Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting Information

S-alkylation of cysteine-containing peptides using thianthenium salts as alkyl source in flow

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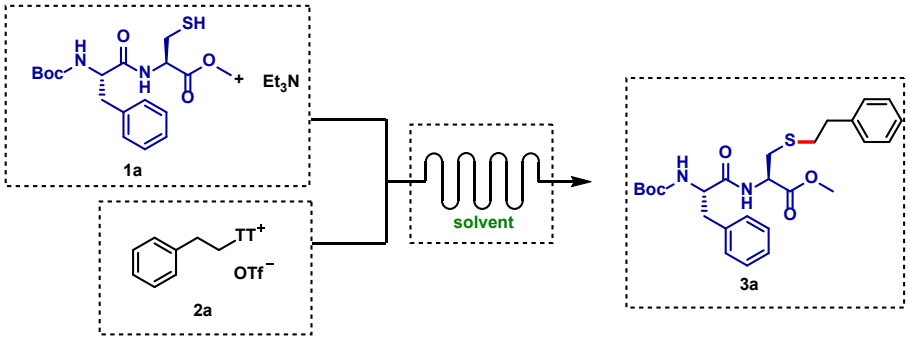
1. General Information

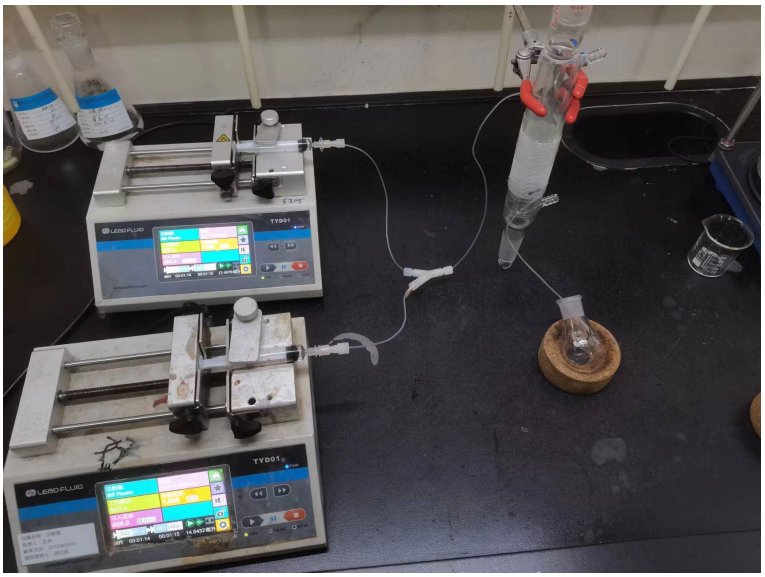
All commercially available reagents and solvents used in this study were purchased from Alfa Aesar, Sigma Aldrich or Energy Chemical and used without further purification. Thin layer chromatography (TLC) was measured on EMD preloaded plates (silica gel 60 F254) and was visualized under ultraviolet light (254 nm and 365 nm). Column chromatography was performed with silica gel (200-300 mesh).

All new compounds were characterized by ^{1}H, ^{13}C and ^{19}F NMR spectroscopy and mass spectrometry. NMR spectra were recorded on a Bruke Avance operating for ^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz, and ^{19}F NMR at 376 MHz. Chemical shifts (δ) were reported in ppm referenced to Tetramethylsilane (TMS) as internal standard. NMR spectra uses the following abbreviations to describe the multiplicity: s = single, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet, td = triple doublet. Coupling constants (*J*) were reported in hertz (Hz). Known products were characterized by comparing to the corresponding ^{1}H NMR, ^{13}C NMR and ^{19}F NMR from literature. NMR data was processed using the MestReNova 9.0.1 software package. High resolution mass spectra were obtained on Agligent Technologies 6520 Accurate Series Q-TOF equipped with ESI. Coil was used commercially available PFA (perfluoroalkoxyalkane) tube with an inner diameter of 0.6 mm.

2. General procedure



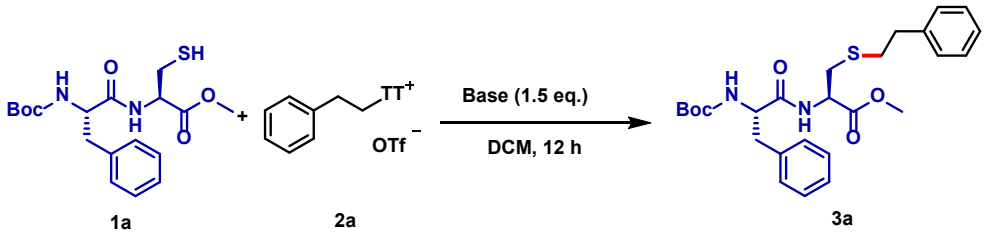
Methyl (tert-butoxycarbonyl)-L-phenylalanyl-L-cysteinate **1a** (0.4 mmol, 1.0 eq.) was dissolved in DMSO (2.0 mL) and then added Et_3N (0.6 mmol, 1.5 eq.). A second reaction solution was to dissolve the thianthrenium salts **2a** (0.48 mmol, 1.2 eq.) in DMSO (2.0 mL). The two solutions were transferred into two 5 mL BD plastic syringes and introduced into the microreactor (a high purity perfluoroalkoxyalkane, PFA capillary tubing, ID = 600 μm) through syringe pump. The two liquid streams were merged with a Y-Mixer before entering the reactor. The flow rate was set to 0.1 mL/min (0.05 mL/min per syringe), thus resulting in 14 min residence time (volume of reactor = 1.4 mL). After reaching steady state, the reaction sample was collected in a glass vial. Solution remaining in the microreactor was then discharged with DMSO (2.0 mL×2) via syringe pump, and was also collected in the same glass vial. After the reaction completed, diluted with DCM and water, and extracted with DCM (10.0 mL) for three times, combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. Purification by flash column chromatography afforded the desired product **3a**.



Supplementary Figure 1. The reaction equipment

3. Optimization of reaction conditions

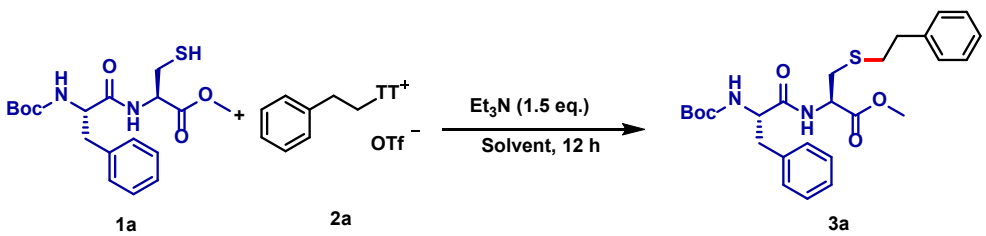
Supplementary Table 1 Screening of bases



Entry [a]	bases	Yield (%) [b]
1	DMAP	60
2	**Et_3N**	**94**
3	TBD	92
4	DIPEA	90
5	TMG	92
6	DBU	86
7	DABCO	17
8	TMEDA	50
9	Pyridine	*N.D.*
10	Cs_2CO_3	90
11	None	*N.D.*

[a] Standard condition: **1a** (1.0 eq., 0.4 mmol), **2a** (1.2 eq., 0.48 mmol), base (1.5 eq., 0.6 mmol), DCM (4.0 mL). Stirred at room temperature for 12 hours. [b] Isolated yield is based on **1a**.

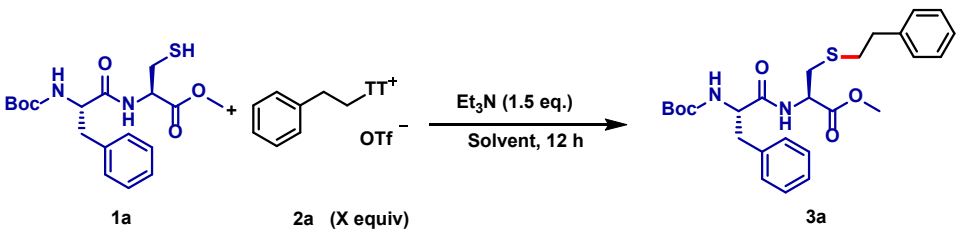
Supplementary Table 2 Screening of solvents



Entry [a]	Solvents	Yield(%) [b]
1	CH_3OH	90
2	THF	92
3	CH_3CN	90
4	DCE	78
5	Acetone	88
6	**DMSO**	**95**
7	DMF	90
8	DMA	89
9	H_2O	73

[a] Standard condition: **1a** (1.0 eq., 0.4 mmol), **2a** (1.2 eq., 0.48 mmol), Et_3N (1.5 eq., 0.6 mmol), Solvent (4.0 mL). Stirred at room temperature for 12 hours. [b] Isolated yield is based on **1a**.

Supplementary Table 3 Screening of amounts of **2a**

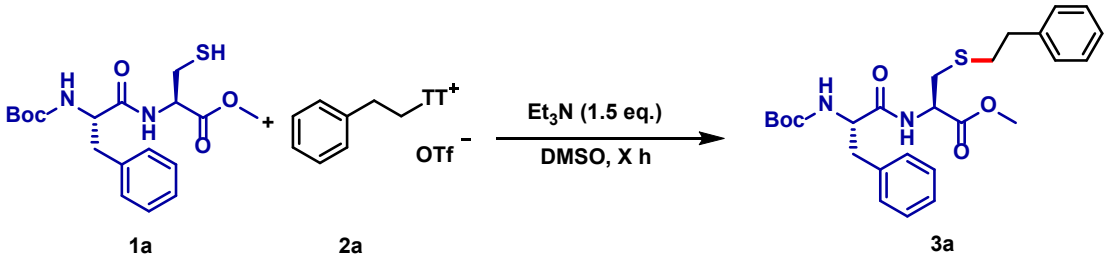


1a 2a (X equiv) 3a

Entry [a]	Amounts of 2a(equiv)	Yield (%)[b]
1	0.5	90
2	1	92
3	1.2	95
4	1.5	89
5	2	87

[a] Standard condition: **1a** (1.0 eq., 0.4 mmol), **2a** (**x** equiv), Et_3N (1.5 eq., 0.6 mmol), Solvent (4.0 mL). Stirred at room temperature for 12 hours. [b] Isolated yield is based on **1a**.

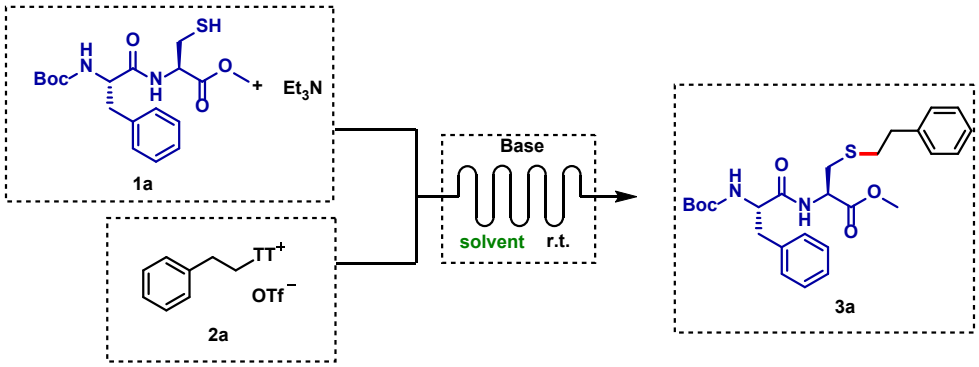
Supplementary Table 4 Screening of reaction time



Entry [a]	Reaction time(h)	Yield (%)[b]
1	6	65
2	8	81
3	10	88
4	12	95

[a] Standard condition: **1a** (1.0 eq., 0.4 mmol), **2a** (1.2 eq., 0.48 mmol), Et_3N (1.5 eq., 0.6 mmol), Solvent (4.0 mL). Stirred at room temperature for **x** hours. [b] Isolated yield is based on **1a**.

Supplementary Table 5 Screening of flow rate

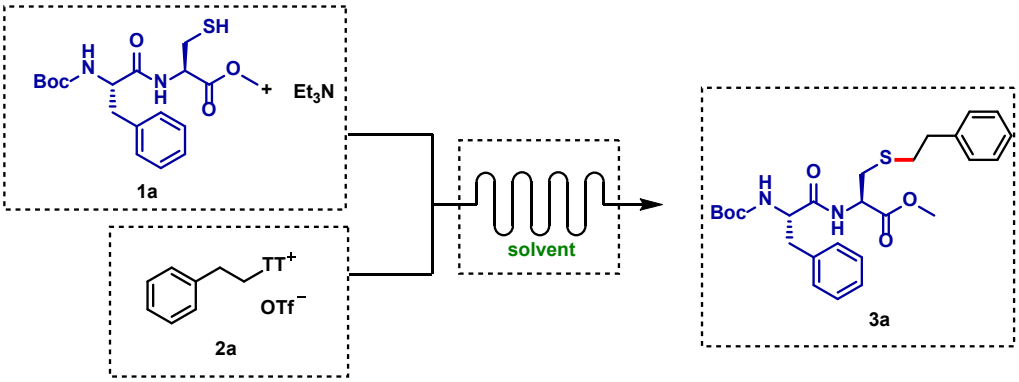


Entry [a]	Rate (mL/min)	Residue time (min)	Yield (%)[b]
1	**0.05**	**14.0**	**96**
2	0.075	9.33	88
3	0.1	7.0	82
4	0.15	4.67	76
5	0.2	3.5	68
6	0.4	1.75	58

[a] Standard condition: **1a** (1.0 eq., 0.4 mmol) and Et_3N (1.5 eq., 0.6 mmol) was dissolved in DMSO (2.0

mL); **2a** (1.2 eq., 0.48 mmol) was dissolved in DMSO (2.0 mL). The solution was transferred into syringe and introduced into microreactor through syringe pump. [b] Isolated yield is based on **1a.**

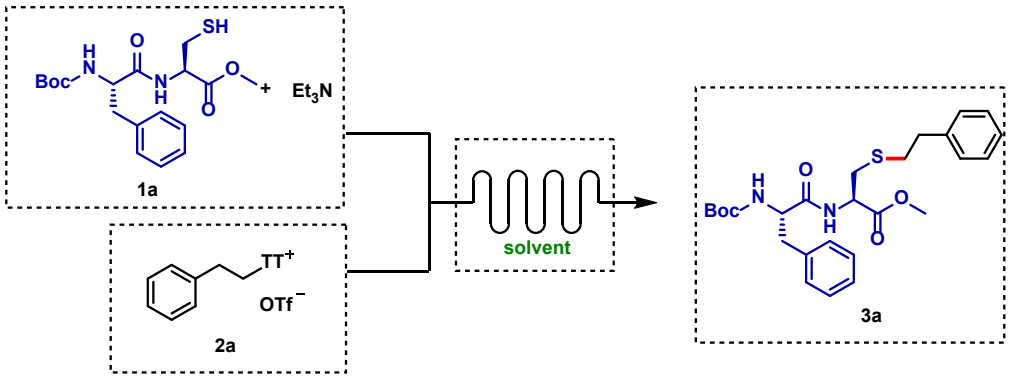
Supplementary Table 6 Screening of flow solvent



Entry [a]	Solvents	Yield (%)[b]
1	CH_3OH	/
2	THF	89
3	CH_3CN	88
4	DCE	80
5	Acetone	85
6	**DMSO**	**96**
7	DMF	87
8	DMA	82
9	DMSO/H_2O(4:1)	88
10	DMSO/H_2O(7:3)	82
11	DMSO/H_2O(3:2)	78
12	DMSO/H_2O(1:1)	69
13	H_2O	/

