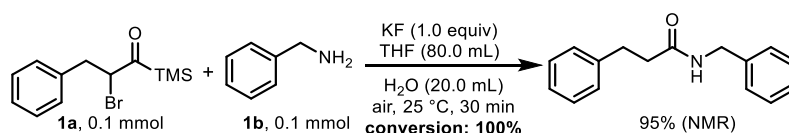


Figure S8. ^1H NMR (CDCl_3 , 400 MHz, 298 K) of the resulting mixtures for **3a** and 1,3,5-trimethoxybenzene (5 sec).

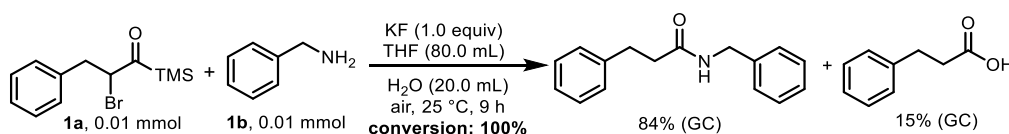
4: Investigation of the impact of concentration

1.0 mM concentration



Under an ambient atmosphere, benzylamine (10.7 mg, 0.1 mmol, 1.0 equiv), tetrahydrofuran (80.0 mL), H_2O (20.0 mL), KF (5.8 mg, 0.1 mmol, 1.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (28.4 mg, 0.1 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (250.0 mL) with a round-bottom flask. The reaction was stirred at 25 °C for 30 min. The sample was analyzed by ^1H NMR. The percentage yield of the product was calculated by using 1,3,5-trimethoxybenzen (16.8 mg, 1.0 equiv) as an internal standard.

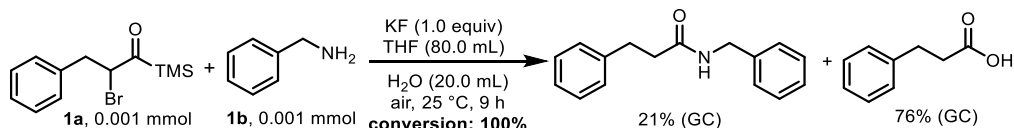
100 μM concentration



Under an ambient atmosphere, benzylamine (0.1 M, 100.0 μL , 1.0 equiv),

tetrahydrofuran (80.0 mL), H₂O (20.0 mL), KF (0.1 M, 100.0 μ L, 1.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (0.1 M, 100.0 μ L, 1.0 equiv) were added to an oven-dried round bottom flask (250.0 mL) with a round-bottom flask. The reaction was stirred at 25 °C for 9 h. The reaction was monitored by GC-MS, using 1,3,5-trimethoxybenzen as an internal standard.

10 μ M concentration



Under an ambient atmosphere, benzylamine (0.01 M, 100.0 μ L, 1.0 equiv), tetrahydrofuran (80.0 mL), H₂O (20.0 mL), KF (0.01 M, 100.0 μ L, 1.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (0.01 M, 100.0 μ L, 1.0 equiv) were added to an oven-dried round bottom flask (250.0 mL) with a round-bottom flask. The reaction was stirred at 25 °C for 9 h. The reaction was monitored by GC-MS, using 1,3,5-trimethoxybenzen as an internal standard.

5: Control experiments on leaving groups and silyl substituents

Under an ambient atmosphere, benzylamine (21.4 mg, 0.2 mmol, 1.0 equiv), tetrahydrofuran (1.6 mL), H₂O (0.4 mL), KF (11.6 mg, 0.2 mmol, 1.0 equiv), and **1a-X/Si** (0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 5 min. The sample was analyzed by ¹H NMR. The percentage yield of the product was calculated by using 1,3,5-trimethoxybenzen as an internal standard.

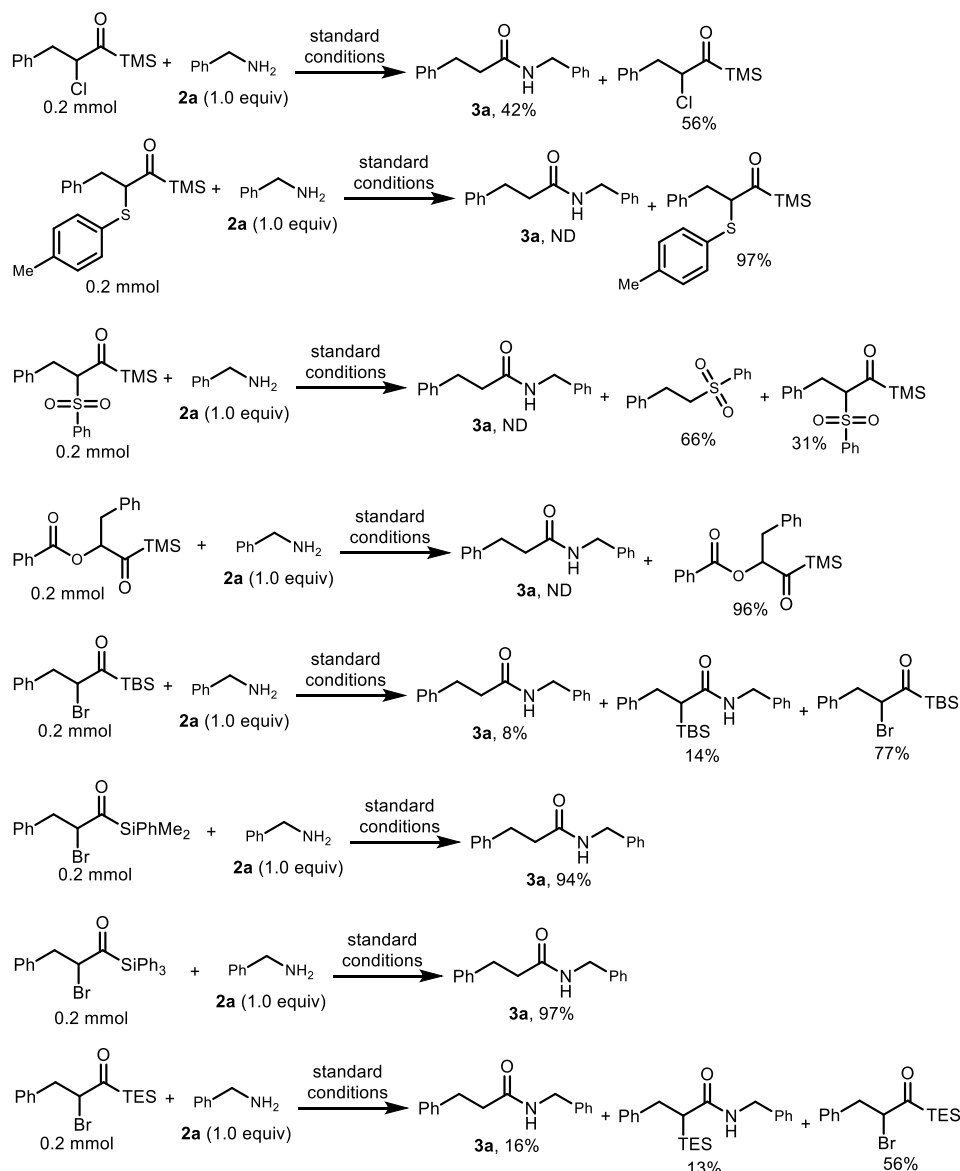
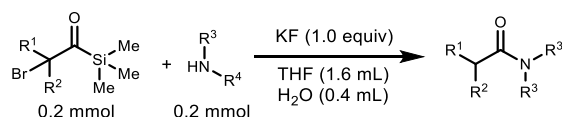


Figure S9. Leaving group and silyl substitution control studies.

6: Procedures for the synthesis of amides

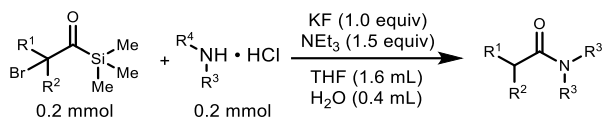
General Procedure III



Under an ambient atmosphere, amine (0.2 mmol, 1.0 equiv), tetrahydrofuran (1.6 mL), H₂O (0.4 mL), KF (11.6 mg, 0.2 mmol, 1.0 equiv), and α -bromo-acylsilanes (0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 2 h. Then water (10.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with EtOAc (3 $\times$ 10.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced

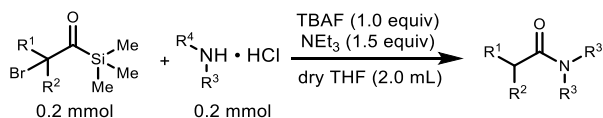
pressure. The crude mixture was purified by silica gel column chromatography to afford amides.

General Procedure IV



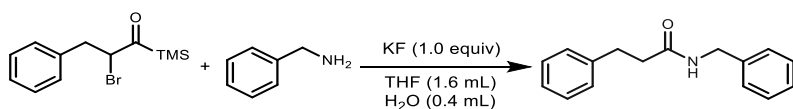
Under an ambient atmosphere, amine hydrochloride (0.2 mmol, 1.0 equiv), NEt₃ (30.3 mg, 0.3 mmol, 1.5 equiv), H₂O (0.4 mL) and KF (11.6 mg, 0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 30 min. Then tetrahydrofuran (1.6 mL) and α -bromo-acylsilanes (0.2 mmol, 1.0 equiv) were added to the reaction mixture and stirred at 25 °C for 2 h. Then water (10.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with EtOAc (3 $\times$ 10.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford amides.

General Procedure V



Under an ambient atmosphere, amine (0.2 mmol, 1.0 equiv), dry tetrahydrofuran (2.0 mL), NEt₃ (30.3 mg, 0.3 mmol, 1.5 equiv), TBAF (0.2 mmol, 1.0 equiv), and α -bromo-acylsilanes (0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 2 h. Then water (10.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with EtOAc (3 $\times$ 10.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford amides.

N-Benzyl-3-phenylpropanamide **3a**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and phenylmethanamine (21.4 mg, 0.2 mmol, 1.0 equiv) to give **3a** as a white solid.

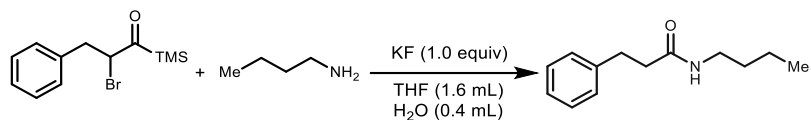
Yield 42.5 mg (89%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.33-7.27 (m, 5H), 7.24-7.21 (m, 3H), 7.17-7.15 (m, 2H), 5.70 (s, 1H), 4.41 (d, *J* = 5.6 Hz, 2H), 3.01 (t, *J* = 7.6 Hz, 2H), 2.53 (t, *J* = 7.6 Hz, 2H).

¹³C NMR (CDCl₃, 150 MHz) δ 172.0, 140.9, 138.3, 128.8, 128.7, 128.5, 127.9, 127.6, 126.4, 43.7, 38.6, 31.9.

N-Butyl-3-phenylpropanamide ³ **3b**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and butan-1-amine (14.6 mg, 0.2 mmol, 1.0 equiv) to give **3b** as a yellow oil.

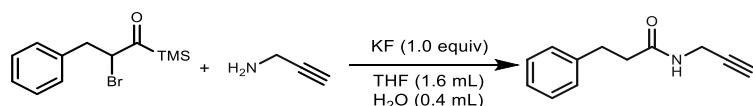
Yield 36.1 mg (88%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.32-7.28 (m, 2H), 7.23-7.20 (m, 3H), 5.36 (s, 1H), 3.22 (q, *J* = 6.7 Hz, 2H), 2.98 (t, *J* = 7.7 Hz, 2H), 2.48 (t, *J* = 7.7 Hz, 2H), 1.46-1.38 (m, 2H), 1.32-1.23 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (CDCl₃, 150 MHz) δ 172.1, 141.1, 128.7, 128.5, 126.4, 39.4, 38.8, 32.0, 31.8, 20.1, 13.8.

3-Phenyl-*N*-(prop-2-yn-1-yl)propanamide ⁴ **3c**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and prop-2-yn-1-amine (11.0 mg, 0.2 mmol, 1.0 equiv) to give **3c** as a white solid.

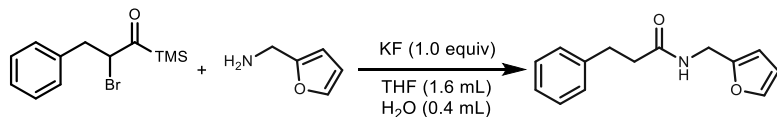
Yield 31.8 mg (85%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.32-7.28 (m, 2H), 7.24-7.20 (m, 3H), 5.86 (s, 1H), 4.04-4.02 (m, 2H), 2.99 (t, *J* = 7.8 Hz, 2H), 2.52 (t, *J* = 7.8 Hz, 2H), 2.22 (s, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ 171.9, 140.8, 128.7, 128.4, 126.4, 79.6, 71.6, 38.2, 31.6, 29.3.

N-(Furan-2-ylmethyl)-3-phenylpropanamide ³ **3d**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and furan-2-ylmethanamine (19.4 mg, 0.2 mmol, 1.0 equiv) to give **3d** as a white solid.

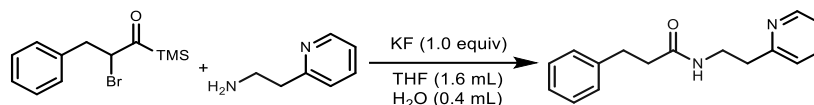
Yield 39.8 mg (87%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.34 (s, 1H), 7.28 (t, *J* = 7.3 Hz, 2H), 7.20 (t, *J* = 8.1 Hz, 3H), 6.32-6.31 (m, 1H), 6.16 (d, *J* = 3.2 Hz, 1H), 5.94 (s, 1H), 4.40 (d, *J* = 5.5 Hz, 2H), 2.98 (t, *J* = 7.8 Hz, 2H), 2.50 (t, *J* = 7.8 Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 172.0, 151.4, 142.2, 140.9, 128.6, 128.4, 126.3, 110.5, 107.5, 38.3, 36.5, 31.7.

3-Phenyl-*N*-(2-(pyridin-2-yl)ethyl)propanamide **3e**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and 2-(pyridin-2-yl)ethan-1-amine (24.4 mg, 0.2 mmol, 1.0 equiv) to give **3e** as a white solid.

Yield 38.5 mg (76%).

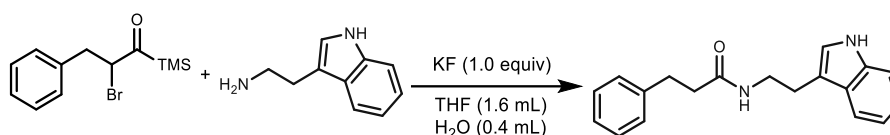
NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 8.48-8.46 (m, 1H), 7.62-7.57 (m, 1H), 7.24-7.22 (m, 2H), 7.17-7.09 (m, 5H), 6.45 (s, 1H), 3.64-3.60 (m, 2H), 2.94-2.88 (m, 4H), 2.45 (t, J = 7.8 Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 172.2, 159.6, 149.1, 141.0, 136.9, 128.5, 128.4, 126.2, 123.7, 121.7, 38.8, 38.6, 36.9, 31.8.

HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{ONa}^+$: 277.1311; Found 277.1304.

N-(2-(1*H*-Indol-3-yl)ethyl)-3-phenylpropanamide **3f**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and 2-(1*H*-indol-3-yl)ethan-1-amine (32.0 mg, 0.2 mmol, 1.0 equiv) to give **3f** as a white solid.

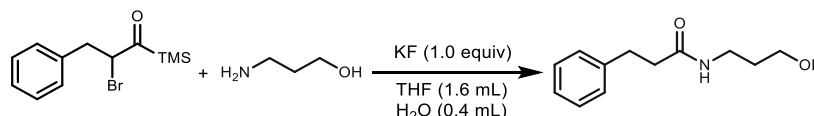
Yield 49.6 mg (85%).

NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 8.42 (s, 1H), 7.59 (d, J = 7.9 Hz, 1H), 7.40 (d, J = 8.1 Hz, 1H), 7.33-7.29 (m, 2H), 7.25-7.13 (m, 5H), 6.88 (d, J = 2.2 Hz, 1H), 5.59 (s, 1H), 3.59 (q, J = 6.5 Hz, 2H), 2.99-2.92 (m, 4H), 2.43 (t, J = 7.7 Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 172.3, 141.0, 136.5, 128.6, 128.5, 127.4, 126.3, 122.22, 122.18, 119.5, 118.7, 112.8, 111.4, 39.8, 38.6, 31.8, 25.3.

N-(3-Hydroxypropyl)-3-phenylpropanamide **3g**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and 3-aminopropan-1-ol (15.0 mg, 0.2 mmol, 1.0 equiv) to give **3g** as a yellow oil.

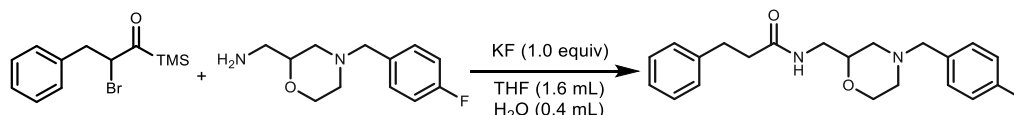
Yield 27.5 mg (66%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.32-7.28 (m, 2H), 7.23-7.20 (m, 3H), 5.96 (s, 1H), 3.53 (t, *J* = 5.6 Hz, 2H), 3.37 (q, *J* = 6.1 Hz, 2H), 2.98 (t, *J* = 7.6 Hz, 2H), 2.69 (s, 1H), 2.51 (t, *J* = 7.6 Hz, 2H), 1.64-1.58 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 173.5, 140.8, 128.7, 128.5, 126.4, 59.4, 38.5, 36.4, 32.2, 31.9.

***N*-((4-(4-Fluorobenzyl)morpholin-2-yl)methyl)-3-phenylpropanamide 3h**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and (4-(4-fluorobenzyl)morpholin-2-yl)methanamine (44.8 mg, 0.2 mmol, 1.0 equiv) to give **3h** as a white solid.

Yield 54.3 mg (76%).

NMR Spectroscopy:

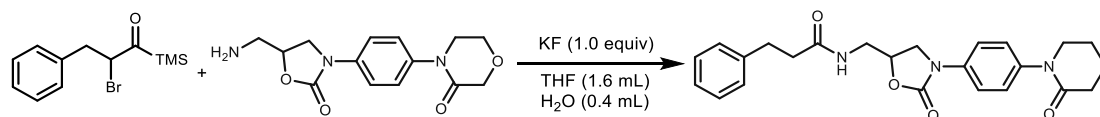
¹H NMR (CDCl₃, 400 MHz) δ 7.31-7.27 (m, 3H), 7.25-7.24 (m, 1H), 7.22-7.18 (m, 3H), 7.03-7.00 (m, 2H), 5.84 (t, *J* = 5.7 Hz, 1H), 3.82-3.78 (m, 1H), 3.63-3.43 (m, 5H), 3.13-3.06 (m, 1H), 2.96 (t, *J* = 7.7 Hz, 2H), 2.67-2.59 (m, 2H), 2.49 (t, *J* = 7.7 Hz, 2H), 2.13-2.06 (m, 1H), 1.82 (t, *J* = 10.6 Hz, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.2, 162.2 (d, *J* = 244.0 Hz), 140.9, 133.3 (d, *J* = 3.0 Hz), 130.6 (d, *J* = 8.0 Hz), 128.6, 128.4, 126.3, 115.2 (d, *J* = 21.0 Hz), 74.5, 66.7, 62.4, 55.7, 52.8, 41.9, 38.4, 31.7.

¹⁹F NMR (CDCl₃, 565 MHz) δ -115.48.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₁H₂₆FN₂O₂⁺: 357.1973; Found 357.1964.

***N*-((2-Oxo-3-(4-(3-oxomorpholino)phenyl)oxazolidin-5-yl)methyl)-3-phenylpropanamide 3i**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and 4-(4-(5-(aminomethyl)-2-oxooxazolidin-3-yl)phenyl)morpholin-3-one (58.2 mg, 0.2 mmol, 1.0 equiv) to give **3i** as a white solid.

Yield 68.5 mg (81%).

NMR Spectroscopy:

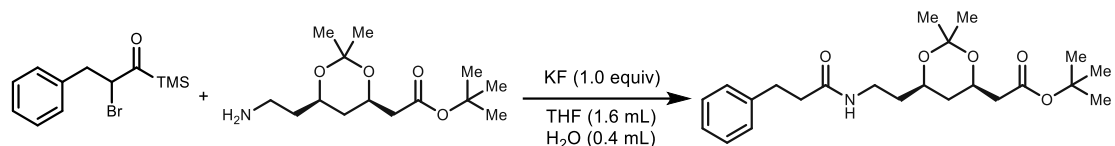
¹H NMR (CDCl₃, 400 MHz) δ 7.50 (d, *J* = 9.0 Hz, 2H), 7.30 (d, *J* = 9.0 Hz, 2H), 7.24-7.21 (m, 2H), 7.16-7.13 (m, 3H), 6.51 (t, *J* = 6.2 Hz, 1H), 4.67-4.61 (m, 1H), 4.32 (s, 2H), 4.02 (t, *J* = 4.8 Hz, 2H), 3.91 (t, *J* = 8.9 Hz, 1H), 3.73-3.65 (m, 3H), 3.54 (t, *J* = 5.4 Hz, 2H), 2.91 (t, *J* = 7.7 Hz, 2H), 2.50 (t, *J* = 7.7 Hz, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 173.4, 167.0, 154.5, 140.7, 137.3, 136.8, 128.6,

128.4, 126.4, 126.3, 119.0, 72.0, 68.6, 64.2, 49.8, 47.6, 41.7, 38.0, 31.6.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{23}H_{25}N_3O_5Na^+$: 446.1686; Found 446.1674.

tert*-Butyl 2-((4*R*,6*R*)-2,2-dimethyl-6-(2-(3-phenylpropanamido)ethyl)-1,3-dioxan-4-yl)acetate **3j*



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and *tert*-butyl 2-((4*R*,6*R*)-6-(2-aminoethyl)-2,2-dimethyl-1,3-dioxan-4-yl)acetate (54.6 mg, 0.2 mmol, 1.0 equiv) to give **3j** as a white solid.

Yield 68.9 mg (85%).

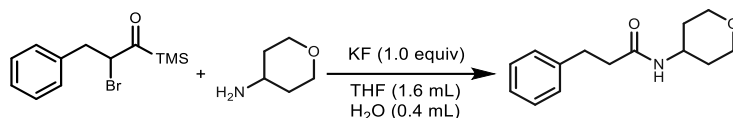
NMR Spectroscopy:

1H NMR ($CDCl_3$, 400 MHz) δ 7.31-7.27 (m, 2H), 7.22-7.18 (m, 3H), 6.06 (t, J = 5.4 Hz, 1H), 4.26-4.19 (m, 1H), 3.91-3.84 (m, 1H), 3.45-3.38 (m, 1H), 3.26-3.18 (m, 1H), 2.94 (t, J = 7.3 Hz, 2H), 2.46-2.38 (m, 3H), 2.31-2.26 (m, 1H), 1.67-1.62 (m, 1H), 1.55-1.48 (m, 2H), 1.45 (s, 9H), 1.40 (s, 3H), 1.34 (s, 3H), 1.28-1.17 (m, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.9, 170.2, 141.0, 128.6, 128.4, 126.3, 98.8, 80.8, 68.7, 66.3, 42.7, 38.8, 36.9, 36.2, 35.1, 31.9, 30.3, 28.2, 19.8.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{23}H_{35}NO_5Na^+$: 428.2407; Found 428.2398.

3-Phenyl-*N*-(tetrahydro-2*H*-pyran-4-yl)propanamide **3k**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and tetrahydro-2*H*-pyran-4-amine (20.2 mg, 0.2 mmol, 1.0 equiv) to give **3k** as a white solid.

Yield 45.3 mg (97%).

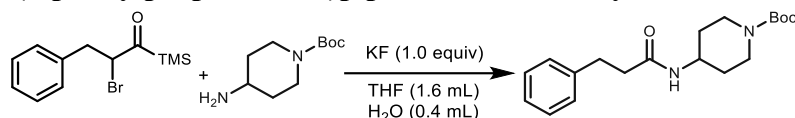
NMR Spectroscopy:

1H NMR ($CDCl_3$, 400 MHz) δ 7.30-7.28 (m, 2H), 7.21-7.18 (m, 3H), 5.23 (s, 1H), 4.00-3.86 (m, 3H), 3.46-3.40 (m, 2H), 2.96 (t, J = 7.5 Hz, 2H), 2.45 (t, J = 7.5 Hz, 2H), 1.82-1.77 (m, 2H), 1.37-1.25 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.5, 140.9, 128.7, 128.5, 126.5, 66.8, 45.6, 38.8, 33.2, 31.9.

HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{14}H_{20}NO_2^+$: 234.1489; Found 234.1483.

***tert*-Butyl 4-(3-phenylpropanamido)piperidine-1-carboxylate ⁷ 3l**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and *tert*-butyl 4-aminopiperidine-1-carboxylate (40.0 mg, 0.2 mmol, 1.0 equiv) to give **3l** as a white solid.

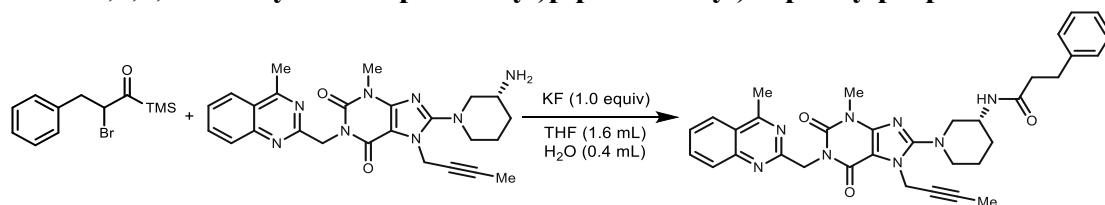
Yield 61.3 mg (92%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.30-7.28 (m, 2H), 7.23-7.18 (m, 3H), 5.38 (s, 1H), 3.99-3.84 (m, 3H), 2.95 (t, *J* = 7.5 Hz, 2H), 2.82 (t, *J* = 12.5 Hz, 2H), 2.45 (t, *J* = 7.6 Hz, 2H), 1.82-1.78 (m, 2H), 1.44 (s, 9H), 1.22-1.12 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 171.5, 154.8, 140.8, 128.6, 128.5, 126.4, 79.7, 46.6, 42.7, 38.7, 32.1, 31.9, 28.5.

(*R*)-*N*-(1-(7-(But-2-yn-1-yl)-3-methyl-1-((4-methylquinazolin-2-yl)methyl)-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purin-8-yl)piperidin-3-yl)-3-phenylpropanamide **3m**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and (*R*)-8-(3-aminopiperidin-1-yl)-7-(but-2-yn-1-yl)-3-methyl-1-((4-methylquinazolin-2-yl)methyl)-3,7-dihydro-1*H*-purine-2,6-dione (94.4 mg, 0.2 mmol, 1.0 equiv) to give **3m** as a white solid.

Yield 112.9 mg (93%).

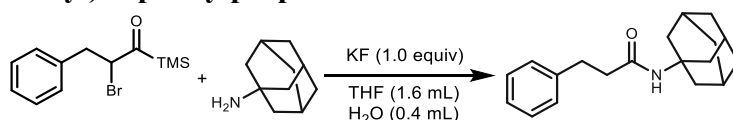
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.00 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.73 (t, *J* = 7.7 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.26-7.22 (m, 2H), 7.17-7.14 (m, 3H), 6.59 (d, *J* = 7.2 Hz, 1H), 5.60-5.51 (m, 2H), 4.81 (d, *J* = 2.5 Hz, 2H), 4.16-4.09 (m, 1H), 3.52 (s, 3H), 3.47-3.37 (m, 2H), 3.34-3.19 (m, 2H), 2.96 (t, *J* = 7.5 Hz, 2H), 2.87 (s, 3H), 2.49 (t, *J* = 7.5 Hz, 2H), 1.77-1.72 (m, 5H), 1.66-1.62 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 171.6, 168.7, 161.1, 155.9, 154.5, 151.9, 150.0, 147.6, 140.8, 133.4, 128.9, 128.6, 128.4, 126.8, 126.4, 124.9, 123.2, 104.6, 81.6, 73.1, 54.0, 51.0, 46.4, 45.1, 38.8, 35.7, 32.0, 29.8, 28.9, 21.92, 21.85, 3.8.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₃₄H₃₇N₈O₃⁺: 605.2983; Found 605.2966.

N-(Adamantan-1-yl)-3-phenylpropanamide **3n**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and adamantan-1-amine (30.2 mg, 0.2 mmol, 1.0 equiv) to give **3n** as a white solid.

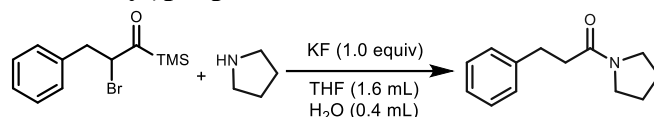
Yield 47.8 mg (84%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.33-7.29 (m, 2H), 7.24-7.21 (m, 3H), 5.10 (s, 1H), 2.96 (t, *J* = 7.6 Hz, 2H), 2.41 (t, *J* = 7.6 Hz, 2H), 2.09-2.07 (m, 3H), 1.96 (d, *J* = 3.0 Hz, 6H), 1.70-1.68 (m, 6H).

¹³C NMR (CDCl₃, 100 MHz) δ 171.3, 141.2, 128.5, 126.2, 51.9, 41.7, 39.6, 36.4, 31.9, 29.5.

3-Phenyl-1-(pyrrolidin-1-yl)propan-1-one **3o**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and pyrrolidine (14.2 mg, 0.2 mmol, 1.0 equiv) to give **3o** as a yellow oil.

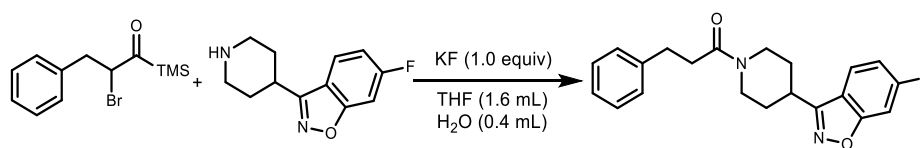
Yield 34.1 mg (84%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.30-7.27 (m, 2H), 7.24-7.17 (m, 3H), 3.46 (t, *J* = 6.7 Hz, 2H), 3.28 (t, *J* = 6.6 Hz, 2H), 3.00-2.96 (m, 2H), 2.58-2.54 (m, 2H), 1.91-1.80 (m, 4H).

¹³C NMR (CDCl₃, 100 MHz) δ 170.9, 141.6, 128.51, 128.48, 126.1, 46.6, 45.7, 36.8, 31.3, 26.1, 24.4.

1-(4-(6-Fluorobenzo[d]isoxazol-3-yl)piperidin-1-yl)-3-phenylpropan-1-one **3p**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and 6-fluoro-3-(piperidin-4-yl)benzo[d]isoxazole (44.0 mg, 0.2 mmol, 1.0 equiv) to give **3p** as a white solid.

Yield 60.6 mg (86%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.60-7.57 (m, 1H), 7.31-7.27 (m, 2H), 7.24-7.17 (m, 4H), 7.08-7.03 (m, 1H), 4.67 (d, *J* = 13.3 Hz, 1H), 3.94 (d, *J* = 13.6 Hz, 1H), 3.32-3.24 (m, 1H), 3.17 (t, *J* = 11.6 Hz, 1H), 3.00 (t, *J* = 7.9 Hz, 2H), 2.88 (t, *J* =

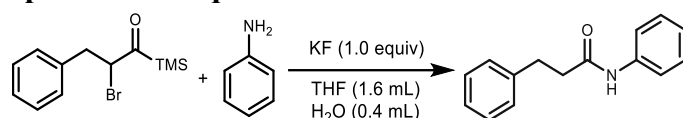
11.4 Hz, 1H), 2.70-2.66 (m, 2H), 2.12-2.02 (m, 2H), 1.90-1.78 (m, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 170.7, 164.2 (d, $J = 249.0$ Hz), 163.9 (d, $J = 13.0$ Hz), 160.2, 141.3, 128.6, 128.5, 126.3, 122.3 (d, $J = 11.0$ Hz), 117.1, 112.6 (d, $J = 25.0$ Hz), 97.6 (d, $J = 27.0$ Hz), 45.4, 41.5, 35.1, 34.3, 31.6, 30.5, 30.2.

^{19}F NMR (CDCl_3 , 376 MHz) δ -109.09.

HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{21}\text{H}_{21}\text{FN}_2\text{O}_2\text{Na}^+$: 375.1479; Found 375.1468.

***N*,3-Diphenylpropanamide ³ 3q**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3q** as a white solid.

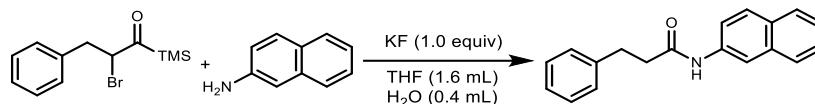
Yield 42.8 mg (95%).

NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 7.44 (d, $J = 8.0$ Hz, 2H), 7.39 (s, 1H), 7.31-7.27 (m, 4H), 7.23-7.20 (m, 3H), 7.09 (t, $J = 7.4$ Hz, 1H), 3.03 (t, $J = 7.7$ Hz, 2H), 2.64 (t, $J = 7.7$ Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 170.7, 140.7, 137.9, 129.0, 128.7, 128.5, 126.5, 124.4, 120.1, 39.5, 31.7.

***N*-(Naphthalen-2-yl)-3-phenylpropanamide ¹⁰ 3r**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and naphthalen-2-amine (28.6 mg, 0.2 mmol, 1.0 equiv) to give **3r** as a white solid.

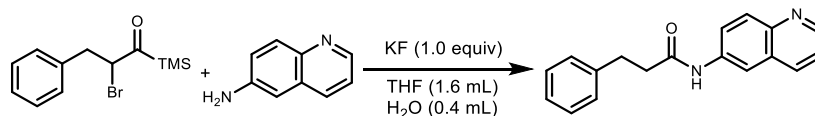
Yield 47.5 mg (86%).

NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 8.20 (s, 1H), 7.82-7.78 (m, 3H), 7.51-7.44 (m, 2H), 7.43-7.39 (m, 2H), 7.37-7.34 (m, 2H), 7.31-7.29 (m, 3H), 3.14 (t, $J = 7.6$ Hz, 2H), 2.76 (t, $J = 7.6$ Hz, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 170.7, 140.7, 135.3, 133.9, 130.8, 128.83, 128.80, 128.5, 127.8, 127.7, 126.65, 126.62, 125.1, 120.0, 116.9, 39.7, 31.7.

3-Phenyl-*N*-(quinolin-6-yl)propenamide 3s



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and quinolin-6-amine (28.8 mg, 0.2 mmol, 1.0 equiv) to give **3s** as a white solid.

Yield 31.4 mg (57%).

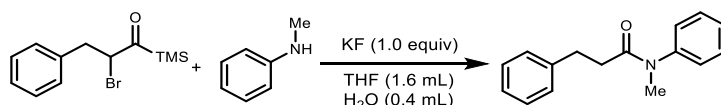
NMR Spectroscopy:

¹H NMR (CDCl₃, 600 MHz) δ 8.80 (d, *J* = 2.4 Hz, 1H), 8.36 (s, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 9.0 Hz, 1H), 7.63 (s, 1H), 7.43-7.42 (m, 1H), 7.39-7.36 (m, 1H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.25-7.21 (m, 3H), 3.09 (t, *J* = 7.6 Hz, 2H), 2.74 (t, *J* = 7.6 Hz, 2H).

¹³C NMR (CDCl₃, 150 MHz) δ 171.0, 149.3, 145.4, 140.6, 136.2, 135.9, 130.0, 129.0, 128.9, 128.5, 126.6, 123.4, 121.8, 116.3, 39.7, 31.7.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₈H₁₆N₂ONa⁺: 299.1155; Found 299.1151.

***N*-Methyl-*N*,3-diphenylpropanamide ¹¹ 3t**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and *N*-methylaniline (21.4 mg, 0.2 mmol, 1.0 equiv) to give **3t** as a white solid.

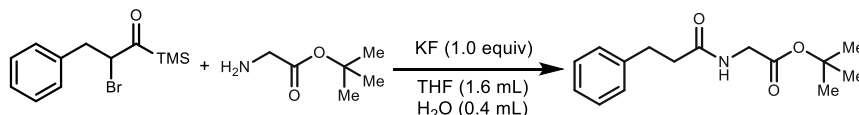
Yield 28.8 mg (60%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.39-7.36 (m, 2H), 7.32-7.28 (m, 1H), 7.24-7.21 (m, 2H), 7.18-7.14 (m, 1H), 7.07-7.01 (m, 4H), 3.25 (s, 3H), 2.91 (t, *J* = 7.8 Hz, 2H), 2.37 (t, *J* = 7.8 Hz, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.4, 144.1, 141.3, 129.8, 128.5, 128.4, 127.9, 127.4, 126.1, 37.5, 36.1, 31.9.

***tert*-Butyl (3-phenylpropanoyl)glycinate ¹² 3u**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and *tert*-butyl glycinate (26.2 mg, 0.2 mmol, 1.0 equiv) to give **3u** as a yellow oil.

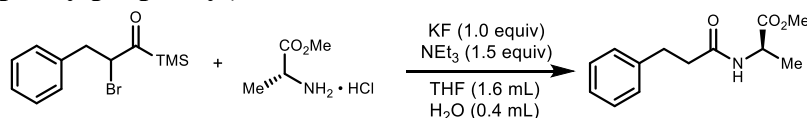
Yield 50.7 mg (96%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.32-7.28 (m, 2H), 7.21-7.19 (m, 3H), 5.94 (s, 1H), 3.94 (d, *J* = 4.8 Hz, 2H), 2.99 (t, *J* = 7.9 Hz, 2H), 2.56 (t, *J* = 7.9 Hz, 2H), 1.48 (s, 9H).

¹³C NMR (CDCl₃, 150 MHz) δ 172.2, 169.3, 140.9, 128.7, 128.4, 126.4, 82.5, 42.2, 38.2, 31.6, 28.2.

Methyl (3-phenylpropanoyl)-*D*-alaninate ¹³ 3v



Prepared via **General Procedure IV** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and methyl *D*-alaninate hydrochloride (27.8 mg, 0.2 mmol, 1.0 equiv) to give **3v** as a white solid.

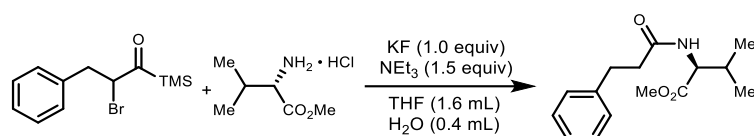
Yield 39.8 mg (85%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.34-7.30 (m, 2H), 7.25-7.21 (m, 3H), 6.07 (d, *J* = 7.1 Hz, 1H), 4.66-4.59 (m, 1H), 3.77 (s, 3H), 3.00 (t, *J* = 7.8 Hz, 2H), 2.63-2.49 (m, 2H), 1.37 (d, *J* = 7.2 Hz, 3H).

¹³C NMR (CDCl₃, 100 MHz) δ 173.7, 172.0, 140.7, 128.6, 128.5, 126.4, 52.6, 48.1, 38.3, 31.6, 18.5.

Methyl (3-phenylpropanoyl)-*L*-valinate ¹⁴ 3w



Prepared via **General Procedure IV** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and methyl *L*-valinate hydrochloride (33.4 mg, 0.2 mmol, 1.0 equiv) to give **3w** as a white solid.

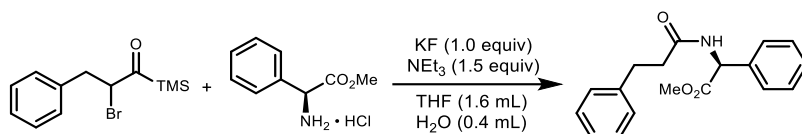
Yield 49.1 mg (93%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.32-7.28 (m, 2H), 7.23-7.19 (m, 3H), 6.02 (d, *J* = 8.3 Hz, 1H), 4.59-4.55 (m, 1H), 3.73 (s, 3H), 3.03-2.94 (m, 2H), 2.64-2.52 (m, 2H), 2.14-2.06 (m, 1H), 0.87-0.83 (m, 6H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.7, 172.0, 140.7, 128.6, 128.4, 126.3, 57.0, 52.2, 38.3, 31.6, 31.3, 18.9, 17.8.

Methyl (*S*)-2-phenyl-2-(3-phenylpropanamido)acetate 3x



Prepared via **General Procedure IV** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and methyl (*S*)-2-amino-2-phenylacetate hydrochloride (40.2 mg, 0.2 mmol, 1.0 equiv) to give **3x** as a white solid.

Yield 51.1 mg (86%).

NMR Spectroscopy:

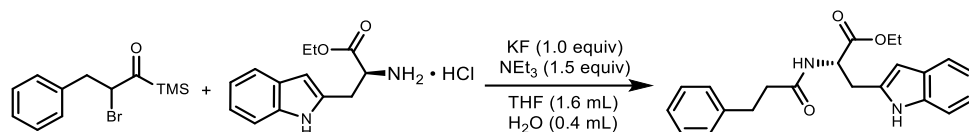
¹H NMR (CDCl₃, 400 MHz) δ 7.30-7.27 (m, 3H), 7.25-7.22 (m, 4H), 7.17-7.12 (m, 3H), 6.46 (d, *J* = 7.2 Hz, 1H), 5.54 (d, *J* = 7.1 Hz, 1H), 3.67 (s, 3H), 2.92 (t, *J* = 7.7 Hz, 2H), 2.59-2.44 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 171.5, 140.7, 136.5, 129.0, 128.62, 128.56, 128.4,

127.3, 126.3, 56.4, 52.9, 38.0, 31.5.

HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{18}H_{20}NO_3^+$: 298.1438; Found 298.1430.

Ethyl (3-phenylpropanoyl)-*L*-tryptophanate **3y**



Prepared via **General Procedure IV** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and ethyl *L*-tryptophanate hydrochloride (53.6 mg, 0.2 mmol, 1.0 equiv) to give **3y** as a white solid.

Yield 68.9 mg (95%).

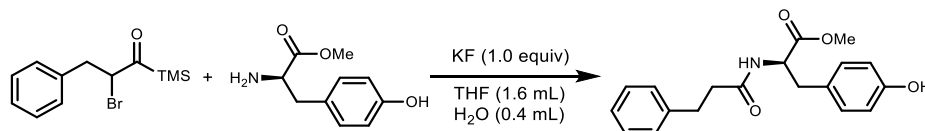
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.22 (s, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.35 (d, J = 8.1 Hz, 1H), 7.30-7.27 (m, 2H), 7.23-7.16 (m, 4H), 7.10 (t, J = 7.5 Hz, 1H), 6.79 (s, 1H), 5.99 (s, 1H), 4.97-4.92 (m, 1H), 4.19-4.06 (m, 2H), 3.28 (d, J = 5.4 Hz, 2H), 3.00-2.88 (m, 2H), 2.53-2.38 (m, 2H), 1.22 (t, J = 7.1 Hz, 3H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.1, 171.8, 140.9, 136.2, 128.6, 128.5, 127.9, 126.3, 122.9, 122.3, 119.7, 118.7, 111.4, 110.1, 61.6, 53.1, 38.3, 31.5, 27.7, 14.2.

HRMS (ESI) m/z : $[M + H]^+$ Calcd for $C_{22}H_{25}N_2O_3^+$: 365.1860; Found 365.1850.

Methyl (3-phenylpropanoyl)-*D*-tyrosinate ¹⁵ **3z**



Prepared via **General Procedure III** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and methyl *D*-tyrosinate (39.0 mg, 0.2 mmol, 1.0 equiv) to give **3z** as a white solid.

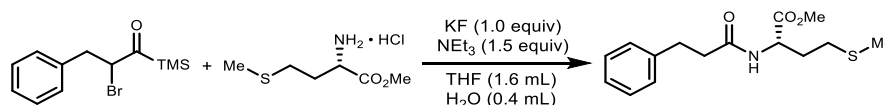
Yield 61.8 mg (94%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.30-7.26 (m, 2H), 7.22-7.16 (m, 3H), 6.79 (d, J = 8.4 Hz, 2H), 6.69 (d, J = 8.4 Hz, 2H), 5.97 (s, 1H), 4.89-4.84 (m, 1H), 3.71 (s, 3H), 3.02-2.87 (m, 4H), 2.57-2.42 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.3, 155.5, 140.6, 130.4, 128.7, 128.5, 127.1, 127.0, 126.5, 115.7, 53.3, 52.5, 38.3, 37.3, 31.6.

Methyl (3-phenylpropanoyl)-*L*-methioninate ¹⁶ **3aa**



Prepared via **General Procedure IV** starting from **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) and methyl *L*-methioninate hydrochloride (39.8 mg, 0.2 mmol, 1.0 equiv) to give **3aa**

as a white solid.

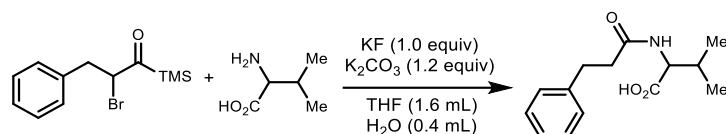
Yield 43.7 mg (74%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.32-7.28 (m, 2H), 7.23-7.19 (m, 3H), 6.11 (d, J = 7.9 Hz, 1H), 4.74-4.68 (m, 1H), 3.75 (s, 3H), 3.05-2.93 (m, 2H), 2.63-2.49 (m, 2H), 2.43-2.31 (m, 2H), 2.15-2.06 (m, 4H), 1.96-1.87 (m, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.6, 171.9, 140.7, 128.7, 128.5, 126.4, 52.6, 51.5, 38.3, 31.8, 31.6, 29.9, 15.5.

(3-Phenylpropanoyl)valine ¹⁷ 3ab



Under an ambient atmosphere, valine (23.4 mg, 0.2 mmol, 1.0 equiv), K₂CO₃ (33.2 mg, 0.24 mmol, 1.2 equiv), H₂O (0.4 mL) and KF (11.6 mg, 0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 30 min. Then tetrahydrofuran (1.6 mL) and **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) were added to the reaction mixture and stirred at 25 °C for 2 h. The reaction mixture was acidified by addition of 1 M aqueous HCl to pH = 1-2. Then water (10.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with DCM (3 × 10.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **3ab** as a white solid.

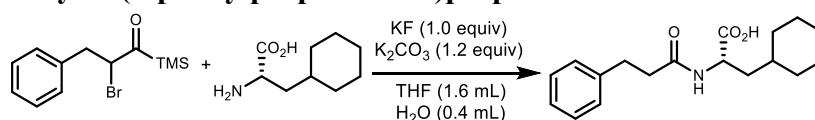
Yield 44.8 mg (90%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.30-7.26 (m, 2H), 7.21-7.17 (m, 3H), 5.92 (d, J = 8.5 Hz, 1H), 4.57-4.54 (m, 1H), 3.03-2.93 (m, 2H), 2.65-2.32 (m, 2H), 2.20-2.12 (m, 1H), 0.89-0.84 (m, 6H).

¹³C NMR (CDCl₃, 100 MHz) δ 175.5, 172.9, 140.5, 128.8, 128.5, 126.5, 57.2, 38.4, 31.7, 31.0, 19.0, 17.7.

(S)-3-Cyclohexyl-2-(3-phenylpropanamido)propanoic acid ¹⁸ 3ac



Under an ambient atmosphere, (S)-2-amino-3-cyclohexylpropanoic acid (34.2 mg, 0.2 mmol, 1.0 equiv), K₂CO₃ (33.2 mg, 0.24 mmol, 1.2 equiv), H₂O (0.4 mL) and KF (11.6 mg, 0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 30 min. Then tetrahydrofuran (1.6 mL) and **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) were added to the reaction mixture and stirred at 25 °C for 2 h. The reaction mixture was acidified by addition of 1 M aqueous

HCl to pH = 1-2. Then water (10.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with DCM (3 × 10.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **3ac** as a white solid.

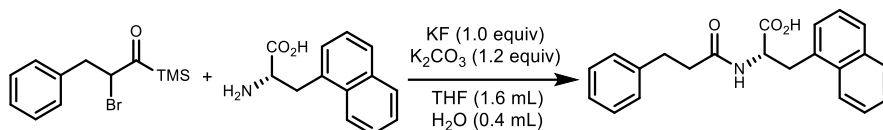
Yield 53.5 mg (88%).

NMR Spectroscopy:

¹H NMR (DMSO-*d*₆, 400 MHz) δ 12.5 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.27-7.15 (m, 5H), 4.27-4.21 (m, 1H), 2.83-2.79 (m, 2H), 2.47-2.36 (m, 2H), 1.66-1.58 (m, 5H), 1.52-1.45 (m, 2H), 1.27-1.04 (m, 4H), 0.93-0.74 (m, 2H).

¹³C NMR (DMSO-*d*₆, 100 MHz) δ 175.6, 172.7, 142.5, 129.5, 129.4, 127.1, 50.6, 39.8, 37.8, 34.7, 34.4, 32.7, 32.2, 27.3, 27.0, 26.8.

(*S*)-3-(Naphthalen-1-yl)-2-(3-phenylpropanamido)propanoic acid 3ad



Under an ambient atmosphere, (*S*)-2-amino-3-(naphthalen-1-yl)propanoic acid (43.0 mg, 0.2 mmol, 1.0 equiv), K₂CO₃ (33.2 mg, 0.24 mmol, 1.2 equiv), H₂O (0.4 mL) and KF (11.6 mg, 0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 30 min. Then tetrahydrofuran (1.6 mL) and **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) were added to the reaction mixture and stirred at 25 °C for 2 h. The reaction mixture was acidified by addition of 1 M aqueous HCl to pH = 1-2. Then water (10.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with DCM (3 × 10.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **3ad** as a white solid.

Yield 55.0 mg (79%).

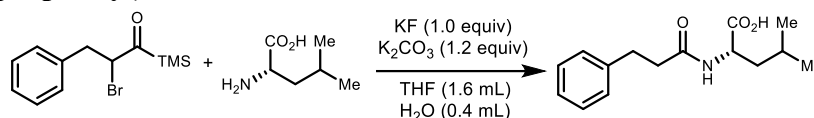
NMR Spectroscopy:

¹H NMR (DMSO-*d*₆, 400 MHz) δ 12.75 (s, 1H), 8.33 (d, *J* = 8.1 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 7.9 Hz, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.3 Hz, 1H), 7.42-7.37 (m, 2H), 7.22 (t, *J* = 7.3 Hz, 2H), 7.23-7.10 (m, 3H), 4.60-4.54 (m, 1H), 3.60-3.56 (m, 1H), 3.27-3.21 (m, 1H), 2.70-2.66 (m, 2H), 2.36-2.32 (m, 2H).

¹³C NMR (DMSO-*d*₆, 100 MHz) δ 174.5, 172.7, 142.4, 134.9, 134.7, 132.7, 130.0, 129.4, 129.3, 128.6, 128.4, 127.5, 127.4, 126.9, 126.6, 124.6, 54.0, 37.9, 35.6, 32.1.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₂H₂₂NO₃⁺: 348.1594; Found 348.1585.

(3-Phenylpropanoyl)-*L*-leucine **3ae**



Under an ambient atmosphere, *L*-leucine (26.2 mg, 0.2 mmol, 1.0 equiv), K₂CO₃ (33.2 mg, 0.24 mmol, 1.2 equiv), H₂O (0.4 mL) and KF (11.6 mg, 0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 30 min. Then tetrahydrofuran (1.6 mL) and **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) were added to the reaction mixture and stirred at 25 °C for 2 h. The reaction mixture was acidified by addition of 1 M aqueous HCl to pH = 1-2. Then water (10.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with DCM (3 × 10.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **3ae** as a white solid.

Yield 47.9 mg (91%).

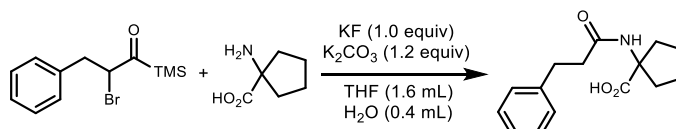
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 10.75 (s, 1H), 7.30-7.27 (m, 2H), 7.21-7.18 (m, 3H), 6.01 (d, *J* = 7.9 Hz, 1H), 4.62-4.57 (m, 1H), 2.97 (t, *J* = 8.1 Hz, 2H), 2.66-2.62 (m, 2H), 1.67-1.62 (m, 1H), 1.54-1.45 (h, *J* = 6.5 Hz, 2H), 0.89 (d, *J* = 5.9 Hz, 6H).

¹³C NMR (CDCl₃, 100 MHz) δ 176.8, 173.1, 140.5, 128.7, 128.5, 126.5, 51.0, 41.2, 38.2, 31.6, 24.8, 22.9, 21.9.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₅H₂₂NO₃⁺: 264.1594; Found 264.1588.

1-(3-Phenylpropanamido)cyclopentane-1-carboxylic acid ¹⁹ **3af**



Under an ambient atmosphere, 1-aminocyclopentane-1-carboxylic acid (25.8 mg, 0.2 mmol, 1.0 equiv), K₂CO₃ (33.2 mg, 0.24 mmol, 1.2 equiv), H₂O (0.4 mL) and KF (11.6 mg, 0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 30 min. Then tetrahydrofuran (1.6 mL) and **1a** (56.8 mg, 0.2 mmol, 1.0 equiv) were added to the reaction mixture and stirred at 25 °C for 2 h. The reaction mixture was acidified by addition of 1 M aqueous HCl to pH = 1-2. Then water (10.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with DCM (3 × 10.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **3af** as a white solid.

Yield 36.4 mg (70%).

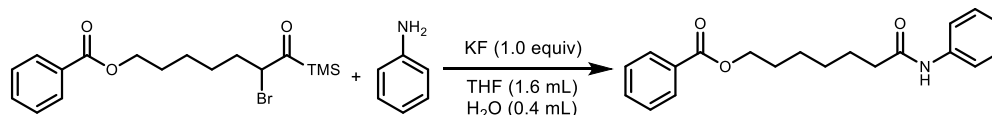
NMR Spectroscopy:

¹H NMR (DMSO-*d*₆, 400 MHz) δ 12.05 (s, 1H), 8.05 (s, 1H), 7.27-7.14 (m, 5H), 2.78 (t, *J* = 7.7 Hz, 2H), 2.36 (t, *J* = 7.7 Hz, 2H), 2.04-1.97 (m, 2H), 1.83-1.77 (m,

2H), 1.59-1.53 (m, 4H).

^{13}C NMR (DMSO- d_6 , 100 MHz) δ 176.6, 172.4, 142.5, 129.44, 129.42, 127.0, 66.0, 37.9, 37.5, 32.2, 25.2.

7-Oxo-7-(phenylamino)heptyl benzoate **3ag**



Prepared via **General Procedure III** starting from **1b** (76.8 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3ag** as a white solid.

Yield 58.0 mg (89%).

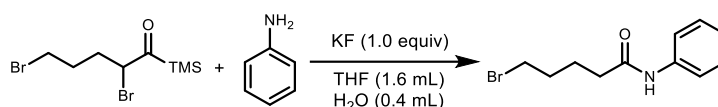
NMR Spectroscopy:

^1H NMR (CDCl₃, 600 MHz) δ 8.03 (d, J = 7.7 Hz, 2H), 7.90 (d, J = 8.0 Hz, 1H), 7.56-7.53 (m, 3H), 7.43 (t, J = 7.7 Hz, 2H), 7.28 (t, J = 7.7 Hz, 2H), 7.07 (t, J = 7.4 Hz, 1H), 4.29 (t, J = 6.6 Hz, 2H), 2.34 (t, J = 7.5 Hz, 2H), 1.77-1.71 (m, 4H), 1.47-1.37 (m, 4H).

^{13}C NMR (CDCl₃, 150 MHz) δ 171.7, 166.9, 138.2, 133.0, 130.4, 129.6, 129.0, 128.4, 124.2, 120.0, 65.0, 37.5, 28.9, 28.6, 25.8, 25.6.

HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for C₂₀H₂₄NO₃⁺: 326.1751; Found 326.1741.

5-Bromo-*N*-phenylpentanamide **3ah**



Prepared via **General Procedure III** starting from **1c** (62.8 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3ah** as a white solid.

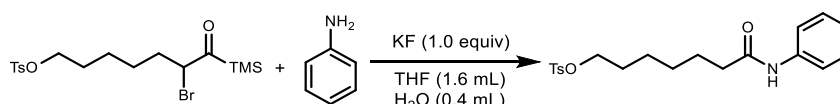
Yield 46.6 mg (91%).

NMR Spectroscopy:

^1H NMR (CDCl₃, 400 MHz) δ 7.73 (s, 1H), 7.51 (d, J = 7.9 Hz, 2H), 7.29 (t, J = 7.7 Hz, 2H), 7.09 (t, J = 7.4 Hz, 1H), 3.40 (t, J = 6.3 Hz, 2H), 2.37 (t, J = 7.0 Hz, 2H), 1.95-1.81 (m, 4H).

^{13}C NMR (CDCl₃, 100 MHz) δ 171.1, 137.9, 129.1, 124.5, 120.2, 36.5, 33.3, 32.1, 24.2.

7-Oxo-7-(phenylamino)heptyl 4-methylbenzenesulfonate **3ai**



Prepared via **General Procedure III** starting from **1d** (86.8 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3ai** as a white solid.

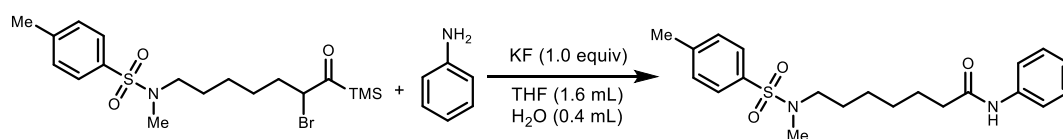
Yield 68.9 mg (92%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.74 (s, 1H), 7.62 (d, *J* = 7.9 Hz, 2H), 7.39 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.12 (t, *J* = 7.7 Hz, 2H), 6.92 (t, *J* = 7.4 Hz, 1H), 3.85 (t, *J* = 6.4 Hz, 2H), 2.28 (s, 3H), 2.15 (t, *J* = 7.5 Hz, 2H), 1.51-1.44 (m, 4H), 1.18-1.12 (m, 4H).

¹³C NMR (CDCl₃, 100 MHz) δ 171.7, 144.9, 138.2, 133.0, 130.0, 128.9, 127.8, 124.1, 119.9, 70.7, 37.3, 28.6, 28.5, 25.3, 25.1, 21.7.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₀H₂₆NO₄S⁺: 376.1577; Found 376.1567.

7-((*N*,4-Dimethylphenyl)sulfonamido)-*N*-phenylheptanamide **3aj**

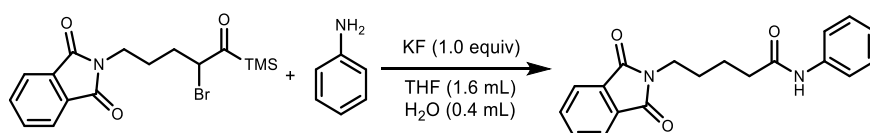
Prepared via **General Procedure III** starting from **1e** (89.4 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3aj** as a white solid.

Yield 71.0 mg (91%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 600 MHz) δ 8.15 (s, 1H), 7.62 (d, *J* = 7.9 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.25 (t, *J* = 7.8 Hz, 2H), 7.04 (t, *J* = 7.4 Hz, 1H), 2.92 (t, *J* = 7.1 Hz, 2H), 2.65 (s, 3H), 2.39 (s, 3H), 2.32 (t, *J* = 7.5 Hz, 2H), 1.69-1.64 (m, 2H), 1.49-1.45 (m, 2H), 1.35-1.28 (m, 4H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.0, 143.4, 138.3, 134.2, 129.7, 128.8, 127.3, 123.9, 119.9, 49.9, 37.3, 34.6, 28.6, 27.2, 26.0, 25.4, 21.5.

5-(1,3-Dioxoisindolin-2-yl)-*N*-phenylpentanamide **3ak**

Prepared via **General Procedure III** starting from **1f** (76.2 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3ak** as a white solid.

Yield 54.7 mg (85%).

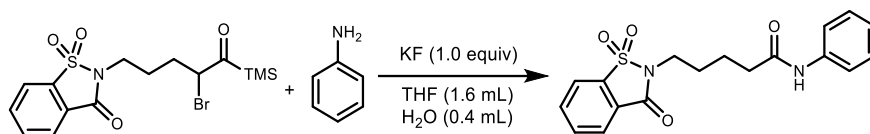
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.85-7.81 (m, 2H), 7.73-7.69 (m, 2H), 7.56-7.52 (m, 3H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 3.74 (t, *J* = 6.4 Hz, 2H), 2.43 (t, *J* = 6.9 Hz, 2H), 1.79-1.74 (m, 4H).

¹³C NMR (CDCl₃, 100 MHz) δ 171.1, 168.7, 138.2, 134.2, 132.2, 129.1, 124.2, 123.4, 119.8, 37.1, 36.9, 28.0, 22.9.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₉H₁₈N₂O₃Na⁺: 345.1210; Found 345.1201.

5-(1,1-Dioxido-3-oxobenzo[d]isothiazol-2(3*H*)-yl)-*N*-phenylpentanamide **3al**



Prepared via **General Procedure III** starting from **1g** (83.4 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3al** as a white solid.

Yield 68.9 mg (96%).

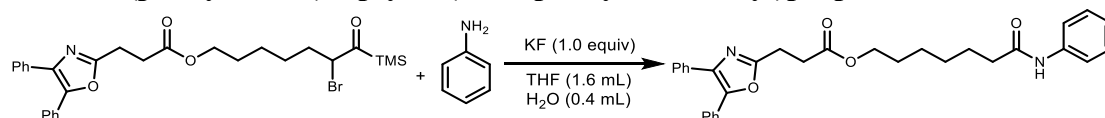
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.04 (d, J = 7.2 Hz, 1H), 7.91 (d, J = 7.3 Hz, 1H), 7.88-7.80 (m, 2H), 7.59 (s, 1H), 7.52 (d, J = 7.9 Hz, 2H), 7.31-7.27 (m, 2H), 7.07 (t, J = 7.4 Hz, 1H), 3.82 (t, J = 6.8 Hz, 2H), 2.42 (t, J = 7.5 Hz, 2H), 1.97-1.90 (m, 2H), 1.88-1.80 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 170.9, 159.3, 138.1, 137.6, 135.0, 134.6, 129.1, 127.4, 125.3, 124.2, 121.1, 119.9, 38.7, 36.8, 27.7, 22.7.

HRMS (ESI) m/z : [M + Na]⁺ Calcd for C₁₈H₁₈N₂O₄SN⁺: 381.0880; Found 381.0869.

7-Oxo-7-(phenylamino)heptyl 3-(4,5-diphenyloxazol-2-yl)propanoate **3am**



Prepared via **General Procedure III** starting from **1h** (111.0 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3am** as a white solid.

Yield 88.9 mg (90%).

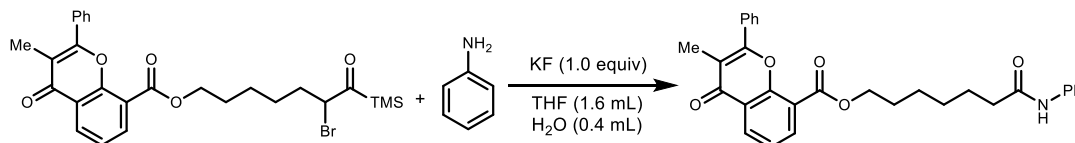
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.04 (d, J = 8.5 Hz, 1H), 7.63 (d, J = 7.4 Hz, 2H), 7.58-7.53 (m, 4H), 7.38-7.28 (m, 8H), 7.07 (t, J = 7.4 Hz, 1H), 4.11 (t, J = 6.5 Hz, 2H), 3.18 (t, J = 7.4 Hz, 2H), 2.91 (t, J = 7.4 Hz, 2H), 2.26 (d, J = 7.5 Hz, 2H), 1.68-1.58 (m, 4H), 1.36-1.30 (m, 4H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.1, 171.7, 161.9, 145.5, 138.2, 135.0, 132.3, 128.9, 128.8, 128.7, 128.6, 128.5, 128.2, 127.9, 126.4, 124.0, 119.9, 64.8, 37.3, 31.1, 28.7, 28.4, 25.6, 25.4, 23.5.

HRMS (ESI) m/z : [M + Na]⁺ Calcd for C₃₁H₃₂N₂O₄Na⁺: 519.2254; Found 519.2242.

7-Oxo-7-(phenylamino)heptyl-3-methyl-4-oxo-2-phenyl-4*H*-chromene-8-carboxylate **3an**



Prepared via **General Procedure III** starting from **1i** (108.4 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3an** as a white solid.

Yield 89.7 mg (93%).

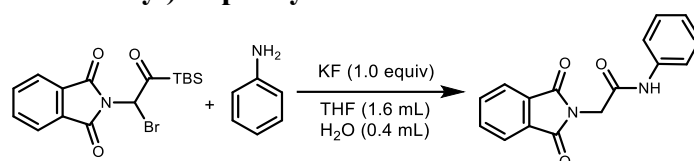
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.40 (d, J = 7.9 Hz, 1H), 8.21 (d, J = 7.3 Hz, 1H), 8.11 (s, 1H), 7.75-7.72 (m, 2H), 7.54-7.46 (m, 5H), 7.38 (t, J = 7.7 Hz, 1H), 7.24 (t, J = 7.8 Hz, 2H), 7.03 (t, J = 7.4 Hz, 1H), 4.29 (t, J = 6.7 Hz, 2H), 2.31 (t, J = 7.4 Hz, 2H), 2.19 (s, 3H), 1.70-1.63 (m, 4H), 1.38-1.26 (m, 4H).

¹³C NMR (CDCl₃, 100 MHz) δ 178.4, 171.6, 164.5, 161.3, 154.4, 138.3, 136.2, 132.9, 130.60, 130.56, 129.3, 128.9, 128.4, 124.1, 124.0, 123.2, 120.8, 119.9, 117.6, 65.6, 37.4, 28.8, 28.5, 25.7, 25.4, 11.8.

HRMS (ESI) m/z : [M + H]⁺ Calcd for C₃₀H₃₀NO₅⁺: 484.2119; Found 484.2106.

2-(1,3-Dioxoisindolin-2-yl)-N-phenylacetamide ²² 3ao



Prepared via **General Procedure III** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3ao** as a white solid.

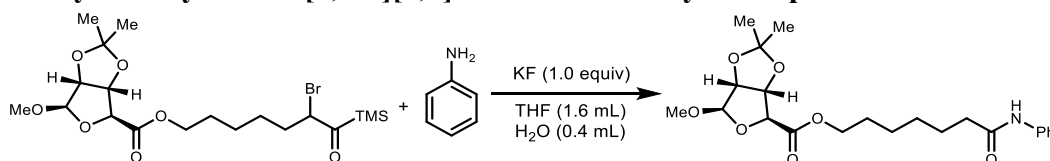
Yield 50.9 mg (91%).

NMR Spectroscopy:

¹H NMR (DMSO-*d*₆, 400 MHz) δ 10.35 (s, 1H), 7.95-7.88 (m, 4H), 7.55 (d, J = 7.9 Hz, 2H), 7.31 (t, J = 7.7 Hz, 2H), 7.07 (t, J = 7.3 Hz, 1H), 4.45 (s, 2H).

¹³C NMR (DMSO-*d*₆, 100 MHz) δ 168.8, 166.1, 139.7, 136.0, 132.9, 130.1, 124.9, 124.6, 120.5, 42.0.

7-Oxo-7-(phenylamino)heptyl (3a*S*,4*S*,6*R*,6a*R*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylate 3ap



Prepared via **General Procedure III** starting from **1k** (96.0 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3ap** as a white solid.

Yield 70.2 mg (83%).

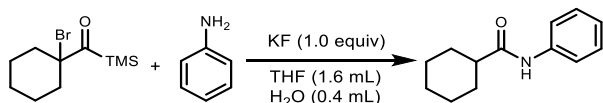
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.60 (s, 1H), 7.51 (d, J = 8.0 Hz, 2H), 7.28 (t, J = 7.9 Hz, 2H), 7.07 (t, J = 7.4 Hz, 1H), 5.19 (d, J = 5.8 Hz, 1H), 5.01 (s, 1H), 4.58 (s, 1H), 4.53 (d, J = 5.8 Hz, 1H), 4.17-4.06 (m, 2H), 3.36 (s, 3H), 2.33 (t, J = 7.5 Hz, 2H), 1.72-1.63 (m, 4H), 1.47 (s, 3H), 1.41-1.35 (m, 4H), 1.31 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz) δ 171.5, 170.3, 138.1, 129.0, 124.3, 120.0, 112.8, 109.4, 84.4, 83.8, 82.2, 65.4, 55.5, 37.5, 28.8, 28.4, 26.5, 25.6, 25.4, 25.1.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{22}H_{31}NO_7Na^+$: 444.1993; Found 444.1982.

N-Phenylcyclohexanecarboxamide **23 3aq**



Prepared via **General Procedure III** starting from **1l** (52.4 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3aq** as a white solid.

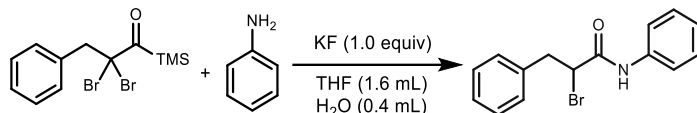
Yield 23.3 mg (57%).

NMR Spectroscopy:

1H NMR ($CDCl_3$, 400 MHz) δ 7.53 (d, J = 8.0 Hz, 2H), 7.30 (t, J = 7.8 Hz, 2H), 7.09 (t, J = 7.4 Hz, 1H), 2.27-2.19 (m, 1H), 1.98-1.94 (m, 2H), 1.86-1.81 (m, 2H), 1.72-1.68 (m, 1H), 1.59-1.50 (m, 2H), 1.36-1.22 (m, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.5, 138.2, 129.1, 124.2, 119.9, 46.7, 29.8, 25.8.

2-Bromo-*N*,3-diphenylpropanamide **3ar**



Prepared via **General Procedure III** starting from **1m** (72.4 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3ar** as a white solid.

Yield 52.9 mg (87%).

NMR Spectroscopy:

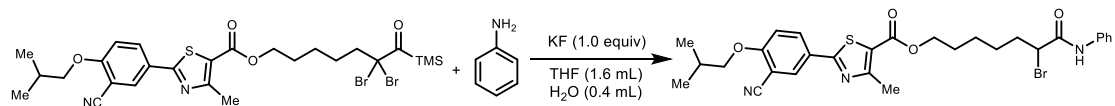
1H NMR ($CDCl_3$, 600 MHz) δ 7.87 (s, 1H), 7.43 (d, J = 8.0 Hz, 2H), 7.32-7.26 (m, 4H), 7.25-7.23 (m, 3H), 7.12 (t, J = 7.4 Hz, 1H), 4.59 (t, J = 6.7 Hz, 1H), 3.61-3.56 (m, 1H), 3.34-3.31 (m, 1H).

^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.2, 137.1, 136.8, 129.6, 129.2, 128.7, 127.5, 125.3, 120.3, 51.9, 41.8.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{15}H_{14}BrNONa^+$: 326.0151; Found 326.0141.

6-Bromo-7-oxo-7-(phenylamino)heptyl methylthiazole-5-carboxylate **3as**

2-(3-cyano-4-isobutoxyphenyl)-4-



Prepared via **General Procedure III** starting from **1n** (131.2 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3as** as a white solid.

Yield 103.9 mg (87%).

NMR Spectroscopy:

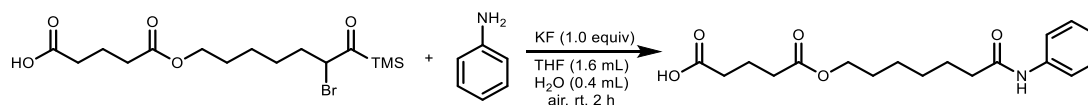
1H NMR ($CDCl_3$, 400 MHz) δ 8.28 (s, 1H), 8.15 (s, 1H), 8.07 (d, J = 8.7 Hz, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.32 (t, J = 7.8 Hz, 2H), 7.12 (t, J = 7.4 Hz, 1H), 6.98 (d,

$J = 8.8$ Hz, 1H), 4.45 (t, $J = 6.8$ Hz, 1H), 4.27 (t, $J = 6.4$ Hz, 2H), 3.88 (d, $J = 6.4$ Hz, 2H), 2.74 (s, 3H), 2.28-2.07 (m, 3H), 1.79-1.73 (m, 2H), 1.62-1.46 (m, 4H), 1.07 (d, $J = 6.7$ Hz, 6H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 167.3, 166.9, 162.6, 162.1, 161.2, 137.3, 132.7, 132.1, 129.1, 125.9, 125.1, 121.8, 120.1, 115.5, 112.7, 102.9, 75.8, 65.2, 51.5, 35.6, 28.5, 28.2, 27.0, 25.4, 19.1, 17.5.

HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{29}\text{H}_{32}\text{BrN}_3\text{O}_4\text{SNa}^+$: 620.1189; Found 620.1176.

5-Oxo-5-((7-oxo-7-(phenylamino)heptyl)oxy)pentanoic acid **3at**



Prepared via **General Procedure III** starting from **1o** (78.8 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3at** as a white solid.

Yield 54.2 mg (81%).

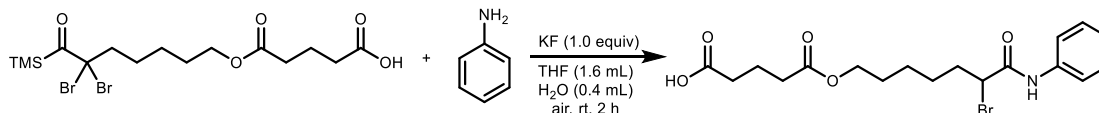
NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 7.69 (s, 1H), 7.49 (s, 2H), 7.30-7.26 (m, 2H), 7.08 (t, $J = 7.3$ Hz, 1H), 4.06 (t, $J = 6.5$ Hz, 2H), 2.42-2.32 (m, 6H), 1.97-1.90 (m, 2H), 1.75-1.67 (m, 2H), 1.64-1.58 (m, 2H), 1.42-1.31 (m, 4H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 177.9, 173.3, 172.0, 138.0, 129.0, 124.4, 120.1, 64.6, 37.5, 33.4, 33.1, 28.8, 28.5, 25.7, 25.5, 20.1.

HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_5\text{Na}^+$: 358.1625; Found 358.1614.

5-((6-bromo-7-oxo-7-(phenylamino)heptyl)oxy)-5-oxopentanoic acid **3au**



Prepared via **General Procedure III** starting from **1p** (94.4 mg, 0.2 mmol, 1.0 equiv) and aniline (18.6 mg, 0.2 mmol, 1.0 equiv) to give **3au** as a white solid.

Yield 65.3 mg (79%).

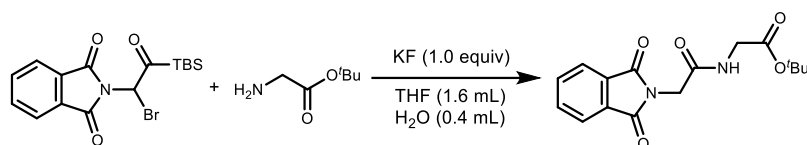
NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 8.26 (s, 1H), 7.53 (d, $J = 7.9$ Hz, 2H), 7.33 (t, $J = 7.8$ Hz, 2H), 7.14 (t, $J = 7.4$ Hz, 1H), 4.46-4.42 (m, 1H), 4.07 (t, $J = 6.5$ Hz, 2H), 2.43-2.37 (m, 4H), 2.26-2.17 (m, 1H), 2.13-2.04 (m, 1H), 1.99-1.91 (m, 2H), 1.68-1.61 (m, 2H), 1.58-1.47 (m, 2H), 1.45-1.36 (m, 2H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 178.4, 173.2, 167.1, 137.2, 129.2, 125.2, 120.2, 64.5, 51.6, 35.7, 33.3, 33.1, 28.4, 27.0, 25.3, 20.0.

HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_5^+$: 414.0911; Found 414.0911.

***tert*-Butyl (2-(1,3-dioxoisindolin-2-yl)acetyl)glycinate ²⁴ 3av**



Prepared via **General Procedure III** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and *tert*-butyl glycinate (26.2 mg, 0.2 mmol, 1.0 equiv) to give **3av** as a white solid.

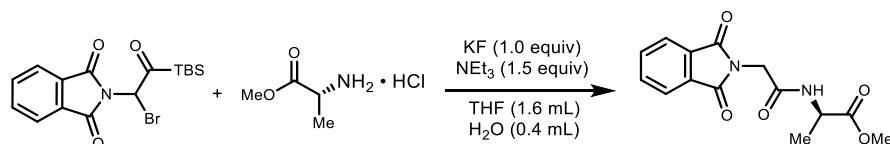
Yield 59.2 mg (93%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.88-7.84 (m, 2H), 7.74-7.70 (m, 2H), 6.45 (t, *J* = 4.9 Hz, 1H), 4.40 (s, 2H), 3.94 (d, *J* = 4.8 Hz, 2H), 1.44 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 168.8, 167.8, 166.1, 134.3, 132.1, 123.7, 82.7, 42.3, 40.6, 28.1.

Methyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-*D*-alaninate ²⁵ 3aw



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and methyl *D*-alaninate hydrochloride (27.8 mg, 0.2 mmol, 1.0 equiv) to give **3aw** as a white solid.

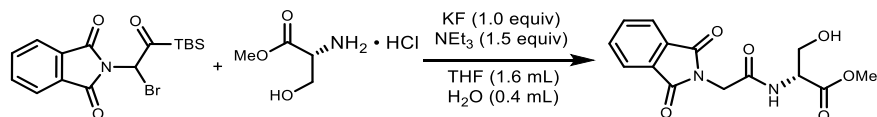
Yield 50.5 mg (87%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.85-7.83 (m, 2H), 7.71-7.69 (m, 2H), 6.72 (d, *J* = 7.3 Hz, 1H), 4.60-4.53 (m, 1H), 4.43-4.33 (m, 2H), 3.71 (s, 3H), 1.38 (d, *J* = 7.2 Hz, 3H).

¹³C NMR (CDCl₃, 100 MHz) δ 173.3, 167.8, 165.8, 134.3, 132.1, 123.7, 52.6, 48.4, 40.6, 18.4.

Methyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-*D*-serinate 3ax



Prepared via **General Procedure IV** starting from **1j** (56.8 mg, 0.2 mmol, 1.0 equiv) and methyl *D*-serinate hydrochloride (31.0 mg, 0.2 mmol, 1.0 equiv) to give **3ax** as a white solid.

Yield 40.3 mg (66%).

NMR Spectroscopy:

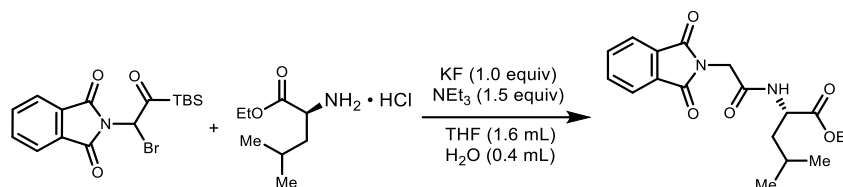
¹H NMR (DMSO-*d*₆, 400 MHz) δ 8.69 (d, *J* = 7.8 Hz, 1H), 7.92-7.86 (m, 4H), 5.15 (t, *J* = 5.5 Hz, 1H), 4.39-4.35 (m, 1H), 4.30 (s, 2H), 3.74-3.68 (m, 1H), 3.64-

3.59 (m, 4H).

^{13}C NMR (DMSO- d_6 , 100 MHz) δ 172.1, 168.8, 167.5, 135.9, 132.9, 124.5, 62.5, 56.1, 53.2, 41.1.

HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_6\text{Na}^+$: 329.0744; Found 329.0735.

Ethyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-*L*-leucinate ²⁶ **3ay**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and ethyl *L*-leucinate hydrochloride (39.0 mg, 0.2 mmol, 1.0 equiv) to give **3ay** as a white solid.

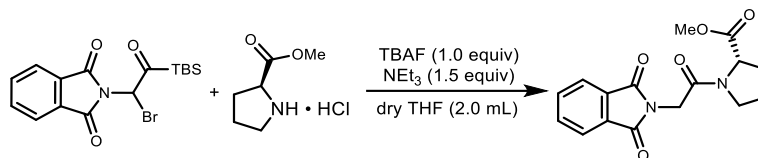
Yield 54.8 mg (79%).

NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 7.86-7.81 (m, 2H), 7.71-7.61 (m, 2H), 6.56 (d, J = 8.3 Hz, 1H), 4.63-4.57 (m, 1H), 4.45-4.34 (m, 2H), 4.19-4.08 (m, 2H), 1.70-1.48 (m, 3H), 1.23 (t, J = 7.1 Hz, 3H), 0.91-0.88 (m, 6H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 173.0, 167.8, 166.0, 134.3, 132.1, 123.6, 61.6, 51.1, 41.9, 40.6, 24.9, 22.8, 22.1, 14.2.

Methyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-*L*-prolinate ²⁷ **3az**



Prepared via **General Procedure V** starting from **1j** (56.8 mg, 0.2 mmol, 1.0 equiv) and methyl *L*-prolinate hydrochloride (33.0 mg, 0.2 mmol, 1.0 equiv) to give **3az** as a white solid.

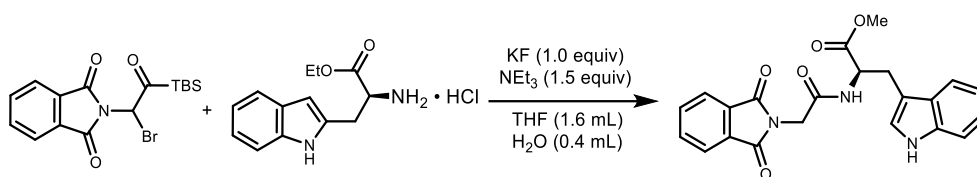
Yield 48.1 mg (76%).

NMR Spectroscopy:

^1H NMR (CDCl_3 , 400 MHz) δ 7.83-7.81 (m, 2H), 7.70-7.67 (m, 2H), 4.58-4.26 (m, 3H), 3.84-3.56 (m, 5H), 2.25-1.92 (m, 4H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 172.2, 167.9, 164.5, 134.1, 132.2, 123.5, 59.2, 52.3, 46.3, 39.7, 29.0, 24.9.

Methyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-*D*-tryptophanate ²⁸ **3ba**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and ethyl *L*-tryptophanate hydrochloride (53.6 mg, 0.2 mmol, 1.0 equiv) to give **3ba** as a white solid.

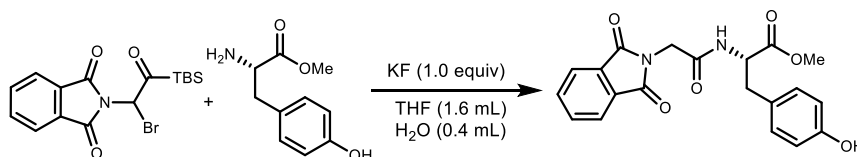
Yield 71.2 mg (88%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.68 (s, 1H), 7.77-7.72 (m, 2H), 7.64-7.60 (m, 2H), 7.46-7.44 (m, 1H), 7.21-7.16 (m, 1H), 7.05-7.00 (m, 2H), 6.93 (d, *J* = 2.3 Hz, 1H), 6.79-6.76 (m, 1H), 4.93-4.89 (m, 1H), 4.33-4.20 (m, 2H), 3.64 (s, 3H), 3.32-3.23 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.2, 167.9, 166.2, 136.0, 134.2, 131.8, 127.5, 123.6, 123.5, 122.0, 119.5, 118.3, 111.4, 109.1, 53.3, 52.6, 40.3, 27.3.

Methyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-*L*-tyrosinate **3bb**



Prepared via **General Procedure III** starting from **1j** (56.8 mg, 0.2 mmol, 1.0 equiv) and methyl *L*-tyrosinate (39.0 mg, 0.2 mmol, 1.0 equiv) to give **3bb** as a white solid.

Yield 70.2 mg (92%).

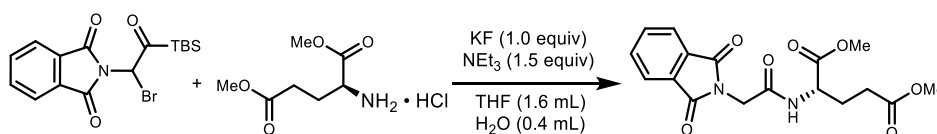
NMR Spectroscopy:

¹H NMR (DMSO-*d*₆, 400 MHz) δ 9.28 (s, 1H), 8.73 (d, *J* = 7.7 Hz, 1H), 7.91-7.84 (m, 4H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.68 (d, *J* = 8.1 Hz, 2H), 4.42-4.36 (m, 1H), 4.22 (s, 2H), 3.59 (s, 3H), 2.92-2.79 (m, 2H).

¹³C NMR (DMSO-*d*₆, 150 MHz) δ 173.0, 168.7, 167.4, 157.4, 135.9, 133.0, 131.3, 128.1, 124.5, 116.4, 55.5, 53.1, 41.1, 37.3.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₀H₁₉N₂O₆⁺: 383.1238; Found 383.1227.

Dimethyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-*L*-glutamate **3bc**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and dimethyl *L*-glutamate hydrochloride (42.2 mg, 0.2 mmol, 1.0 equiv) to give **3bc** as a white solid.

Yield 61.4 mg (85%).

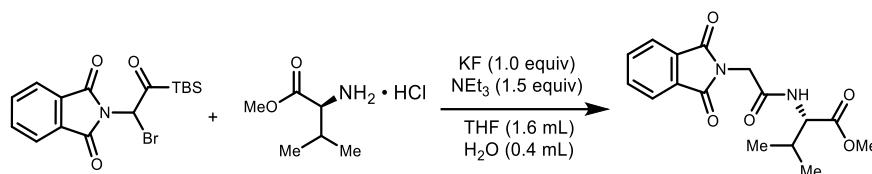
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.92-7.87 (m, 2H), 7.78-7.73 (m, 2H), 6.82 (d, *J* = 7.6 Hz, 1H), 4.66-4.61 (m, 1H), 4.47-4.36 (m, 2H), 3.76 (s, 3H), 3.64 (s, 3H), 2.50-2.36 (m, 2H), 2.26-2.18 (m, 1H), 2.09-1.99 (m, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ 173.7, 172.0, 167.8, 166.3, 134.3, 132.2, 123.7, 52.8, 52.2, 52.0, 40.7, 30.1, 27.2.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₇H₁₈N₂O₇Na⁺: 385.1006; Found 385.0994.

Methyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-L-valinate ²⁶ **3bd**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and methyl *L*-valinate hydrochloride (33.4 mg, 0.2 mmol, 1.0 equiv) to give **3bd** as a white solid.

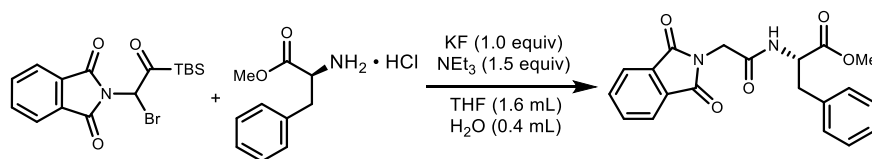
Yield 49.6 mg (78%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.86-7.83 (m, 2H), 7.71-7.69 (m, 2H), 6.62 (d, *J* = 8.7 Hz, 1H), 4.57-4.53 (m, 1H), 4.47-4.36 (m, 2H), 3.70 (s, 3H), 2.18-2.09 (m, 1H), 0.92-0.86 (m, 6H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.4, 167.8, 166.2, 134.3, 132.1, 123.7, 57.4, 52.3, 40.7, 31.6, 18.9, 17.8.

Methyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-L-phenylalaninate ²⁹ **3be**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and methyl *L*-phenylalaninate hydrochloride (43.0 mg, 0.2 mmol, 1.0 equiv) to give **3be** as a white solid.

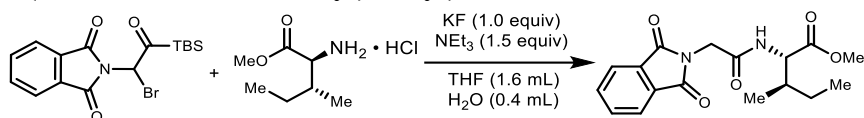
Yield 56.2 mg (77%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.86-7.84 (m, 2H), 7.73-7.71 (m, 2H), 7.23-7.14 (m, 3H), 7.07 (d, *J* = 7.3 Hz, 2H), 6.54 (d, *J* = 7.7 Hz, 1H), 4.86-4.81 (m, 1H), 4.40-4.28 (m, 2H), 3.70 (s, 3H), 3.15-3.02 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 171.7, 167.7, 165.9, 135.6, 134.3, 132.1, 129.4, 128.6, 127.2, 123.7, 53.5, 52.5, 40.6, 37.7.

Methyl (2-(1,3-dioxisoindolin-2-yl)acetyl)-*L*-alloisoleucinate **3bf**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and methyl *L*-alloisoleucinate hydrochloride (36.2 mg, 0.2 mmol, 1.0 equiv) to give **3bf** as a white solid.

Yield 53.8 mg (81%).

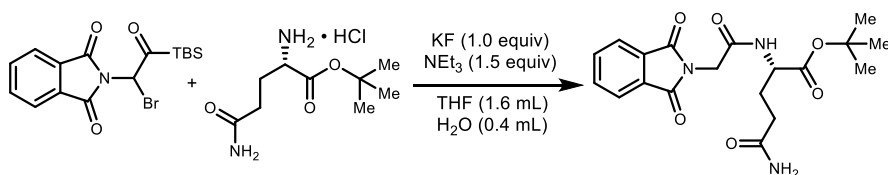
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.85-7.83 (m, 2H), 7.71-7.69 (m, 2H), 6.63 (d, *J* = 8.6 Hz, 1H), 4.61-4.57 (m, 1H), 4.46-4.35 (m, 2H), 3.70 (s, 3H), 1.92-1.82 (m, 1H), 1.44-1.34 (m, 1H), 1.20-1.10 (m, 1H), 0.89-0.85 (m, 6H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.3, 167.8, 166.0, 134.3, 132.1, 123.7, 56.7, 52.3, 40.7, 38.2, 25.2, 15.4, 11.6.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₇H₂₀N₂O₅Na⁺: 355.1264; Found 355.1254.

tert-Butyl (2-(1,3-dioxisoindolin-2-yl)acetyl)-*L*-glutamate **3bg**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and *tert*-butyl *L*-glutamate hydrochloride (47.6 mg, 0.2 mmol, 1.0 equiv) to give **3bg** as a white solid.

Yield 66.4 mg (85%).

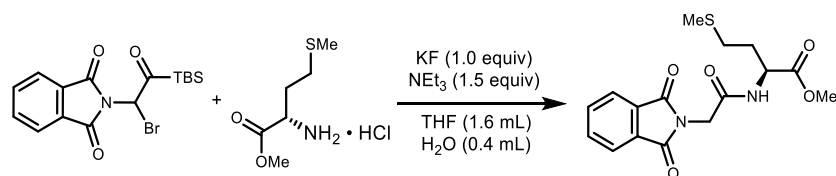
NMR Spectroscopy:

¹H NMR (DMSO-*d*₆, 400 MHz) δ 8.56 (d, *J* = 7.6 Hz, 1H), 7.93-7.85 (m, 4H), 7.29 (s, 1H), 6.77 (s, 1H), 4.25 (s, 2H), 4.13-4.07 (m, 1H), 2.13 (t, *J* = 7.8 Hz, 2H), 1.96-1.87 (m, 1H), 1.81-1.71 (m, 1H), 1.39 (s, 9H).

¹³C NMR (DMSO-*d*₆, 100 MHz) δ 174.5, 172.0, 168.7, 167.4, 135.8, 133.0, 124.4, 82.0, 53.8, 41.1, 32.3, 28.8, 28.1.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₉H₂₃N₃O₆Na⁺: 412.1479; Found 412.1468.

Methyl (2-(1,3-dioxisoindolin-2-yl)acetyl)-*L*-methioninate **3bh**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and methyl *L*-methioninate hydrochloride (39.8 mg, 0.2 mmol, 1.0 equiv) to give **3bh**

as a white solid.

Yield 61.2 mg (87%).

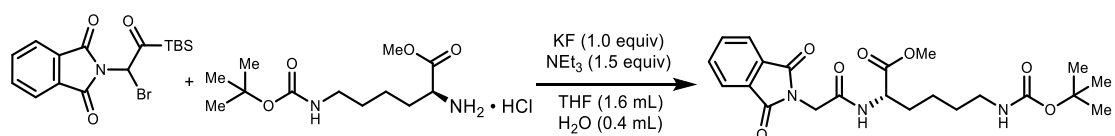
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.87-7.83 (m, 2H), 7.73-7.69 (m, 2H), 6.85 (d, *J* = 7.8 Hz, 1H), 4.72-4.67 (m, 1H), 4.46-4.35 (m, 2H), 3.72 (s, 3H), 2.49 (t, *J* = 7.3 Hz, 2H), 2.20-2.10 (m, 1H), 2.03 (s, 3H), 2.00-1.93 (m, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.3, 167.8, 166.2, 134.3, 132.0, 123.7, 52.8, 51.8, 40.7, 31.4, 29.9, 15.5.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₆H₁₈N₂O₅Na⁺: 373.0829; Found 373.0819.

Methyl *N*⁶-(*tert*-butoxycarbonyl)-*N*²-(2-(1,3-dioxoisindolin-2-yl)acetyl)-*L*-lysinate **3bi**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and methyl *N*⁶-(*tert*-butoxycarbonyl)-*L*-lysinate hydrochloride (59.2 mg, 0.2 mmol, 1.0 equiv) to give **3bi** as a white solid.

Yield 76.9 mg (86%).

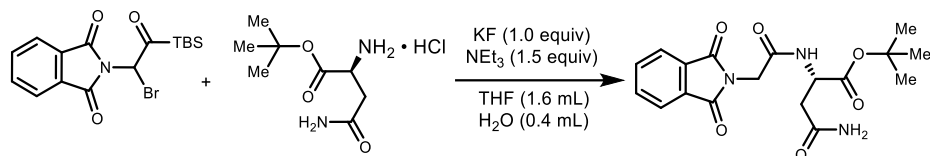
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.86-7.81 (m, 2H), 7.72-7.67 (m, 2H), 6.88 (d, *J* = 7.8 Hz, 1H), 4.78 (s, 1H), 4.59-4.54 (m, 1H), 4.44-4.33 (m, 2H), 3.69 (s, 3H), 3.11-3.02 (m, 2H), 1.88-1.79 (m, 1H), 1.72-1.63 (m, 1H), 1.47-1.30 (m, 13H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.7, 167.8, 166.2, 156.3, 134.3, 132.1, 123.6, 79.1, 52.5, 52.4, 40.6, 40.1, 31.9, 29.6, 28.5, 22.4.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₂₂H₂₉N₃O₇Na⁺: 470.1898; Found 470.1887.

tert*-Butyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-*L*-asparaginate **3bj*



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and *tert*-butyl *L*-asparaginate hydrochloride (44.8 mg, 0.2 mmol, 1.0 equiv) to give **3bj** as a white solid.

Yield 61.5 mg (82%).

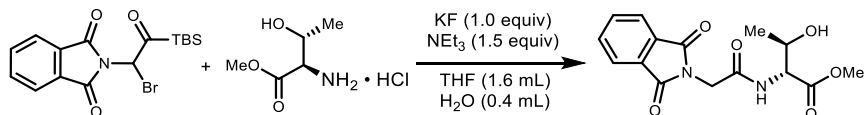
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.87-7.85 (m, 2H), 7.74-7.71 (m, 2H), 7.52 (d, *J* = 7.8 Hz, 1H), 6.22 (s, 1H), 6.00 (s, 1H), 4.69-4.64 (m, 1H), 4.52-4.39 (m, 2H), 2.92-2.75 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (CDCl_3 , 100 MHz) δ 172.7, 169.8, 168.0, 166.5, 134.3, 132.2, 123.7, 82.7, 50.1, 40.6, 37.1, 28.0.

HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{21}\text{N}_3\text{O}_6\text{Na}^+$: 398.1323; Found 398.1312.

Methyl (2-(1,3-dioxisoindolin-2-yl)acetyl)-*D*-allothreoninate **3bk**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and methyl *D*-allothreoninate hydrochloride (33.8 mg, 0.2 mmol, 1.0 equiv) to give **3bk** as a white solid.

Yield 55.2 mg (86%).

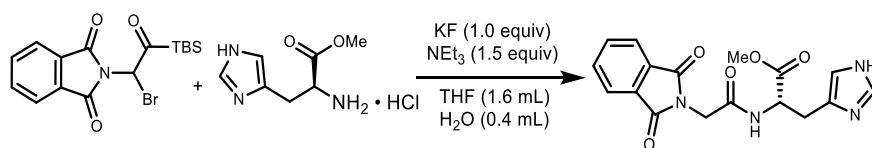
NMR Spectroscopy:

^1H NMR ($\text{DMSO}-d_6$, 400 MHz) δ 8.51 (d, $J = 8.5$ Hz, 1H), 7.93-7.87 (m, 4H), 5.05 (d, $J = 5.2$ Hz, 1H), 4.36 (s, 2H), 4.34-4.31 (m, 1H), 4.17-4.10 (m, 1H), 3.65 (s, 3H), 1.08 (d, $J = 6.3$ Hz, 3H).

^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz) δ 172.0, 168.7, 167.8, 135.8, 132.9, 124.4, 67.5, 59.2, 53.1, 41.0, 21.3

HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_6\text{Na}^+$: 343.0901; Found 343.0892.

Methyl (2-(1,3-dioxisoindolin-2-yl)acetyl)-*L*-histidinate **3bl**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and methyl *L*-histidinate hydrochloride (41.0 mg, 0.2 mmol, 1.0 equiv) to give **3bl** as a white solid.

Yield 44.4 mg (62%).

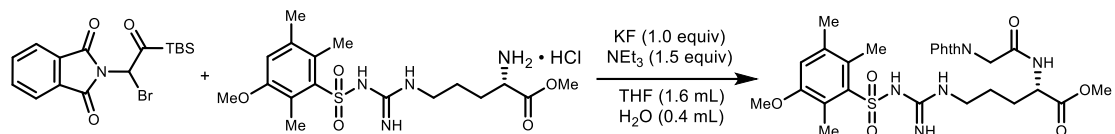
NMR Spectroscopy:

^1H NMR ($\text{DMSO}-d_6$, 600 MHz) δ 8.73 (d, $J = 7.6$ Hz, 1H), 7.92-7.87 (m, 4H), 7.63 (s, 1H), 6.87 (s, 1H), 4.51-4.48 (m, 1H), 4.23 (s, 2H), 3.60 (s, 3H), 2.97-2.94 (m, 1H), 2.90-2.86 (m, 1H).

^{13}C NMR ($\text{DMSO}-d_6$, 150 MHz) δ 172.8, 168.7, 167.4, 136.0, 135.9, 134.0, 132.9, 124.5, 117.7, 53.7, 53.2, 41.1, 30.0.

HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_4\text{O}_5\text{Na}^+$: 379.1013; Found 379.1003.

Methyl *N*²-(2-(1,3-dioxoisindolin-2-yl)acetyl)-*N*^W-((3-methoxy-2,5,6-Trimethylphenyl)sulfonyl)-*L*-argininate **3bm**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and methyl *N*^W-((3-methoxy-2,5,6-trimethylphenyl)sulfonyl)-*L*-argininate hydrochloride (87.2 mg, 0.2 mmol, 1.0 equiv) to give **3bm** as a white solid.

Yield 67.4 mg (57%).

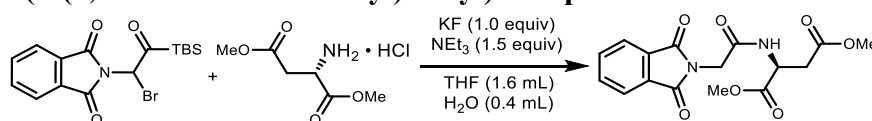
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.80-7.76 (m, 2H), 7.68-7.63 (m, 2H), 7.45 (d, *J* = 7.9 Hz, 1H), 6.50 (s, 1H), 6.30 (s, 2H), 6.15 (s, 1H), 4.51-4.46 (m, 1H), 4.43-4.34 (m, 2H), 3.78 (s, 3H), 3.67 (s, 3H), 3.22-3.17 (m, 2H), 2.65 (s, 3H), 2.56 (s, 3H), 2.08 (s, 3H), 1.90-1.82 (m, 1H), 1.78-1.69 (m, 1H), 1.62-1.56 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz) δ 172.4, 168.0, 167.1, 158.6, 156.4, 138.6, 136.6, 134.3, 133.4, 132.0, 124.9, 123.6, 111.8, 55.5, 52.6, 52.5, 40.7, 40.3, 29.2, 25.4, 24.2, 18.4, 12.0.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₂₇H₃₃N₅O₈Na⁺: 610.1942; Found 610.1925.

Dimethyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-*L*-aspartate ³⁰ **3bn**



Prepared via **General Procedure IV** starting from **1j** (76.2 mg, 0.2 mmol, 1.0 equiv) and dimethyl *L*-aspartate hydrochloride (39.4 mg, 0.2 mmol, 1.0 equiv) to give **3bn** as a white solid.

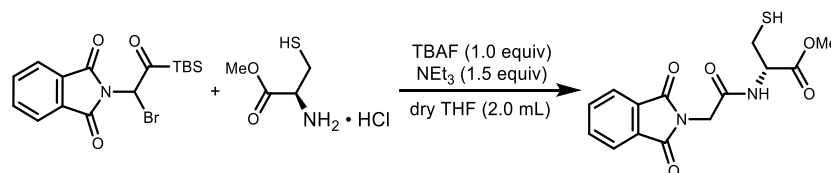
Yield 57.8 mg (83%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.89-7.85 (m, 2H), 7.75-7.70 (m, 2H), 6.88 (d, *J* = 8.0 Hz, 1H), 4.87-4.83 (m, 1H), 4.46-4.34 (m, 2H), 3.75 (s, 3H), 3.68 (s, 3H), 3.06-3.00 (m, 1H), 2.90-2.85 (m, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ 171.6, 170.9, 167.8, 166.0, 134.3, 132.2, 123.7, 53.1, 52.2, 48.9, 40.6, 36.0.

Methyl (2-(1,3-dioxoisindolin-2-yl)acetyl)-*D*-cysteinate **3bo**



Prepared via **General Procedure V** starting from **1j** (56.8 mg, 0.2 mmol, 1.0 equiv)

and methyl *D*-cysteinate hydrochloride (34.2 mg, 0.2 mmol, 1.0 equiv) to give **3bo** as a white solid.

Yield 32.8 mg (51%).

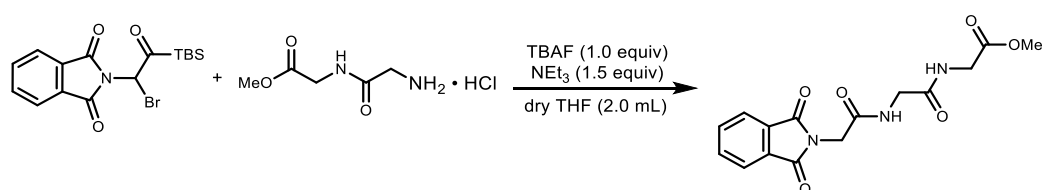
NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.89-7.87 (m, 2H), 7.75-7.73 (m, 2H), 6.78 (d, *J* = 7.2 Hz, 1H), 4.89-4.86 (m, 1H), 4.49-4.38 (m, 2H), 3.79 (s, 3H), 3.10-2.96 (m, 2H), 1.45 (t, *J* = 9.1 Hz, 1H).

¹³C NMR (CDCl₃, 100 MHz) δ 170.4, 167.8, 166.0, 134.4, 132.1, 123.8, 54.1, 53.1, 40.8, 26.8.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₄H₁₄N₂O₅SNa⁺: 345.0516; Found 345.0507.

Methyl (2-(1,3-dioxisoindolin-2-yl)acetyl)glycylglycinate 3bp



Prepared via **General Procedure V** starting from **1j** (56.8 mg, 0.2 mmol, 1.0 equiv) and methyl glycylglycinate hydrochloride (36.4 mg, 0.2 mmol, 1.0 equiv) to give **3bp** as a white solid.

Yield 49.8 mg (75%).

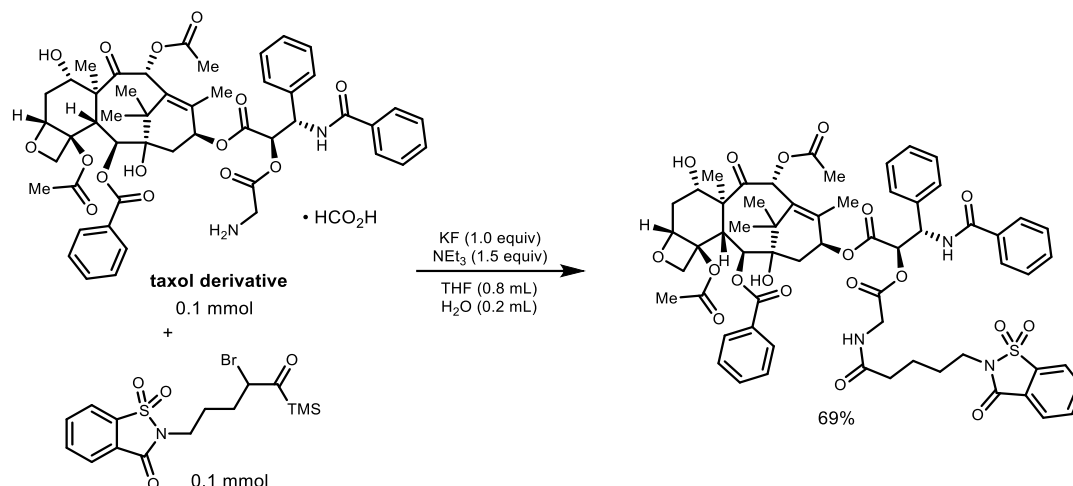
NMR Spectroscopy:

¹H NMR (DMSO-*d*₆, 400 MHz) δ 8.60 (t, *J* = 5.8 Hz, 1H), 8.38 (t, *J* = 5.9 Hz, 1H), 7.92-7.86 (m, 4H), 4.28 (s, 2H), 3.86 (d, *J* = 5.7 Hz, 2H), 3.78 (d, *J* = 5.7 Hz, 2H), 3.63 (s, 3H).

¹³C NMR (DMSO-*d*₆, 100 MHz) δ 171.5, 170.4, 168.8, 167.8, 135.9, 133.0, 124.5, 53.0, 43.0, 41.8, 41.3.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₅H₁₅N₃O₆Na⁺: 356.0853; Found 356.0843.

(2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-9-(((2*R*,3*S*)-3-Benzamido-2-(((5-(1,1-dioxido-3-oxobenzo[d]isothiazol-2(3*H*)-yl)pentanoyl)glycyl)oxy)-3-phenylpropanoyl)oxy)-12-(benzoyloxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate **5**



Under an ambient atmosphere, (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-9-(((2*R*,3*S*)-3-benzamido-2-(glycyloxy)-3-phenylpropanoyl)oxy)-12-(benzoyloxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate formate (95.6 mg, 0.1 mmol, 1.0 equiv), NEt₃ (15.1 mg, 0.15 mmol, 1.5 equiv), H₂O (0.2 mL) and KF (5.8 mg, 0.1 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 30 min. Then tetrahydrofuran (0.8 mL) and **1g** (41.7 mg, 0.1 mmol, 1.0 equiv) were added to the reaction mixture and stirred at 25 °C for 2 h. Then water (5.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 5.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **5** as a white solid.

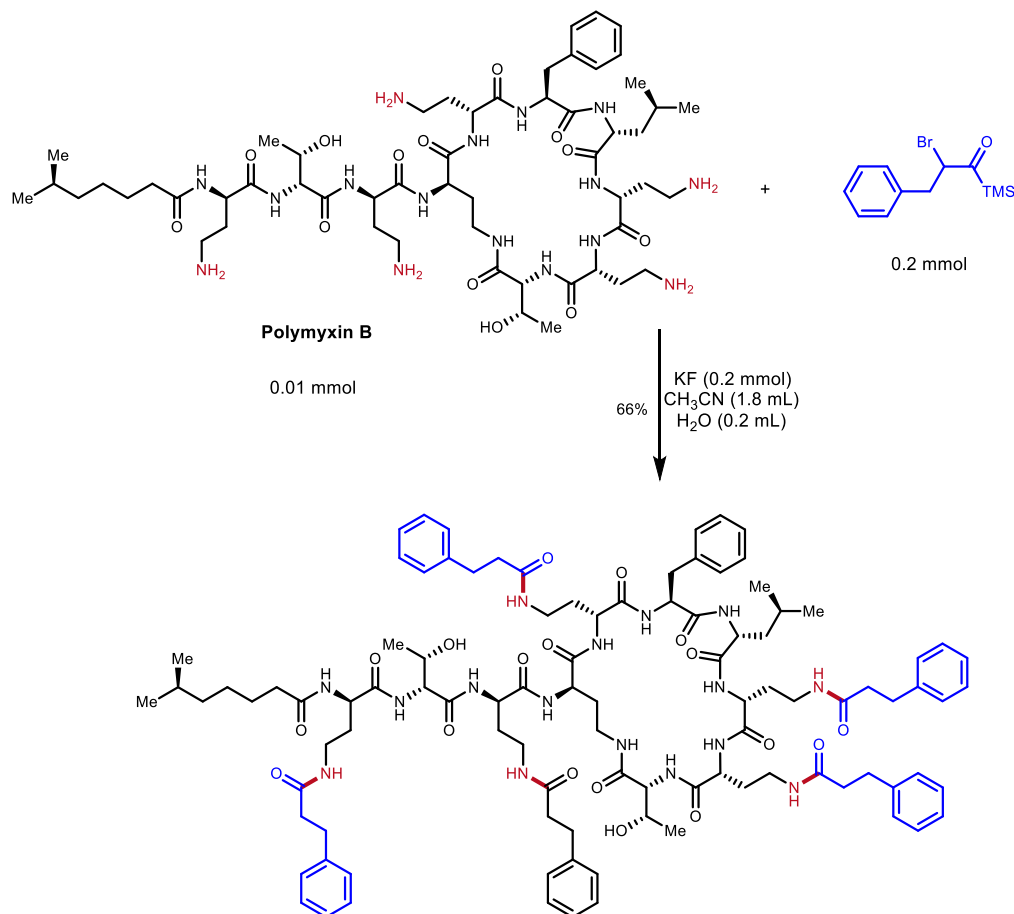
Yield 80.9 mg (69%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 8.11 (d, *J* = 7.8 Hz, 2H), 7.98 (d, *J* = 7.3 Hz, 1H), 7.88-7.73 (m, 5H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.51-7.28 (m, 11H), 6.33 (d, *J* = 5.6 Hz, 1H), 6.28 (s, 1H), 6.18 (t, *J* = 9.1 Hz, 1H), 5.95-5.92 (m, 1H), 5.65 (d, *J* = 7.0 Hz, 1H), 5.50 (d, *J* = 3.8 Hz, 1H), 4.94 (d, *J* = 9.4 Hz, 1H), 4.42-4.38 (m, 1H), 4.27 (d, *J* = 8.5 Hz, 1H), 4.17 (d, *J* = 8.6 Hz, 1H), 4.14-4.01 (m, 2H), 3.77 (d, *J* = 7.0 Hz, 1H), 3.72 (t, *J* = 7.0 Hz, 2H), 2.55-2.47 (m, 2H), 2.41 (s, 3H), 2.36-2.04 (m, 10H), 1.88 (s, 3H), 1.85-1.77 (m, 2H), 1.70-1.62 (m, 4H), 1.19 (s, 3H), 1.11 (s, 3H).
¹³C NMR (CDCl₃, 100 MHz) δ 203.9, 173.1, 171.2, 170.0, 169.3, 168.0, 167.5, 167.0, 159.2, 142.5, 137.6, 136.8, 134.9, 134.5, 133.74, 133.66, 133.0, 132.1, 130.3, 129.3, 129.2, 128.8, 128.7, 127.3, 126.8, 125.3, 121.0, 84.5, 81.1, 79.0, 77.4, 76.5, 75.7, 75.2, 74.9, 72.2, 72.1, 58.5, 53.2, 45.8, 43.3, 41.3, 38.7, 35.7, 35.6, 35.2, 29.8, 27.7, 26.8, 22.8, 22.5, 22.2, 20.9, 14.8, 9.7.

HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{61}H_{65}N_3O_{19}Na^+$: 1198.3825; Found 1198.3817.

***N,N',N''*-(((2*R*,5*S*,8*R*,11*R*,14*R*,17*R*,22*R*)-5-benzyl-22-(((*R*)-2-(((2*R*,3*S*)-3-hydroxy-2-((*R*)-2-(6-methylheptanamido)-4-(3-phenylpropanamido)butanamido)butanamido)-4-(3-phenylpropanamido)butanamido)-17-((*S*)-1-hydroxyethyl)-8-isobutyl-3,6,9,12,15,18,23-heptaaxo-1,4,7,10,13,16,19-heptaazacyclotricosane-2,11,14-triyl)tris(ethane-2,1-diyl))tris(3-phenylpropanamide) 6**



Under an ambient atmosphere, polymyxin B (12.0 mg, 0.01 mmol, 1.0 equiv), acetonitrile (1.8 mL), H₂O (0.2 mL), KF (11.6 mg, 0.2 mmol, 1.0 equiv), and **1a** (56.8 mg, 0.2 mmol, 20.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 3 h. Then the crude product was filtrated and washed with H₂O (3 × 5.0 mL), DCM (3 × 5.0 mL) and CH₃CN (3 × 5.0 mL). The crude product is dissolved with DMSO, which was purified by semi-preparative HPLC to give **6** as a white solid (12.0, 66%).

HPLC condition: InfinityLab Poroshell 120 EC-C18 4.6 × 150 mm column; H₂O (solvent A), MeCN (solvent B); gradient 10%-100% (solvent B) in 22 min; flow rate = 1.0 mL/min; detection wavelength = 214 nm.

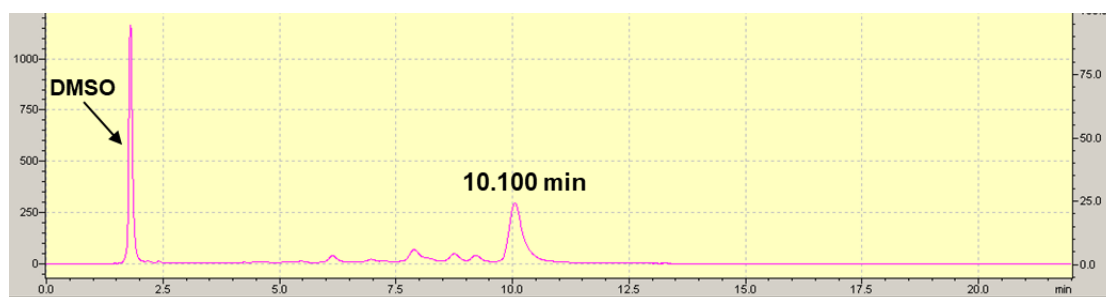


Figure S10: LC trace of reaction mixture of compound **6**.

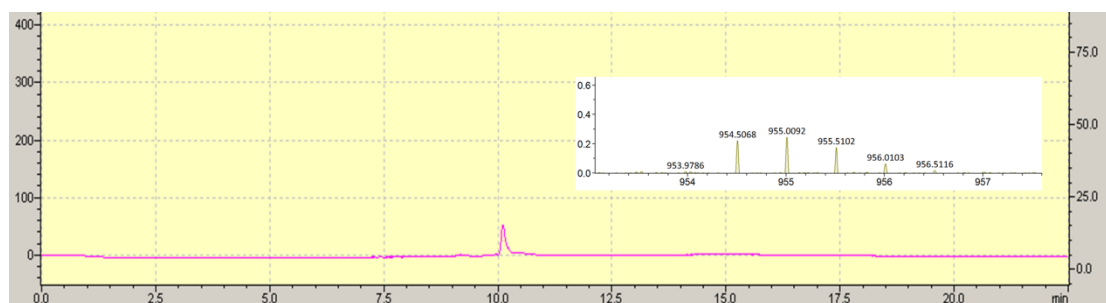
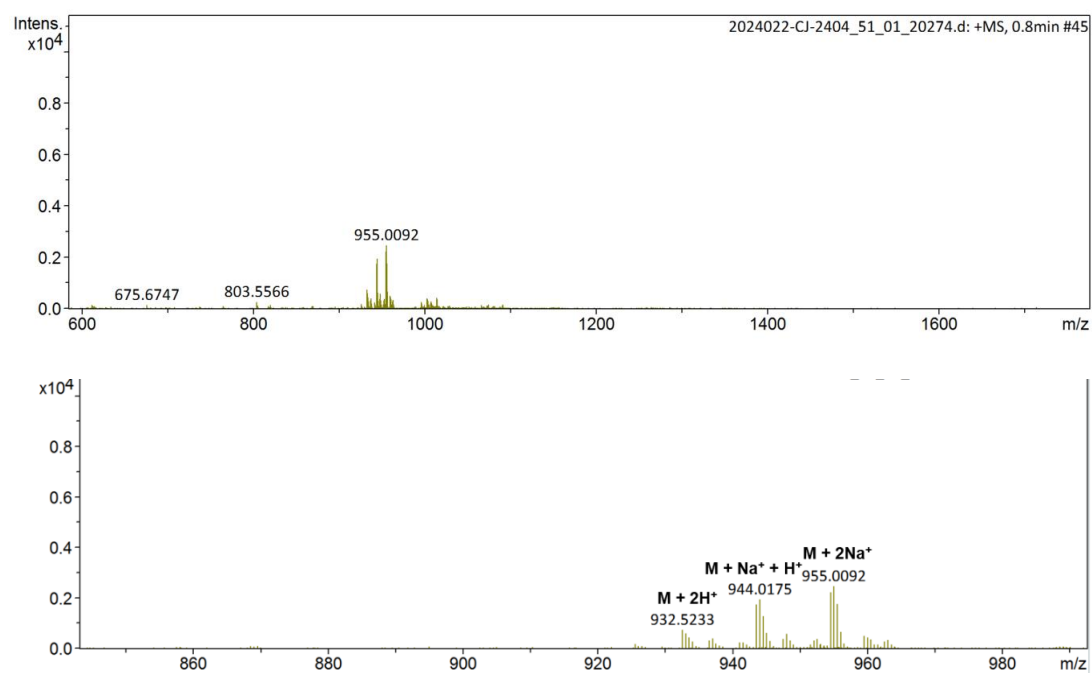


Figure S11: LC trace of purified compound **6**.

HRMS Data of **6** from LC/MS



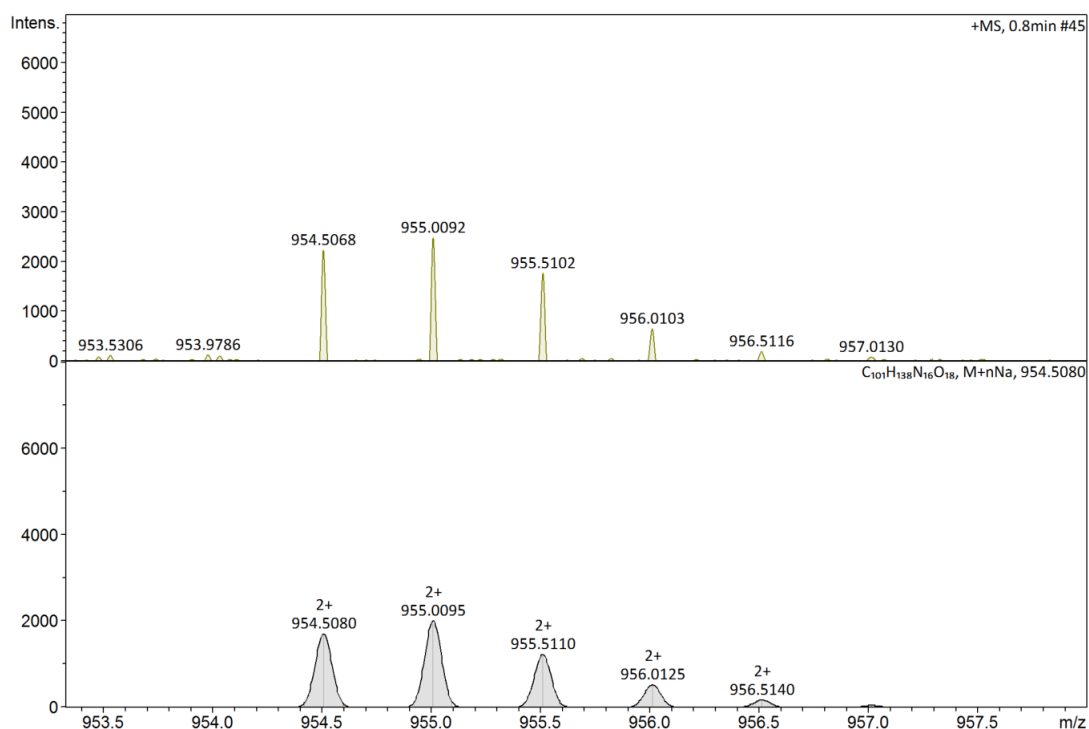
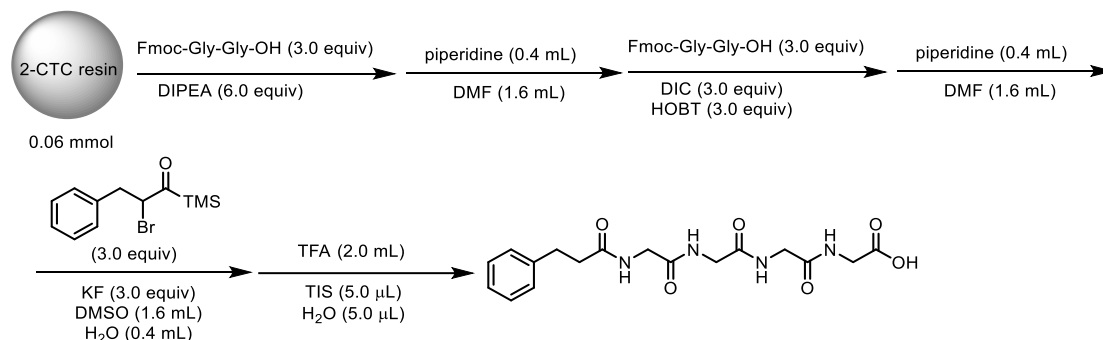


Figure S12: HRMS (ESI) m/z of compound **6**: $[M + 2Na]^+$ Calcd for $C_{101}H_{138}N_{16}O_{18}Na_2^+$: 954.5080; found: 954.5068.

7: Solid-phase synthesis³¹

(3-phenylpropanoyl)glycylglycylglycylglycine **3bo**



General procedure for incorporating the first amino acid on the solid support

2-CTC resin (78.0 mg, 0.06 mmol) with a loading of 0.77 mmol/g was placed in a 25.0 mL fritted syringe, and the resin was swollen in 6.0 mL DCM for 0.5 h. Then the syringe was drained, and Fmoc-Gly-Gly-OH (63.7 mg, 3.0 equiv), *N,N*-diisopropylethylamine (DIEA, 46.4 mg, 6.0 equiv), and 6.0 mL of a 1:1 DMF/DCM mixture (v/v) were added to the fritted syringe and react at 25 °C for 2 h. Then the syringe was drained. The resin was washed with DMF (4 × 3.0 mL) and DCM (4 × 3.0 mL).

General procedure for removing Fmoc-protection

The solution of 20% piperidine in DMF (2.0 mL) was added to the fritted syringe to react for 15 min before being drained. A further 2.0 mL of 20% piperidine was added to react for 15 min. Then, the resin was again carefully washed with DMF (4 × 2.0 mL) and DCM (4 × 2.0 mL) before being drained.

General procedure for peptide elongation

The Fmoc-Gly-Gly-OH (63.7 mg, 3.0 equiv) was added to the fritted syringe, followed by a solution of HOBt (24.3, 3.0 equiv) and DIC (22.7 mg, 3.0 equiv) in 6.0 mL DMF and react at 25 °C for 3 h. Then, the resin was washed with DMF (4 × 2.0 mL) and DCM (4 × 2.0 mL) before being drained.

DMSO (1.6 mL), H₂O (0.4 mL), KF (10.5 mg, 0.18 mmol, 3.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (51.2 mg, 0.18 mmol, 3.0 equiv) were added to the fritted syringe and react at 25 °C for 1 h. Then the syringe was drained. The resin was washed with DMF (4 × 3.0 mL) and DCM (4 × 3.0 mL).

General procedure of resin cleavage

The resin was washed with DCM (4 × 2.0 mL) and diethyl ether (4 × 2.0 mL) immediately after synthesis was completed. Cleavage was then performed with 2.0 mL of a freshly prepared TFA/TIS/H₂O (95:2.5:2.5) solution for 2 h. The resin was then filtered and washed with pure TFA (3 × 0.5 mL). After combining the TFA solution and concentrated under reduced pressure to afford (3-phenylpropanoyl)glycine as a white solid.

Yield 9.6 mg (42%).

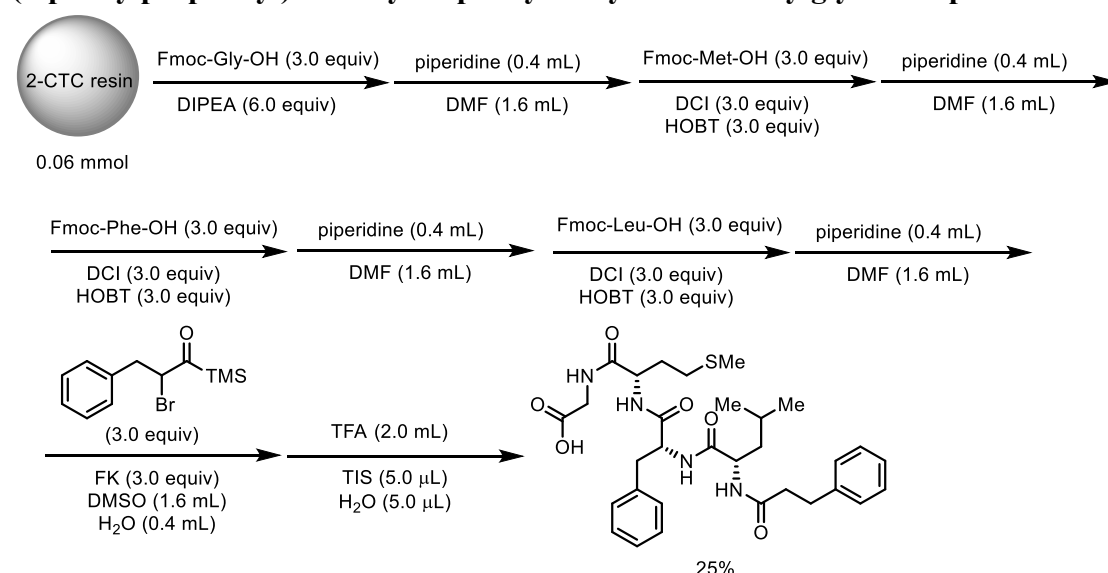
NMR Spectroscopy:

¹H NMR (DMSO-*d*₆, 400 MHz) δ 8.18-8.06 (m, 3H), 7.29-7.17 (m, 5H), 3.76-3.72 (m, 8H), 2.81 (t, *J* = 8.1 Hz, 2H), 2.45 (t, *J* = 8.1 Hz, 2H).

¹³C NMR (DMSO-*d*₆, 100 MHz) δ 173.2, 172.3, 170.7, 170.4, 142.6, 129.5, 129.4, 127.1, 43.4, 43.3, 43.0, 41.8, 38.0, 32.1.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₇H₂₂N₄O₆Na⁺: 401.1432; Found 401.1436.

(3-phenylpropanoyl)-*L*-leucyl-*D*-phenylalanyl-*L*-methionylglycine 3bp



General procedure for incorporating the first amino acid on the solid support

2-CTC resin (78.0 mg, 0.06 mmol) with a loading of 0.77 mmol/g was placed in a 25.0 mL fritted syringe, and the resin was swollen in 6 mL DCM for 0.5 h. Then the syringe was drained, and Fmoc-Gly-OH (53.5 mg, 3.0 equiv), *N,N*-diisopropylethylamine

(DIEA, 46.4 mg, 6.0 equiv), and 6.0 mL of a 1:1 DMF/DCM mixture (v/v) were added to the fritted syringe and react at 25 °C for 2 h. Then the syringe was drained. The resin was washed with DMF (4 × 3.0 mL) and DCM (4 × 3.0 mL).

General procedure for removing Fmoc-protection

The solution of 20% piperidine in DMF (2.0 mL) was added to the fritted syringe to react for 15 min before being drained. A further 2.0 mL of 20% piperidine was added to react for 15 min. Then, the resin was again carefully washed with DMF (4 × 2.0 mL) and DCM (4 × 2.0 mL) before being drained.

General procedure for peptide elongation

The Fmoc-protected amino acid (3.0 equiv) was added to the fritted syringe, followed by a solution of HOBt (24.3, 3.0 equiv) and DIC (22.7 mg, 3.0 equiv) in 6.0 mL DMF. The loading reaction was left to proceed until the resin gave a negative color test. Then, the resin was washed with DMF (4 × 2.0 mL) and DCM (4 × 2.0 mL) before being drained.

DMSO (1.6 mL), H₂O (0.4 mL), KF (10.5 mg, 0.18 mmol, 3.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (51.2 mg, 0.18 mmol, 3.0 equiv) were added to the fritted syringe and react at 25 °C for 1 h. Then the syringe was drained. The resin was washed with DMF (4 × 3.0 mL) and DCM (4 × 3.0 mL).

General procedure of resin cleavage

The resin was washed with DCM (4 × 2.0 mL) and diethyl ether (4 × 2.0 mL) immediately after synthesis was completed. Cleavage was then performed with 2.0 mL of a freshly prepared TFA/TIS/H₂O (95:2.5:2.5) solution for 2 h. The resin was then filtered and washed with pure TFA (3 × 0.5 mL). After combining the TFA solution and concentrated under reduced pressure to afford (3-phenylpropanoyl)glycine as a white solid.

Yield 9.0 mg (25%).

NMR Spectroscopy:

¹H NMR (DMSO-*d*₆, 400 MHz) δ 8.37-8.29 (m, 2H), 8.22 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 7.0 Hz, 1H), 7.26-7.13 (m, 10H), 4.52-4.38 (m, 2H), 4.18-4.13 (m, 1H), 3.87-3.70 (m, 4H), 2.79-2.75 (m, 2H), 2.48 (s, 3H), 2.40-2.33 (m, 4H), 2.04-1.91 (m, 2H), 1.15-1.08 (m, 3H), 0.72-0.66 (m, 6H).

¹³C NMR (DMSO-*d*₆, 150 MHz) δ 173.6, 172.8, 172.3, 172.2, 172.1, 142.2, 139.0, 130.4, 129.4, 129.1, 127.4, 127.0, 55.3, 52.6, 50.4, 41.9, 39.3, 39.1, 38.5, 37.8, 32.2, 30.2, 25.0, 23.9, 23.1.

HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₃₁H₄₂N₄O₆SN⁺: 621.2717; Found 621.2716.

8: Experiments of protein modification

8.1: Screening of conditions for lysozyme modification

The optimal reaction conditions of lysozyme were determined by preliminary screening of solvent type, equivalent and time, the experimental method was described in the general procedure below.

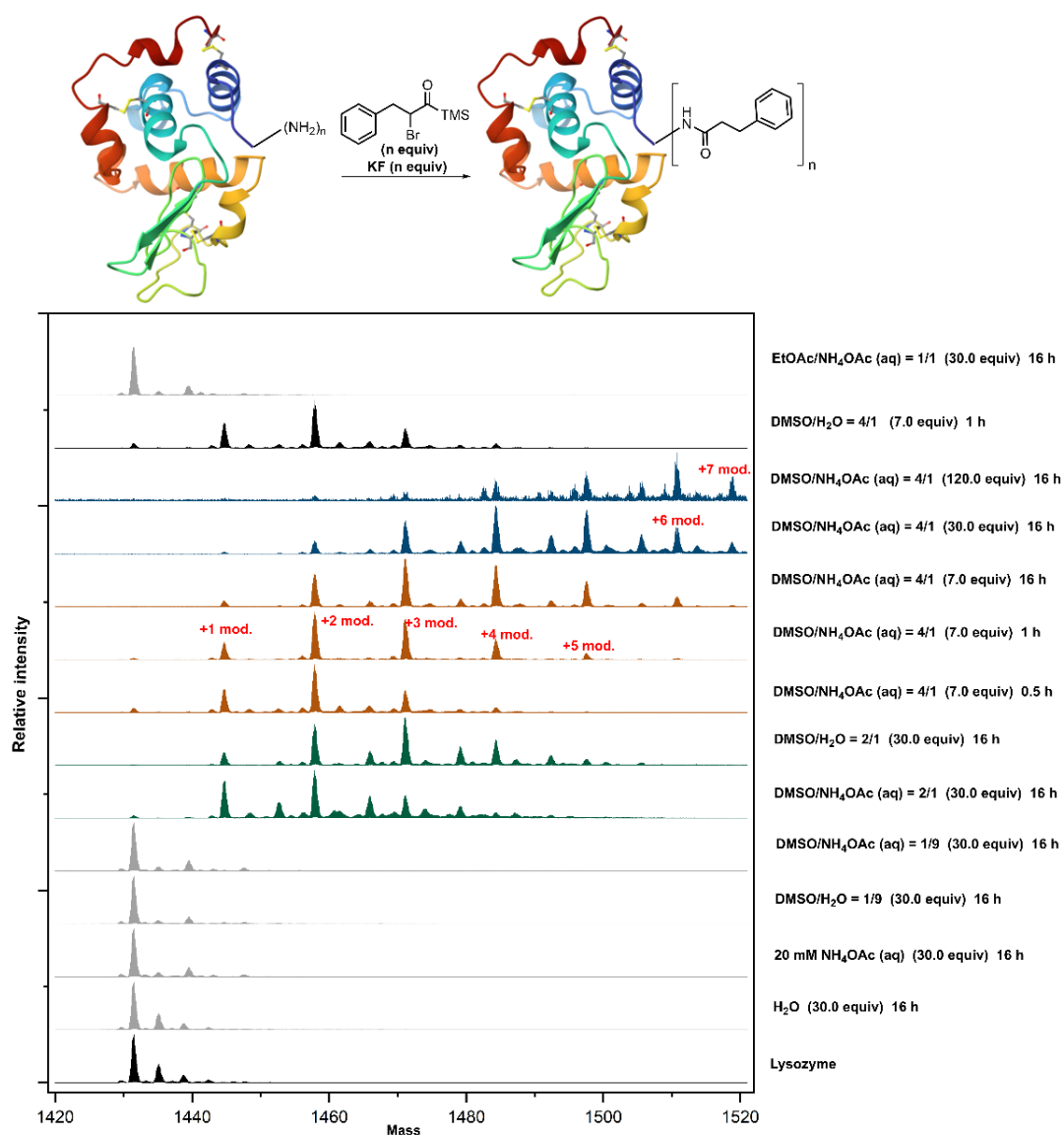


Figure S13. Screening of conditions for lysozyme modification.

8.2: Procedure for reactions of protein modification

ESI-MS was performed on a quadrupole time-of-flight mass spectrometer (Waters acquity UPLC I-CLASS/Synapt G2-Si). The mass spectrometry results had not been deconvoluted, the number of added ions had been marked in the figure. Lysozyme, from egg white was purchased from Amreco. Ribonuclease A, from bovine pancreas was purchased from MedChemExpress (MCE). Chymotrypsinogen A and myoglobin were purchased from Aladdin, and used without further purification.

Sequence of protein lysozyme:

Lysozyme is composed of 129 amino acids and 6 lysines.

KVFGRCELAAAMKRHGLDNYRGYSLGNWVCAAKFESNFNTQATNRNTDGS
TDYGILQINSRWWCNDGRTPGSRNLCNIPCSALLSSDITASVNC AKKIVSDGN
GMNAWVAWRNRCKGTDVQAWIRGCRL

Sequence of protein chymotrypsinogen A:

Chymotrypsinogen A composed of 245 amino acids and 14 lysines.

CGVPAIQPVLSGLSRIVNGEEAVPGSWPWQVSLQDKTGFHFCGGSLINENWV
VTAAHCGVTTSDVVVAGEFDQGSSEKIQLKIAKVFKNSKYNSLTINNDITLL
KLSTAASFSTVSAVCLPSASDDFAAGTTCVTTGWGLTRYTNANTPDRLQQAS
LPLLSNTNCKKYWGTEKIKDAMICAGASGVSSCMGDSGGPLVCKKNGAWTLV
GIVSWGSSCTSTSTPGVYARVTALVNWVQQTLAAN

Sequence of protein myoglobin:

Myoglobin is composed of 153 amino acids and 19 lysines.

GLSDGEWQQVLNVWGKVEADIAGHGQEVLRFTGHPETLEKFDKFKHLKT
EAEMKASEDLKKHGTVVLTALGGILKKKGHHEAELKPLAQSHATKHKIPIKY
LEFISDAIIHVLHSHKHPGDFGADAQGAMTKALELFRNDIAAKYKELGFQG

Sequence of protein ribonuclease A:

Ribonuclease A is composed of 124 amino acids and 10 lysines.

KETAAAKFERQHMDSSSTAASSSNYCNQMMKSRNLTKDRCKPVNTFVHESL
ADVQAVCSQKNVACKNGQTNCYQSYSTMSITDCRETGSSKYPNCAYKTTQA
NKHIIVACEGNPYVPVHFDASV

8.3: General procedure for reactions of lysozyme with 1a: To a 10 mL reaction tube, **1a** (2.0 mg, 7.0 equiv, 7.0 μmol) and potassium fluoride (0.4 mg, 7.0 equiv, 7.0 μmol) was added to 1.0 mM of lysozyme (14.3 mg, 1.0 equiv, 1.0 μmol) in co-solvent of DMSO and ammonium acetate buffer solution (DMSO, 0.8 mL, NH_4OAc buffer, 0.2 mL, 20 mM). After vigorously stirring for 1 h at 25 $^\circ\text{C}$, the reaction mixture was added to the desalting column (BeyoDesaltTM G-25 Midi Desalting Column), eluted with pure water (3.0 mL) for three times, added with elution buffer, and centrifuged with 1000 g for two minutes to collect the flow through solution. A 300 μL aliquot of the reaction mixture was evaluated by performing ESI-MS and the conjugated species was detected. Other equivalent reactions were completed in the same procedure.

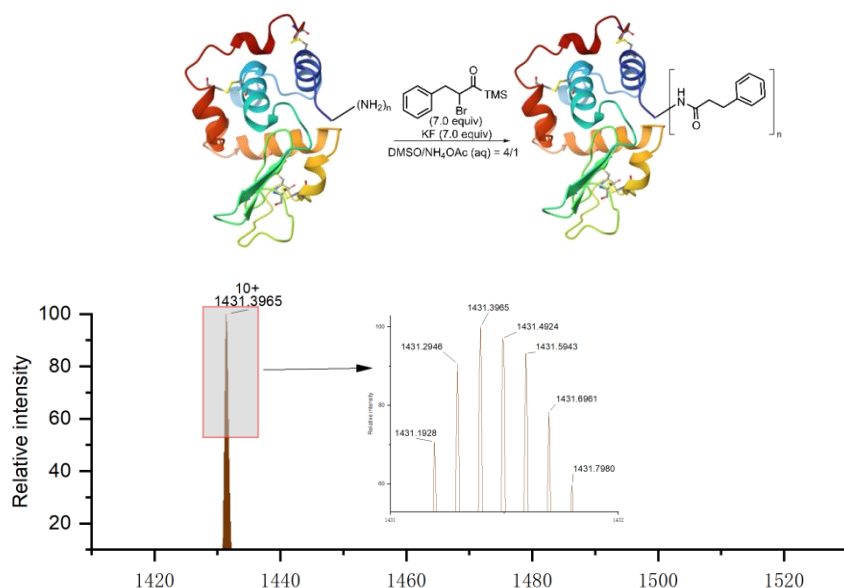
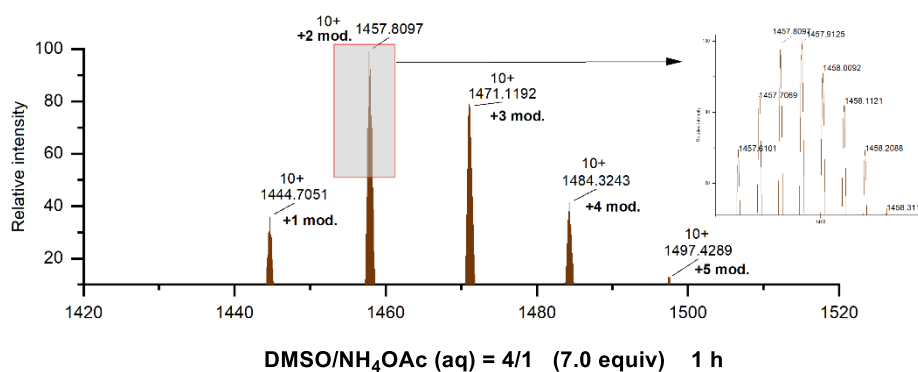


Figure S14. Mass spectrum of unmodified lysozyme.



+1 mod.	+2 mod.	+3 mod.	+4 mod.	+5 mod.	+6 mod.	+7 mod.
13.46%	37.19%	29.30%	15.42%	4.62%	0%	0%

Figure S15. Modification result of lysozyme with **1a** (7.0 equiv), Percentages were determined through the relative ratio of peak intensities in the mass spectrum of the product mixture.

8.4: Procedure for reactions and SDS-PAGE analysis of lysozyme with 1i: After reaction with the above general method, a 300 μ L aliquot of the reaction mixture was evaluated by performing ESI-MS, a 10 μ L aliquot from the elution fraction was mixed with one-fourth amount of $5 \times$ SDS loading buffer and heated at 98 $^{\circ}$ C for 8 min, before loading onto 12% SDS-PAGE gel. Electrophoresis was completed in 100 V constant voltage mode for 30 min, and the gel was imaged and analyzed by Fluorescent & Chemiluminescence Gel Imaging System (Shanghai JiaPeng science technology Co., Ltd, JP-K600), then the gel was dyed in Coomassie brilliant blue for 20 min.

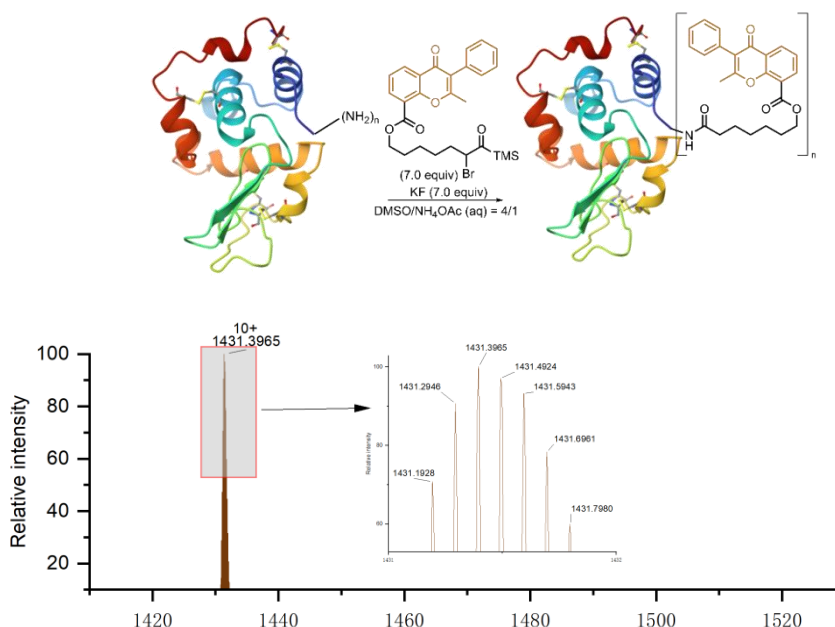
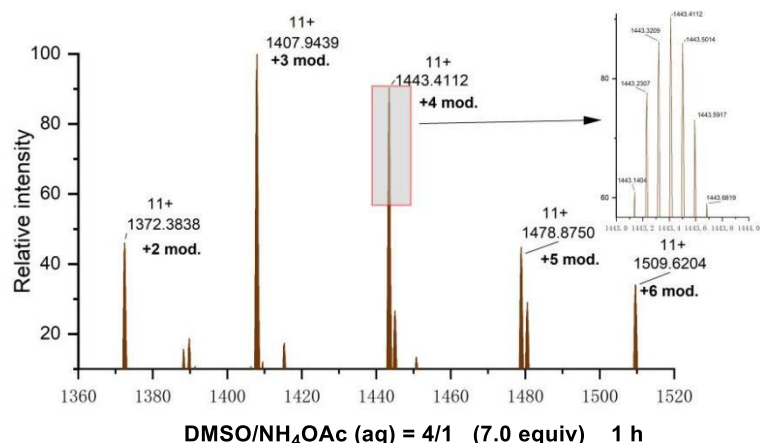


Figure S16. Mass spectrum of unmodified lysozyme.



DMSO/NH₄OAc (aq) = 4/1 (7.0 equiv) 1 h

+1 mod.	+2 mod.	+3 mod.	+4 mod.	+5 mod.	+6 mod.	+7 mod.
0%	14.42%	32.05%	28.84%	14.10%	10.58%	0%

Figure S17. Modification result of lysozyme with **1j** (7.0 equiv), Percentages were determined through the relative ratio of peak intensities in the mass spectrum of the product mixture.

8.5: General procedure for reactions of chymotrypsinogen A with 1a: To a 10 mL reaction tube, **1a** (4.3 mg, 15.0 equiv, 15.0 μ mol) and potassium fluoride (1.0 mg, 15.0 equiv, 15.0 μ mol) were added to 1.0 mM of chymotrypsinogen A (25.6 mg, 1.0 equiv, 1.0 μ mol) in mixed solution (DMSO, 0.8 mL, NH₄OAc buffer, 0.2 mL, 20 mM). After vigorously stirring for 1 h at 25 °C, the reaction mixture was added to the desalting column (BeyoDesalt™ G-25 Midi Desalting Column), eluted with pure water (3.0 mL) for three times, added with elution buffer, and centrifuged with 1000 g for 2 min to collect the flow through solution. A 300 μ L aliquot of the reaction mixture was evaluated by performing ESI-MS and the conjugated species was detected. Other equivalent reactions were completed in the same procedure.

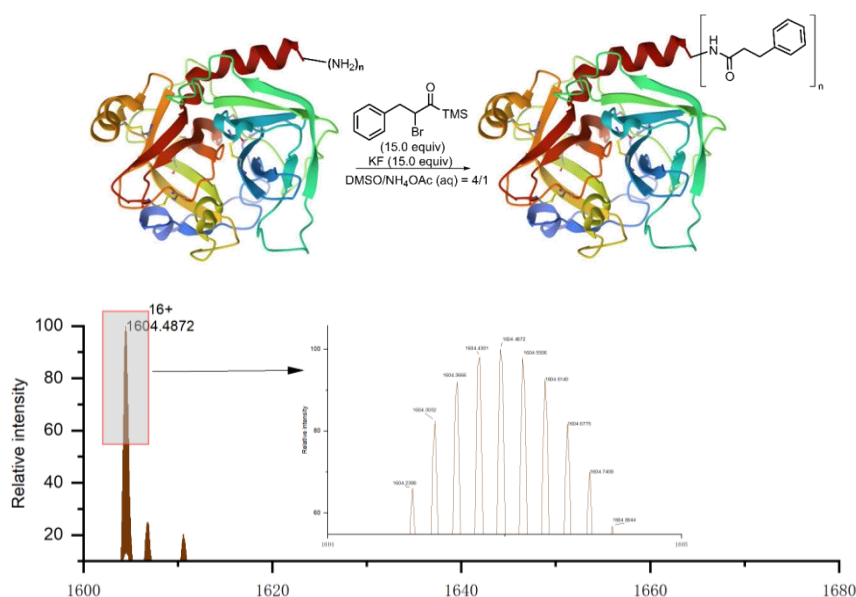
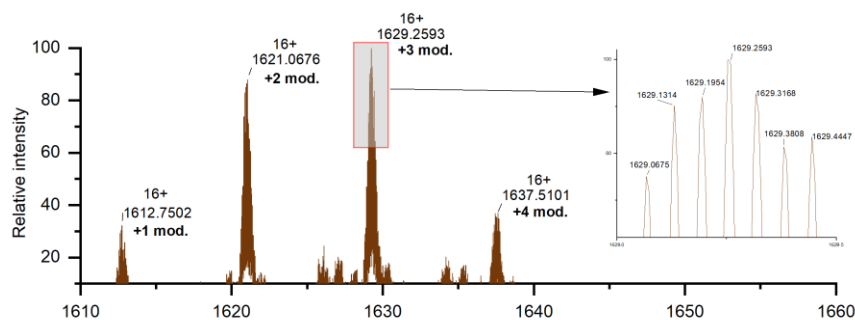


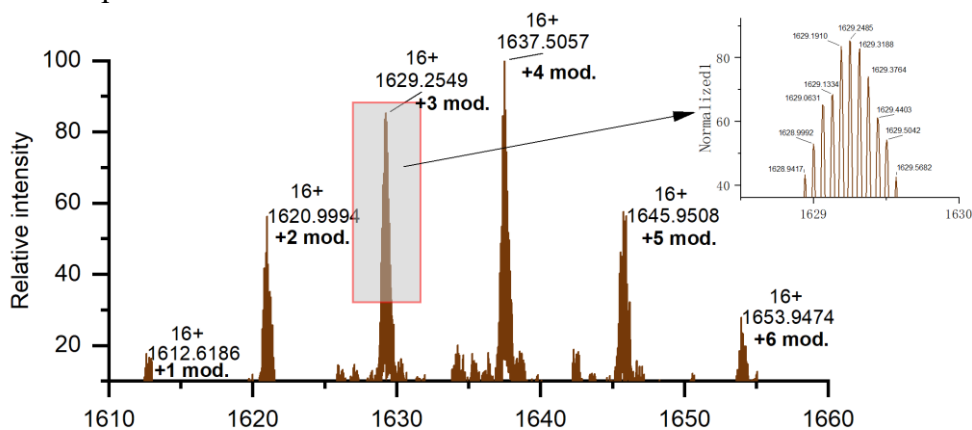
Figure S18. Mass spectrum of unmodified chymotrypsinogen A.



DMSO/NH₄OAc (aq) = 4/1 (7.0 equiv) 1 h

+1 mod.	+2 mod.	+3 mod.	+4 mod.	+5 mod.	+6 mod.	+7 mod.
12.60%	34.25%	39.37%	13.78%	0%	0%	0%

Figure S19. Modification result of chymotrypsinogen A with **1a** (7.0 equiv), Percentages were determined through the relative ratio of peak intensities in the mass spectrum of the product mixture.



DMSO/NH₄OAc (aq) = 4/1 (15.0 equiv) 1 h

+1 mod.	+2 mod.	+3 mod.	+4 mod.	+5 mod.	+6 mod.	+7 mod.
4.72%	16.52%	24.78%	29.50%	16.52%	7.96%	0%

Figure S20. Modification result of chymotrypsinogen A with **1a** (15.0 equiv), Percentages were determined through the relative ratio of peak intensities in the mass spectrum of the product mixture.

8.6: General procedure for reactions of myoglobin with 1a: To a 10 mL reaction tube, **1a** (2.0 mg, 7.0 equiv, 7.0 μ mol) and potassium fluoride (0.4 mg, 7.0 equiv, 7.0 μ mol) were added to 1.0 mM of myoglobin (16.9 mg, 1.0 equiv, 1.0 μ mol) in mixed solution (DMSO, 0.8 mL, NH₄OAc buffer, 0.2 mL, 20 mM). After vigorously stirring for 1 h at 25 $^{\circ}$ C, the reaction mixture was added to the desalting column (BeyoDesalt™ G-25 Midi Desalting Column), eluted with pure water (3.0 mL) for three times, added with elution buffer, and centrifuged with 1000 g for 2 min to collect the flow through solution. A 300 μ L aliquot of the reaction mixture was evaluated by performing ESI-MS and the conjugated species was detected. Other equivalent reactions were completed in the

same procedure.

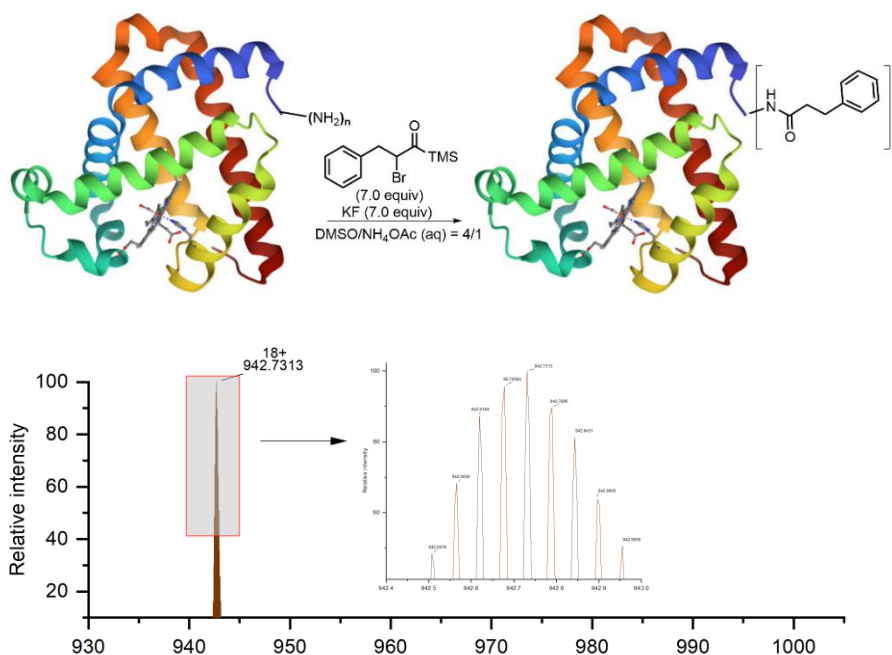
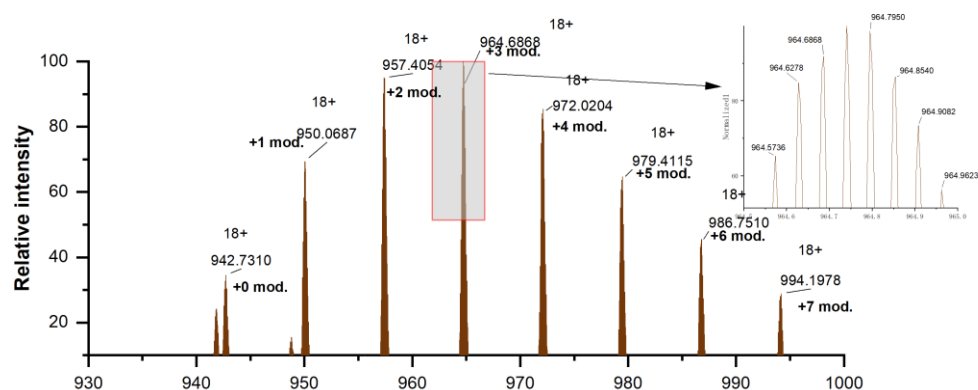


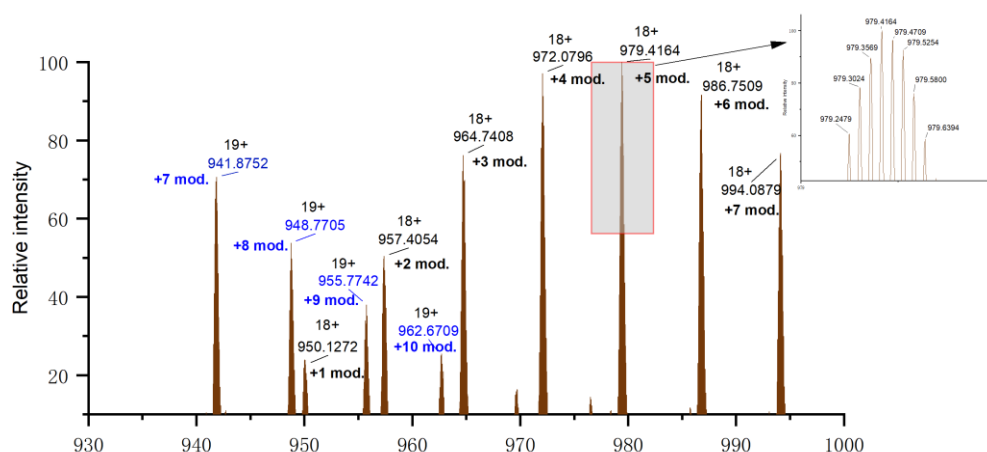
Figure S21. Mass spectrum of unmodified myoglobin.



DMSO/NH₄OAc (aq) = 4/1 (7.0 equiv) 1 h

+0 mod.	+1 mod.	+2 mod.	+3 mod.	+4 mod.	+5 mod.	+6 mod.	+7 mod.
6.56%	13.32%	18.34%	19.31%	16.41%	12.16%	8.49%	5.40%

Figure S22. Modification result of myoglobin with **1a** (7.0 equiv), percentages were determined through the relative ratio of peak intensities in the mass spectrum of the product mixture.

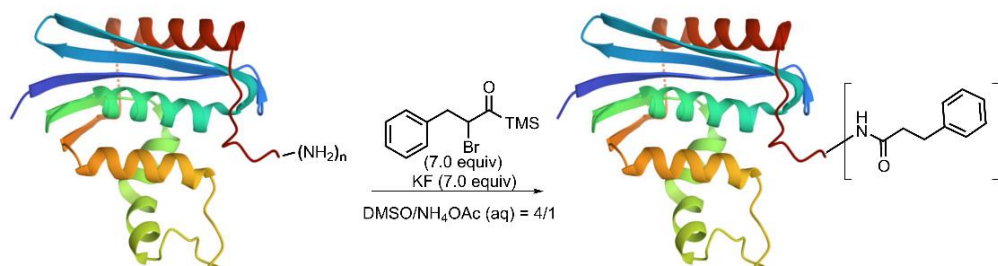


DMSO/NH₄OAc (aq) = 4/1 (20.0 equiv) 1 h

+1 mod.	+2 mod.	+3 mod.	+4 mod.	+5 mod.	+6 mod.	+7 mod.	+8 mod.	+9 mod.	+10 mod.
3.70%	8.05%	11.76%	15.46%	16.10%	14.49%	12.24%	8.53%	5.79%	3.86%

Figure S23. Modification result of myoglobin with **1a** (20.0 equiv). Percentages were determined through the relative ratio of peak intensities in the mass spectrum of the product mixture.

8.7: General procedure for reactions of ribonuclease A with 1a: To a 10 mL reaction tube, **1a** (1.98 mg, 7.0 equiv, 7.0 μ mol) and potassium fluoride (0.41 mg, 7.0 equiv, 7.0 μ mol) were added to 1.0 mM of ribonuclease A (13.69 mg, 1.0 equiv, 1.0 μ mol) in mixed solution (DMSO, 0.8 mL, NH₄OAc buffer, 0.2 mL, 20 mM). After vigorously stirring for 1 h at 25 $^{\circ}$ C, the reaction mixture was added to the desalting column (BeyoDesaltTM G-25 Midi Desalting Column), eluted with pure water (3.0 mL) for three times, added with elution buffer, and centrifuged with 1000 g for 2 min to collect the flow through solution. A 300 μ L aliquot of the reaction mixture was evaluated by performing ESI-MS and the conjugated species was detected. Other equivalent reactions were completed in the same procedure.



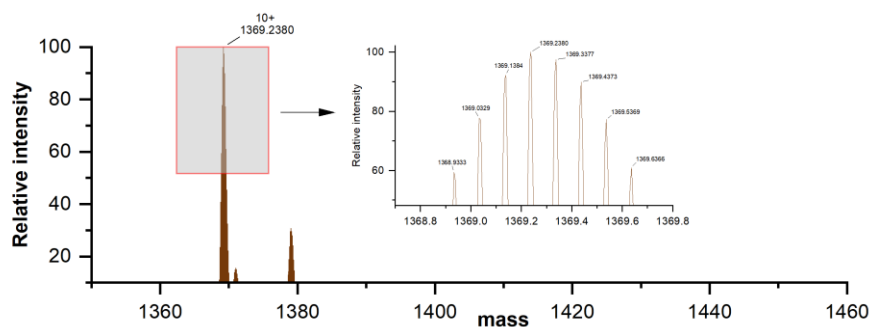
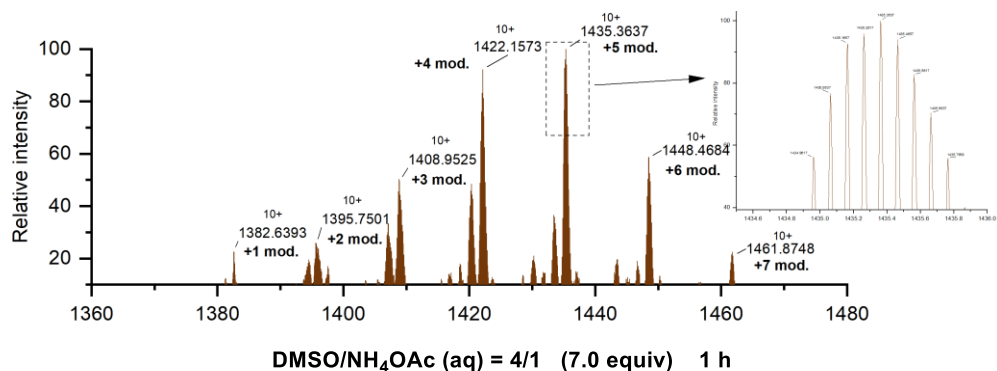
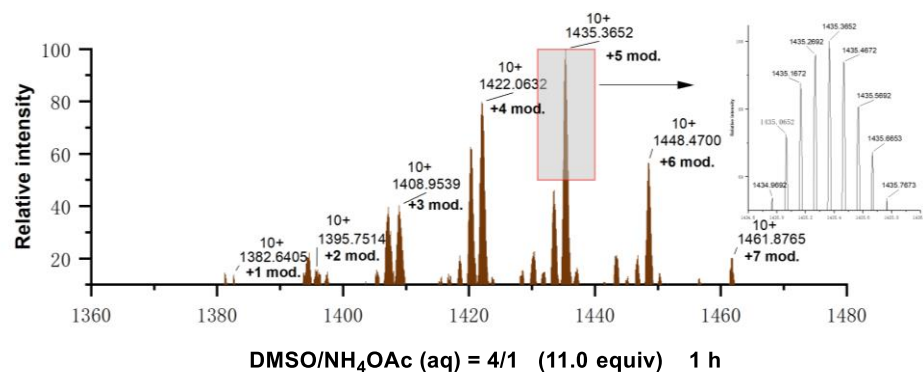


Figure S24. Mass spectrum of unmodified ribonuclease A.



+1 mod.	+2 mod.	+3 mod.	+4 mod.	+5 mod.	+6 mod.	+7 mod.
5.99%	6.81%	13.35%	25.07%	27.25%	15.80%	5.72%

Figure S25. Modification result of ribonuclease A with **1a** (7.0 equiv). Percentages were determined through the relative ratio of peak intensities in the mass spectrum of the product mixture.



+1 mod.	+2 mod.	+3 mod.	+4 mod.	+5 mod.	+6 mod.	+7 mod.
4.08%	4.72%	11.64%	24.84%	31.45%	16.98%	6.29%

Figure S26. Modification result of ribonuclease A with **1a** (11.0 equiv). Percentages were determined through the relative ratio of peak intensities in the mass spectrum of the product mixture.

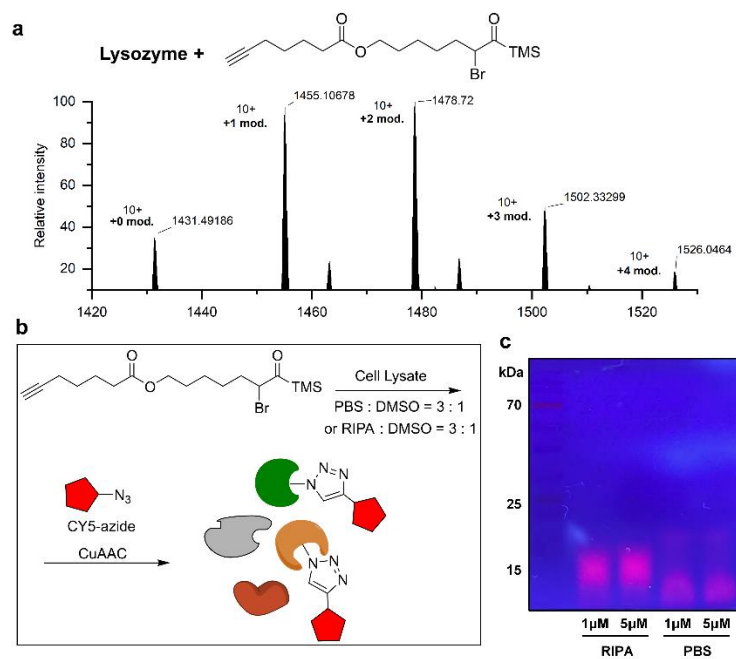


Figure S27. (a) Coupling of lysozyme to alkyne bearing substrates (7.0 equiv). (b) CY-5 labeling of proteins in cell lysates. (c) Gel imaging after Cy5 labeling.

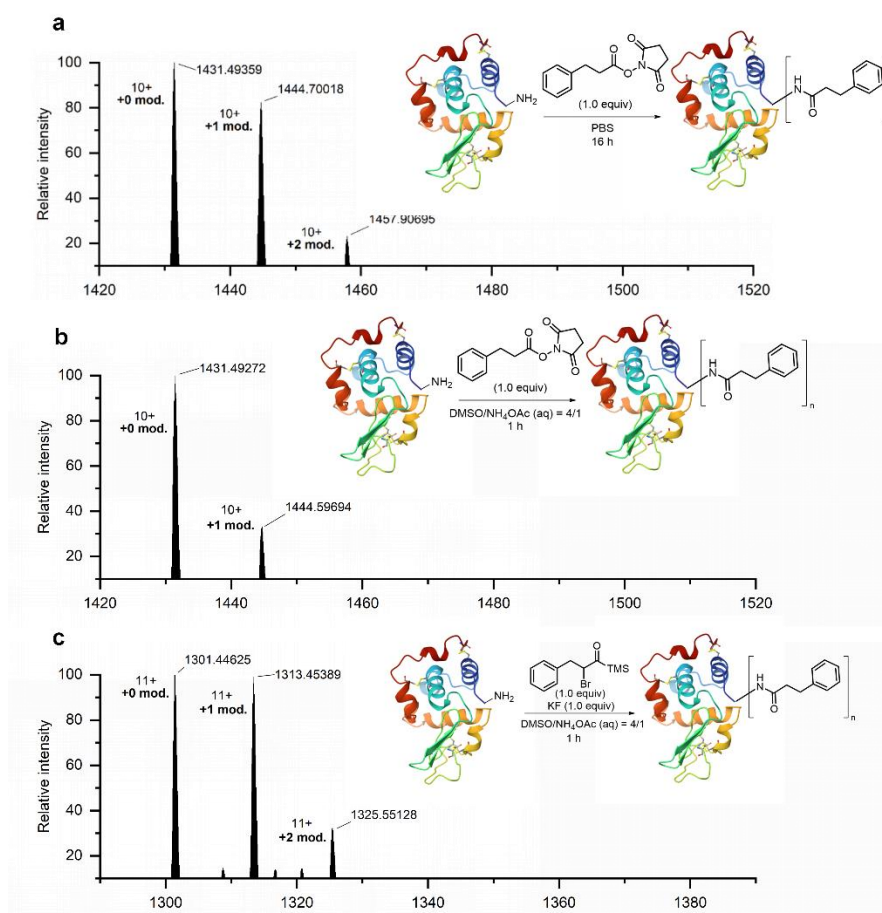


Figure S28. Comparison with NHS ester modified protein amino acids under standard conditions (1 equiv).

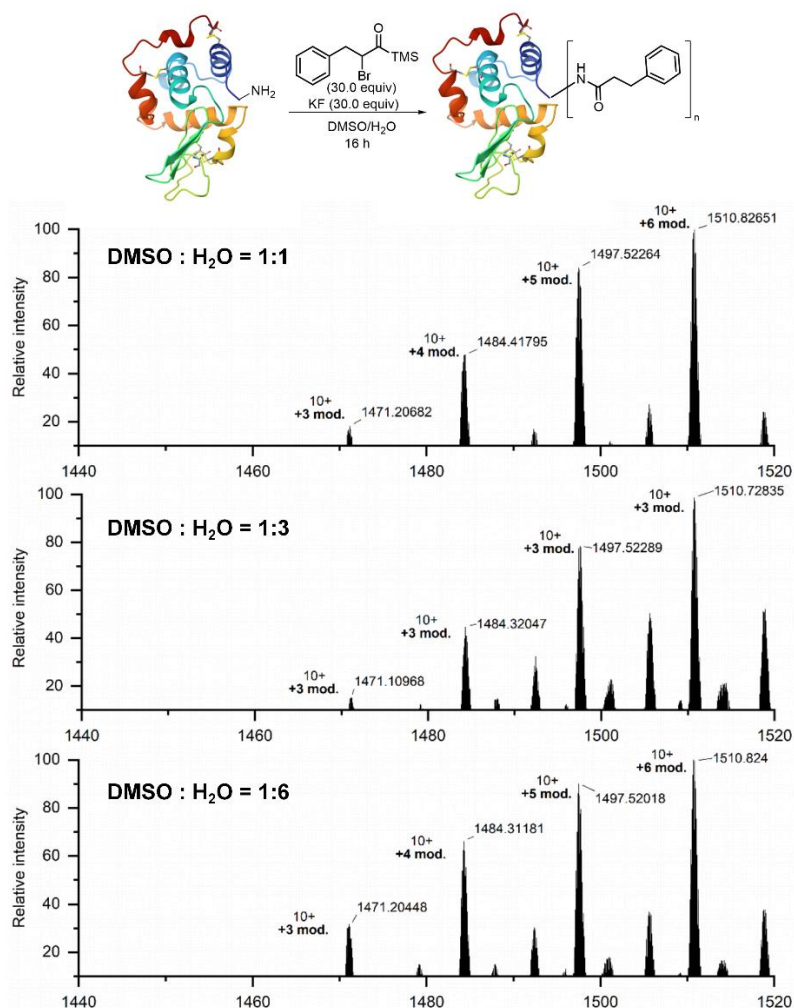


Figure S29. The lysozyme modification under different conditions was detected by mass spectrum.

8.8: General procedure for reactions of ribonuclease A with 1a: Lysozyme activity was measured using the ADP-Glo™ Max Assay (Promega, V7001) to evaluate DMSO solvent effects. Lysozyme (10 µg/mL in 50 mM Tris-HCl, 150 mM NaCl, pH 7.5) was pre-incubated with 80% or 50% (v/v) DMSO for 10 or 30 min at 25 °C, followed by reaction initiation with 0.2 mg/mL *Micrococcus lysodeikticus* substrate (37 °C, 15 min). Reactions were terminated by ADP-Glo™ Reagent (10 µL), incubated for 40 min (25 °C), and kinase detection reagent (20 µL) was added for luminescence measurement (SpectraMax iD3). Activity retention (%) was normalized to untreated controls (no DMSO) and blank (substrate-only), calculated as $[(RLU_{\text{sample}} - RLU_{\text{blank}})/(RLU_{\text{control}} - RLU_{\text{blank}})] \times 100$. Triplicate data (mean $\pm$ SD) were analyzed via one-way ANOVA with Tukey's post hoc test (* $p < 0.05$).

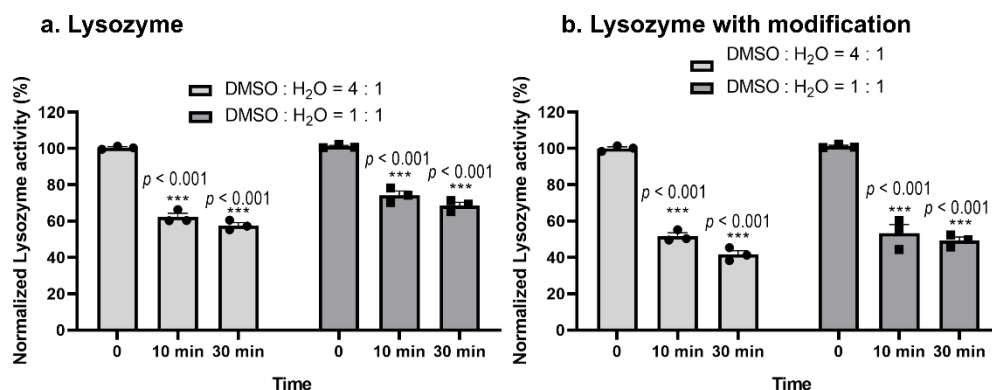


Figure S30. The lysozyme activity under different conditions was detected by ADP-Glo. All data represent three independent biological replicates ($n=3$), presented as mean $\pm$ SEM. Significance was determined by one-way ANOVA with Tukey's multiple comparisons test, GraphPad Prism. (***) $p<0.001$.

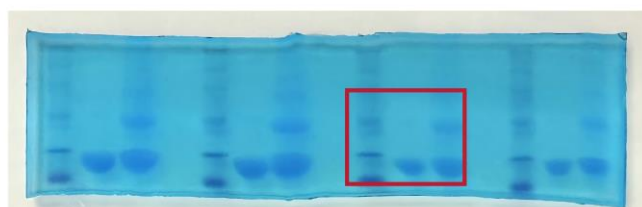


Figure 6B

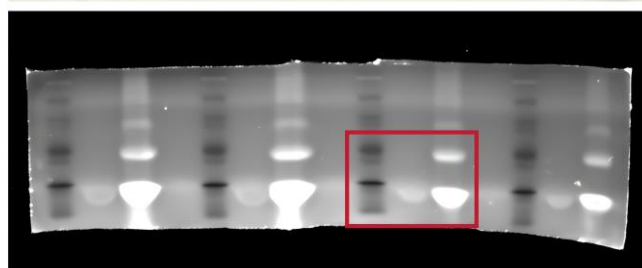


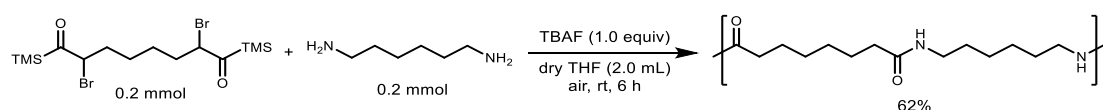
Figure 6B



Figure S27c

Figure S31. Uncropped scans of gel images.

9: Polyamide synthesis



Under an ambient atmosphere, hexane-1,6-diamine (23.2 mg, 0.2 mmol, 1.0 equiv), dry tetrahydrofuran (2.0 mL), TBAF (0.4 mmol, 2.0 equiv), and 2,7-dibromo-1,8-bis(trimethylsilyl)octane-1,8-dione (88.2 mg, 0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at

25 °C for 6 h. Then the polyamide was filtrated and washed with H₂O (3 × 5.0 mL), (3 × 5.0 mL) and (3 × 5.0 mL). The resulting polyamide was dried to a constant weight to afford **9** as a white powder (31.7 mg, 62%) and characterized by GPC.

Mn: 32.1 kg/mol, Đ: 1.48.

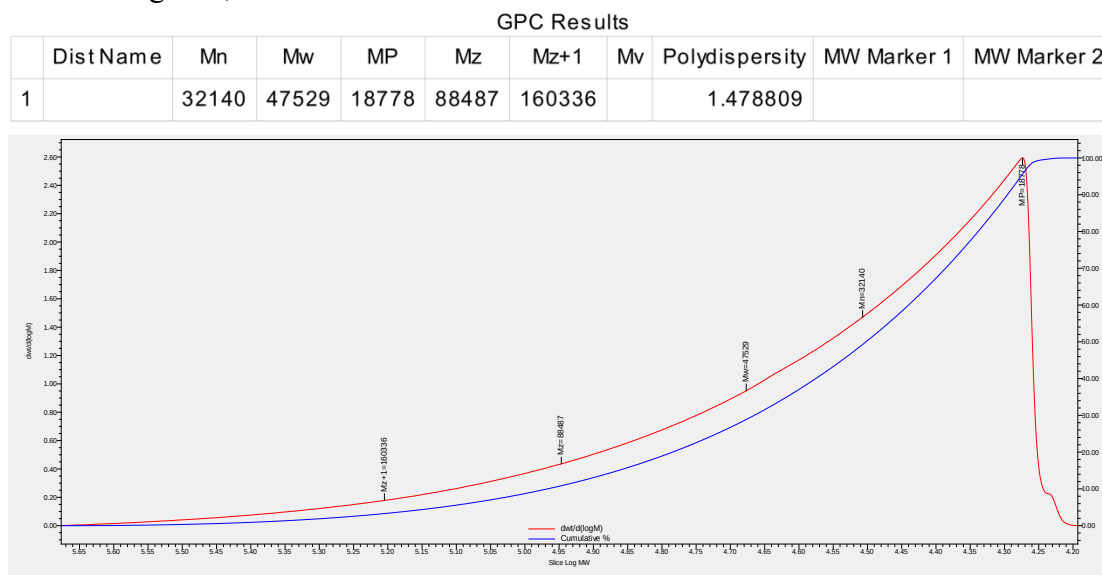
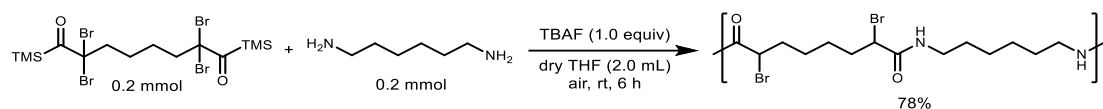


Figure S32. GPC curves of **9**.



Under an ambient atmosphere, hexane-1,6-diamine (23.2 mg, 0.2 mmol, 1.0 equiv), dry tetrahydrofuran (2.0 mL), TBAF (0.4 mmol, 2.0 equiv), and 2,2,7,7-tetrabromo-1,8-bis(trimethylsilyl)octane-1,8-dione (119.6 mg, 0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 6 h. Then the polyamide was filtrated and washed with H₂O (3 × 5.0 mL), THF (3 × 5.0 mL) and n-hexane (3 × 5.0 mL). The resulting polyamide was dried to a constant weight to afford **11** as a white powder (64.3 mg, 78%) and characterized by GPC.

Mn: 27.3 kg/mol, Đ: 1.16.

GPC Results										
	Dist Name	Mn	Mw	MP	Mz	Mz+1	Mv	Polydispersity	MW Marker 1	MW Marker 2
1		27341	31733	27245	36895	42623		1.160634		

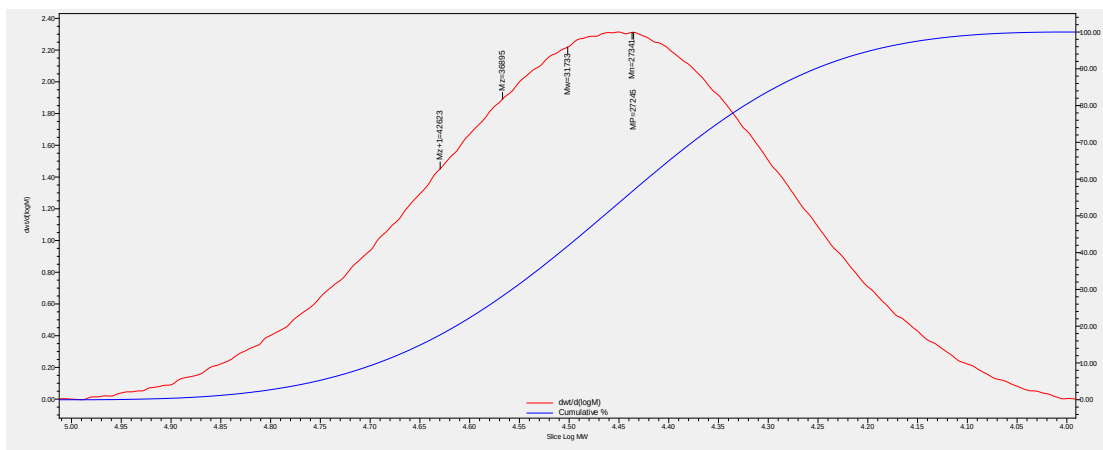
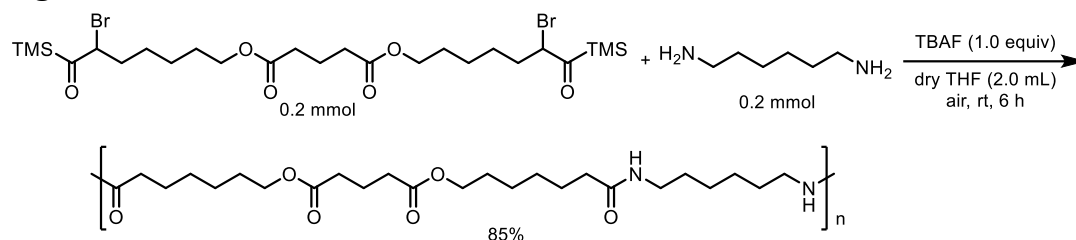


Figure S33. GPC curves of **11**.



Under an ambient atmosphere, hexane-1,6-diamine (23.2 mg, 0.2 mmol, 1.0 equiv), dry tetrahydrofuran (2.0 mL), TBAF (0.4 mmol, 2.0 equiv), and bis(6-bromo-7-oxo-7-(trimethylsilyl)heptyl) glutarate (131.2 mg, 0.2 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 6 h. Then the polyamide was filtrated and washed with H₂O (3 × 5.0 mL), THF (3 × 5.0 mL) and n-hexane (3 × 5.0 mL). The resulting polyamide was dried to a constant weight to afford **13** as a white powder (79.8 mg, 85%) and characterized by GPC.

Mn: 105.1 kg/mol, Đ: 1.30.

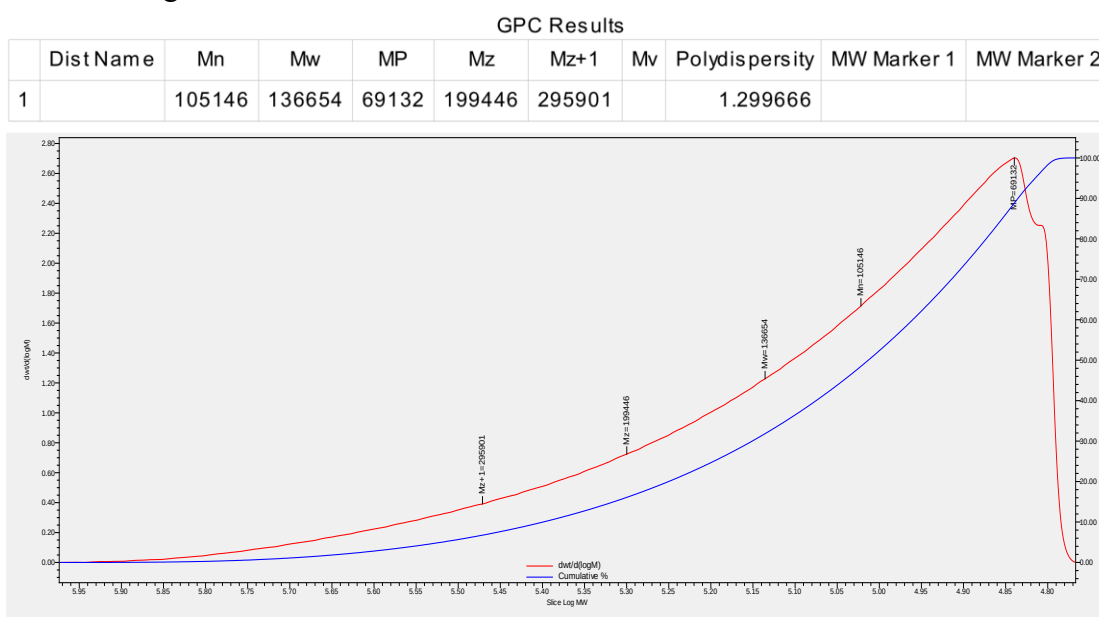
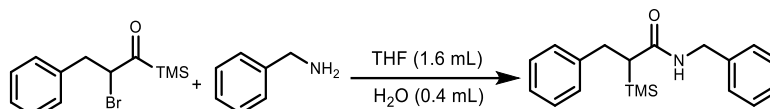


Figure S34. GPC curves of **13**.

10: Mechanistic studies

(1) Control experiments on the potential intermediate

N-Benzyl-3-phenyl-2-(trimethylsilyl)propenamide ³² **3-Int**



Under an ambient atmosphere, amine (10.7 mg, 0.1 mmol, 1.0 equiv), tetrahydrofuran (0.8 mL), H₂O (0.2 mL), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (28.4 mg, 0.1 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 5 min. Then water (10.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 10.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **3-Int**.

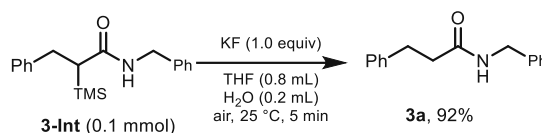
Yield 16.8 mg (54%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.25-7.21 (m, 8H), 7.01 (d, *J* = 6.5 Hz, 2H), 5.34 (s, 1H), 4.48-4.43 (m, 1H), 4.24-4.19 (m, 1H), 3.19 (t, *J* = 12.9 Hz, 1H), 2.74 (d, *J* = 13.9 Hz, 1H), 1.94 (d, *J* = 11.6 Hz, 1H), 0.14 (s, 9H).

¹³C NMR (CDCl₃, 100 MHz) δ 173.8, 142.5, 138.7, 128.62, 128.55, 128.5, 127.9, 127.3, 126.1, 43.6, 42.7, 33.4, -2.5.

HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₉H₂₆NOSi⁺: 312.1778; Found 312.1765.



Under an ambient atmosphere, **3-Int** (31.1 mg, 0.1 mmol, 1.0 equiv), tetrahydrofuran (1.6 mL), H₂O (0.4 mL) and KF (5.8 mg, 0.1 mmol, 1.0 equiv) were added to an oven-dried 10.0 mL microwave tube with a magnetic bar. The reaction was stirred at 25 °C for 5 min. Then water (5.0 mL) was added, the organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 5.0 mL). After that, the organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography to afford **3a** as a white solid.

Yield 22.0 mg (92%).

NMR Spectroscopy:

¹H NMR (CDCl₃, 400 MHz) δ 7.33-7.27 (m, 5H), 7.24-7.21 (m, 3H), 7.17-7.15 (m, 2H), 5.70 (s, 1H), 4.41 (d, *J* = 5.6 Hz, 2H), 3.01 (t, *J* = 7.6 Hz, 2H), 2.53 (t, *J* = 7.6 Hz, 2H).

¹³C NMR (CDCl₃, 150 MHz) δ 172.0, 140.9, 138.3, 128.8, 128.7, 128.5, 127.9,

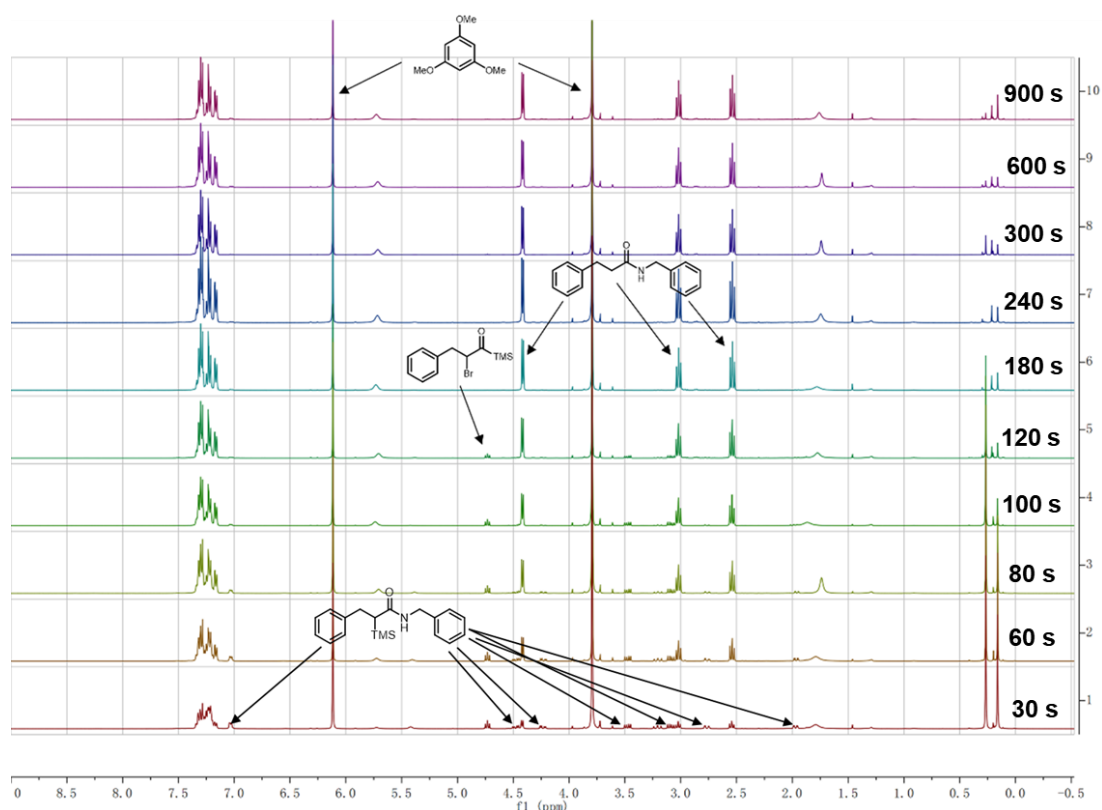


Figure S36. ^1H NMR (CDCl₃, 400 MHz, 298 K) of the reaction varying with time (second run).

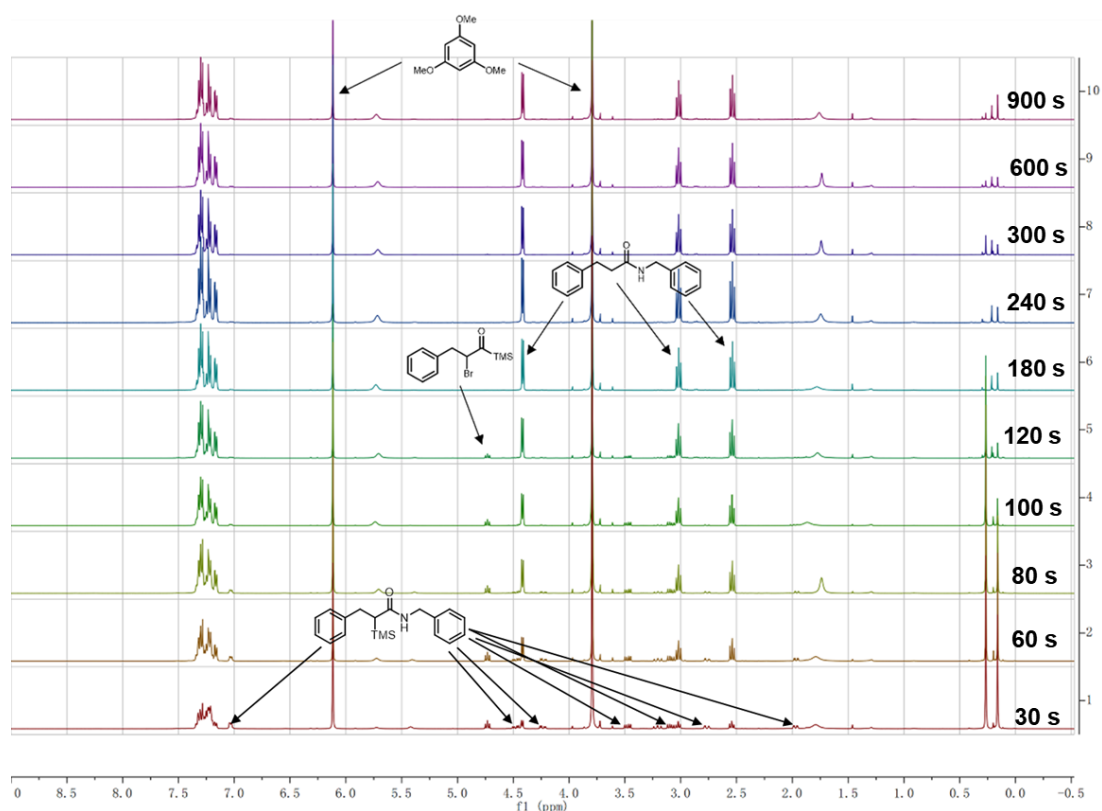
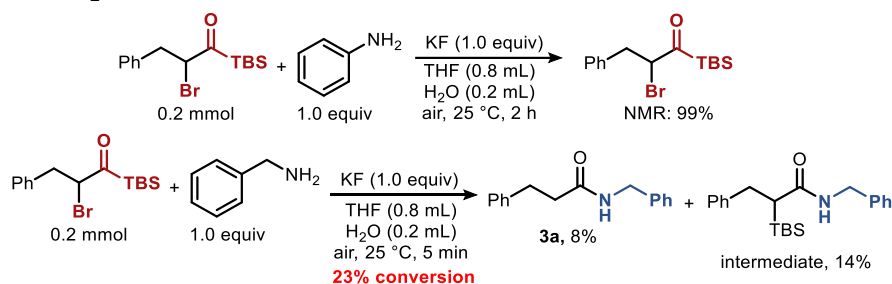
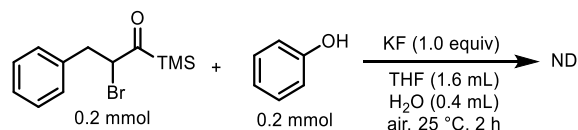


Figure S37. ^1H NMR (CDCl₃, 400 MHz, 298 K) of the reaction varying with time (third run).

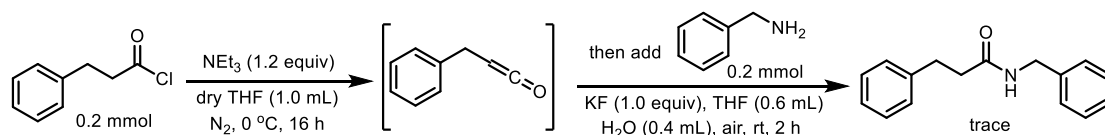
(3) Control experiments



To confirm that the reaction starts with amine reacting with the acyl silane, not the acyl silane with KF, we used more hindered TBS acyl silane and less reactive aniline. No reaction occurred after 2 h. But when we switched to benzylamine, 8% of the desired product and 14% of the intermediate formed within 5 min. This shows the reaction is initiated by the amine reacting with the acyl silane.

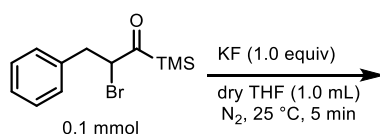


Under an ambient atmosphere, phenol (18.8 mg, 0.2 mmol, 1.0 equiv), THF (1.6 mL), H₂O (0.4 mL), KF (11.6 mg, 0.2 mmol, 1.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (56.8 mg, 0.2 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (10.0 mL) with a magnetic bar. The reaction was monitored by GC-MS.



Ketene were prepared according to the literature.³³ Under a nitrogen atmosphere, hydrocinnamoyl chloride (33.7 mg, 0.2 mmol, 1.0 equiv) and dry tetrahydrofuran (1.0 mL) were added to an oven-dried Schlenk tube (10.0 mL) with a magnetic bar. The reaction mixture was cooled to 0 °C and stirred for 5 min. Then, NEt₃ (24.2 mg, 1.2 equiv) was added dropwise to the reaction mixture and stirred at 0 °C for 16 h to afford ketene quantitatively which was used directly without further purification for the next step.

Under an ambient atmosphere, benzylamine (21.4 mg, 0.2 mmol, 1.0 equiv), tetrahydrofuran (0.6 mL), H₂O (0.4 mL), KF (11.6 mg, 0.2 mmol, 1.0 equiv) were added to an 10.0 mL microwave tube with a magnetic bar. Then ketene solution added to the reaction mixture and stirred at 25 °C for 2 h. The reaction was monitored by GC-MS.



Under a nitrogen atmosphere, dry tetrahydrofuran (1.0 mL), KF (5.8 mg, 0.1 mmol, 10.0 equiv), and 2-bromo-3-phenyl-1-(trimethylsilyl)propan-1-one (28.4 mg, 0.1 mmol, 1.0 equiv) were added to an oven-dried round bottom flask (10.0 mL) with a magnetic bar. The reaction was monitored by GC-MS.

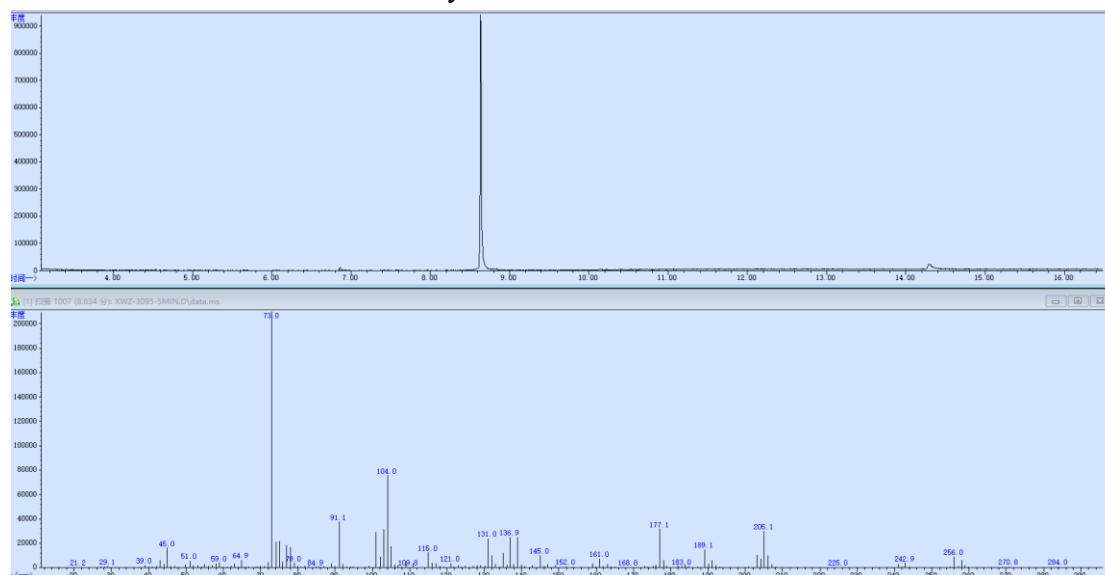


Figure S38. GC-MS spectrum after 5 min of reaction

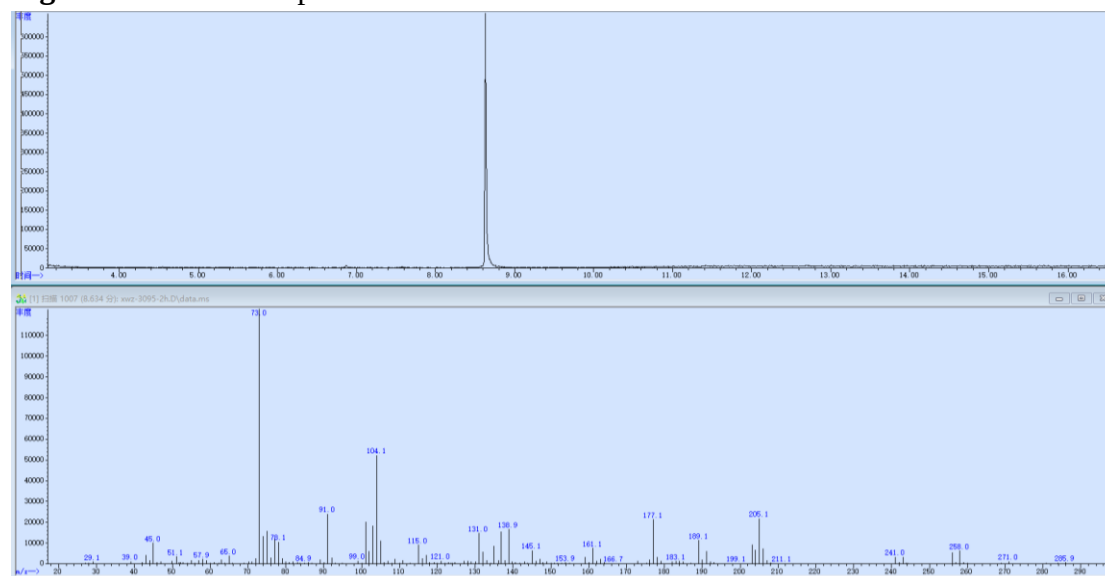


Figure S39. GC-MS spectrum after 2 h of reaction

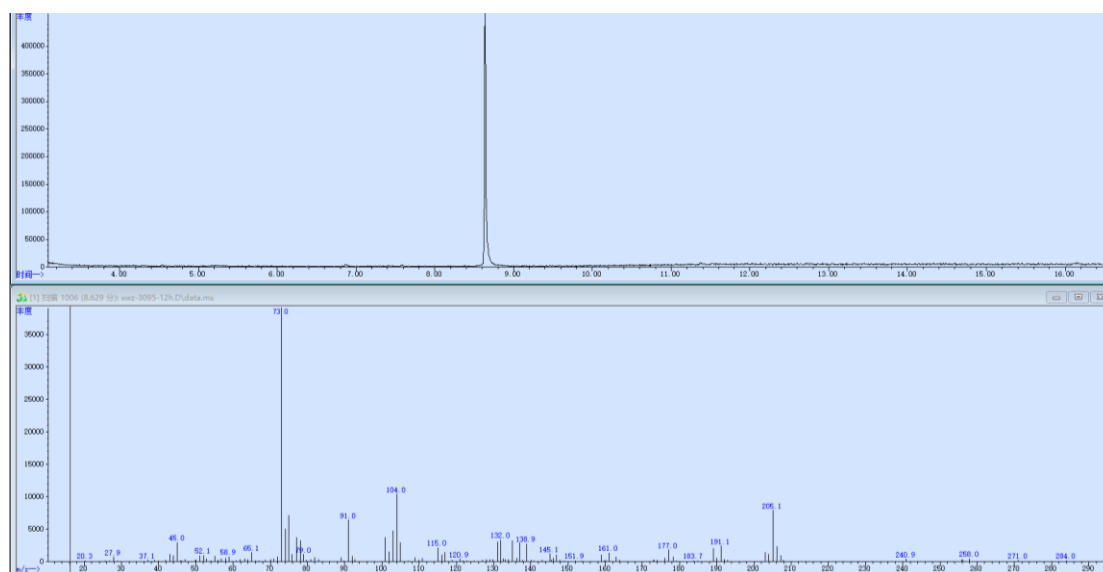


Figure S40. GC-MS spectrum after 12 h of reaction

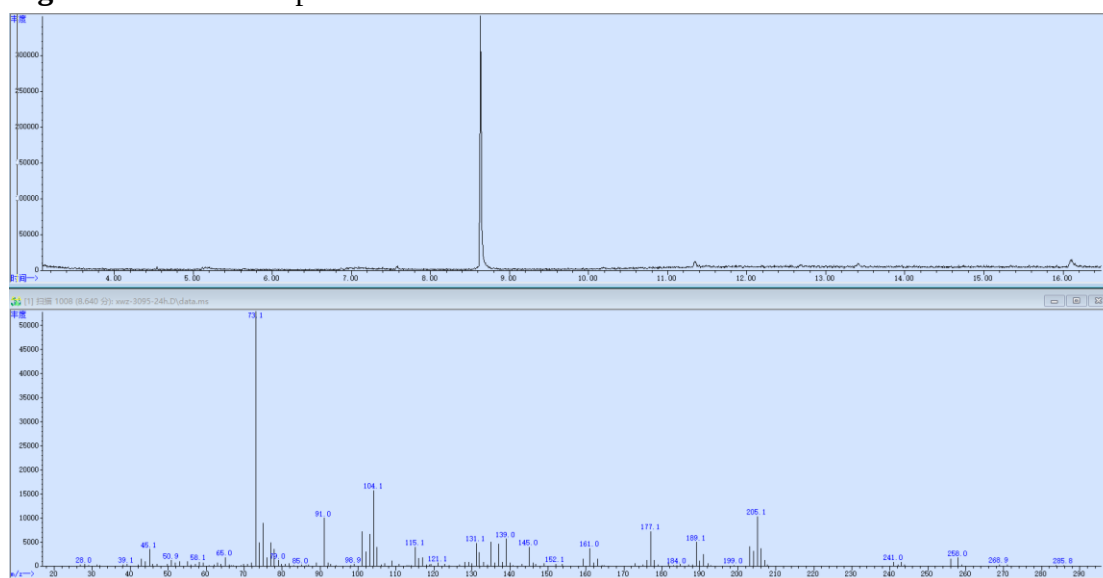
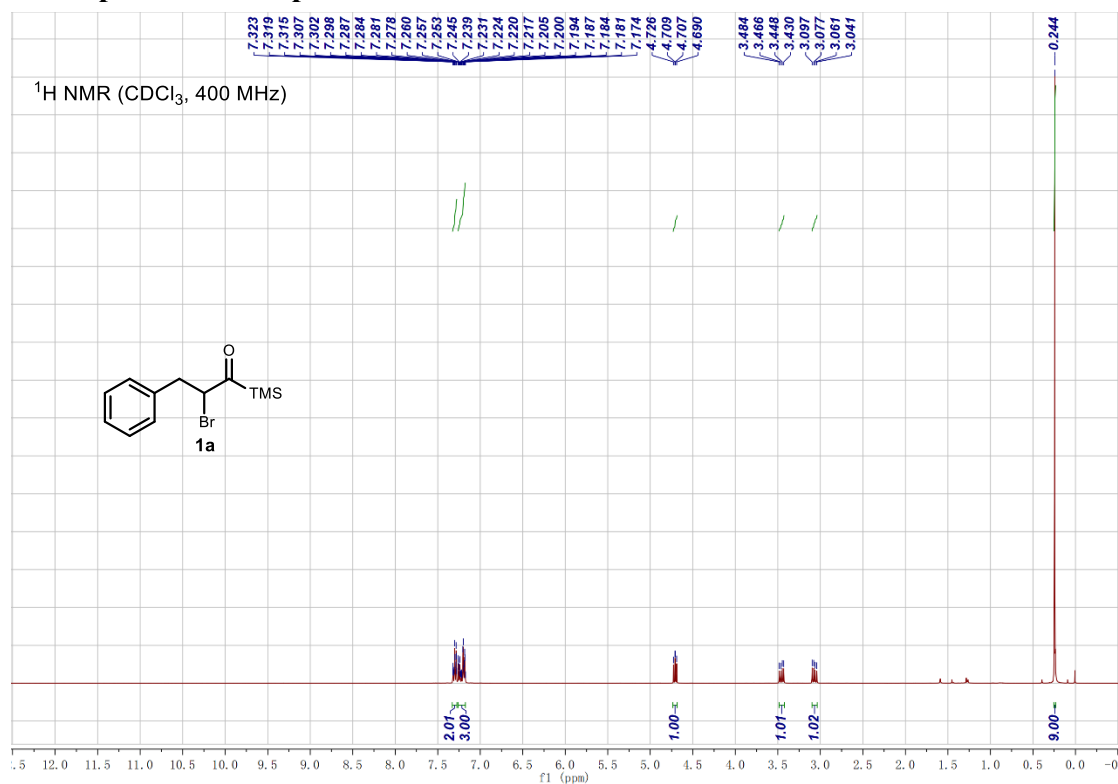
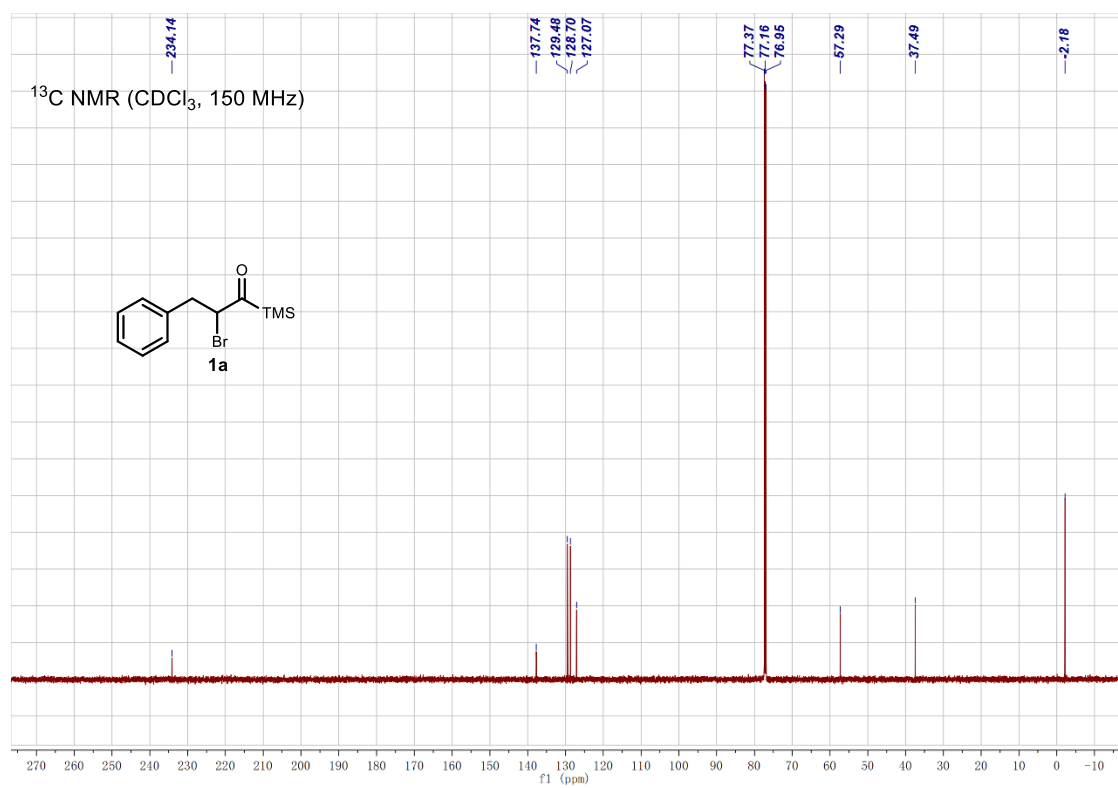


Figure S41. GC-MS spectrum after 24 h of reaction

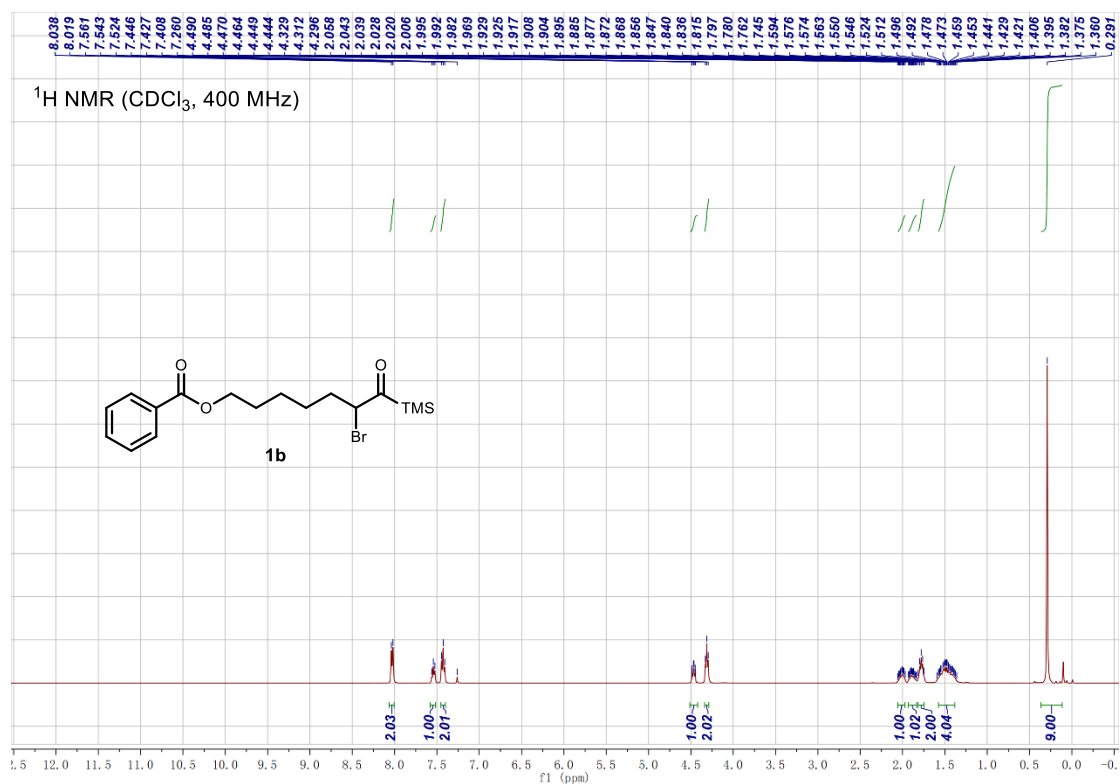
11: Copies of NMR spectra



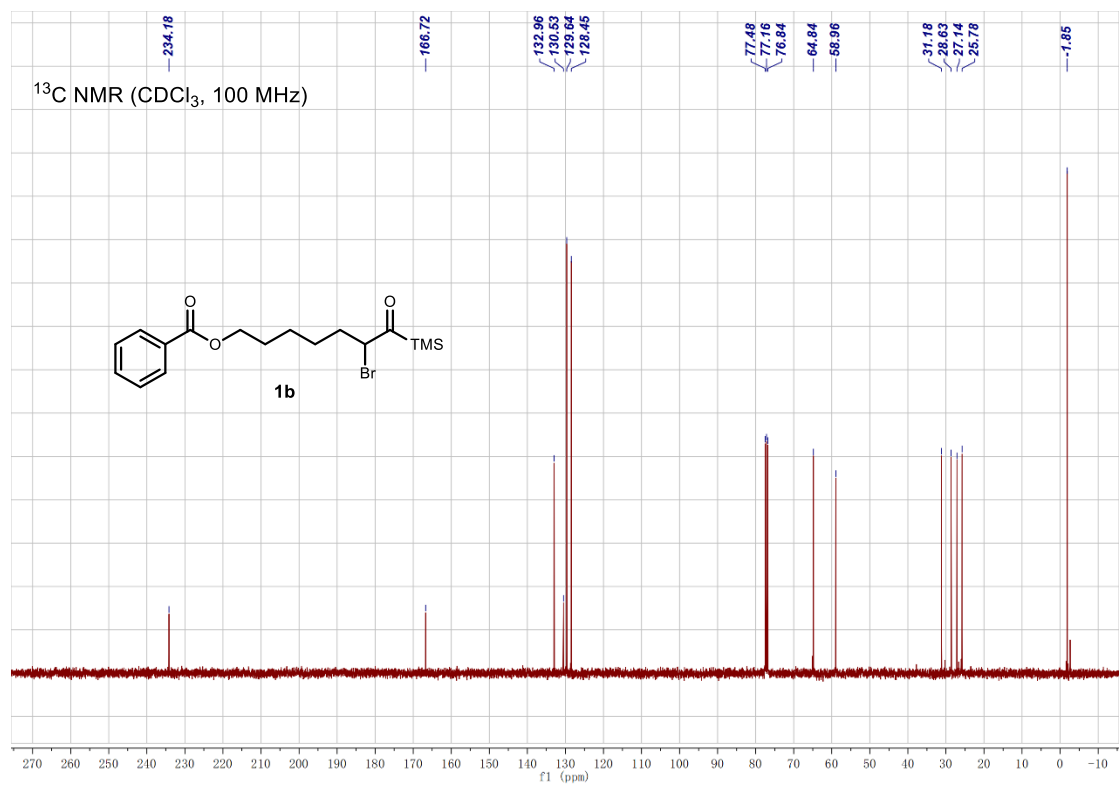
¹H NMR of **1a** (400 MHz, CDCl₃, 298 K)



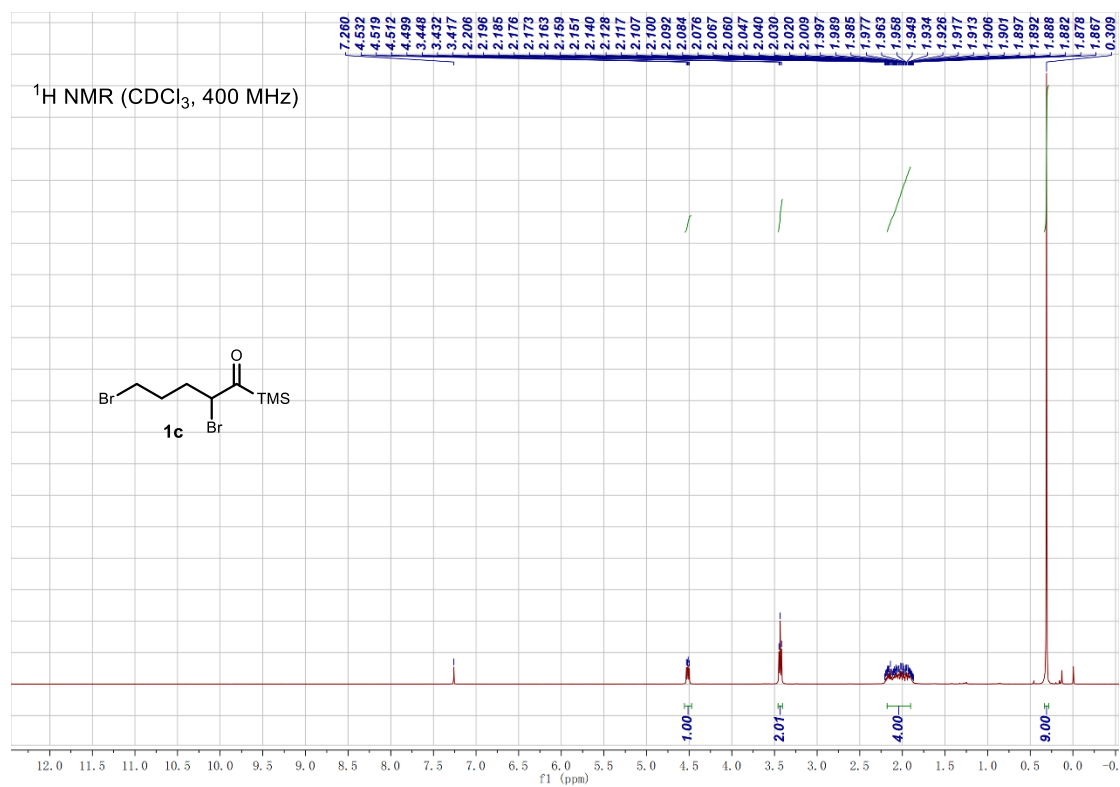
¹³C NMR of **1a** (150 MHz, CDCl₃, 298 K)



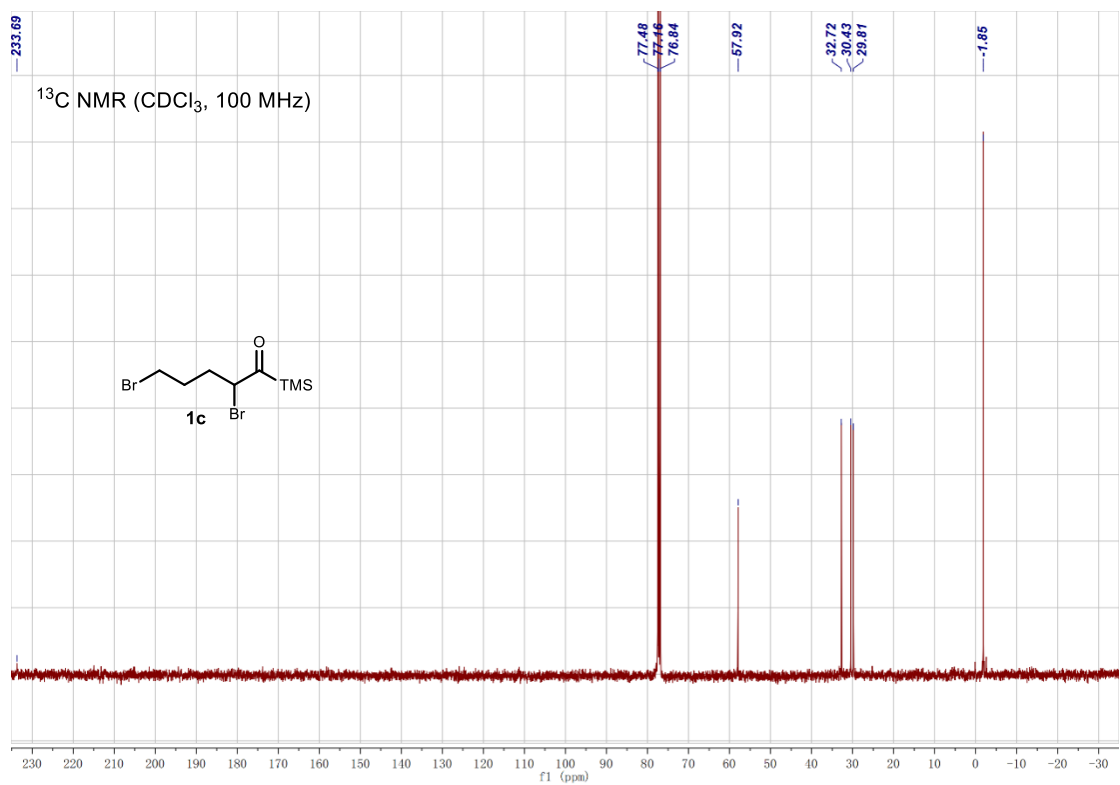
¹H NMR of **1b** (400 MHz, CDCl₃, 298 K)



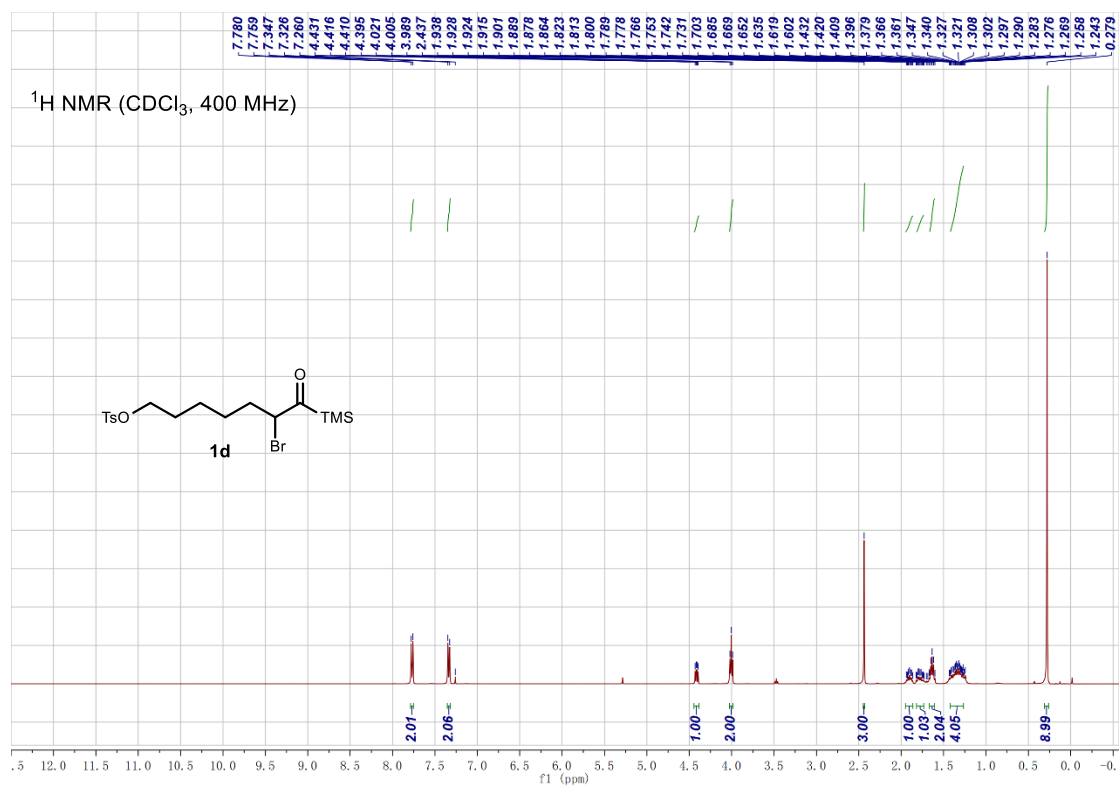
¹³C NMR of **1b** (100 MHz, CDCl₃, 298 K)



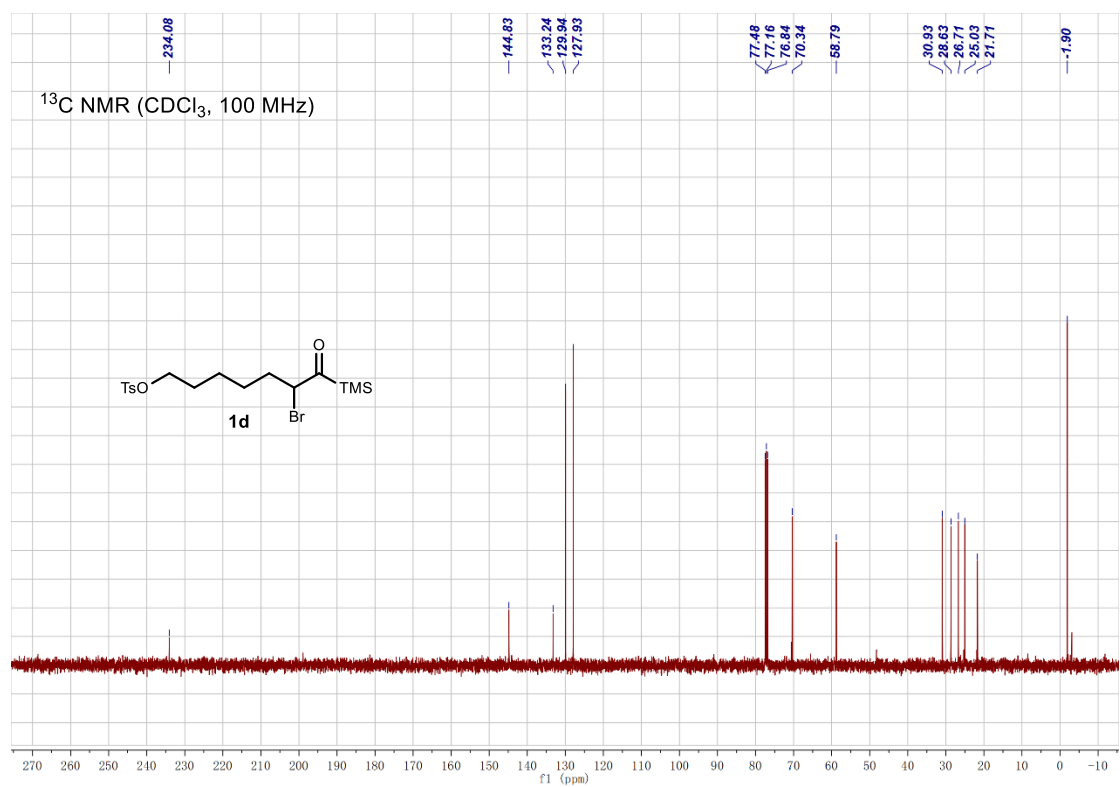
¹H NMR of **1c** (400 MHz, CDCl₃, 298 K)



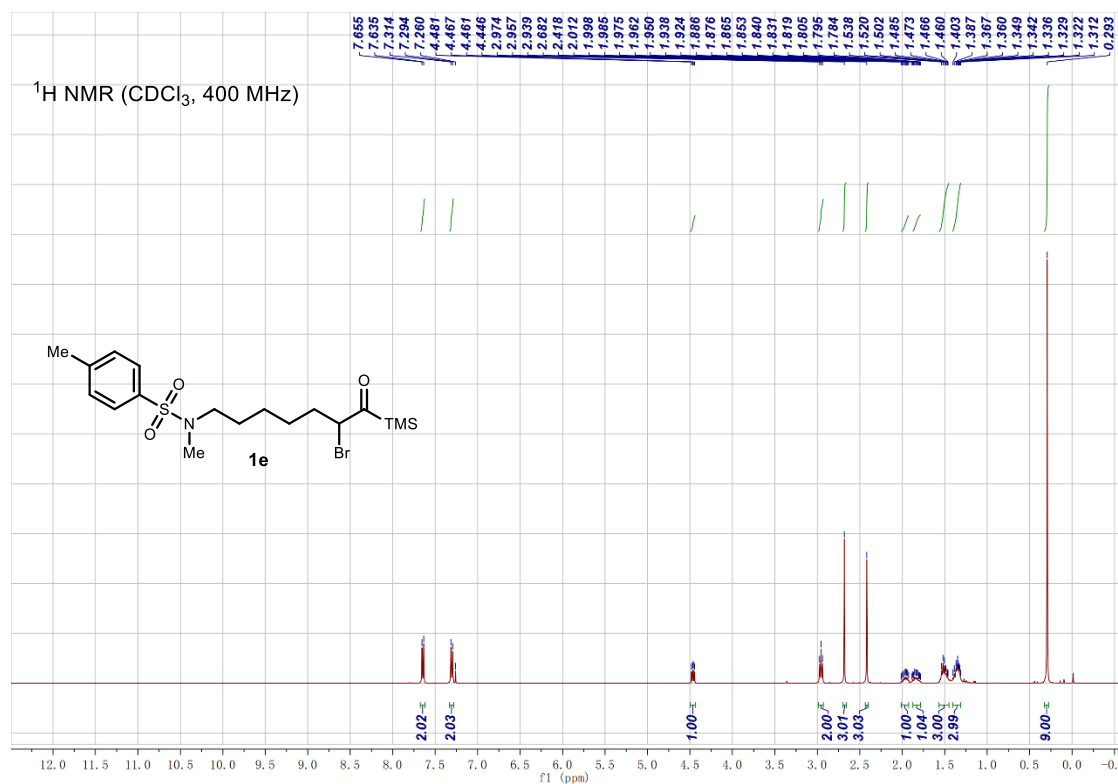
¹³C NMR of **1c** (100 MHz, CDCl₃, 298 K)



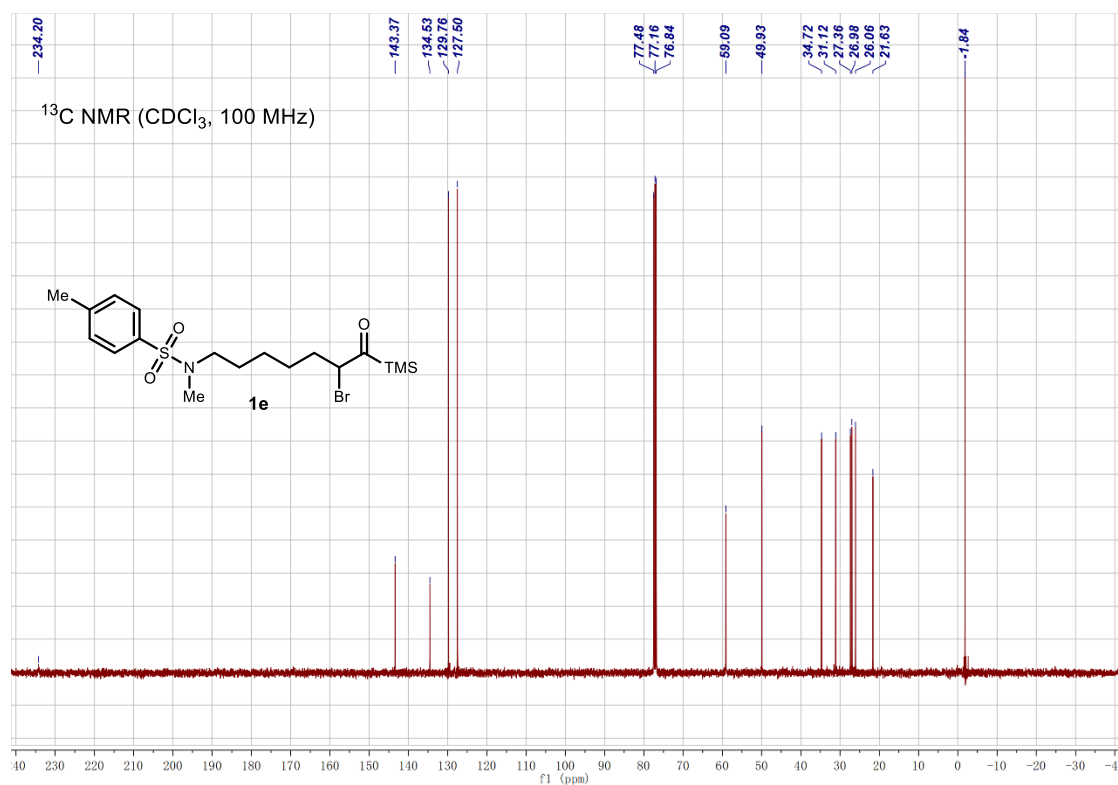
¹H NMR of **1d** (400 MHz, CDCl₃, 298 K)



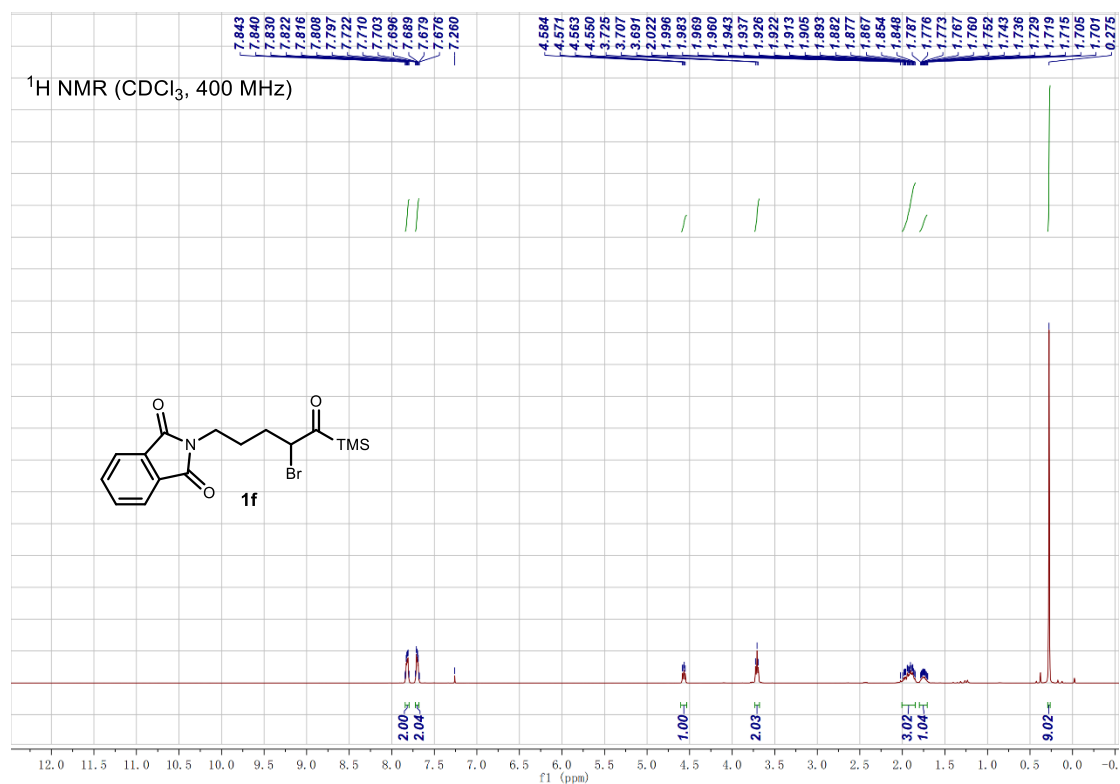
¹³C NMR of **1d** (100 MHz, CDCl₃, 298 K)



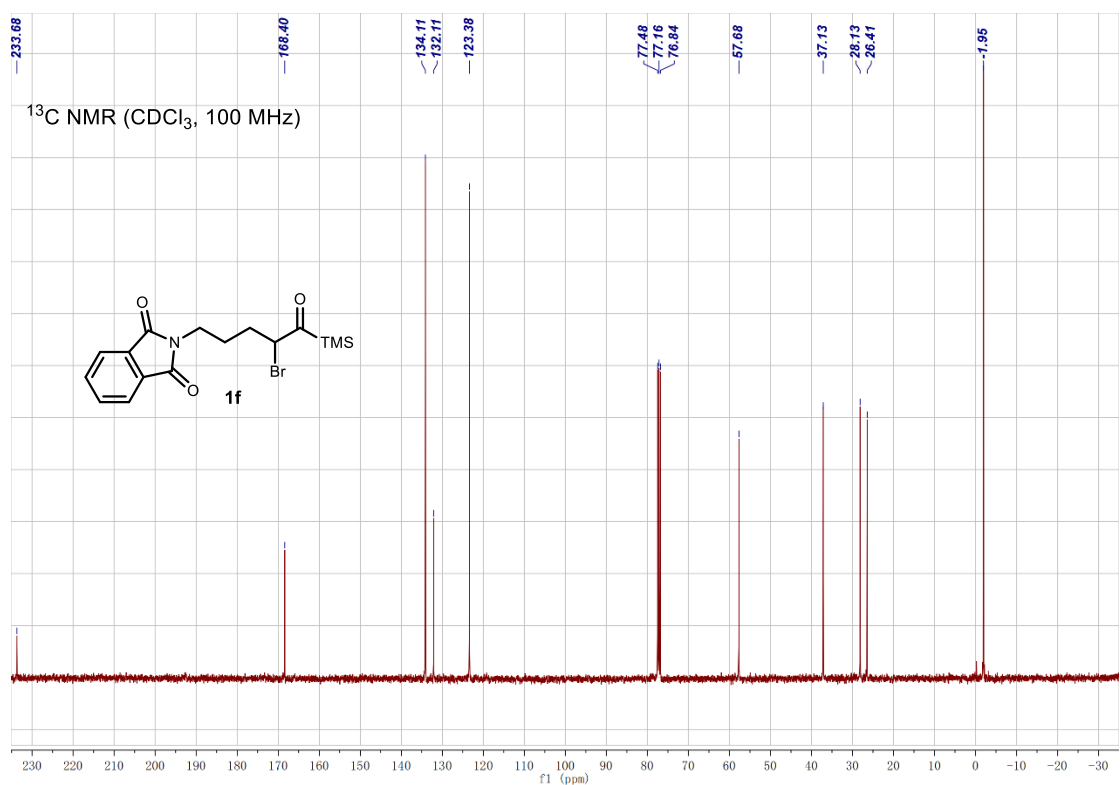
¹H NMR of **1e** (400 MHz, CDCl₃, 298 K)



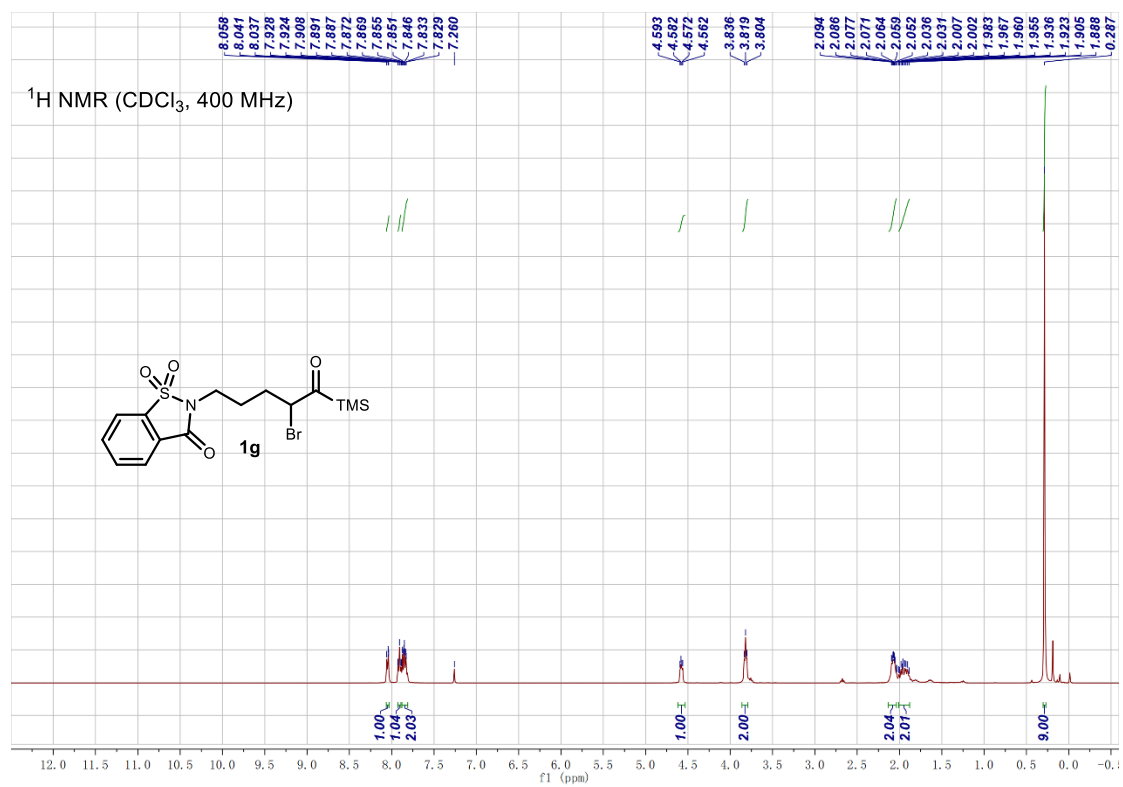
¹³C NMR of **1e** (100 MHz, CDCl₃, 298 K)



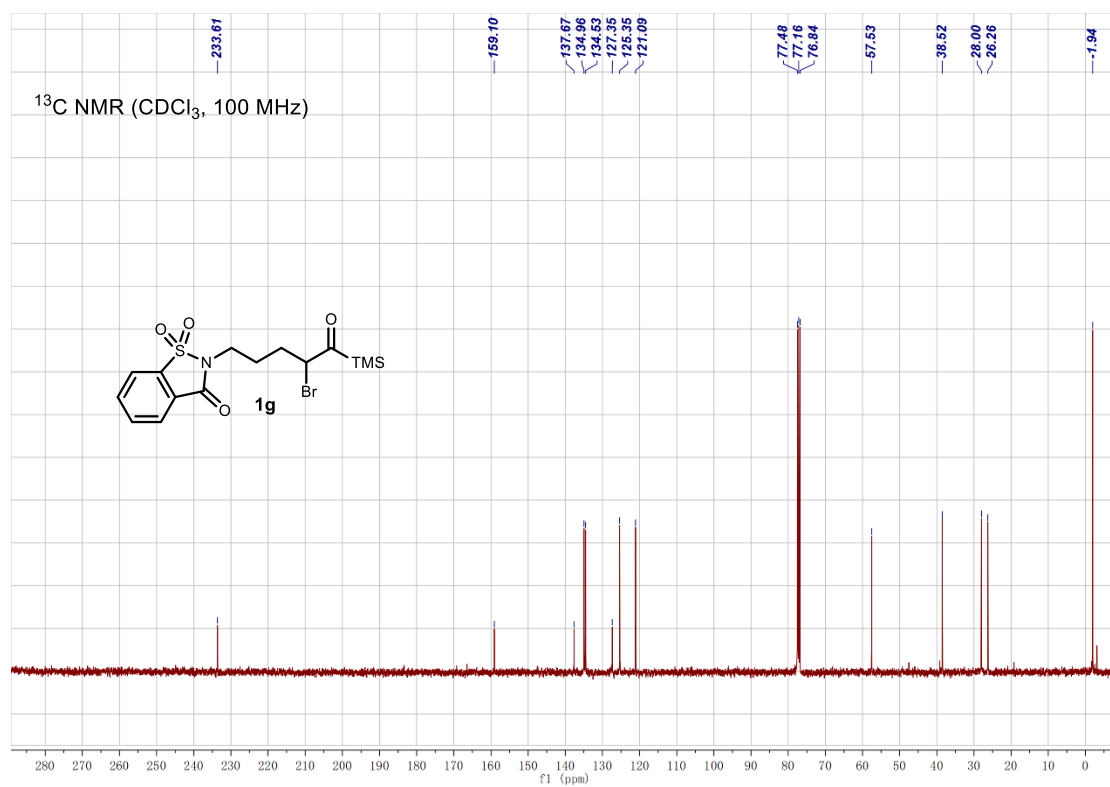
¹H NMR of **1f** (400 MHz, CDCl₃, 298 K)



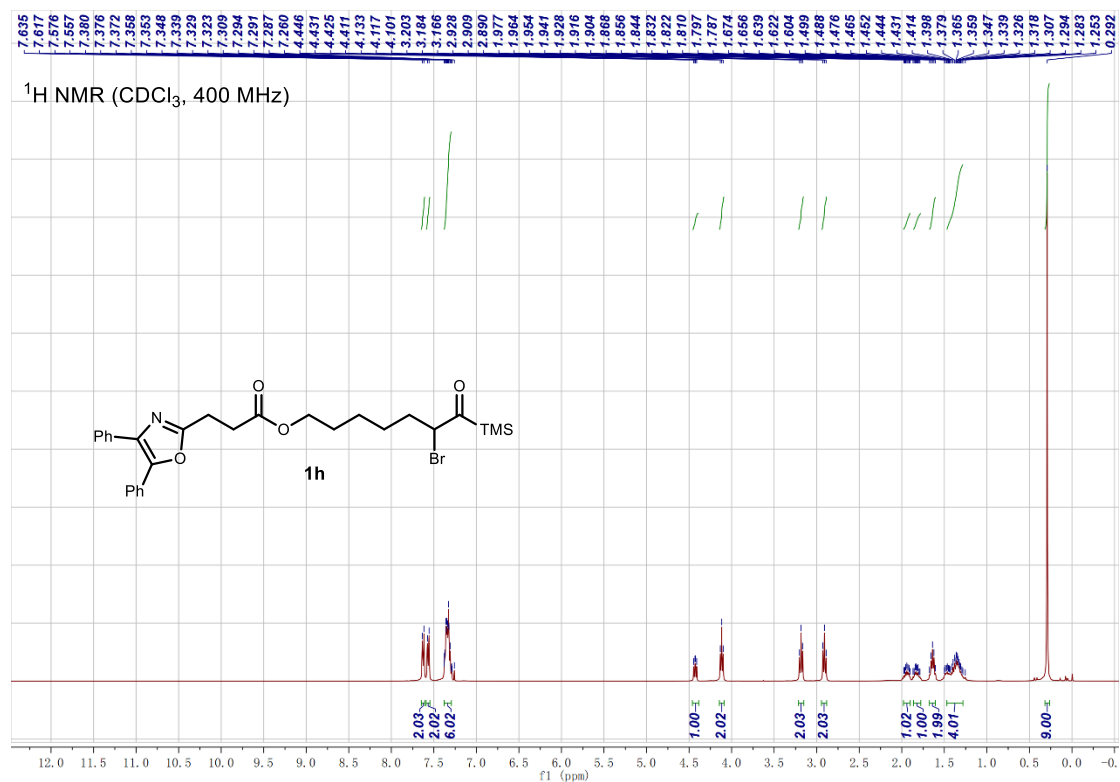
¹³C NMR of **1f** (100 MHz, CDCl₃, 298 K)



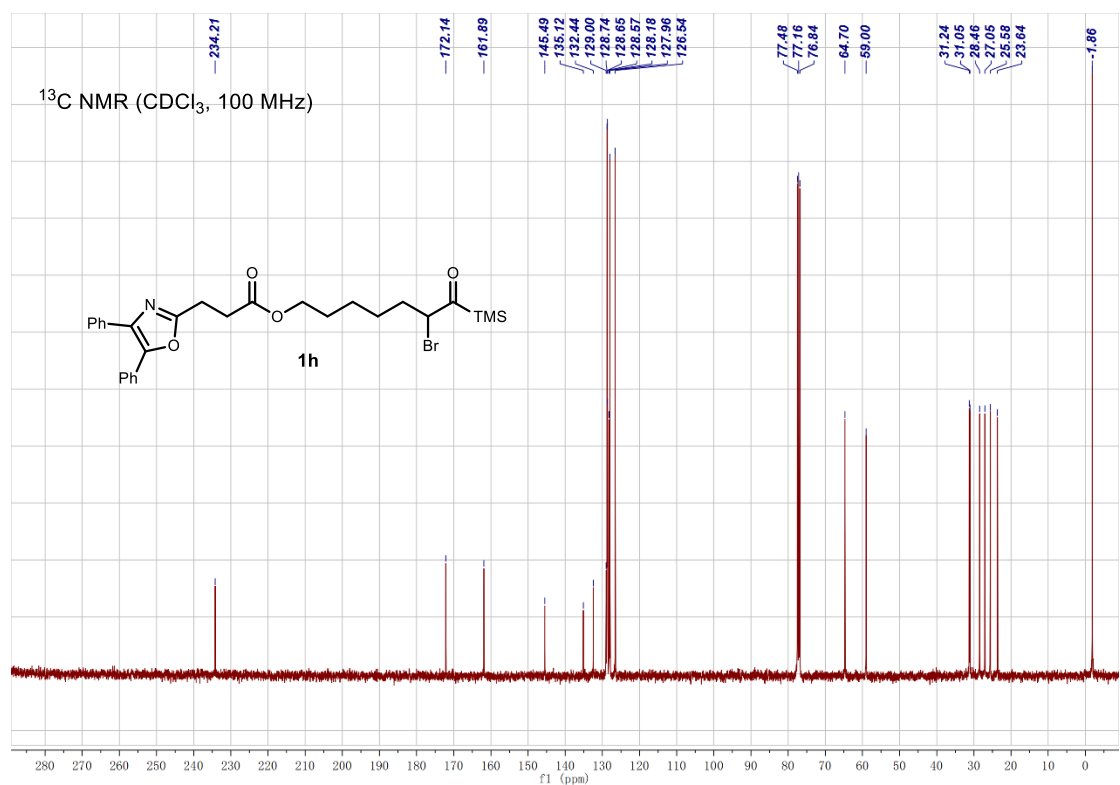
¹H NMR of **1g** (400 MHz, CDCl₃, 298 K)



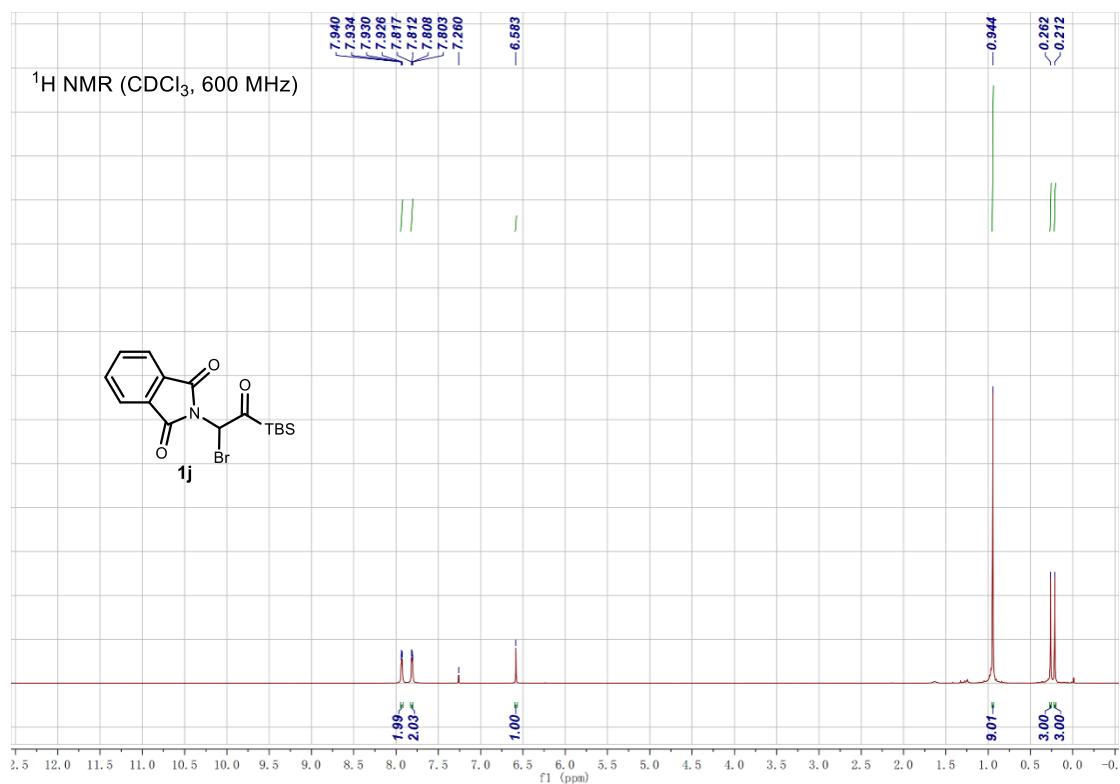
¹³C NMR of **1g** (100 MHz, CDCl₃, 298 K)



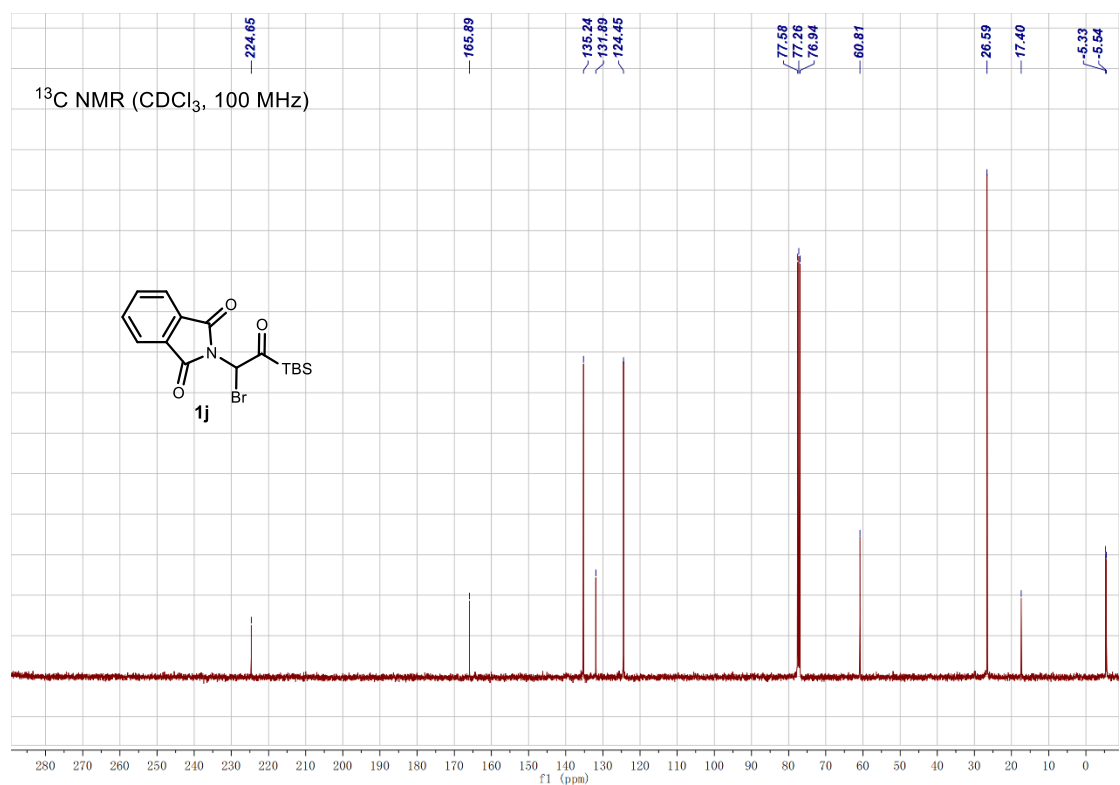
¹H NMR of **1h** (400 MHz, CDCl₃, 298 K)



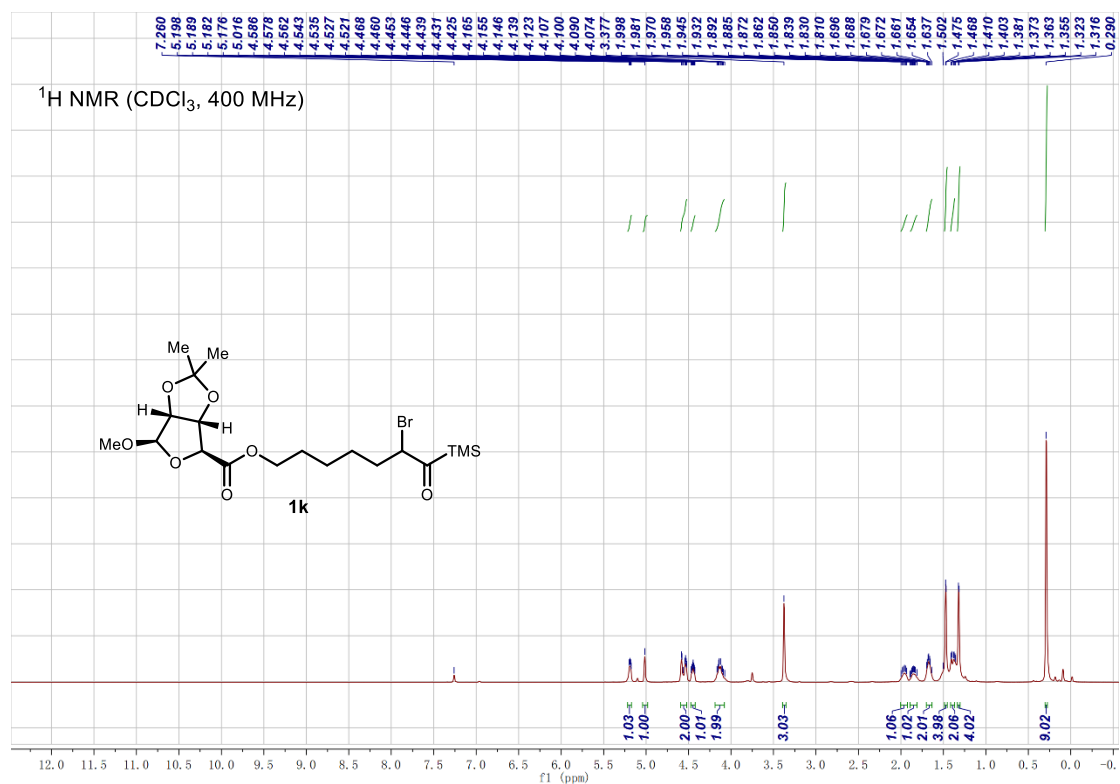
¹³C NMR of **1h** (100 MHz, CDCl₃, 298 K)



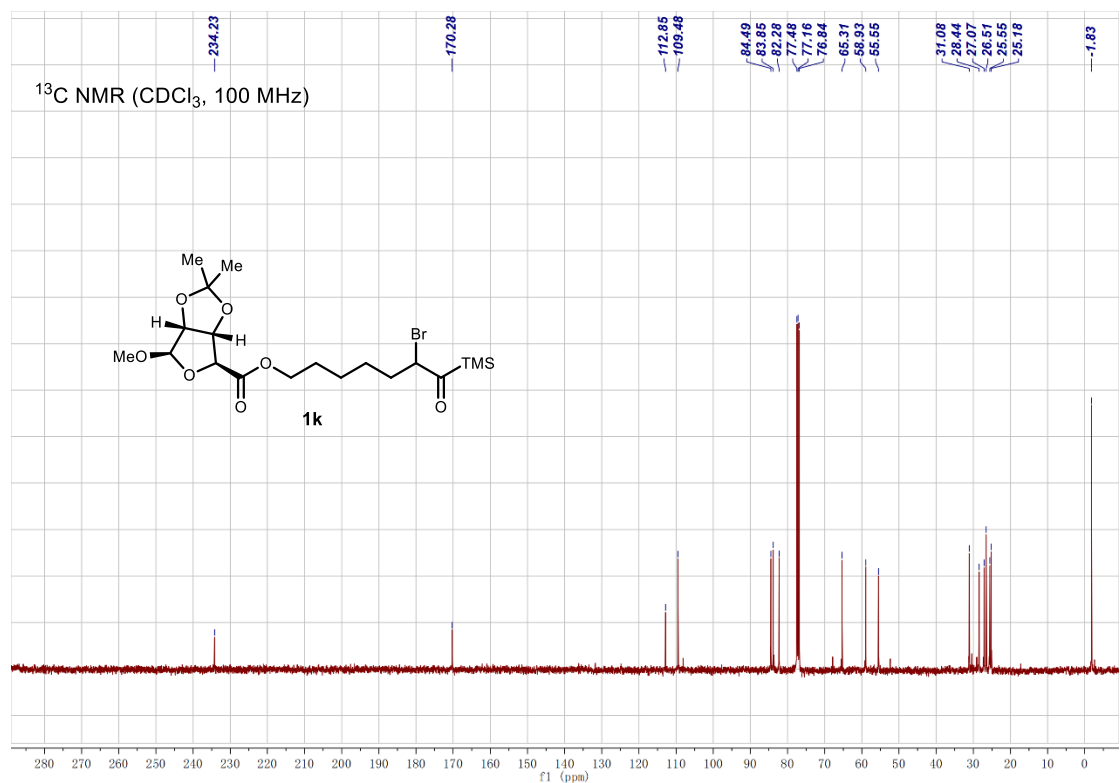
¹H NMR of **1j** (600 MHz, CDCl₃, 298 K)



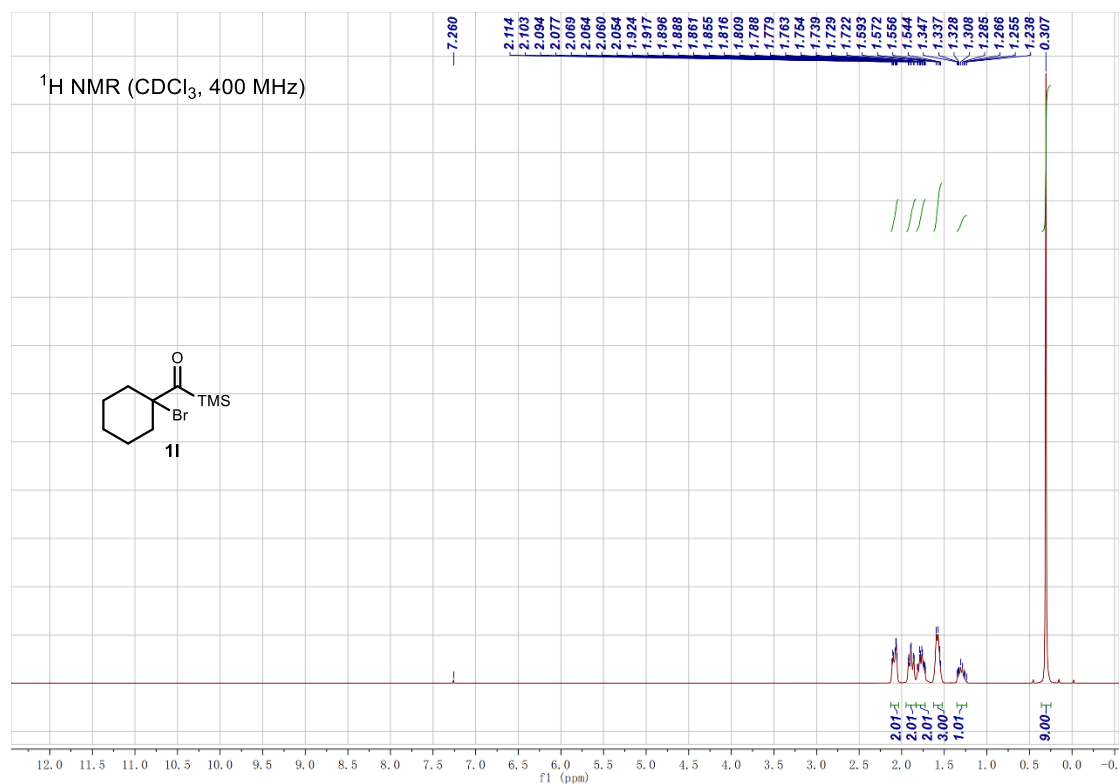
¹³C NMR of **1j** (100 MHz, CDCl₃, 298 K)



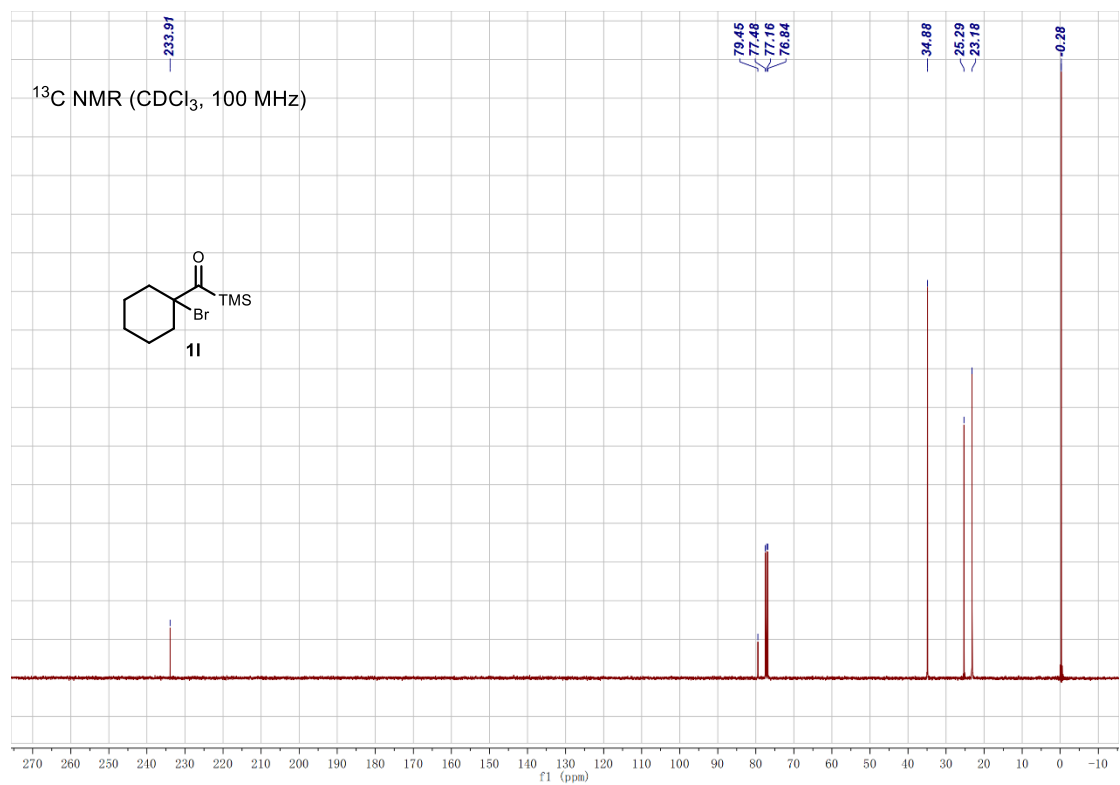
¹H NMR of **1k** (400 MHz, CDCl₃, 298 K)



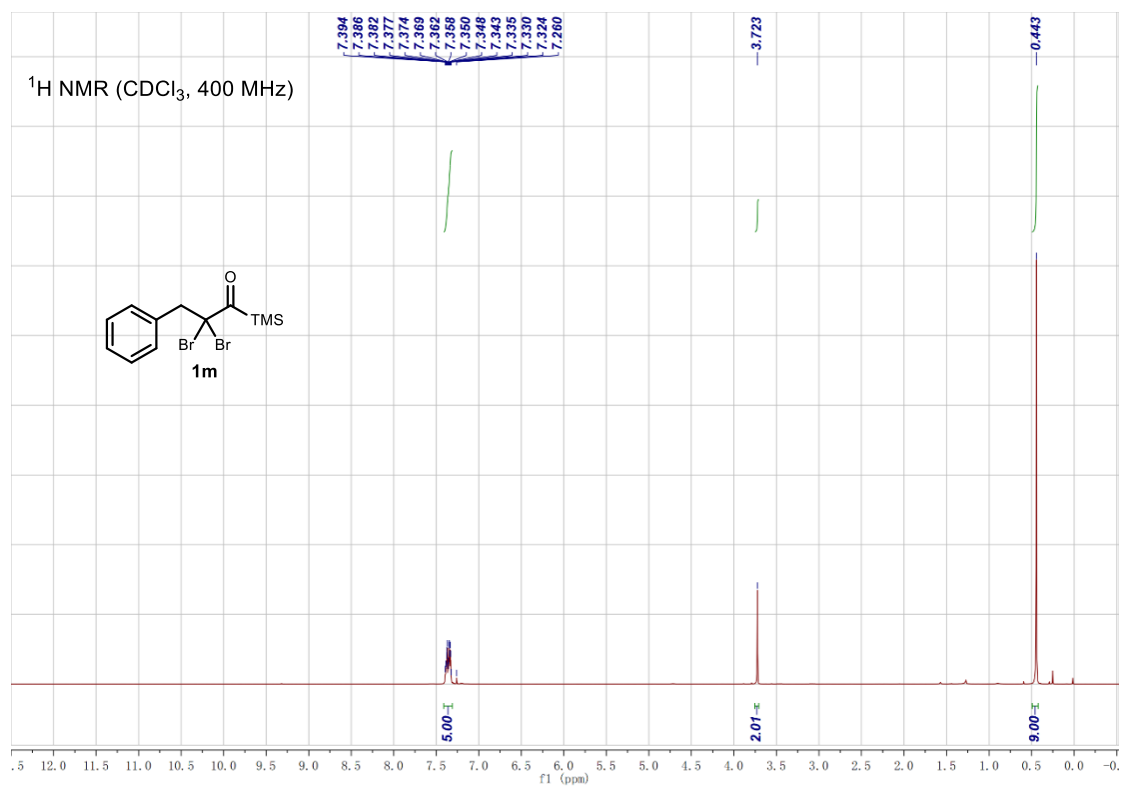
¹³C NMR of **1k** (100 MHz, CDCl₃, 298 K)



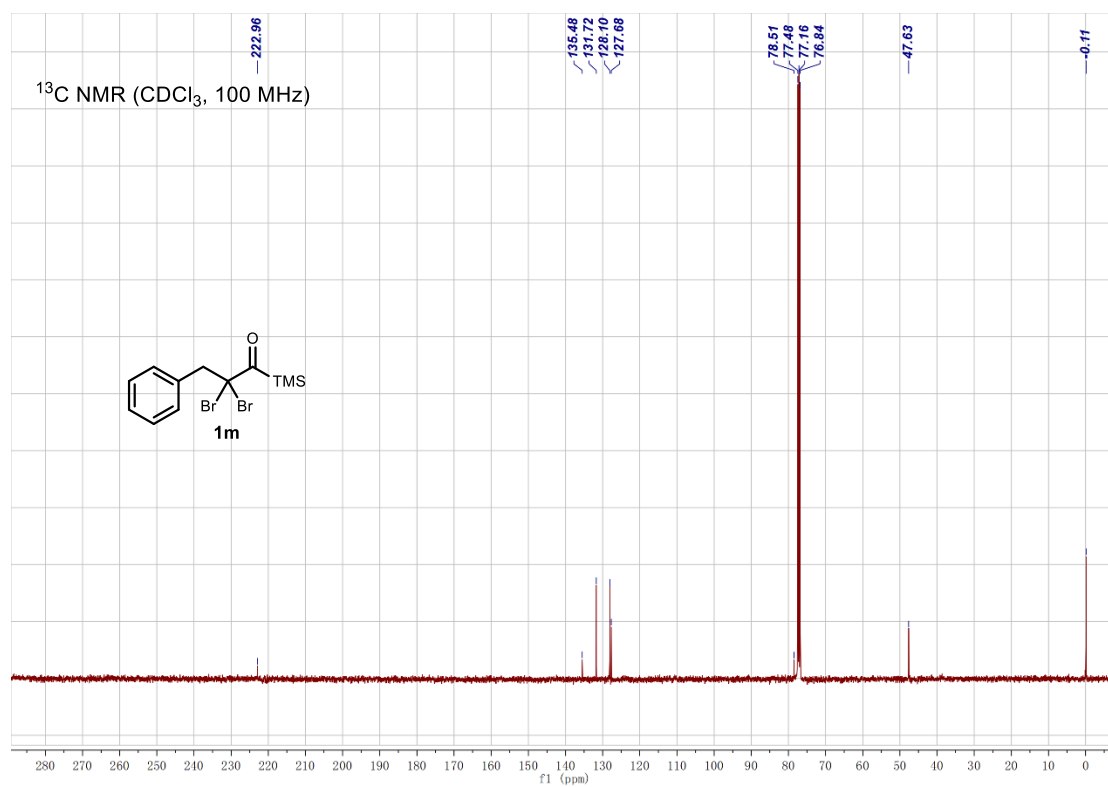
¹H NMR of **11** (400 MHz, CDCl₃, 298 K)



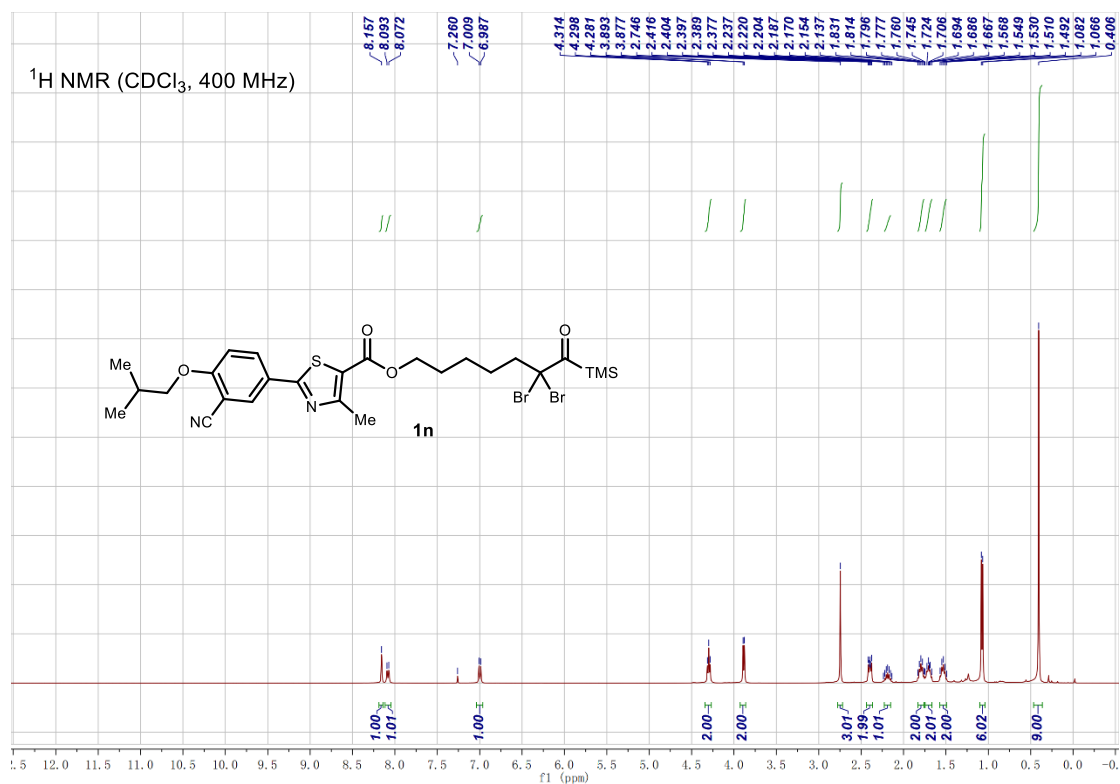
¹³C NMR of **11** (100 MHz, CDCl₃, 298 K)



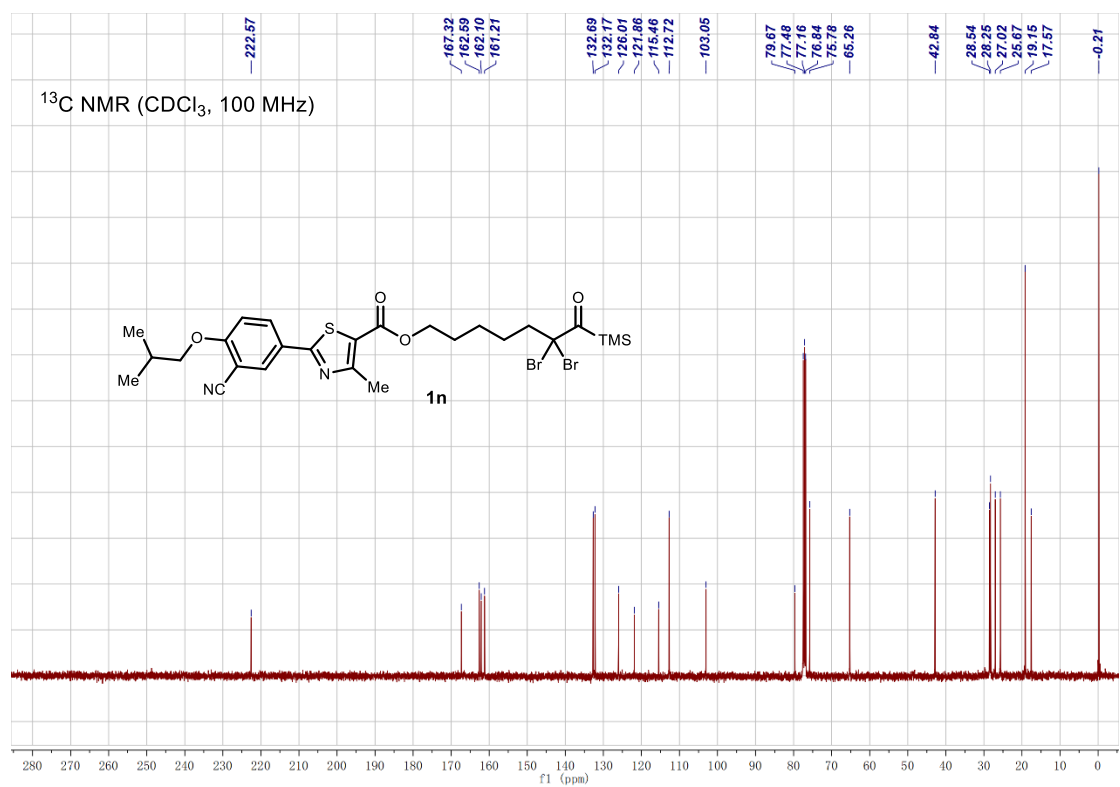
¹H NMR of **1m** (400 MHz, CDCl₃, 298 K)



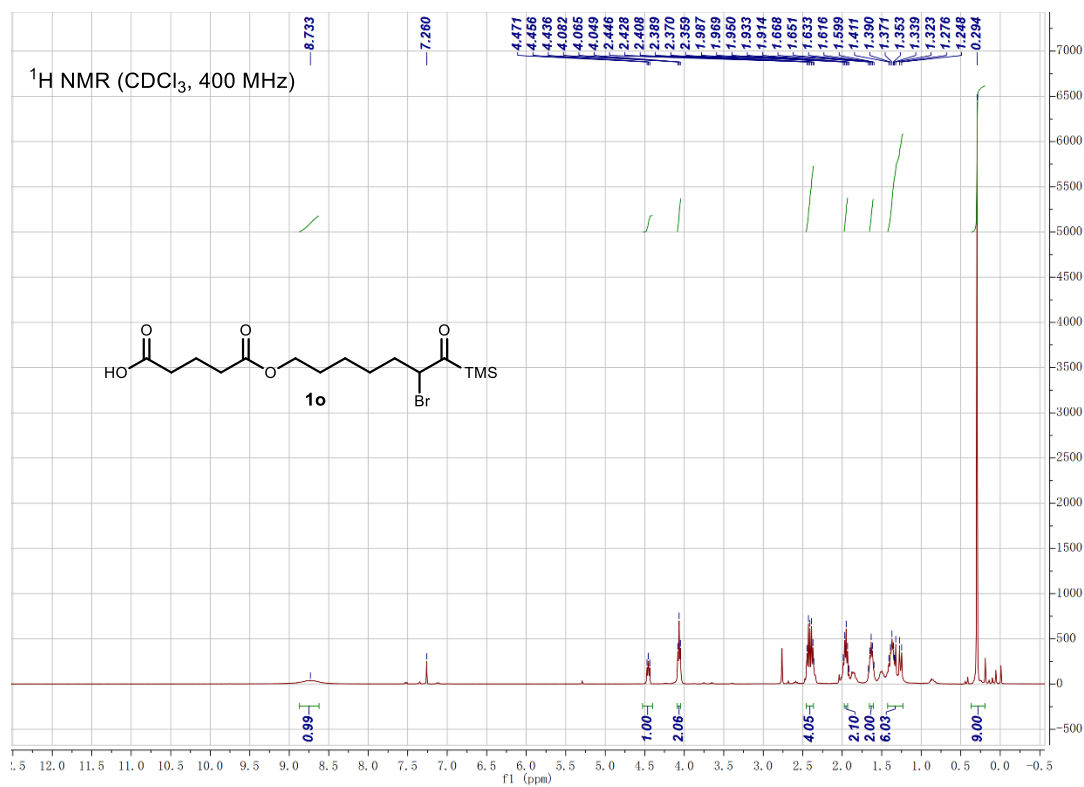
¹³C NMR of **1m** (100 MHz, CDCl₃, 298 K)



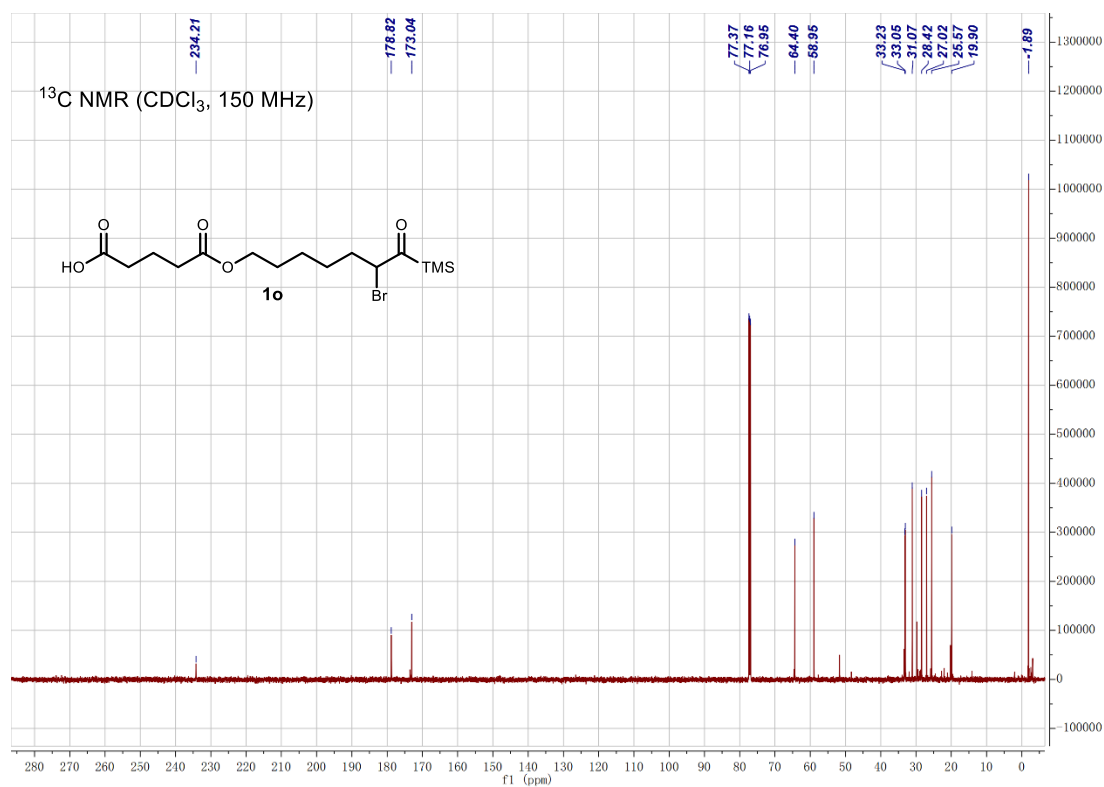
¹H NMR of **1n** (400 MHz, CDCl₃, 298 K)



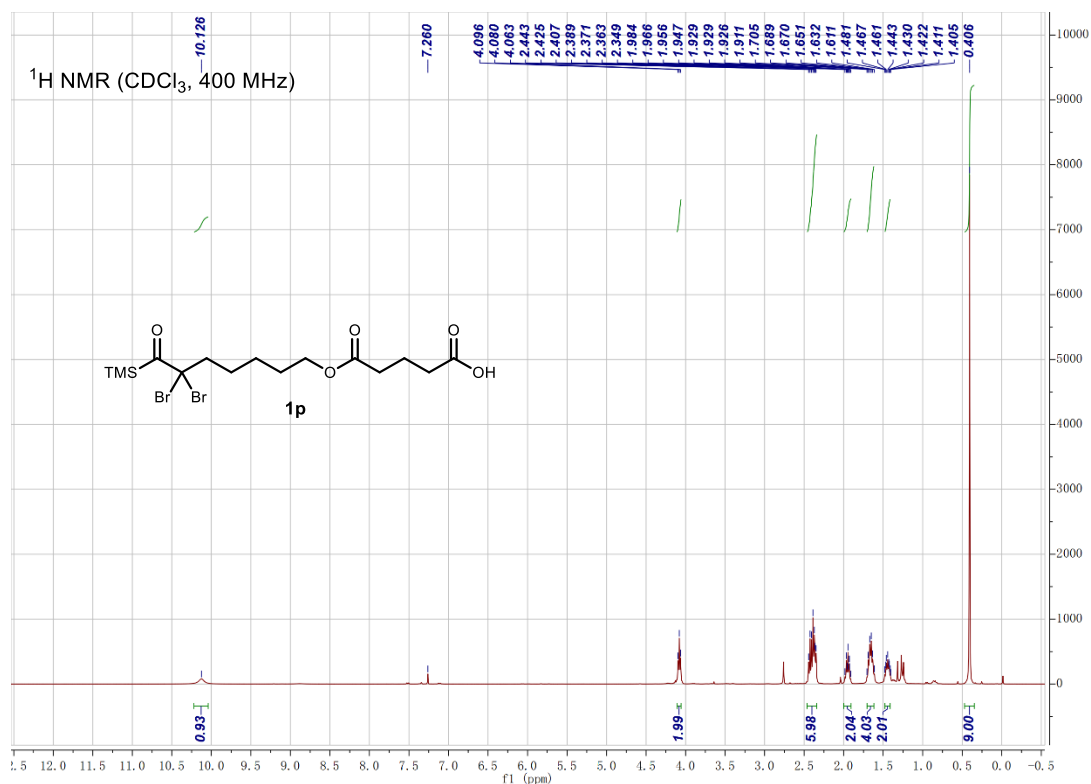
¹³C NMR of **1n** (100 MHz, CDCl₃, 298 K)