[a] Standard condition: **1a** (1.0 eq., 0.4 mmol) and Et_3N (1.5 eq., 0.6 mmol) were dissolved in Solvents (2.0 mL); **2a** (1.2 eq., 0.48 mmol) was dissolved in Solvents (2.0 mL). The solution was transferred into syringe and introduced into microreactor through syringe pump (PFA tube, ID = 600 μm) for 14 min. [b] Isolated yield is based on **1a.**

Supplementary Table 7 Screening of flow pipe diameter



Entry [a]	diameter	Yield (%)[b]
1	500 μm	94
2	**600 μm**	**96**
3	800 μm	88
4	1000 μm	79

[a] Standard condition: **1a** (1.0 eq., 0.4 mmol) and Et_3N (1.5 eq., 0.6 mmol) was dissolved in DMSO (2.0 mL); **2a** (1.2 eq., 0.48 mmol) was dissolved in DMSO (2.0 mL). The solution was transferred into syringe and introduced into microreactor through syringe pump for 14 min. [b] Isolated yield is based on **1a.**

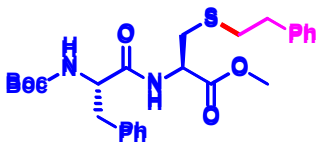
Supplementary Table 8 The comparison between batch and flow

Product	Isolated yield (%)[a] (in batch)	Time[a] (in batch)	Space time yield (mol/L·h)[a] (in batch)	Isolated yield (%)[b] (in flow)	Time[b] (in flow)	Space time yield (mol/L·h)[b] (in flow)
3a	95	12 h	$8.3*10^{-3}$	96	14 min	$6.1*10^{-1}$
4a	87	12 h	$8.3*10^{-3}$	92	14 min	$6.1*10^{-1}$
5a	81	12 h	$8.3*10^{-3}$	85	14 min	$6.1*10^{-1}$

[a] Reaction condition: **1a** (0.2 mmol), **2a** (0.24 mmol), Et_3N (0.3 mmol), Solvent (2.0 mL). Stirred in the seal reaction tube (25 mL) at room temperature

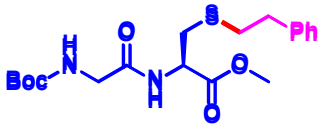
[b] Reaction conditions: the reaction was carried out in the microfluidic chip reactor (1.4 mL) with a flow rate of 0.05mL/min at room temperature

4. NMR Spectra



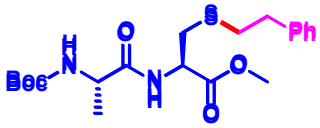
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-phenethyl-L-cysteinate (3a)

White solid (Flow:186.6 mg, 96% yield; Batch:184.7 mg, 95% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.25 (m, 4H), 7.24 – 7.16 (m, 6H), 6.69 (d, *J* = 7.2 Hz, 1H), 4.99 (s, 1H), 4.78 – 4.70 (m, 1H), 4.47 – 4.33 (m, 1H), 3.71 (s, 3H), 3.13 – 3.02 (m, 2H), 2.97 – 2.89 (m, 2H), 2.86 – 2.79 (m, 2H), 2.77 – 2.69 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.1, 170.7, 155.4, 140.0, 136.5, 129.3, 128.7, 128.5(3), 128.5(0), 127.0, 126.5, 80.3, 52.6, 52.0, 38.2, 36.1, 34.2, 34.0, 28.3. HRMS (ESI) m/z: calcd for $C_{26}H_{34}N_2O_5SNa$ $[M+Na]^+$: 509.2081, found: 509.2076.



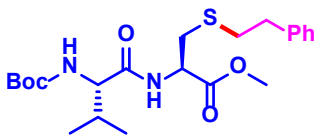
Methyl *N*-((tert-butoxycarbonyl)glycyl)-*S*-phenethyl-L-cysteinate (3b)

Light yellow oil (Flow:112.5 mg, 71% yield; Batch:109.3mg, 69% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23-7.18 (m, 2H), 7.15 – 7.03 (m, 4H), 5.36 (t, *J* = 5.5 Hz, 1H), 4.77 – 4.71 (m, 1H), 3.81 – 3.70 (m, 2H), 3.65 (s, 3H), 2.95 – 2.84 (m, 2H), 2.80 – 2.74 (m, 2H), 2.72 – 2.66 (m, 2H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.1, 169.6, 156.1, 140.0, 128.5, 126.5, 80.2, 52.7, 51.9, 44.2, 36.1, 34.1, 34.0, 28.3. HRMS (ESI) m/z: calcd for $C_{19}H_{28}N_2O_5SNa$ $[M+Na]^+$: 419.1611, found: 419.1615.



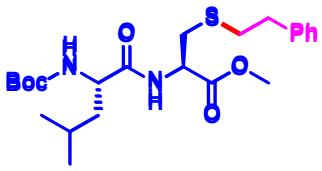
Methyl *N*-((tert-butoxycarbonyl)-L-alanyl)-*S*-phenethyl-L-cysteinate (3c)

Colorless oil (Flow:137.6 mg, 84% yield; Batch:137.7mg, 81% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 – 7.18 (m, 2H), 7.14 – 7.08 (m, 3H), 7.02 (s, 1H), 5.25 – 5.09 (m, 1H), 4.74 – 4.68 (m, 1H), 4.16 (s, 1H), 3.65 (s, 3H), 2.95 – 2.84 (m, 2H), 2.79 – 2.74 (m, 2H), 2.71 – 2.66 (m, 2H), 1.36 (s, 9H), 1.27 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.8, 171.1, 155.4, 140.1, 128.5, 126.4, 80.0, 52.6, 51.9, 50.0, 36.1, 34.1, 34.0, 28.3, 18.3. HRMS (ESI) m/z: calcd for $C_{20}H_{30}N_2O_5SNa$ $[M+Na]^+$: 433.1768, found: 433.1771.



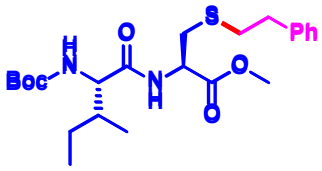
Methyl *N*-((tert-butoxycarbonyl)-L-valyl)-*S*-phenethyl-L-cysteinate (3d)

Colorless oil (Flow:151.6 mg, 87% yield; Batch:144.6mg, 83% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.18 (m, 2H), 7.14 – 7.08 (m, 3H), 6.87 (d, *J* = 7.3 Hz, 1H), 5.16 (d, *J* = 8.5 Hz, 1H), 4.75 – 4.69 (m, 1H), 4.01 – 3.88 (m, 1H), 3.64 (s, 3H), 2.93 – 2.86 (m, 2H), 2.79 – 2.74 (m, 2H), 2.72 – 2.66 (m, 2H), 2.11 – 2.01 (m, 1H), 1.36 (s, 9H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.7, 171.1, 155.8, 140.0, 128.5, 126.4, 79.8, 52.6, 51.8, 36.1, 34.1, 34.0, 31.0, 28.3, 19.2, 17.7. HRMS (ESI) m/z: calcd for $C_{22}H_{34}N_2O_5SNa$ $[M+Na]^+$: 461.2081, found: 461.2082.



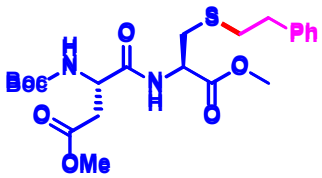
Methyl *N*-((tert-butoxycarbonyl)-L-leucyl)-*S*-phenethyl-L-cysteinate (3e)

Colorless oil (Flow: 166.6 mg, 92% yield; Batch: 159.4mg, 88% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 – 7.17 (m, 2H), 7.14 – 7.08 (m, 3H), 7.04 (d, *J* = 5.9 Hz, 1H), 5.05 (d, *J* = 7.4 Hz, 1H), 4.74 – 4.66 (m, 1H), 4.11 (s, 1H), 3.64 (s, 3H), 2.95 – 2.85 (m, 2H), 2.79 – 2.74 (m, 2H), 2.71 – 2.65 (m, 2H), 1.64 – 1.53 (m, 2H), 1.43 – 1.39 (m, 1H), 1.36 (s, 9H), 0.85 (dd, *J* = 6.2, 3.3 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.0, 171.2, 155.7, 140.1, 128.5(0), 128.4(7), 126.4, 79.7, 53.0, 52.5, 52.1, 41.2, 36.0, 33.9, 33.9, 28.3, 24.6, 23.0, 22.0. HRMS (ESI) m/z: calcd for $C_{23}H_{36}N_2O_5SNa$ $[M+Na]^+$: 475.2237, found: 475.2240.



Methyl *N*-((tert-butoxycarbonyl)-L-isoleucyl)-*S*-phenethyl-L-cysteinate (3f)

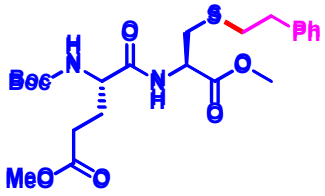
Colorless oil (Flow: 161.8 mg, 89% yield; Batch: 165.4mg, 91% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 – 7.18 (m, 2H), 7.14 – 7.08 (m, 3H), 6.86 (d, *J* = 7.2 Hz, 1H), 5.14 (d, *J* = 8.4 Hz, 1H), 4.75 – 4.69 (m, 1H), 4.02 – 3.92 (m, 1H), 3.65 (s, 3H), 2.92 – 2.87 (m, 2H), 2.79 – 2.74 (m, 2H), 2.72 – 2.65 (m, 2H), 1.85 – 1.75 (m, 1H), 1.48 – 1.41 (m, 1H), 1.36 (s, 9H), 1.11 – 1.01 (m, 1H), 0.88 – 0.80 (m, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.9, 171.3, 140.2, 128.5(0), 128.4(7), 126.4, 79.6, 59.1, 52.5, 51.9, 37.4, 36.0, 33.9, 28.3, 24.7, 15.4, 11.4. HRMS (ESI) m/z: calcd for $C_{23}H_{36}N_2O_5SNa$ $[M+Na]^+$: 475.2237, found: 475.2239.



Methyl (*S*)-3-((tert-butoxycarbonyl)amino)-4-(((*R*)-1-methoxy-1-oxo-3-(phenethyl thio) propan -2-yl)amino)-4-oxobutanoate (3g)

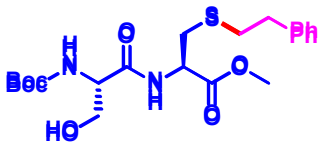
Colorless oil (Flow: 157.4 mg, 84% yield; Batch: 148mg, 79% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 (d, *J* = 7.2 Hz, 1H), 7.22 – 7.18 (m, 2H), 7.12 (t, *J* = 7.4 Hz, 3H), 5.69 (d, *J* = 8.1 Hz, 1H), 4.71 – 4.65 (m, 1H), 4.55 – 4.45 (m, 1H), 3.65 (s, 3H), 3.59 (s, 3H), 2.92 – 2.85 (m, 3H), 2.80

– 2.75 (m, 2H), 2.72 – 2.59 (m, 3H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.1, 170.8, 170.7, 155.5, 140.1, 128.5, 126.4, 80.5, 52.6, 52.1(2), 52.0(7), 50.6, 36.1, 35.8, 34.0, 33.9, 28.3. HRMS (ESI) m/z: calcd for $C_{22}H_{32}N_2O_7SNa$ $[M+Na]^+$: 491.1822, found: 491.1823.



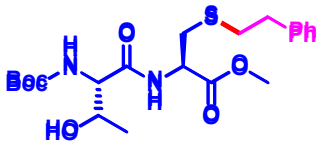
Methyl (*S*)-4-((tert-butoxycarbonyl)amino)-5-(((*R*)-1-methoxy-1-oxo-3-(phenethyl thio) propan -2-yl)amino)-5-oxopentanoate (3h)

Colorless oil (Flow: 167.2 mg, 87% yield; Batch: 159.5mg, 83% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.18 (m, 2H), 7.17 – 7.07 (m, 4H), 5.39 (d, *J* = 7.4 Hz, 1H), 4.73 – 4.66 (m, 1H), 4.27 – 4.10 (m, 1H), 3.65 (s, 3H), 3.59 (s, 3H), 2.94 – 2.85 (m, 2H), 2.80 – 2.75 (m, 2H), 2.72 – 2.66 (m, 2H), 2.45 – 2.35 (m, 2H), 2.12 – 2.02 (m, 1H), 1.92 – 1.81 (m, 1H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.7, 171.7, 171.0, 155.6, 140.0, 128.4(8), 128.4(6), 126.4, 79.8, 53.5, 52.6, 52.0, 51.8, 36.0, 33.8, 30.1, 28.3, 27.9. HRMS (ESI) m/z: calcd for $C_{23}H_{34}N_2O_7SNa$ $[M+Na]^+$: 505.1979, found: 505.1979.



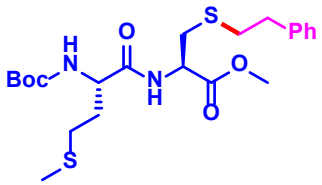
Methyl *N*-((tert-butoxycarbonyl)-L-seryl)-*S*-phenethyl-L-cysteinate (3i)

Colorless oil (Flow: 115.8 mg, 68% yield; Batch: 107.3mg, 63% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (s, 1H), 7.24 – 7.19 (m, 2H), 7.16 – 7.08 (m, 3H), 5.56 (d, *J* = 7.1 Hz, 1H), 4.76 – 4.66 (m, 1H), 4.17 (s, 1H), 3.94 (s, 1H), 3.67 (s, 3H), 3.63 – 3.56 (m, 1H), 3.26 (s, 1H), 2.98 – 2.84 (m, 2H), 2.80 – 2.75 (m, 2H), 2.73 – 2.66 (m, 2H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.3, 171.1, 155.9, 140.0, 128.5(3), 128.4(9), 126.5, 80.5, 63.0, 55.3, 52.8, 52.0, 36.0, 34.0, 33.9, 28.3. HRMS (ESI) m/z: calcd for $C_{20}H_{30}N_2O_6SNa$ $[M+Na]^+$: 449.1717, found: 449.1716.



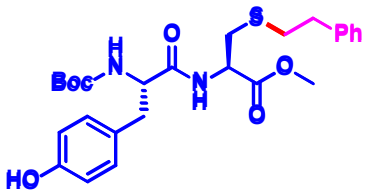
Methyl *N*-((tert-butoxycarbonyl)-L-threonyl)-*S*-phenethyl-L-cysteinate (3j)

Colorless oil (Flow: 141.2 mg, 80% yield; Batch: 134.1mg, 76% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 – 7.48 (m, 1H), 7.30 – 7.25 (m, 2H), 7.22 – 7.15 (m, 3H), 5.76 – 5.67 (m, 1H), 4.84 – 4.75 (m, 1H), 4.31 (s, 1H), 4.21 (d, *J* = 7.1 Hz, 1H), 3.82 (d, *J* = 10.5 Hz, 1H), 3.73 (s, 3H), 3.03 – 2.98 (m, 1H), 2.94 – 2.89 (m, 1H), 2.87 – 2.82 (m, 2H), 2.80 – 2.74 (m, 2H), 1.45 (s, 9H), 1.19 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 171.1, 156.2, 140.0, 128.5, 126.5, 80.3, 67.2, 58.6, 52.7, 51.9, 36.0, 34.0, 33.8, 28.3, 18.2. HRMS (ESI) m/z: calcd for $C_{21}H_{32}N_2O_6SNa$ $[M+Na]^+$: 463.1873, found: 463.1873.



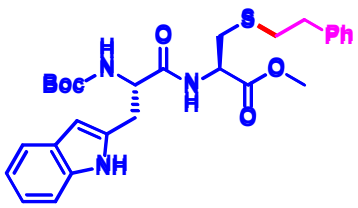
Methyl *N*-((tert-butoxycarbonyl)-L-methionyl)-*S*-phenethyl-L-cysteinate (3k)

Colorless oil (Flow: 165.6 mg, 88% yield; Batch: 158.1mg, 84% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.19 (m, 2H), 7.16 – 7.05 (m, 4H), 5.32 (d, *J* = 7.5 Hz, 1H), 4.74 – 4.68 (m, 1H), 4.36 – 4.19 (m, 1H), 3.66 (s, 3H), 2.93 – 2.87 (m, 2H), 2.80 – 2.75 (m, 2H), 2.72 – 2.67 (m, 2H), 2.51 (t, *J* = 7.2 Hz, 2H), 2.05 – 1.98 (m, 4H), 1.91 – 1.83 (m, 1H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.7, 171.0, 155.5, 140.0, 128.5, 126.4, 80.0, 53.3, 52.7, 51.9, 36.0, 33.9, 31.8, 30.0, 28.3, 15.2. HRMS (ESI) m/z: calcd for $C_{22}H_{34}N_2O_5S_2Na$ $[M+Na]^+$: 493.1801, found: 493.1801.



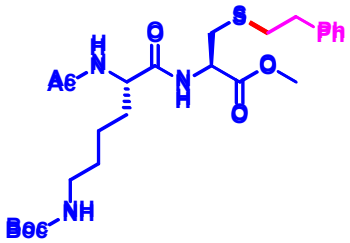
Methyl *N*-((tert-butoxycarbonyl)-L-tyrosyl)-*S*-phenethyl-L-cysteinate (3l)

Colorless oil (Flow: 171.4 mg, 85% yield; Batch: 159.3mg, 79% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (s, 1H), 7.29-7.24 (m, 2H), 7.21-7.14 (m, 3H), 7.07-6.95 (m, 3H), 6.74 (d, *J* = 7.2 Hz, 2H), 5.28 (s, 1H), 4.74 (s, 1H), 4.38 (s, 1H), 3.67 (s, 3H), 3.01 – 2.88 (m, 4H), 2.84 – 2.79 (m, 2H), 2.76 – 2.68 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.0, 170.9, 155.7, 155.6, 140.1, 130.4, 128.5, 127.3, 126.5, 115.7, 80.5, 56.0, 52.8, 52.1, 37.6, 36.0, 34.0, 33.9, 28.3. HRMS (ESI) m/z: calcd for $C_{26}H_{34}N_2O_6SNa$ $[M+Na]^+$: 525.2030, found: 425.2024.



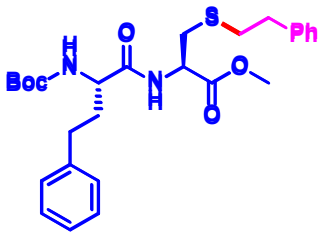
Methyl *N*-((tert-butoxycarbonyl)-L-tryptophyl)-*S*-phenethyl-L-cysteinate (3m)

Light yellow oil (Flow: 189.2 mg, 90% yield; Batch: 185mg, 88% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.34 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.23 – 7.17 (m, 3H), 7.16 – 7.11 (m, 1H), 7.09 – 6.98 (m, 4H), 6.92 (s, 1H), 6.63 (d, *J* = 7.5 Hz, 1H), 5.14 (s, 1H), 4.63 – 4.54 (m, 1H), 4.41 (s, 1H), 3.54 (s, 3H), 3.27 – 3.16 (m, 1H), 3.13 – 3.06 (m, 1H), 2.76 – 2.63 (m, 4H), 2.52 – 2.44 (m, 2H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.8, 170.8, 155.6, 140.2, 136.4, 128.6, 127.5, 126.5, 123.6, 122.1, 119.6, 118.8, 111.4, 110.0, 80.3, 55.2, 52.7, 52.1, 36.0, 34.1, 34.0, 28.4. HRMS (ESI) m/z: calcd for $C_{28}H_{35}N_3O_5SNa$ $[M+Na]^+$: 548.2190, found: 548.2186.



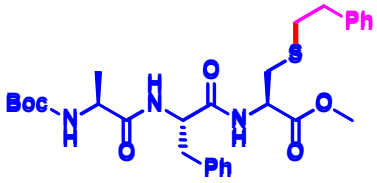
Methyl *N*-(*N*^{2}-acetyl-*N*^{6}-(tert-butoxycarbonyl)-L-lysyl)-*S*-phenethyl-L-cysteinate (3n)

White solid (Flow: 192.4 mg, 94% yield; Batch: 169.9mg, 83% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.27 (m, 2H), 7.23 – 7.17 (m, 3H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.37 (d, *J* = 7.0 Hz, 1H), 4.78 – 4.71 (m, 2H), 4.53 – 4.47 (m, 1H), 3.75 (s, 3H), 3.14 – 3.05 (m, 2H), 3.00 – 2.94 (m, 2H), 2.88 – 2.82 (m, 2H), 2.79 – 2.74 (m, 2H), 2.01 – 1.95 (m, 4H), 1.88 – 1.81 (m, 1H), 1.70 – 1.63 (m, 1H), 1.52 – 1.47 (m, 2H), 1.43 (s, 9H), 1.38 – 1.35 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.7, 171.0, 170.3, 156.2, 140.0, 128.5, 126.5, 79.1, 52.9, 52.7, 51.9, 39.9, 36.0, 33.9(8), 33.9(6), 31.9, 29.6, 28.5, 23.1, 22.3. HRMS (ESI) m/z: calcd for $C_{25}H_{39}N_3O_6SNa$ [M+Na]$^+$: 532.2452, found: 532.2456.



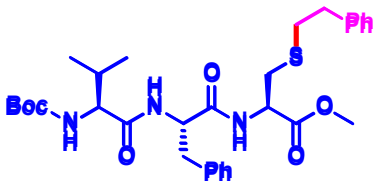
Methyl *N*-((*S*)-2-((tert-butoxycarbonyl)amino)-4-phenylbutanoyl)-*S*-phenethyl-L- cysteinate (3o)

Colorless oil (Flow: 172.6 mg, 86% yield; Batch: 162.6mg, 81% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.24 (m, 4H), 7.22-7.15 (m, 6H), 6.86 (d, *J* = 7.2 Hz, 1H), 5.09 (d, *J* = 8.0 Hz, 1H), 4.80 – 4.75 (m, 1H), 4.22 – 4.08 (m, 1H), 3.73 (s, 3H), 3.01 – 2.93 (m, 2H), 2.87 – 2.82 (m, 2H), 2.79 – 2.73 (m, 2H), 2.69 (t, *J* = 7.8 Hz, 2H), 2.20 – 2.12 (m, 1H), 1.94 – 1.88 (m, 1H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.8, 171.0, 155.5, 140.9, 140.0, 128.5(3), 128.5(1), 128.4(6), 126.5, 126.2, 80.2, 54.2, 52.7, 51.9, 36.1, 34.1(4), 34.0(7), 34.0, 31.7, 28.3. HRMS (ESI) m/z: calcd for $C_{27}H_{36}N_2O_5SNa$ [M+Na]$^+$: 523.2237, found: 523.2254.



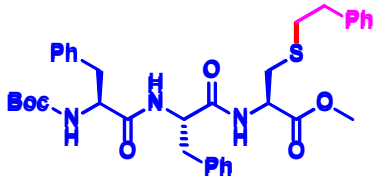
Methyl *N*-(tert-butoxycarbonyl)-L-alanyl-L-phenylalanyl-*S*-phenethyl-L-cysteinate (4a)

White solid (Flow: 205.6 mg, 92% yield; Batch: 194.4mg, 87% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.22 (m, 4H), 7.22 – 7.14 (m, 6H), 7.13 – 7.06 (m, 1H), 6.98 (d, *J* = 7.0 Hz, 1H), 5.24 (s, 1H), 4.84 – 4.76 (m, 1H), 4.75 – 4.67 (m, 1H), 4.19 (s, 1H), 3.69 (s, 3H), 3.08 (d, *J* = 5.8 Hz, 2H), 2.95 – 2.78 (m, 4H), 2.75 – 2.68 (m, 2H), 1.41 (s, 9H), 1.27 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.7, 170.8, 170.7, 155.5, 140.1, 136.3, 129.4, 128.6, 128.5, 126.9, 126.4, 80.1, 54.1, 52.6, 52.1, 50.3, 38.2, 36.0, 34.0, 33.9, 28.4, 18.5. HRMS (ESI) m/z: calcd for $C_{29}H_{39}N_3O_6SNa$ [M+Na]$^+$: 580.2452, found: 580.2456.



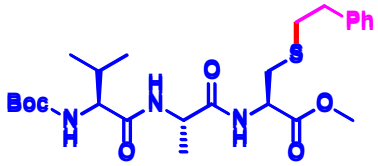
Methyl *N*-(tert-butoxycarbonyl)-L-valyl-L-phenylalanyl-*S*-phenethyl-L-cysteinate (4b)

White solid (Flow: 208.2 mg, 89% yield; Batch: 187.1mg, 80% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.13 (m, 10H), 7.10 – 7.00 (m, 1H), 6.90 (d, *J* = 7.0 Hz, 1H), 5.24 (d, *J* = 7.9 Hz, 1H), 4.88 – 4.77 (m, 1H), 4.75 – 4.66 (m, 1H), 3.98 (s, 1H), 3.69 (s, 3H), 3.06 (d, *J* = 6.3 Hz, 2H), 2.91 – 2.77 (m, 4H), 2.72 (d, *J* = 6.5 Hz, 2H), 2.15 – 2.01 (m, 1H), 1.43 (s, 9H), 0.89 (d, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 5.5 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.7, 170.7(2), 170.6(6), 155.9, 140.1, 136.3, 129.4, 128.6, 128.5, 126.9, 126.4, 79.9, 60.0, 54.1, 52.6, 52.0, 38.4, 36.0, 34.0, 33.9, 30.8, 28.4, 19.3, 17.7. HRMS (ESI) m/z: calcd for $C_{31}H_{43}N_3O_6SNa$ $[M+Na]^+$: 608.2765, found: 608.2772.



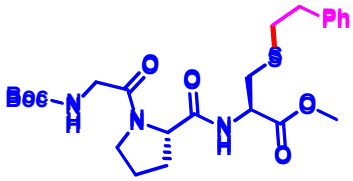
Methyl *N*-(tert-butoxycarbonyl)-L-phenylalanyl-L-phenylalanyl-*S*-phenethyl-L- cysteinate (4c)

White solid (Flow: 210.2 mg, 83% yield; Batch: 212.7mg, 84% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.12 (m, 14H), 7.11 – 7.07 (m, 2H), 6.88 (d, *J* = 7.8 Hz, 1H), 5.23 (d, *J* = 6.6 Hz, 1H), 4.81 (q, *J* = 6.9 Hz, 1H), 4.69 (q, *J* = 5.9 Hz, 1H), 4.43 (s, 1H), 3.68 (s, 3H), 3.08 – 2.94 (m, 4H), 2.92 – 2.84 (m, 2H), 2.83 – 2.78 (m, 2H), 2.74 – 2.68 (m, 2H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.4, 170.8, 170.5, 155.5, 140.1, 136.7, 136.2, 129.5, 129.4, 128.6(4), 128.5(8), 128.5, 126.9, 126.4, 80.1, 55.7, 54.1, 52.6, 52.2, 38.4, 38.3, 36.1, 34.0, 33.9, 28.3. HRMS (ESI) m/z: calcd for $C_{35}H_{43}N_3O_6SNa$ $[M+Na]^+$: 656.2765, found: 656.2768.



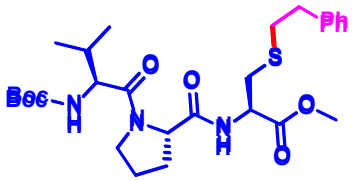
Methyl *N*-(tert-butoxycarbonyl)-L-valyl-L-alanyl-*S*-phenethyl-L-cysteinate (4d)

White solid (Flow: 189.0 mg, 93% yield; Batch: 176.8mg, 87% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.25 (m, 3H), 7.23 – 7.16 (m, 3H), 6.93 (d, *J* = 6.8 Hz, 1H), 5.34 (d, *J* = 8.8 Hz, 1H), 4.81 – 4.74 (m, 1H), 4.68 – 4.59 (m, 1H), 4.06 – 3.96 (m, 1H), 3.74 (s, 3H), 2.95 (d, *J* = 5.7 Hz, 2H), 2.87 – 2.81 (m, 2H), 2.79 – 2.73 (m, 2H), 2.15 – 2.06 (m, 1H), 1.44 (s, 9H), 1.39 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.1, 171.6, 171.0, 156.0, 140.1, 128.5, 126.4, 79.8, 59.8, 52.6, 52.0, 48.8, 36.0, 34.0, 33.9, 31.1, 28.3, 19.4, 18.5, 17.8. HRMS (ESI) m/z: calcd for $C_{25}H_{39}N_3O_6SNa$ $[M+Na]^+$: 532.2452, found: 532.2455.



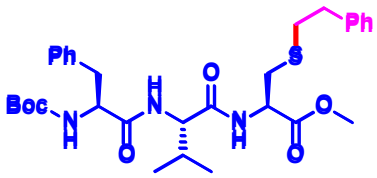
Methyl *N*-(tert-butoxycarbonyl)glycyl-L-prolyl-*S*-phenethyl-L-cysteinate (4e)

Colorless oil (Flow: 155.6 mg, 79% yield; Batch: 149.7mg, 76% yield, d:r = 1:4.3). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 7.7 Hz, 1H), 7.31 – 7.25 (m, 2H), 7.22 – 7.16 (m, 3H), 5.62 – 5.49 (m, 1H), 4.78 – 4.70 (m, 1H), 4.64 – 4.56 (m, 1H), 4.01 – 3.91 (m, 1H), 3.85 – 3.78 (m, 1H), 3.73 (s, 3H), 3.49 – 3.30 (m, 2H), 3.03 – 2.89 (m, 2H), 2.88 – 2.81 (m, 2H), 2.79 – 2.72 (m, 2H), 2.34 – 2.25 (m, 1H), 2.13 – 2.03 (m, 1H), 1.99 – 1.86 (m, 2H), 1.46 – 1.40 (m, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.1, 170.9, 168.6, 155.8, 140.1, 128.5, 126.4, 79.6, 59.9, 52.6, 52.2, 46.2, 43.0, 36.1, 34.0, 33.9, 28.3, 27.7, 24.7. HRMS (ESI) m/z: calcd for $C_{24}H_{35}N_3O_6SNa$ [M+Na]$^{+}$: 516.2139, found: 516.2144.