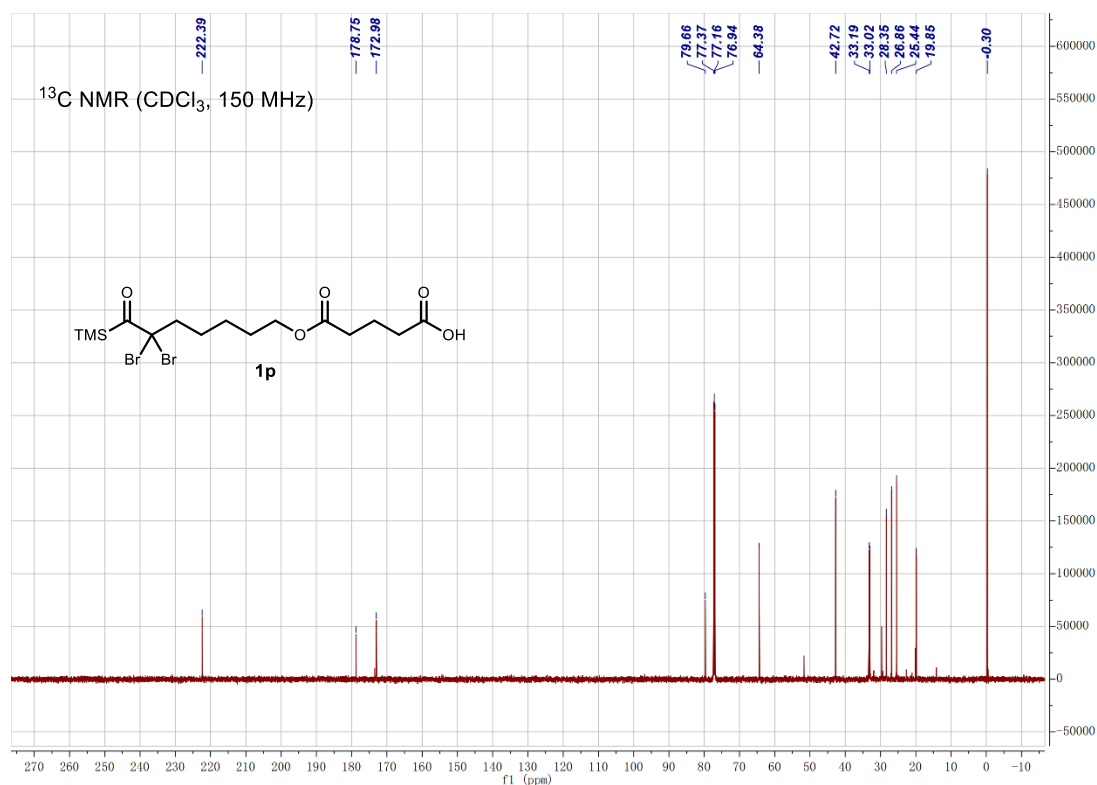
¹H NMR of **1o** (400 MHz, CDCl₃, 298 K)



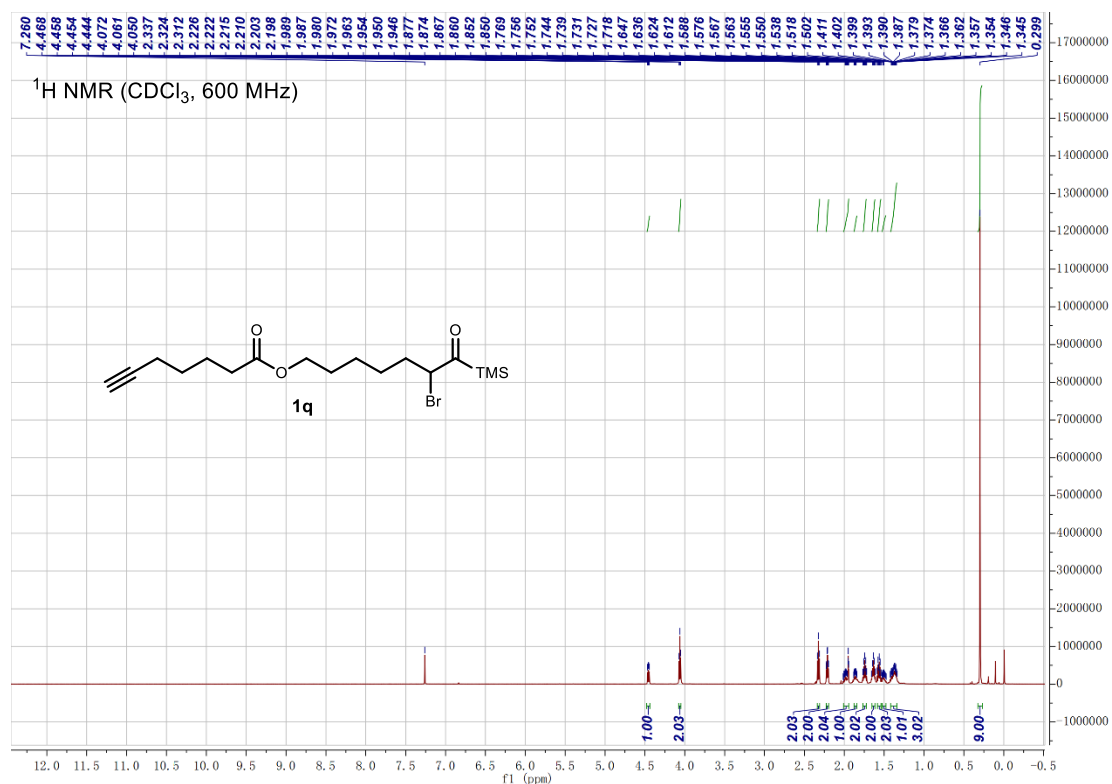
¹³C NMR of **1o** (150 MHz, CDCl₃, 298 K)



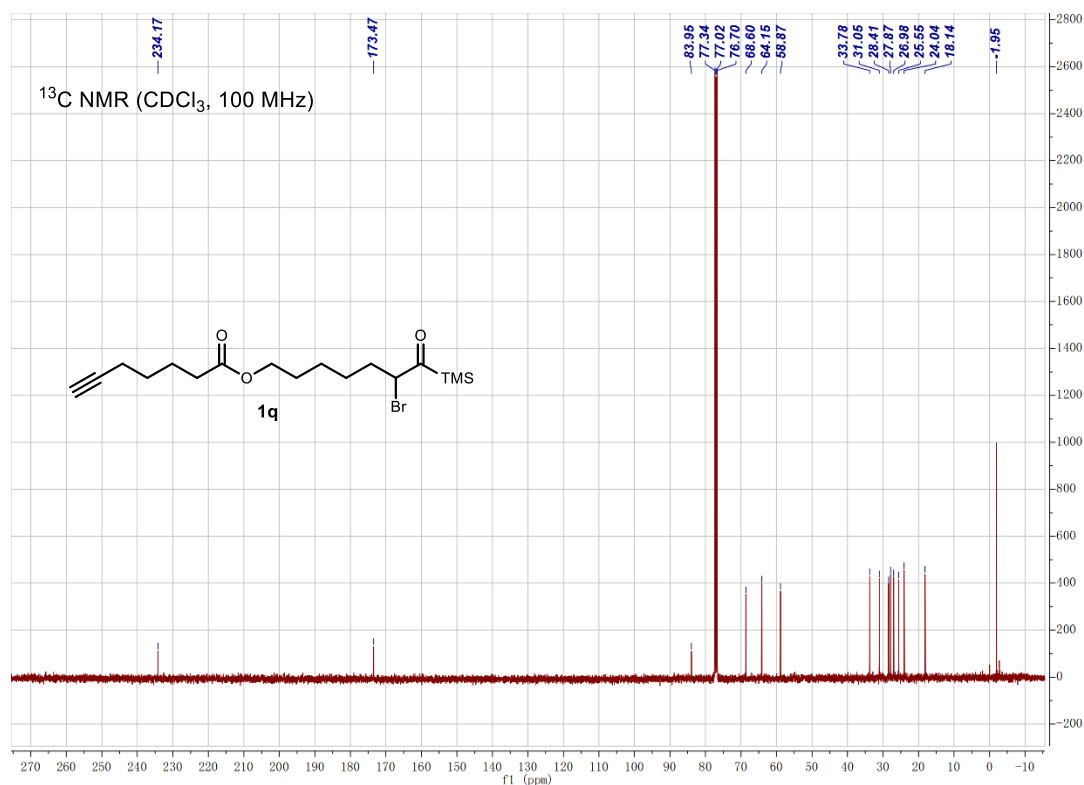
¹H NMR of **1p** (400 MHz, CDCl₃, 298 K)



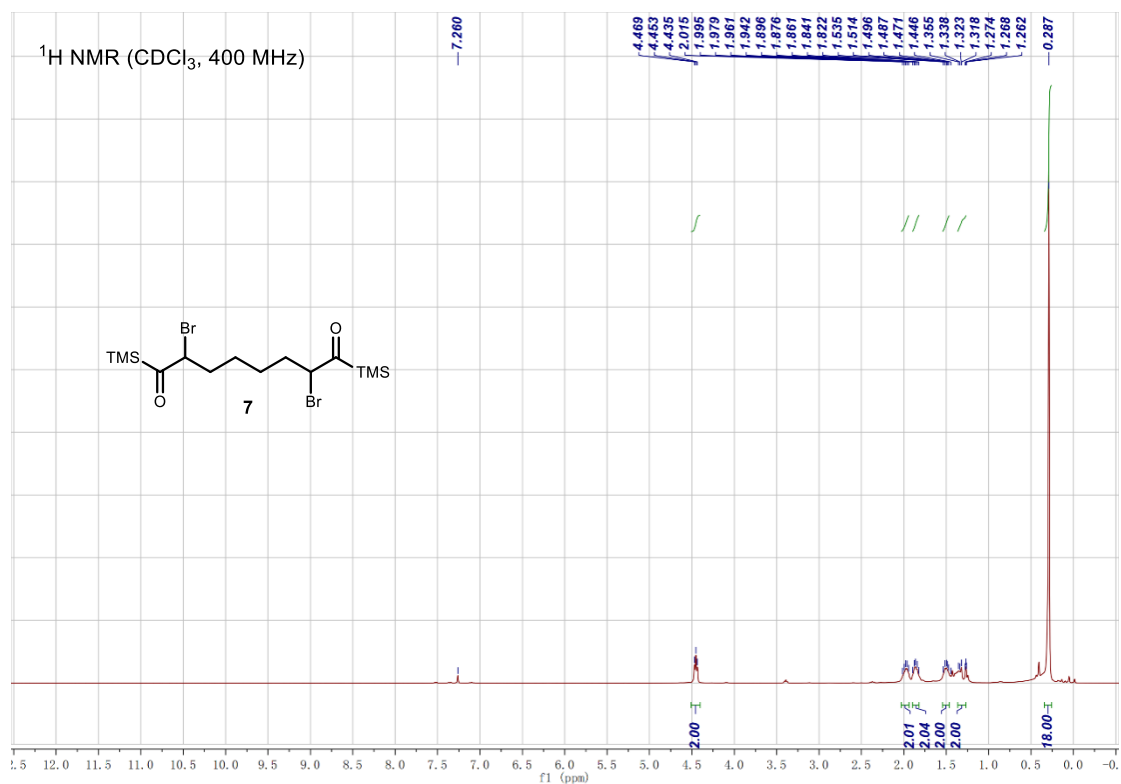
¹³C NMR of **1p** (150 MHz, CDCl₃, 298 K)



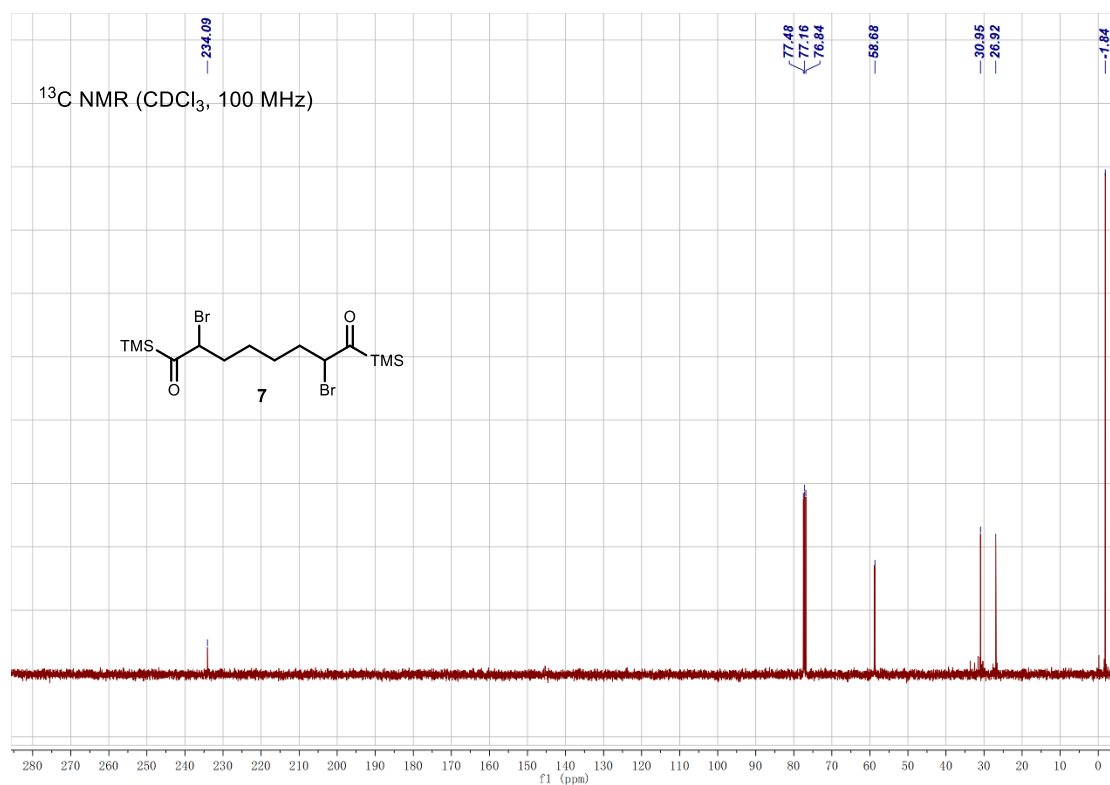
¹H NMR of **1q** (600 MHz, CDCl₃, 298 K)



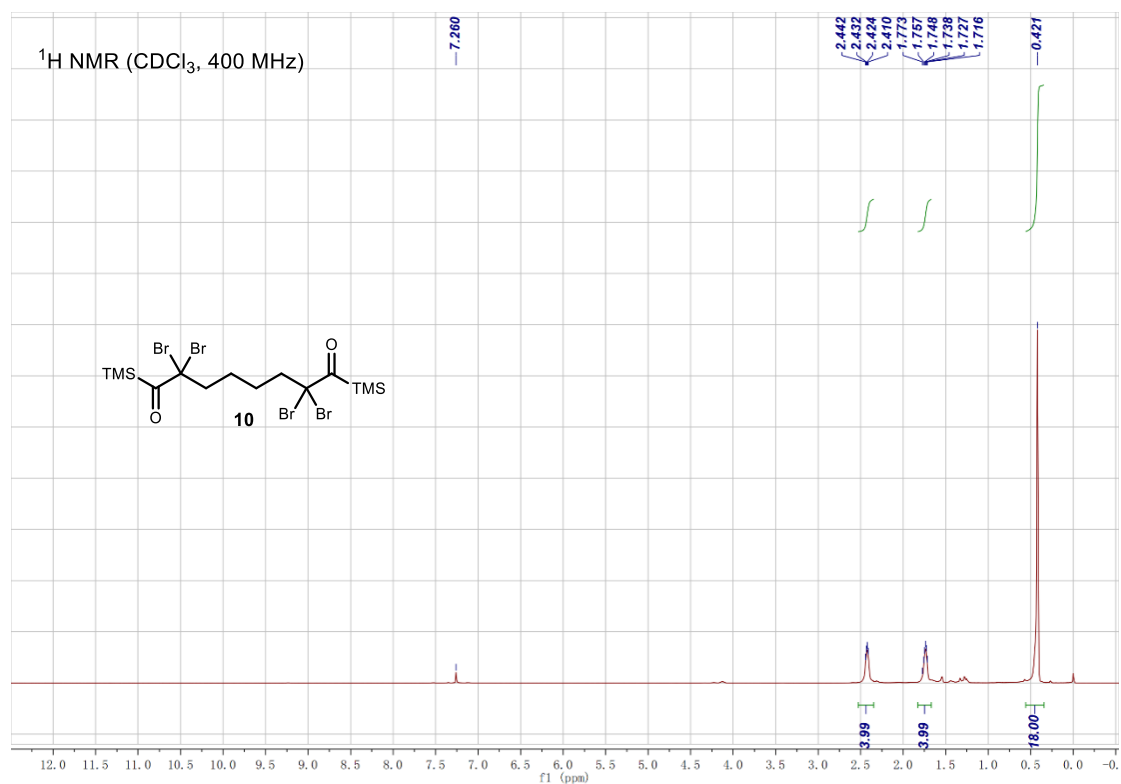
¹³C NMR of **1q** (100 MHz, CDCl₃, 298 K)



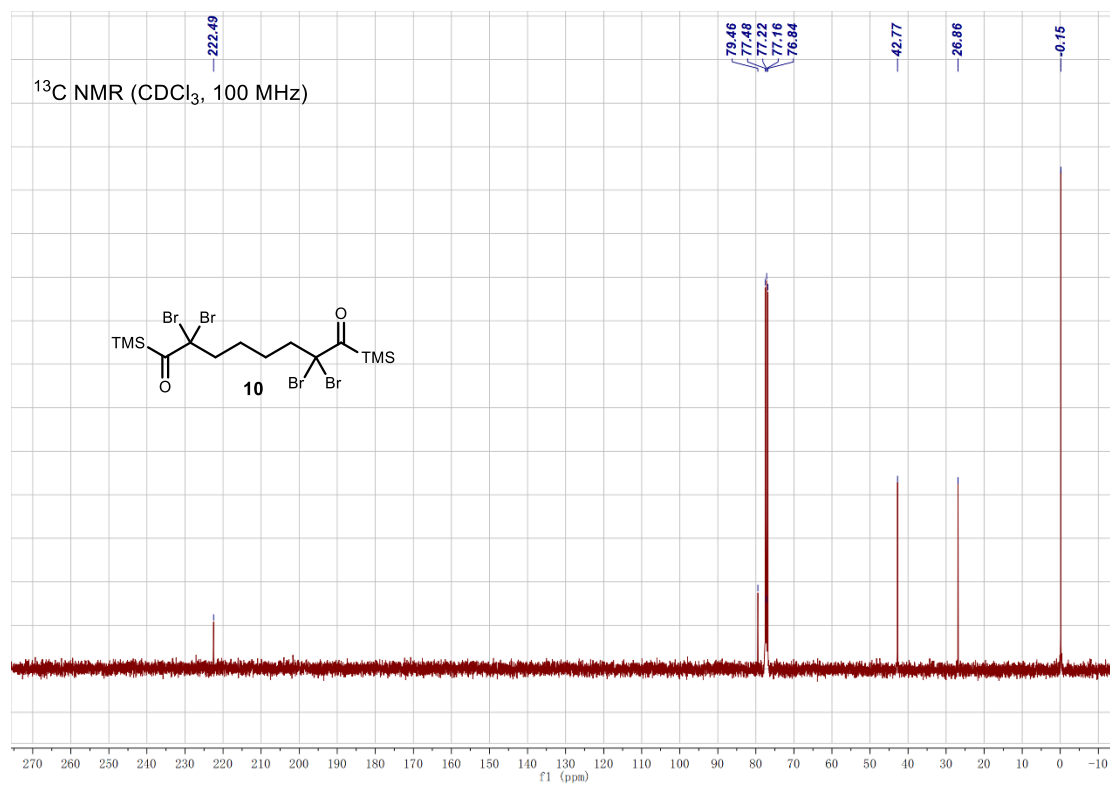
¹H NMR of 7 (400 MHz, CDCl₃, 298 K)



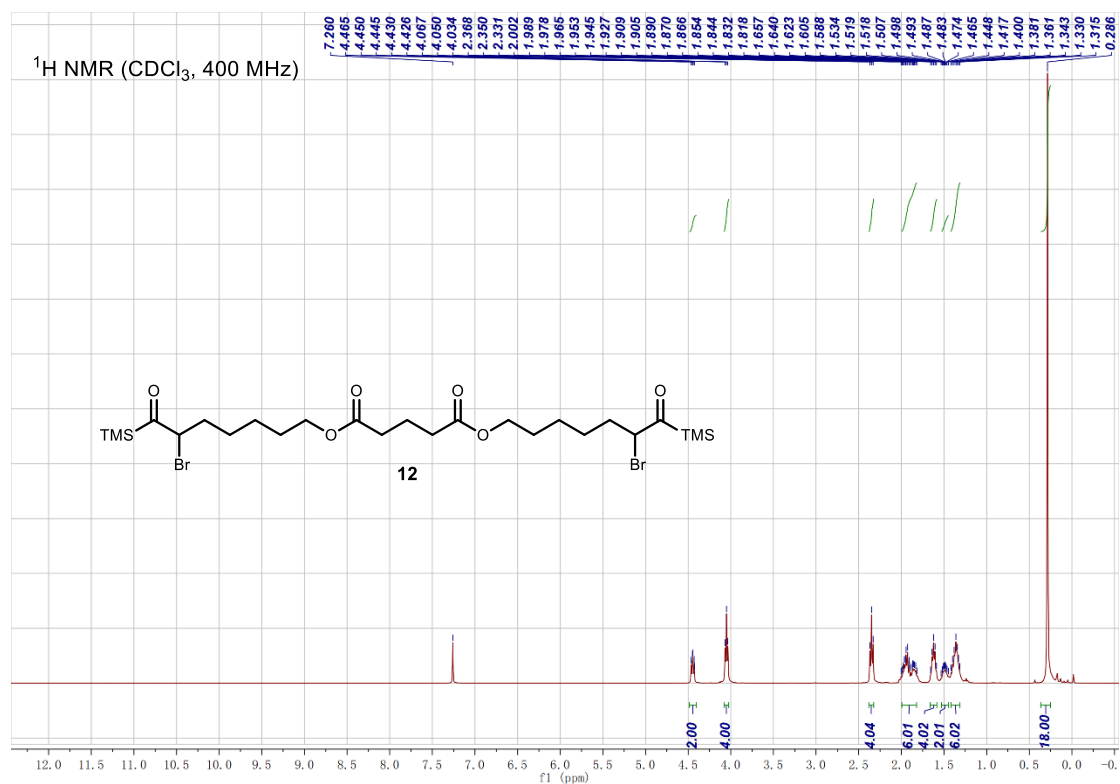
¹³C NMR of 7 (100 MHz, CDCl₃, 298 K)



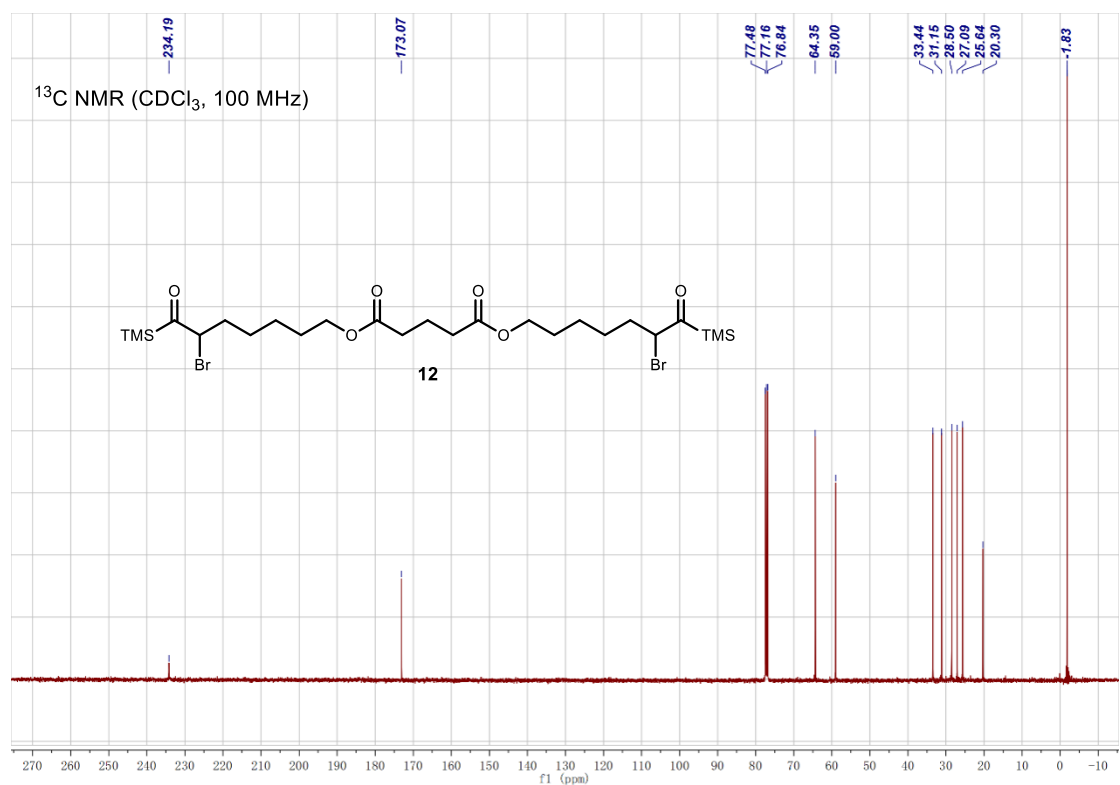
¹H NMR of **10** (400 MHz, CDCl₃, 298 K)



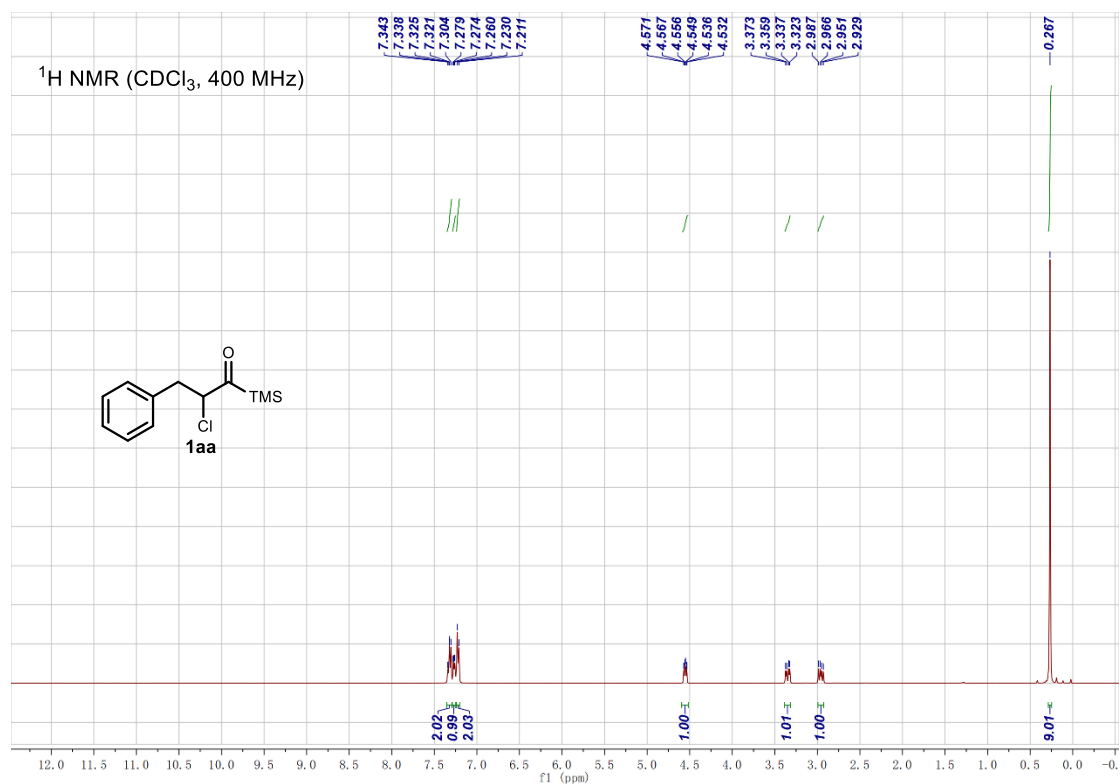
¹³C NMR of **10** (100 MHz, CDCl₃, 298 K)



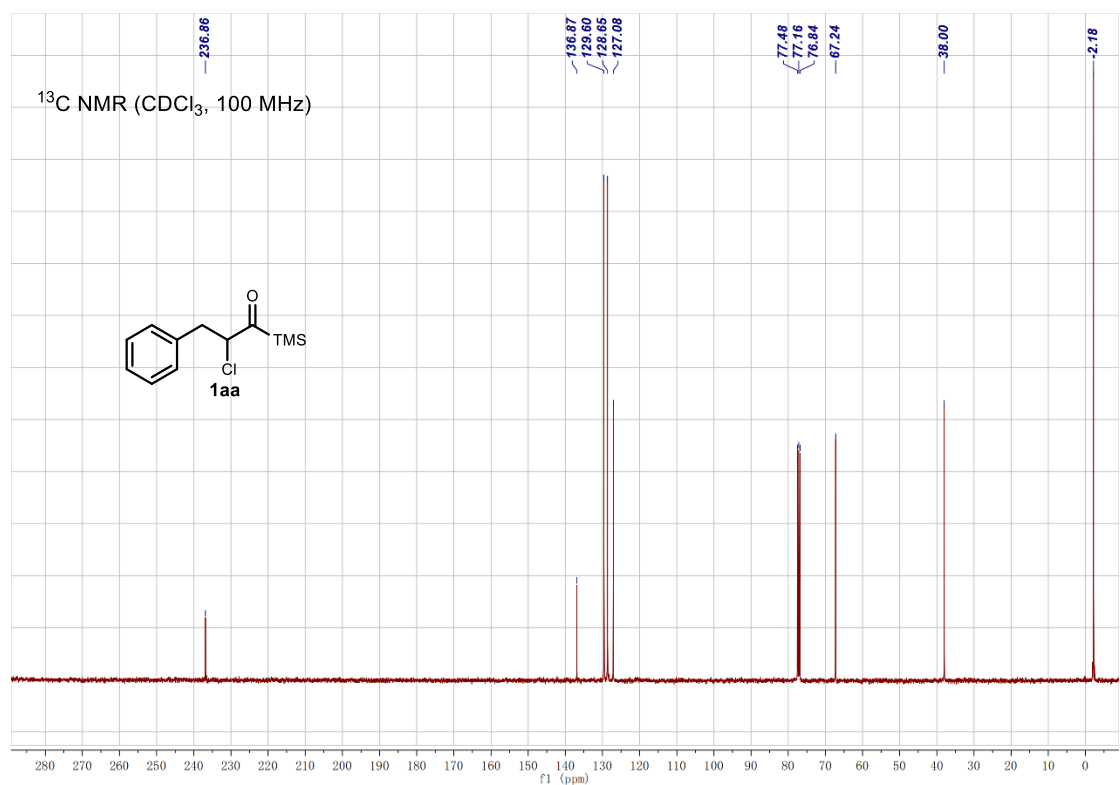
¹H NMR of **12** (400 MHz, CDCl₃, 298 K)



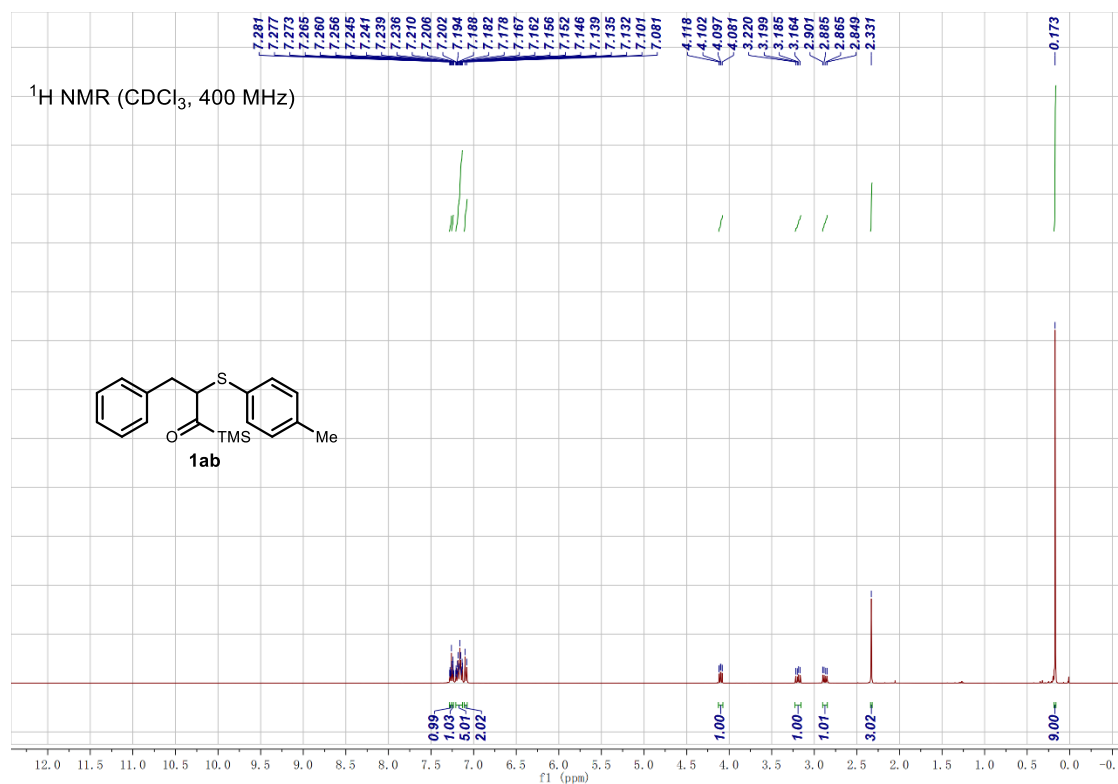
¹³C NMR of **12** (100 MHz, CDCl₃, 298 K)



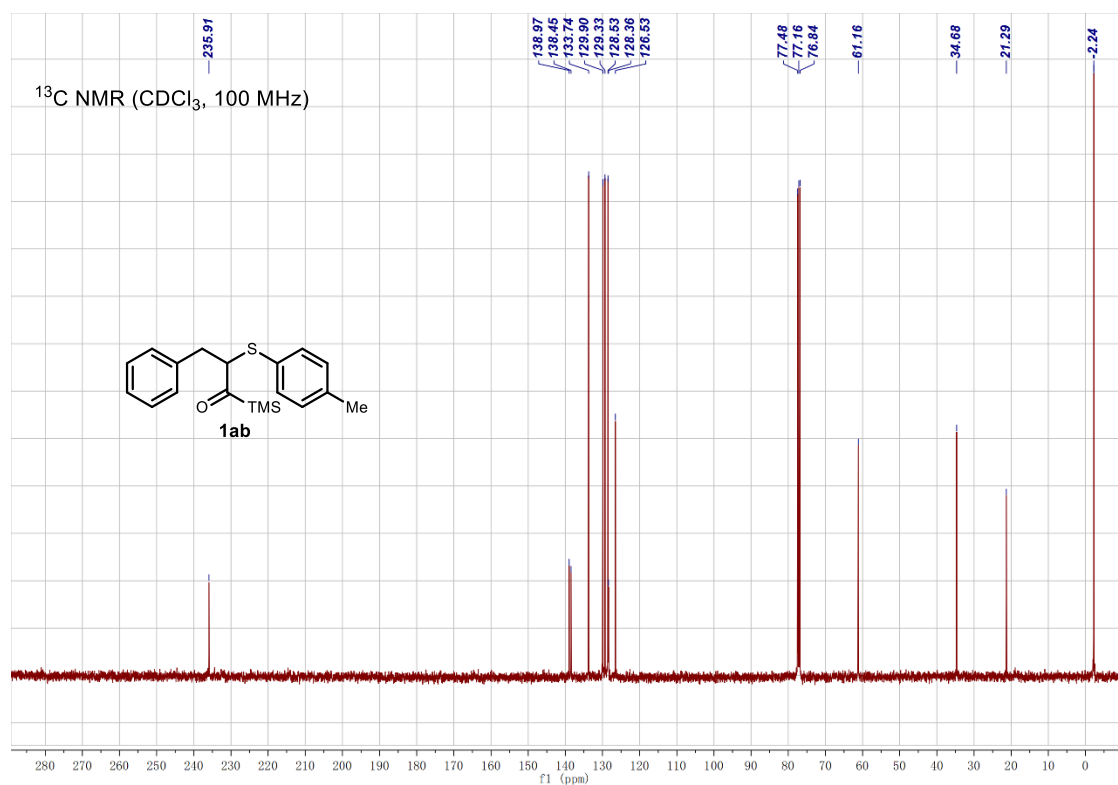
¹H NMR of **1aa** (400 MHz, CDCl₃, 298 K)



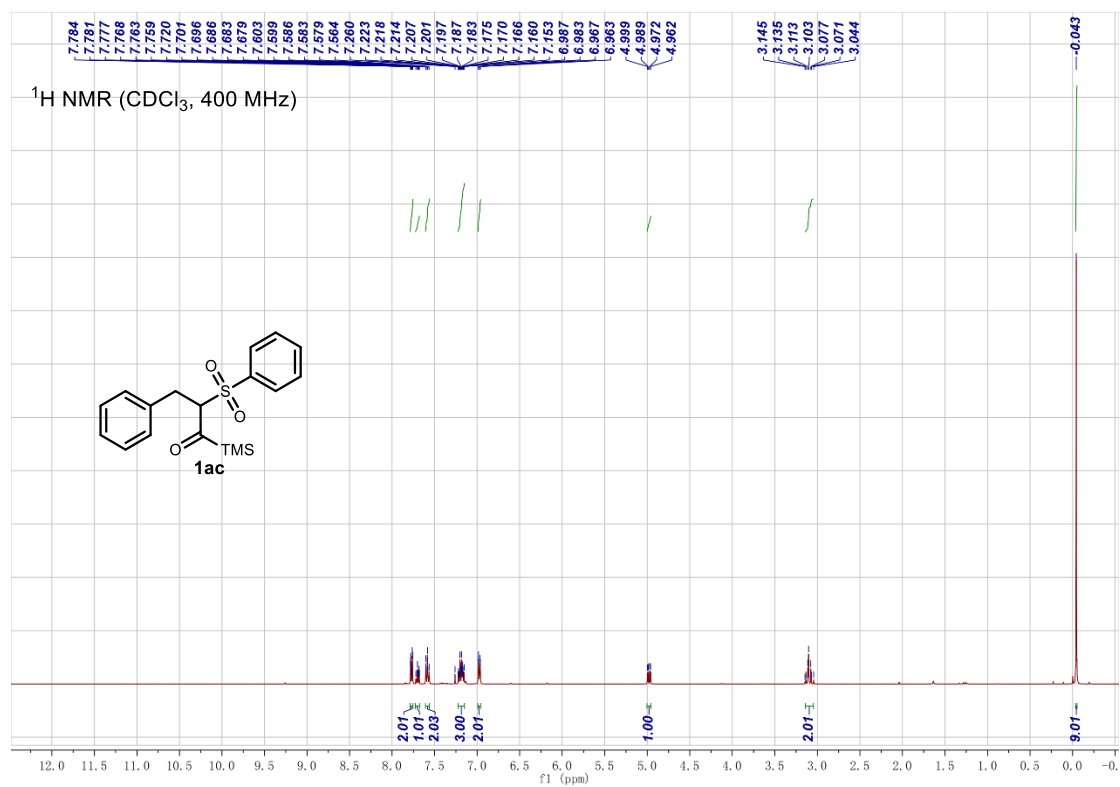
¹³C NMR of **1aa** (100 MHz, CDCl₃, 298 K)



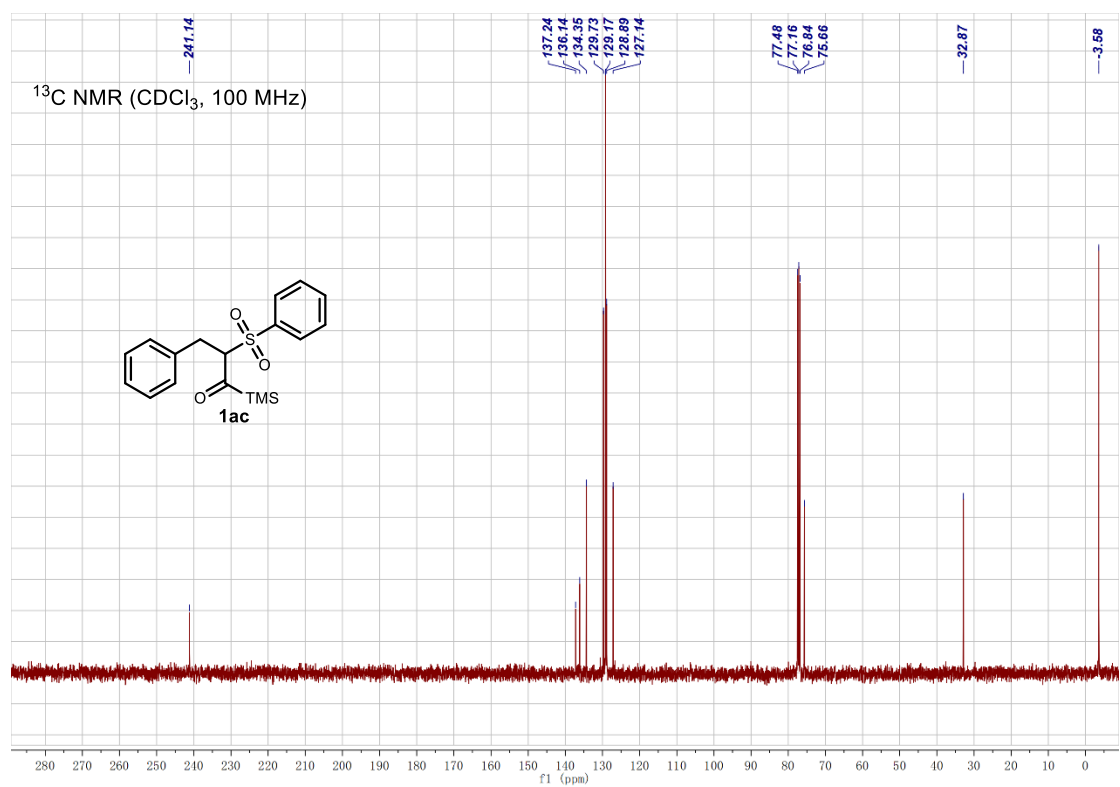
¹H NMR of **1ab** (400 MHz, CDCl₃, 298 K)



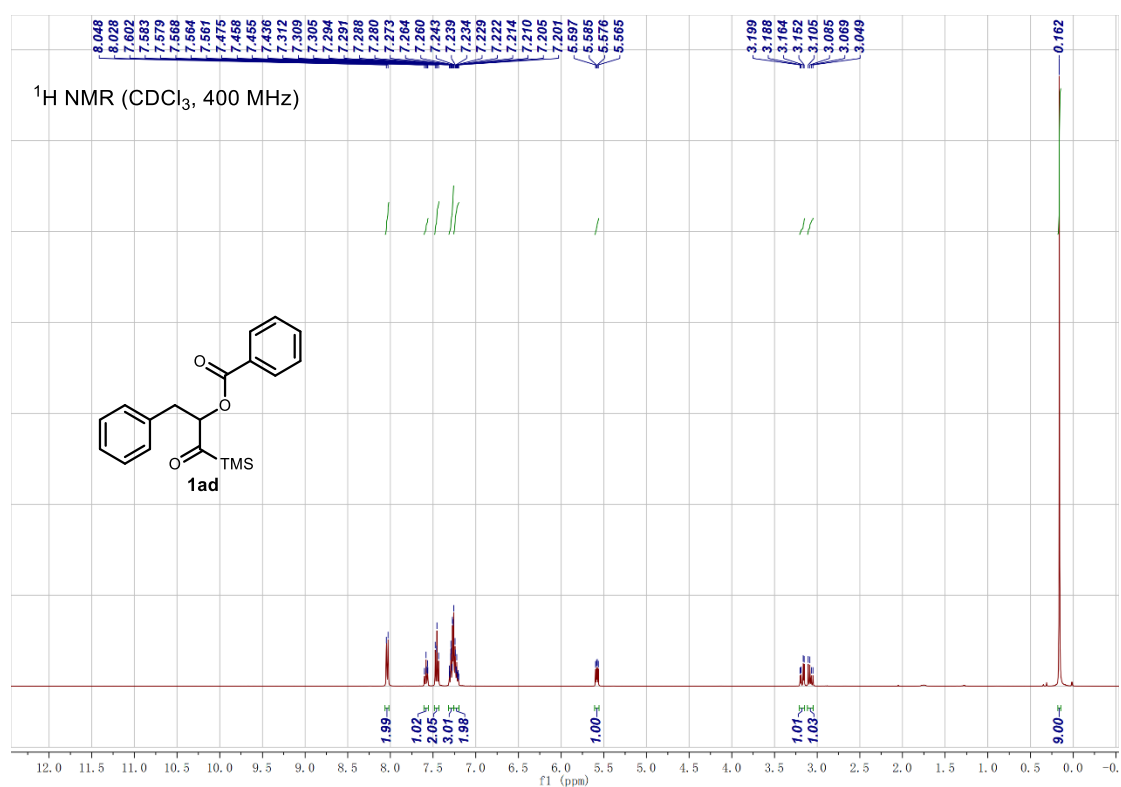
¹³C NMR of **1ab** (100 MHz, CDCl₃, 298 K)



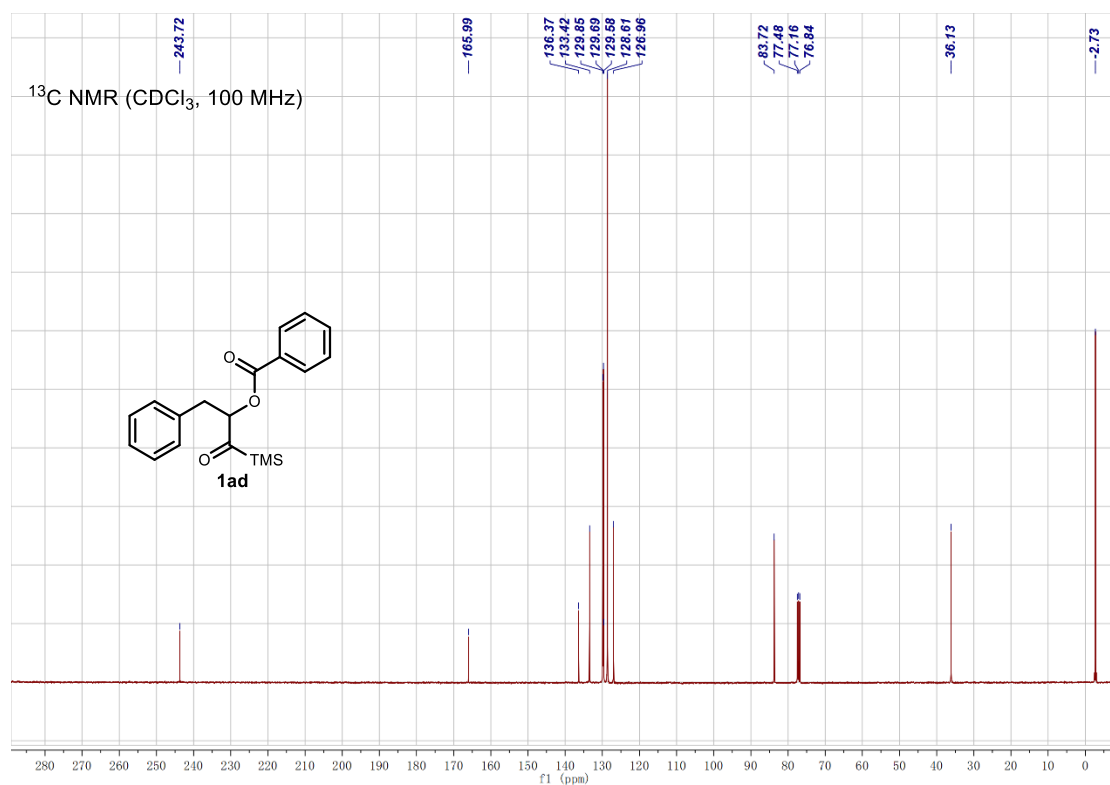
¹H NMR of **1ac** (400 MHz, CDCl₃, 298 K)



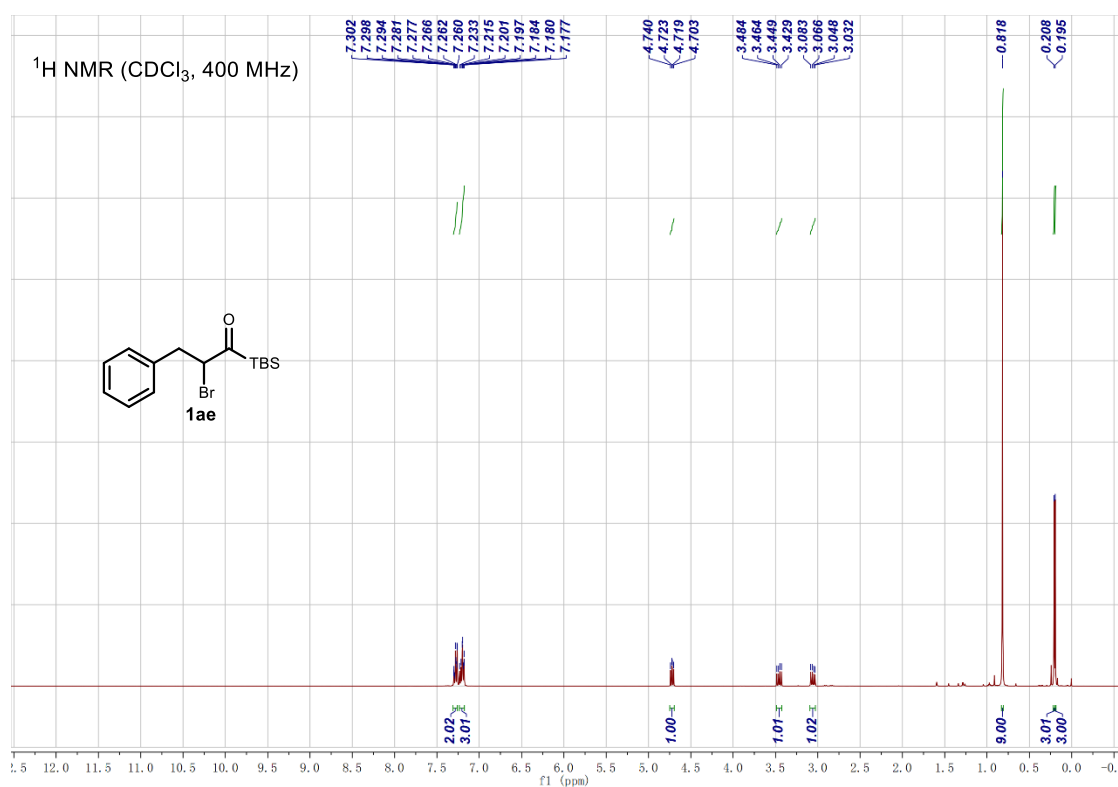
¹³C NMR of **1ac** (100 MHz, CDCl₃, 298 K)



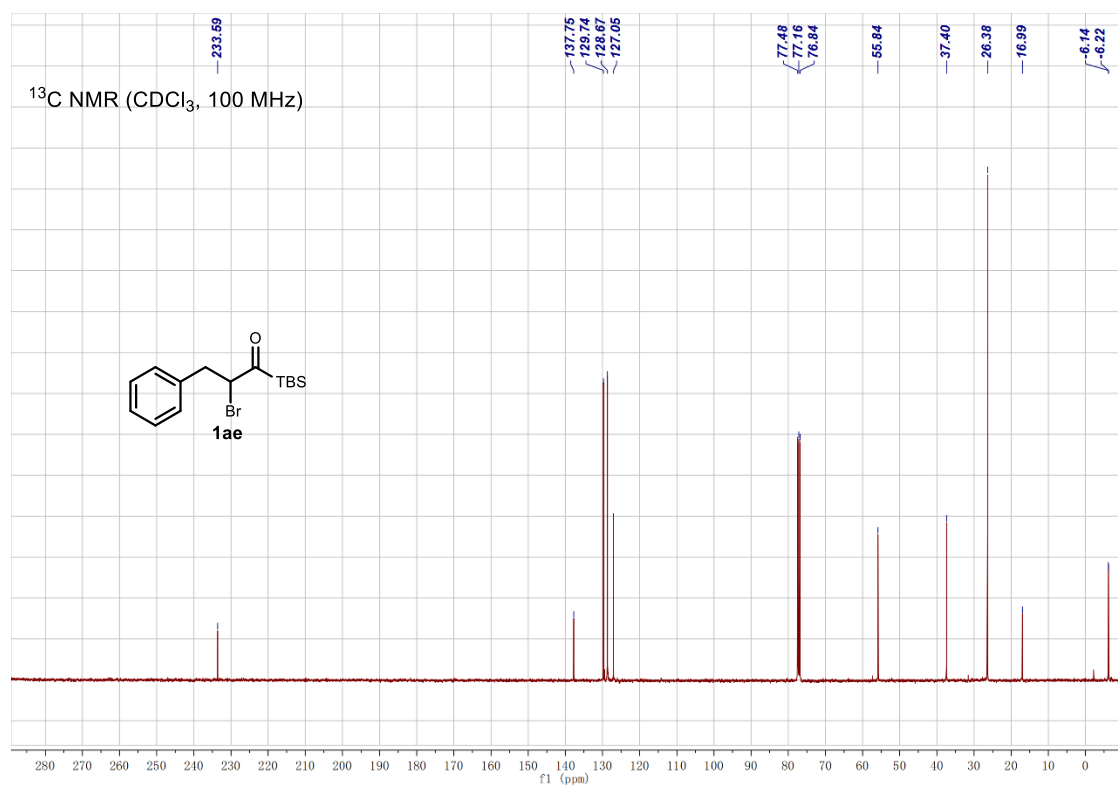
¹H NMR of **1ad** (400 MHz, CDCl₃, 298 K)



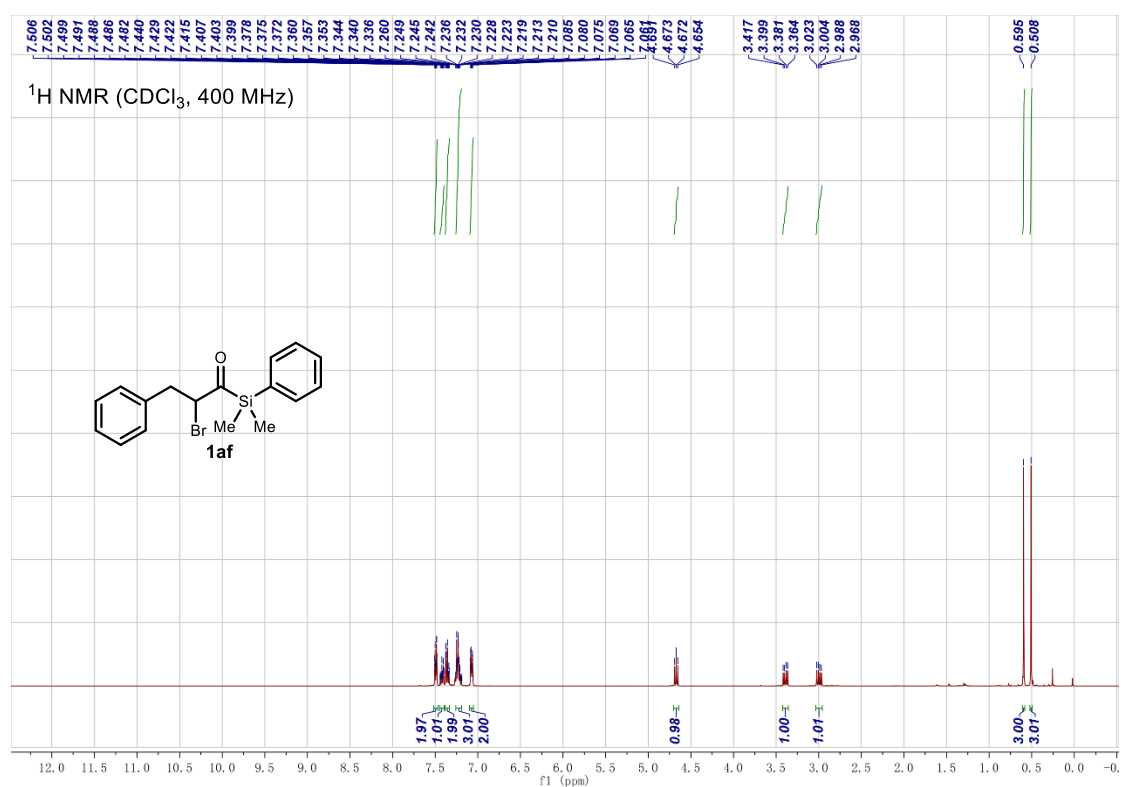
¹³C NMR of **1ad** (100 MHz, CDCl₃, 298 K)



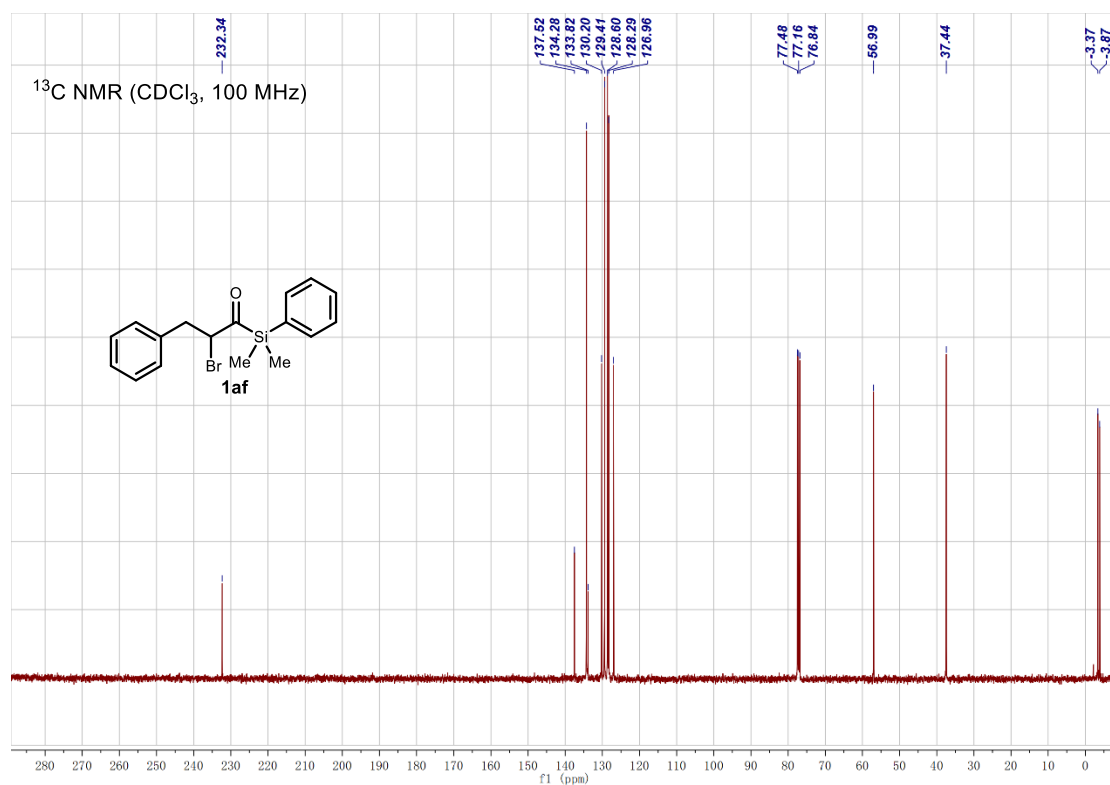
¹H NMR of **1ae** (400 MHz, CDCl₃, 298 K)



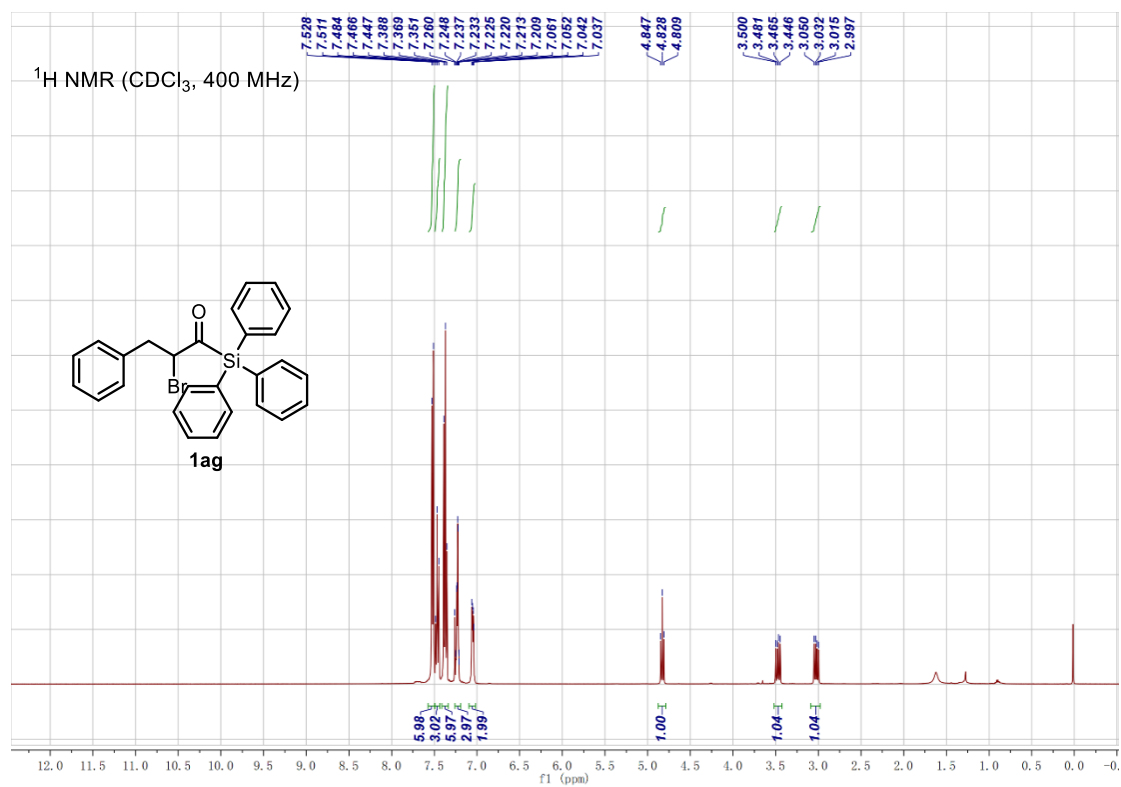
¹³C NMR of **1ae** (100 MHz, CDCl₃, 298 K)



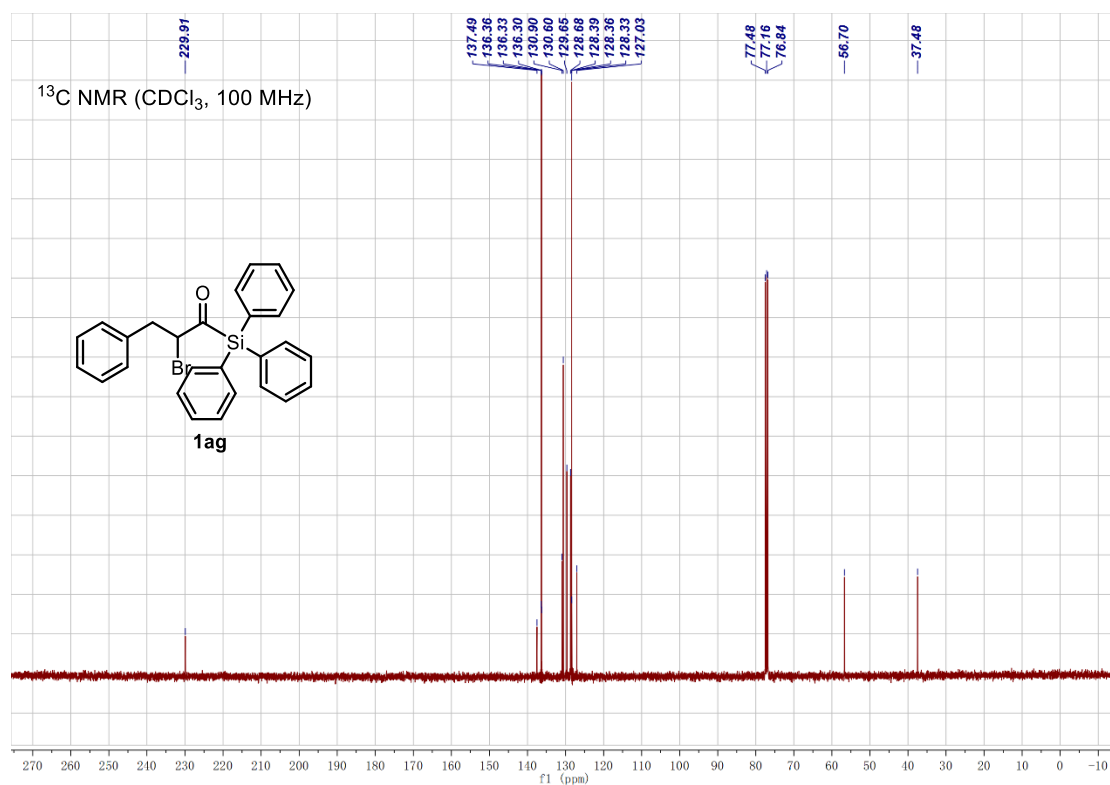
¹H NMR of **1af** (400 MHz, CDCl₃, 298 K)



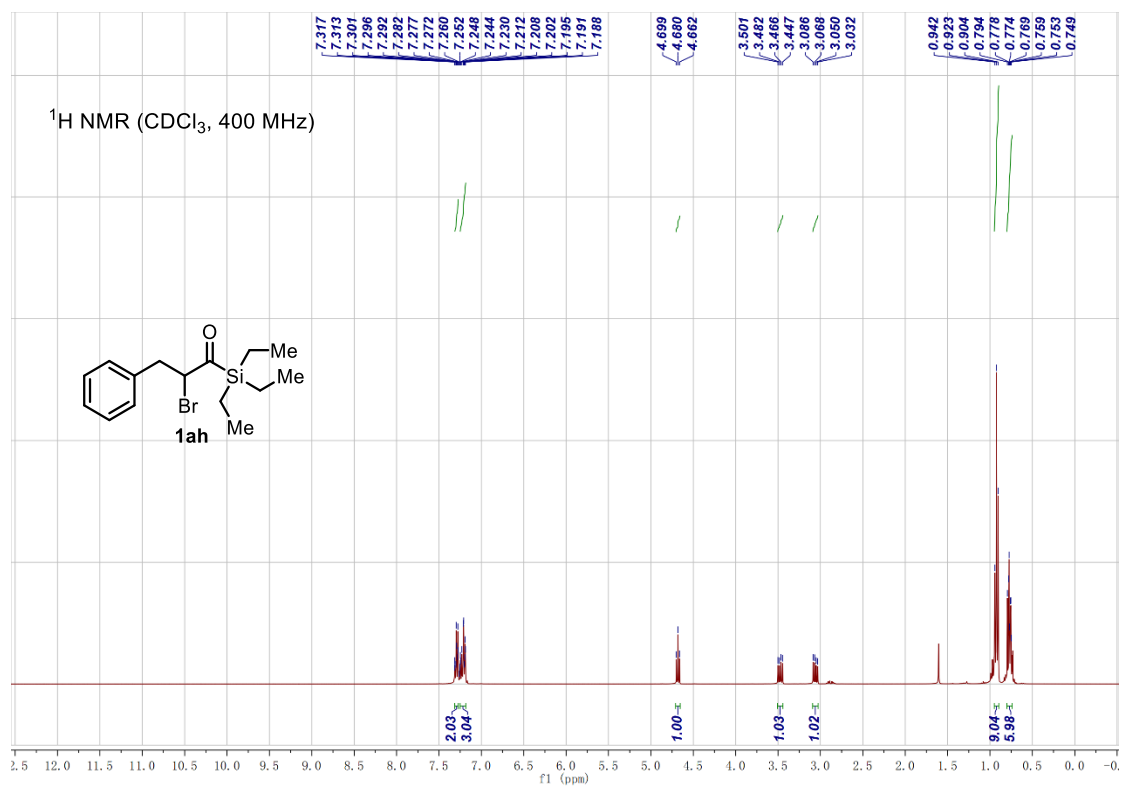
¹³C NMR of **1af** (100 MHz, CDCl₃, 298 K)



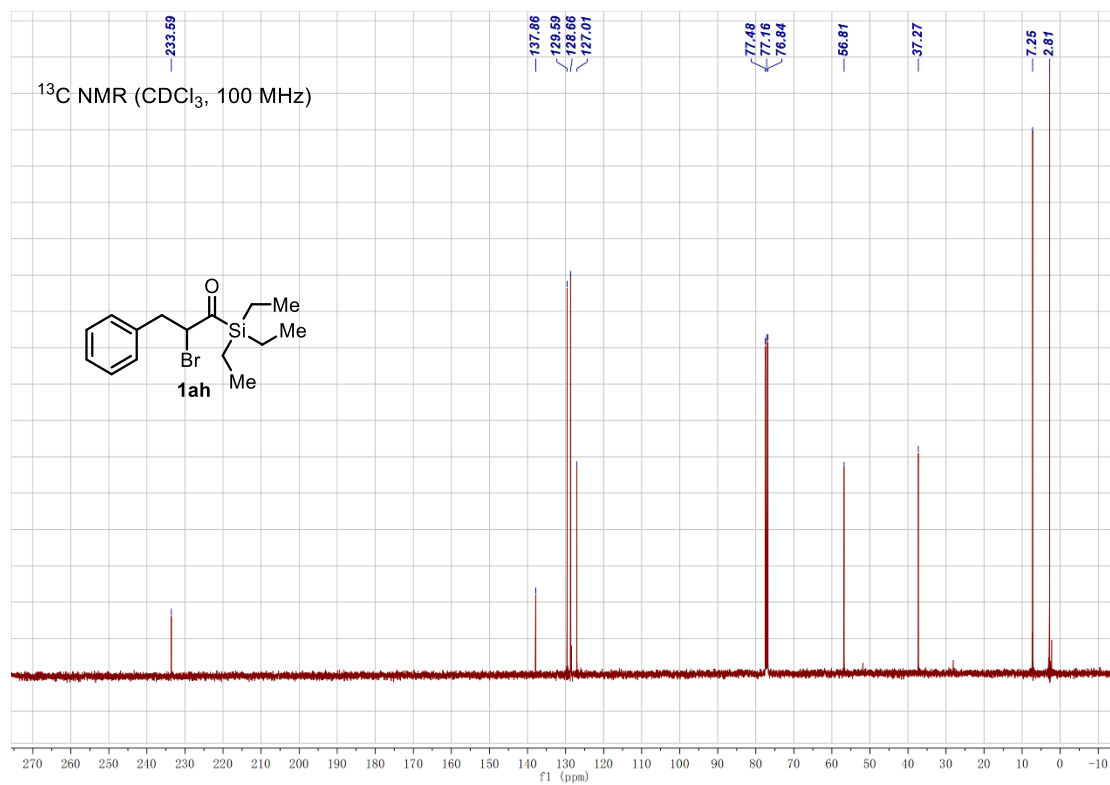
¹H NMR of **1ag** (400 MHz, CDCl₃, 298 K)



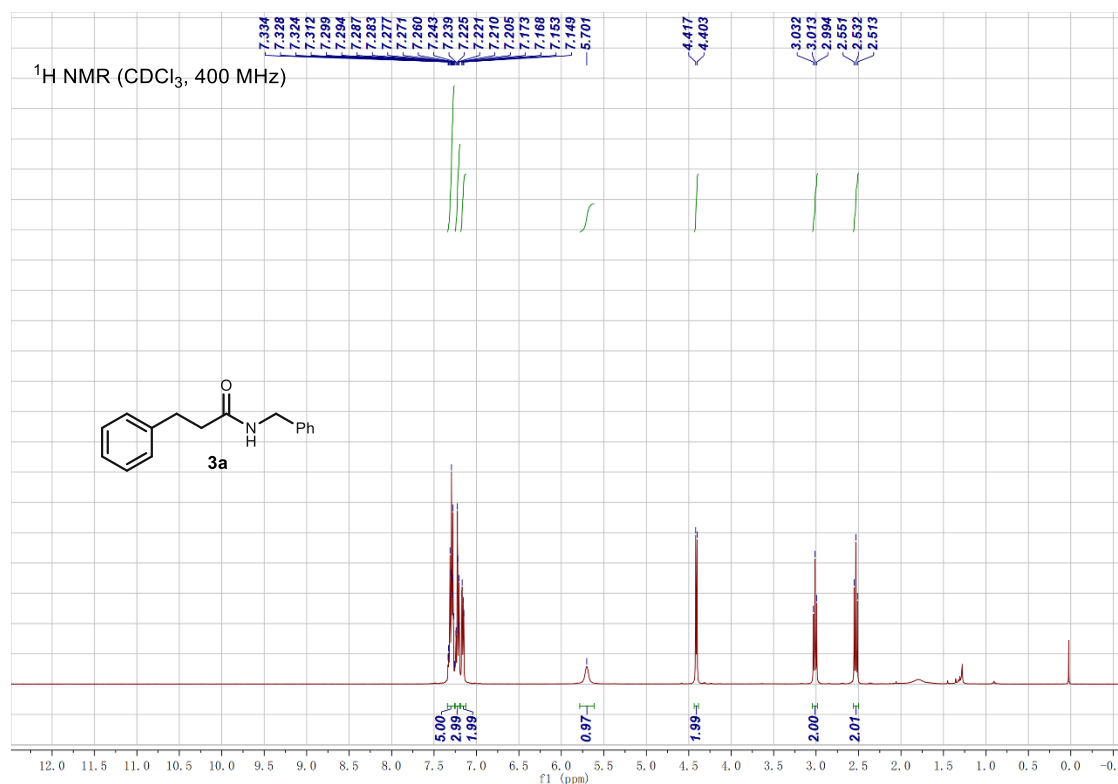
¹³C NMR of **1ag** (100 MHz, CDCl₃, 298 K)



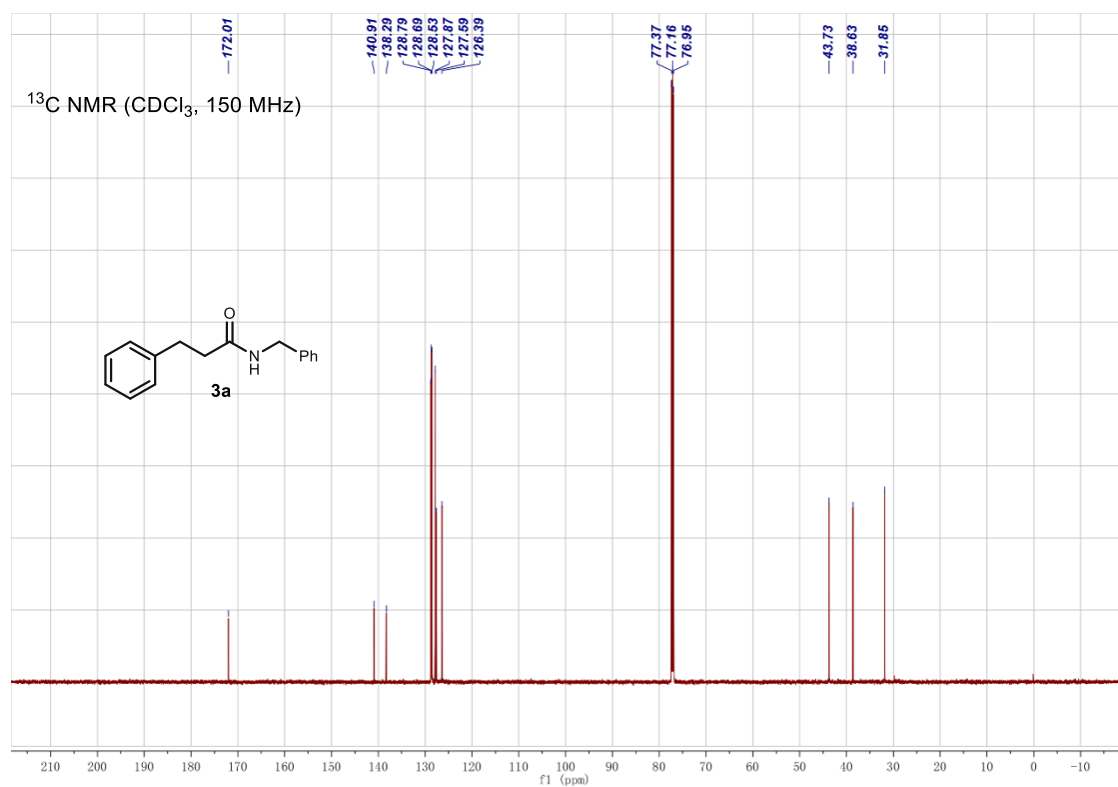
¹H NMR of **1ah** (400 MHz, CDCl₃, 298 K)



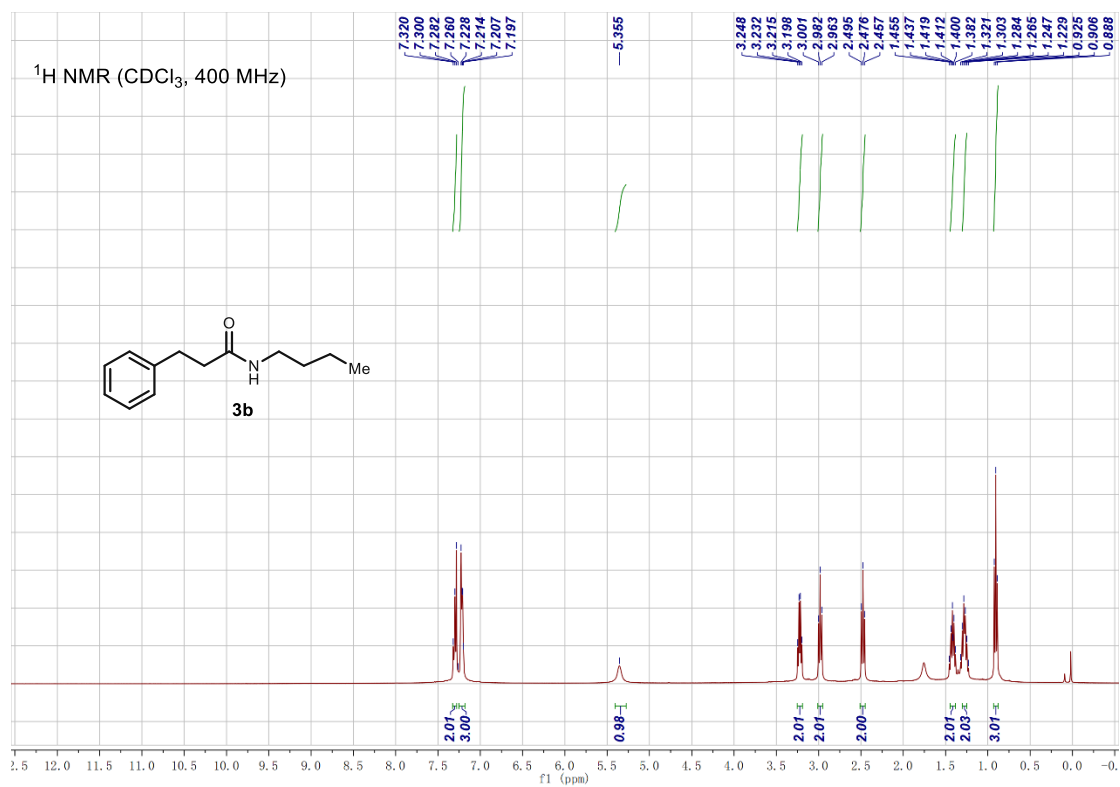
¹³C NMR of **1ah** (100 MHz, CDCl₃, 298 K)



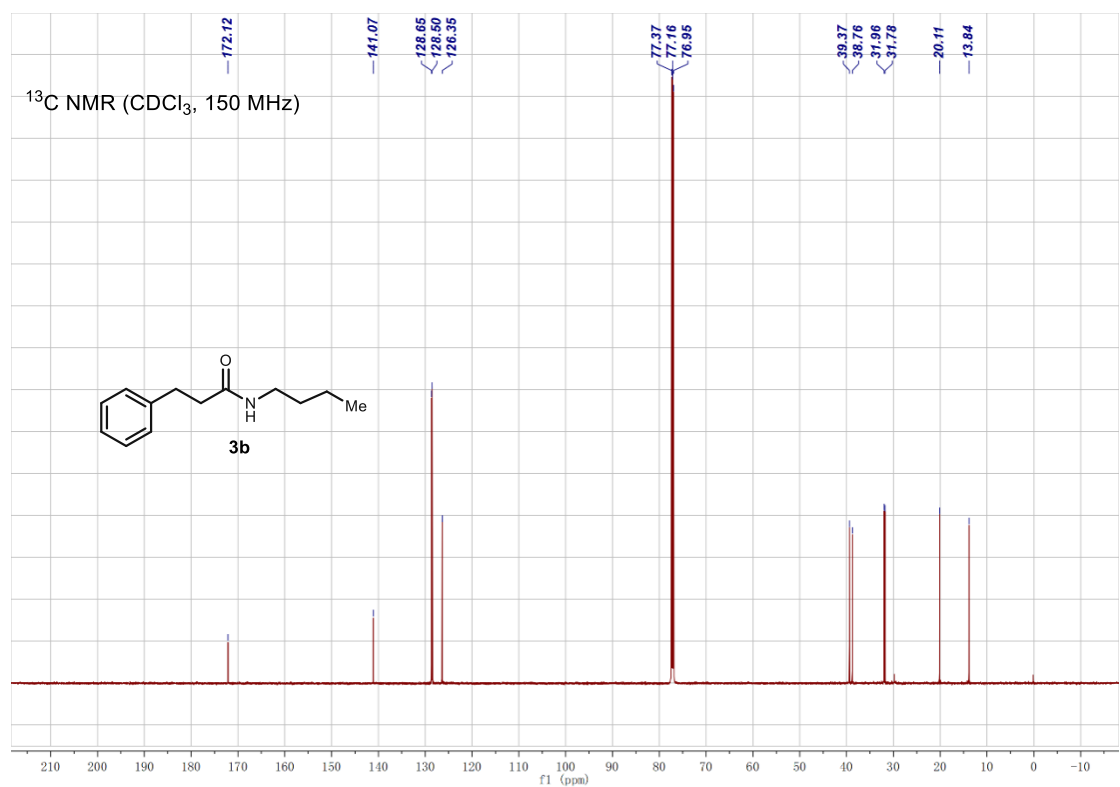
¹H NMR of **3a** (400 MHz, CDCl₃, 298 K)



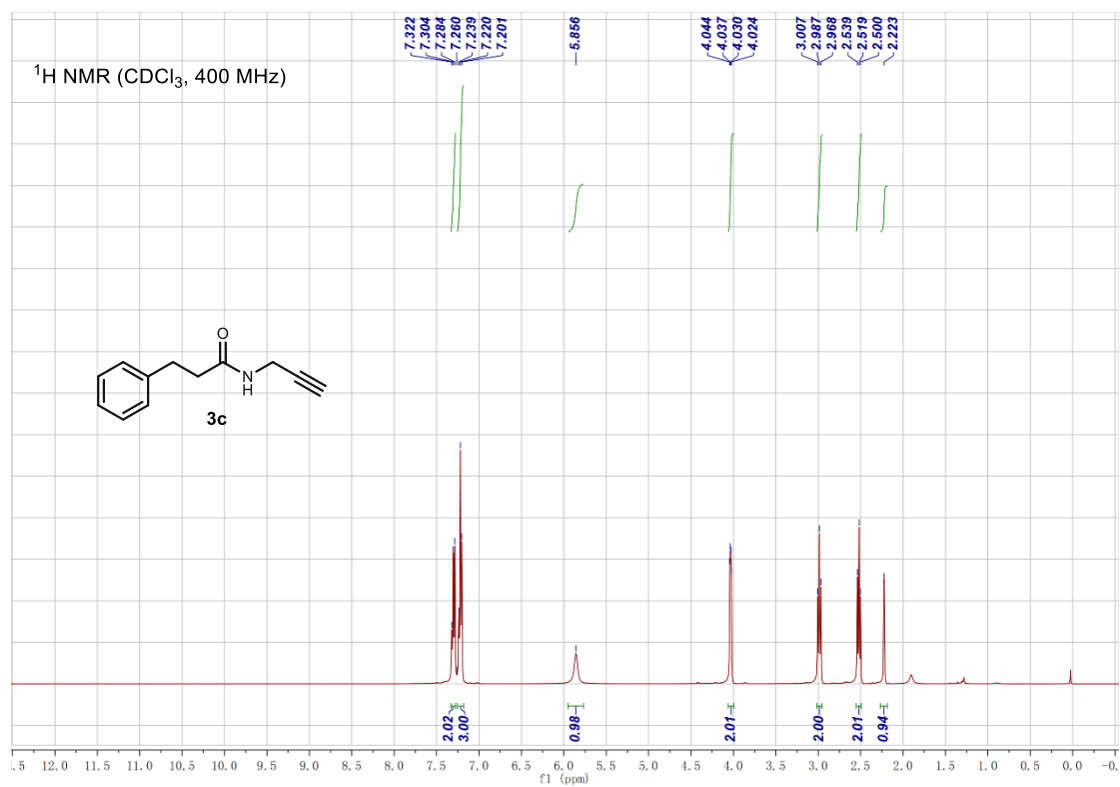
¹³C NMR of **3a** (150 MHz, CDCl₃, 298 K)



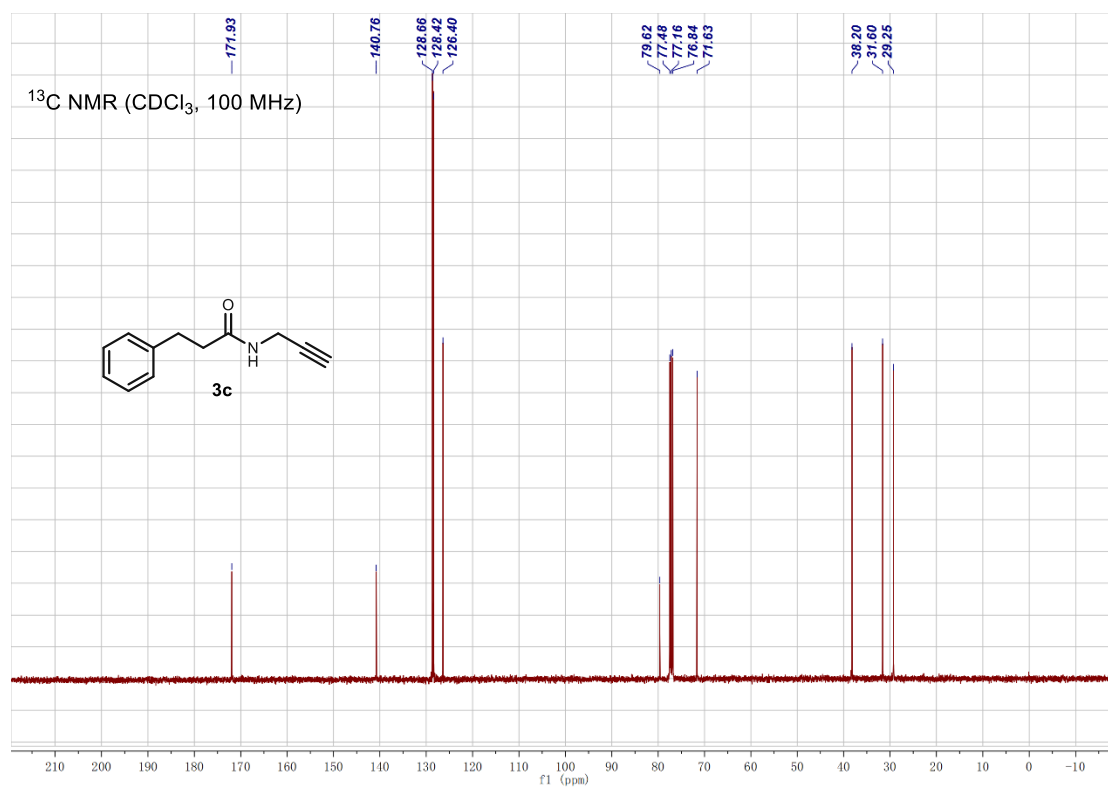
¹H NMR of **3b** (400 MHz, CDCl₃, 298 K)



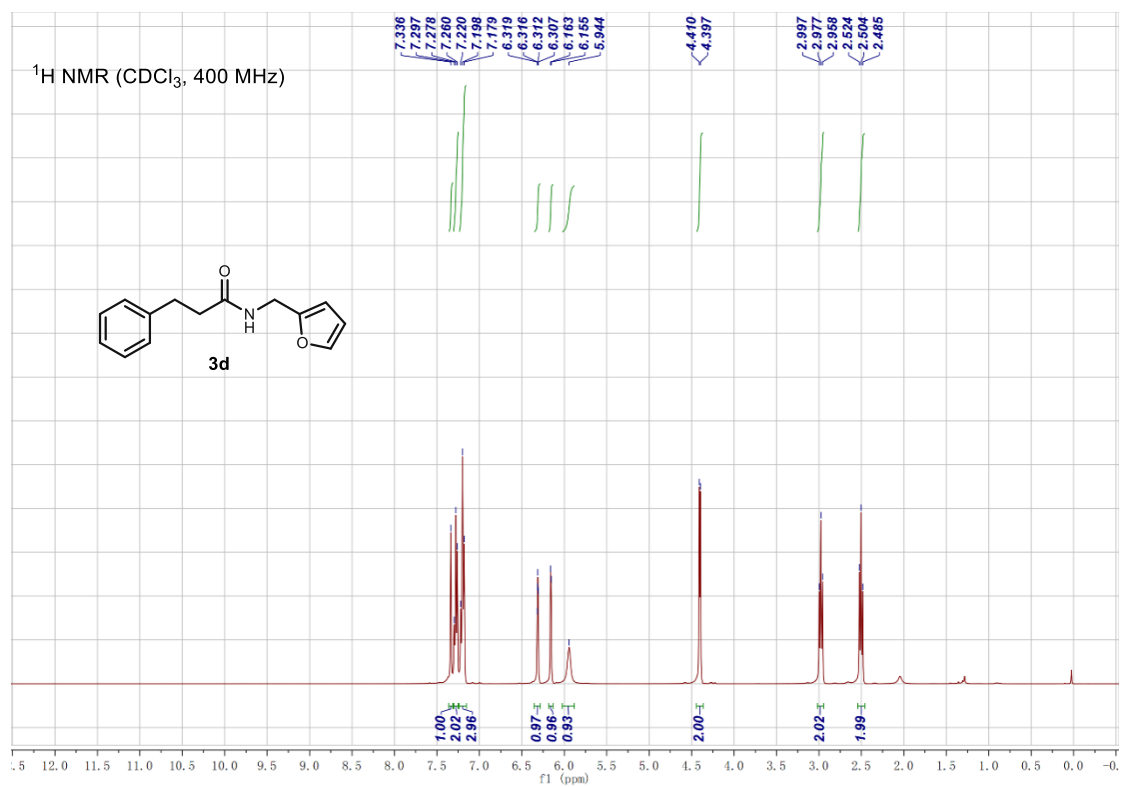
¹³C NMR of **3b** (150 MHz, CDCl₃, 298 K)



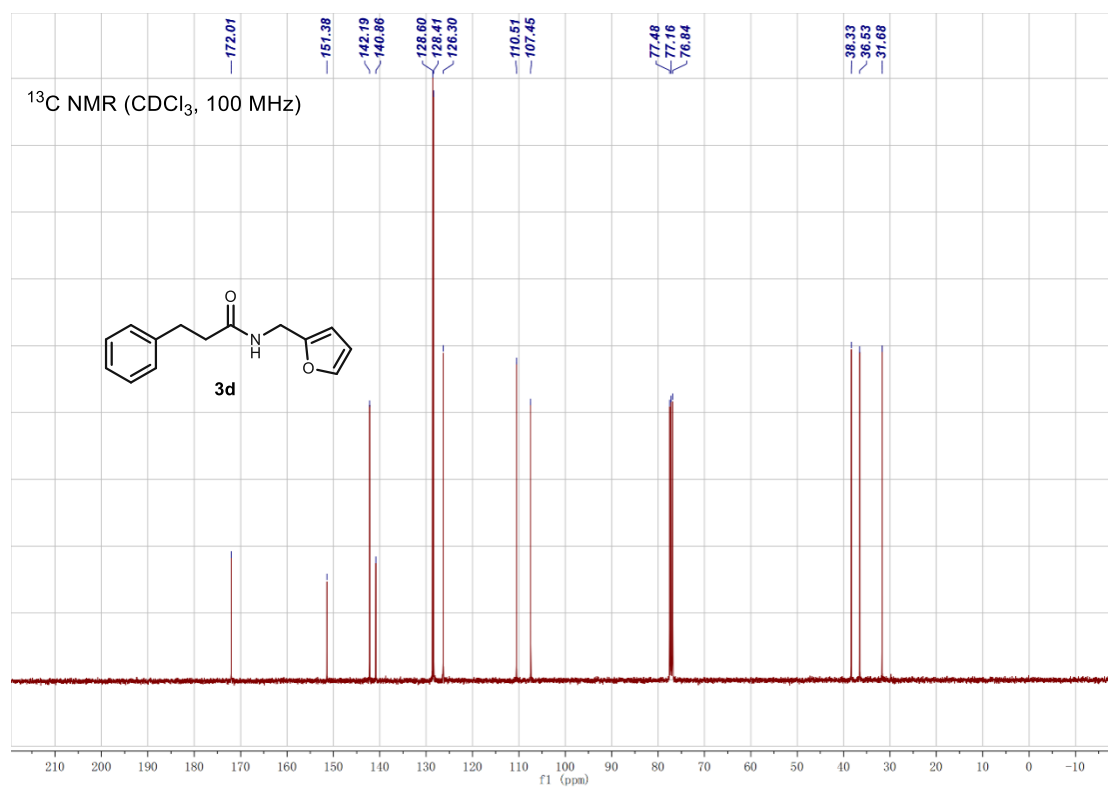
¹H NMR of **3c** (400 MHz, CDCl₃, 298 K)



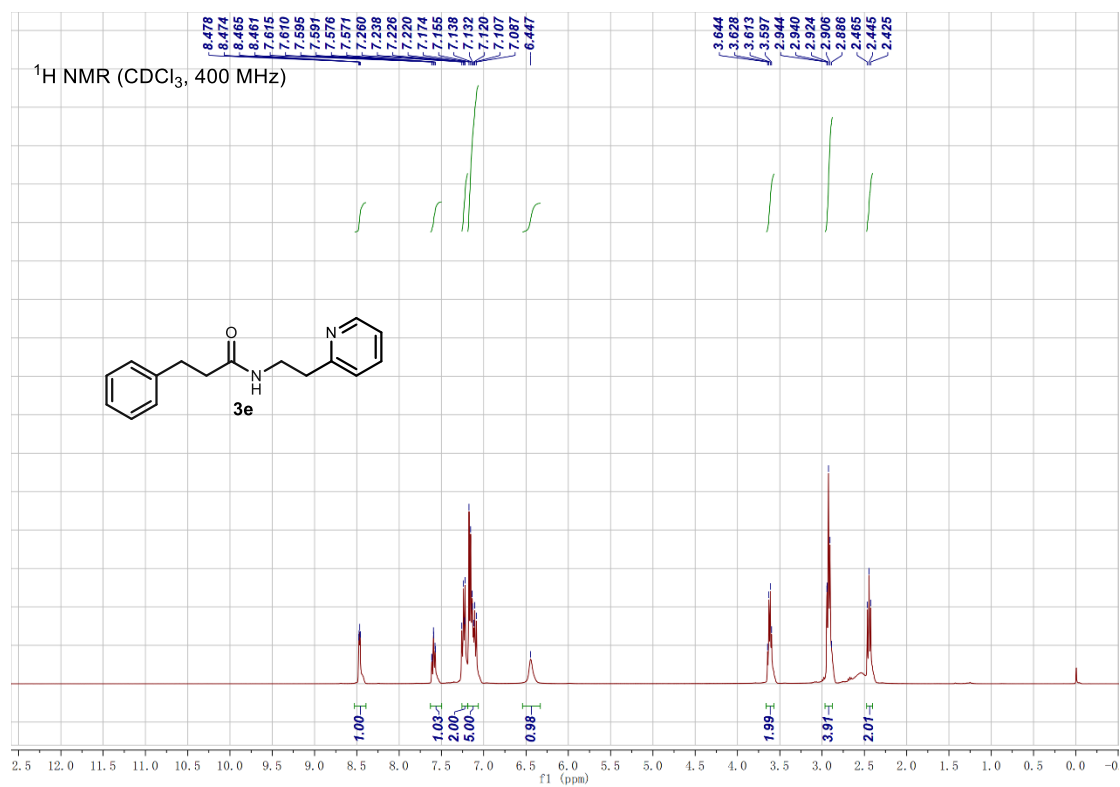
¹³C NMR of **3c** (100 MHz, CDCl₃, 298 K)