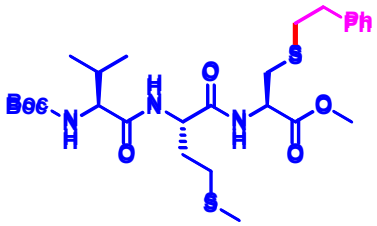
Methyl *N*-(tert-butoxycarbonyl)-L-valyl-L-prolyl-*S*-phenethyl-L-cysteinate (4f)

Colorless oil (Flow: 177.6 mg, 83% yield; Batch: 171.2mg, 80% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 7.6 Hz, 1H), 7.31 – 7.26 (m, 2H), 7.22 – 7.17 (m, 3H), 5.33 (d, *J* = 9.3 Hz, 1H), 4.76 – 4.70 (m, 1H), 4.64 – 4.58 (m, 1H), 4.32 – 4.25 (m, 1H), 3.73 (s, 3H), 3.69 (d, *J* = 4.2 Hz, 1H), 3.59 – 3.52 (m, 1H), 2.98 – 2.90 (m, 2H), 2.87 – 2.82 (m, 2H), 2.80 – 2.74 (m, 2H), 2.29 (d, *J* = 9.5 Hz, 1H), 2.05 – 1.90 (m, 4H), 1.43 (s, 9H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.4, 171.1, 171.0, 155.8, 140.1, 128.5, 128.4, 126.4, 79.5, 59.9, 56.7, 52.5, 52.1, 47.5, 36.0, 34.1, 33.9, 31.4, 28.3, 27.5, 25.0, 19.6, 17.4. HRMS (ESI) m/z: calcd for $C_{27}H_{41}N_3O_6SNa$ [M+Na]$^{+}$: 558.2608, found: 558.2611.



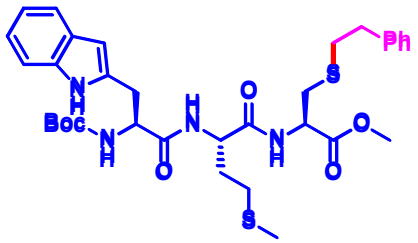
Methyl *N*-(tert-butoxycarbonyl)-L-phenylalanyl-L-valyl-*S*-phenethyl-L-cysteinate (4g)

White solid (Flow: 201.3 mg, 86% yield, Batch: 191.9mg, 82% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 7.6 Hz, 1H), 7.27 – 7.22 (m, 4H), 7.20 – 7.14 (m, 6H), 6.97 (d, *J* = 7.4 Hz, 1H), 5.39 (d, *J* = 7.3 Hz, 1H), 4.81 – 4.75 (m, 1H), 4.53 – 4.42 (m, 2H), 3.72 (s, 3H), 3.13-3.07 (m, 1H), 3.04 – 2.98 (m, 1H), 2.94 (d, *J* = 5.6 Hz, 2H), 2.86 – 2.80 (m, 2H), 2.78 – 2.73 (m, 2H), 2.16 – 2.06 (m, 1H), 1.37 (s, 9H), 0.92 (dd, *J* = 12.8, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.6, 171.1, 170.9, 155.6, 140.1, 136.8, 129.4, 128.6, 128.5, 126.8, 126.4, 80.0, 58.4, 55.8, 52.6, 52.0, 38.1, 36.1, 34.0, 33.9, 31.2, 28.3, 19.0, 18.1. HRMS (ESI) m/z: calcd for $C_{31}H_{43}N_3O_6SNa$ [M+Na]$^{+}$: 608.2765, found: 608.2771.



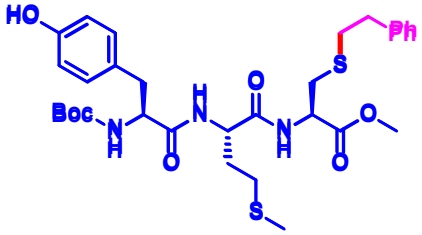
Methyl *N*-(tert-butoxycarbonyl)-L-valyl-L-methionyl-*S*-phenethyl-L-cysteinate (4h)

White solid (Flow: 193.6 mg, 85% yield; Batch: 184.5mg, 81% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 (d, *J* = 7.7 Hz, 1H), 7.33 – 7.25 (m, 3H), 7.22 – 7.16 (m, 3H), 5.46 (d, *J* = 8.5 Hz, 1H), 4.79 (q, *J* = 5.9 Hz, 2H), 4.05 (d, *J* = 7.2 Hz, 1H), 3.73 (s, 3H), 2.95 (d, *J* = 5.7 Hz, 2H), 2.87 – 2.81 (m, 2H), 2.80 – 2.73 (m, 2H), 2.58 (t, *J* = 7.2 Hz, 2H), 2.13 – 1.99 (m, 6H), 1.44 (s, 9H), 0.95 – 0.89 (dd, *J* = 10.9, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.9, 171.0, 170.9, 155.9, 140.0, 128.5, 126.4, 79.7, 59.9, 52.6, 52.0, 36.0, 33.9, 31.7, 31.0, 29.8, 28.4, 19.3, 18.0, 15.1. HRMS (ESI) m/z: calcd for $C_{27}H_{43}N_3O_6S_2Na$ $[M+Na]^+$: 592.2485, found: 592.2490.



Methyl *N*-(tert-butoxycarbonyl)-L-tryptophyl-L-methionyl-*S*-phenethyl-L-cysteinate (4i)

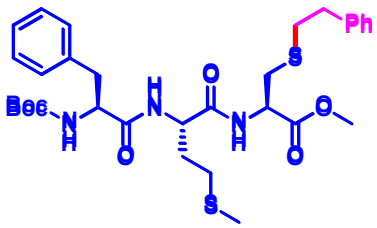
White solid (Flow: 241.4 mg, 92% yield; Batch: 228.3mg, 87% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.59 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.27 (t, *J* = 7.2 Hz, 3H), 7.21 – 7.13 (m, 4H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.03 (s, 1H), 6.98 – 6.89 (m, 1H), 5.29 (d, *J* = 7.0 Hz, 1H), 4.71 – 4.59 (m, 2H), 4.53 – 4.41 (m, 1H), 3.70 (s, 3H), 3.34 – 3.16 (m, 2H), 2.94 – 2.79 (m, 4H), 2.76 – 2.70 (m, 2H), 2.37 (t, *J* = 6.5 Hz, 2H), 1.99 – 1.84 (m, 5H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.0, 170.9, 170.8, 155.7, 140.1, 136.3, 128.5, 127.5, 126.5, 123.5, 122.2, 119.7, 118.8, 111.4, 110.1, 80.3, 55.4, 52.7, 52.4, 52.0, 36.0, 33.9, 33.8, 30.8, 29.6, 28.4, 28.1, 14.9. HRMS (ESI) m/z: calcd for $C_{33}H_{43}N_3O_6S_2Na$ $[M+Na]^+$: 679.2594, found: 679.2597.



Methyl *N*-(tert-butoxycarbonyl)-L-tyrosyl-L-methionyl-*S*-phenethyl-L-cysteinate (4j)

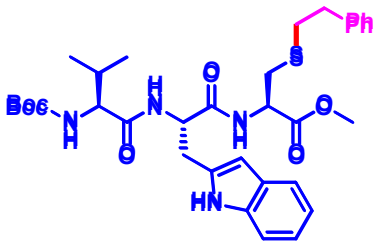
White solid (Flow: 230.4 mg, 91% yield; Batch: 222.8mg, 88% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (s, 1H), 7.45 (d, *J* = 7.0 Hz, 1H), 7.29 – 7.13 (m, 6H), 6.98 (d, *J* = 8.1 Hz, 2H), 6.75 (d, *J* = 8.1 Hz, 2H), 5.39 – 5.26 (m, 1H), 4.79 – 4.67 (m, 2H), 4.43 – 4.28 (m, 1H), 3.71 (s, 3H), 2.96 (s, 4H), 2.86 – 2.80 (m, 2H), 2.79 – 2.73 (m, 2H), 2.51 (t, *J* = 6.8 Hz, 2H), 2.01 (d, *J* = 13.3 Hz, 5H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.0, 171.1, 170.9, 155.8, 155.6, 140.0,

130.4, 128.5, 127.4, 126.5, 115.7, 80.5, 56.0, 52.7, 52.3, 52.1, 37.4, 36.0, 33.9, 33.8, 31.3, 29.7, 28.3, 15.1. HRMS (ESI) m/z: calcd for $C_{31}H_{43}N_3O_7S_2Na$ $[M+Na]^+$: 656.2435, found: 656.2437.



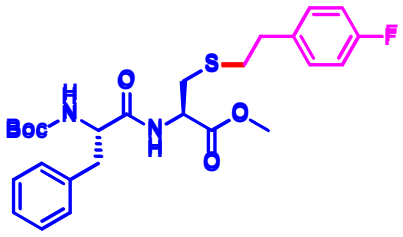
Methyl *N*-(tert-butoxycarbonyl)-L-phenylalanyl-L-methionyl-*S*-phenethyl-L-cys teinate (4k)

White solid (Flow: 229.6 mg, 93% yield; Batch: 219.7mg, 89% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 7.8 Hz, 1H), 7.29 – 7.24 (m, 4H), 7.22 – 7.20 (m, 1H), 7.20 – 7.14 (m, 6H), 5.29 (d, *J* = 6.7 Hz, 1H), 4.79 – 4.71 (m, 2H), 4.51 – 4.39 (m, 1H), 3.72 (s, 3H), 3.11 – 3.01 (m, 2H), 2.95 (d, *J* = 5.3 Hz, 2H), 2.87 – 2.82 (m, 2H), 2.79 – 2.73 (m, 2H), 2.51 (t, *J* = 7.3 Hz, 2H), 2.05 (s, 3H), 2.03 – 1.94 (m, 2H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.5, 170.9, 170.8, 155.5, 140.0, 136.6, 129.4, 128.6, 128.5, 126.9, 126.4, 80.1, 55.7, 52.6, 52.2, 52.0, 38.2, 36.1, 33.9, 31.5, 29.7, 28.3, 15.1. HRMS (ESI) m/z: calcd for $C_{31}H_{43}N_3O_6S_2Na$ $[M+Na]^+$: 640.2485, found: 640.2490.



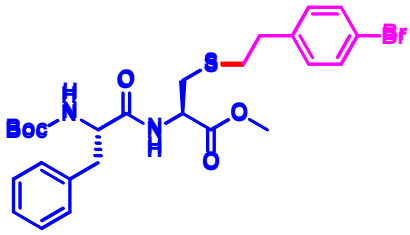
Methyl *N*-(tert-butoxycarbonyl)-L-valyl-L-tryptophyl-*S*-phenethyl-L-cysteinate (4l)

White solid (Flow: 234.6 mg, 94% yield; Batch: 234.6mg, 94% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.49 (s, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.31 – 7.24 (m, 3H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.16 – 7.06 (m, 4H), 7.02 (s, 1H), 6.93 – 6.83 (m, 2H), 5.18 (d, *J* = 7.3 Hz, 1H), 4.88 – 4.76 (m, 1H), 4.65 – 4.58 (m, 1H), 4.06 – 3.94 (m, 1H), 3.62 (s, 3H), 3.35 – 3.26 (m, 1H), 3.18 – 3.09 (m, 1H), 2.81 – 2.75 (m, 4H), 2.65 – 2.57 (m, 2H), 2.18 – 2.07 (m, 1H), 1.40 (s, 9H), 0.90 (d, *J* = 6.7 Hz, 3H), 0.80 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.6, 171.2, 170.7, 156.0, 140.1, 136.3, 128.5(4), 128.5(1), 127.5, 126.5, 123.8, 122.1, 119.6, 118.7, 111.4, 109.9, 80.0, 60.1, 53.8, 52.5, 52.2, 36.0, 34.0, 33.9, 30.8, 28.3, 28.1, 19.3, 17.5. HRMS (ESI) m/z: calcd for $C_{33}H_{44}N_4O_6SNa$ $[M+Na]^+$: 647.2874, found: 647.2878.



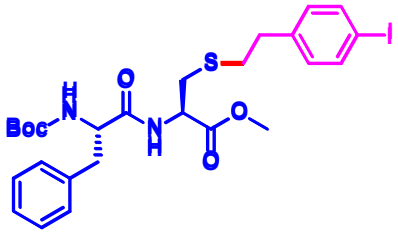
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(4-fluorophenethyl)-L-cysteinate (5a)

White solid (Flow: 171.0 mg, 85% yield; Batch: 162.9mg, 81% yield).^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.24 (m, 2H), 7.23 – 7.18 (m, 3H), 7.15 – 7.09 (m, 2H), 6.99 – 6.93 (m, 2H), 6.87 (d, *J* = 7.2 Hz, 1H), 5.16 (d, *J* = 8.0 Hz, 1H), 4.78 – 4.70 (m, 1H), 4.51 – 4.34 (m, 1H), 3.70 (s, 3H), 3.14 – 3.00 (m, 2H), 2.97 – 2.86 (m, 2H), 2.82 – 2.76 (m, 2H), 2.74 – 2.65 (m, 2H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.3, 170.8, 161.6 (d, *J* = 242.7 Hz, 1C), 155.4, 136.5, 135.7 (d, *J* = 3.0 Hz, 1C), 130.0, 129.9, 129.3, 128.6, 127.7, 126.9, 80.2, 55.7, 52.6, 52.0, 38.3, 35.2, 34.1, 34.0, 28.3. ^{19}F NMR (376 MHz, Chloroform-*d*) δ 116.60. HRMS (ESI) m/z: calcd for $C_{26}H_{33}FN_2O_5SNa$ $[M+Na]^+$: 527.1986, found: 527.1991.



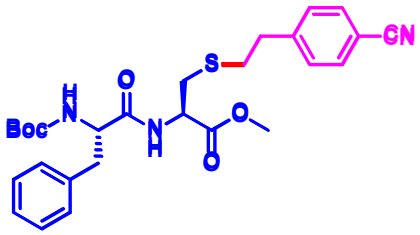
Methyl *S*-(4-bromophenethyl)-*N*-((tert-butoxycarbonyl)-L-phenylalanyl)-L-cysteinate (5b)

White solid (Flow: 209.8 mg, 93% yield; Batch: 196.3mg, 87% yield).^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 8.3 Hz, 2H), 7.30 – 7.25 (m, 2H), 7.23 – 7.18 (m, 3H), 7.05 (d, *J* = 8.3 Hz, 2H), 6.81 (d, *J* = 7.5 Hz, 1H), 5.09 (d, *J* = 7.9 Hz, 1H), 4.78 – 4.70 (m, 1H), 4.48 – 4.35 (m, 1H), 3.70 (s, 3H), 3.13 – 3.02 (m, 2H), 2.97 – 2.87 (m, 2H), 2.81 – 2.74 (m, 2H), 2.74 – 2.65 (m, 2H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.3, 170.7, 155.4, 139.0, 136.5, 131.6, 130.3, 129.3, 128.7, 127.0, 120.3, 80.2, 55.7, 52.7, 52.0, 38.3, 35.4, 34.2, 33.7, 28.3. HRMS (ESI) m/z: calcd for $C_{26}H_{33}BrN_2O_5SNa$ $[M+Na]^+$: 587.1186, found: 587.1178.



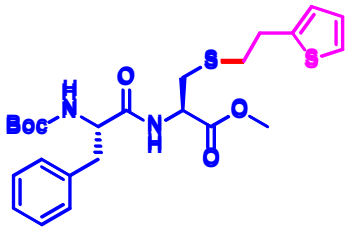
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(4-iodophenethyl)-L-cysteinate (5c)

White solid (Flow: 209.4 mg, 86% yield; Batch: 202.1mg, 83% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 8.1 Hz, 2H), 7.30 – 7.25 (m, 2H), 7.24 – 7.18 (m, 3H), 6.92 (d, *J* = 8.1 Hz, 2H), 6.77 (d, *J* = 7.0 Hz, 1H), 5.10 – 5.00 (m, 1H), 4.78 – 4.69 (m, 1H), 4.47 – 4.35 (m, 1H), 3.70 (s, 3H), 3.13 – 3.01 (m, 2H), 2.97 – 2.86 (m, 2H), 2.79 – 2.74 (m, 2H), 2.73 – 2.65 (m, 2H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 170.7, 155.3, 139.6, 137.5, 136.5, 130.6, 129.3, 128.7, 127.0, 91.7, 80.2, 55.7, 52.7, 52.0, 38.3, 35.5, 34.2, 33.7, 28.3. HRMS (ESI) m/z: calcd for $C_{26}H_{33}IN_2O_5SNa$ $[M+Na]^+$: 635.1047, found: 635.1051.



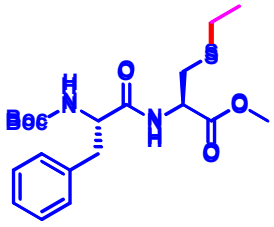
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(4-cyanophenethyl)-L-cysteinate (5d)

White solid (Flow: 121.9 mg, 60% yield; Batch: 136.1mg, 67% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 7.7 Hz, 2H), 7.33 – 7.26 (m, 4H), 7.25 – 7.17 (m, 3H), 6.69 (s, 1H), 5.00 (s, 1H), 4.78 – 4.69 (m, 1H), 4.47 – 4.28 (m, 1H), 3.71 (s, 3H), 3.13 – 3.01 (m, 2H), 2.99 – 2.86 (m, 4H), 2.82 – 2.70 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.3, 170.7, 155.4, 145.5, 136.4, 132.3, 129.4, 129.3, 128.7, 127.0, 118.9, 110.3, 80.2, 55.7, 52.7, 52.0, 38.3, 35.9, 34.2, 33.2, 28.2. HRMS (ESI) m/z: calcd for $C_{26}H_{33}FN_2O_5SNa$ $[M+Na]^+$: 527.1986, found: 527.1991. HRMS (ESI) m/z: calcd for $C_{27}H_{33}N_3O_5SNa$ $[M+Na]^+$: 534.2033, found: 534.2045.



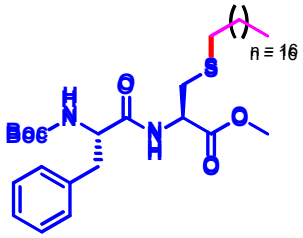
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(2-(thiophen-2-yl)ethyl)-L- cysteinate (5e)

White solid (Flow: 148.2 mg, 75% yield; Batch: 144.2mg, 73% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.25 (m, 2H), 7.23 – 7.18 (m, 3H), 7.14 – 7.10 (m, 1H), 6.93 – 6.89 (m, 1H), 6.85 – 6.69 (m, 2H), 5.10 (d, *J* = 7.8 Hz, 1H), 4.78 – 4.71 (m, 1H), 4.49 – 4.36 (m, 1H), 3.71 (s, 3H), 3.13 – 3.00 (m, 4H), 2.98 – 2.89 (m, 2H), 2.78 – 2.72 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 170.7, 155.3, 142.5, 136.5, 129.4, 128.7, 126.9, 126.9, 125.1, 123.8, 80.2, 55.7, 52.7, 52.1, 38.3, 34.2(1), 34.1(6), 30.3, 28.3. HRMS (ESI) m/z: calcd for $C_{24}H_{32}N_2O_5S_2Na$ $[M+Na]^+$: 515.1645, found: 515.1653.



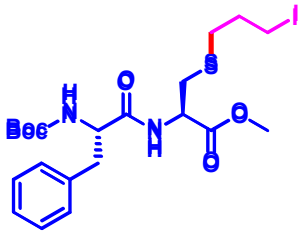
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-ethyl-L-cysteinate (5f)

White solid (Flow: 146.0 mg, 89% yield; Batch: 142.7mg, 87% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.18 (m, 2H), 7.17 – 7.12 (m, 3H), 6.82 (d, *J* = 7.3 Hz, 1H), 5.14 (d, *J* = 8.0 Hz, 1H), 4.67 (q, *J* = 5.4 Hz, 1H), 4.46 – 4.29 (m, 1H), 3.65 (s, 3H), 3.07 – 2.94 (m, 2H), 2.90 – 2.80 (m, 2H), 2.41 (q, *J* = 7.4 Hz, 2H), 1.32 (s, 9H), 1.12 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.3, 170.9, 155.3, 136.6, 129.4, 128.6, 126.9, 80.0, 55.6, 52.6, 52.0, 38.3, 33.5, 28.3, 26.4, 14.6. HRMS (ESI) m/z: calcd for $C_{20}H_{30}N_2O_5SNa$ $[M+Na]^+$: 433.1768, found: 433.1770.



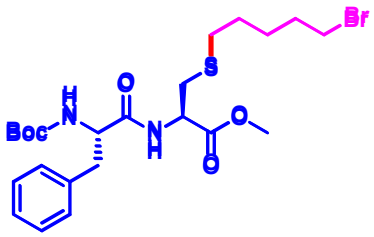
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-octadecyl-L-cysteinate (5g)

White solid (Flow: 227.0 mg, 90% yield; Batch: 216.7mg, 87% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.24 (m, 2H), 7.23 – 7.18 (m, 3H), 6.89 (d, *J* = 7.5 Hz, 1H), 5.21 (d, *J* = 8.0 Hz, 1H), 4.74 (d, *J* = 7.1 Hz, 1H), 4.52 – 4.36 (m, 1H), 3.71 (s, 3H), 3.15 – 3.01 (m, 2H), 2.96 – 2.85 (m, 2H), 2.45 (t, *J* = 7.4 Hz, 2H), 1.54 – 1.48 (m, 2H), 1.40 (s, 9H), 1.33 – 1.21 (m, 30H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 170.9, 155.3, 136.6, 129.4, 128.5, 126.8, 80.0, 55.6, 52.5, 52.0, 38.4, 34.0, 32.6, 31.9, 29.6(9), 29.6(5), 29.6, 29.5(2), 29.4(9), 29.3, 29.2, 28.8, 28.2, 22.7, 14.1. HRMS (ESI) m/z: calcd for $C_{36}H_{62}N_2O_5SNa$ $[M+Na]^+$: 657.4272, found: 657.4279.



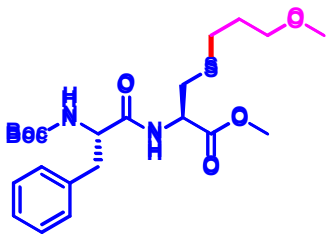
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(3-iodopropyl)-L-cysteinate (5h)

White solid (Flow: 186.6 mg, 85% yield; Batch: 173.4mg, 79% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 2H), 7.25 – 7.19 (m, 3H), 6.90 (d, *J* = 6.8 Hz, 1H), 5.18 (d, *J* = 8.0 Hz, 1H), 4.78 – 4.72 (m, 1H), 4.54 – 4.34 (m, 1H), 3.74 (s, 3H), 3.23 (t, *J* = 6.7 Hz, 2H), 3.14 – 3.01 (m, 2H), 2.99 – 2.87 (m, 2H), 2.57 (t, *J* = 6.9 Hz, 2H), 2.03 – 1.96 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.3, 170.7, 155.3, 136.5, 129.4, 128.6, 126.9, 80.2, 55.6, 52.7, 52.1, 38.3, 34.0, 33.0, 32.6, 28.3, 4.8. HRMS (ESI) m/z: calcd for $C_{21}H_{31}IN_2O_5SNa$ $[M+Na]^+$: 573.0891, found: 573.0897.



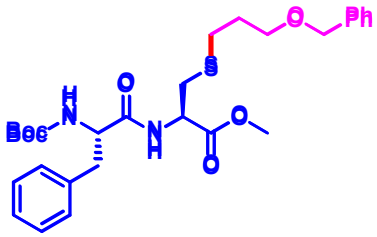
Methyl *S*-(5-bromopentyl)-*N*-((tert-butoxycarbonyl)-L-phenylalanyl)-L-cysteinate (5i)

Light yellow solid (Flow :187.2 mg, 88% yield; Batch: 180.8mg, 85% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 2H), 7.25 – 7.19 (m, 3H), 6.86 (d, *J* = 7.4 Hz, 1H), 5.15 (d, *J* = 7.9 Hz, 1H), 4.77 – 4.69 (m, 1H), 4.50 – 4.34 (m, 1H), 3.73 (s, 3H), 3.39 (t, *J* = 6.7 Hz, 2H), 3.14 – 3.01 (m, 2H), 2.97 – 2.86 (m, 2H), 2.48 (t, *J* = 6.8 Hz, 2H), 1.88 – 1.81 (m, 2H), 1.60 – 1.47 (m, 4H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 170.8, 155.3, 136.5, 129.3, 128.6, 126.9, 80.1, 55.6, 52.6, 52.0, 38.3, 34.0, 33.5, 32.3, 32.2, 28.5, 28.3, 27.2. HRMS (ESI) m/z: calcd for $C_{23}H_{35}BrN_2O_5SNa$ $[M+Na]^+$: 553.1342, found: 553.1363.



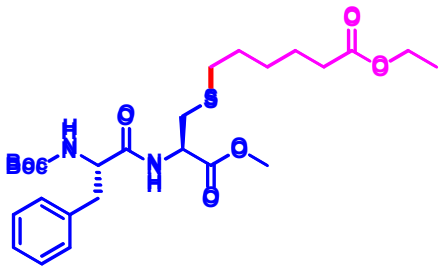
Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-(3-methoxypropyl)-L-cysteinate (5j)

Colorless oil (Flow: 155.6 mg, 86% yield; Batch: 152mg, 84% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.25 (m, 2H), 7.24 – 7.19 (m, 3H), 7.00 (d, *J* = 6.9 Hz, 1H), 5.32 (d, *J* = 8.2 Hz, 1H), 4.81 – 4.73 (m, 1H), 4.46 (s, 1H), 3.72 (s, 3H), 3.44 – 3.38 (m, 2H), 3.31 (s, 3H), 3.18 – 3.11 (m, 1H), 3.04 – 2.97 (m, 1H), 2.96 – 2.85 (m, 2H), 2.59 – 2.51 (m, 2H), 1.82 – 1.73 (m, 2H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.3, 170.8, 155.4, 136.7, 129.3, 128.5, 126.8, 80.0, 70.8, 58.5, 55.5, 52.5, 52.2, 38.2, 33.9, 29.5, 29.3, 28.2. HRMS (ESI) m/z: calcd for $C_{22}H_{34}N_2O_6SNa$ $[M+Na]^+$: 477.2030, found: 477.2033.



Methyl *S*-(3-(benzyloxy)propyl)-*N*-((tert-butoxycarbonyl)-L-phenylalanyl)-L- cysteinate (5k)

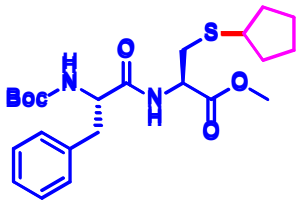
Light yellow solid (Flow: 182.2 mg, 86% yield; Batch: 175.8mg, 83% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.24 (m, 7H), 7.22 – 7.18 (m, 3H), 6.91 (d, *J* = 6.7 Hz, 1H), 5.21 (d, *J* = 7.4 Hz, 1H), 4.77 – 4.71 (m, 1H), 4.48 (s, 2H), 4.43 (s, 1H), 3.69 (s, 3H), 3.51 (t, *J* = 6.1 Hz, 2H), 3.15 – 2.99 (m, 2H), 2.96 – 2.87 (m, 2H), 2.57 (t, *J* = 7.3 Hz, 2H), 1.86 – 1.78 (m, 2H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.3, 170.8, 155.4, 138.3, 136.6, 129.4, 128.6, 128.4, 127.7, 127.6, 126.9, 80.1, 73.0, 68.5, 55.6, 52.6, 52.1, 38.3, 34.0, 29.7, 29.4, 28.3. HRMS (ESI) m/z: calcd for $C_{28}H_{38}N_2O_6SNa$ $[M+Na]^+$: 553.2343, found: 553.2346.



Ethyl (6*S*,9*R*)-6-benzyl-9-(methoxycarbonyl)-2,2-dimethyl-4,7-dioxo-3-oxa-11-thia-5,8- diazahep tadecan-17-oate (5l)

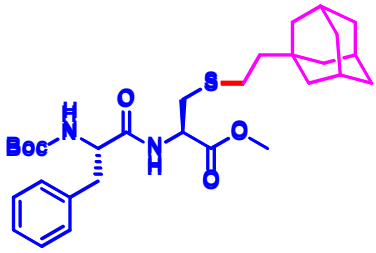
White solid (Flow: 94.7 mg, 45% yield; Batch: 111.5mg, 53% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.27 (m, 2H), 7.25 – 7.20 (m, 3H), 6.75 (d, *J* = 7.4 Hz, 1H), 5.18 – 5.02 (m, 1H), 4.77 – 4.70 (m, 1H), 4.47 – 4.35 (m, 1H), 4.16 – 4.08 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 3H), 3.15 – 3.02 (m, 2H), 2.97 – 2.86 (m, 2H), 2.47 (t, *J* = 7.2 Hz, 2H), 2.29 (t, *J* = 7.4 Hz, 2H), 1.66 – 1.58 (m, 2H),

1.57 – 1.51 (m, 2H), 1.41 (s, 9H), 1.39 – 1.32 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.6, 171.1, 170.8, 155.3, 136.5, 129.3, 128.6, 126.9, 80.2, 60.3, 55.6, 52.6, 52,0, 38.2, 34.1(1), 34.0(8), 32.4, 29.0, 28.3, 28.1, 24.4, 14.2. HRMS (ESI) m/z: calcd for $C_{26}H_{40}N_2O_7SNa$ $[M+Na]^+$: 547.2448, found: 547.2458.