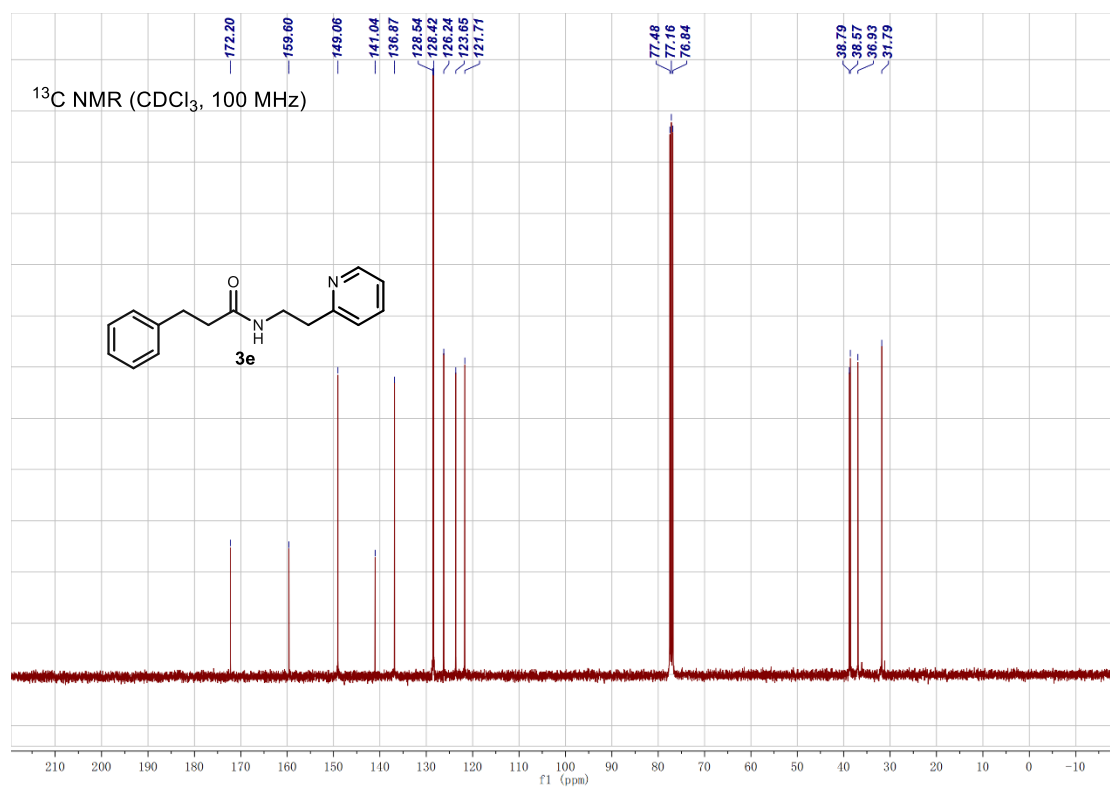
¹H NMR of **3d** (400 MHz, CDCl₃, 298 K)



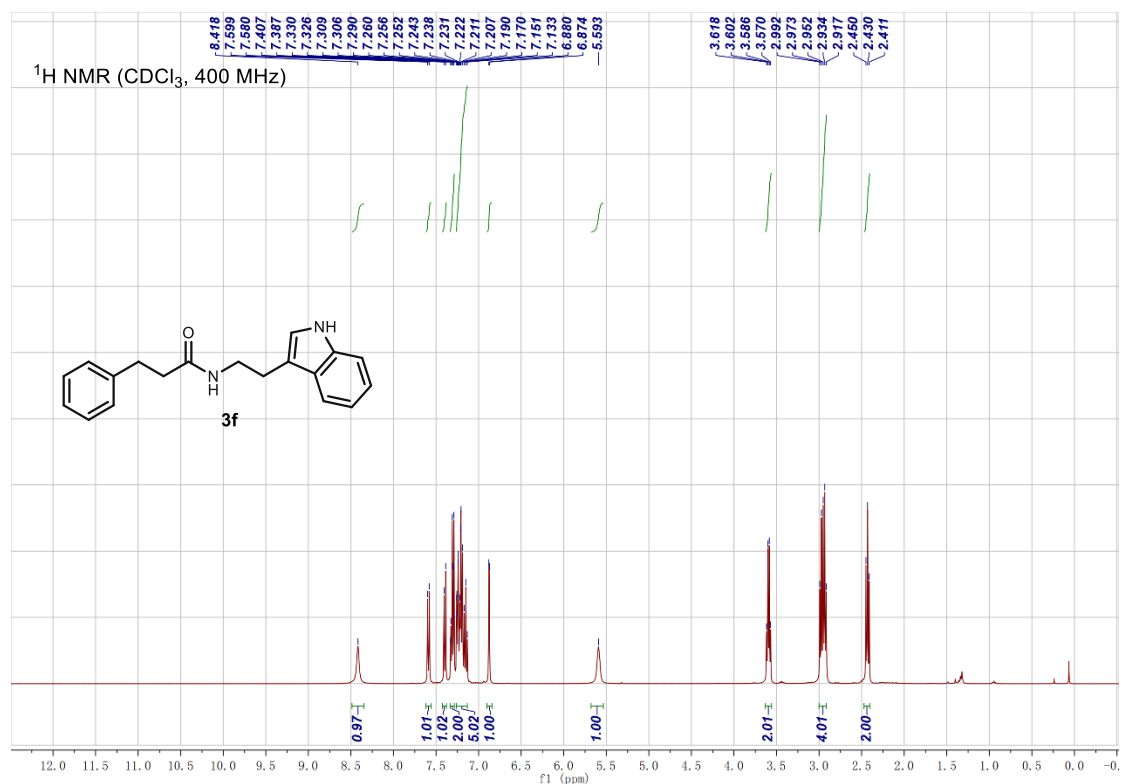
¹³C NMR of **3d** (100 MHz, CDCl₃, 298 K)



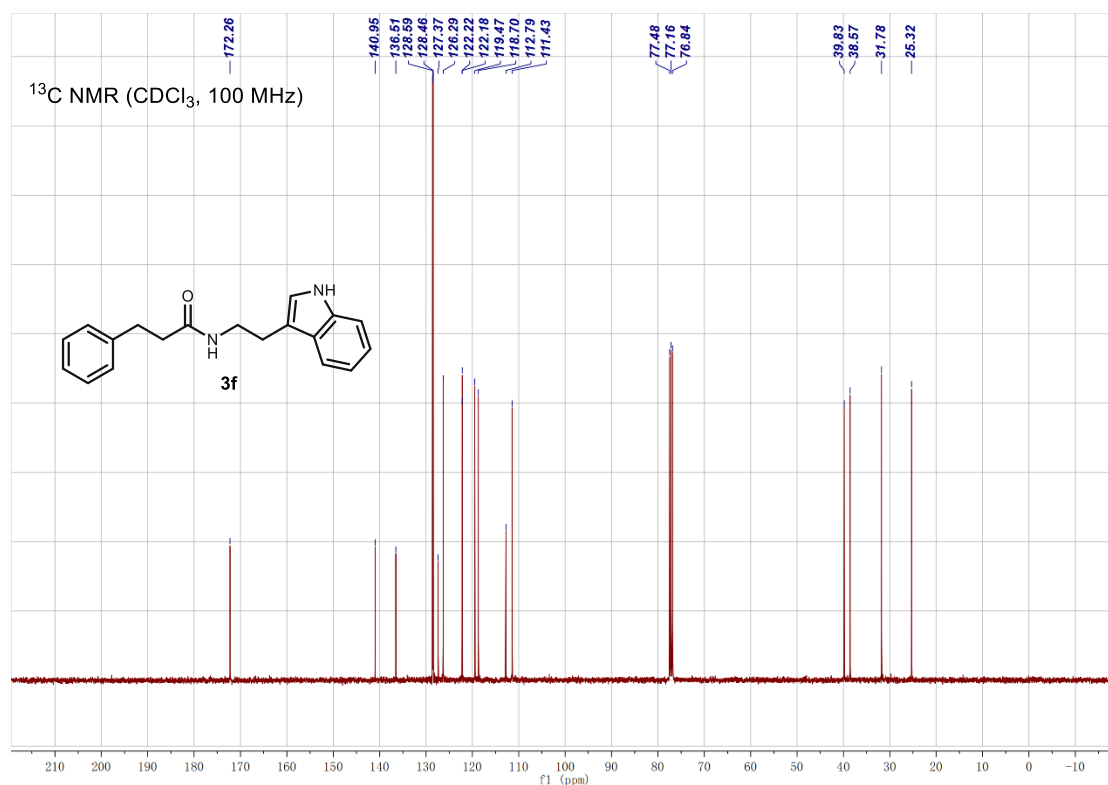
¹H NMR of **3e** (400 MHz, CDCl₃, 298 K)



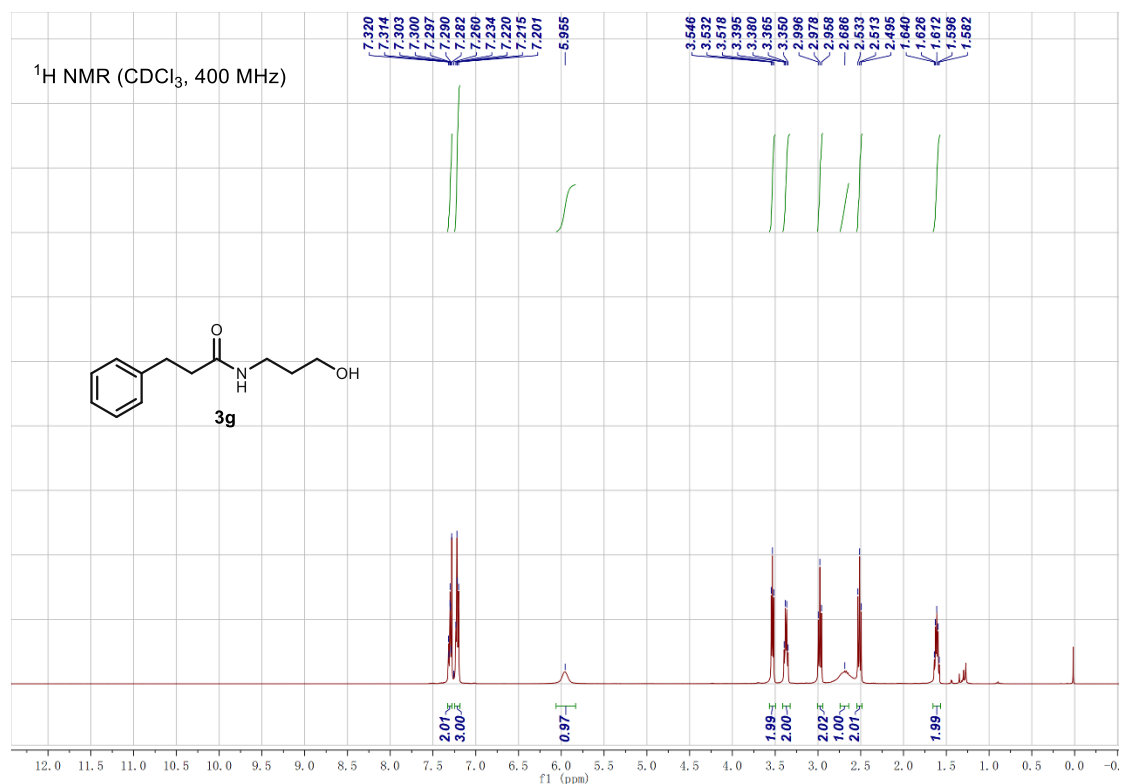
¹³C NMR of **3e** (100 MHz, CDCl₃, 298 K)



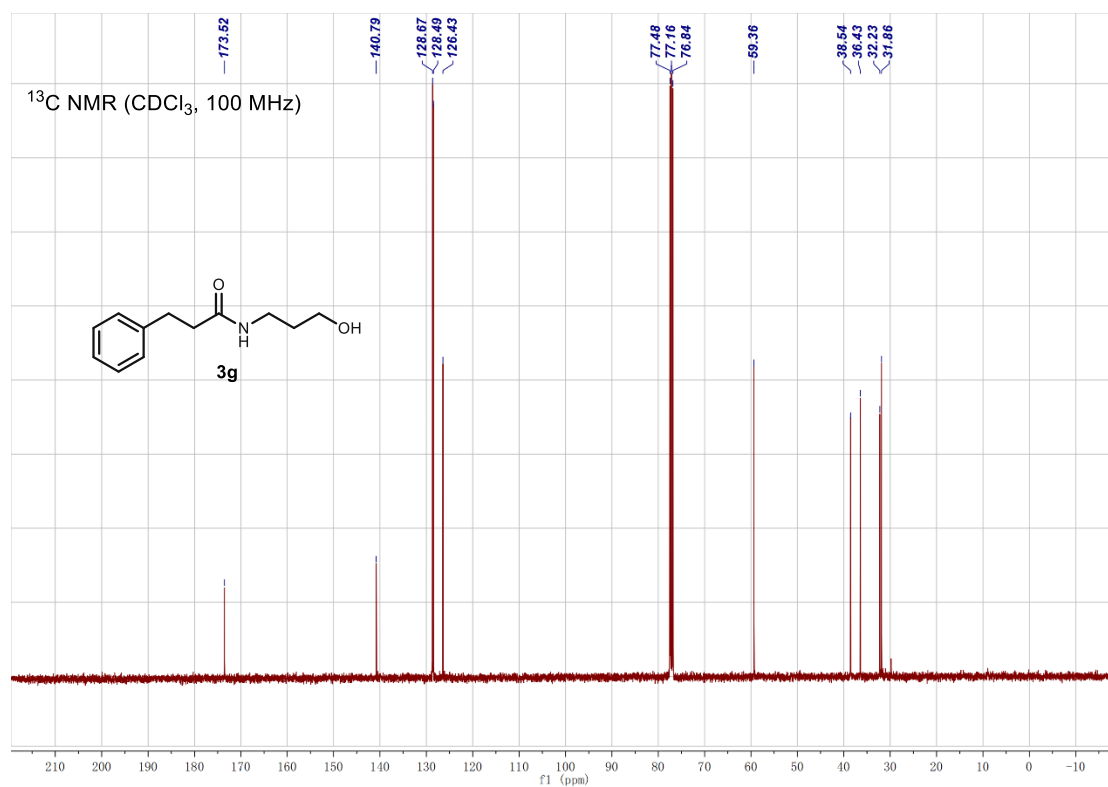
¹H NMR of **3f** (400 MHz, CDCl₃, 298 K)



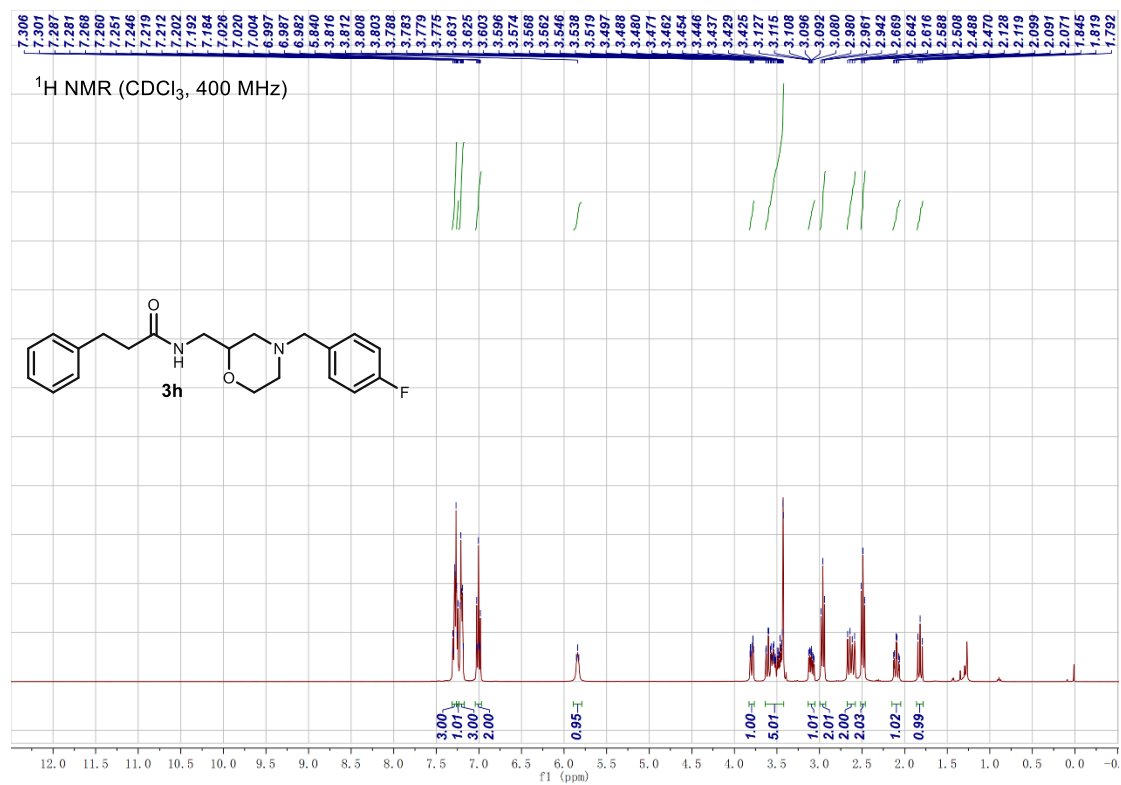
¹³C NMR of **3f** (100 MHz, CDCl₃, 298 K)



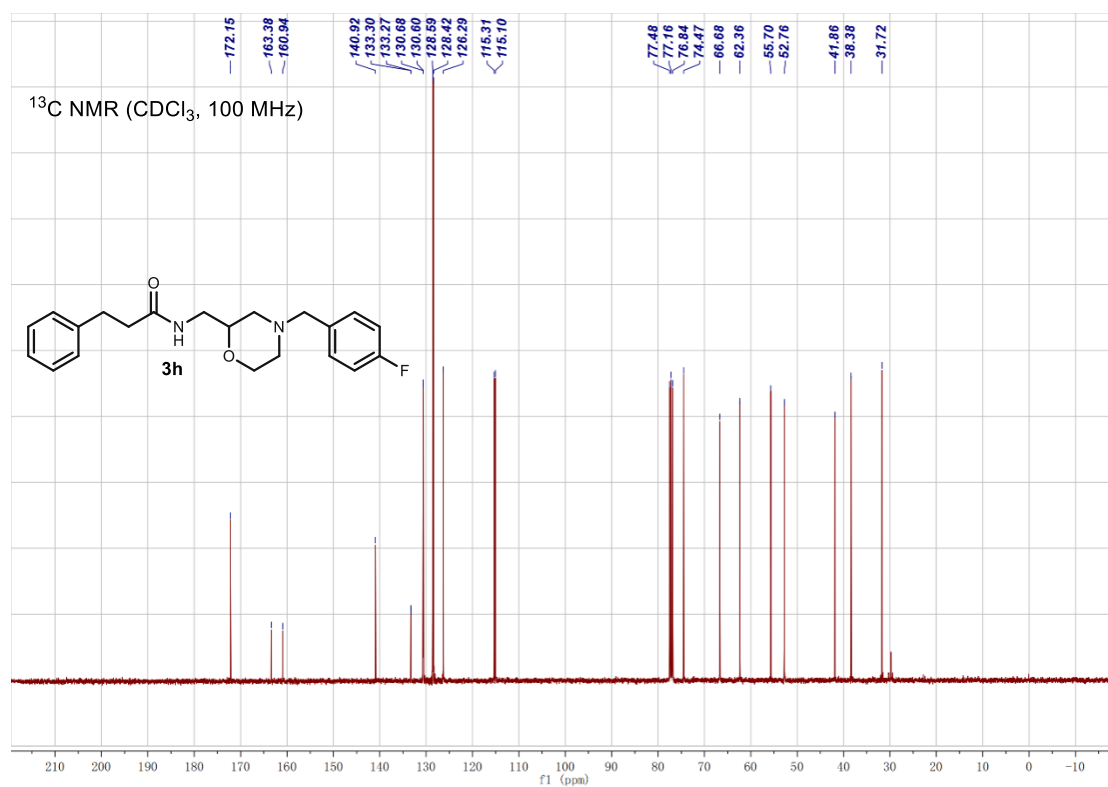
¹H NMR of **3g** (400 MHz, CDCl₃, 298 K)



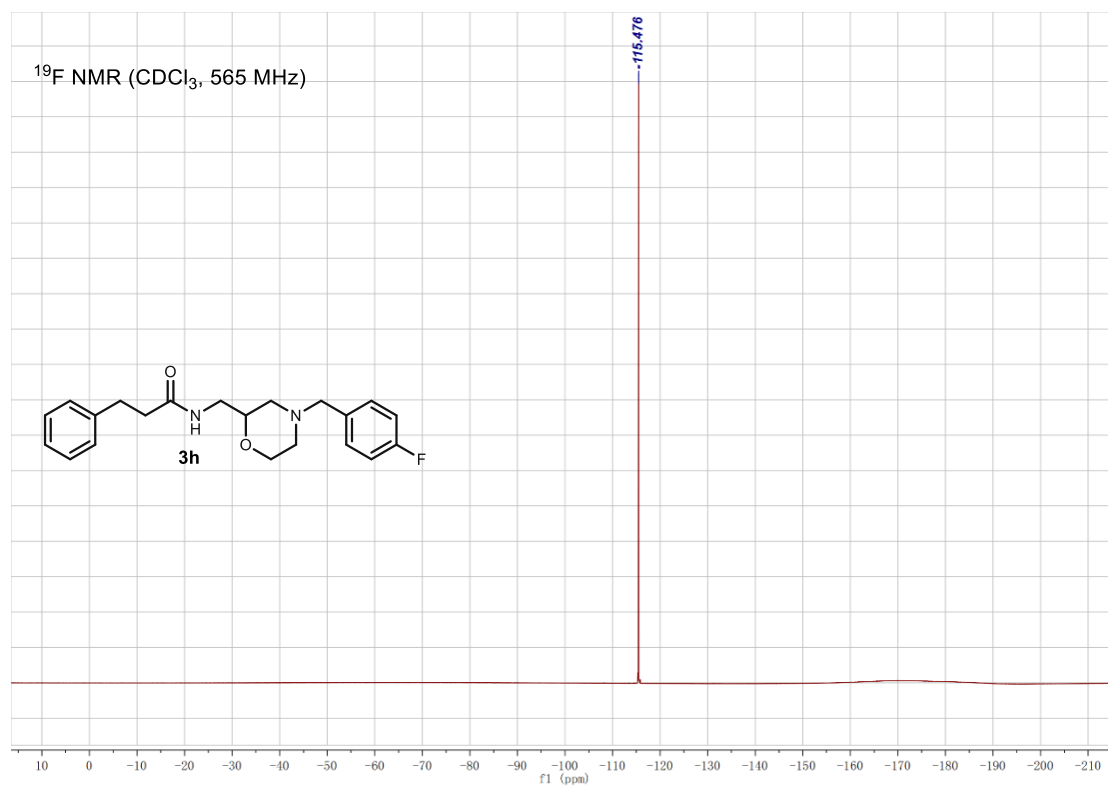
¹³C NMR of **3g** (100 MHz, CDCl₃, 298 K)



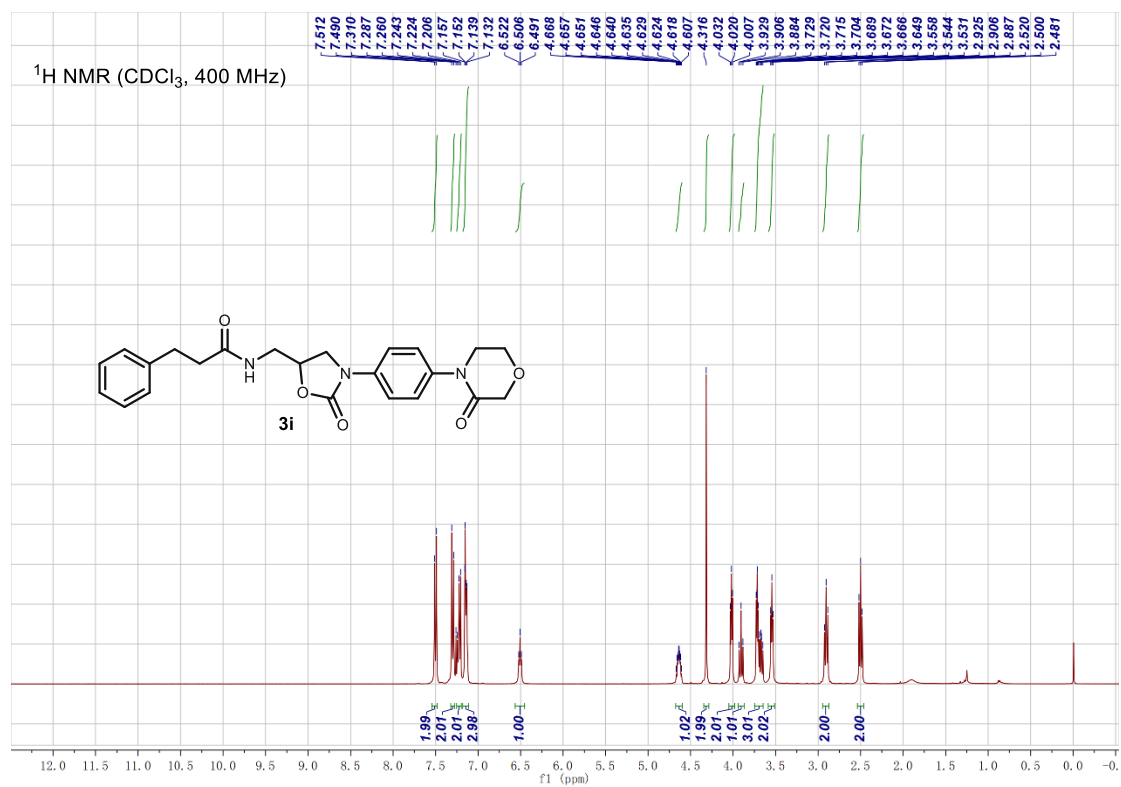
¹H NMR of **3h** (400 MHz, CDCl₃, 298 K)



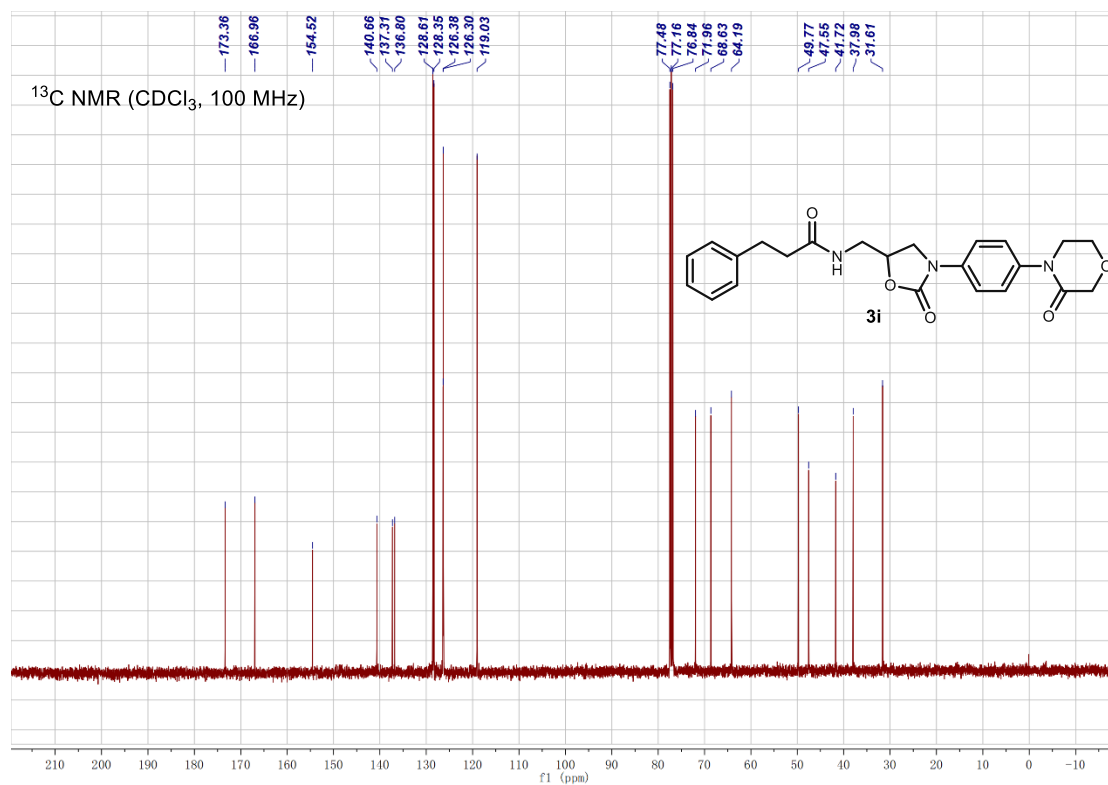
¹³C NMR of **3h** (100 MHz, CDCl₃, 298 K)



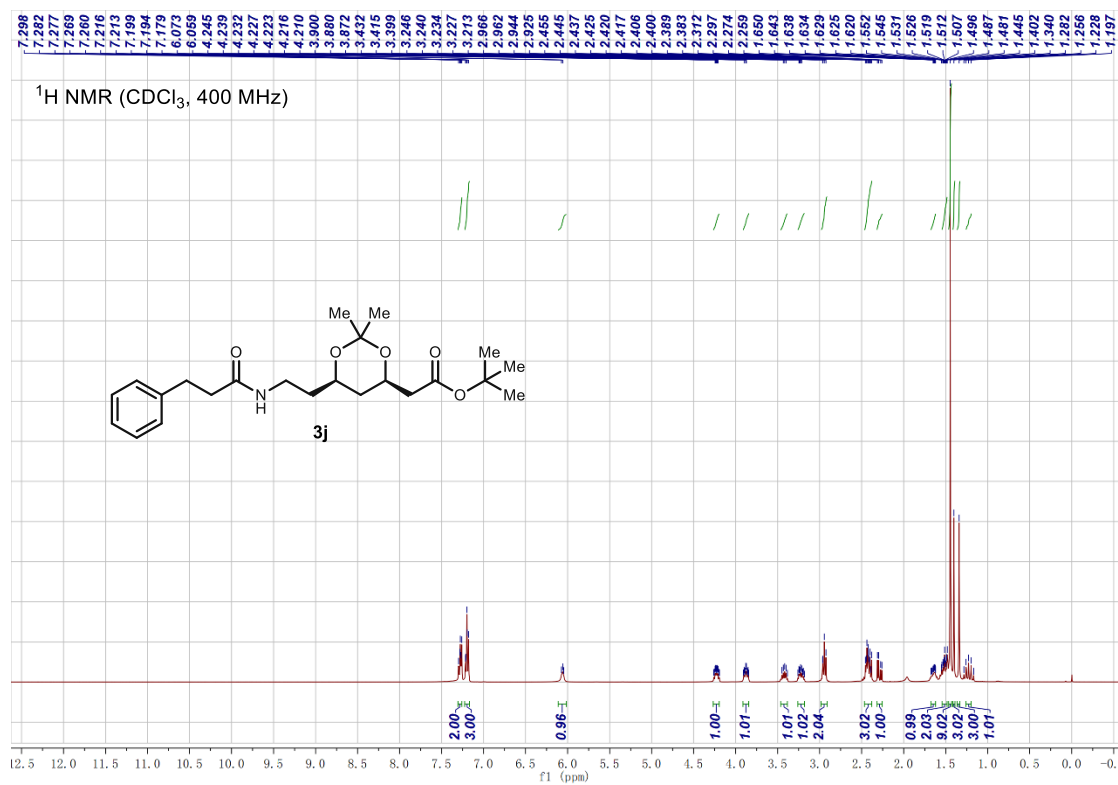
^{19}F NMR of **3h** (565 MHz, CDCl_3 , 298 K)



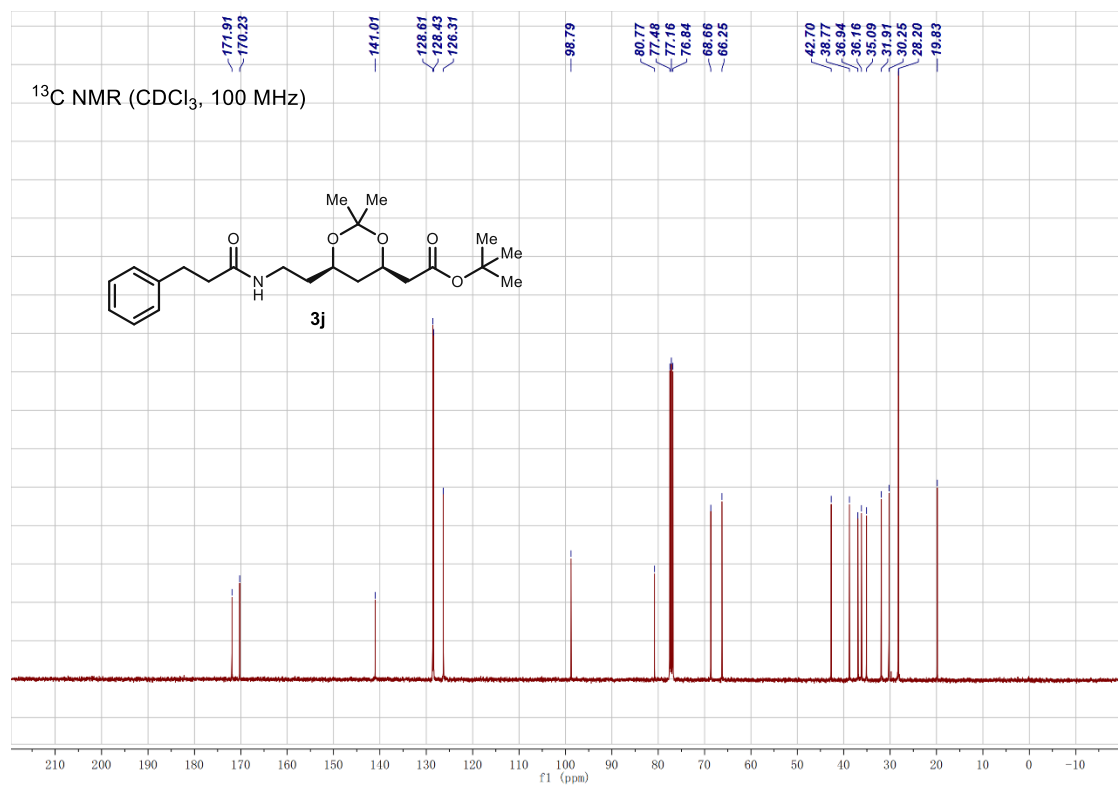
¹H NMR of **3i** (400 MHz, CDCl₃, 298 K)



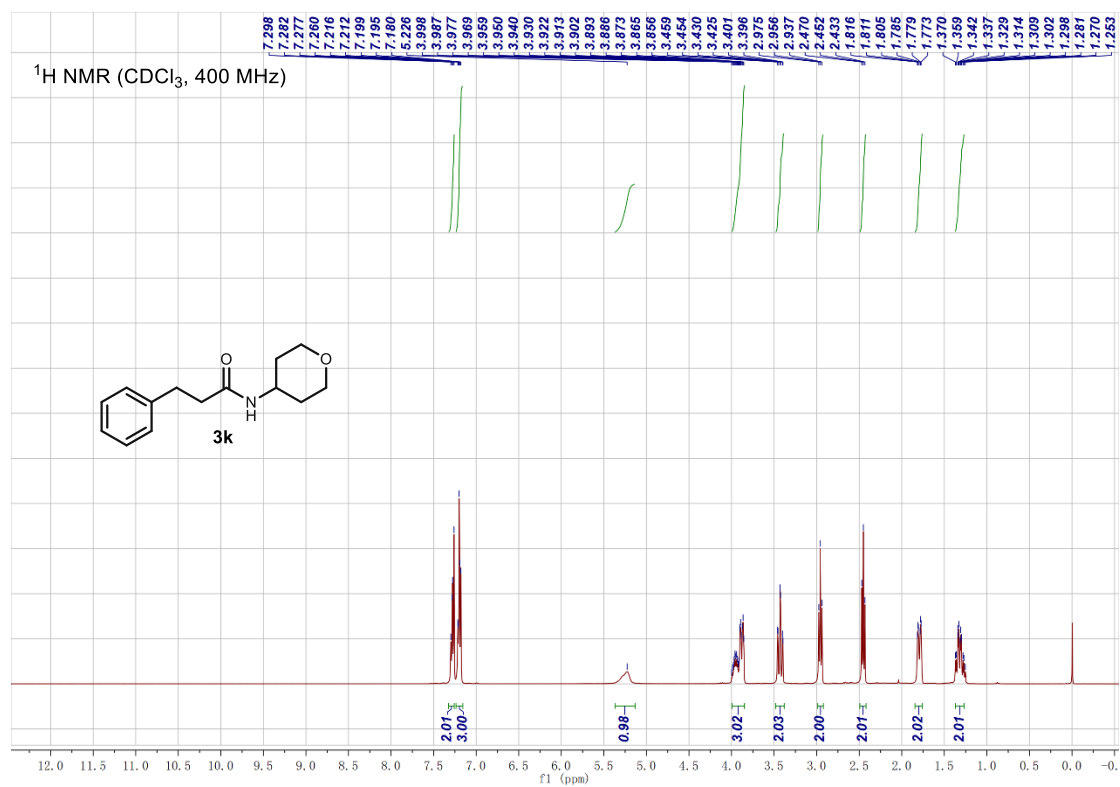
¹³C NMR of **3i** (100 MHz, CDCl₃, 298 K)



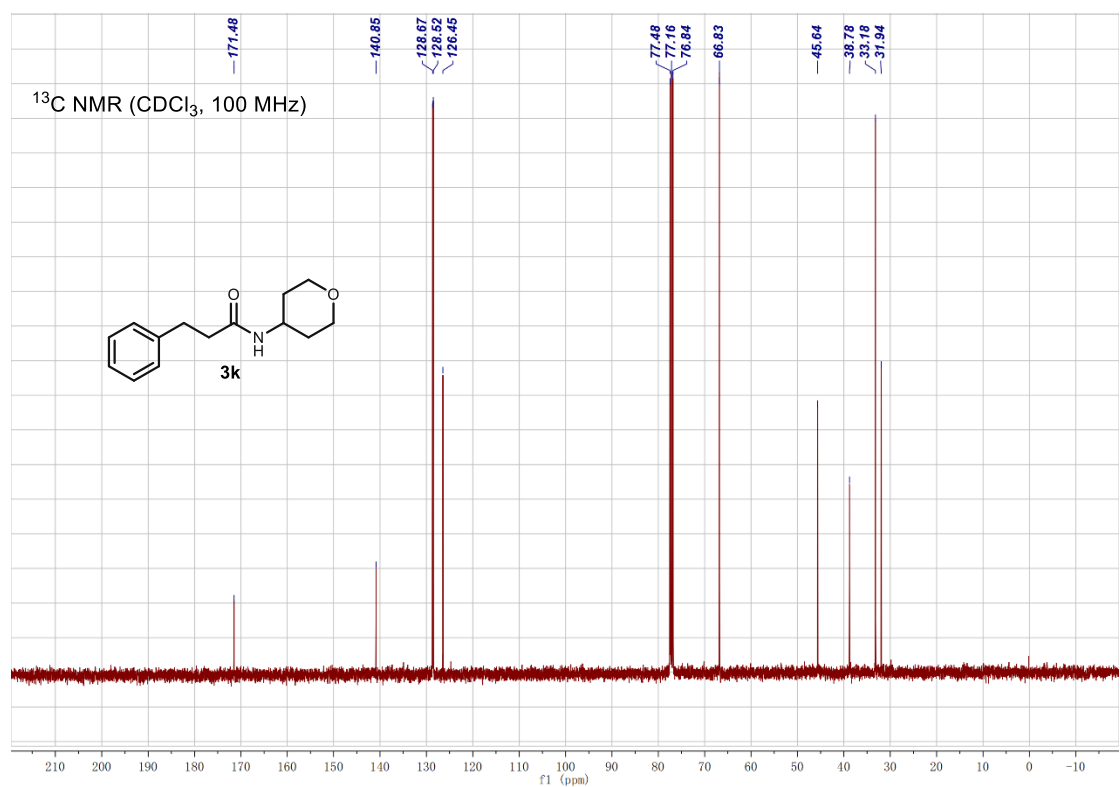
¹H NMR of **3j** (400 MHz, CDCl₃, 298 K)



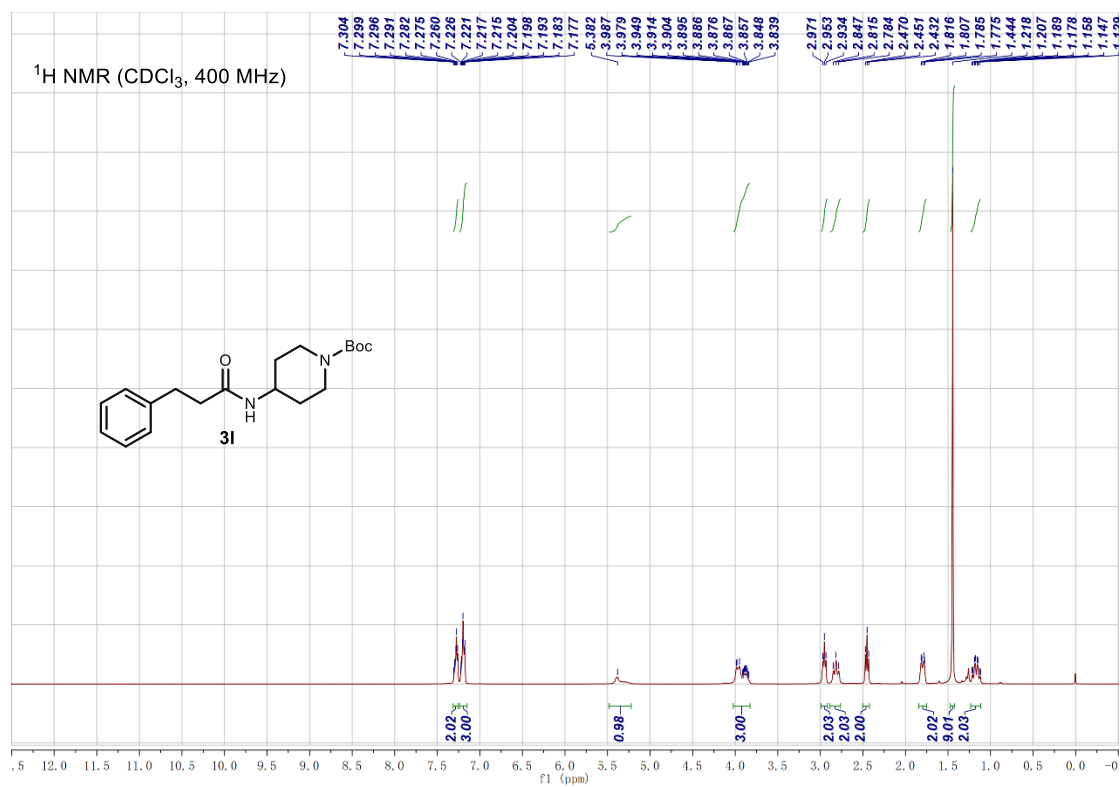
¹³C NMR of **3j** (100 MHz, CDCl₃, 298 K)



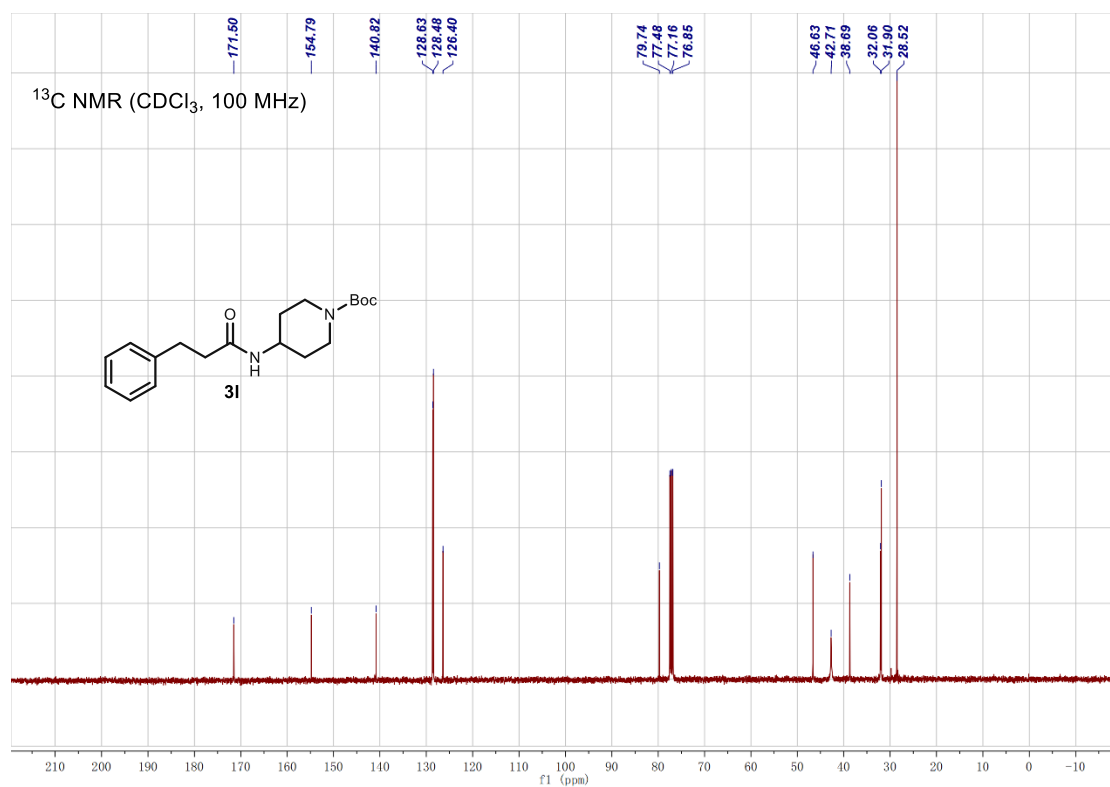
¹H NMR of **3k** (400 MHz, CDCl₃, 298 K)



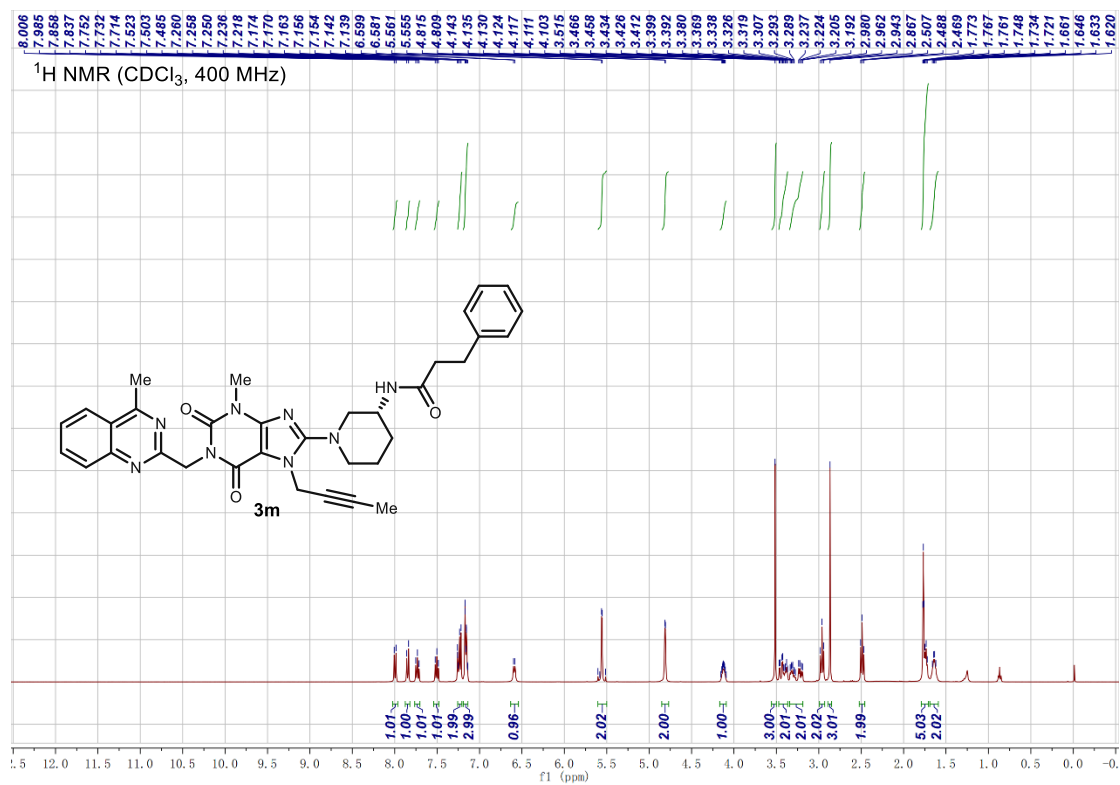
¹³C NMR of **3k** (100 MHz, CDCl₃, 298 K)



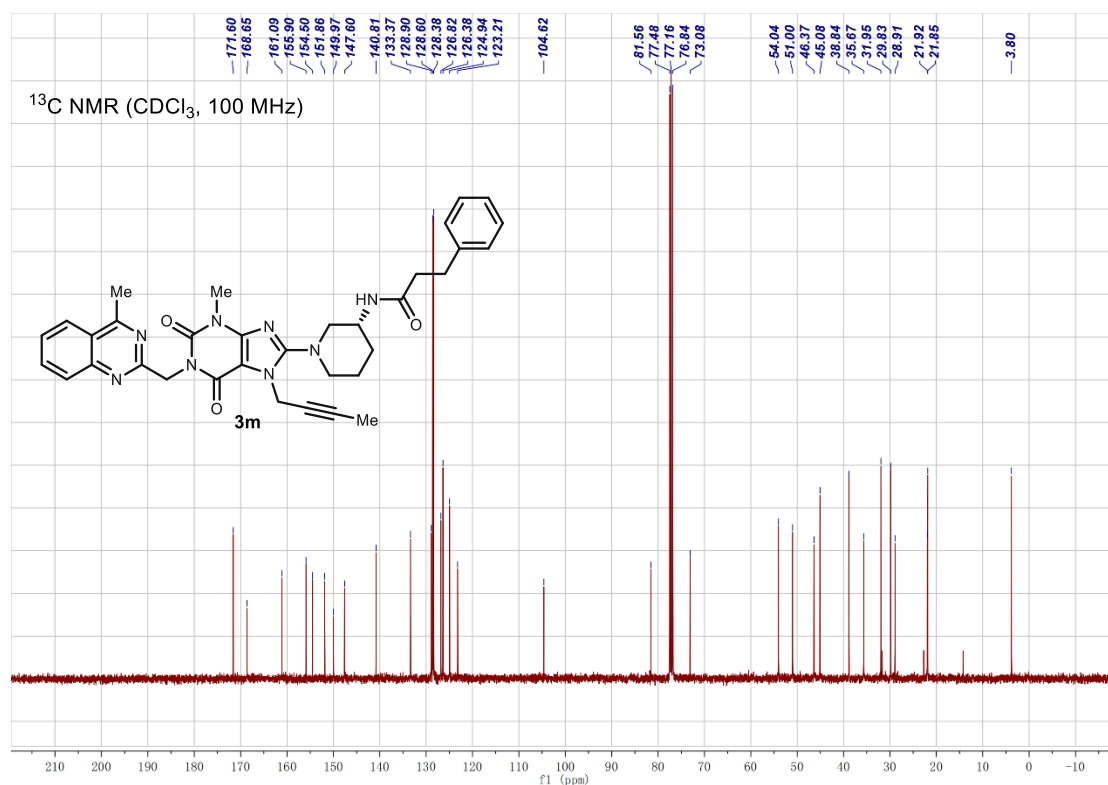
¹H NMR of **3I** (400 MHz, CDCl₃, 298 K)



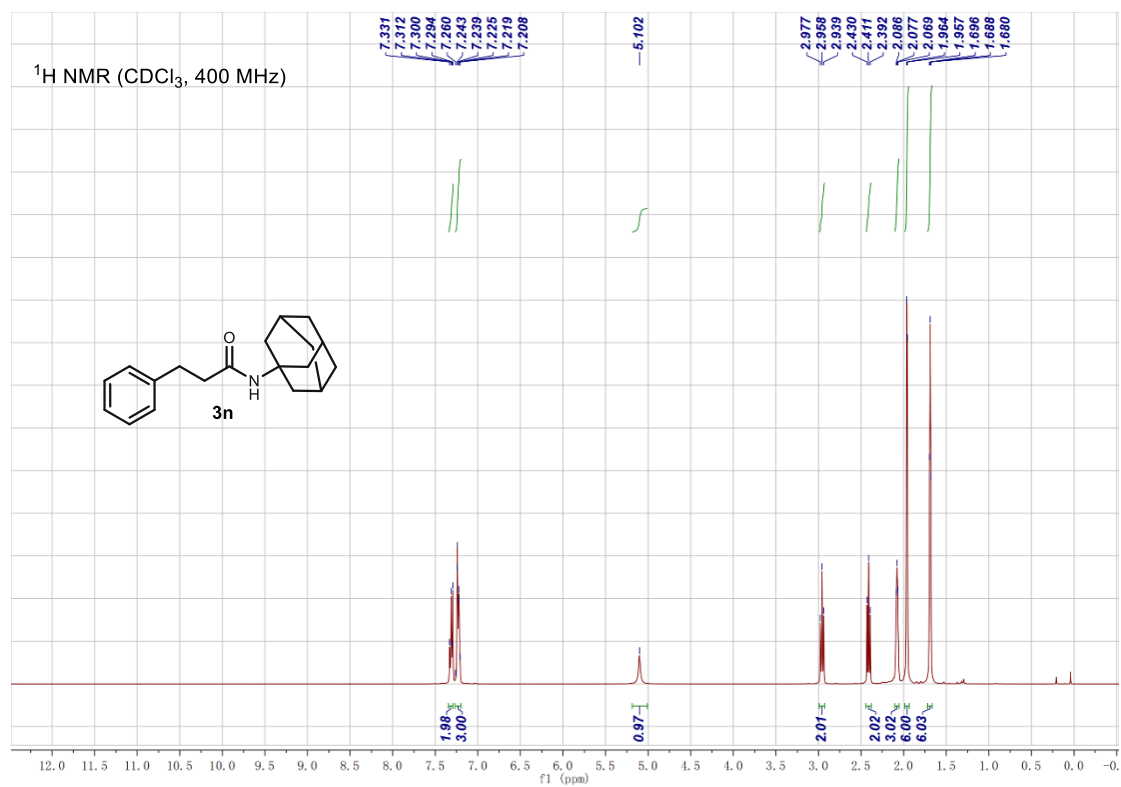
¹³C NMR of **3I** (100 MHz, CDCl₃, 298 K)



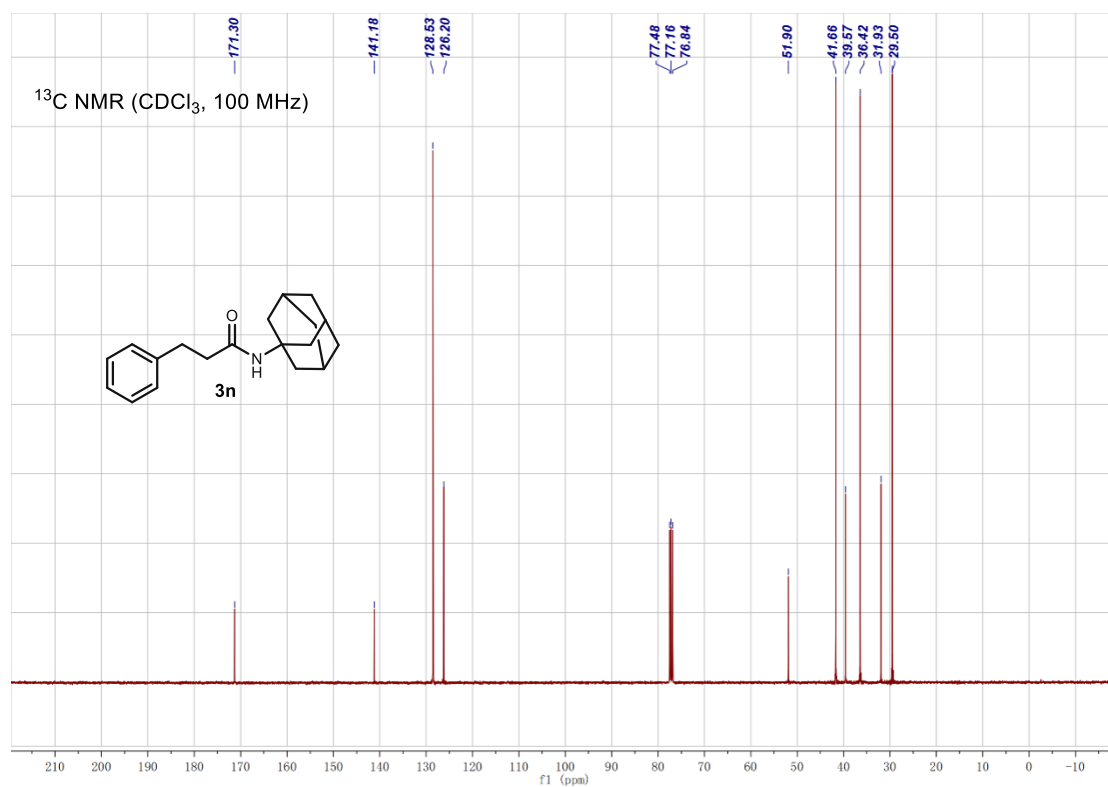
¹H NMR of **3m** (400 MHz, CDCl₃, 298 K)



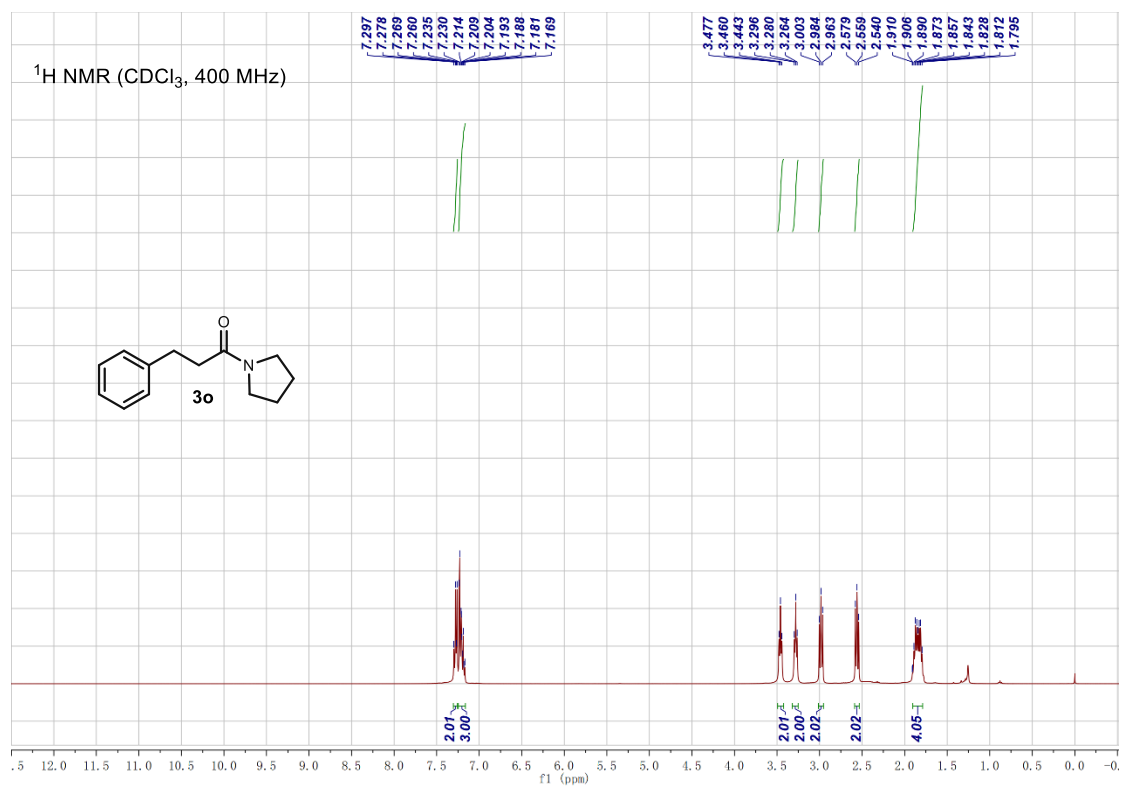
¹³C NMR of **3m** (100 MHz, CDCl₃, 298 K)



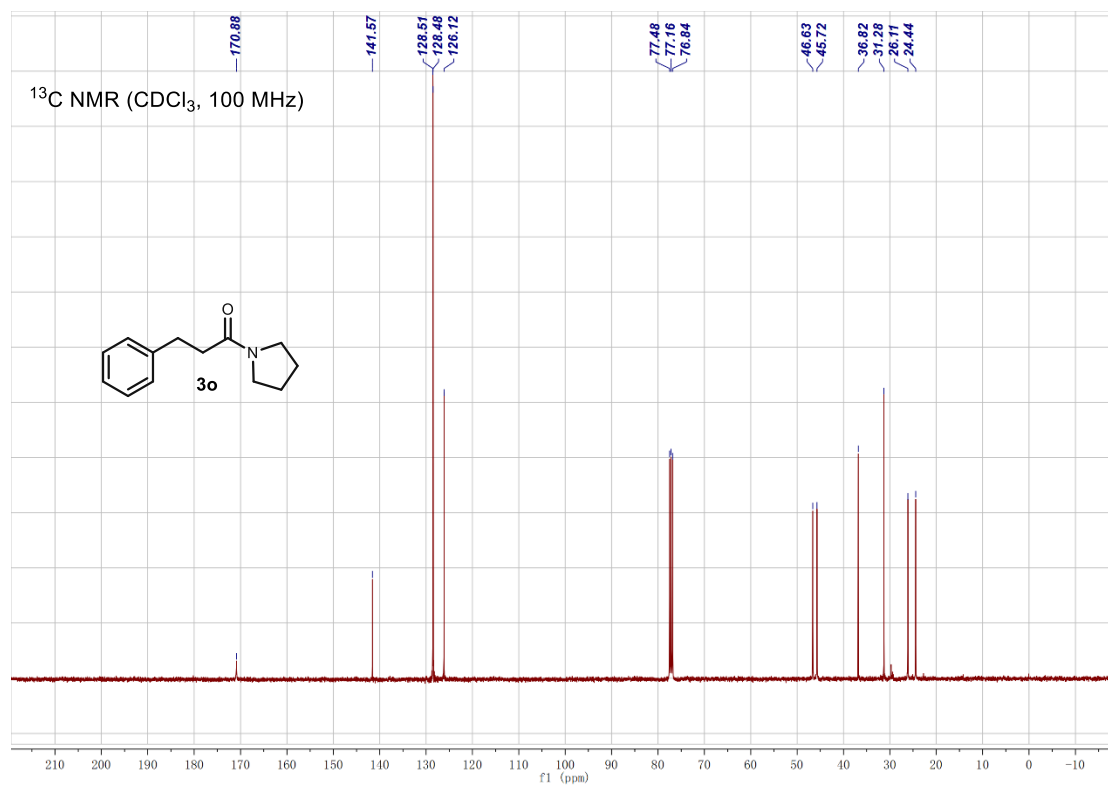
¹H NMR of **3n** (400 MHz, CDCl₃, 298 K)



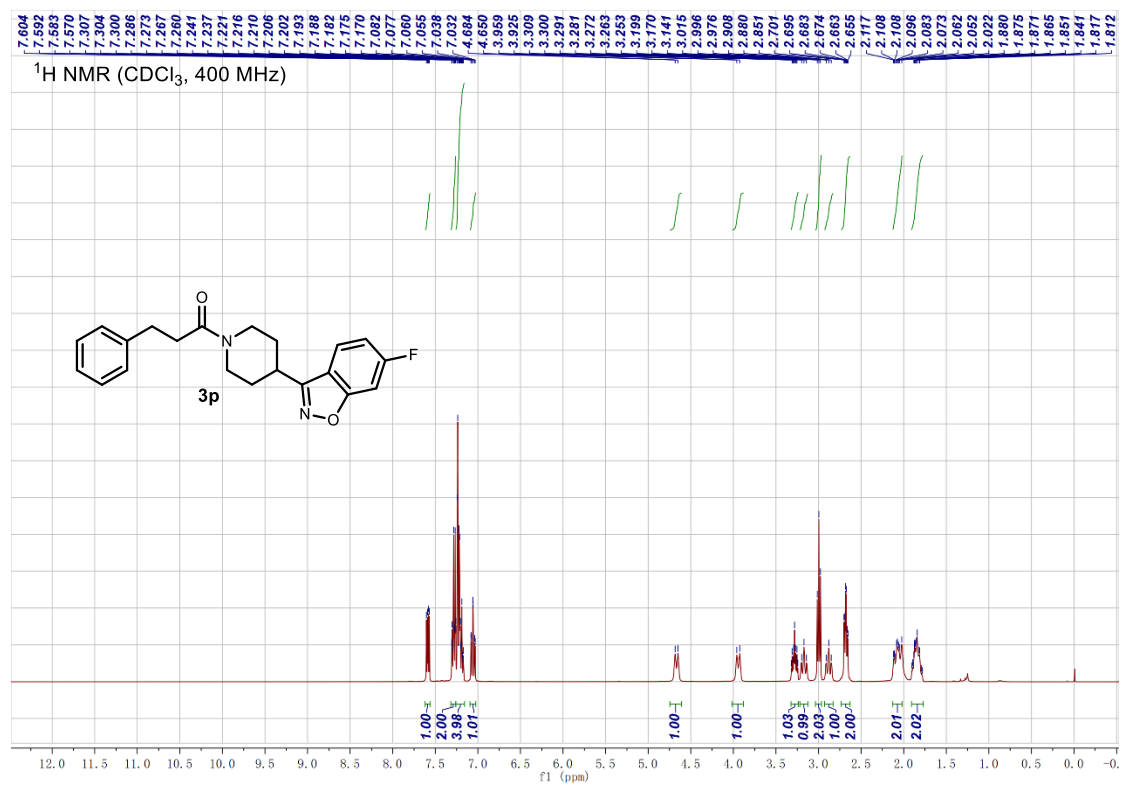
¹³C NMR of **3n** (100 MHz, CDCl₃, 298 K)



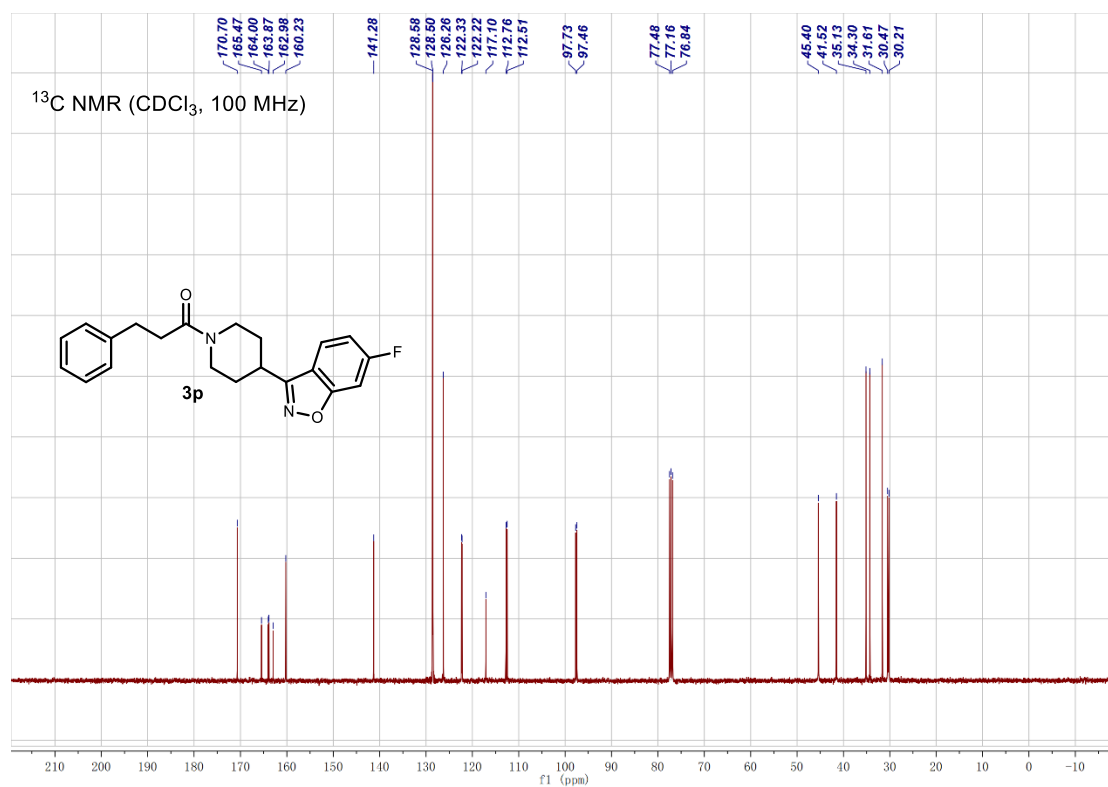
¹H NMR of **3o** (400 MHz, CDCl₃, 298 K)



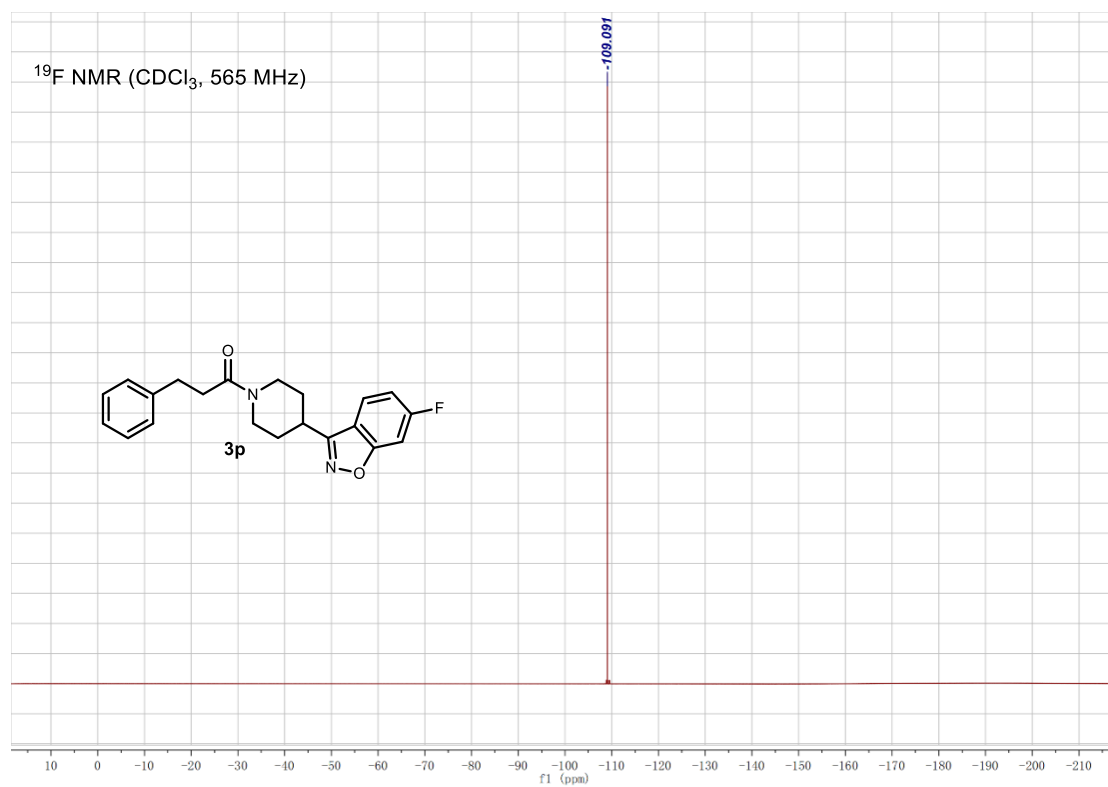
¹³C NMR of **3o** (100 MHz, CDCl₃, 298 K)



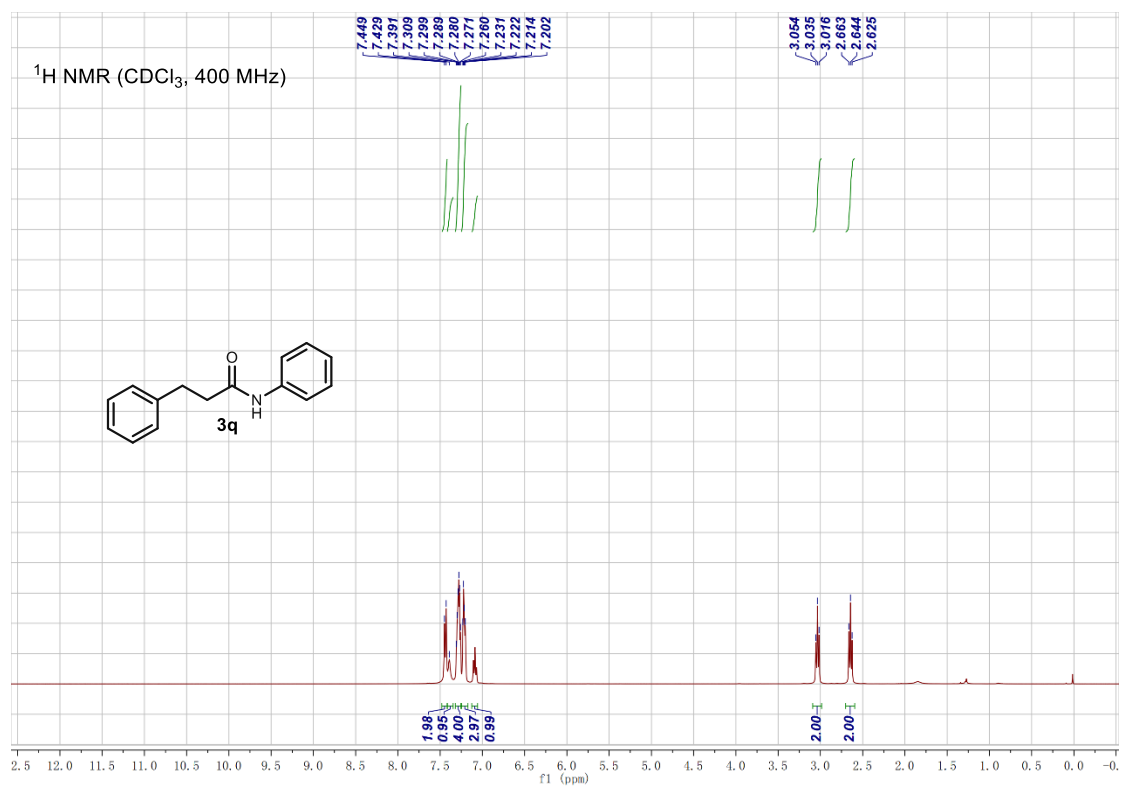
¹H NMR of **3p** (400 MHz, CDCl₃, 298 K)



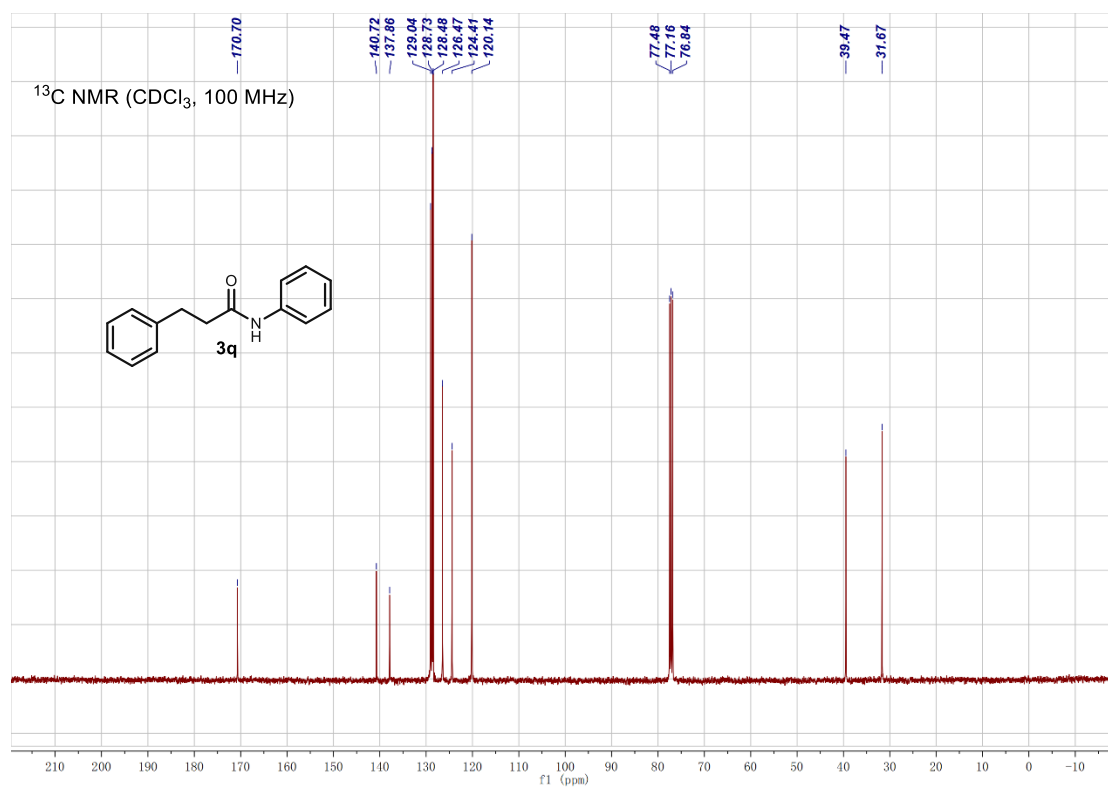
¹³C NMR of **3p** (100 MHz, CDCl₃, 298 K)



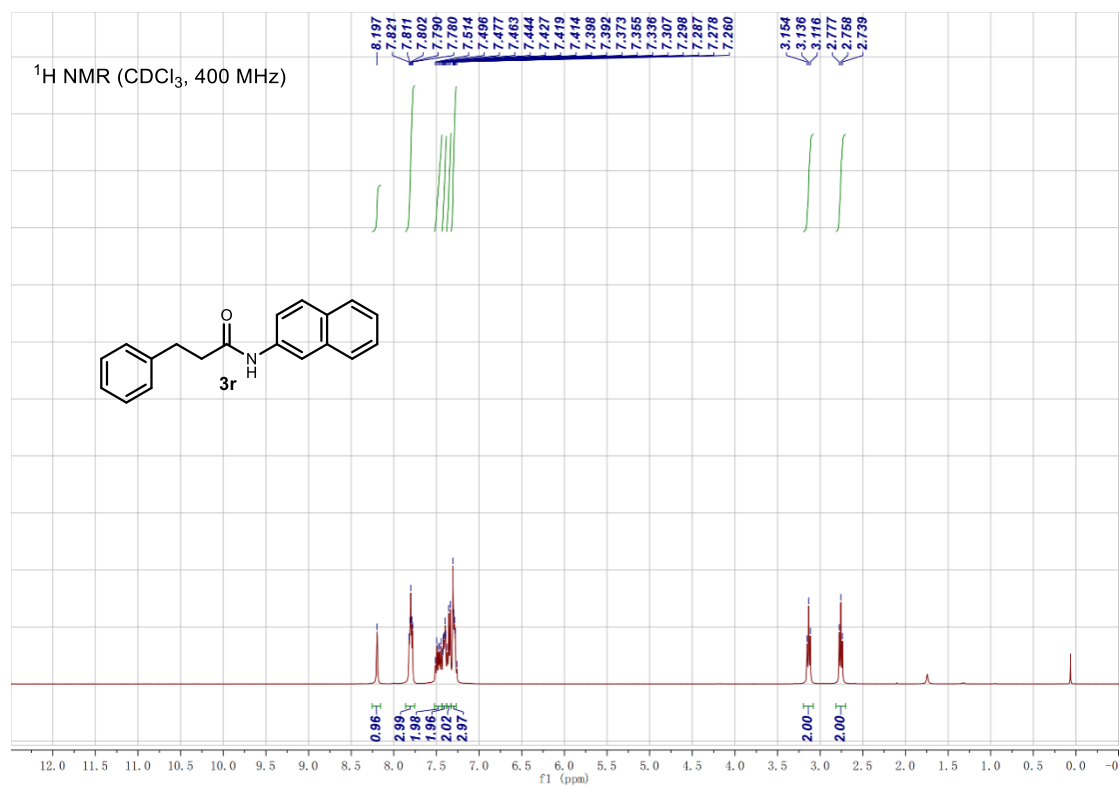
^{19}F NMR of **3p** (565 MHz, CDCl_3 , 298 K)



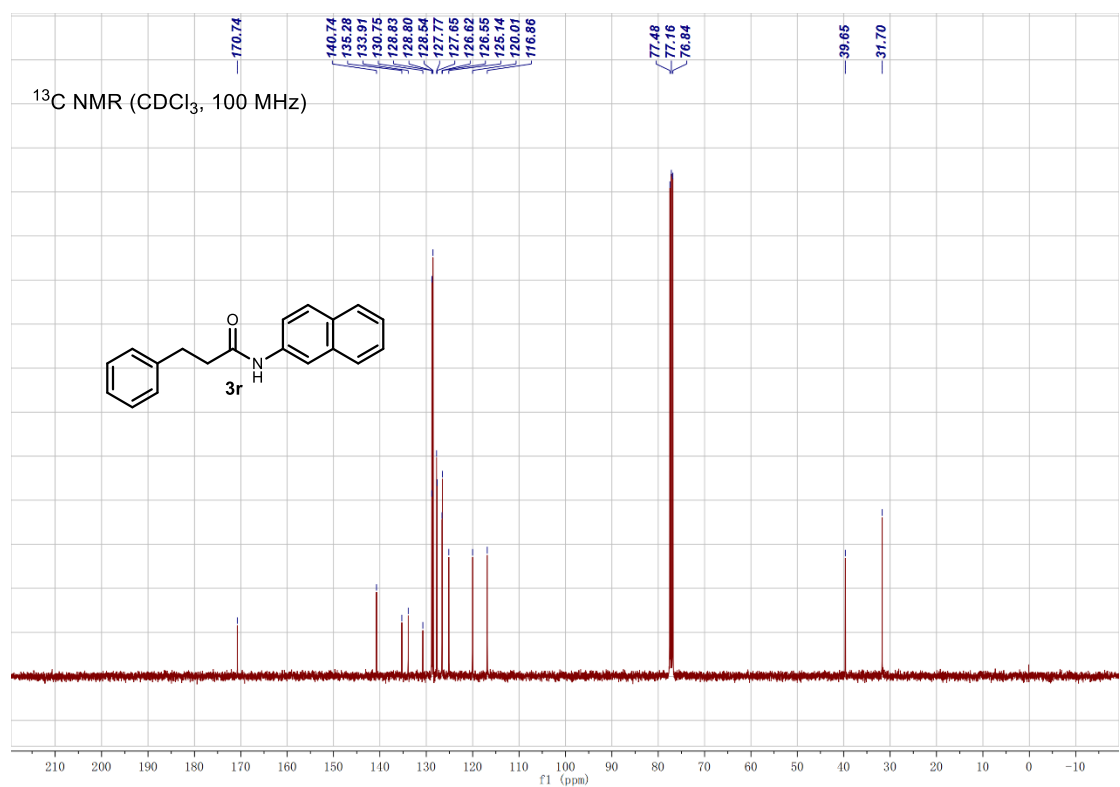
¹H NMR of **3q** (400 MHz, CDCl₃, 298 K)



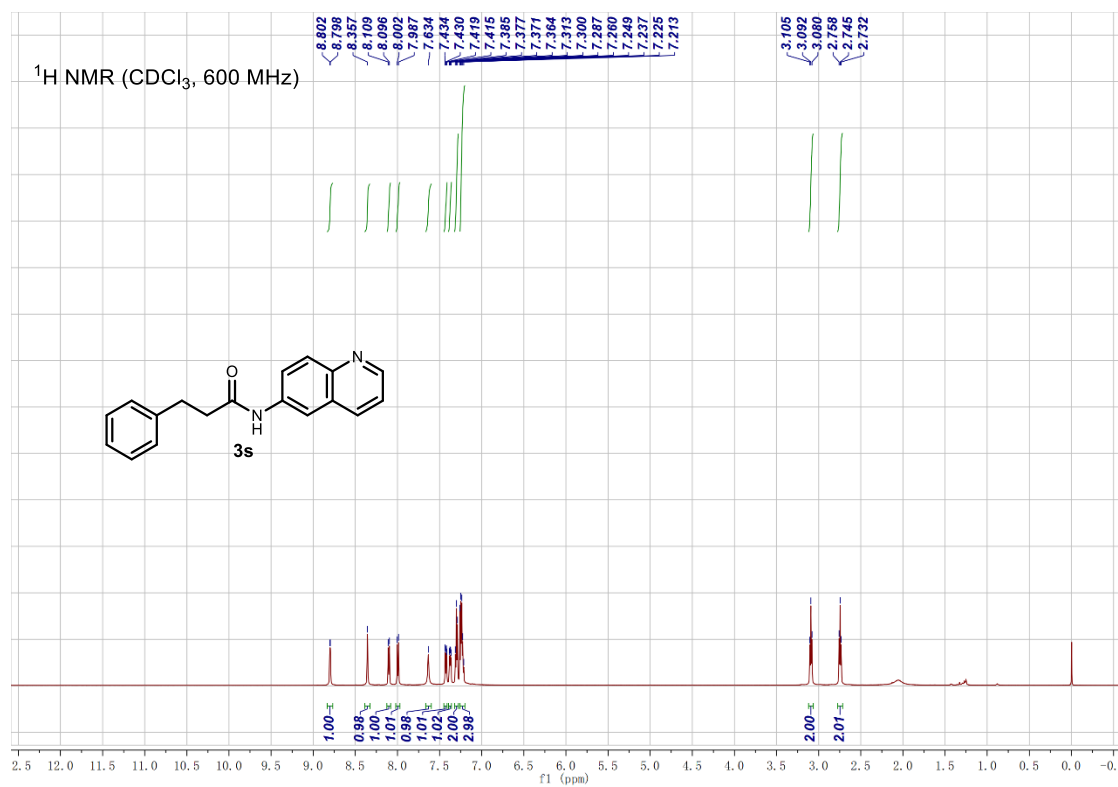
¹³C NMR of **3q** (100 MHz, CDCl₃, 298 K)



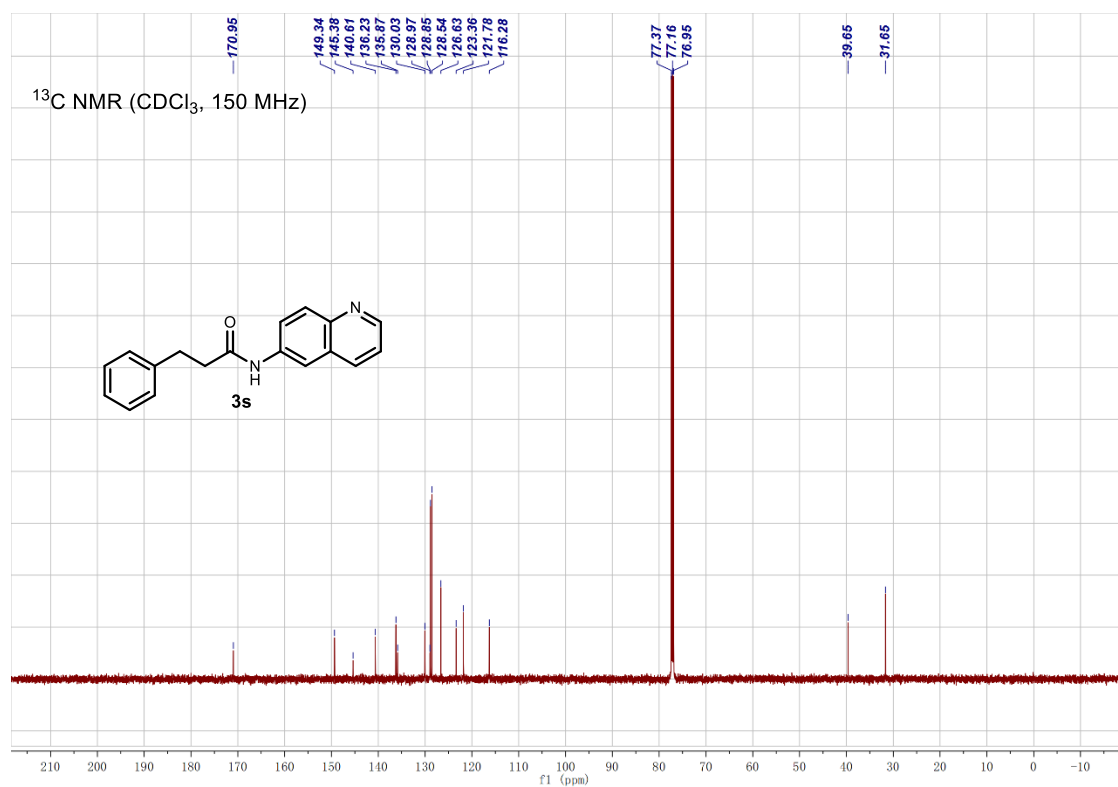
¹H NMR of **3r** (400 MHz, CDCl₃, 298 K)



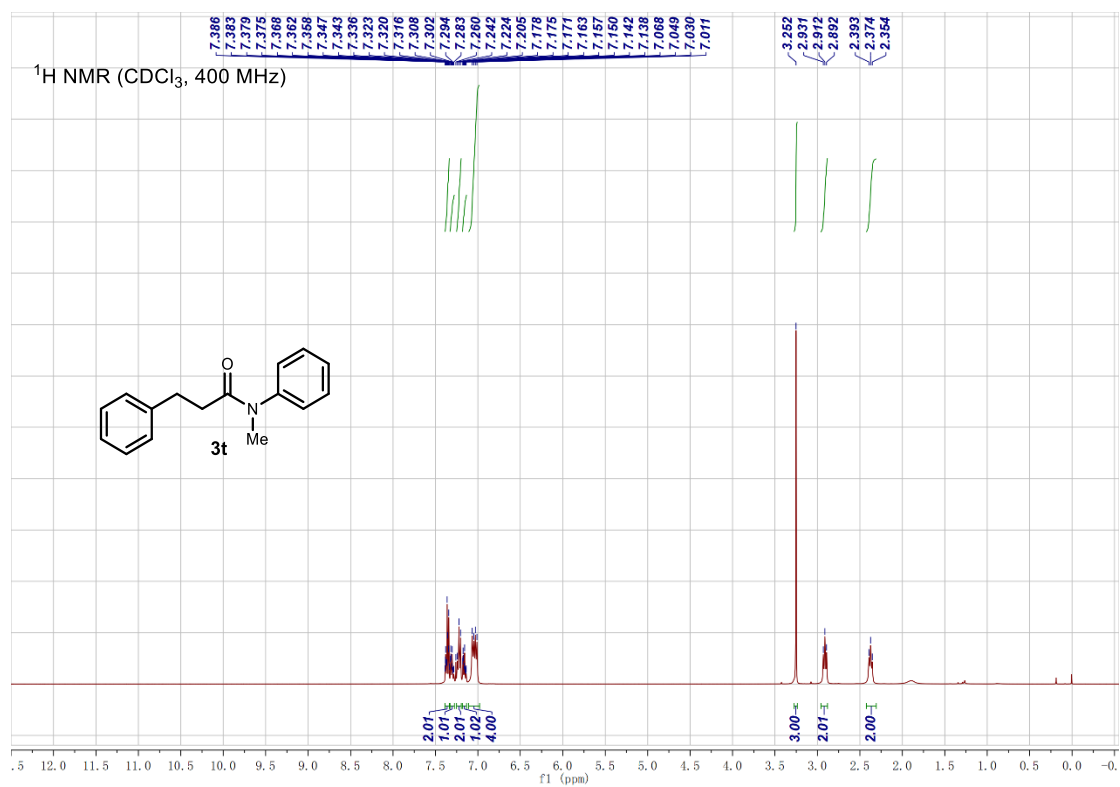
¹³C NMR of **3r** (100 MHz, CDCl₃, 298 K)



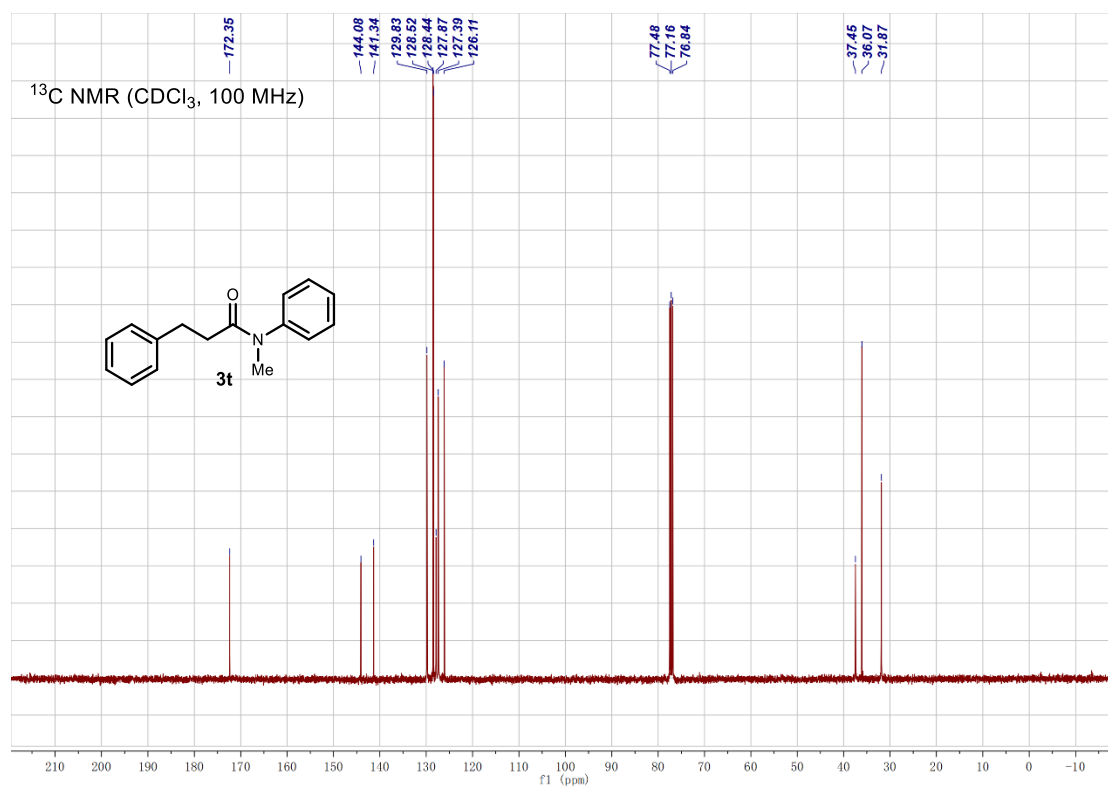
¹H NMR of **3s** (600 MHz, CDCl₃, 298 K)