Methyl *N*-((tert-butoxycarbonyl)-L-phenylalanyl)-*S*-cyclopentyl-L-cysteinate (5m)

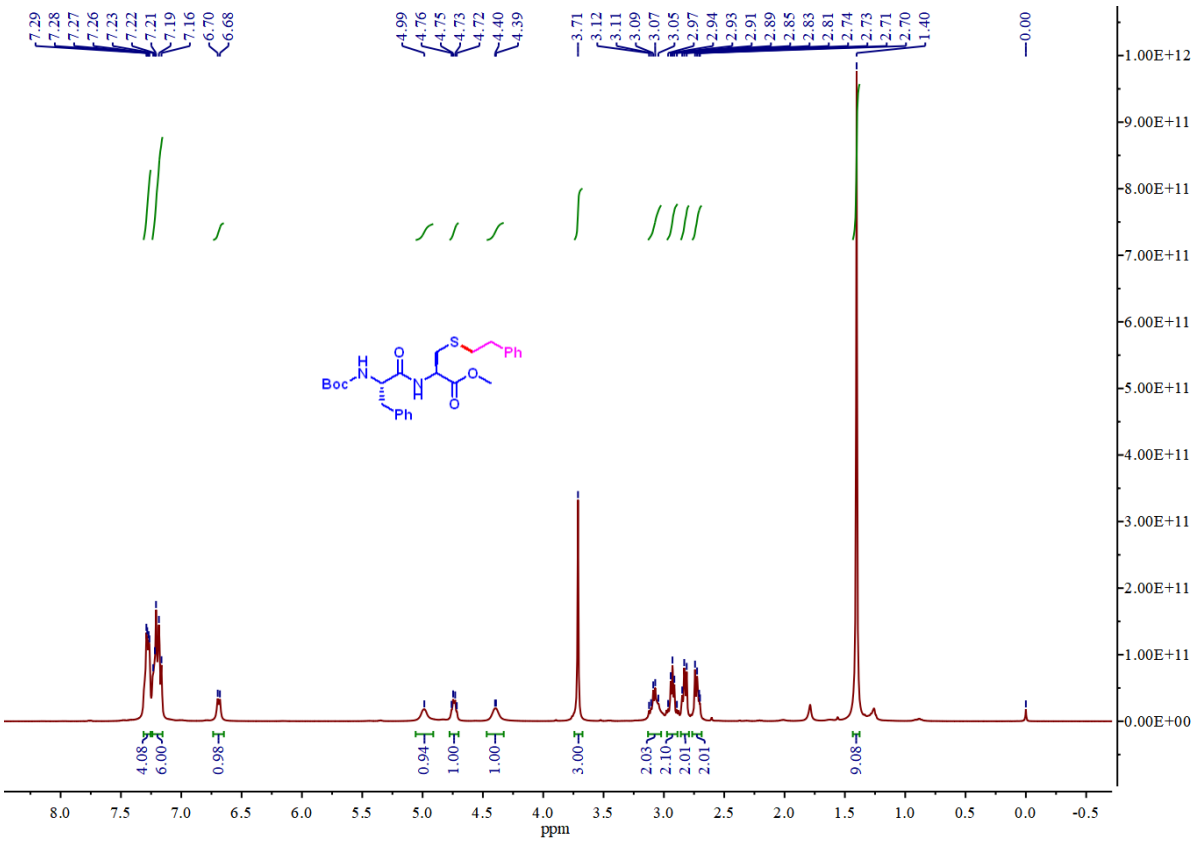
White solid (Flow: 117.2 mg, 65% yield; Batch: 110mg, 61% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.27 (m, 2H), 7.26 – 7.20 (m, 3H), 6.71 (d, *J* = 7.3 Hz, 1H), 5.12 – 4.98 (m, 1H), 4.78 – 4.71 (m, 1H), 4.47 – 4.36 (m, 1H), 3.73 (s, 3H), 3.14 – 3.01 (m, 3H), 2.98 – 2.90 (m, 2H), 1.98 – 1.90 (m, 2H), 1.76 – 1.66 (m, 2H), 1.59 – 1.51 (m, 2H), 1.47 – 1.38 (m, 11H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.1, 179.8, 155.3, 136.5, 129.4, 128.6, 126.9, 80.2, 55.6, 52.6, 52.0, 44.1, 38.4, 33.7(4), 33.7(1), 33.6(7), 28.3, 24.7. HRMS (ESI) m/z: calcd for $C_{23}H_{34}N_2O_5SNa$ $[M+Na]^+$: 473.2081, found: 473.2089.



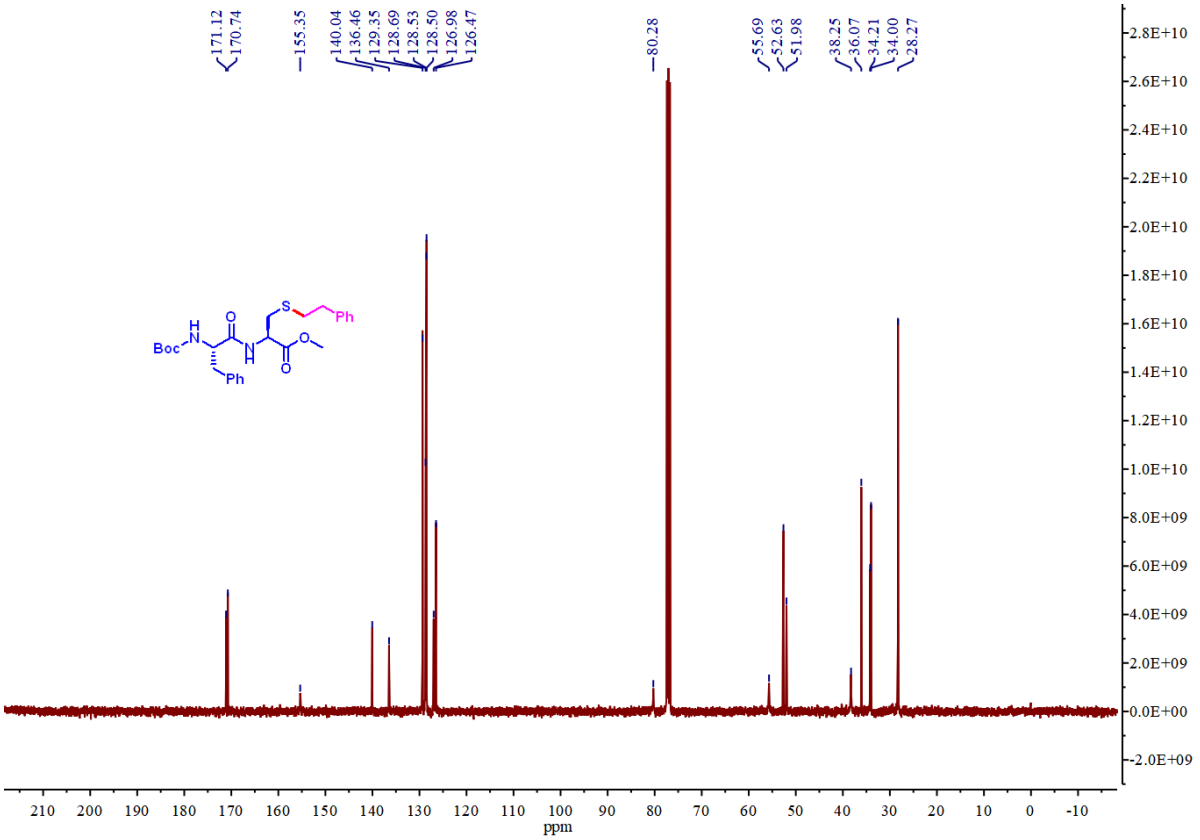
Methyl *S*-(2-((3*R*,5*R*,7*R*)-adamantan-1-yl)ethyl)-*N*-((tert-butoxycarbonyl)-L-phenyl alanyl) -L-cysteinate (5n)

Colorless oil (Flow: 204.5 mg, 94% yield; Batch: 193.6mg, 89% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.27 (m, 2H), 7.25 – 7.20 (m, 3H), 6.76 (d, *J* = 7.4 Hz, 1H), 5.13 – 5.01 (m, 1H), 4.77 – 4.70 (m, 1H), 4.48 – 4.35 (m, 1H), 3.73 (s, 3H), 3.14 – 3.03 (m, 2H), 2.97 – 2.86 (m, 2H), 2.45 – 2.38 (m, 2H), 1.94 (s, 2H), 1.72 – 1.66 (m, 3H), 1.64 – 1.58 (m, 3H), 1.45 (s, 6H), 1.41 (s, 9H), 1.32 – 1.24 (m, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.2, 170.9, 155.3, 136.5, 129.4, 128.6, 126.9, 80.2, 55.6, 52.6, 51.9, 44.2, 42.2, 38.3, 37.0, 34.1, 32.7, 28.6, 28.3, 26.6. HRMS (ESI) m/z: calcd for $C_{30}H_{44}N_2O_5SNa$ $[M+Na]^+$: 567.2864, found: 567.2873.

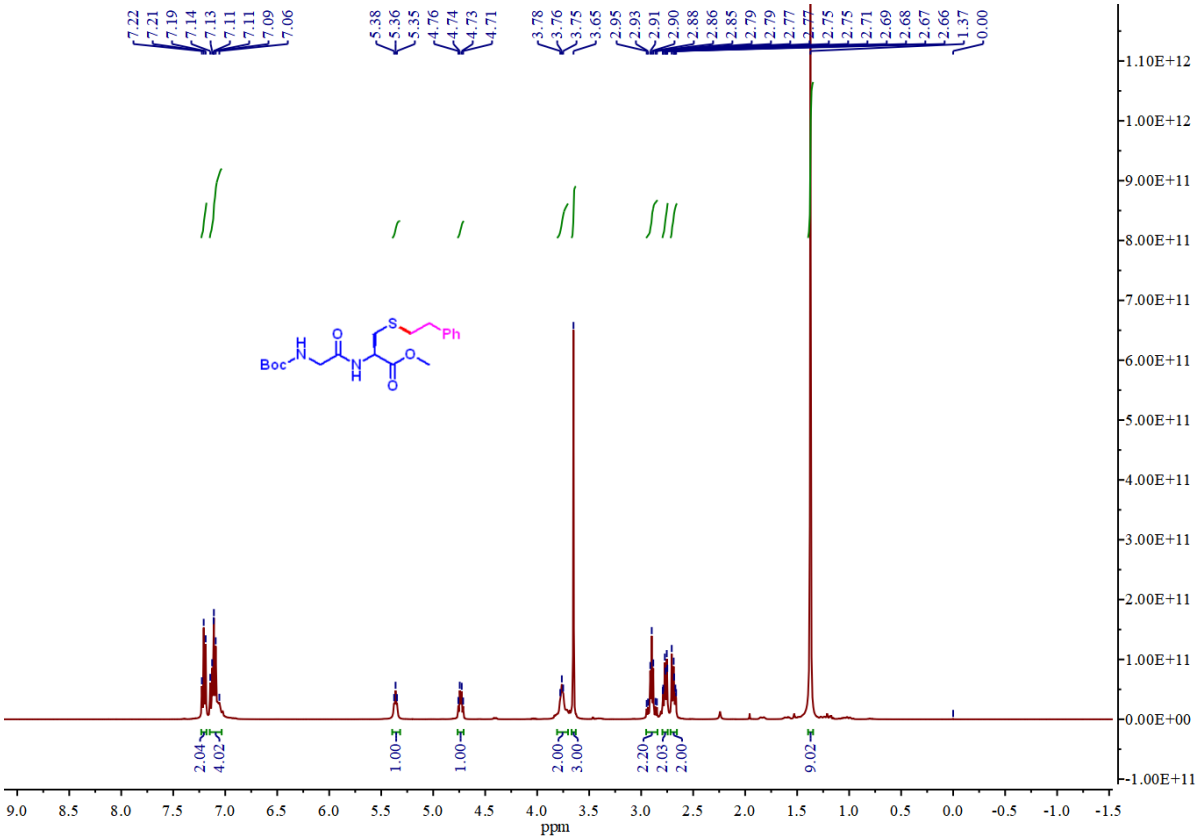
5. Cpoies of NMR Spectra



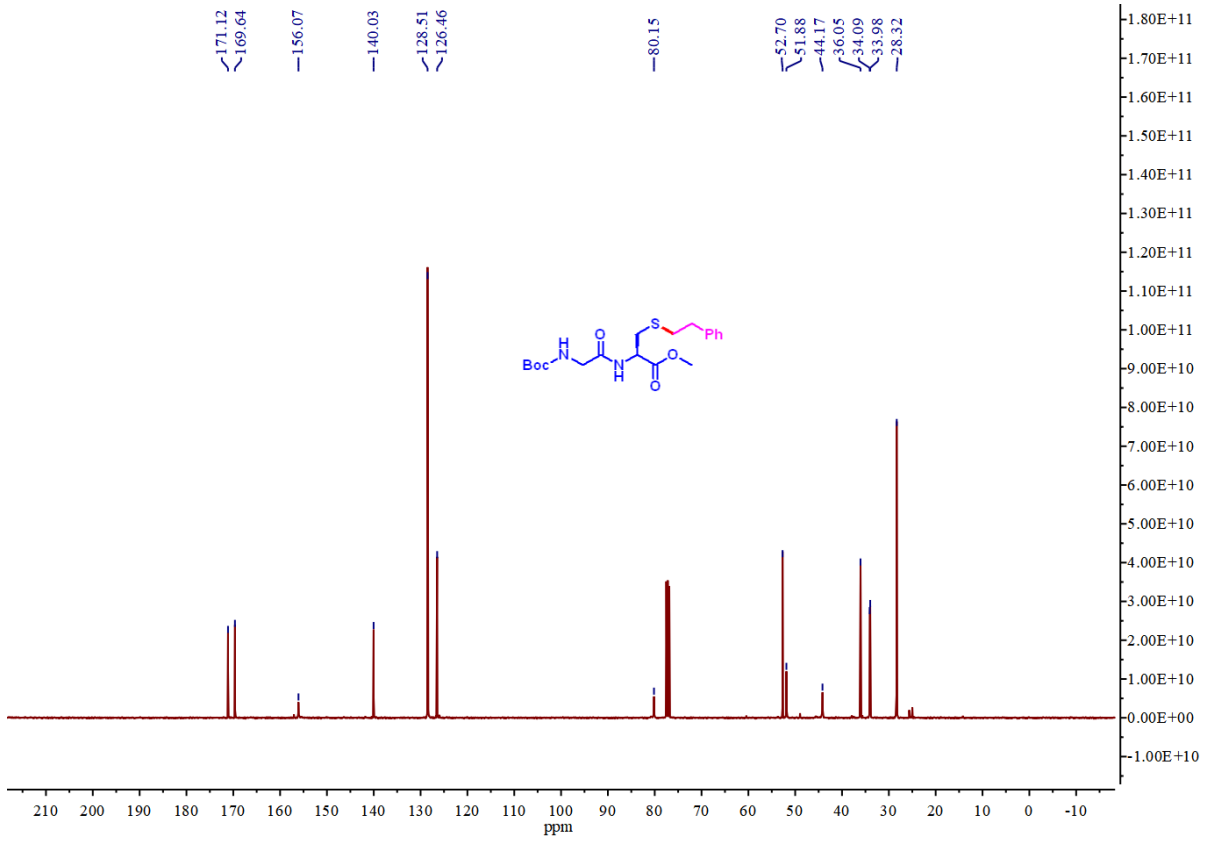
^{1}H NMR Spectrum of Compound **3a** (400 MHz, $CDCl_3$)



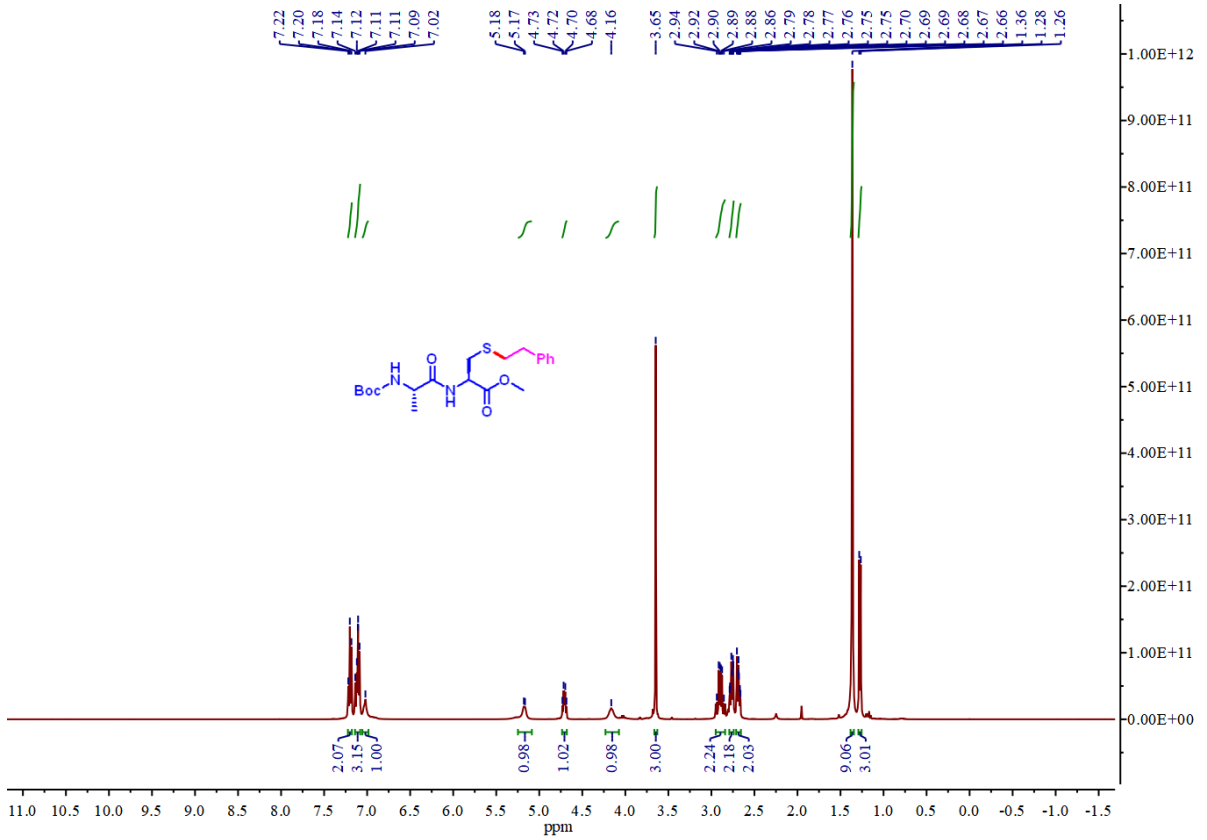
^{13}C NMR Spectrum of Compound **3a** (100 MHz, $CDCl_3$)