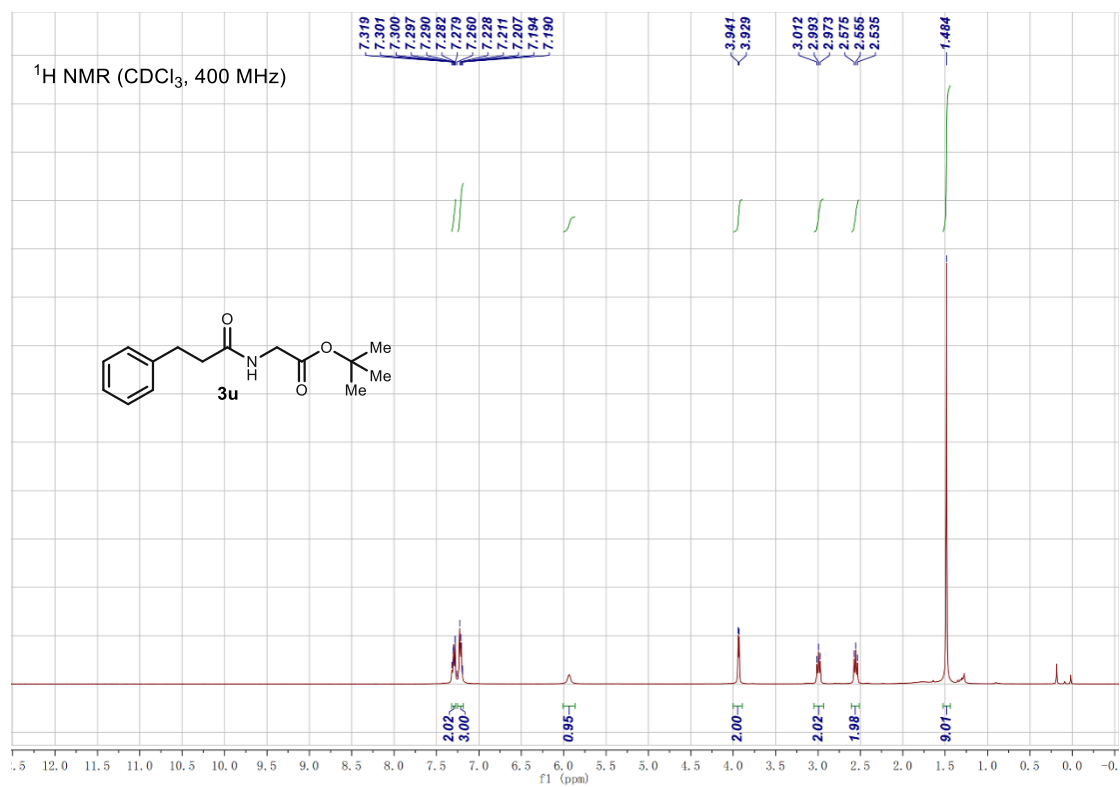
¹³C NMR of **3s** (150 MHz, CDCl₃, 298 K)



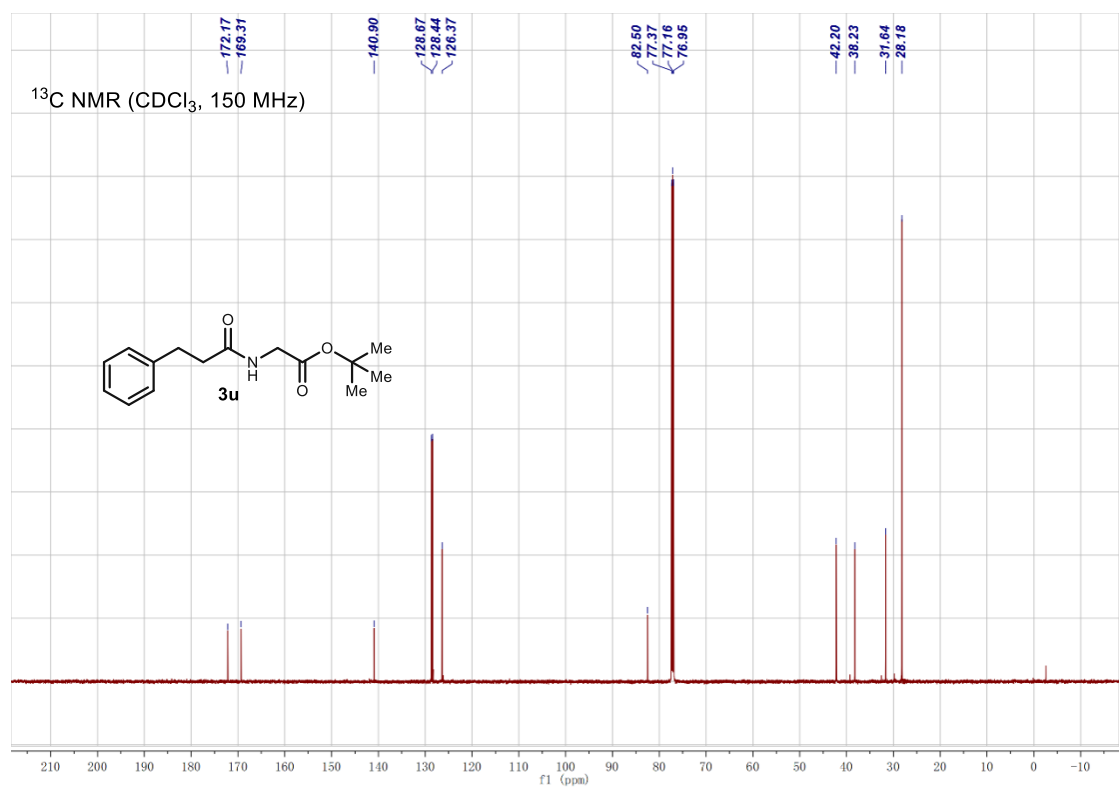
¹H NMR of **3t** (400 MHz, CDCl₃, 298 K)



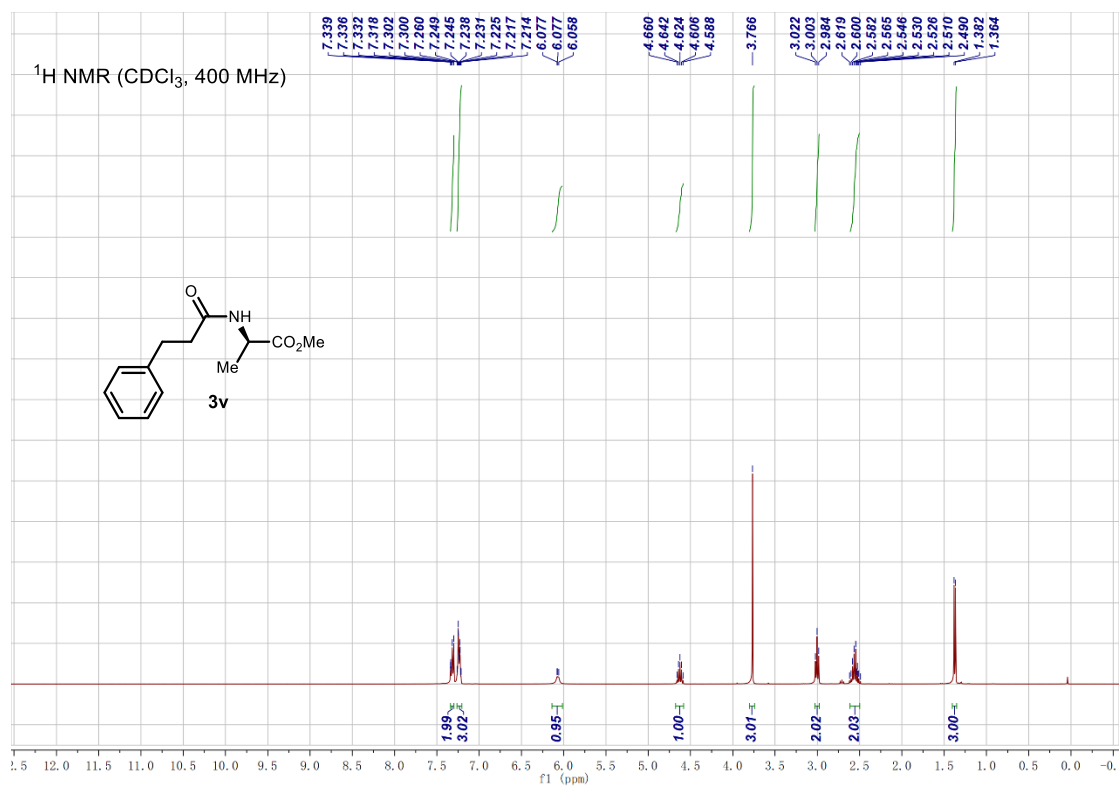
¹³C NMR of **3t** (100 MHz, CDCl₃, 298 K)



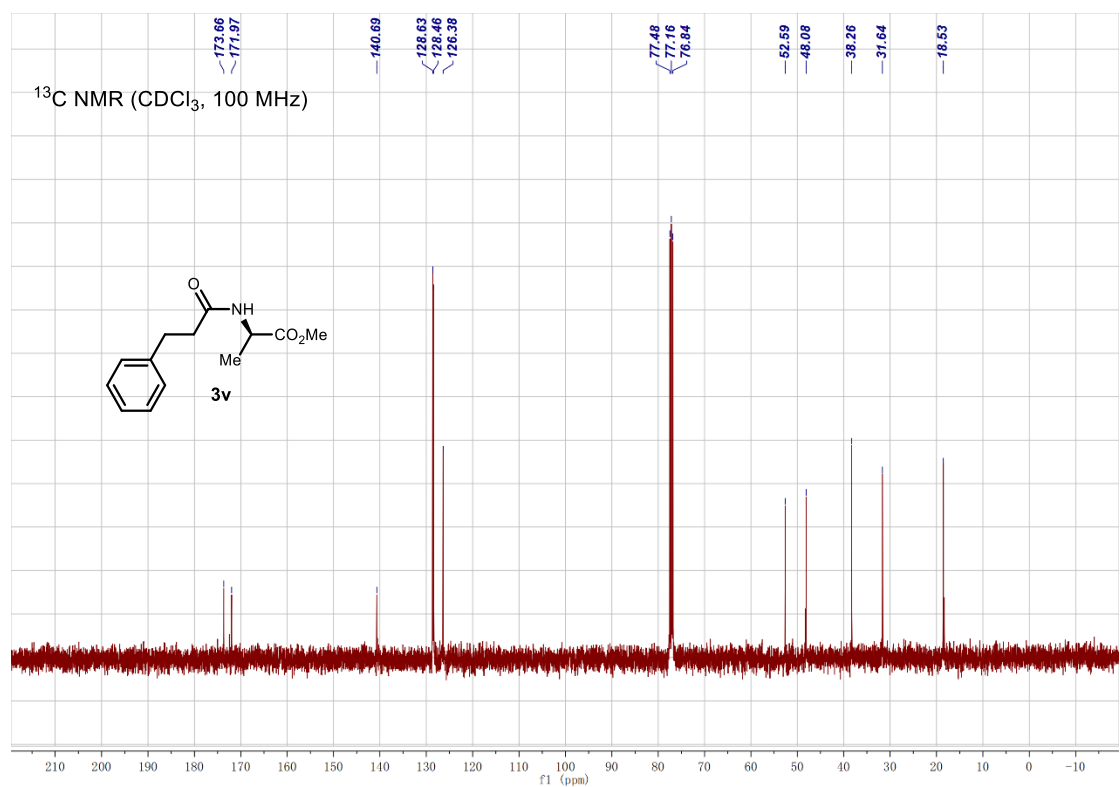
¹H NMR of **3u** (400 MHz, CDCl₃, 298 K)



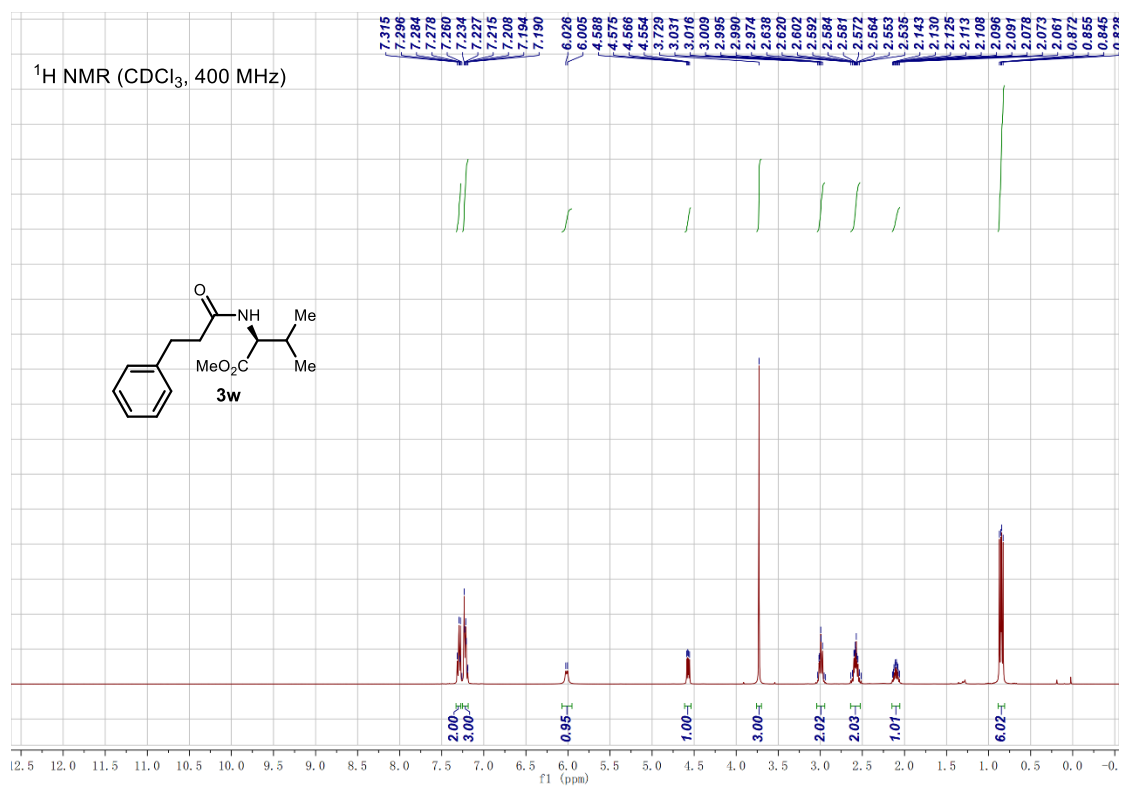
¹³C NMR of **3u** (150 MHz, CDCl₃, 298 K)



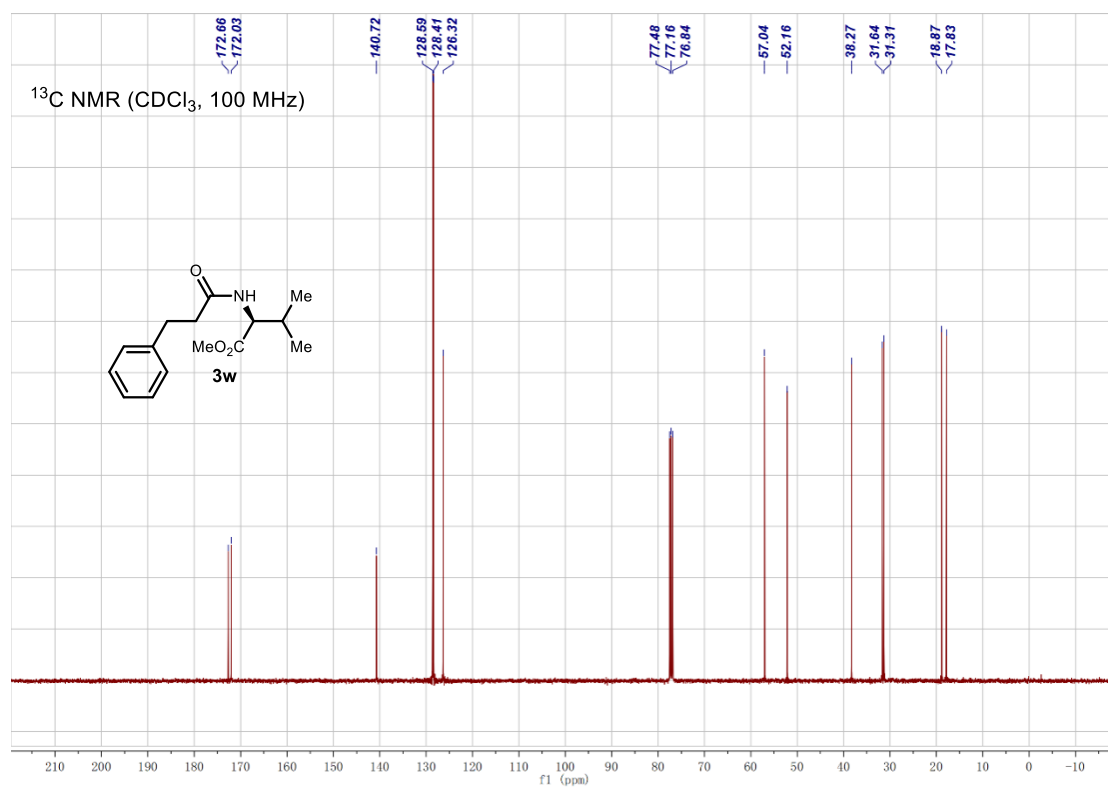
¹H NMR of **3v** (400 MHz, CDCl₃, 298 K)



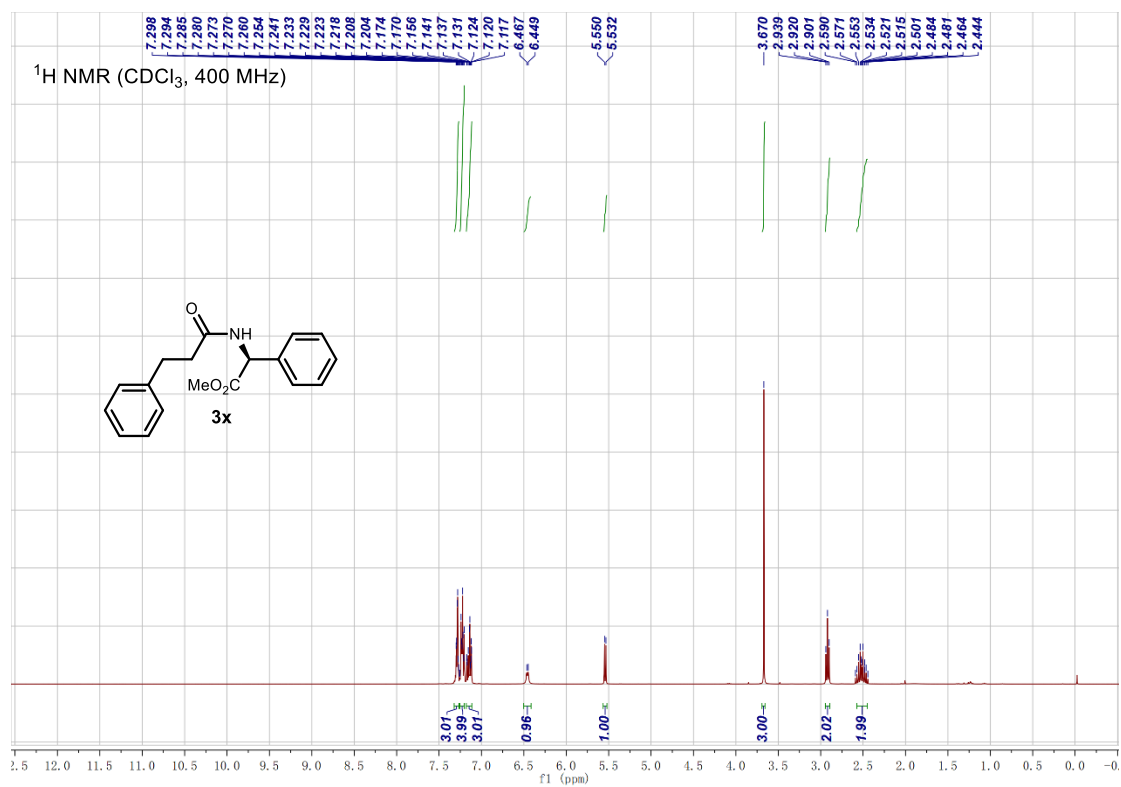
¹³C NMR of **3v** (100 MHz, CDCl₃, 298 K)



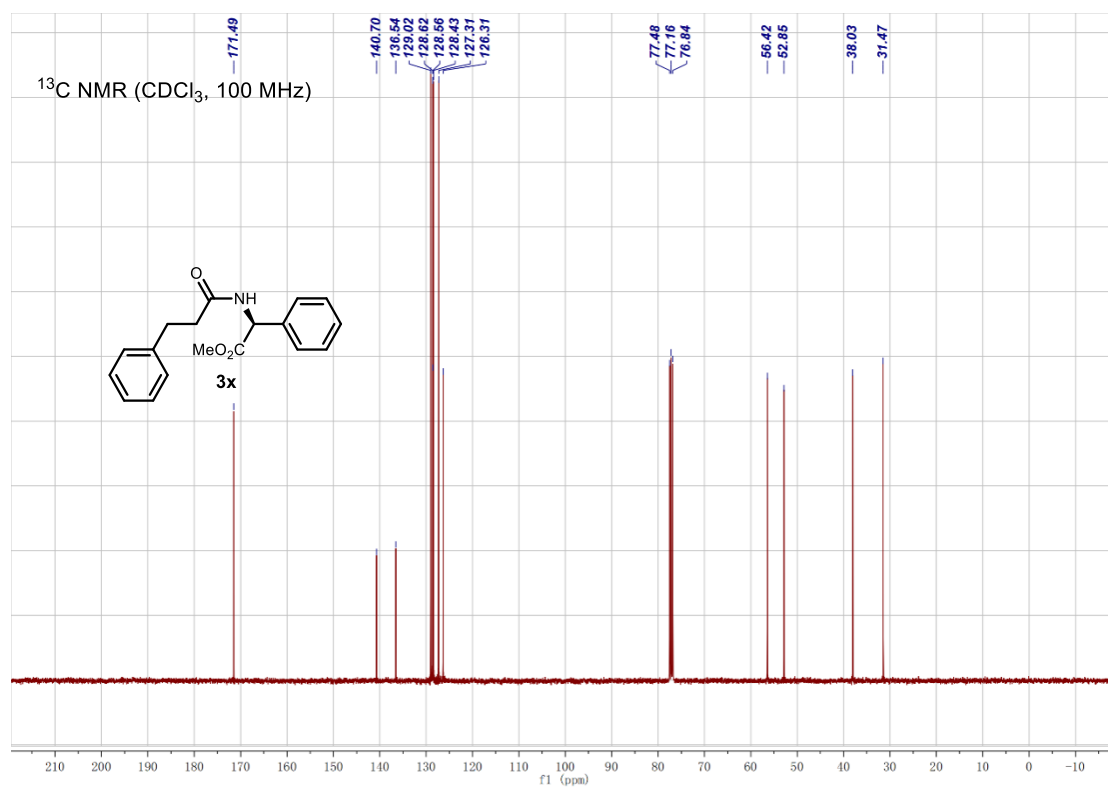
¹H NMR of **3w** (400 MHz, CDCl₃, 298 K)



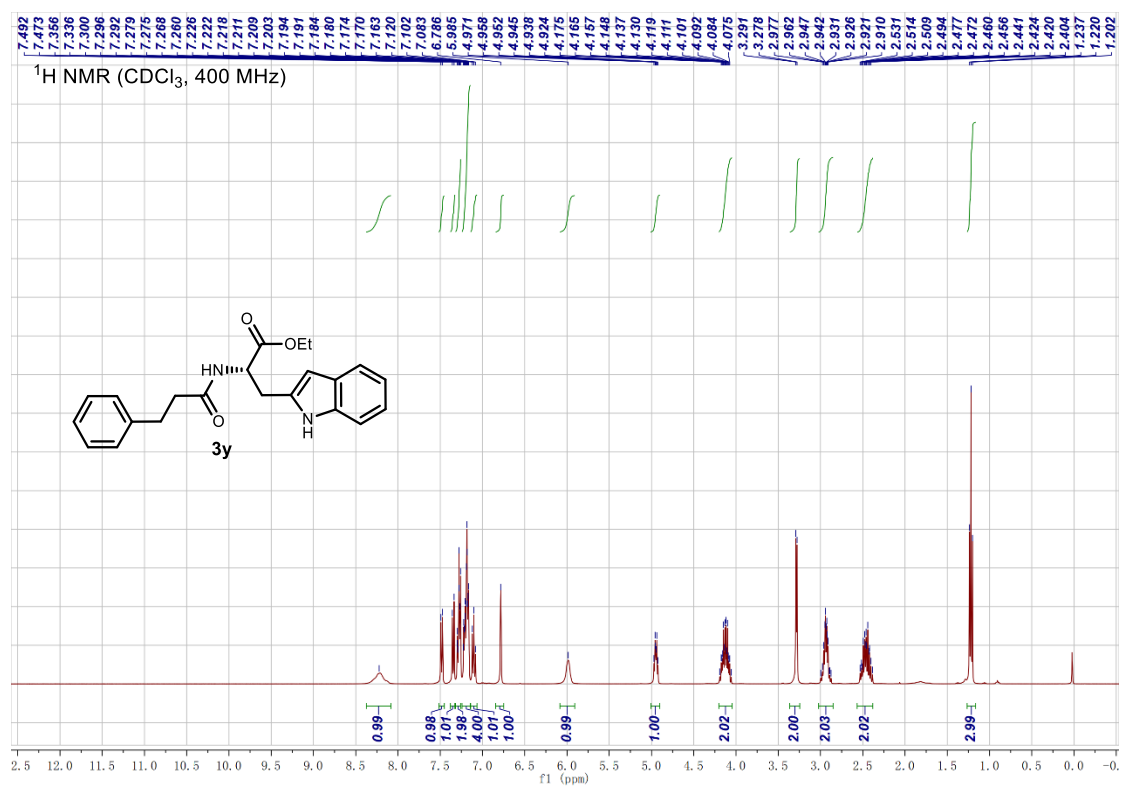
¹³C NMR of **3w** (100 MHz, CDCl₃, 298 K)



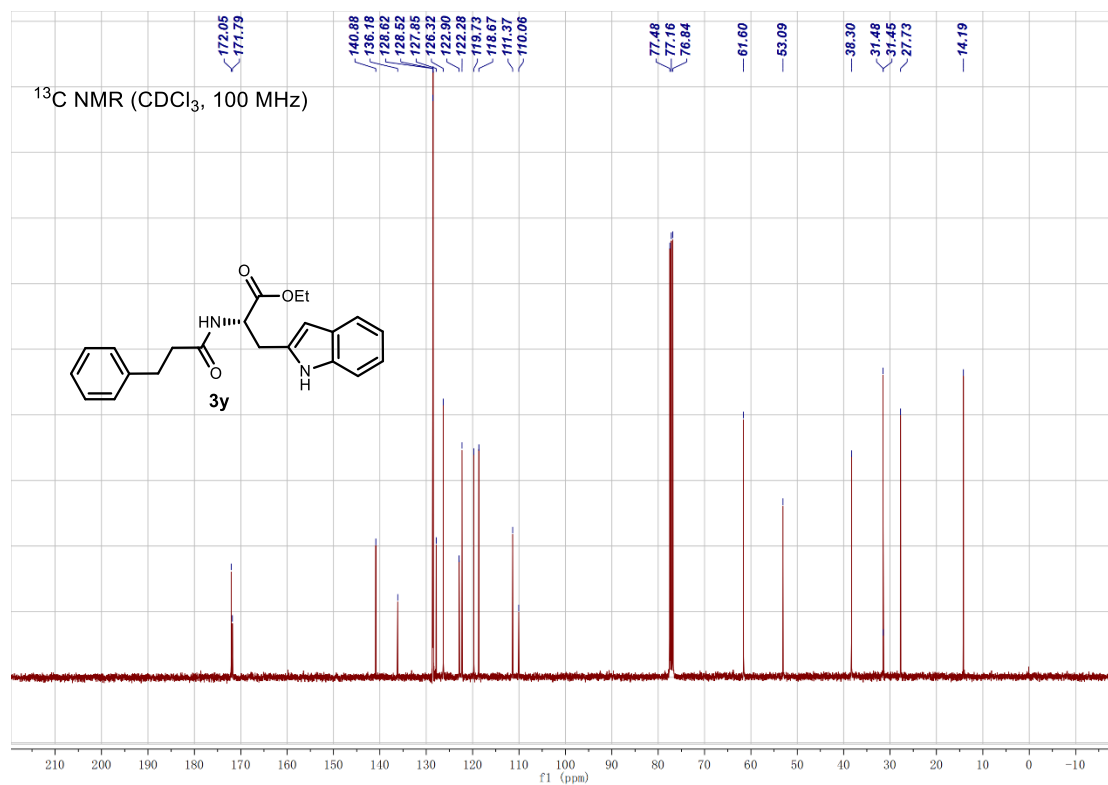
¹H NMR of **3x** (400 MHz, CDCl₃, 298 K)



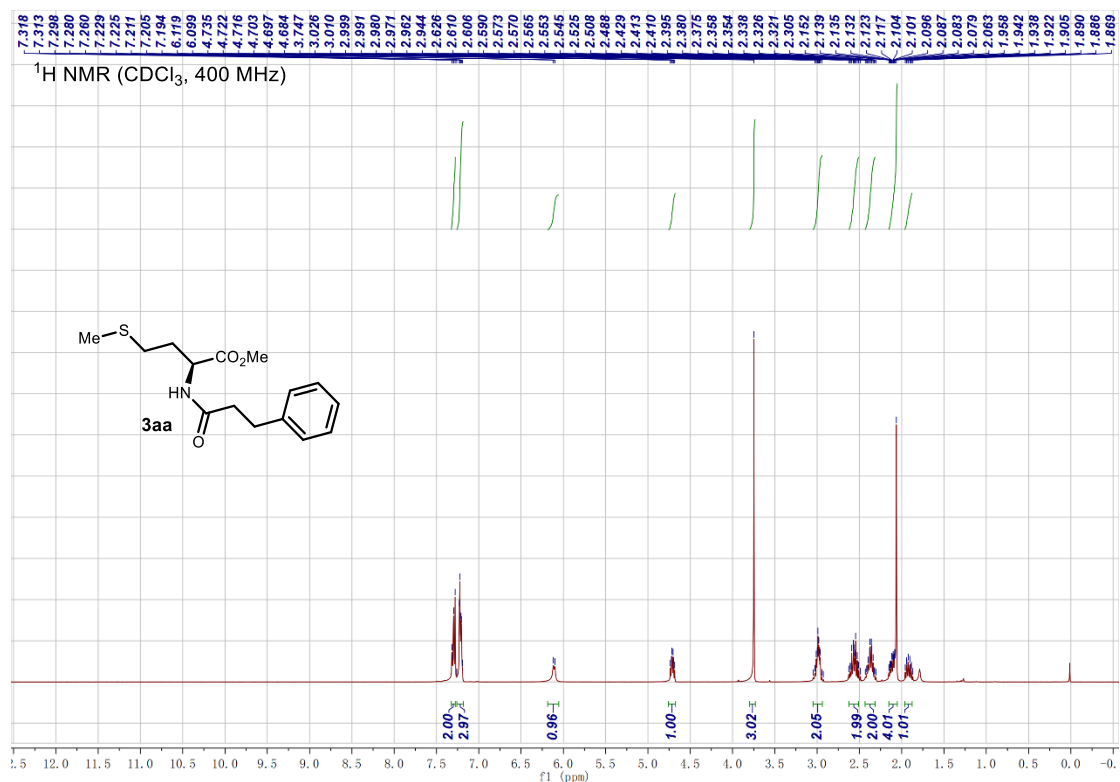
¹³C NMR of **3x** (100 MHz, CDCl₃, 298 K)



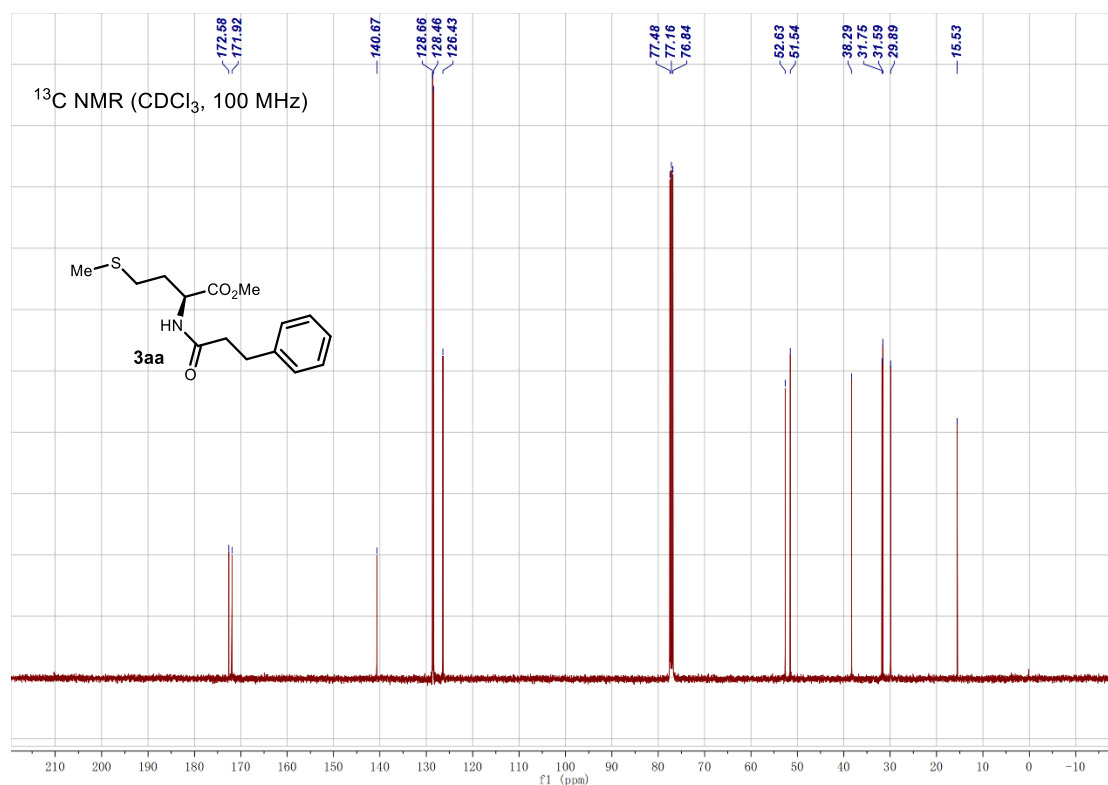
¹H NMR of **3y** (400 MHz, CDCl₃, 298 K)



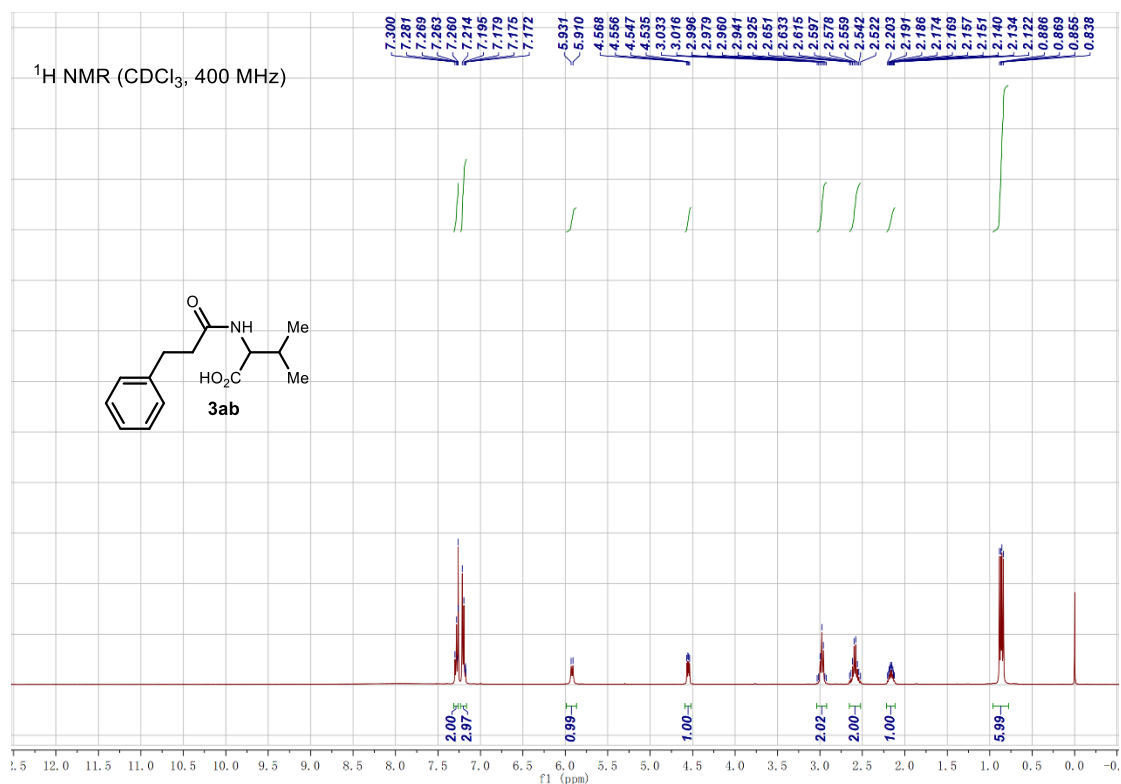
¹³C NMR of **3y** (100 MHz, CDCl₃, 298 K)



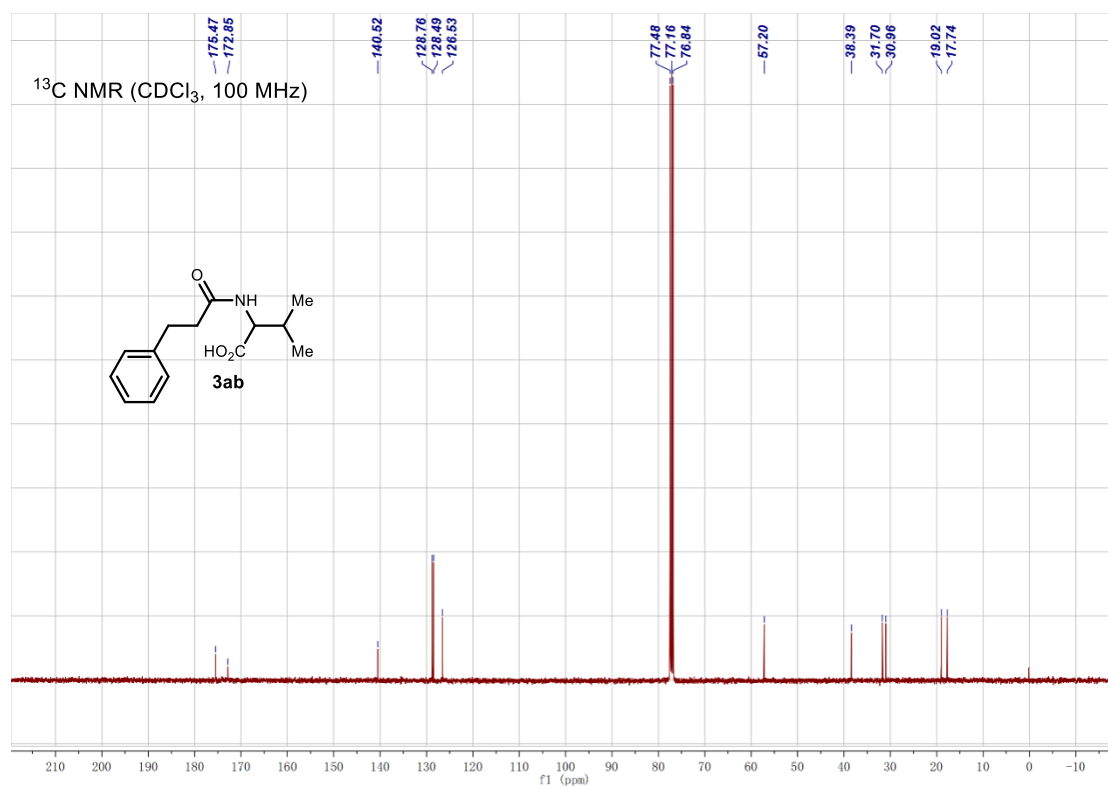
¹H NMR of **3aa** (400 MHz, CDCl₃, 298 K)



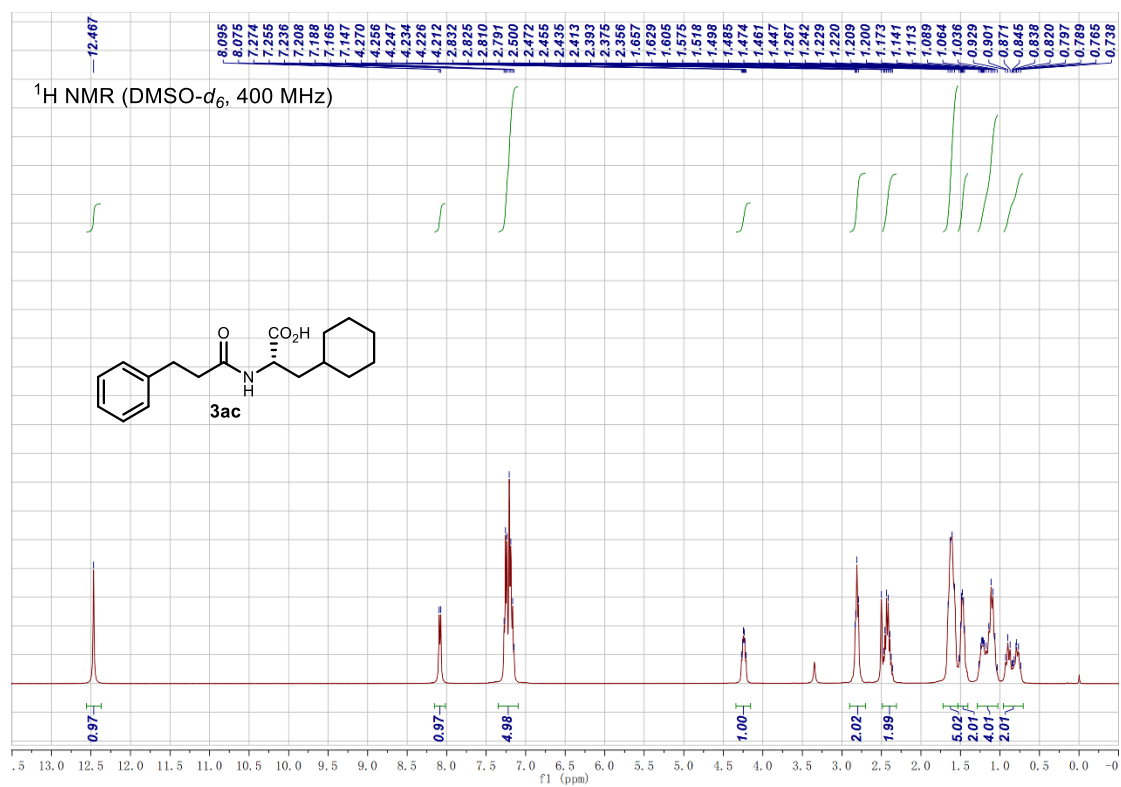
¹³C NMR of **3aa** (100 MHz, CDCl₃, 298 K)



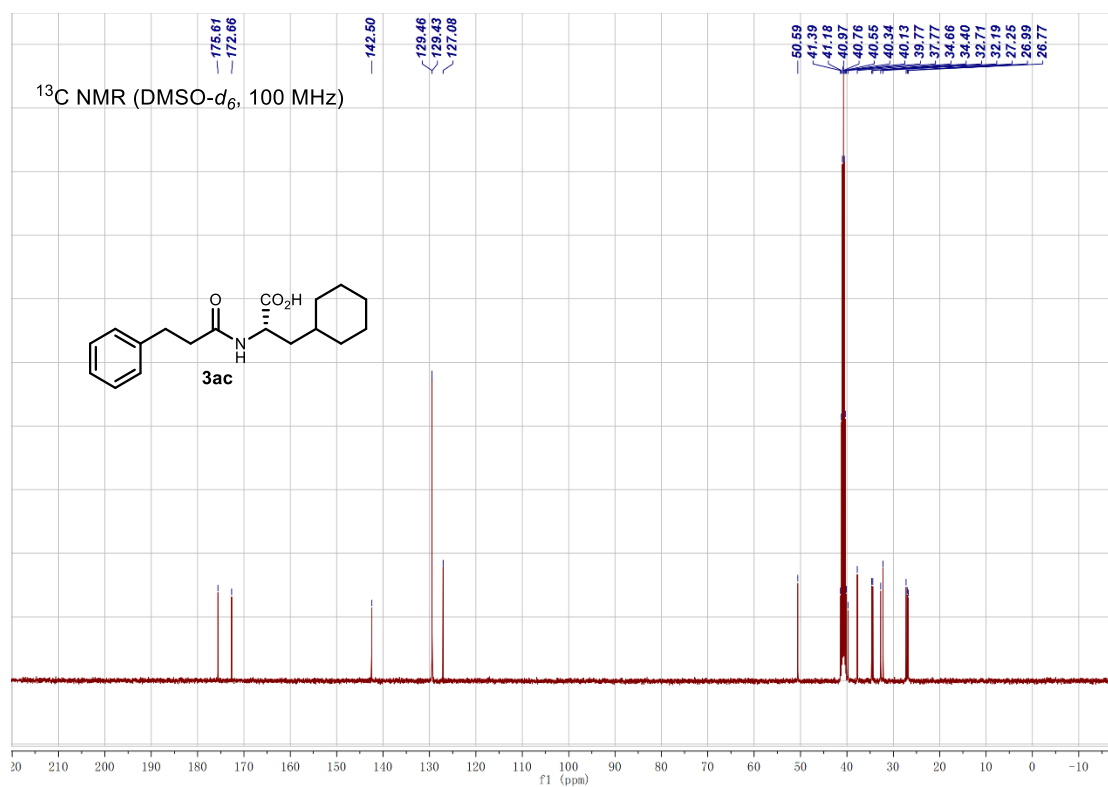
¹H NMR of **3ab** (400 MHz, CDCl₃, 298 K)



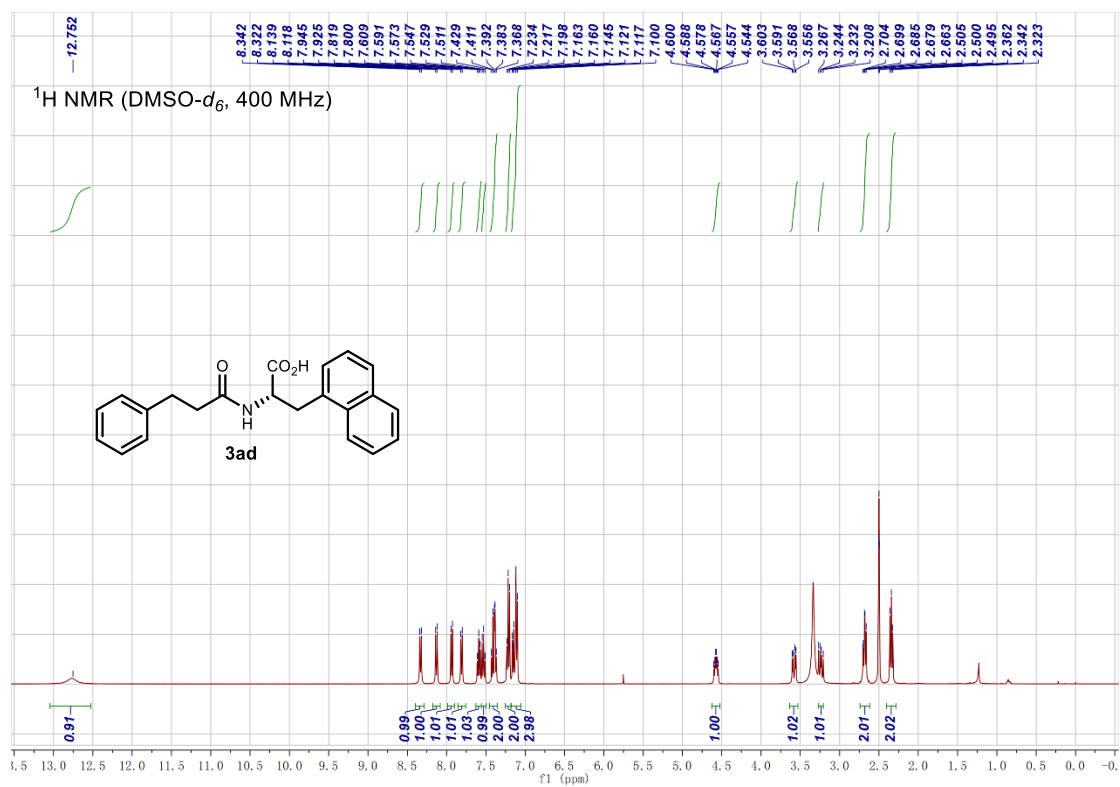
¹³C NMR of **3ab** (100 MHz, CDCl₃, 298 K)



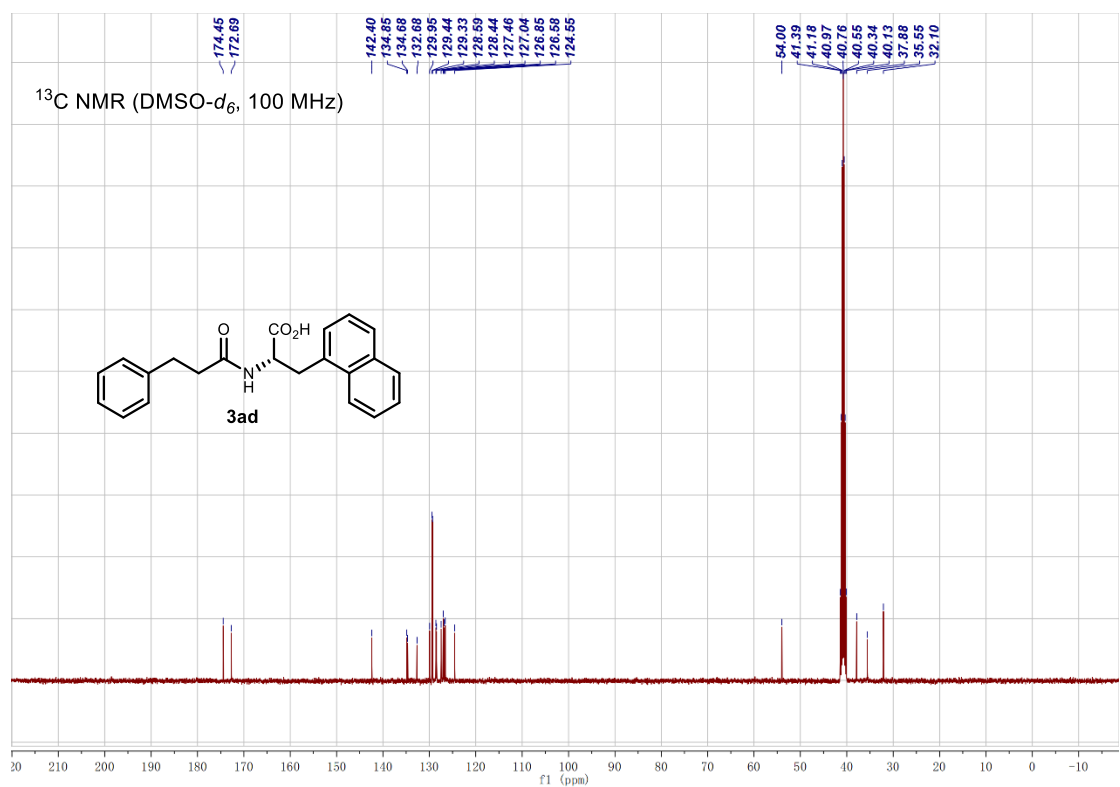
¹H NMR of **3ac** (400 MHz, DMSO-*d*₆, 298 K)



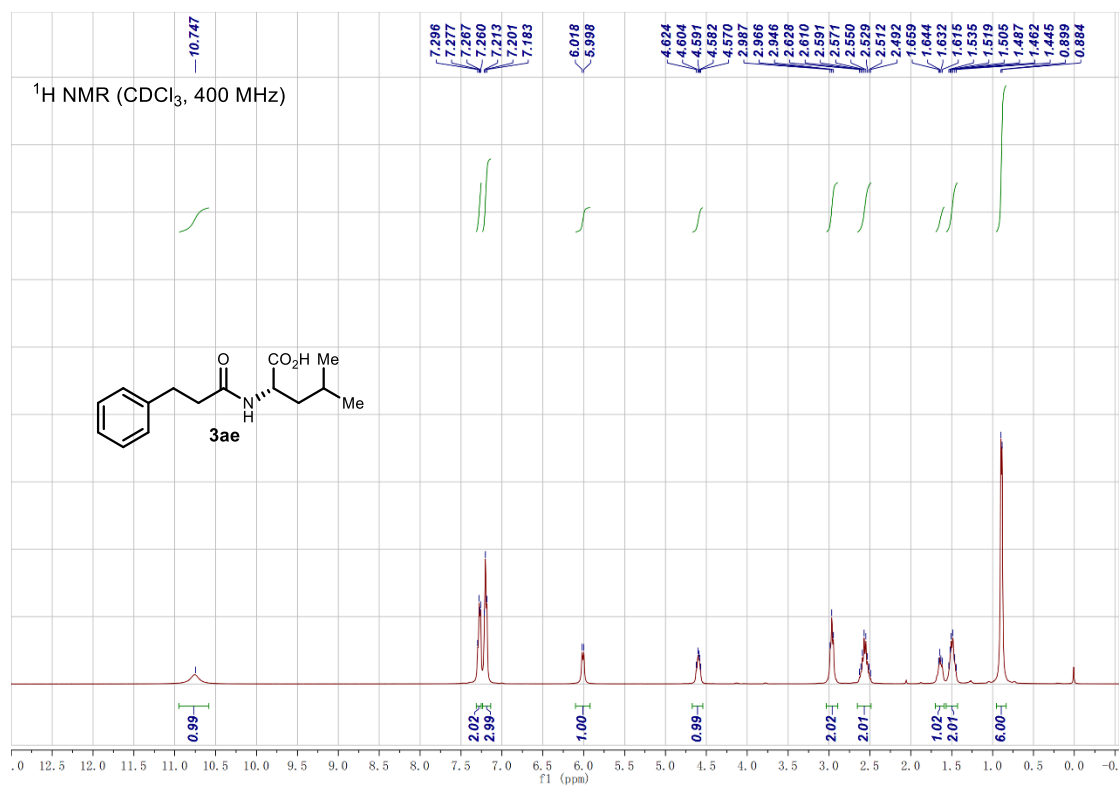
¹³C NMR of **3ac** (100 MHz, DMSO-*d*₆, 298 K)



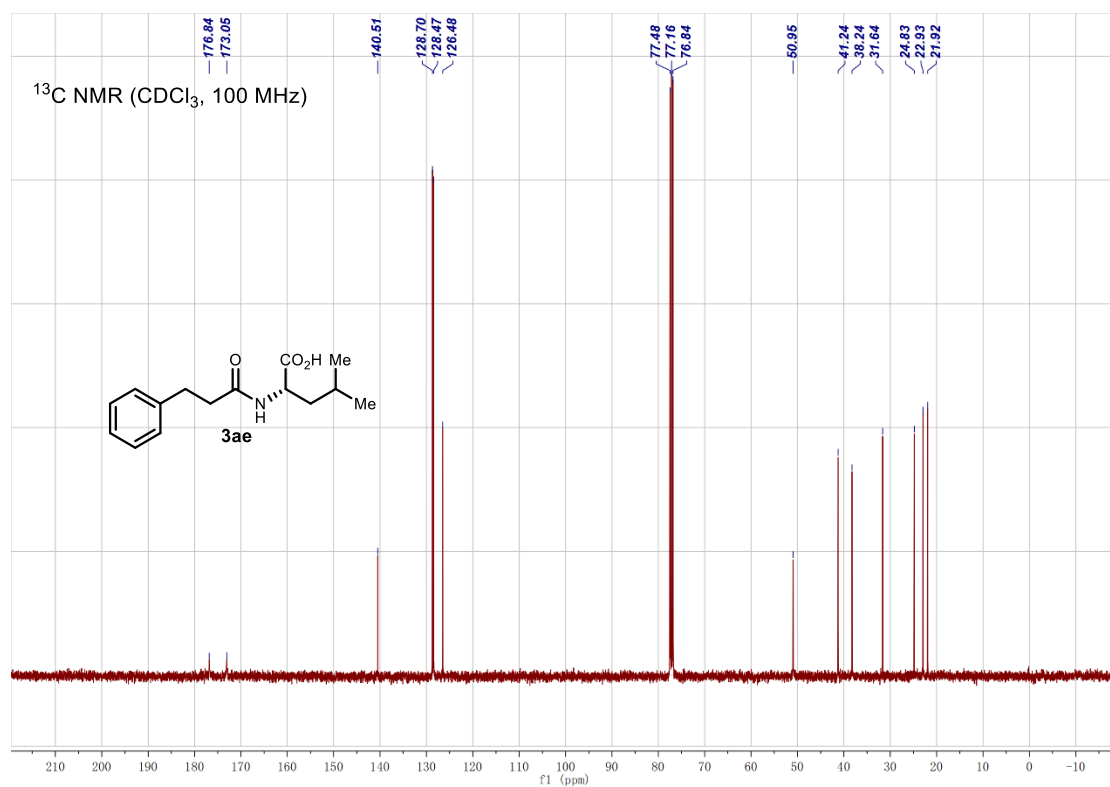
¹H NMR of **3ad** (400 MHz, DMSO-*d*₆, 298 K)



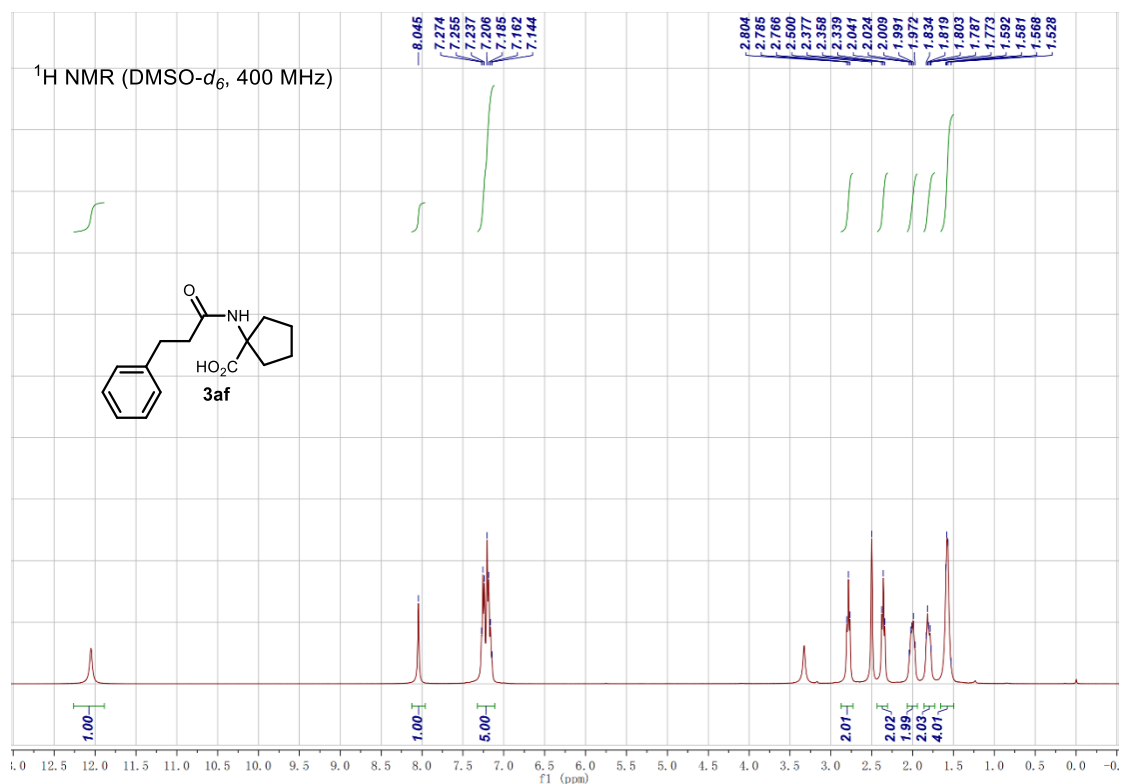
¹³C NMR of **3ad** (100 MHz, DMSO-*d*₆, 298 K)



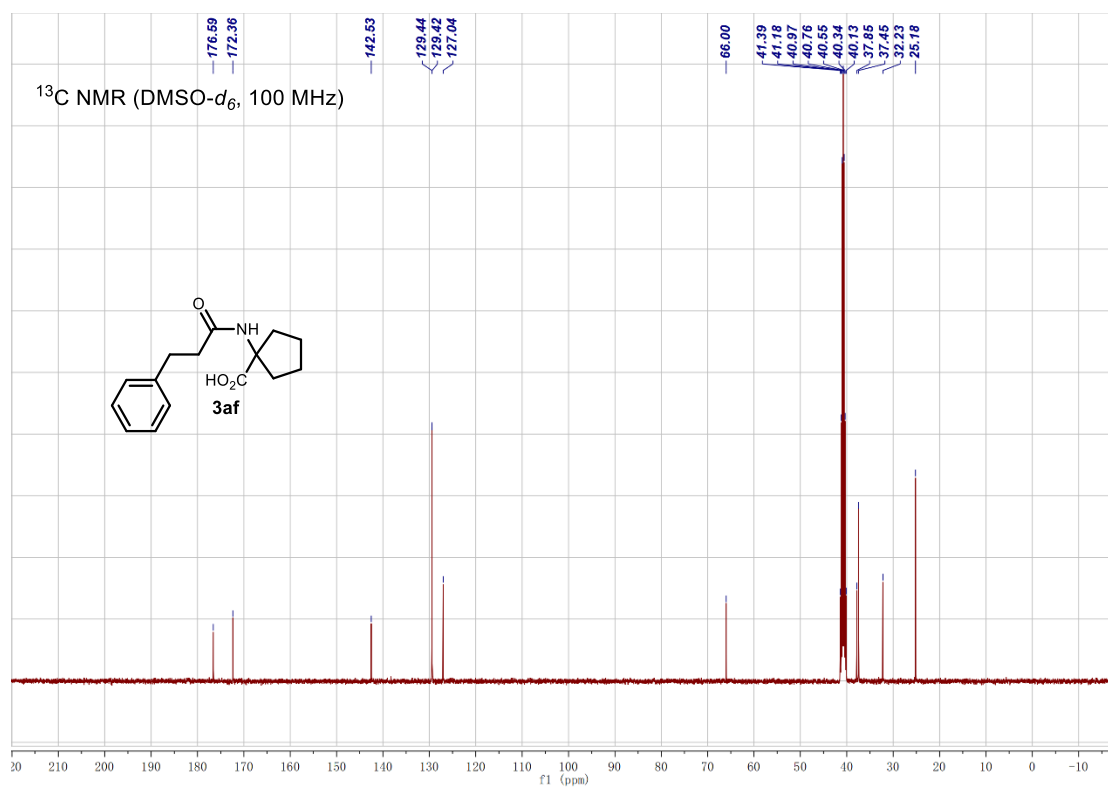
¹H NMR of **3ae** (400 MHz, CDCl₃, 298 K)



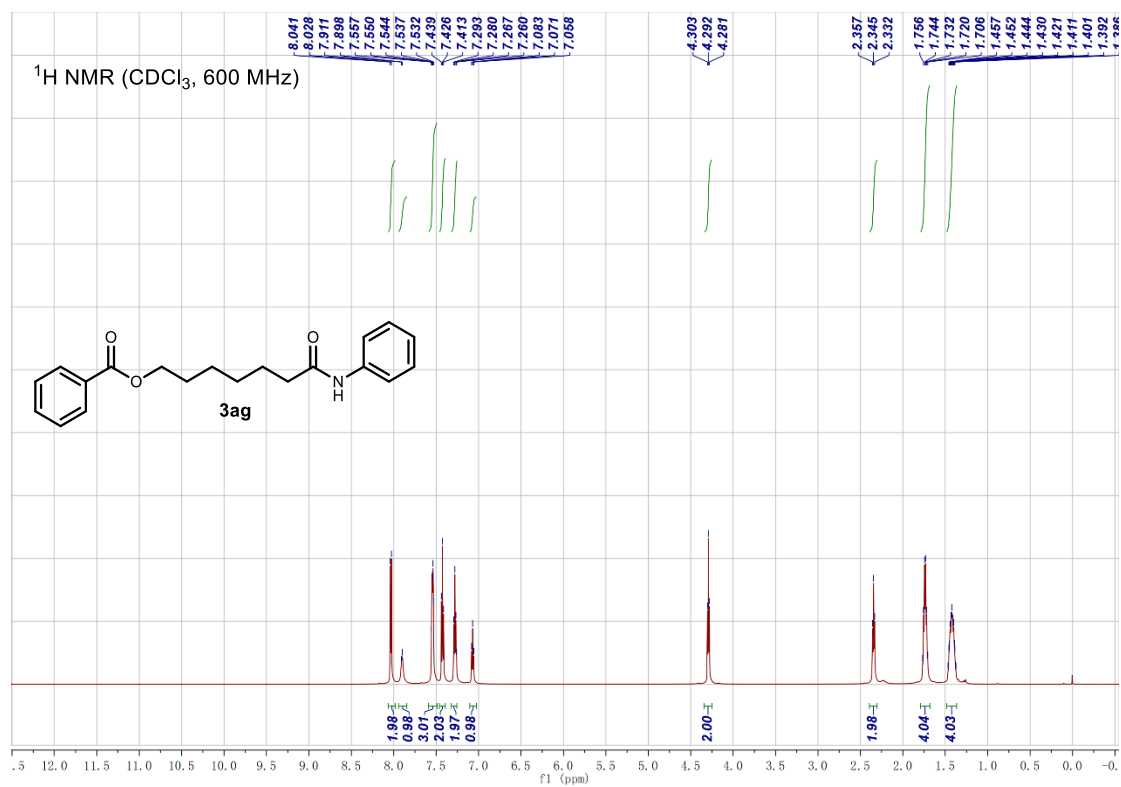
¹³C NMR of **3ae** (100 MHz, CDCl₃, 298 K)



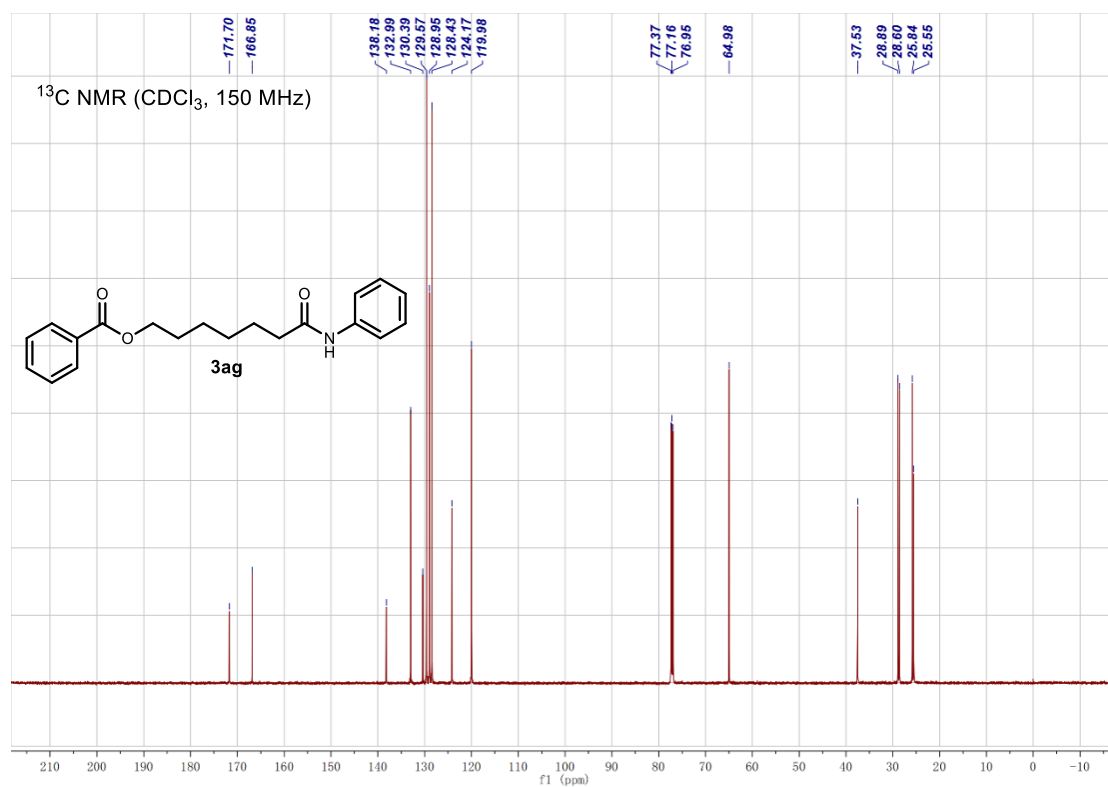
¹H NMR of **3af** (400 MHz, DMSO-*d*₆, 298 K)



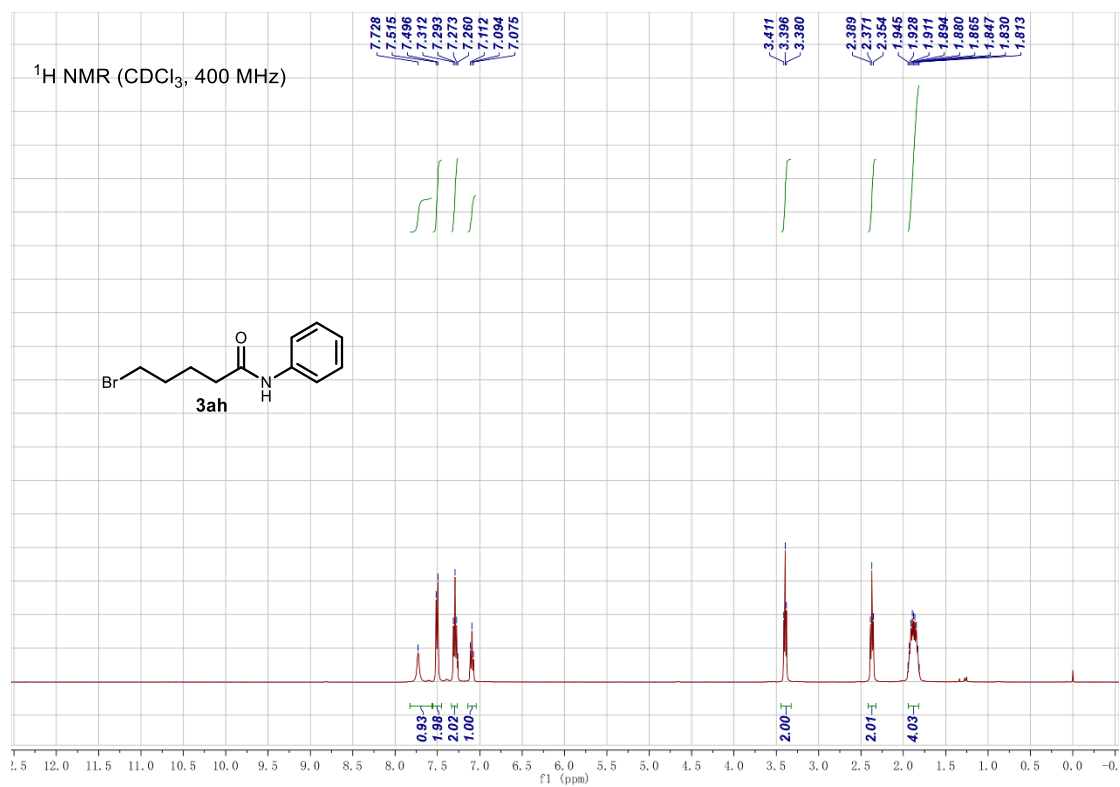
¹³C NMR of **3af** (100 MHz, DMSO-*d*₆, 298 K)



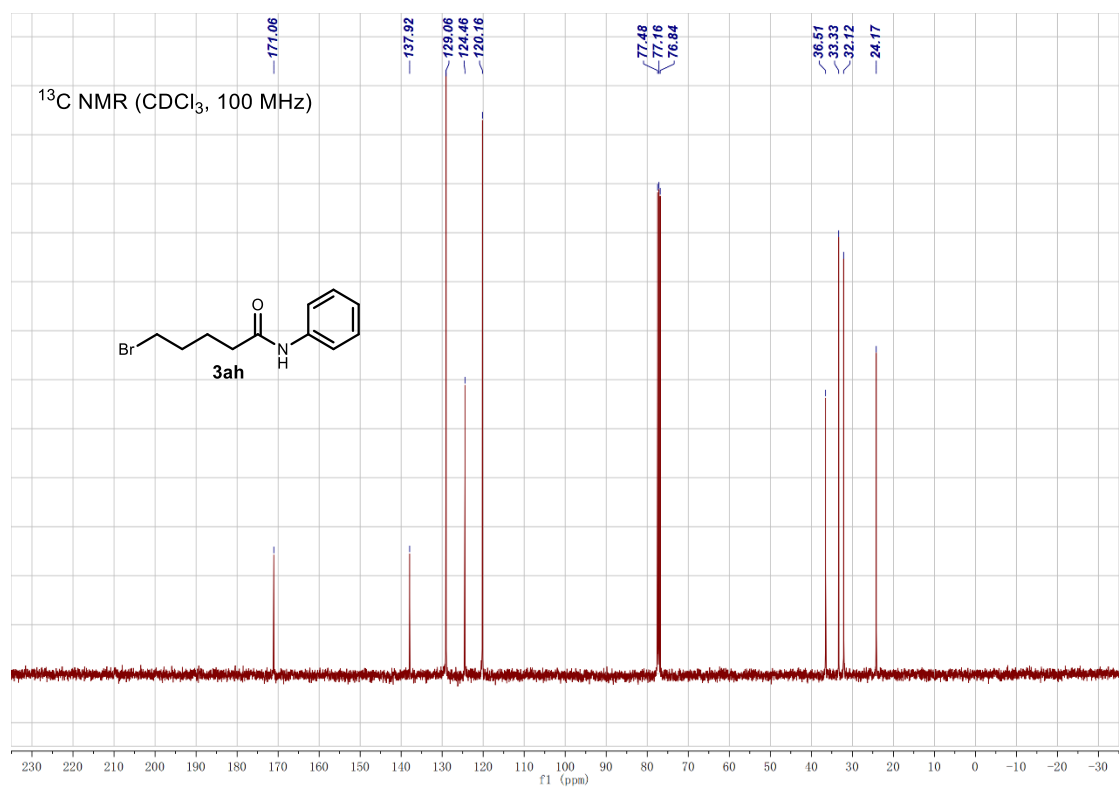
¹H NMR of **3ag** (600 MHz, CDCl₃, 298 K)



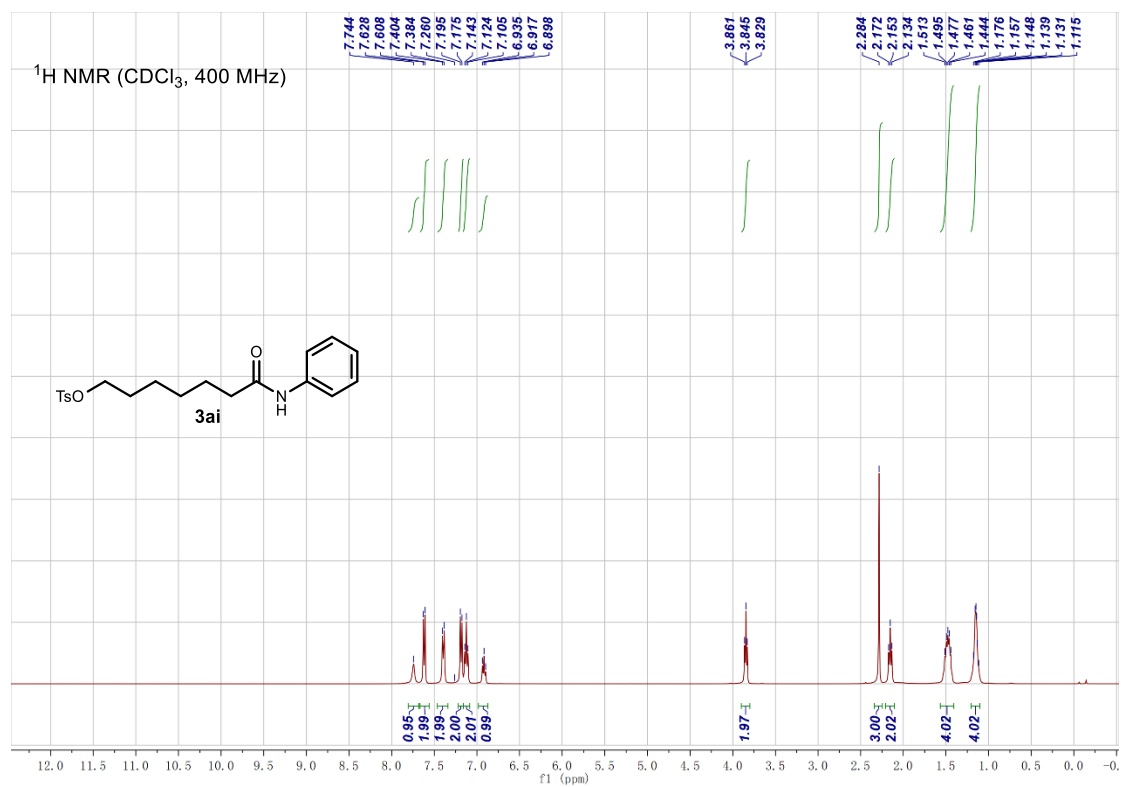
¹³C NMR of **3ag** (150 MHz, CDCl₃, 298 K)



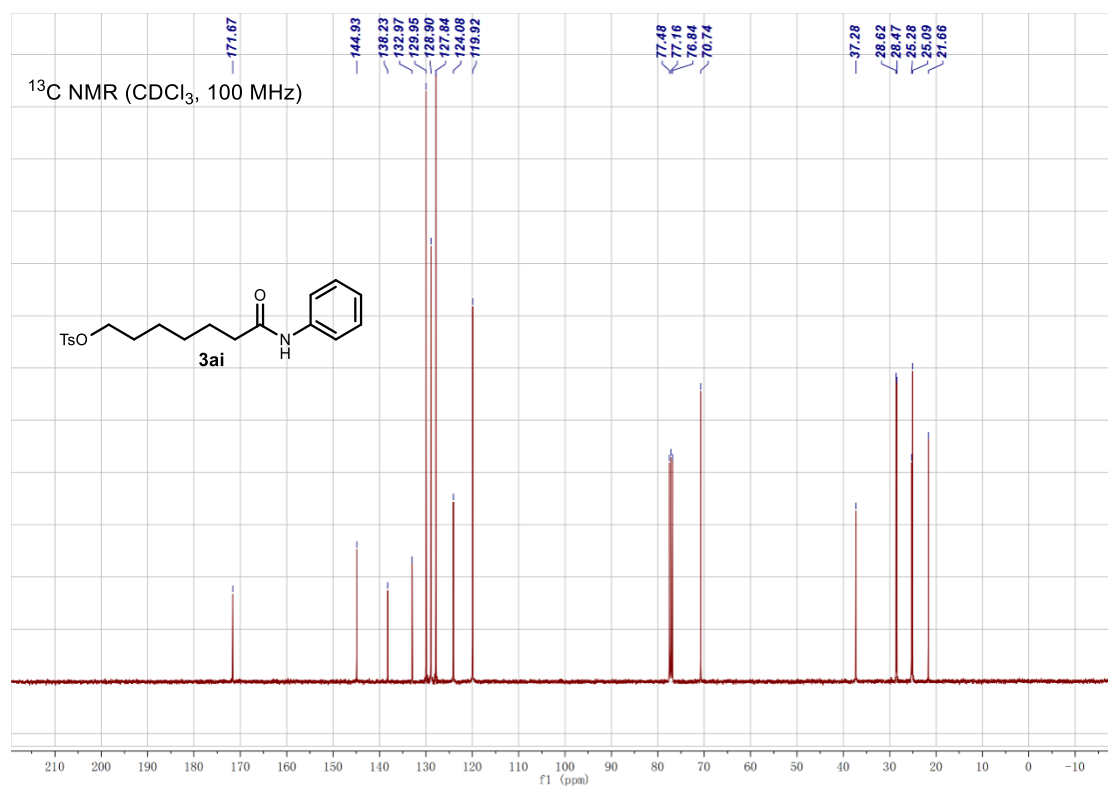
¹H NMR of **3ah** (400 MHz, CDCl₃, 298 K)



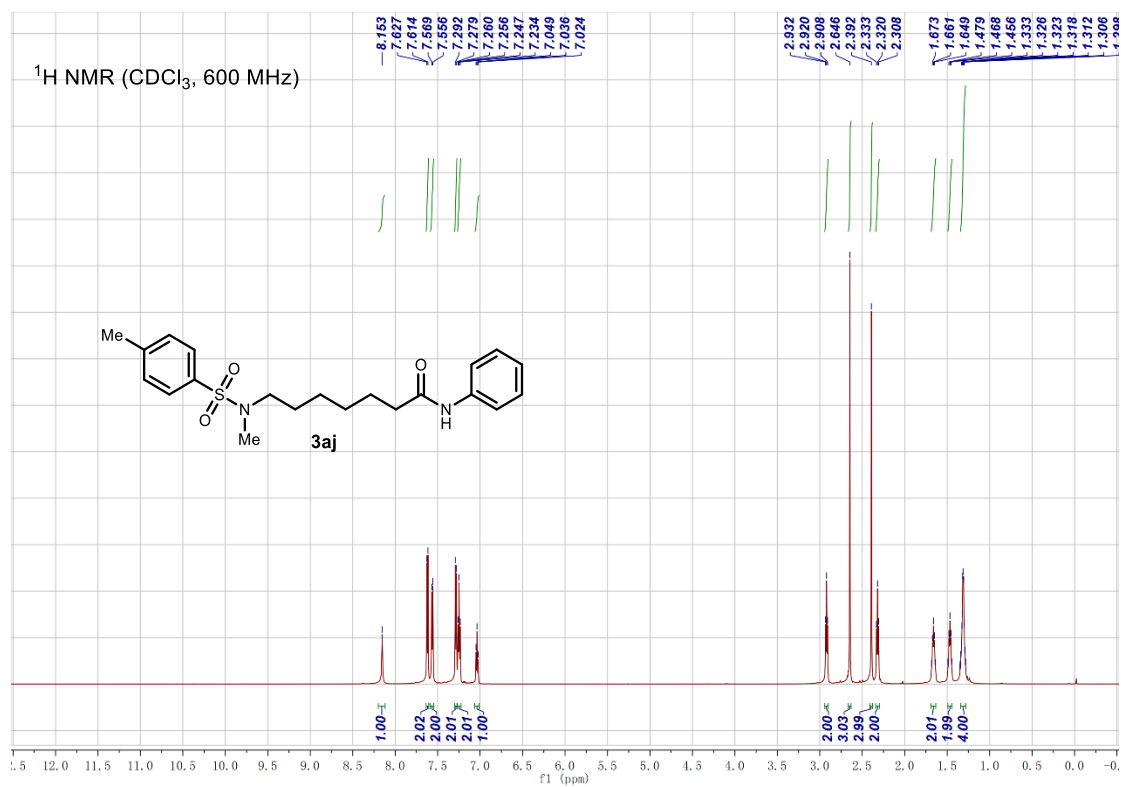
¹³C NMR of **3ah** (100 MHz, CDCl₃, 298 K)



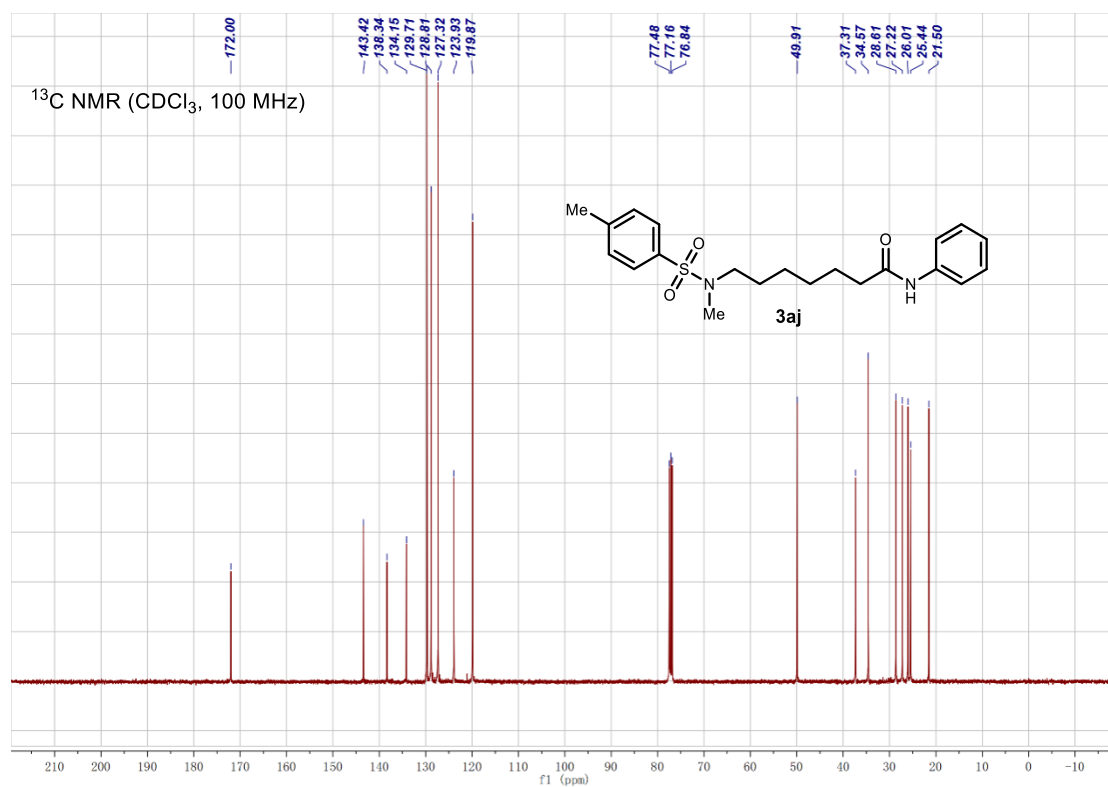
¹H NMR of **3ai** (400 MHz, CDCl₃, 298 K)



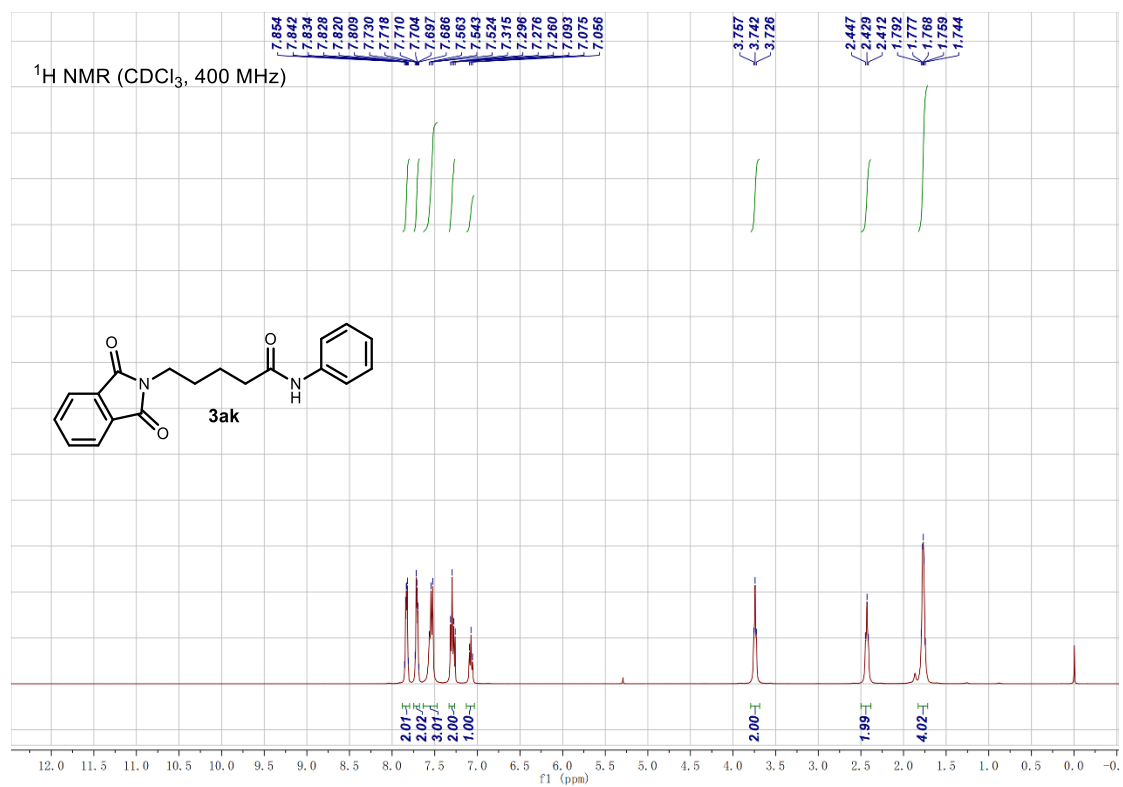
¹³C NMR of **3ai** (100 MHz, CDCl₃, 298 K)



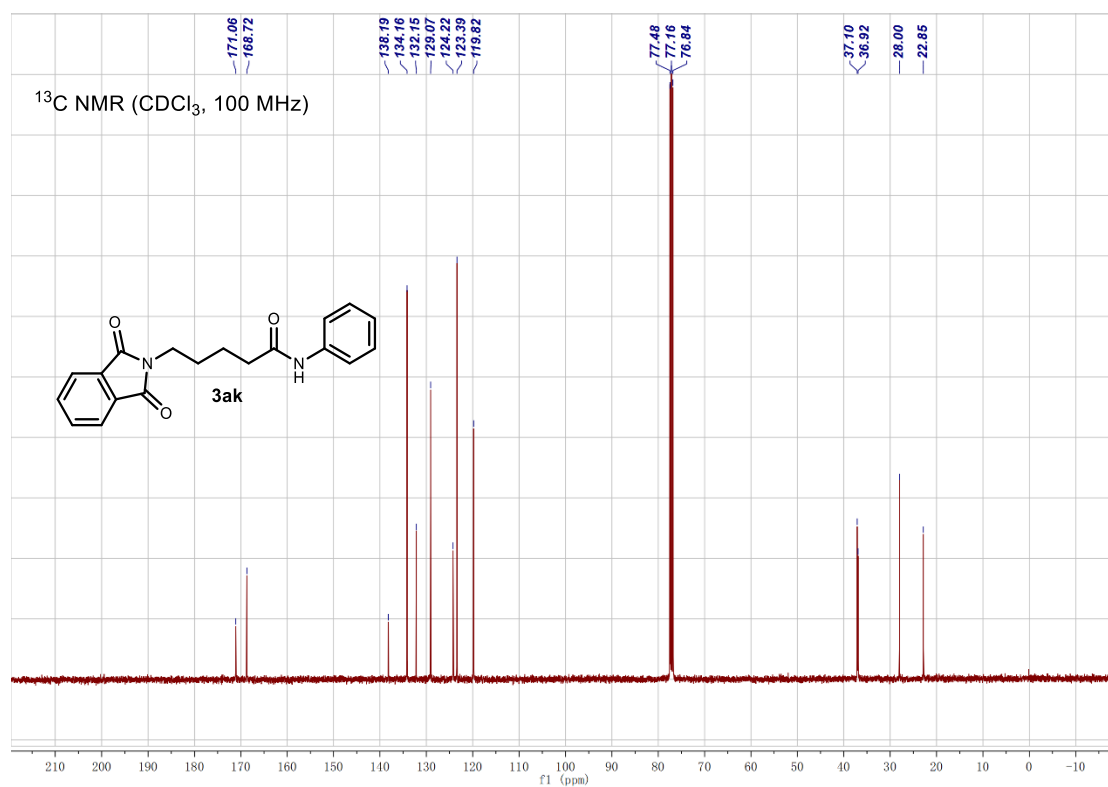
¹H NMR of **3aj** (600 MHz, CDCl₃, 298 K)



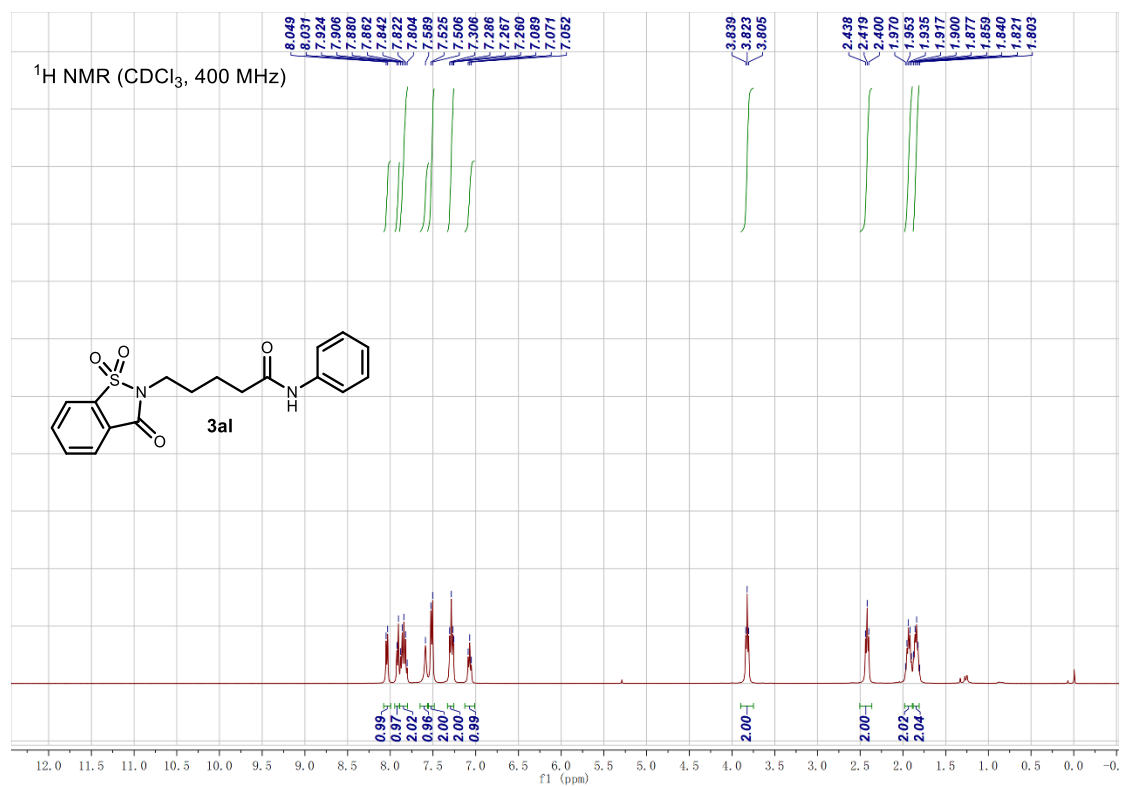
¹³C NMR of **3aj** (100 MHz, CDCl₃, 298 K)



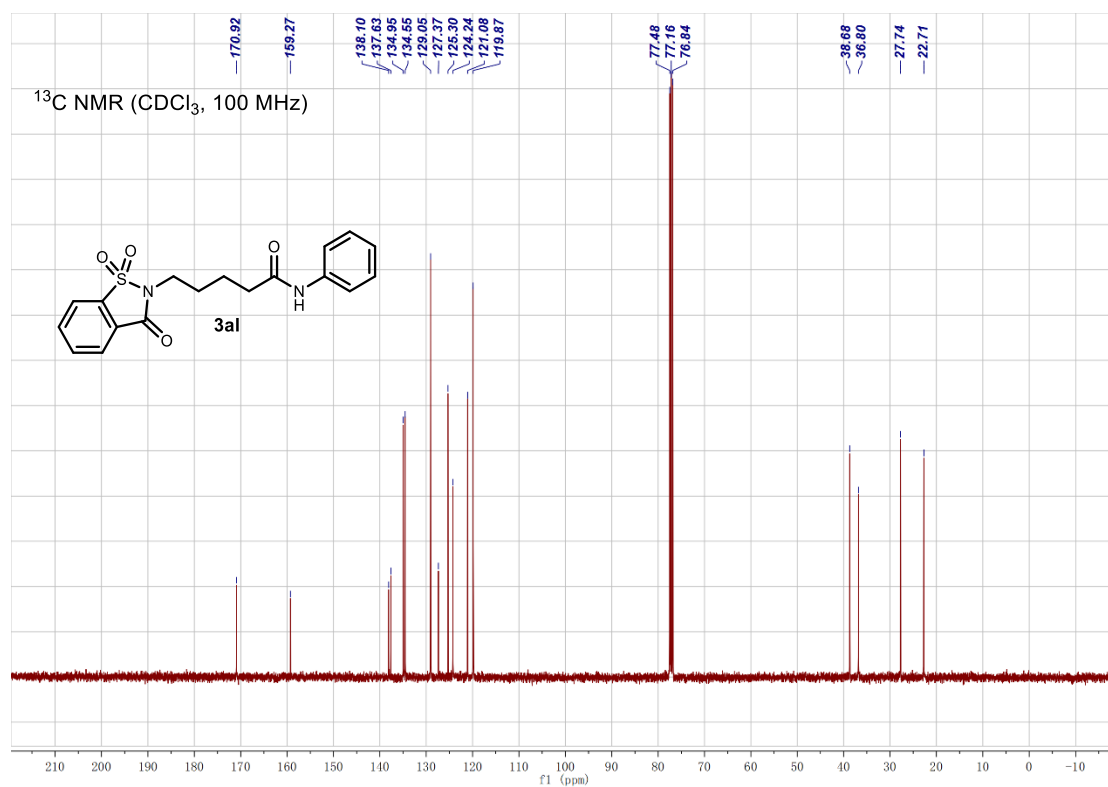
¹H NMR of **3ak** (400 MHz, CDCl₃, 298 K)



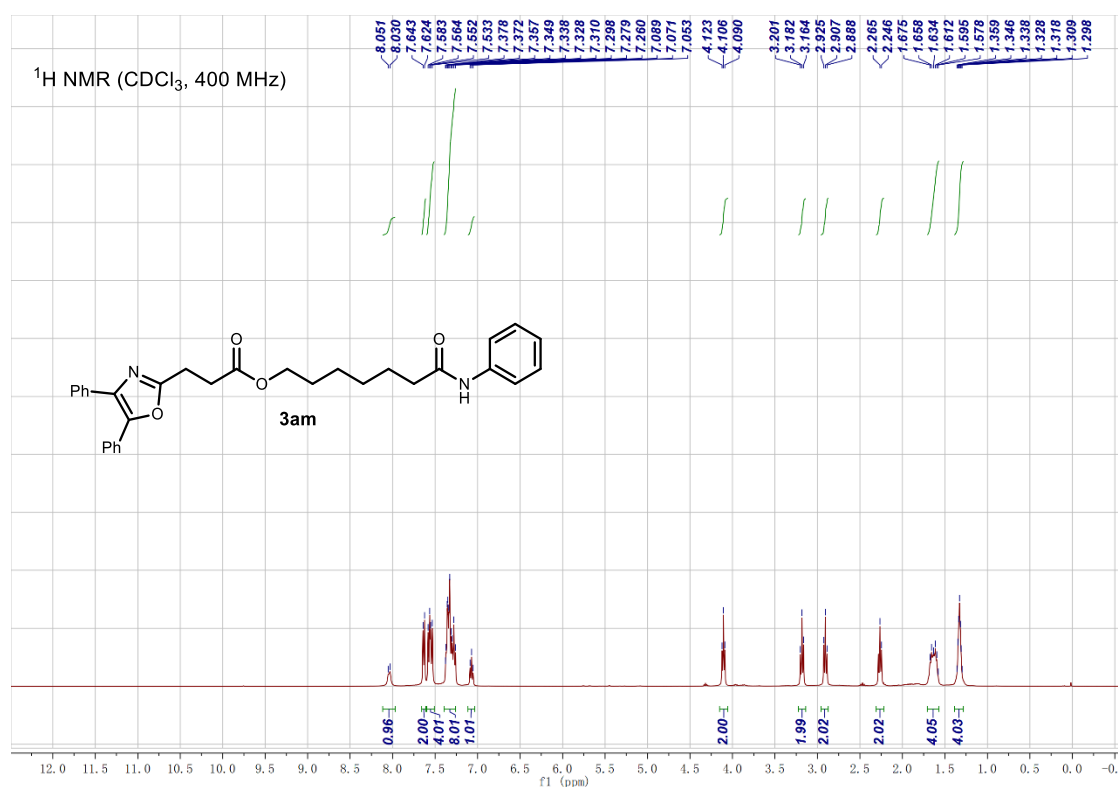
¹³C NMR of **3ak** (100 MHz, CDCl₃, 298 K)



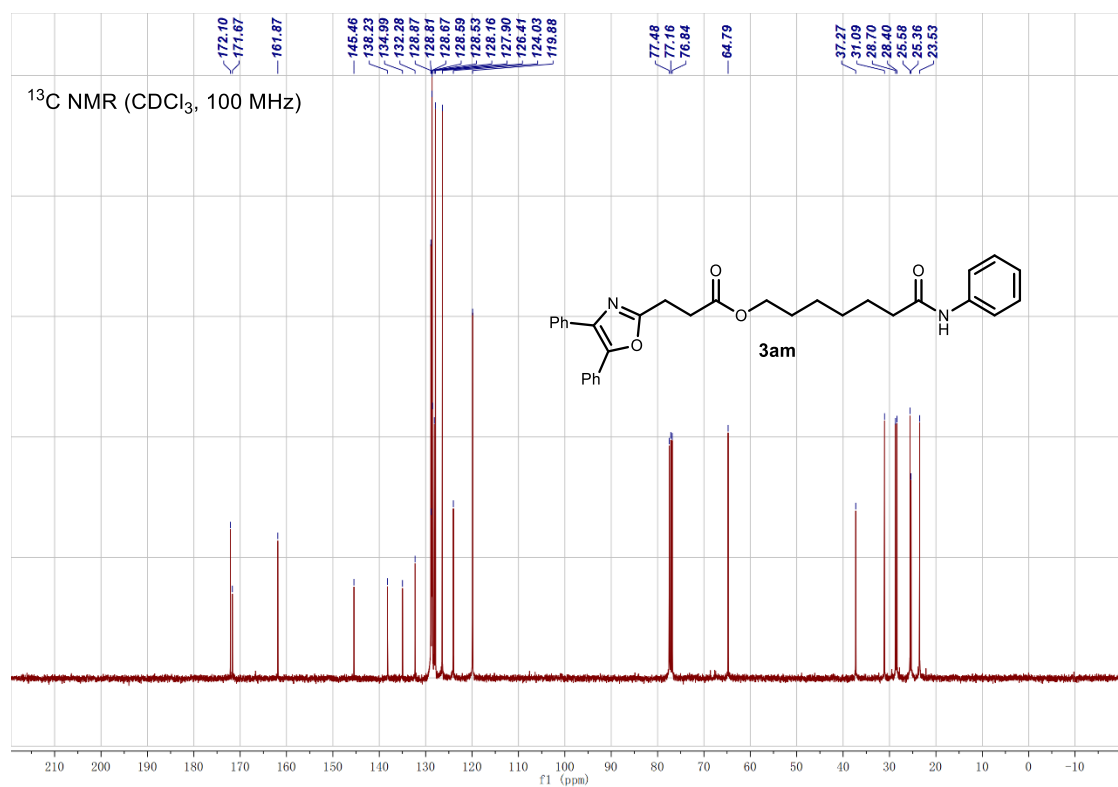
¹H NMR of **3al** (400 MHz, CDCl₃, 298 K)



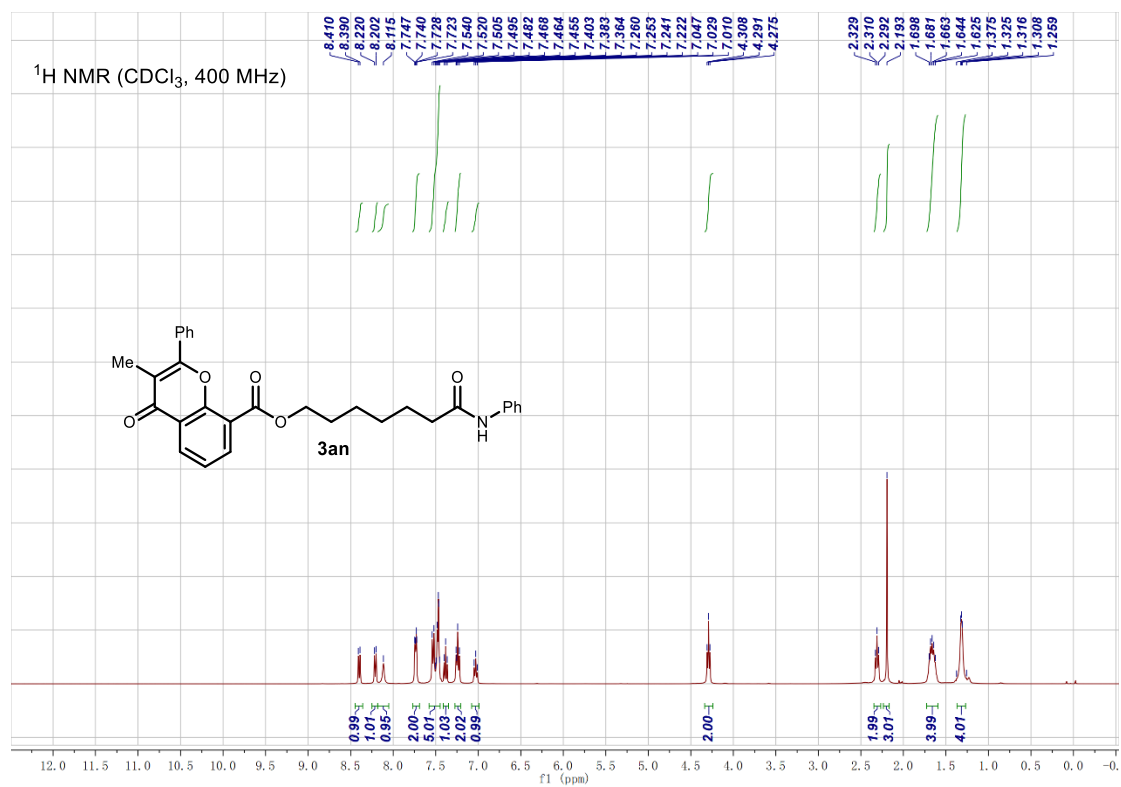
¹³C NMR of **3al** (100 MHz, CDCl₃, 298 K)



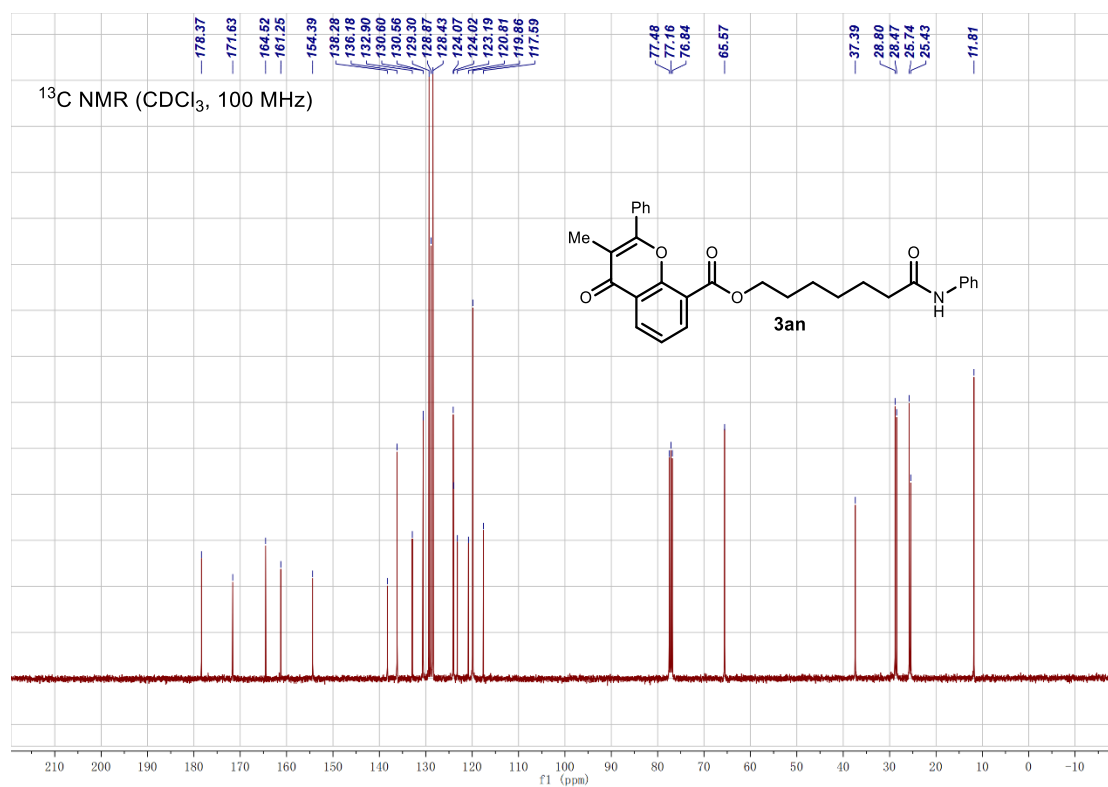
¹H NMR of **3am** (400 MHz, CDCl₃, 298 K)



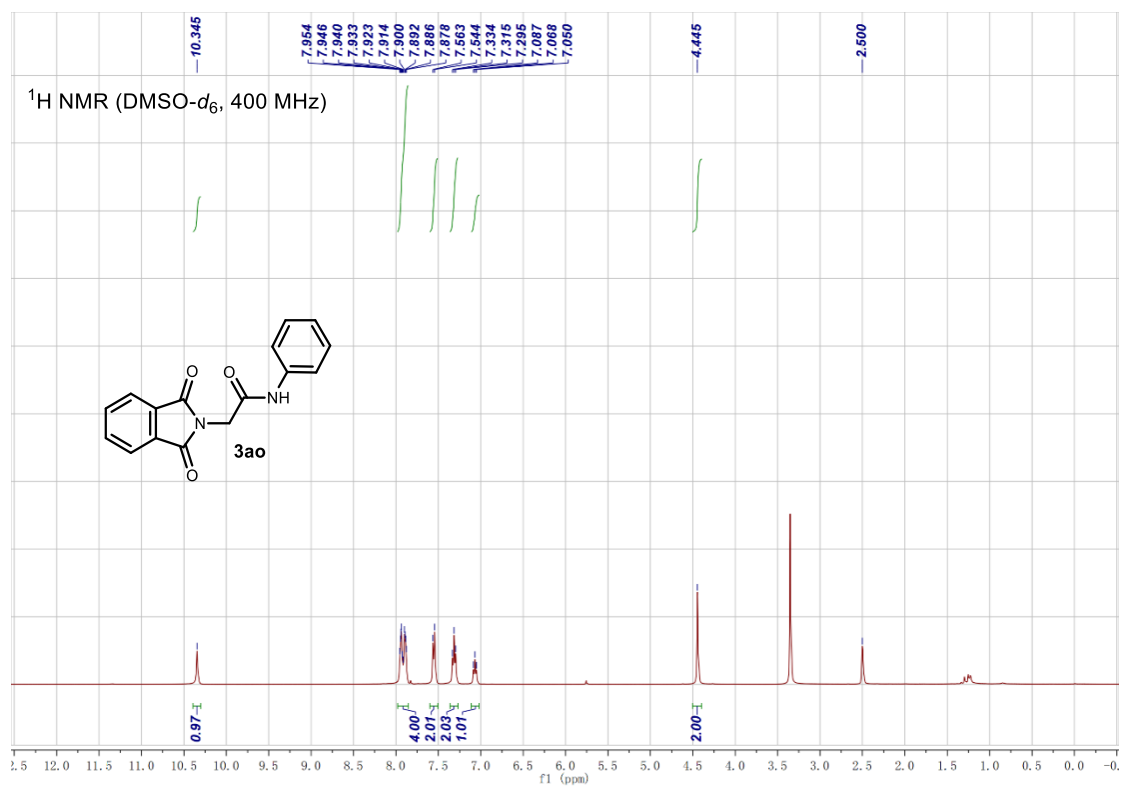
¹³C NMR of **3am** (100 MHz, CDCl₃, 298 K)



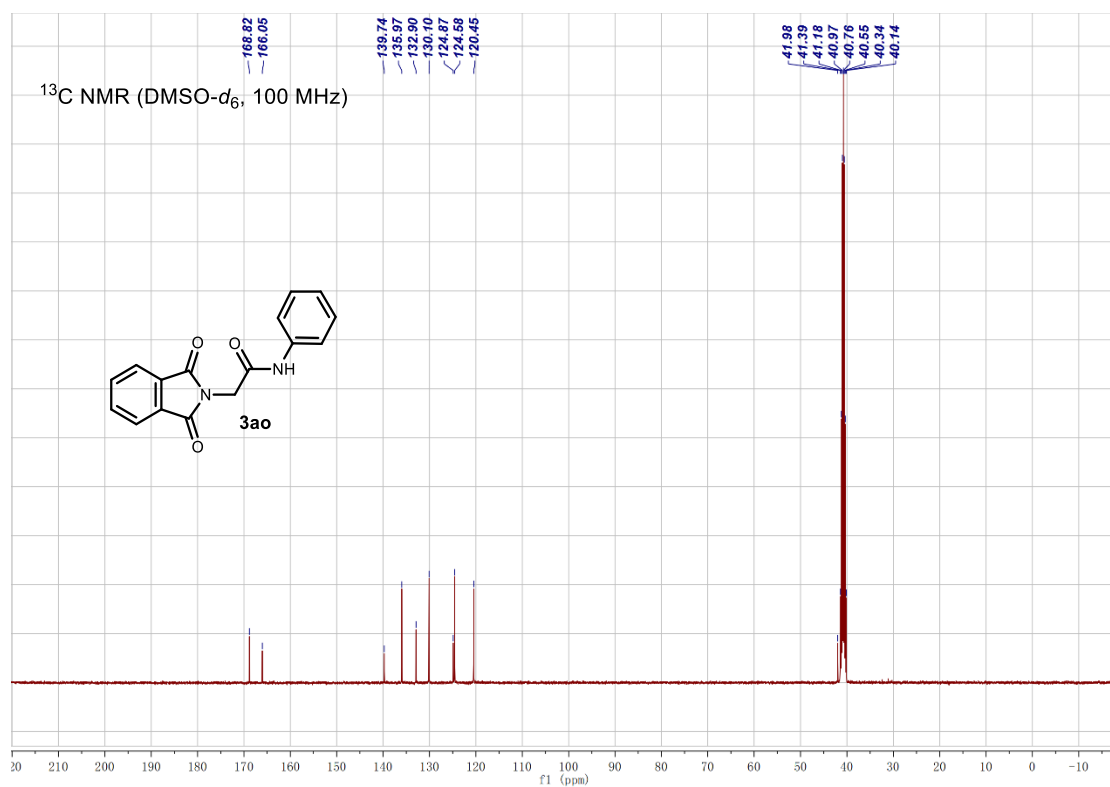
¹H NMR of **3an** (400 MHz, CDCl₃, 298 K)



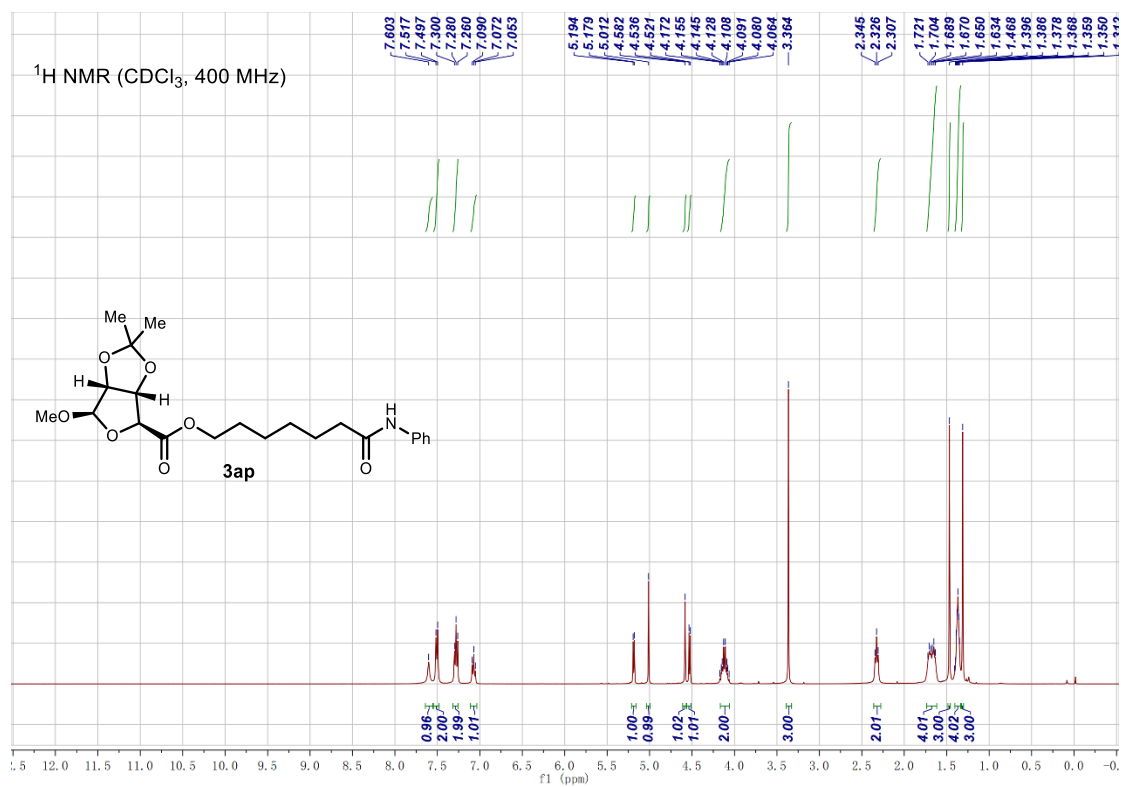
¹³C NMR of **3an** (100 MHz, CDCl₃, 298 K)



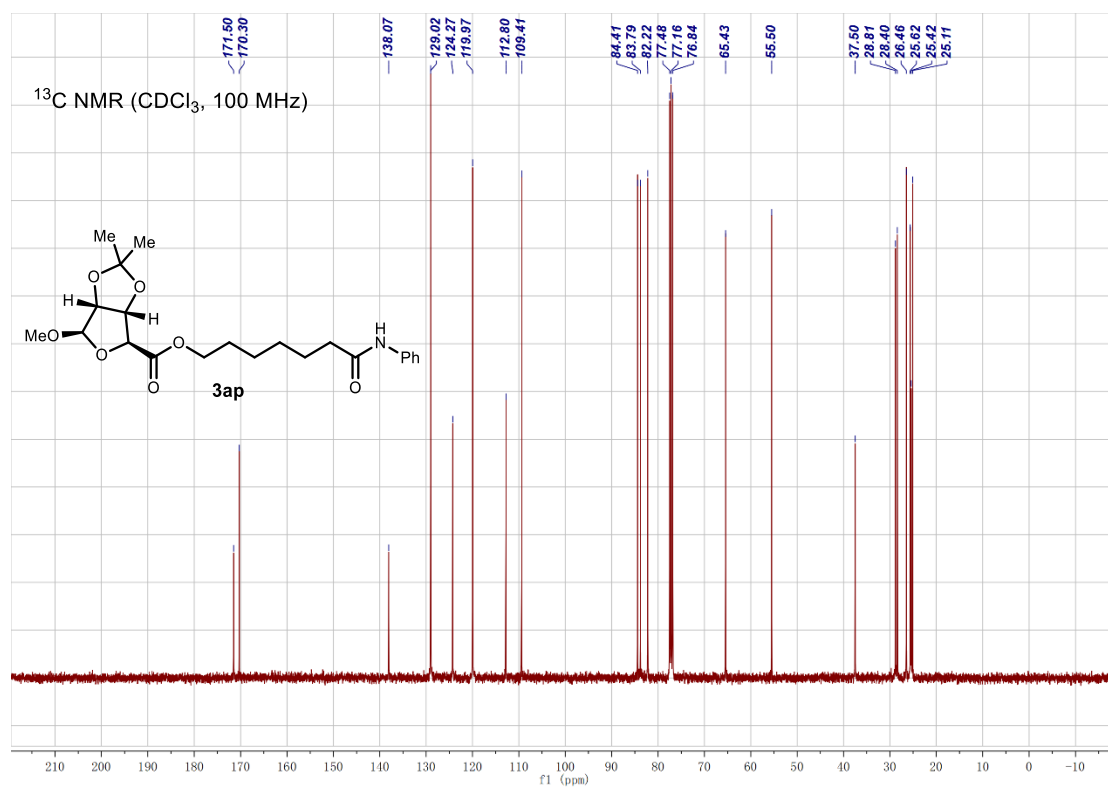
¹H NMR of **3ao** (400 MHz, DMSO-*d*₆, 298 K)



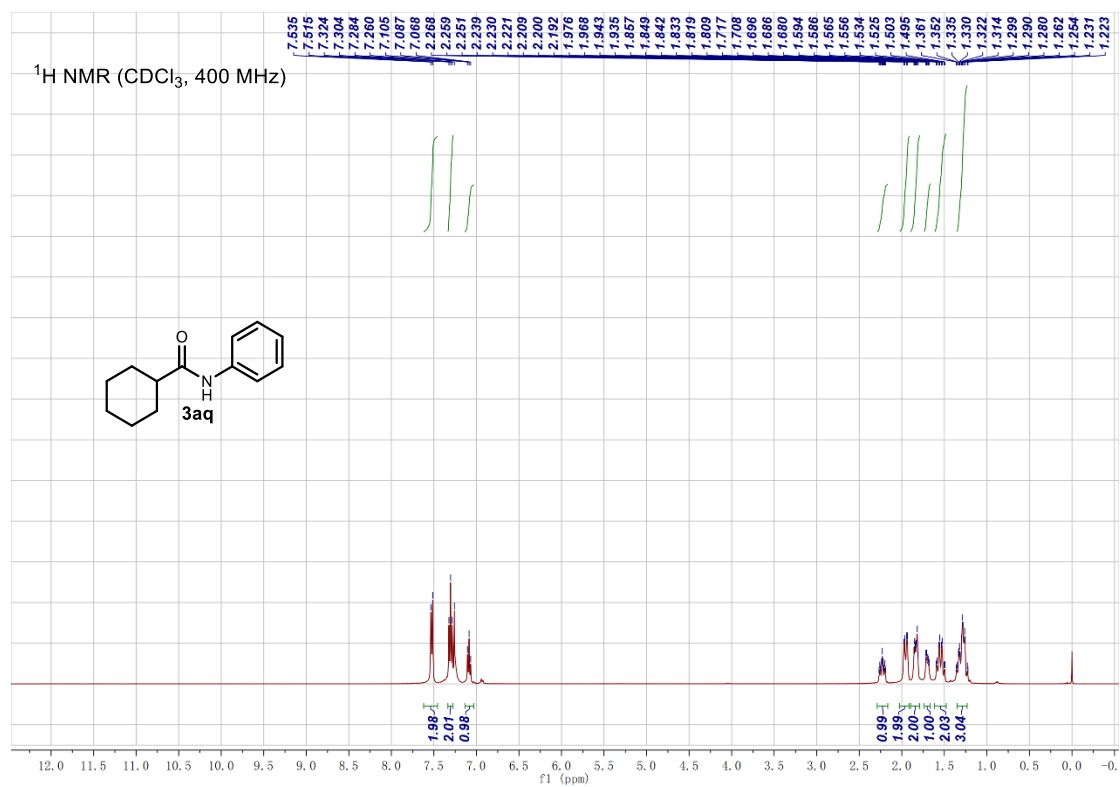
¹³C NMR of **3ao** (100 MHz, DMSO-*d*₆, 298 K)



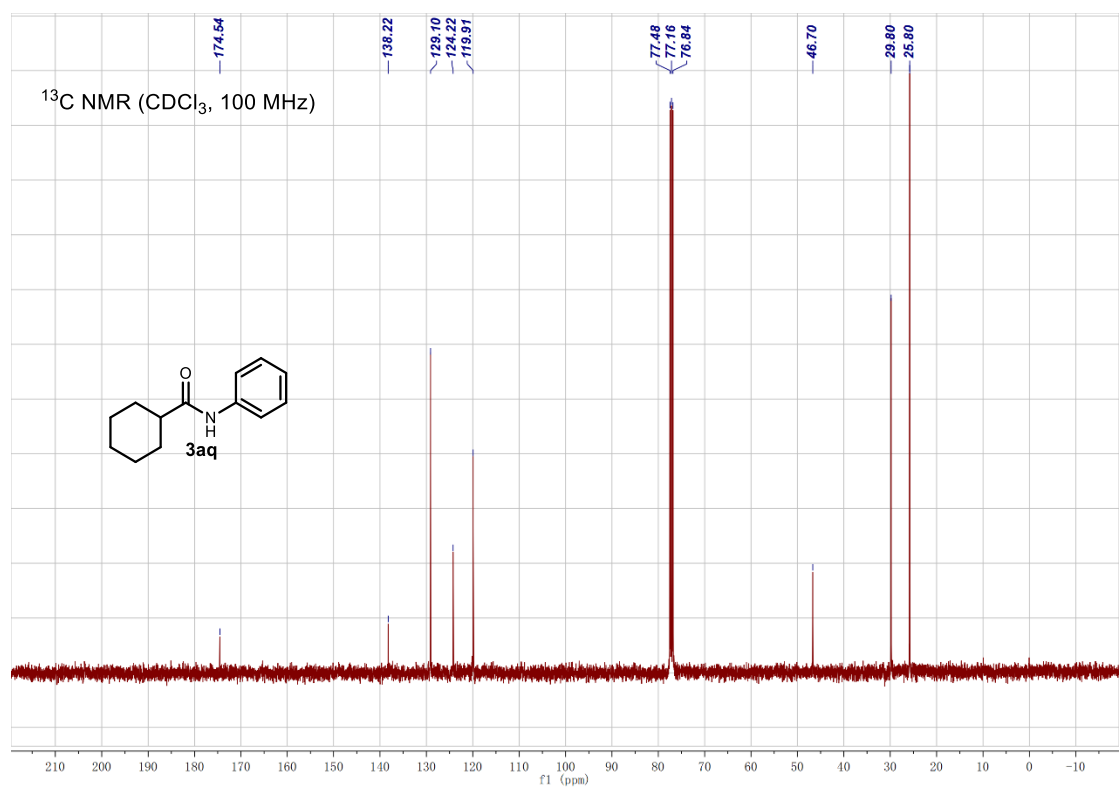
¹H NMR of **3ap** (400 MHz, CDCl₃, 298 K)



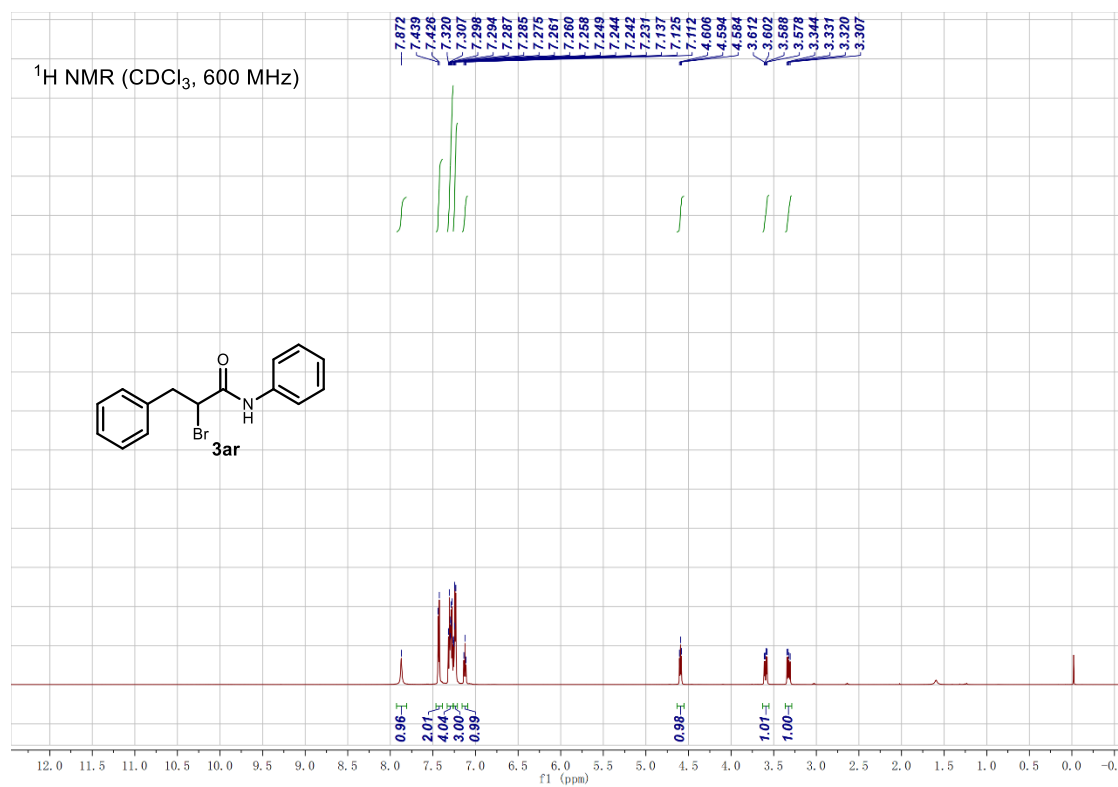
¹³C NMR of **3ap** (100 MHz, CDCl₃, 298 K)



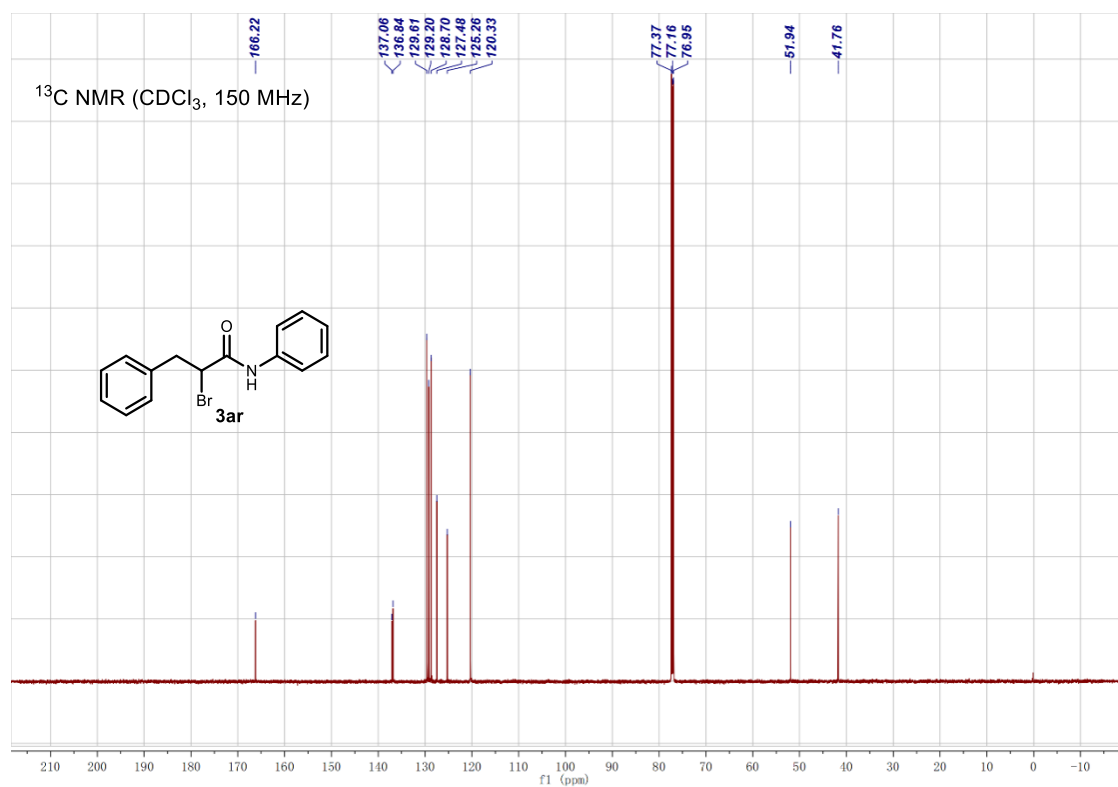
¹H NMR of **3aq** (400 MHz, CDCl₃, 298 K)



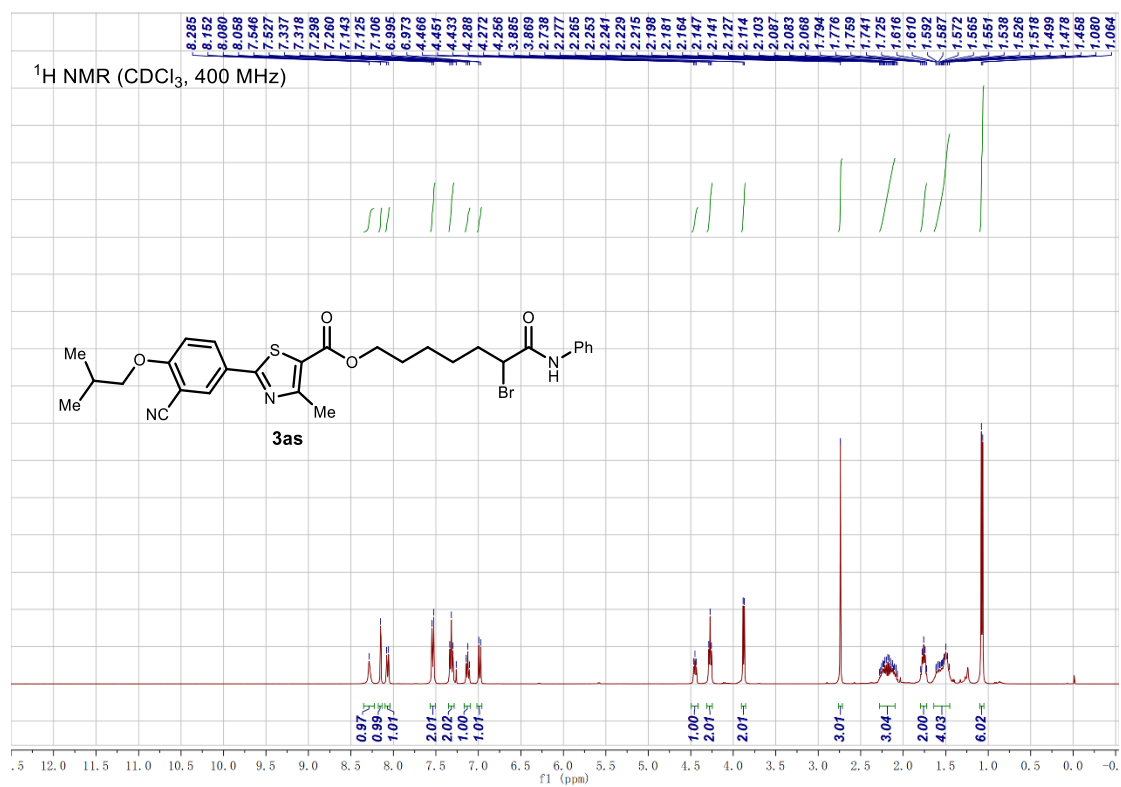
¹³C NMR of **3aq** (100 MHz, CDCl₃, 298 K)



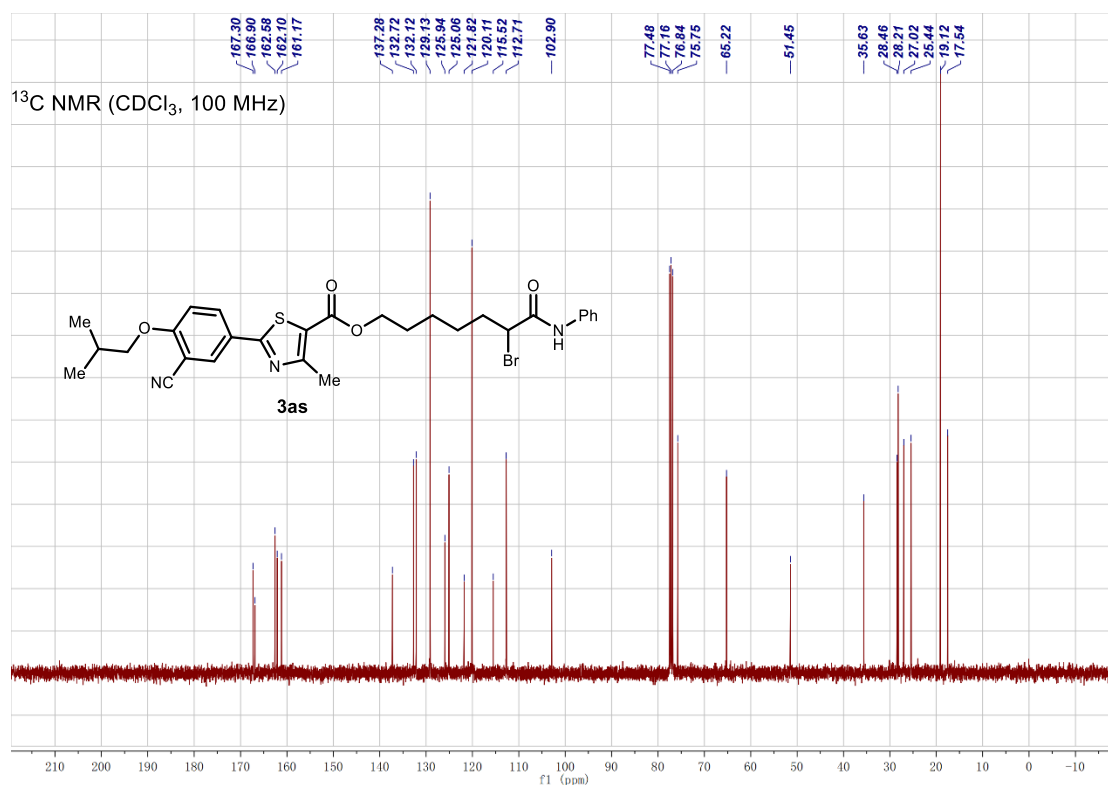
¹H NMR of **3ar** (600 MHz, CDCl₃, 298 K)



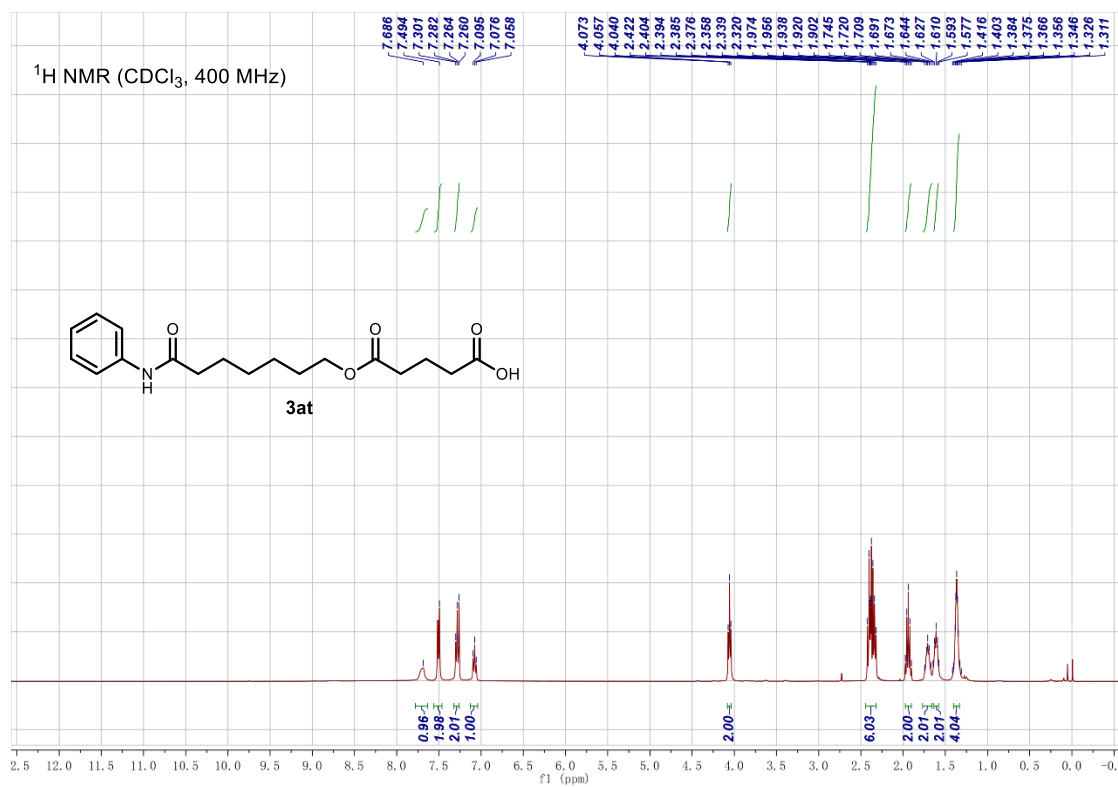
¹³C NMR of **3ar** (150 MHz, CDCl₃, 298 K)



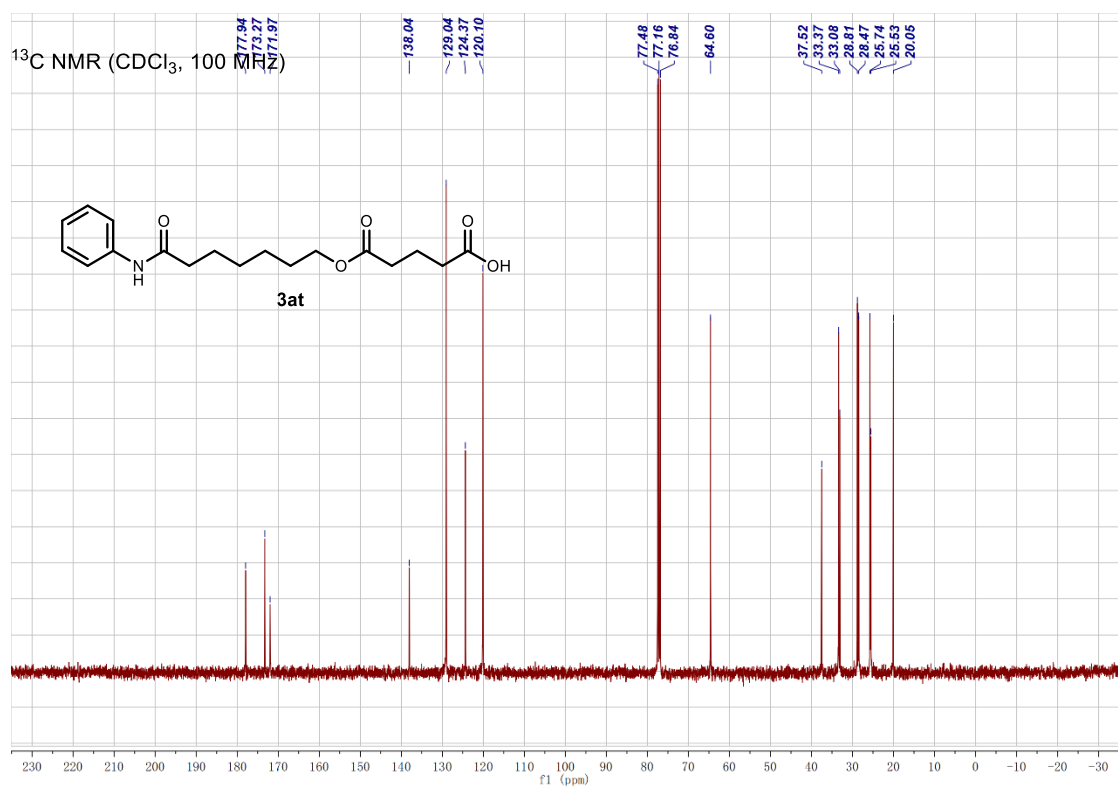
¹H NMR of **3as** (400 MHz, CDCl₃, 298 K)



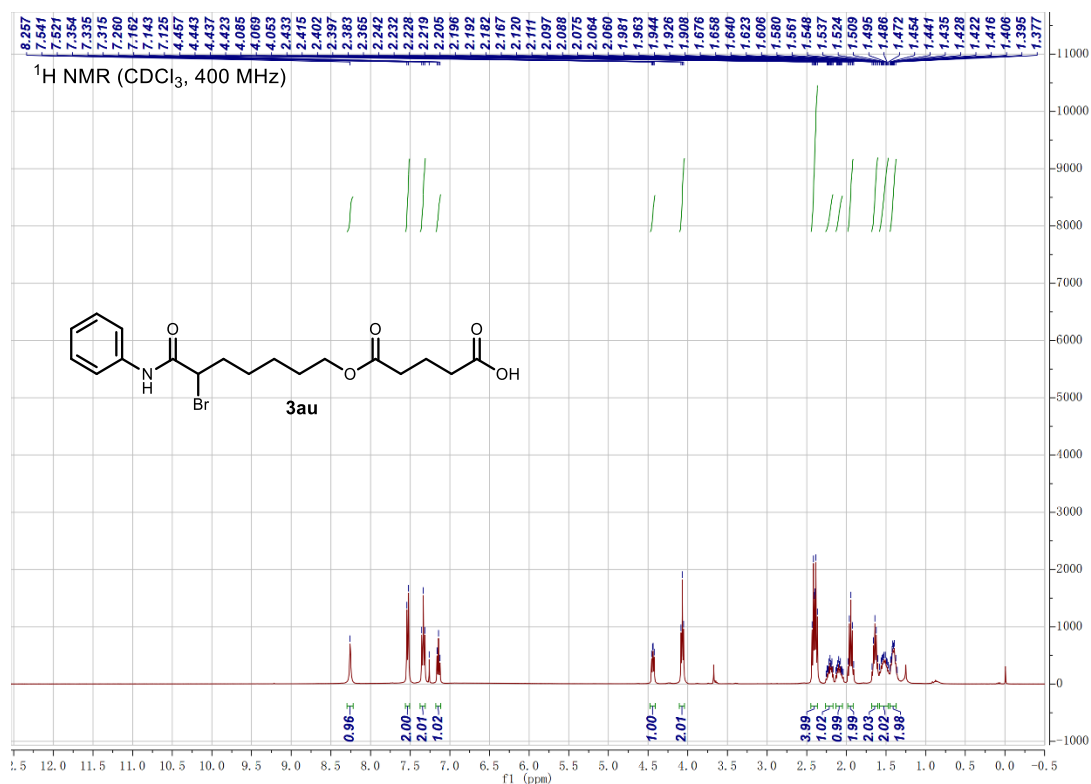
¹³C NMR of **3as** (100 MHz, CDCl₃, 298 K)



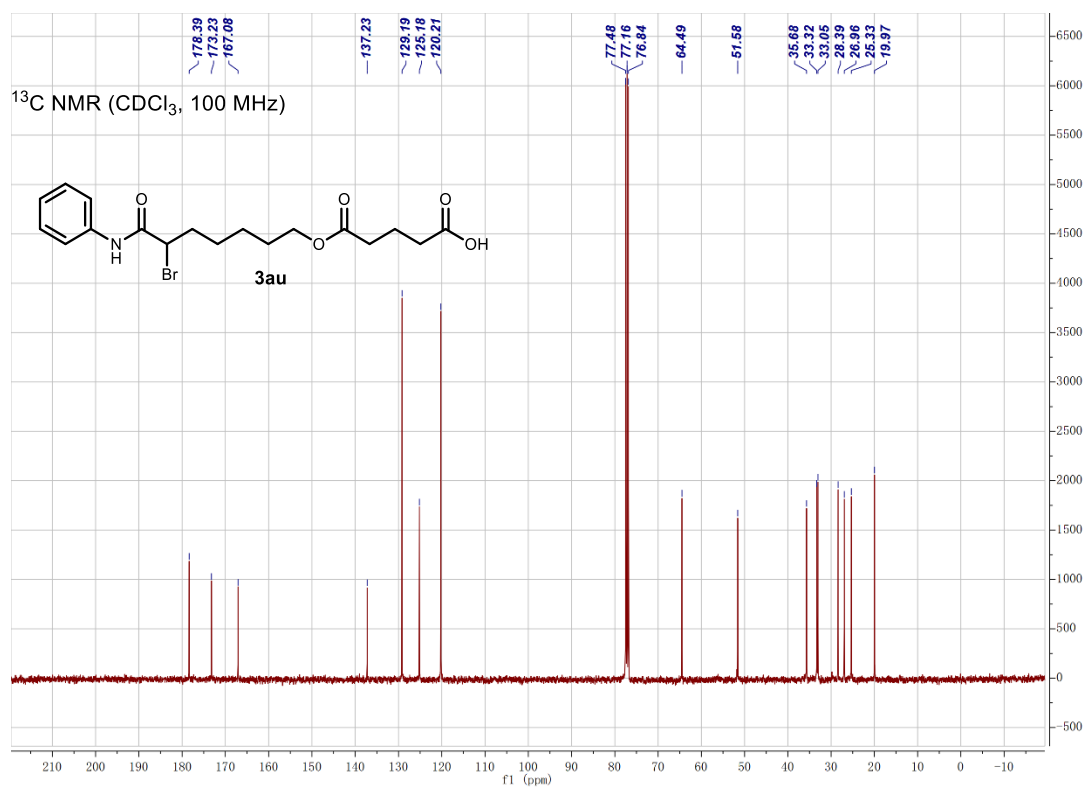
¹H NMR of **3at** (400 MHz, CDCl₃, 298 K)



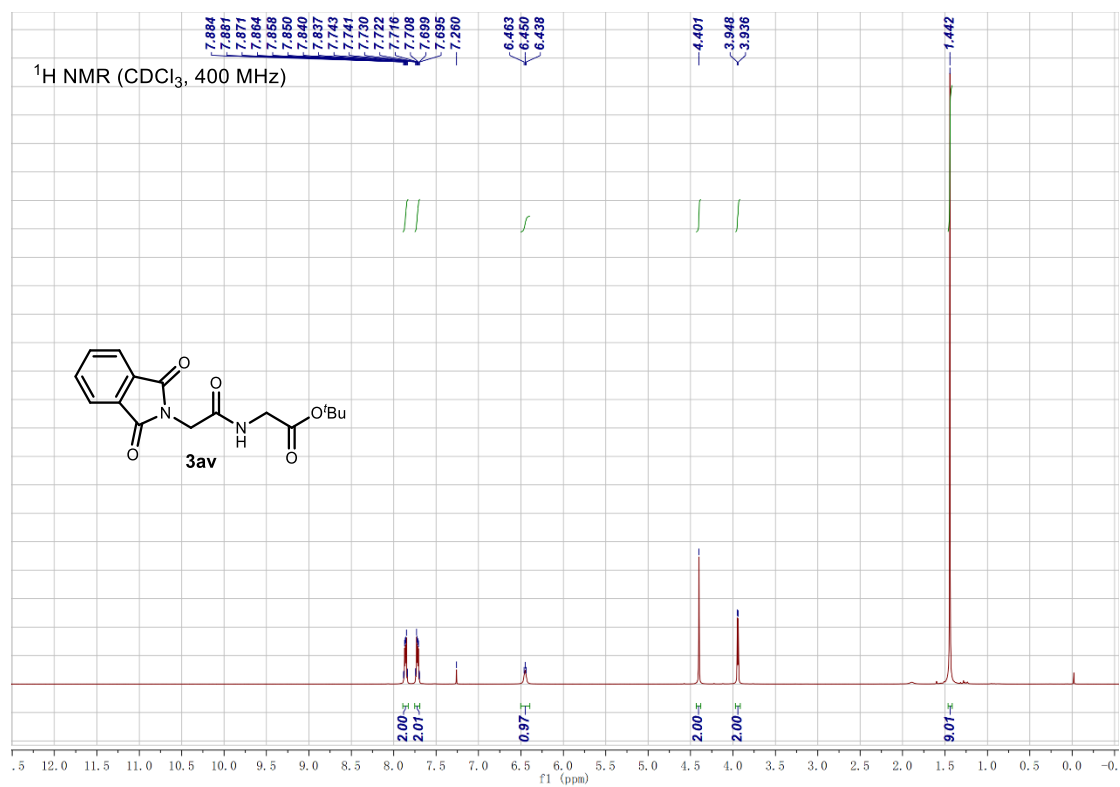
¹³C NMR of **3at** (100 MHz, CDCl₃, 298 K)



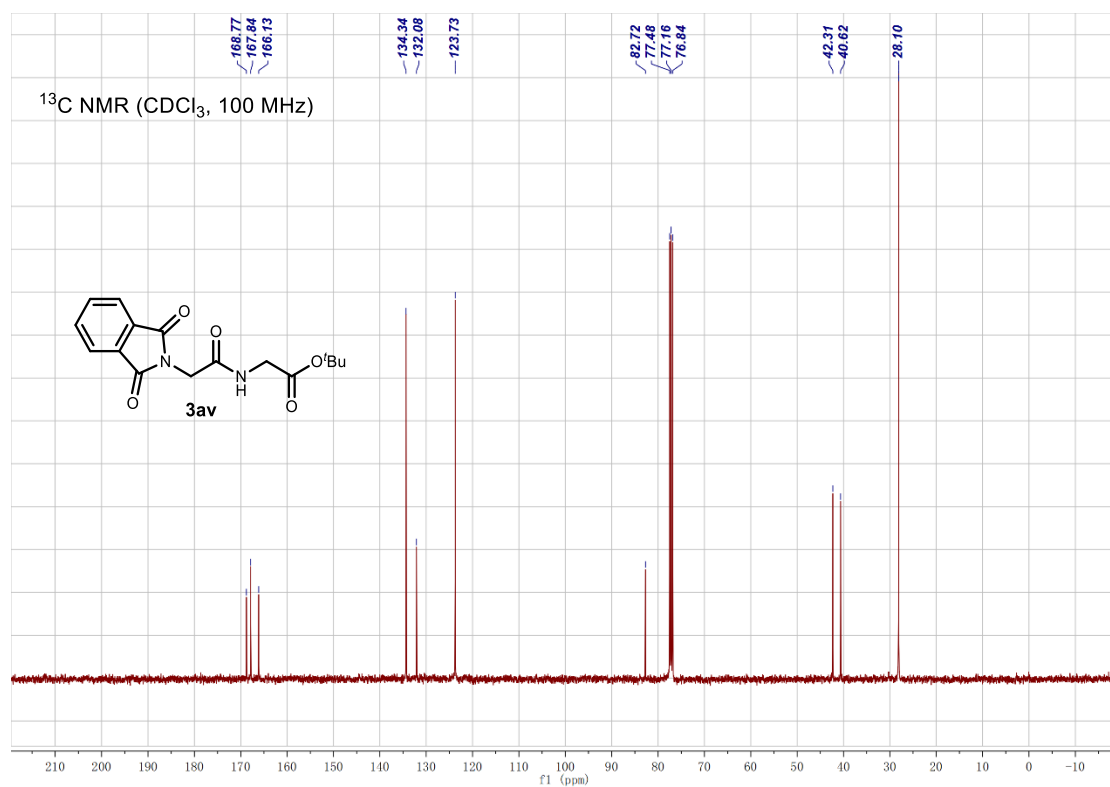
¹H NMR of **3au** (400 MHz, CDCl₃, 298 K)



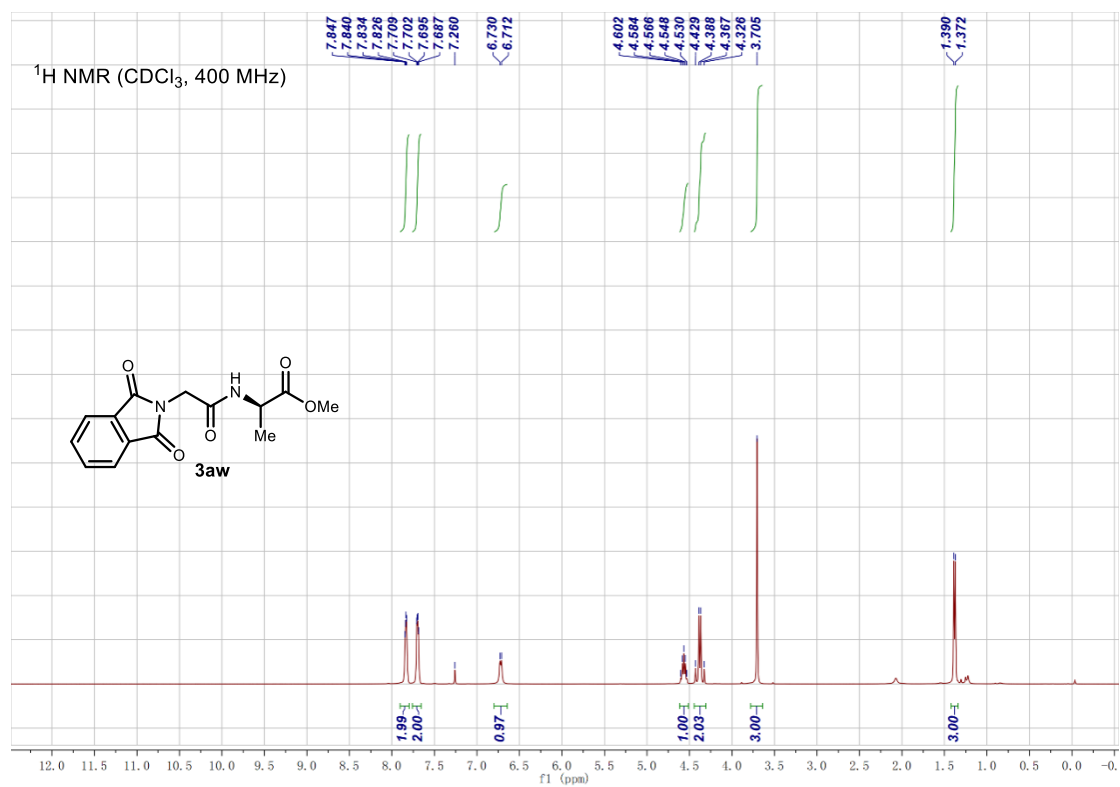
¹³C NMR of **3au** (100 MHz, CDCl₃, 298 K)



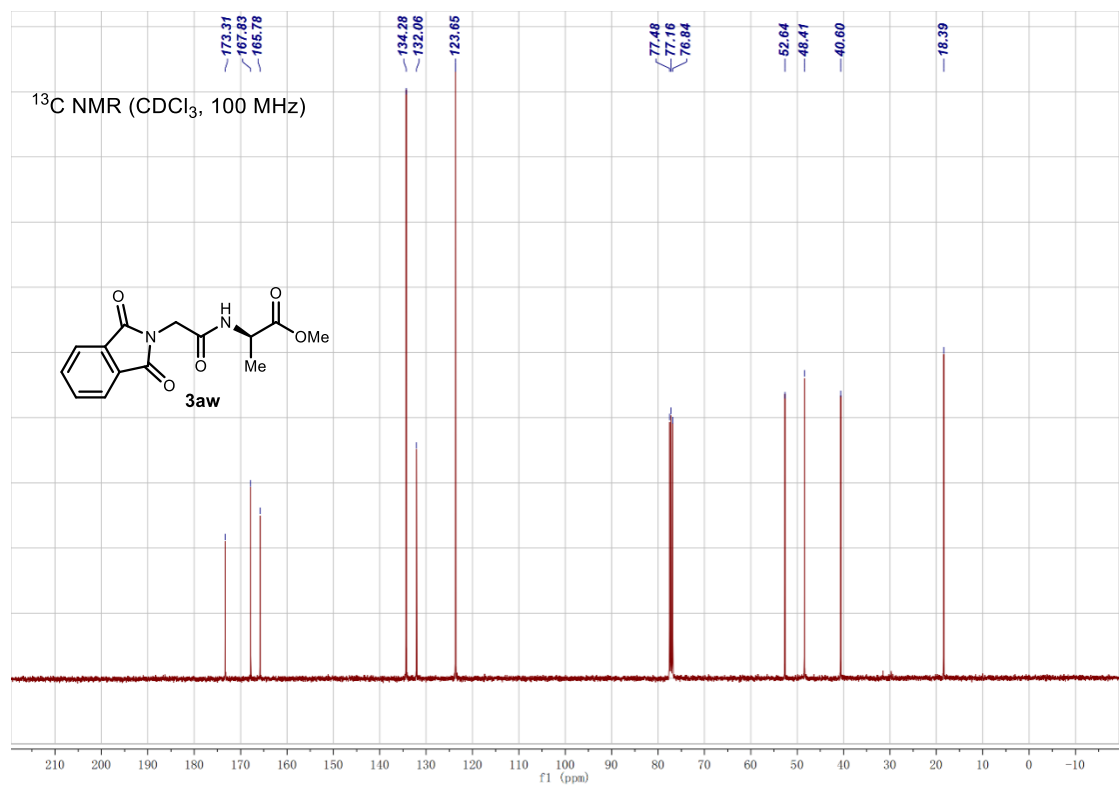
¹H NMR of **3av** (400 MHz, CDCl₃, 298 K)



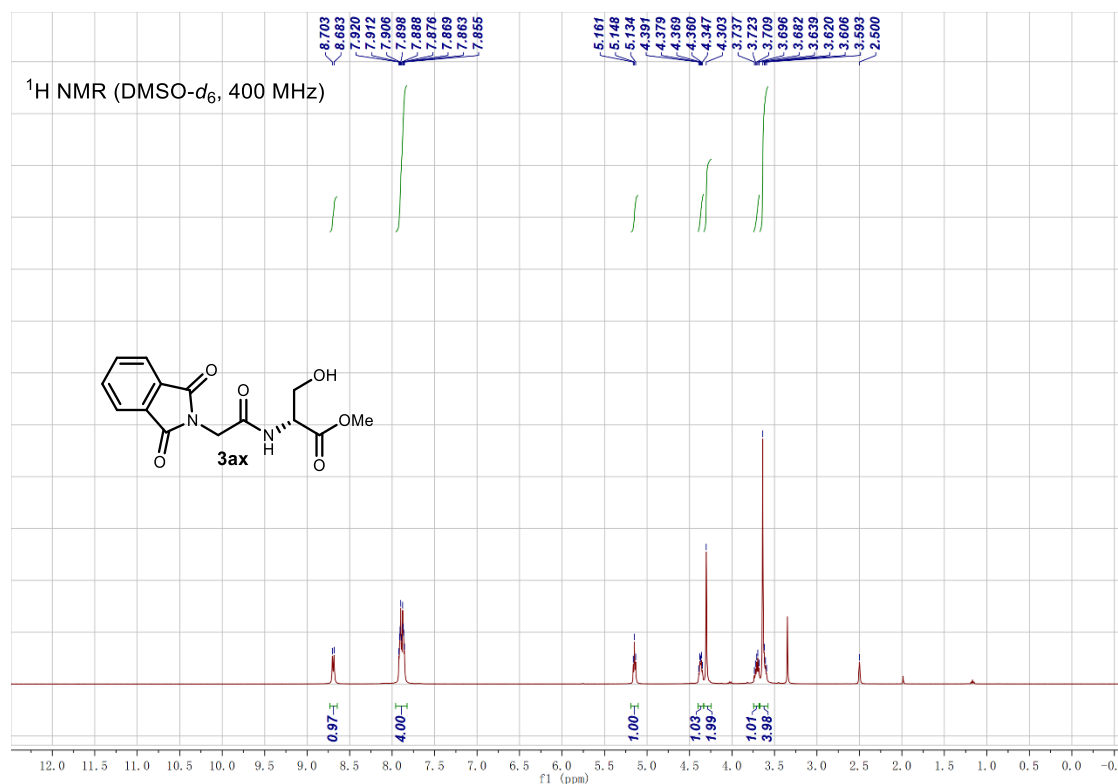
¹³C NMR of **3av** (100 MHz, CDCl₃, 298 K)



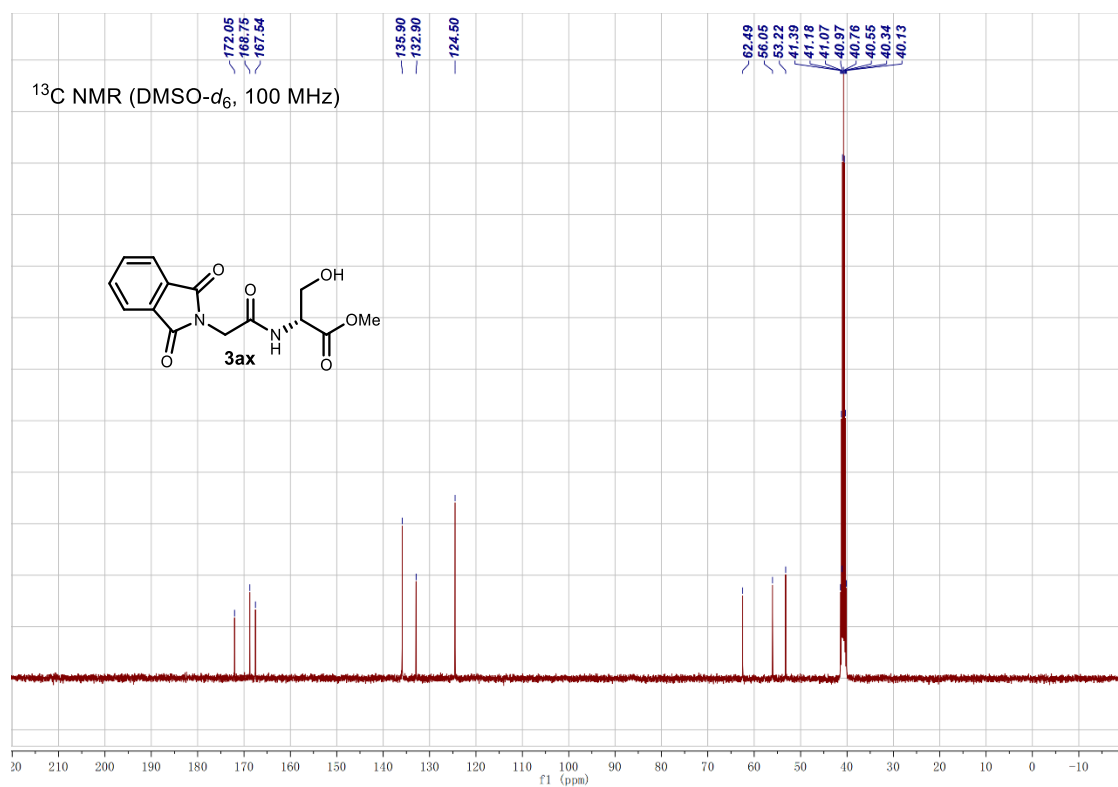
¹H NMR of **3aw** (400 MHz, CDCl₃, 298 K)



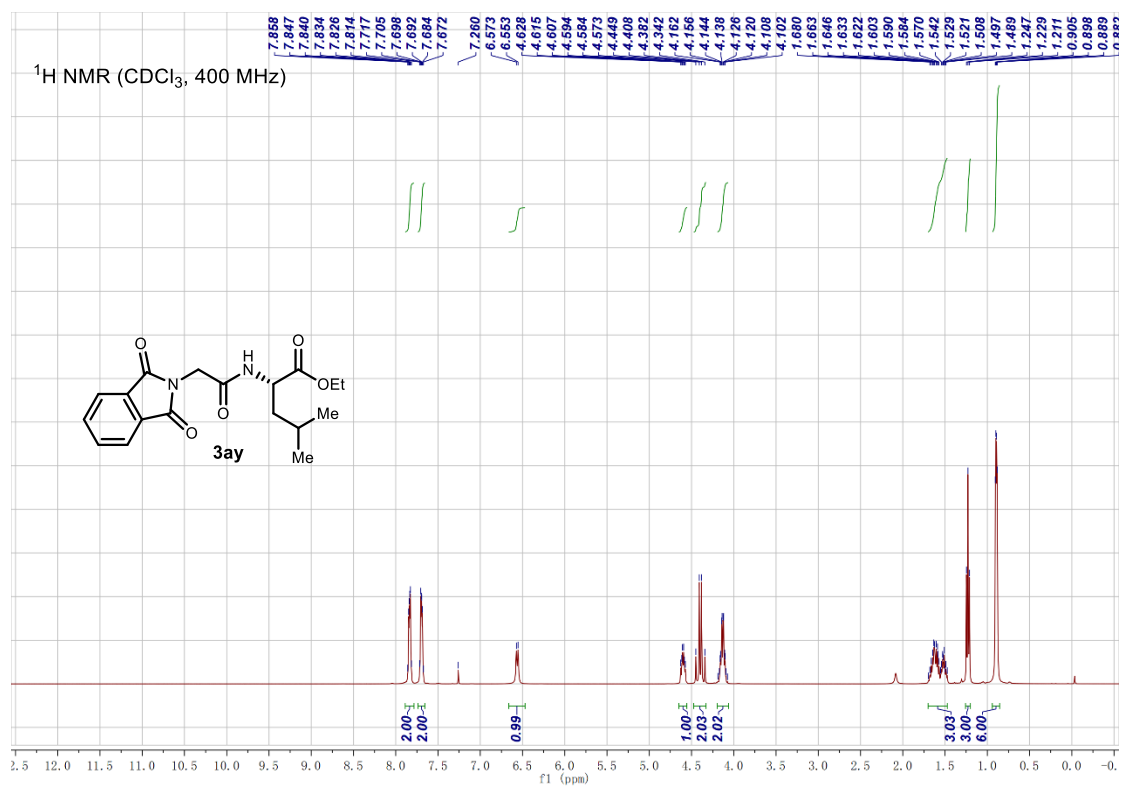
¹³C NMR of **3aw** (100 MHz, CDCl₃, 298 K)



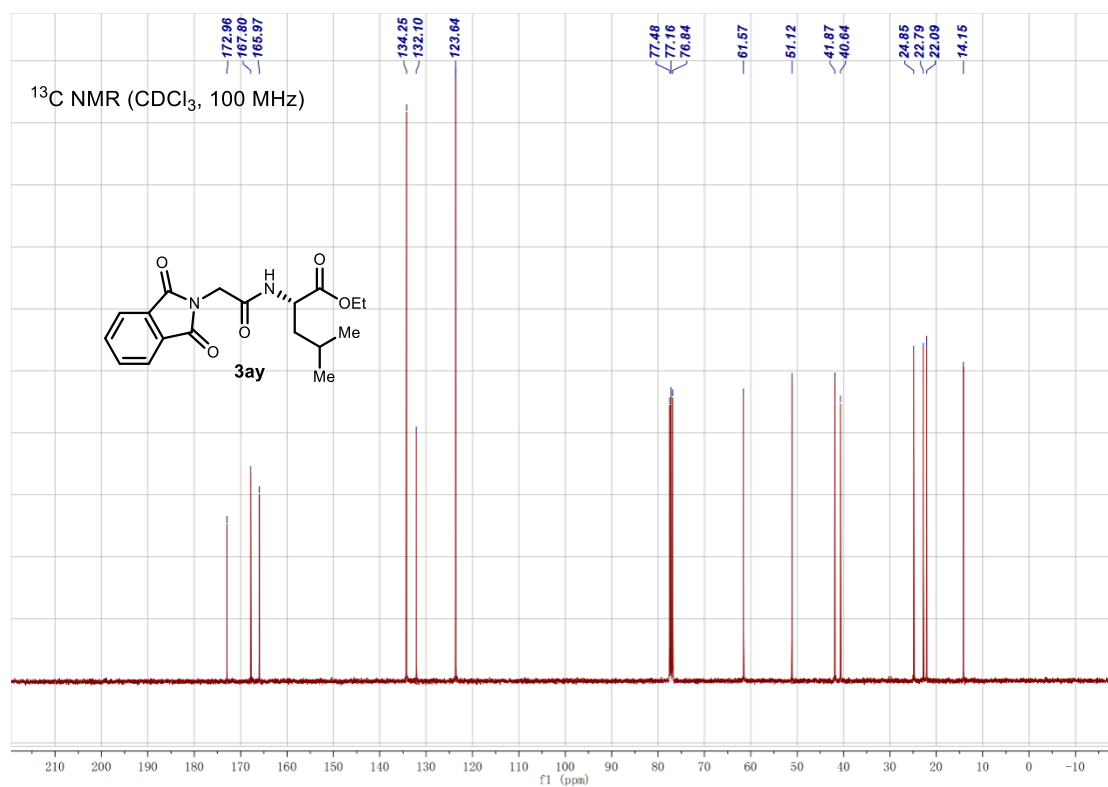
¹H NMR of **3ax** (400 MHz, DMSO-*d*₆, 298 K)



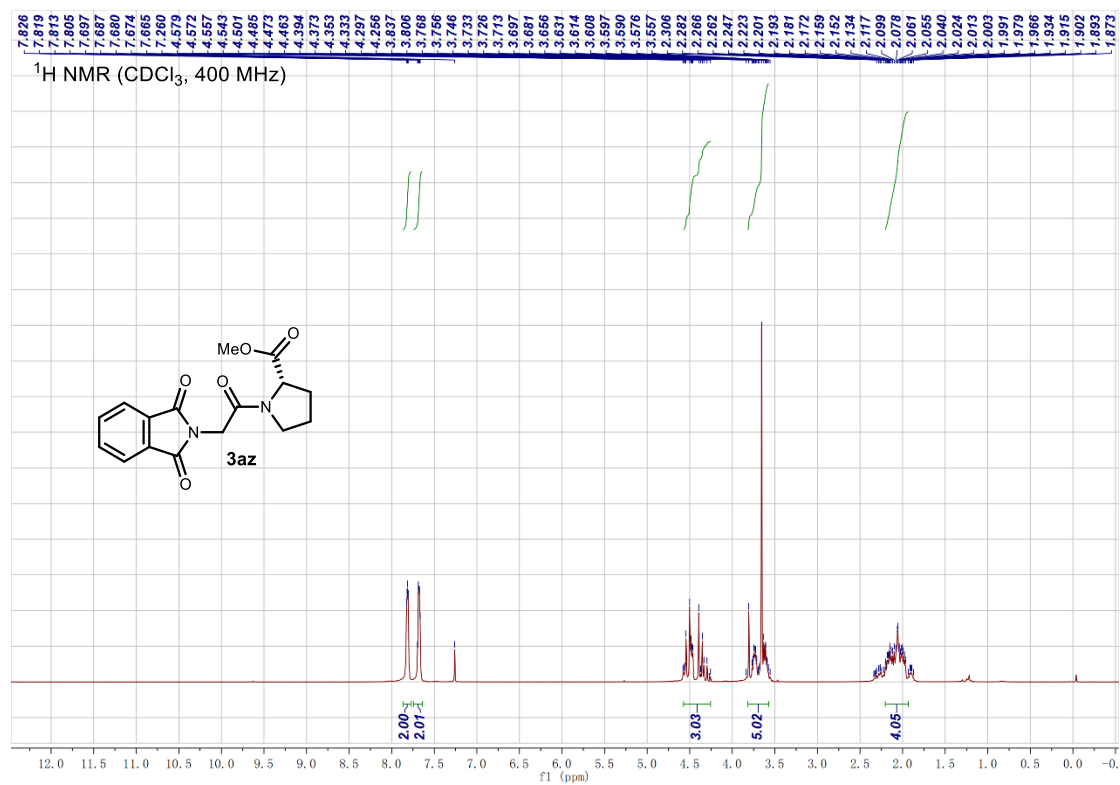
¹³C NMR of **3ax** (100 MHz, DMSO-*d*₆, 298 K)



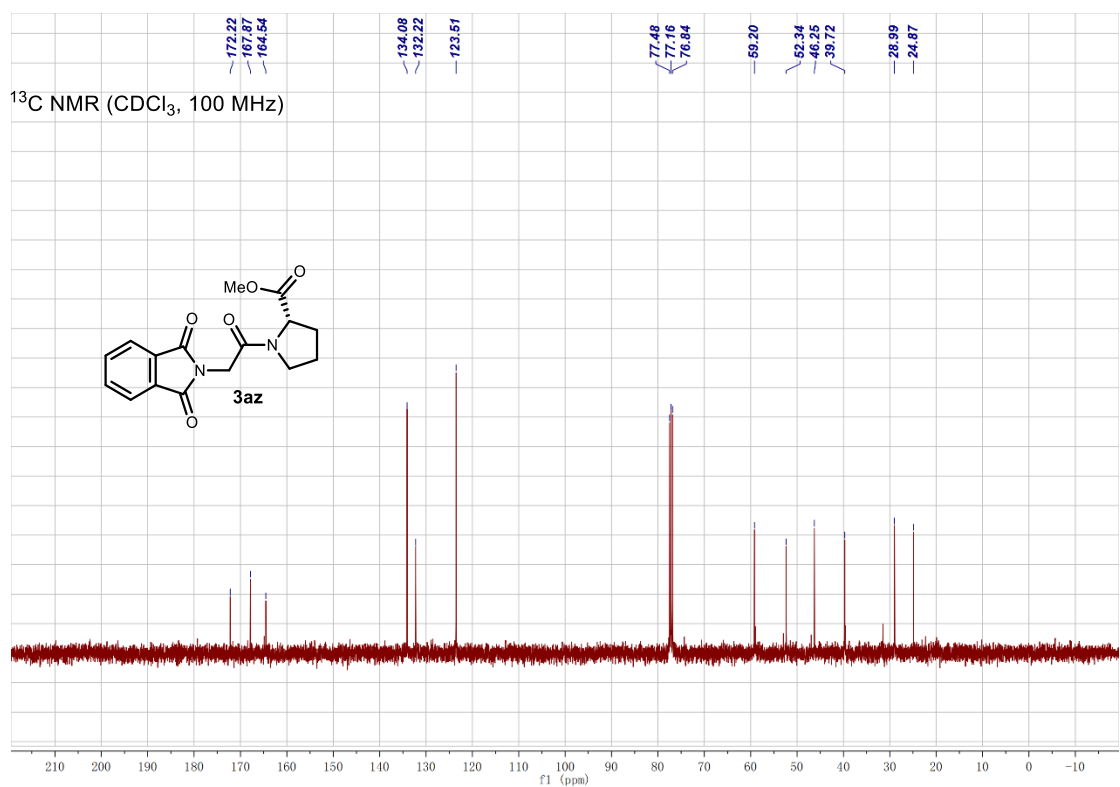
¹H NMR of **3ay** (400 MHz, CDCl₃, 298 K)



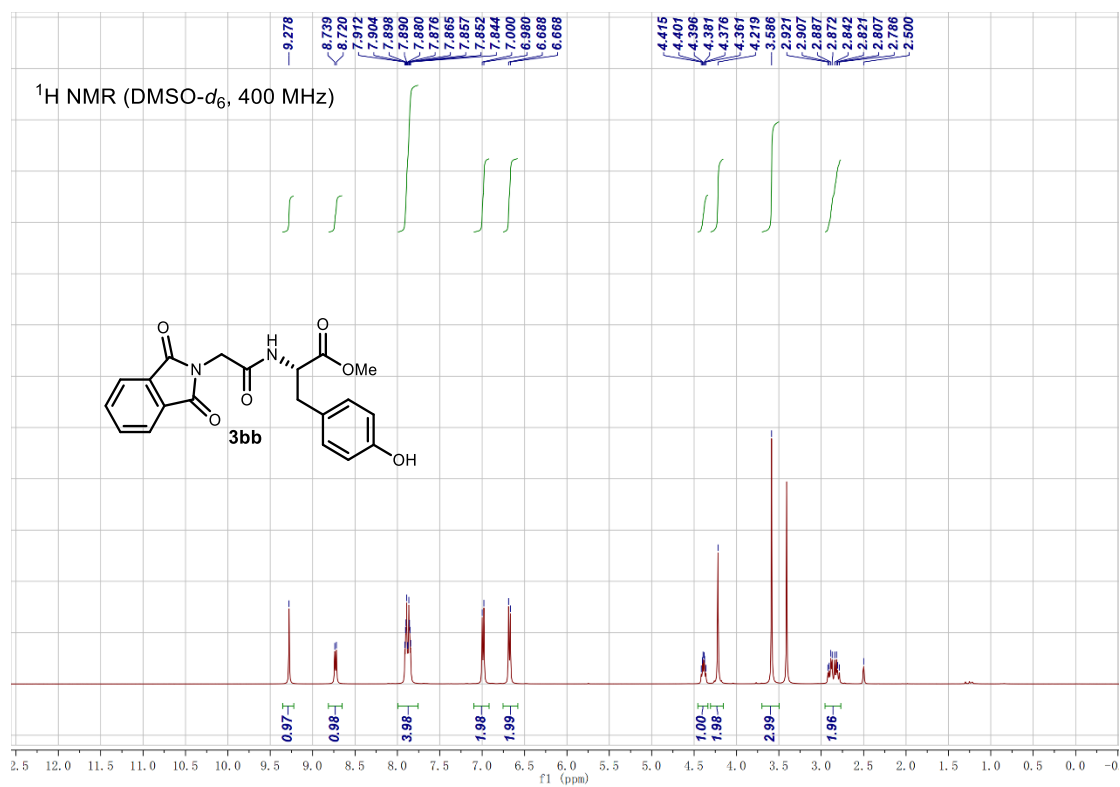
¹³C NMR of **3ay** (100 MHz, CDCl₃, 298 K)



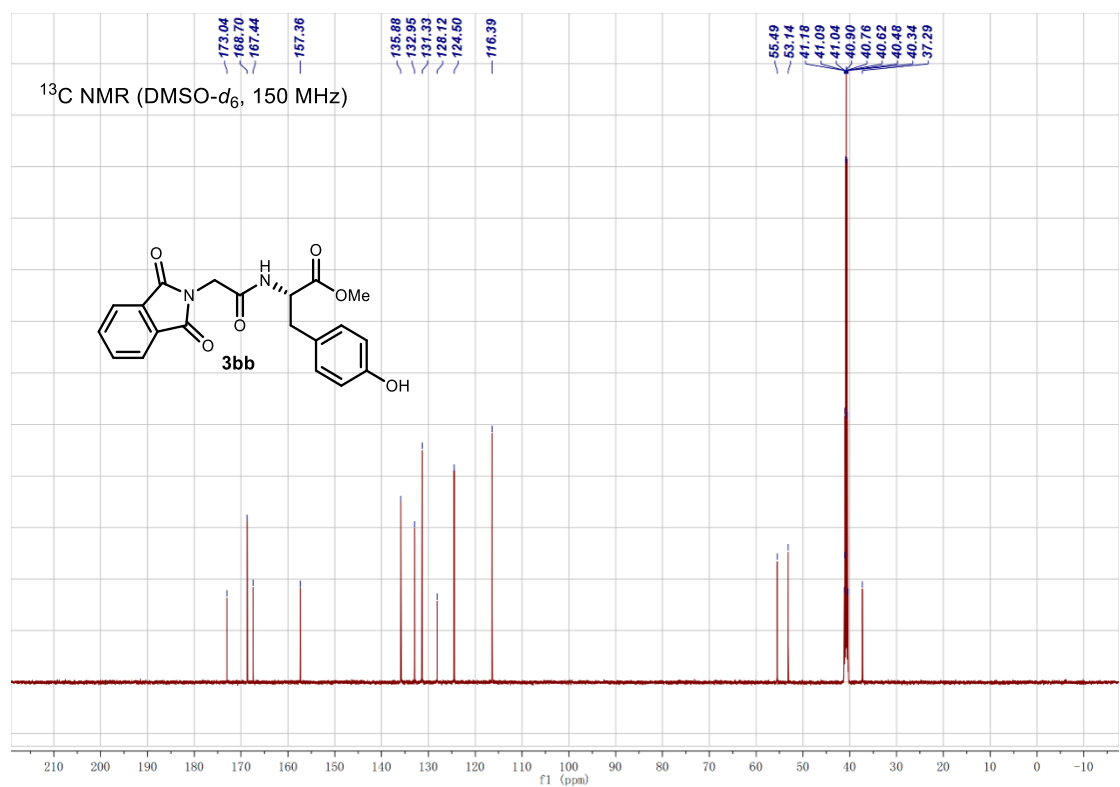
¹H NMR of **3az** (400 MHz, CDCl₃, 298 K)



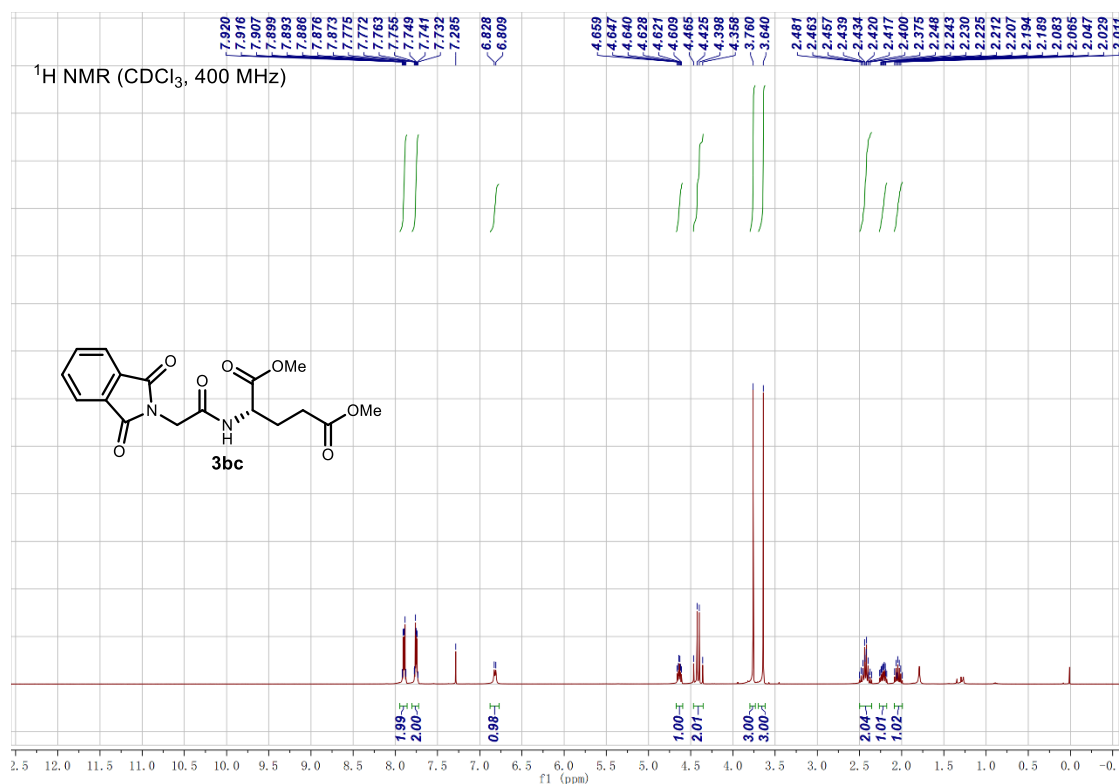
¹³C NMR of **3az** (100 MHz, CDCl₃, 298 K)



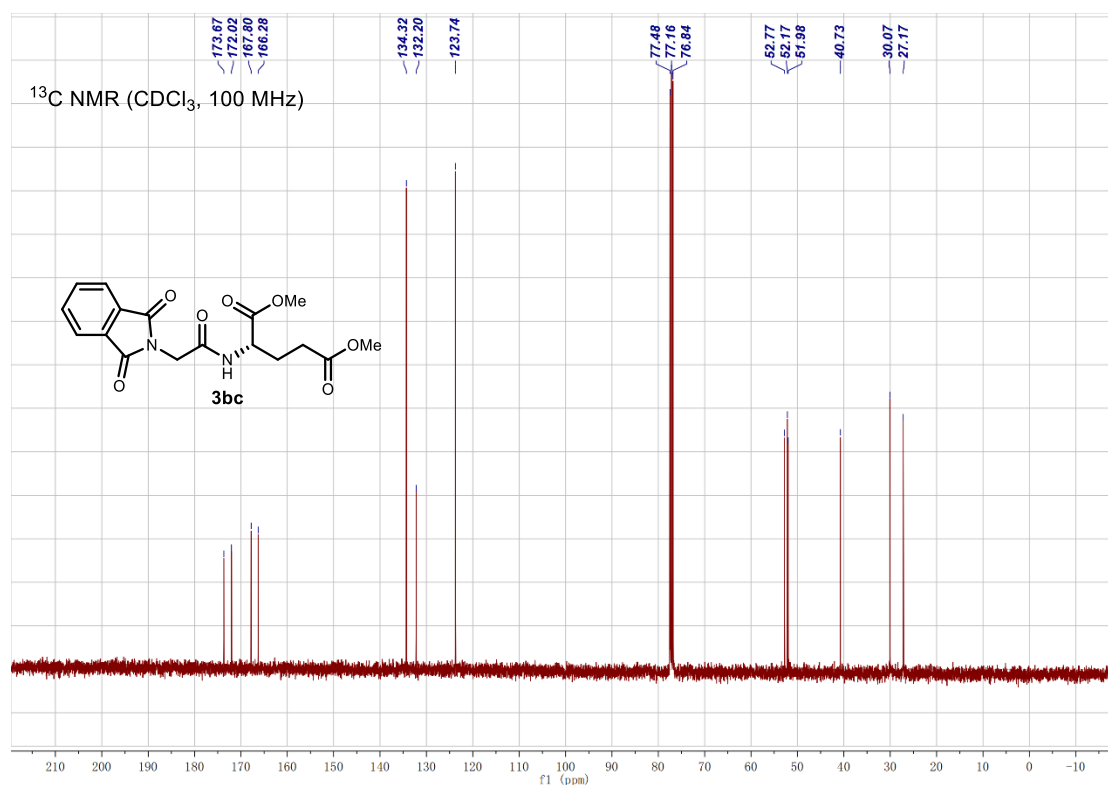
¹H NMR of **3bb** (400 MHz, DMSO-*d*₆, 298 K)



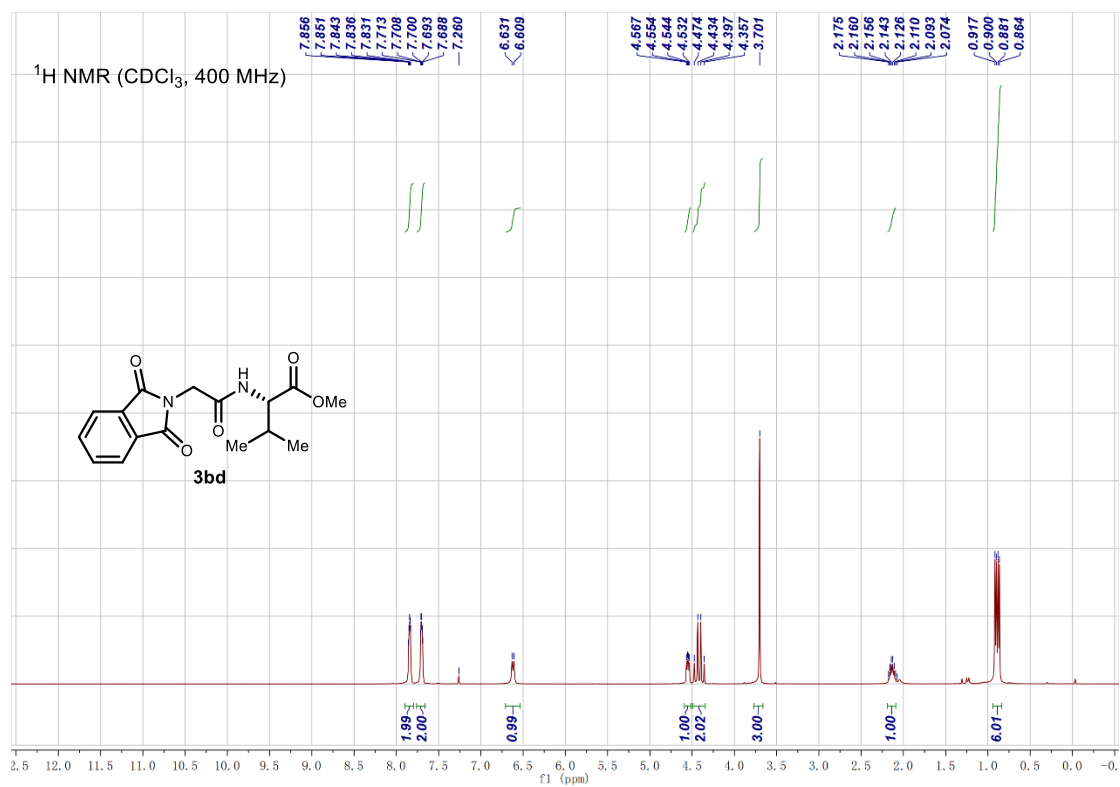
¹³C NMR of **3bb** (150 MHz, DMSO-*d*₆, 298 K)