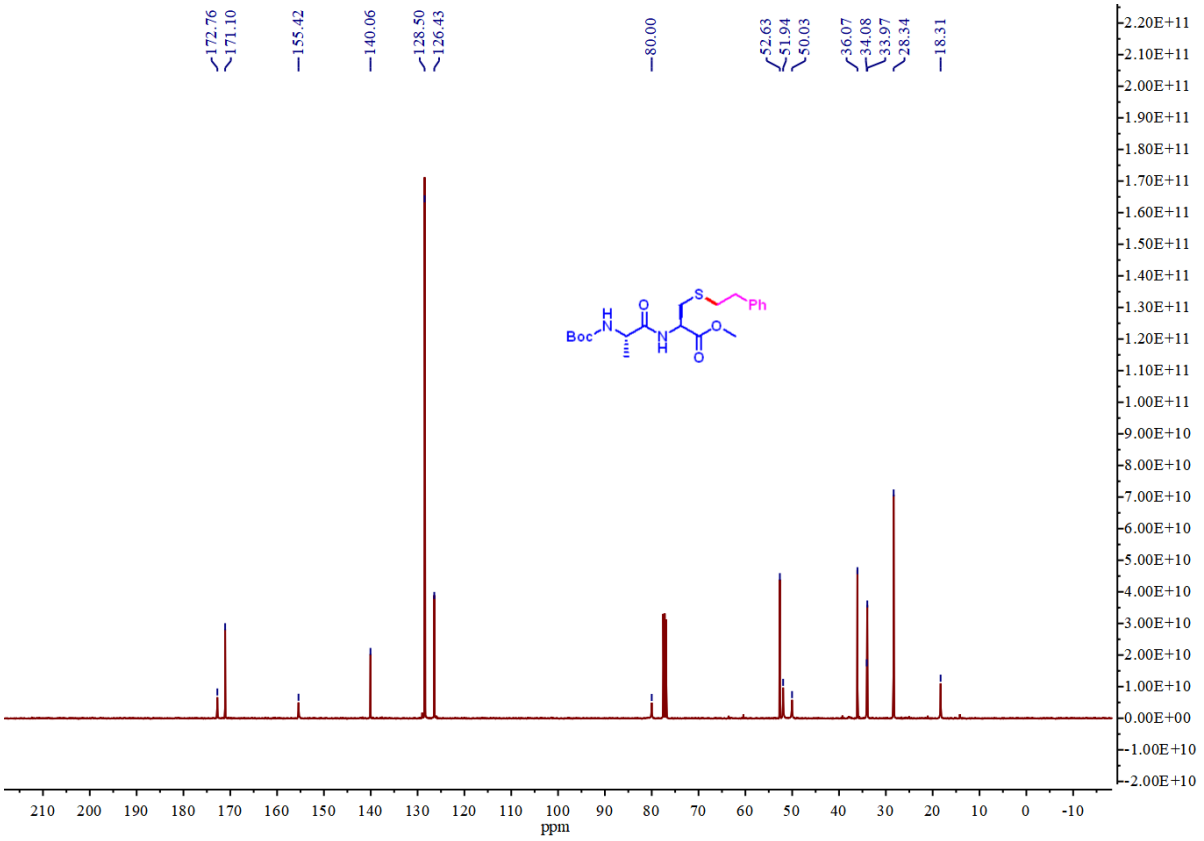
^{1}H NMR Spectrum of Compound **3b** (400 MHz, $CDCl_3$)



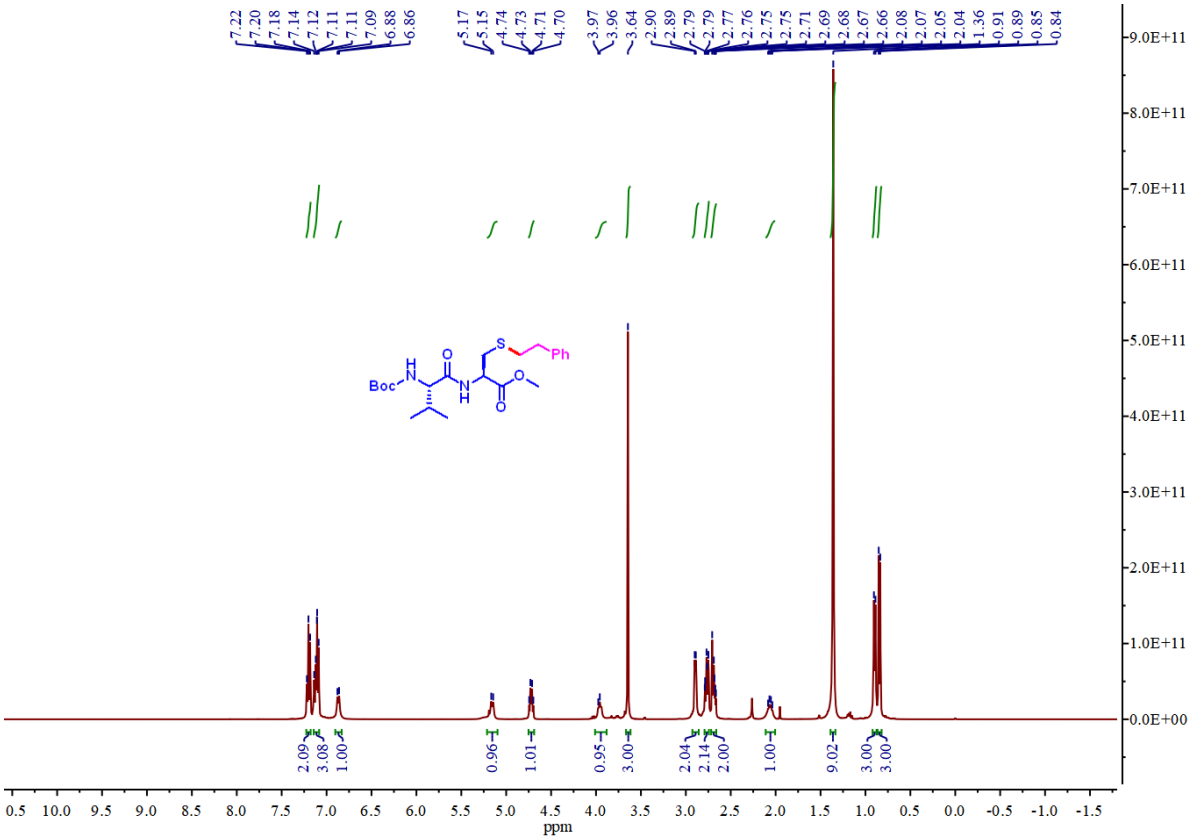
^{13}C NMR Spectrum of Compound **3b** (100 MHz, $CDCl_3$)



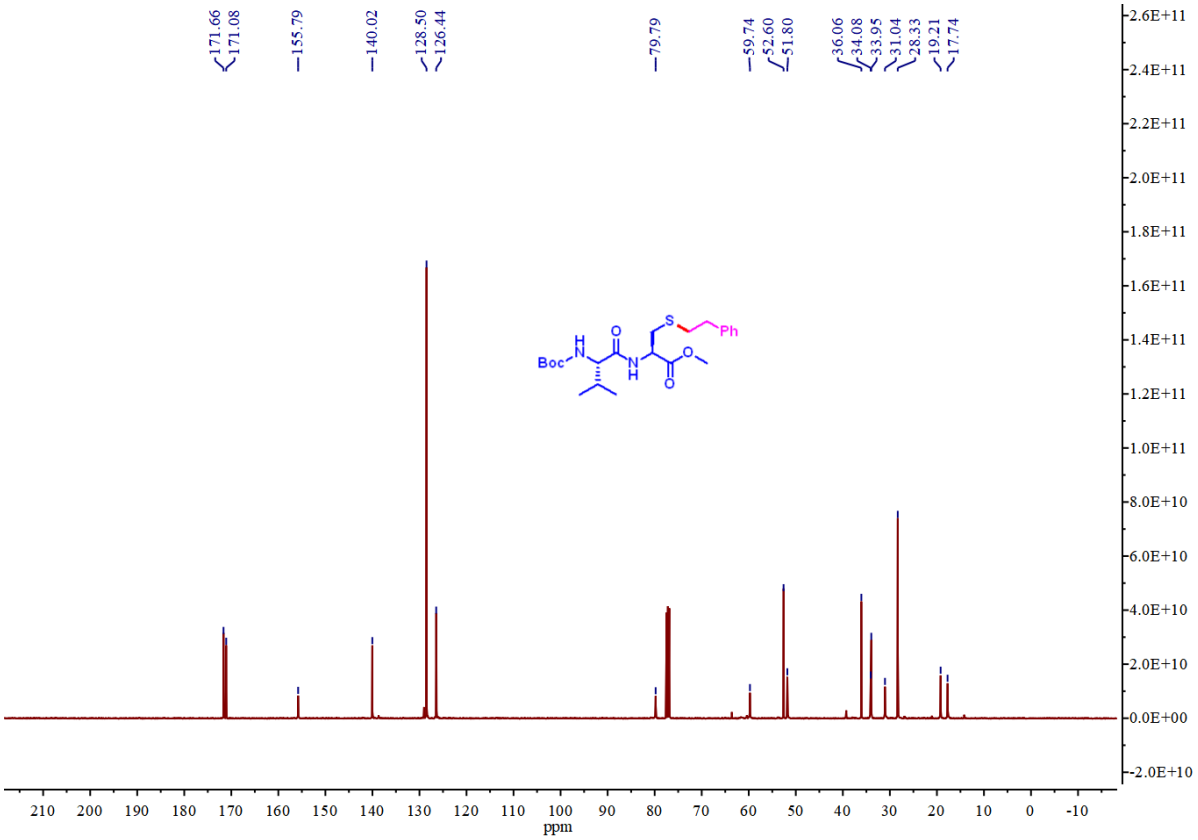
^{1}H NMR Spectrum of Compound **3c** (400 MHz, $CDCl_3$)



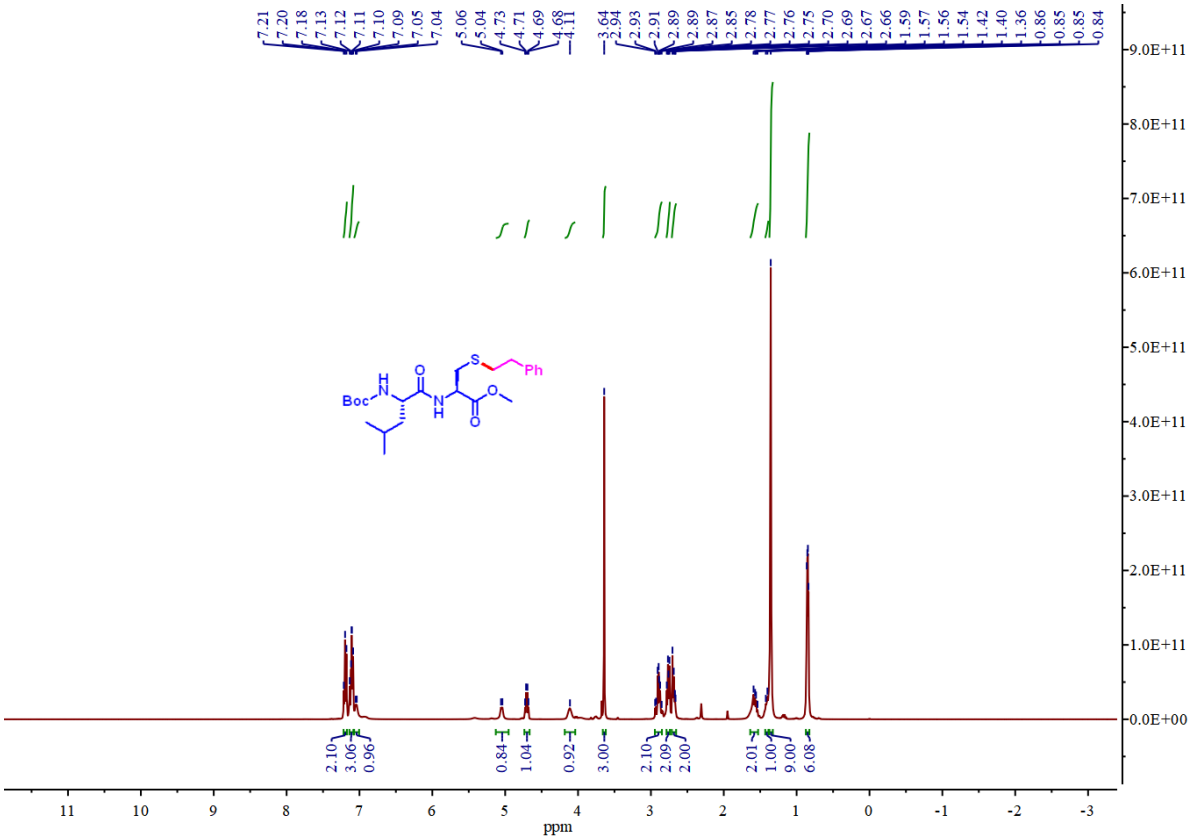
^{13}C NMR Spectrum of Compound **3c** (100 MHz, $CDCl_3$)