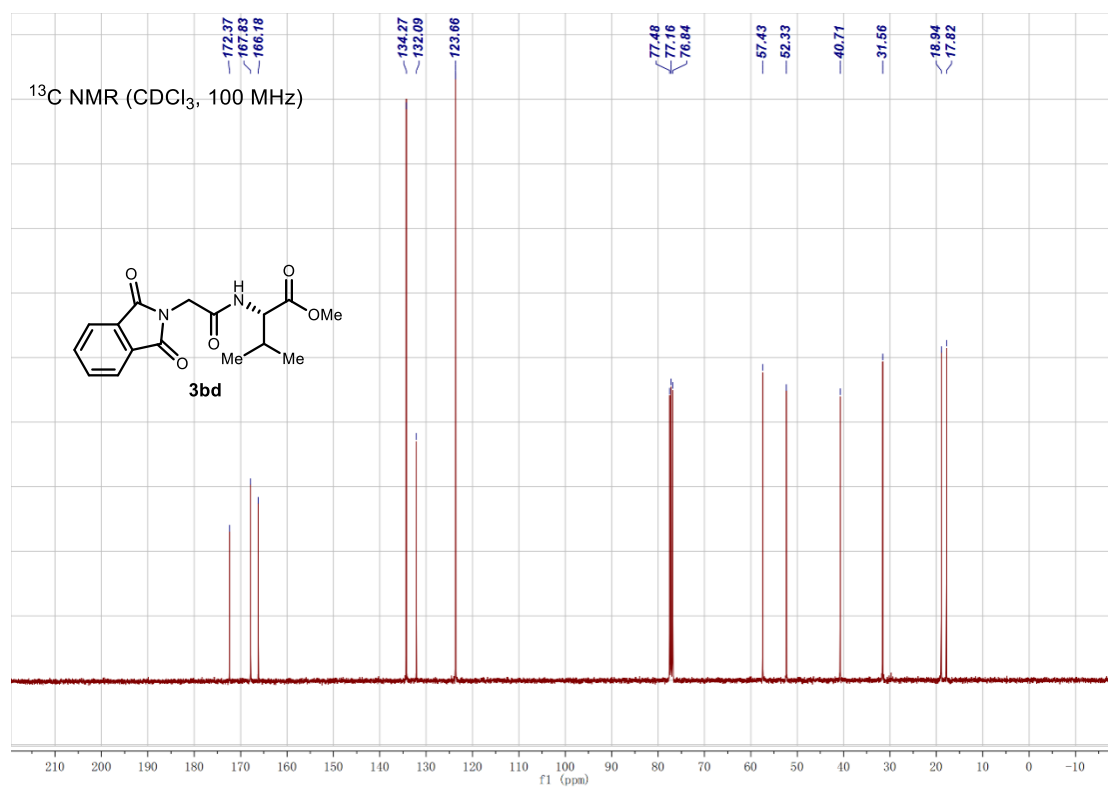
¹H NMR of **3bc** (400 MHz, CDCl₃, 298 K)



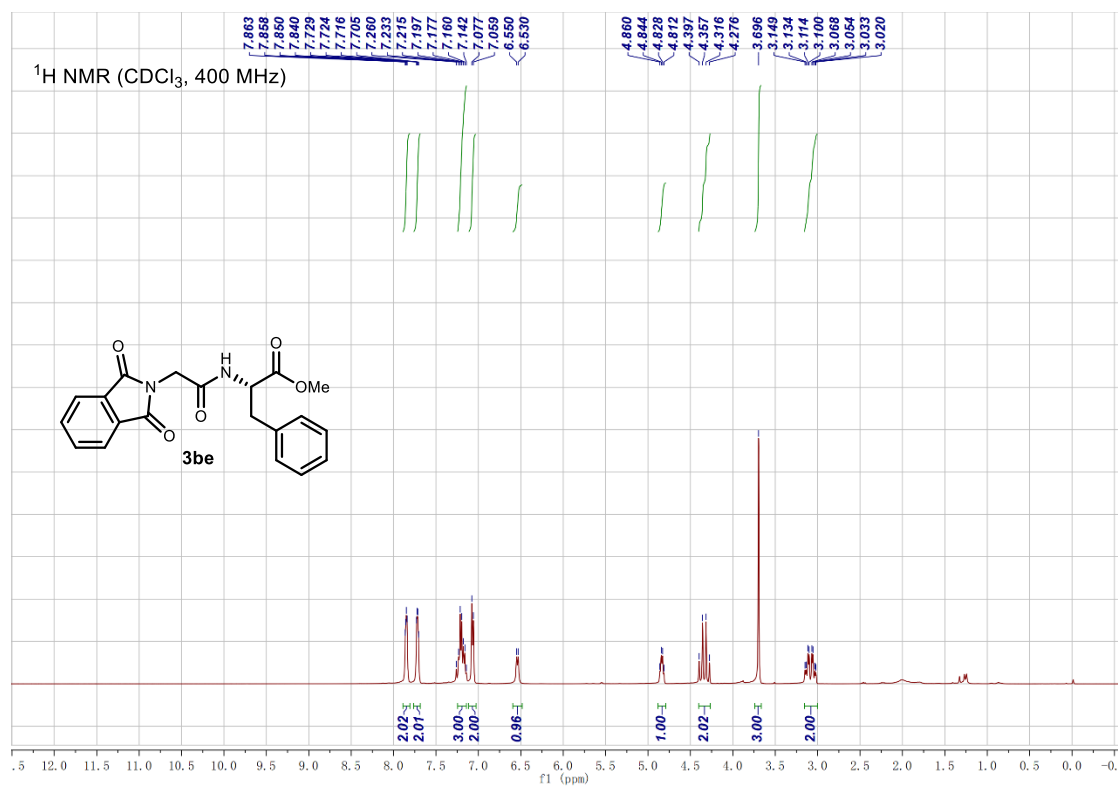
¹³C NMR of **3bc** (100 MHz, CDCl₃, 298 K)



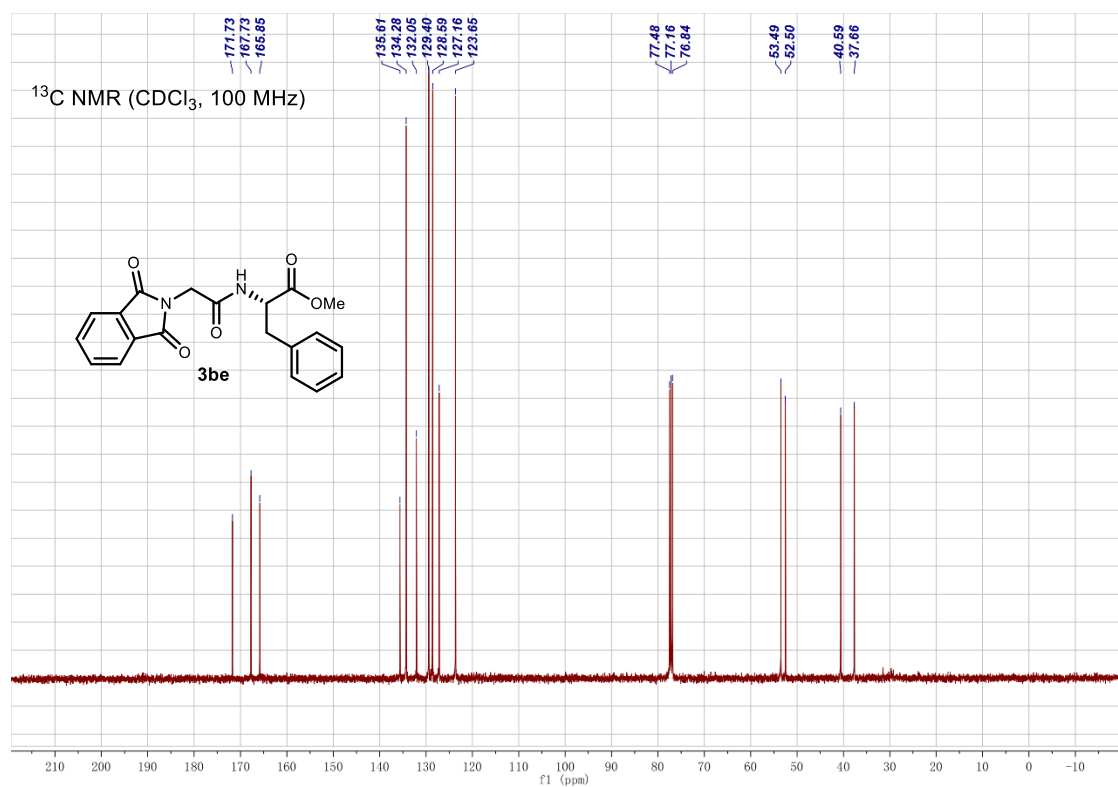
¹H NMR of **3bd** (400 MHz, CDCl₃, 298 K)



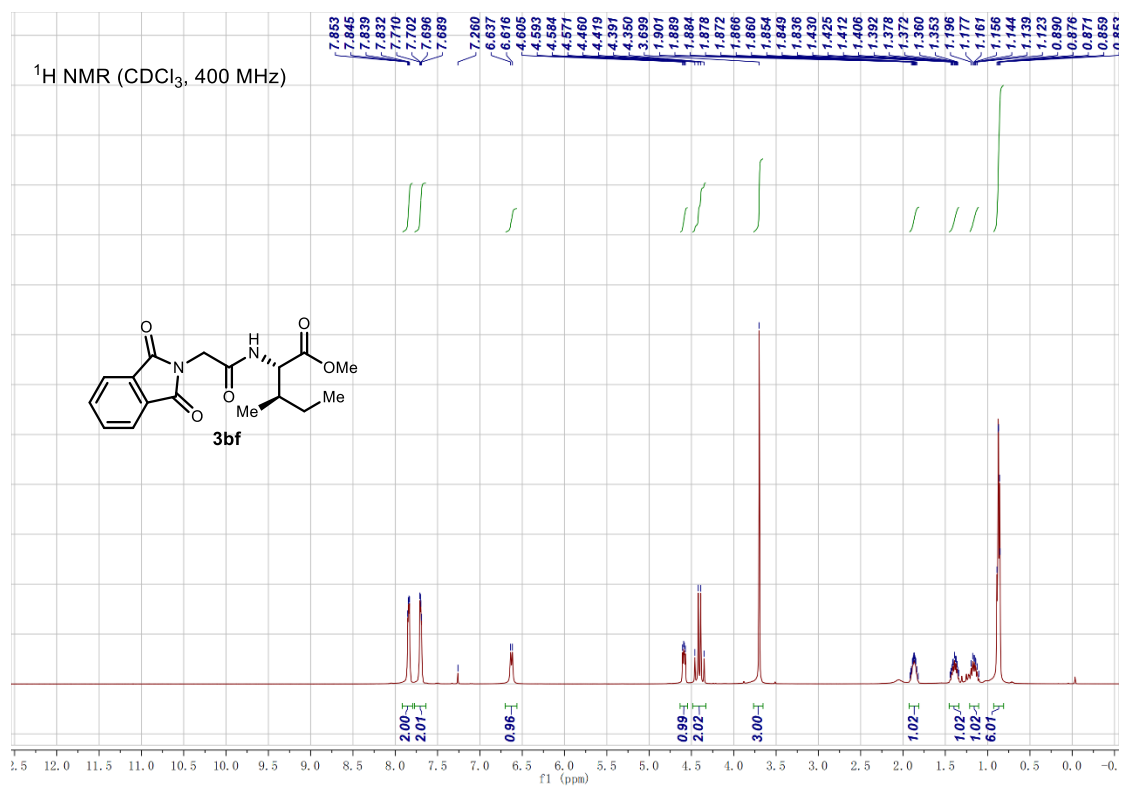
¹³C NMR of **3bd** (100 MHz, CDCl₃, 298 K)



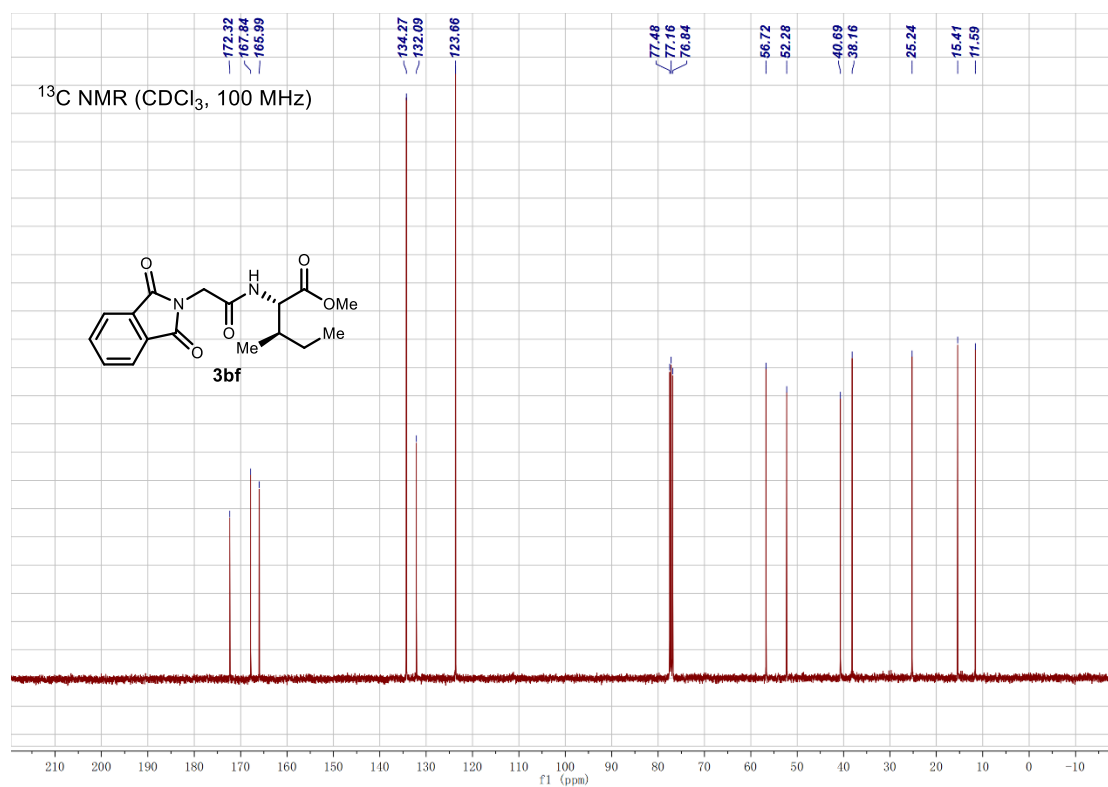
¹H NMR of **3be** (400 MHz, CDCl₃, 298 K)



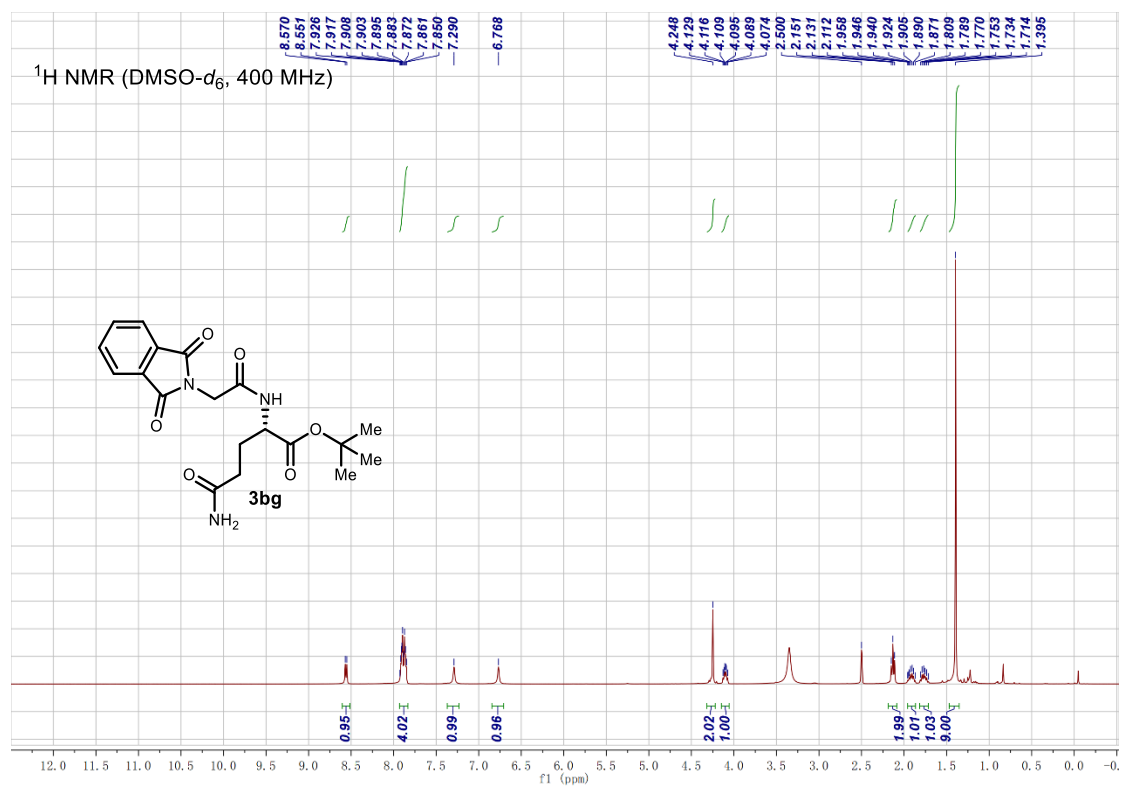
¹³C NMR of **3be** (100 MHz, CDCl₃, 298 K)



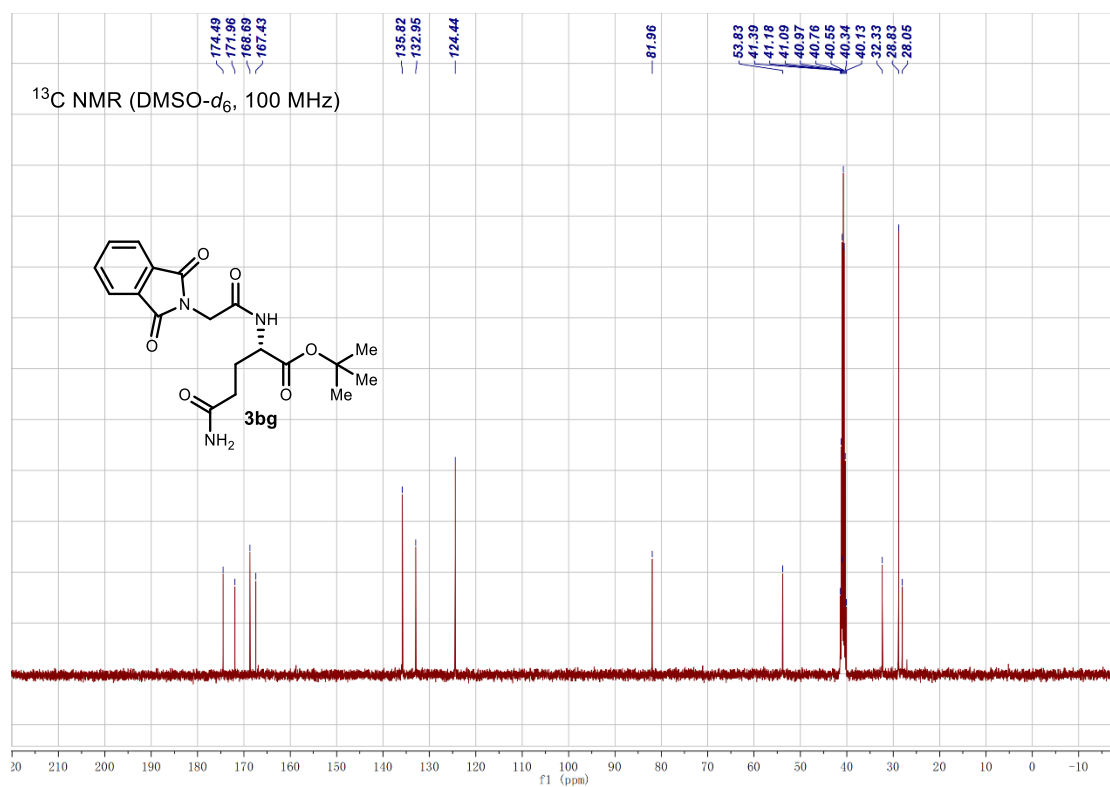
¹H NMR of **3bf** (400 MHz, CDCl₃, 298 K)



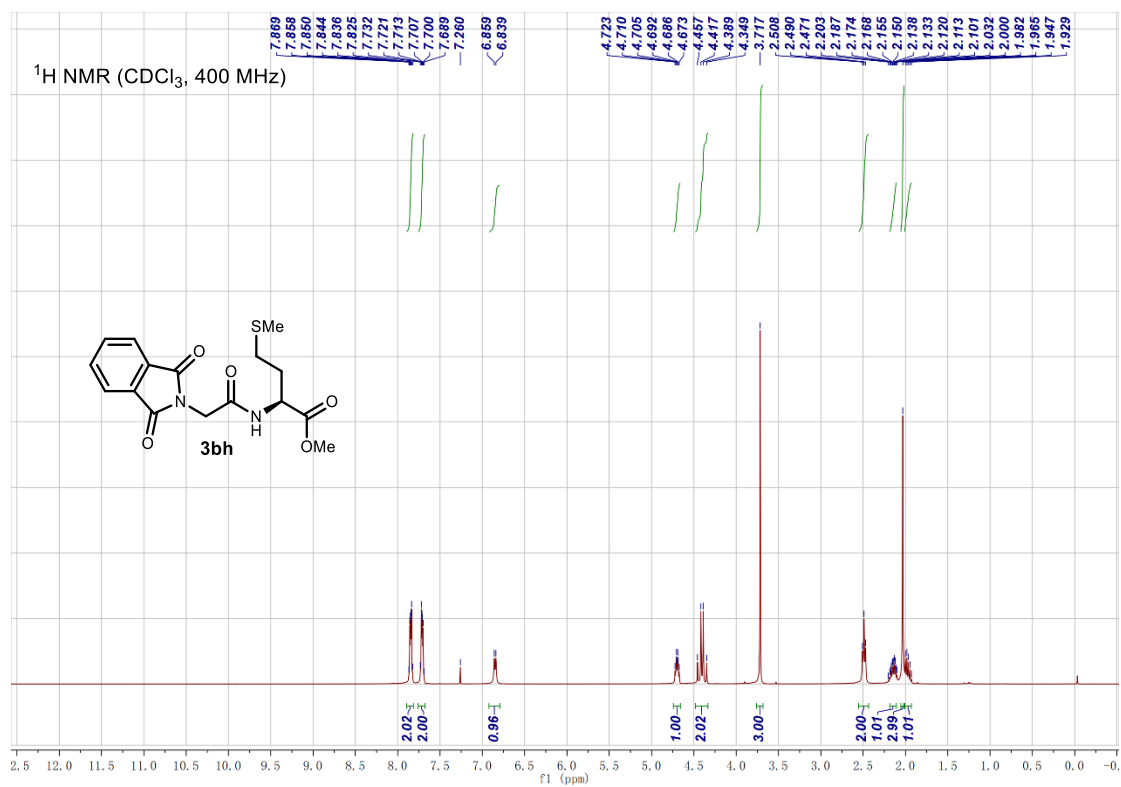
¹³C NMR of **3bf** (100 MHz, CDCl₃, 298 K)



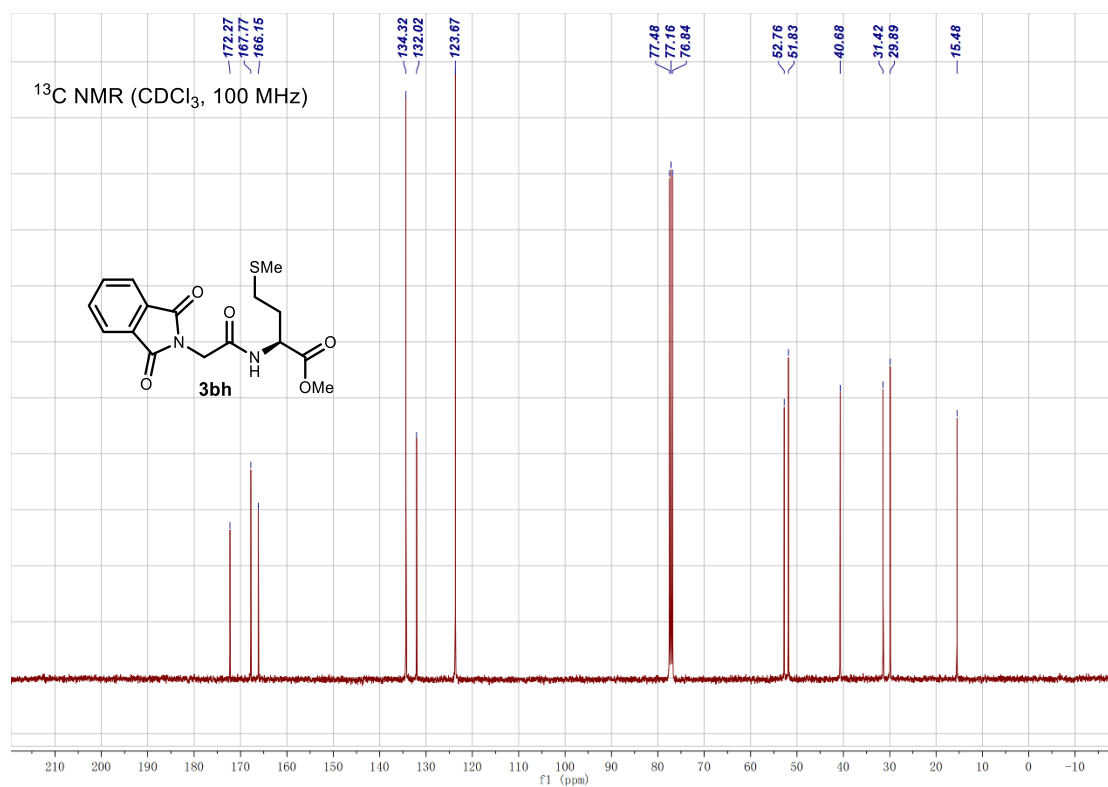
¹H NMR of **3bg** (400 MHz, DMSO-*d*₆, 298 K)



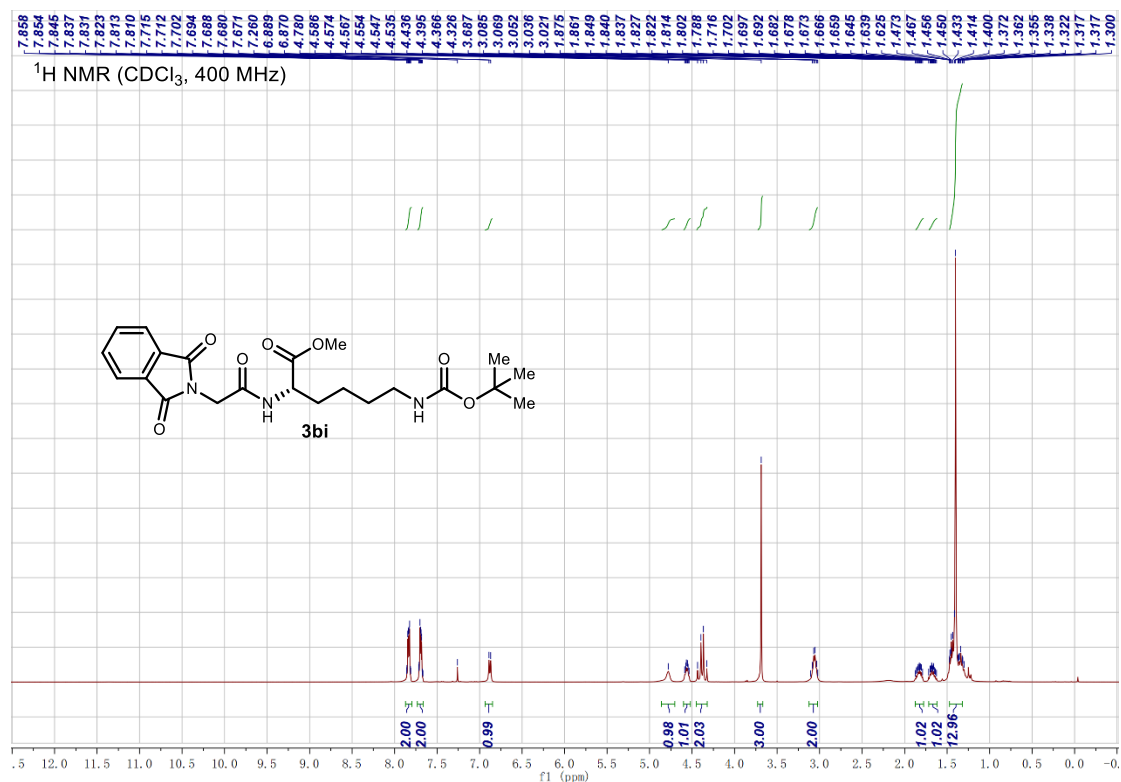
¹³C NMR of **3bg** (100 MHz, DMSO-*d*₆, 298 K)



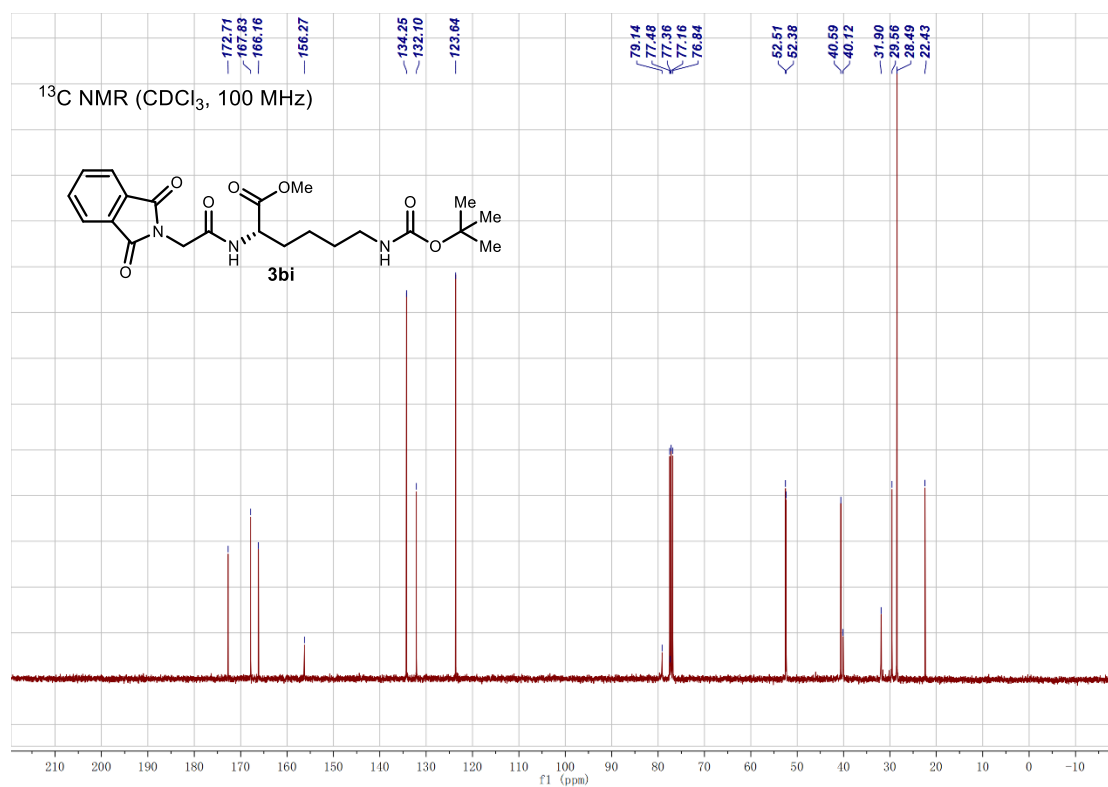
¹H NMR of **3bh** (400 MHz, CDCl₃, 298 K)



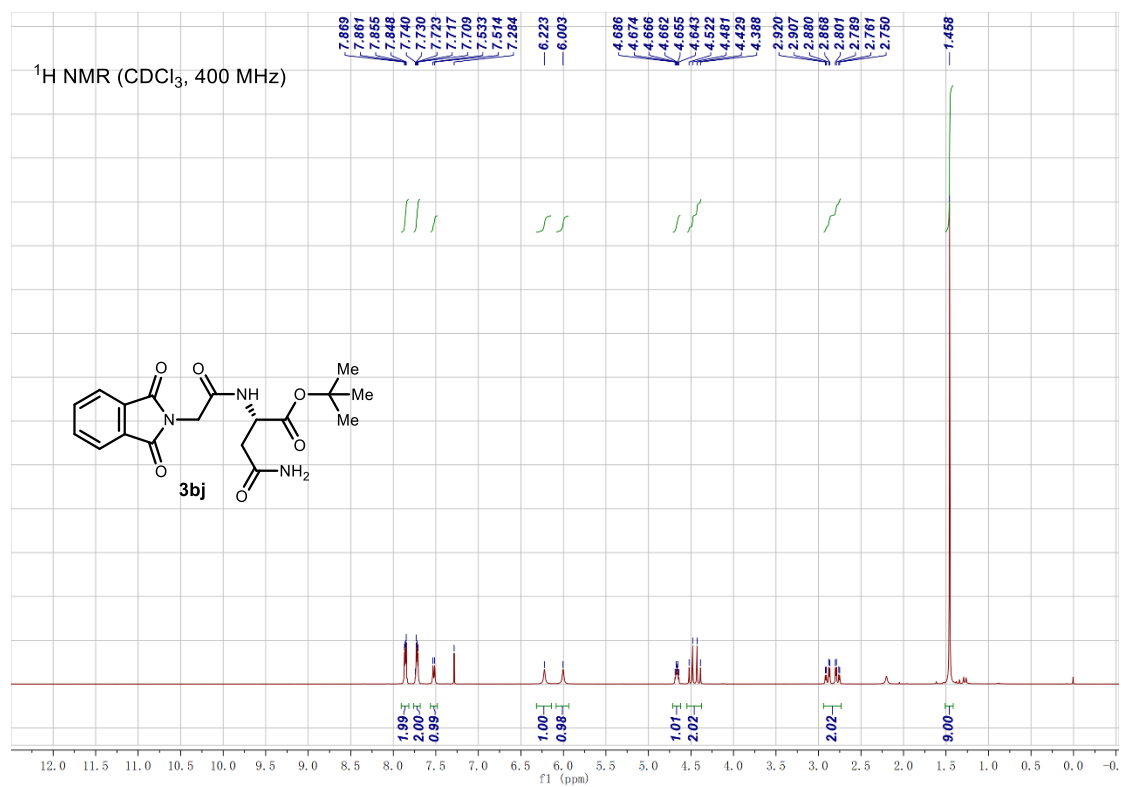
¹³C NMR of **3bh** (100 MHz, CDCl₃, 298 K)



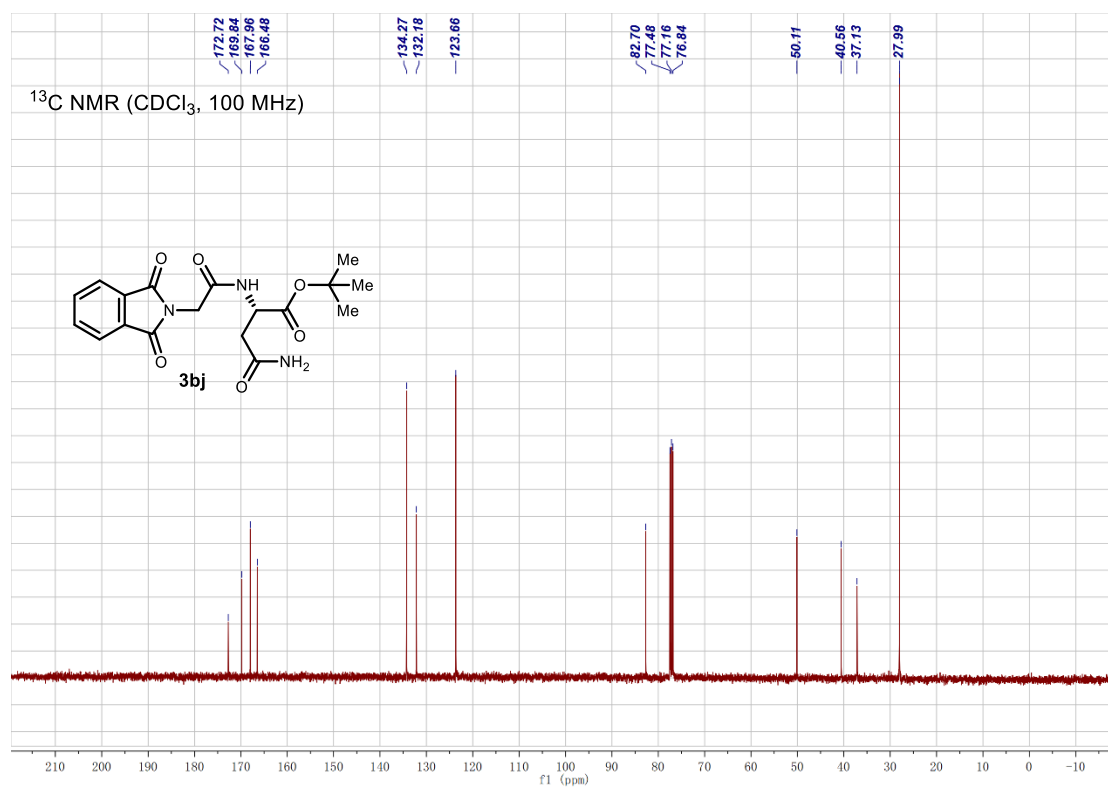
¹H NMR of **3bi** (400 MHz, CDCl₃, 298 K)



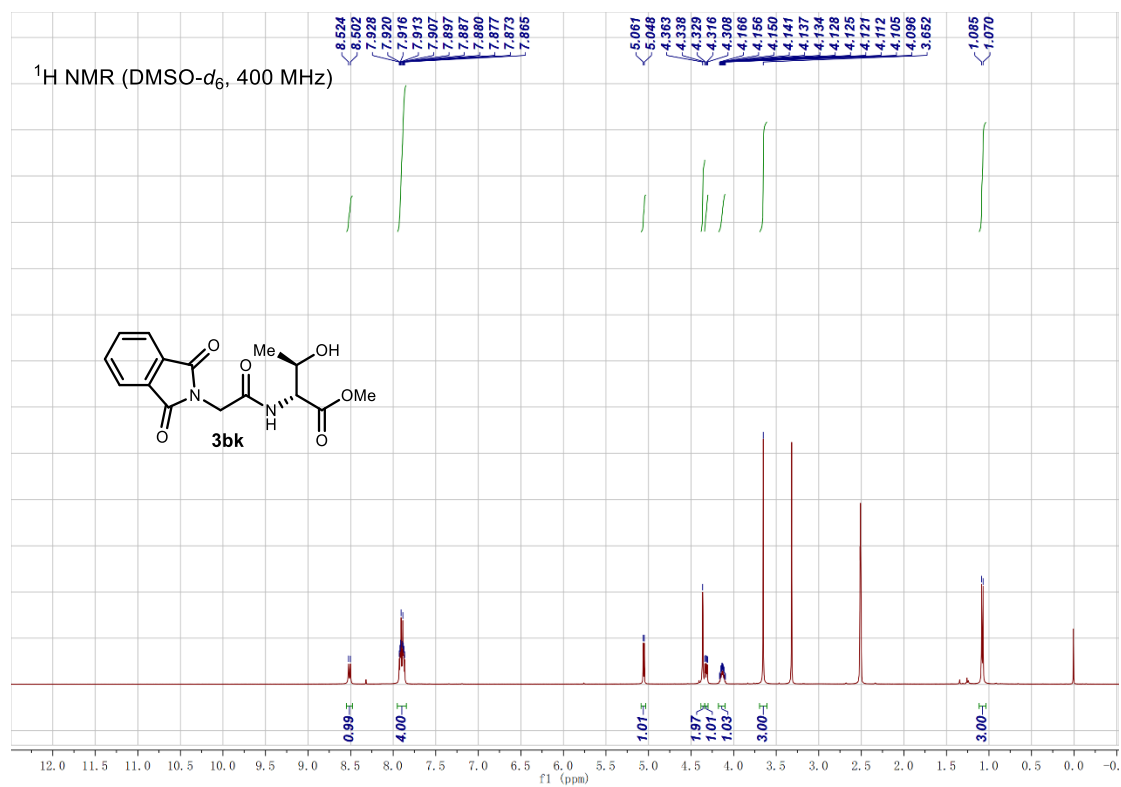
¹³C NMR of **3bi** (100 MHz, CDCl₃, 298 K)



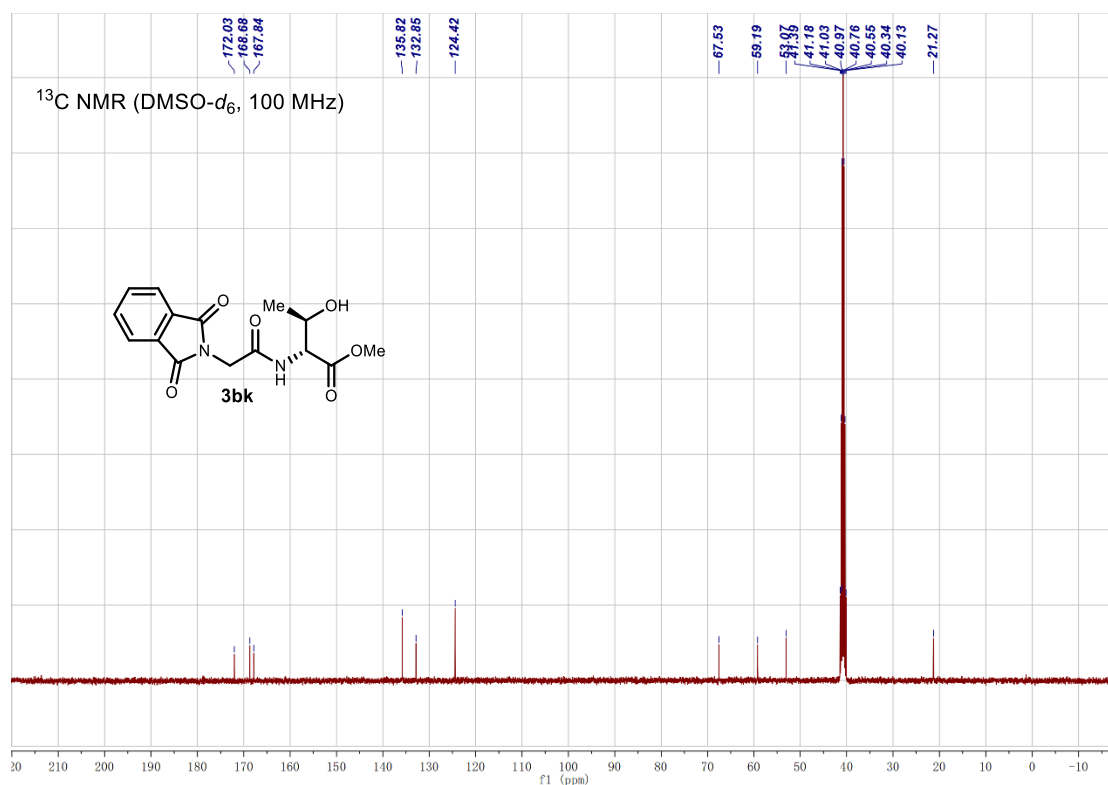
¹H NMR of **3bj** (400 MHz, CDCl₃, 298 K)



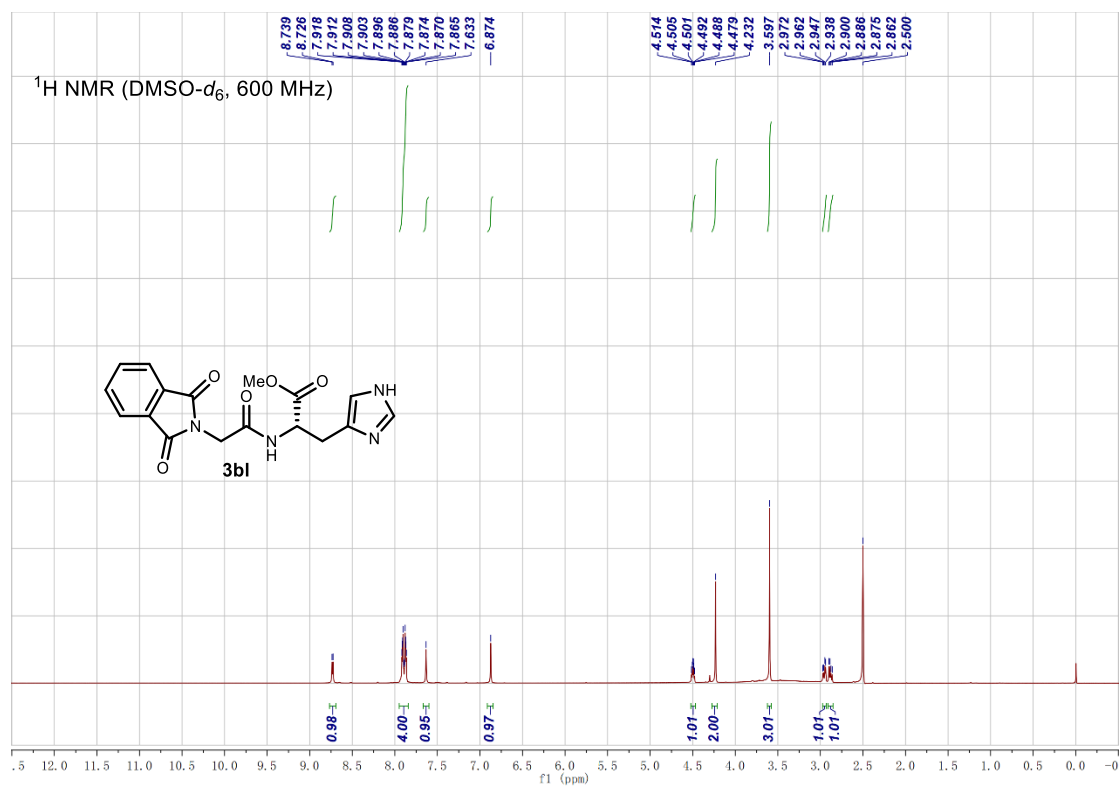
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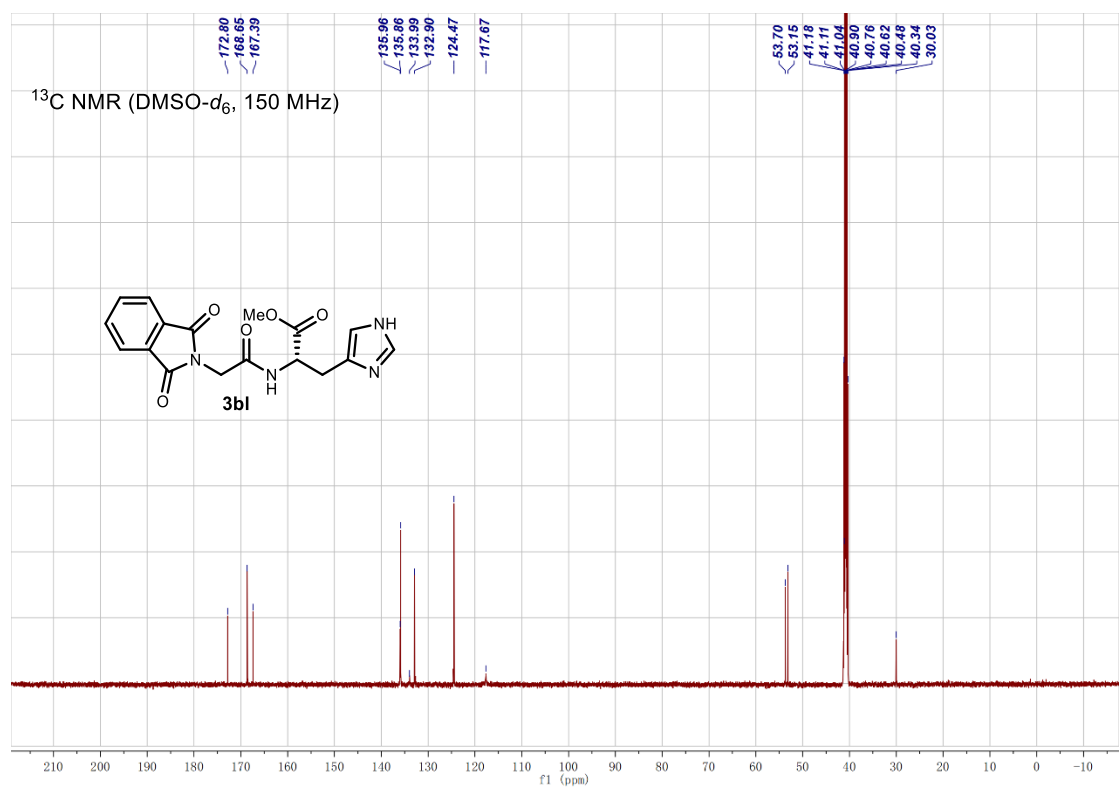
¹H NMR of **3bk** (400 MHz, DMSO-*d*₆, 298 K)



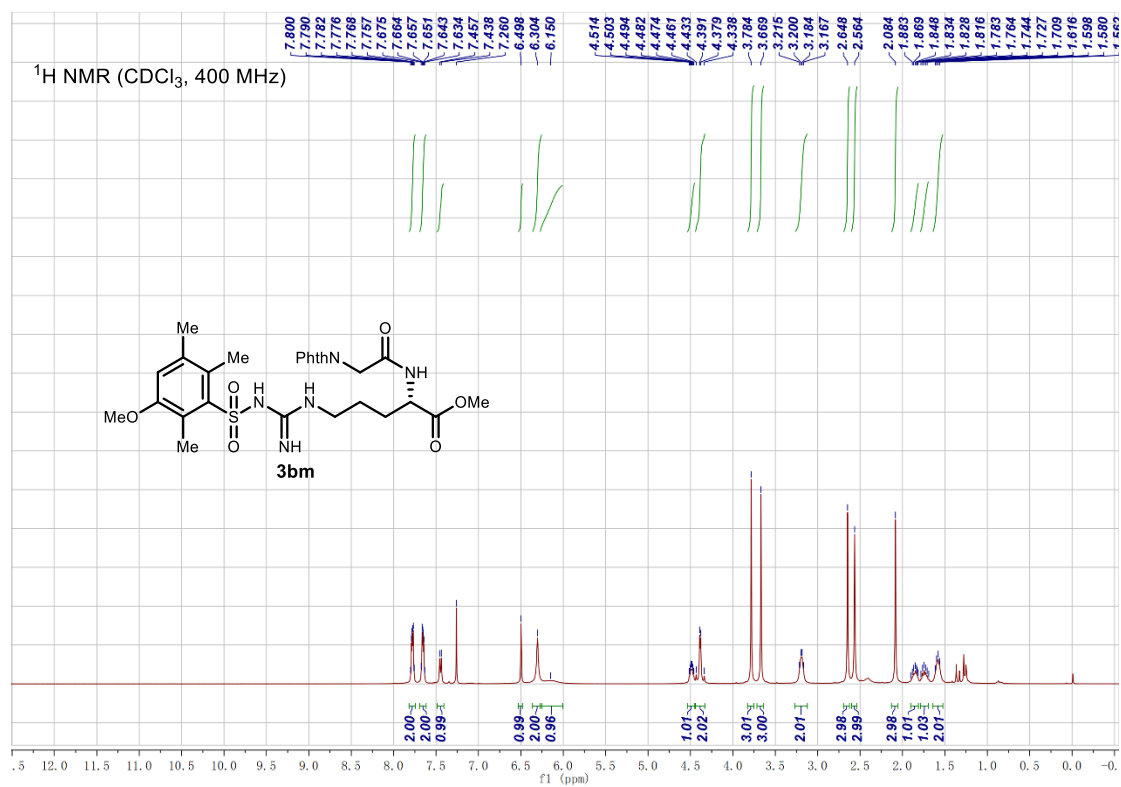
¹³C NMR of **3bk** (100 MHz, DMSO-*d*₆, 298 K)



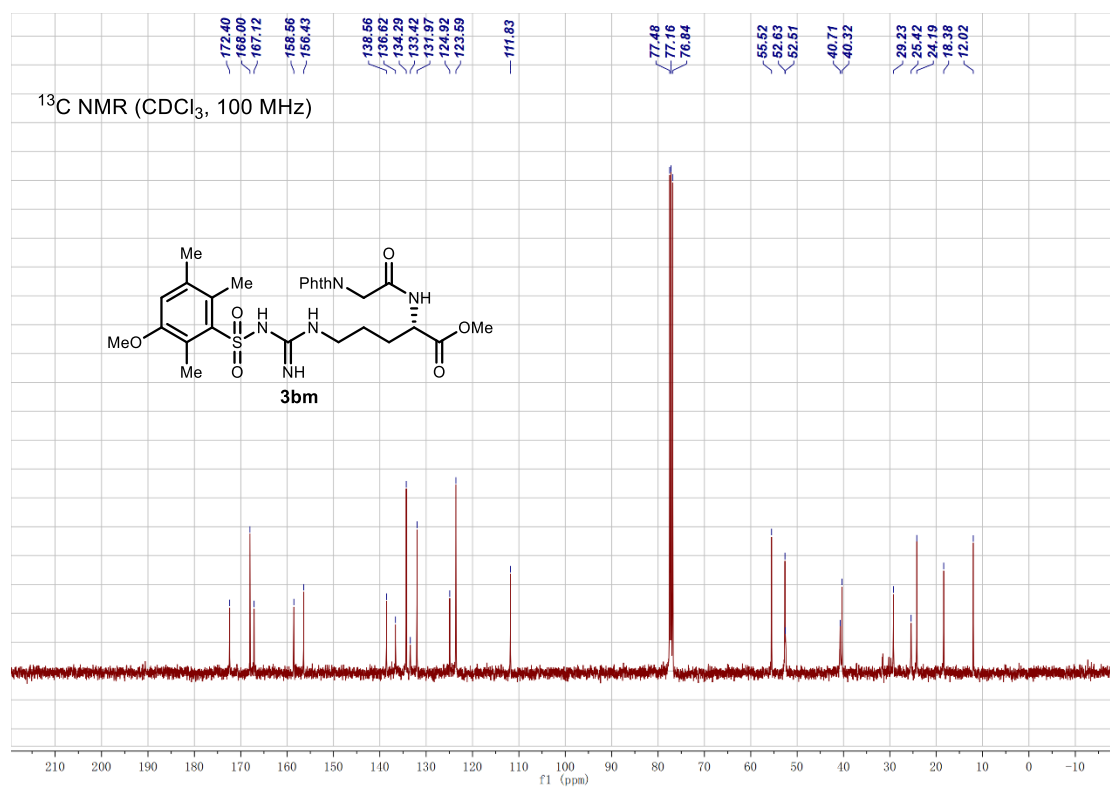
¹H NMR of **3bl** (600 MHz, DMSO-*d*₆, 298 K)



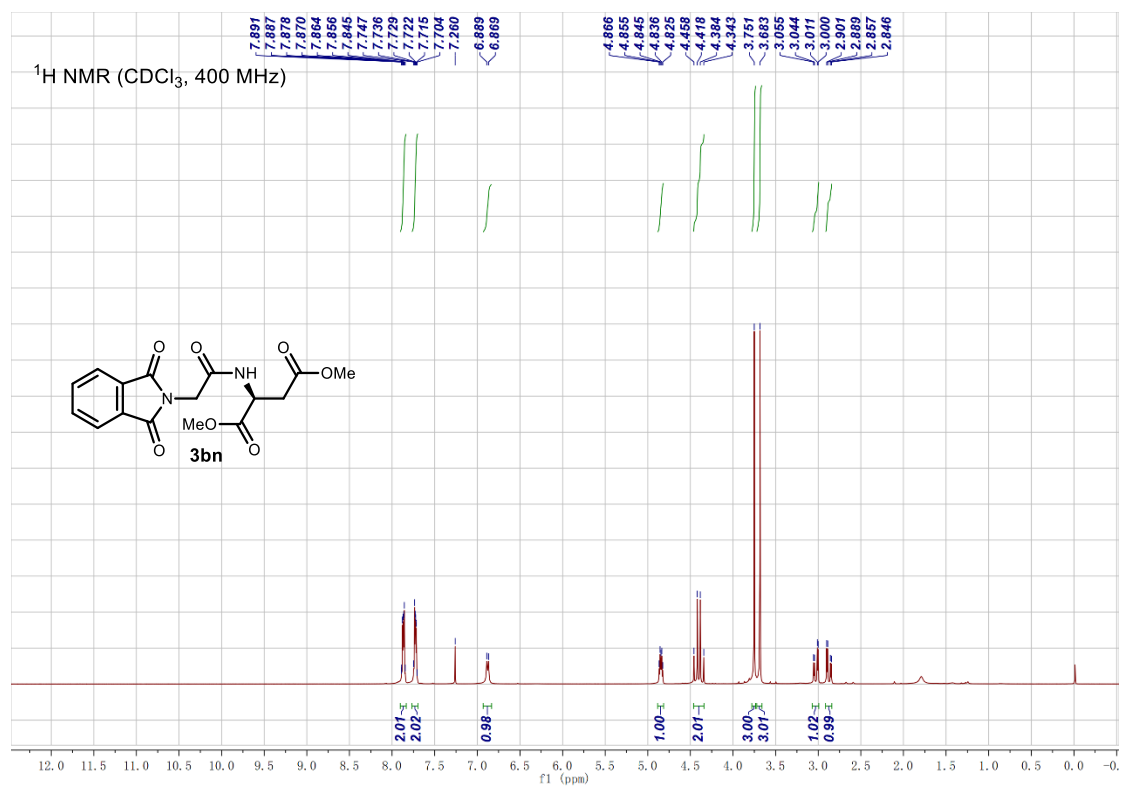
¹³C NMR of **3bl** (150 MHz, DMSO-*d*₆, 298 K)



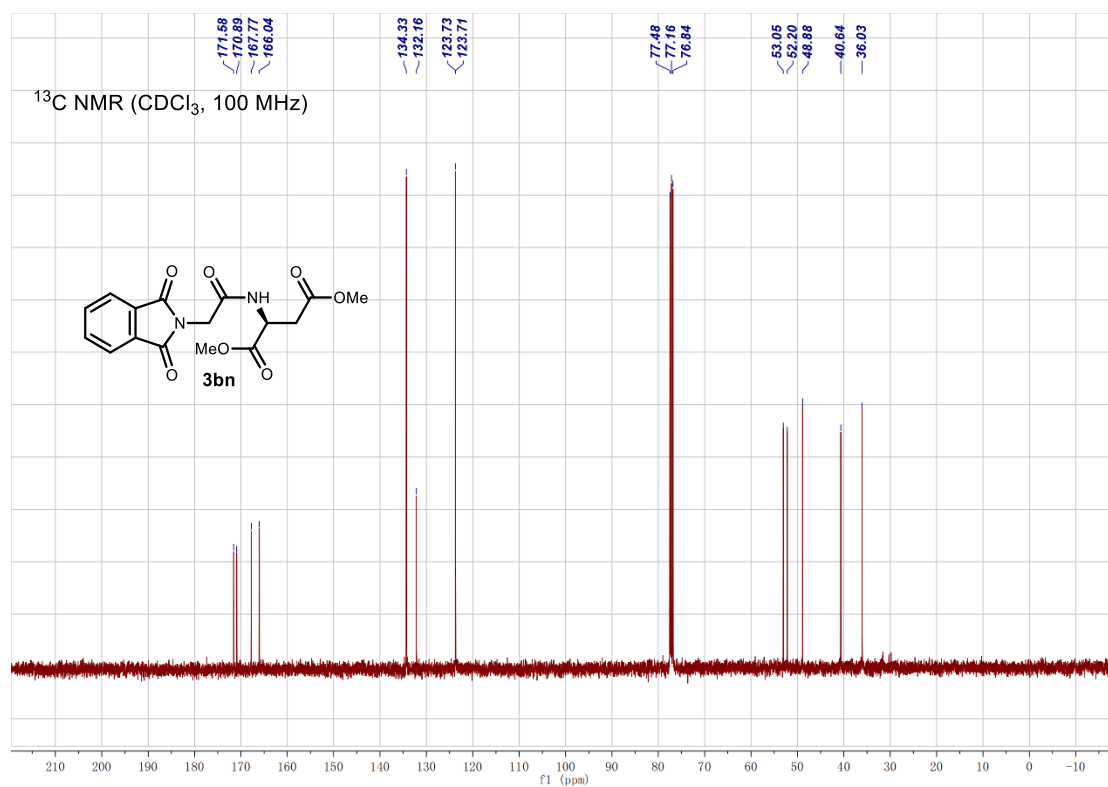
¹H NMR of **3bm** (400 MHz, CDCl₃, 298 K)



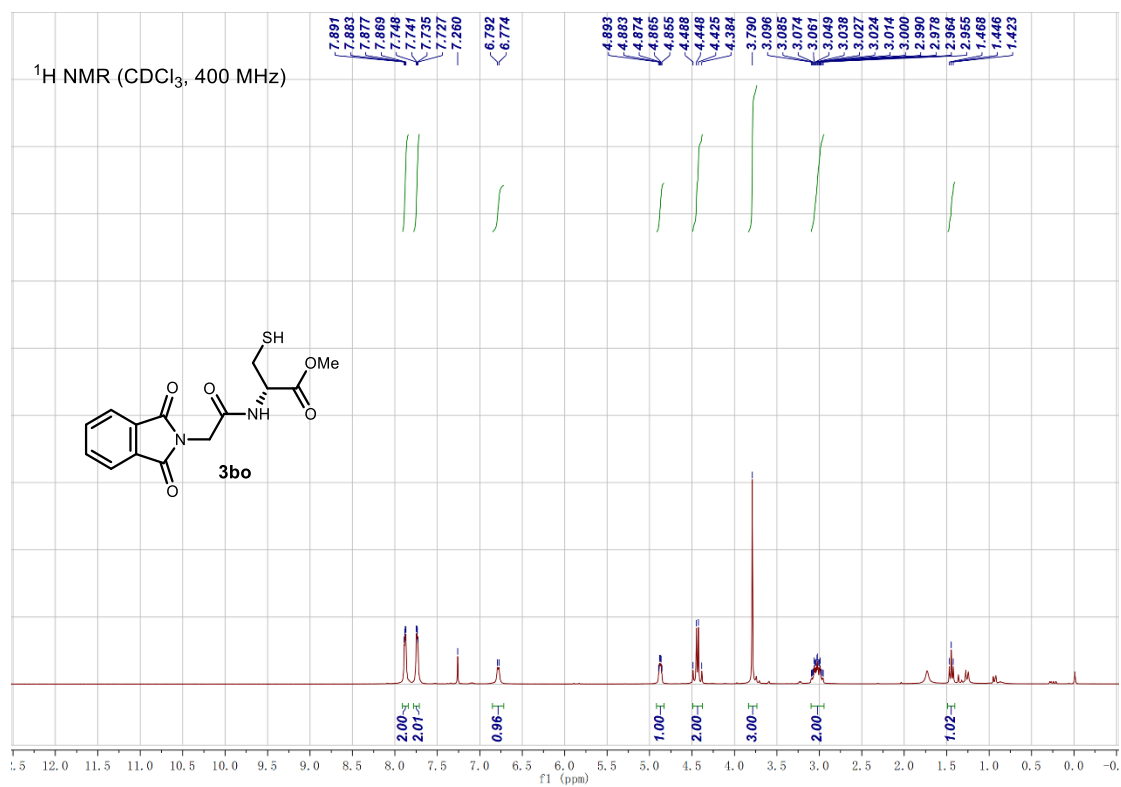
¹³C NMR of **3bm** (100 MHz, CDCl₃, 298 K)



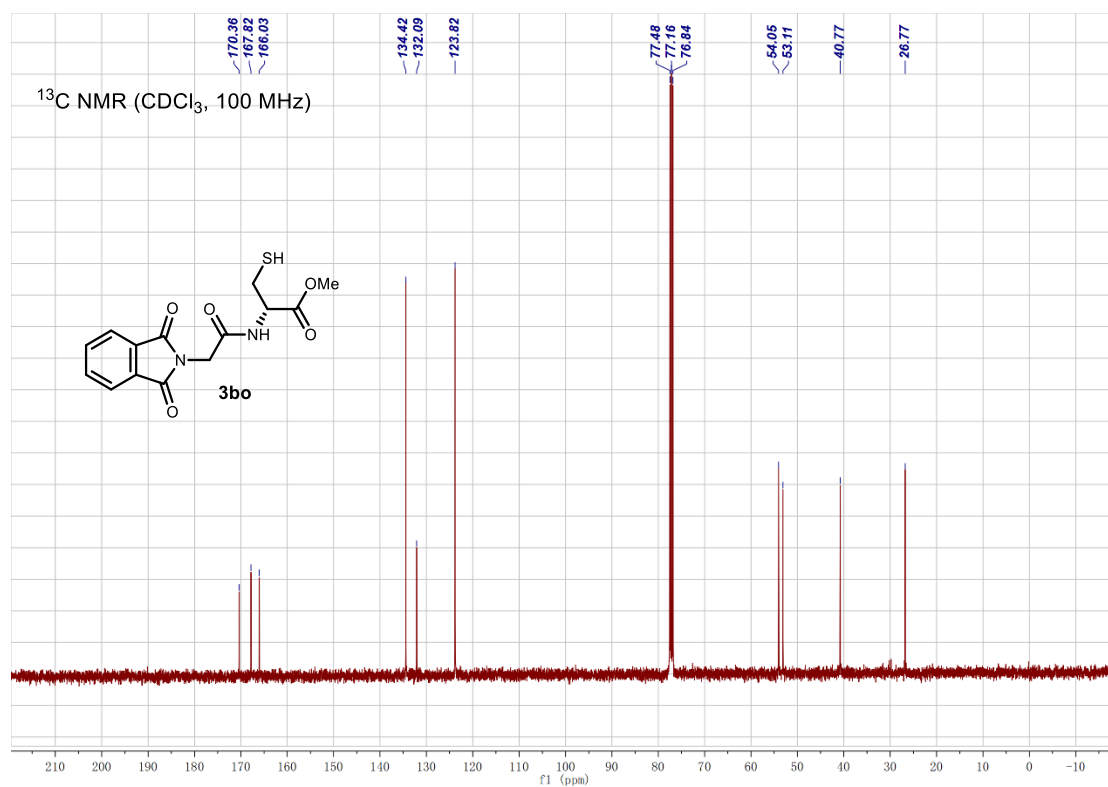
¹H NMR of **3bn** (400 MHz, CDCl₃, 298 K)



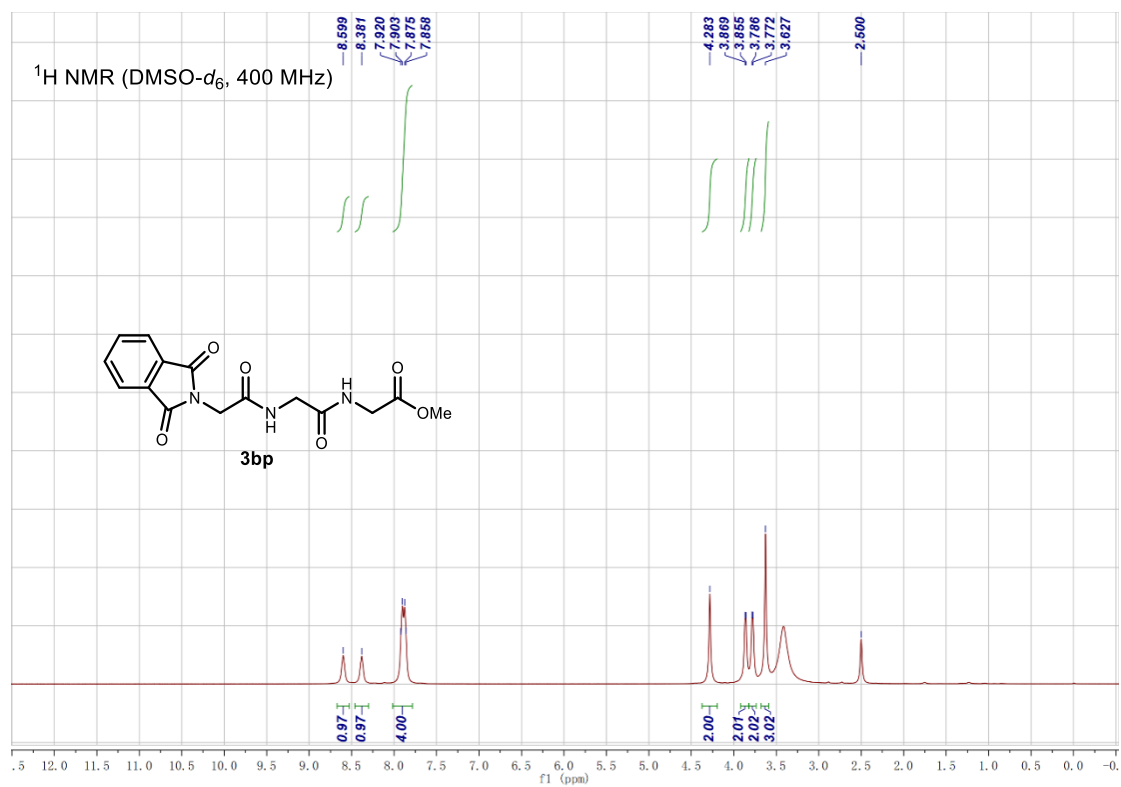
¹³C NMR of **3bn** (100 MHz, CDCl₃, 298 K)



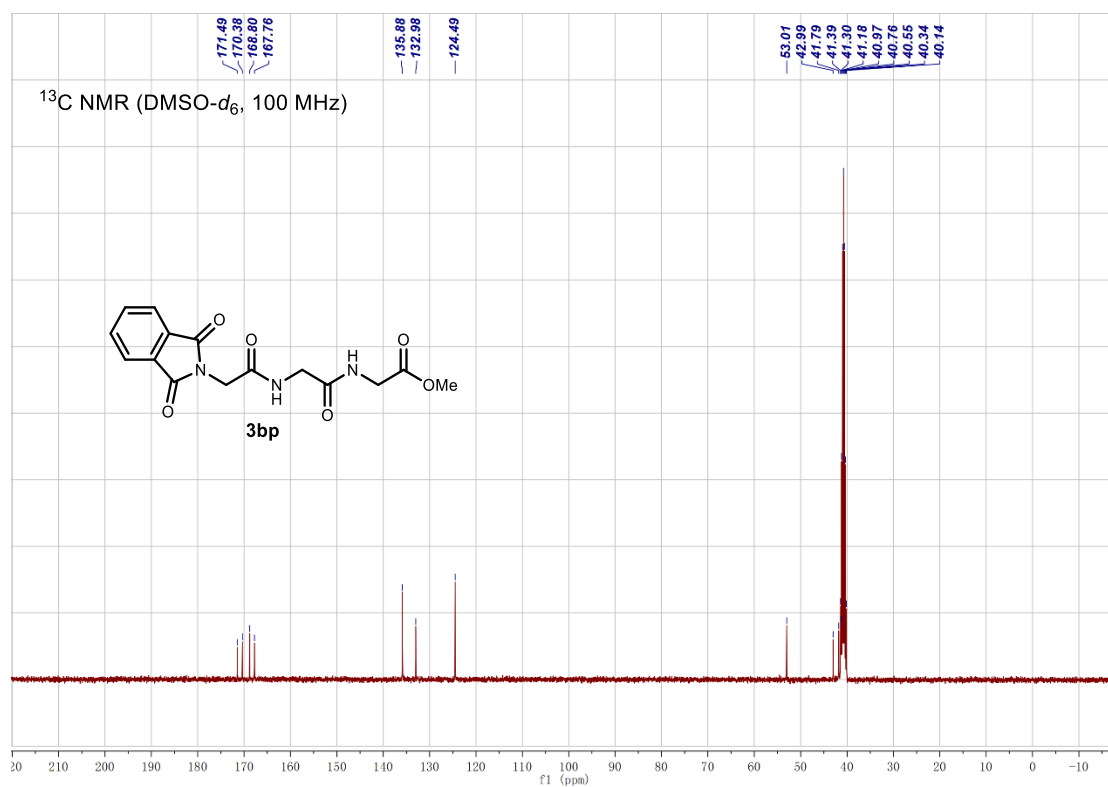
¹H NMR of **3bo** (400 MHz, CDCl₃, 298 K)



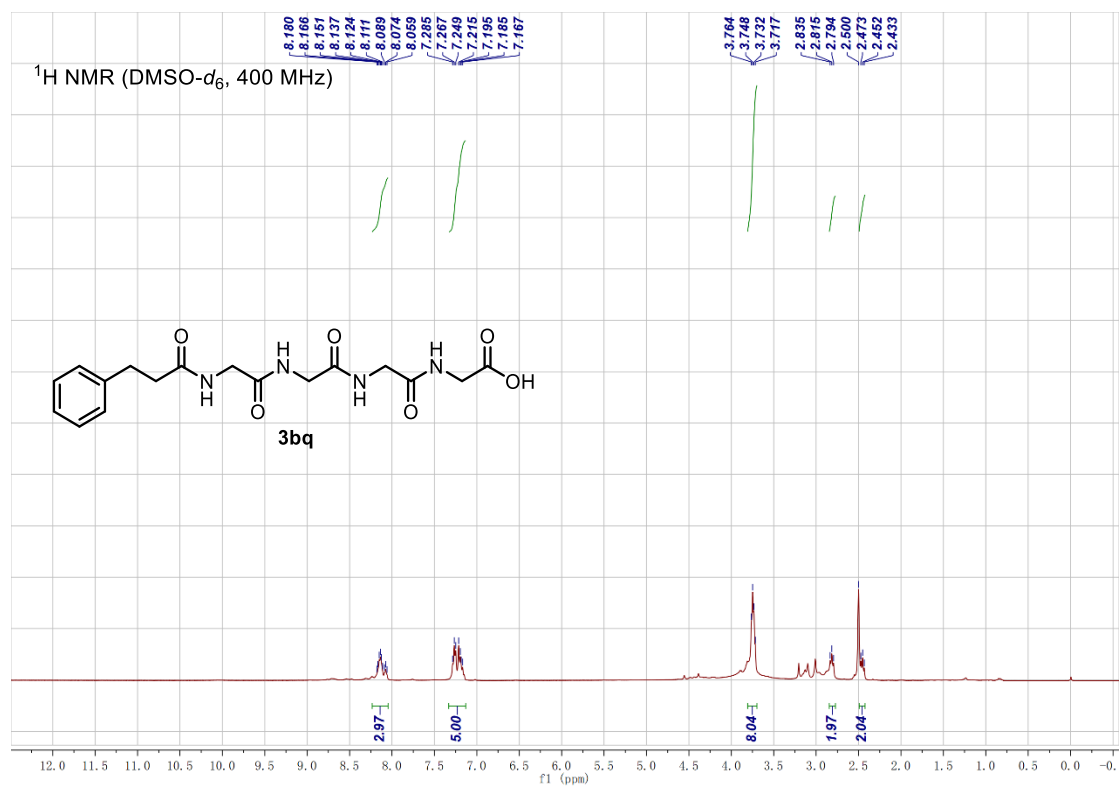
¹³C NMR of **3bo** (100 MHz, CDCl₃, 298 K)



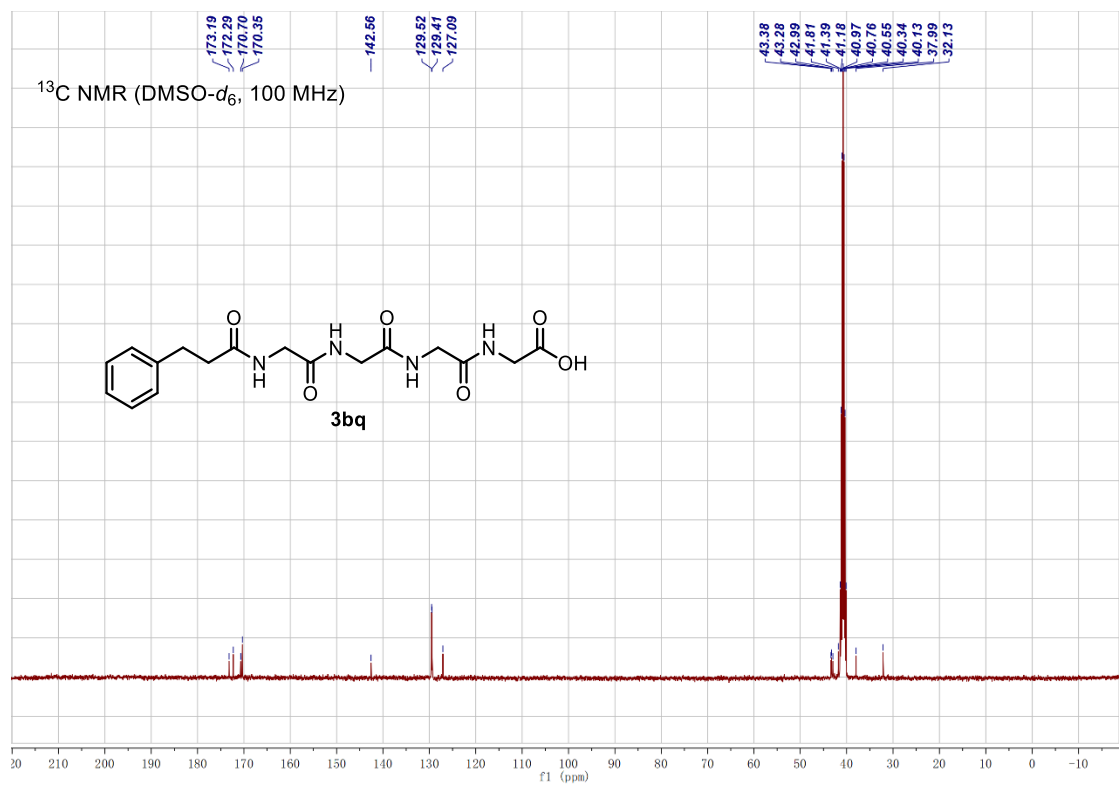
¹H NMR of **3bp** (400 MHz, DMSO-*d*₆, 298 K)



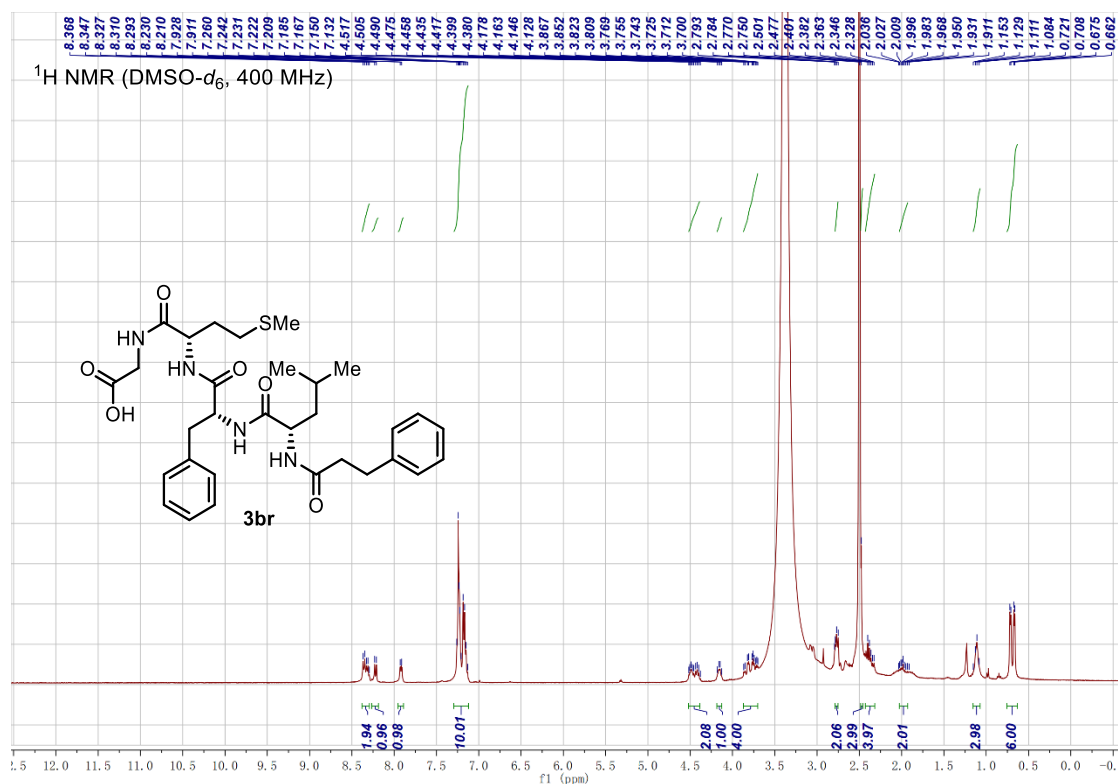
¹³C NMR of **3bp** (100 MHz, DMSO-*d*₆, 298 K)



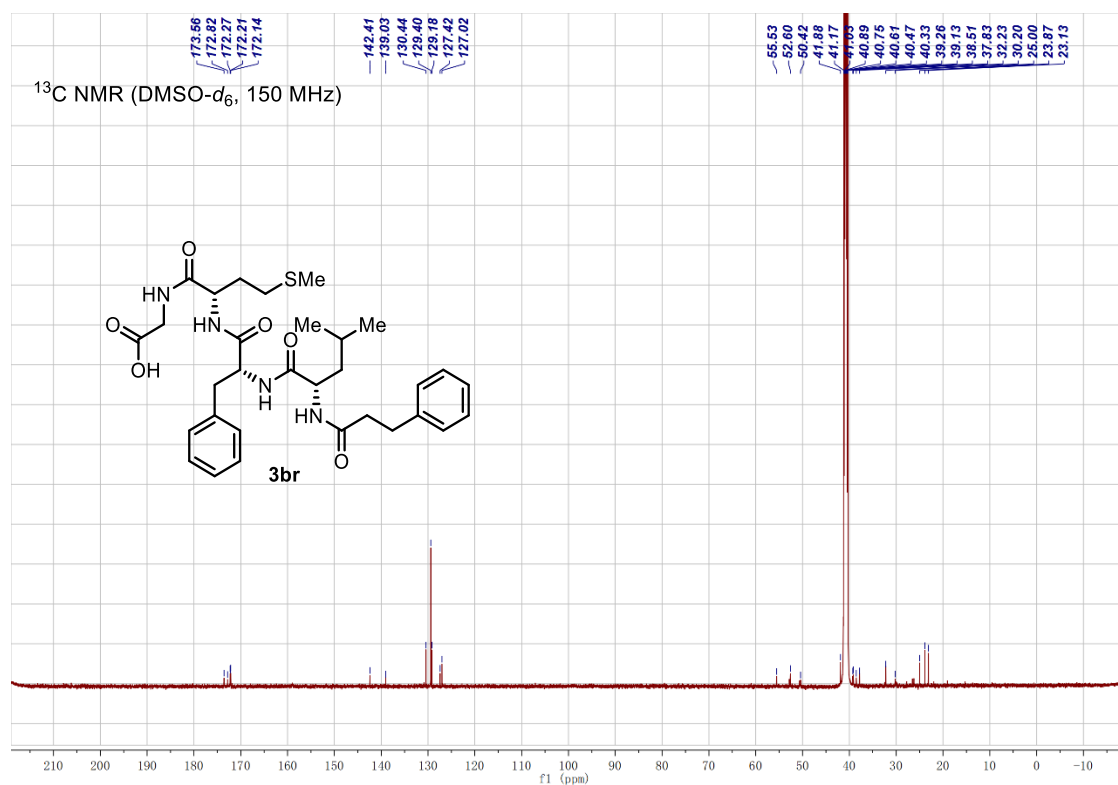
¹H NMR of **3bq** (400 MHz, DMSO-*d*₆, 298 K)



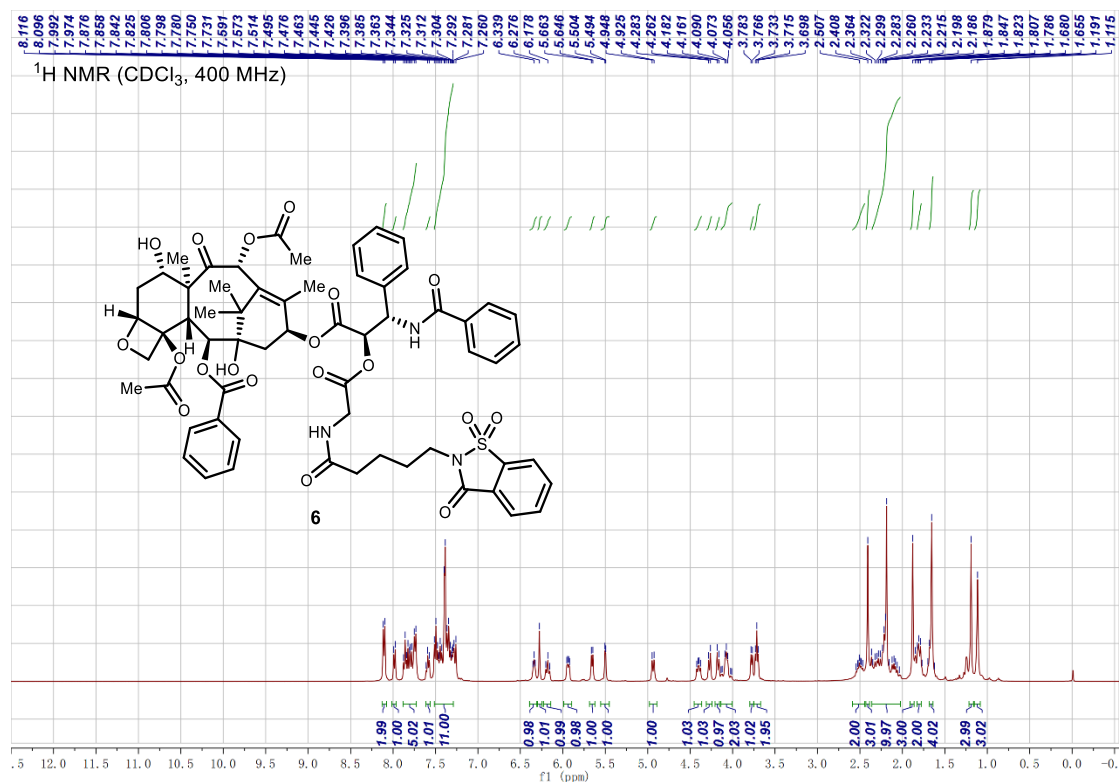
¹³C NMR of **3bq** (100 MHz, DMSO-*d*₆, 298 K)



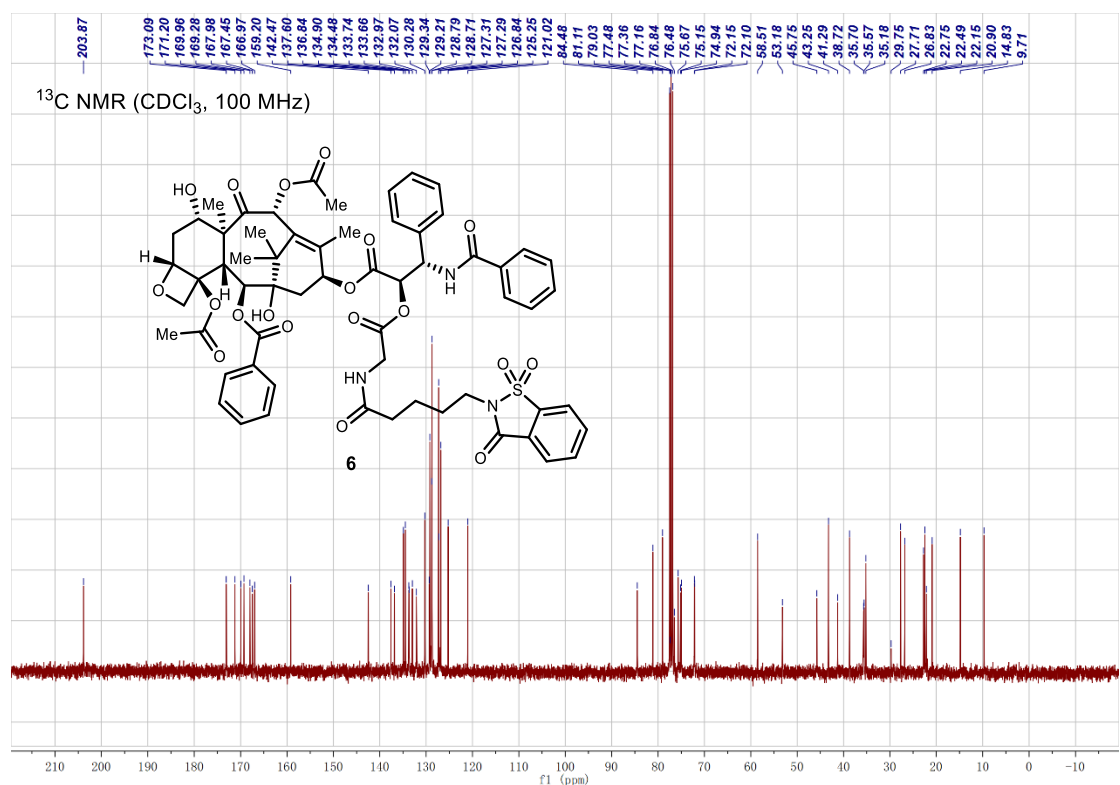
¹H NMR of **3br** (400 MHz, DMSO-*d*₆, 298 K)



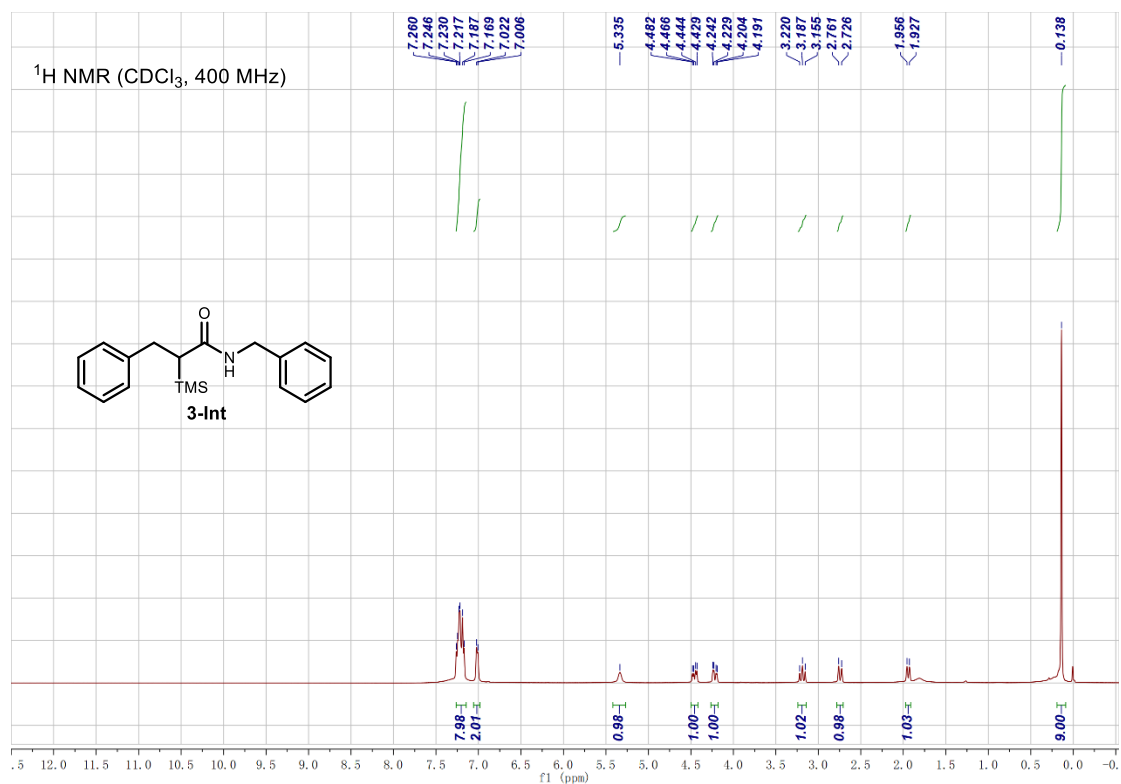
¹³C NMR of **3br** (150 MHz, DMSO-*d*₆, 298 K)



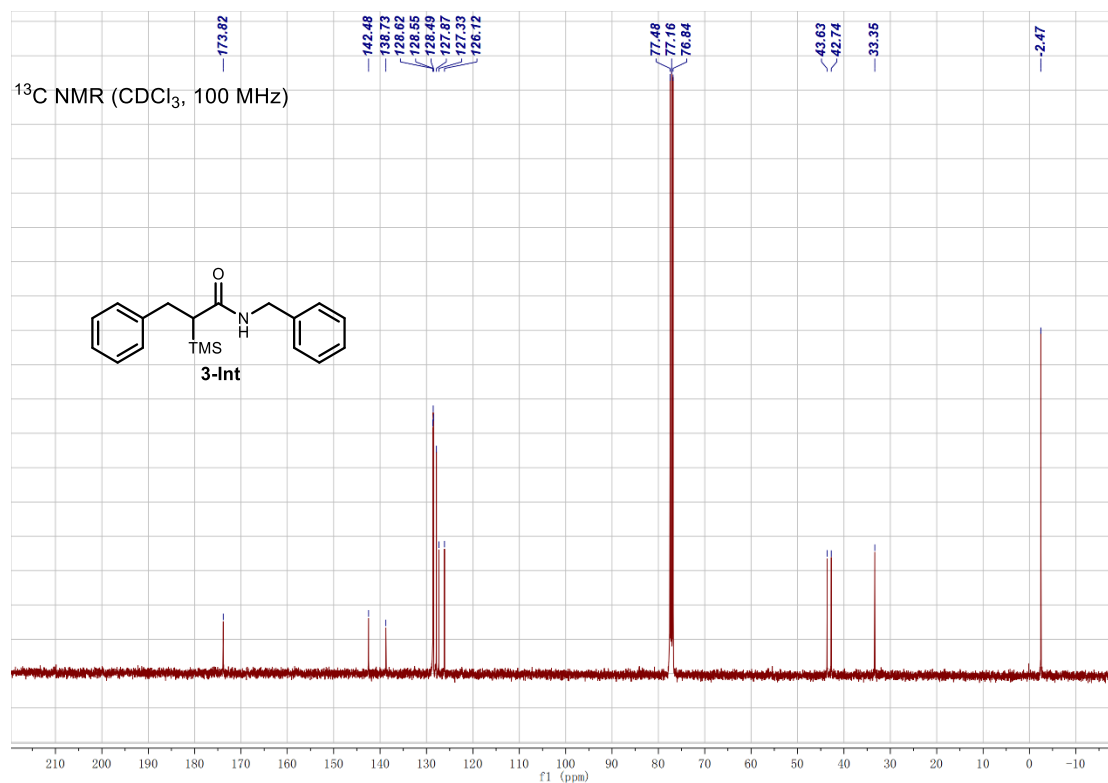
¹H NMR of **6** (400 MHz, CDCl₃, 298 K)



¹³C NMR of **6** (100 MHz, CDCl₃, 298 K)



¹H NMR of **3-Int** (400 MHz, CDCl₃, 298 K)



¹³C NMR of **3-Int** (100 MHz, CDCl₃, 298 K)

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