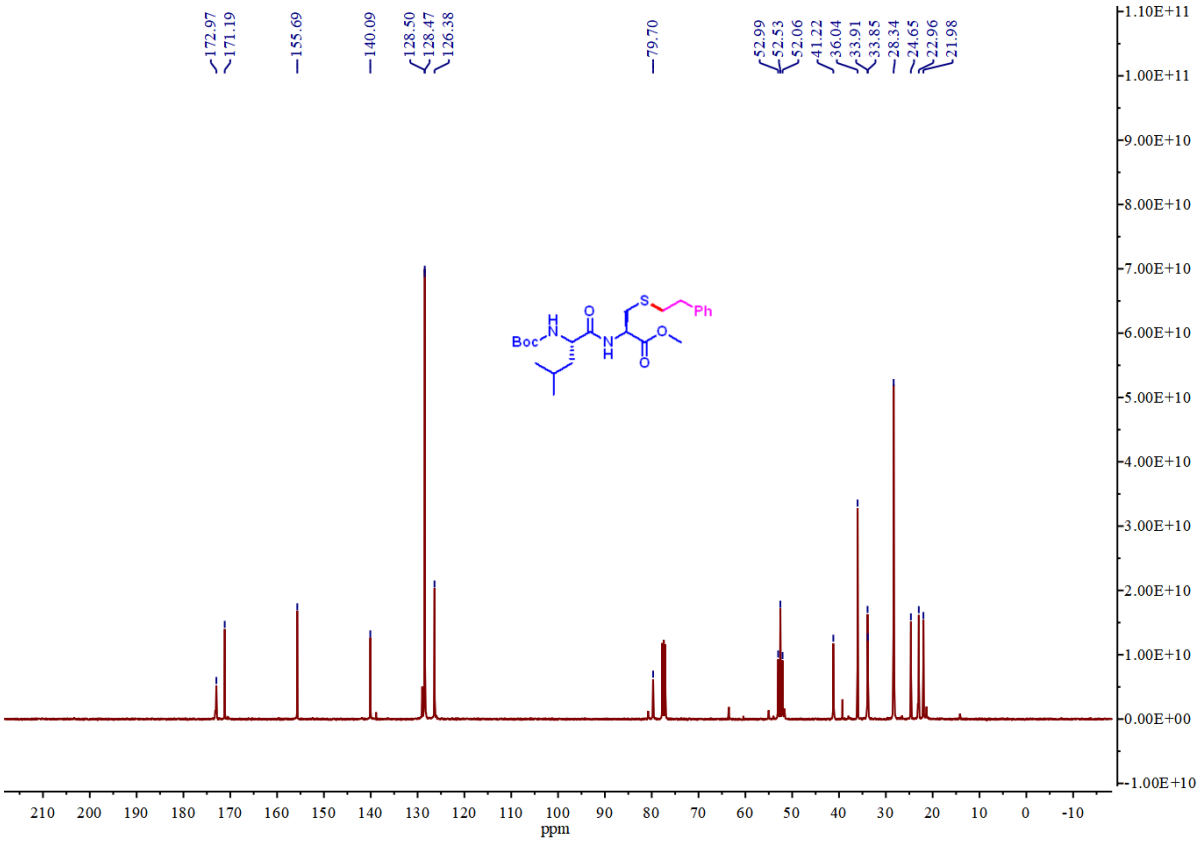
^{1}H NMR Spectrum of Compound **3d** (400 MHz, $CDCl_3$)



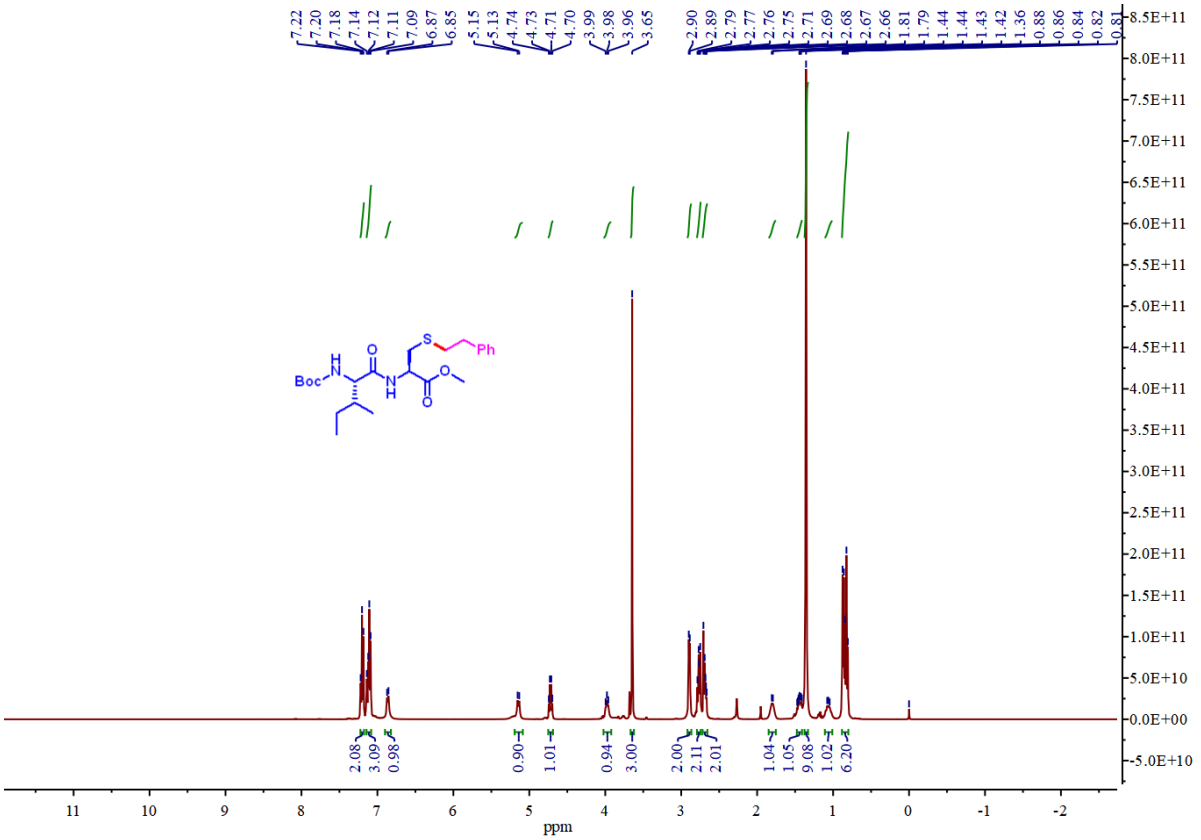
^{13}C NMR Spectrum of Compound **3d** (100 MHz, $CDCl_3$)



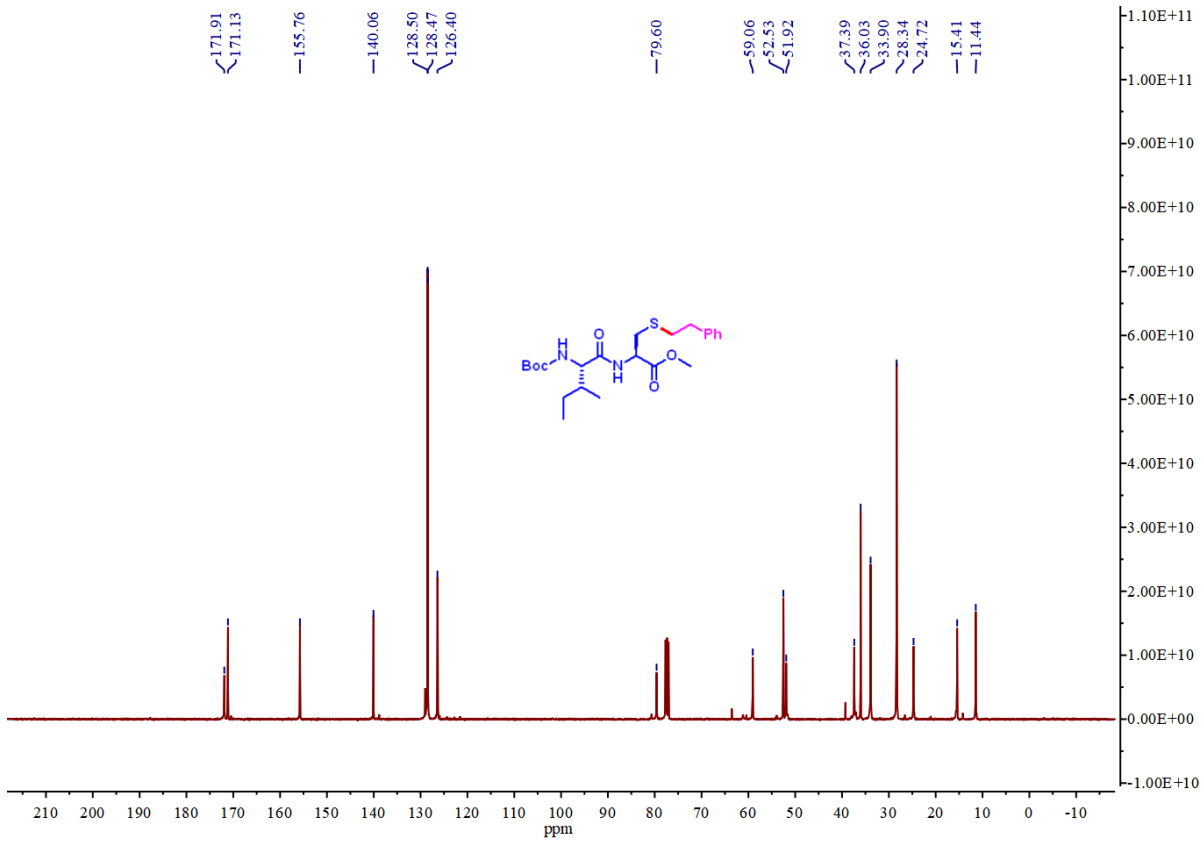
^{1}H NMR Spectrum of Compound **3e** (400 MHz, $CDCl_3$)



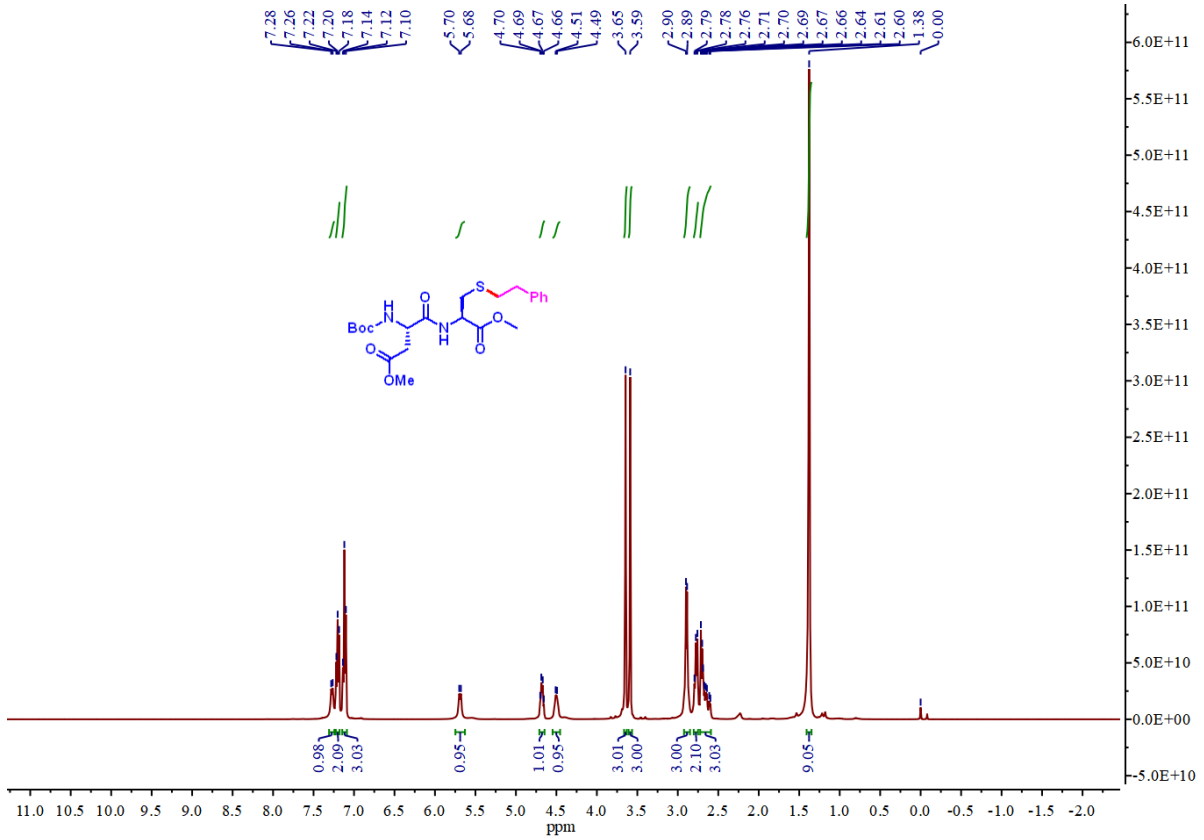
^{13}C NMR Spectrum of Compound **3e** (100 MHz, $CDCl_3$)



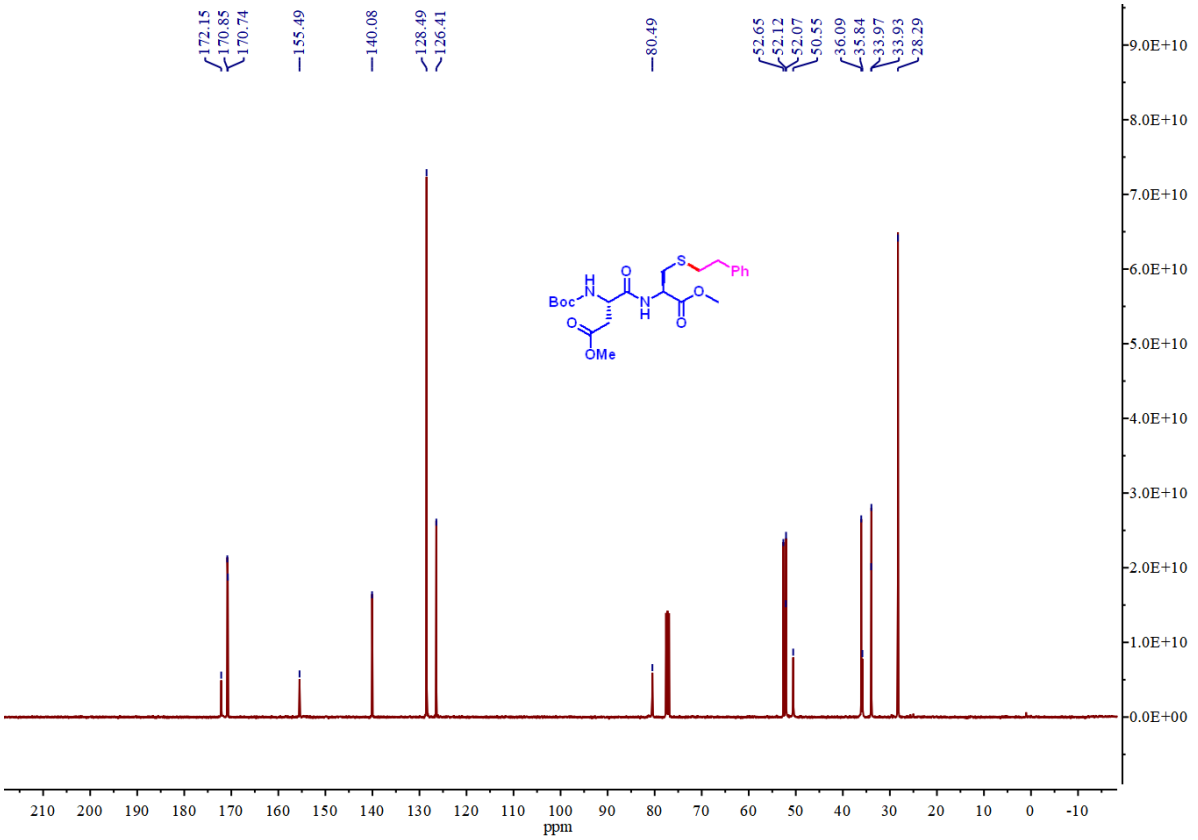
^{1}H NMR Spectrum of Compound **3f** (400 MHz, $CDCl_3$)



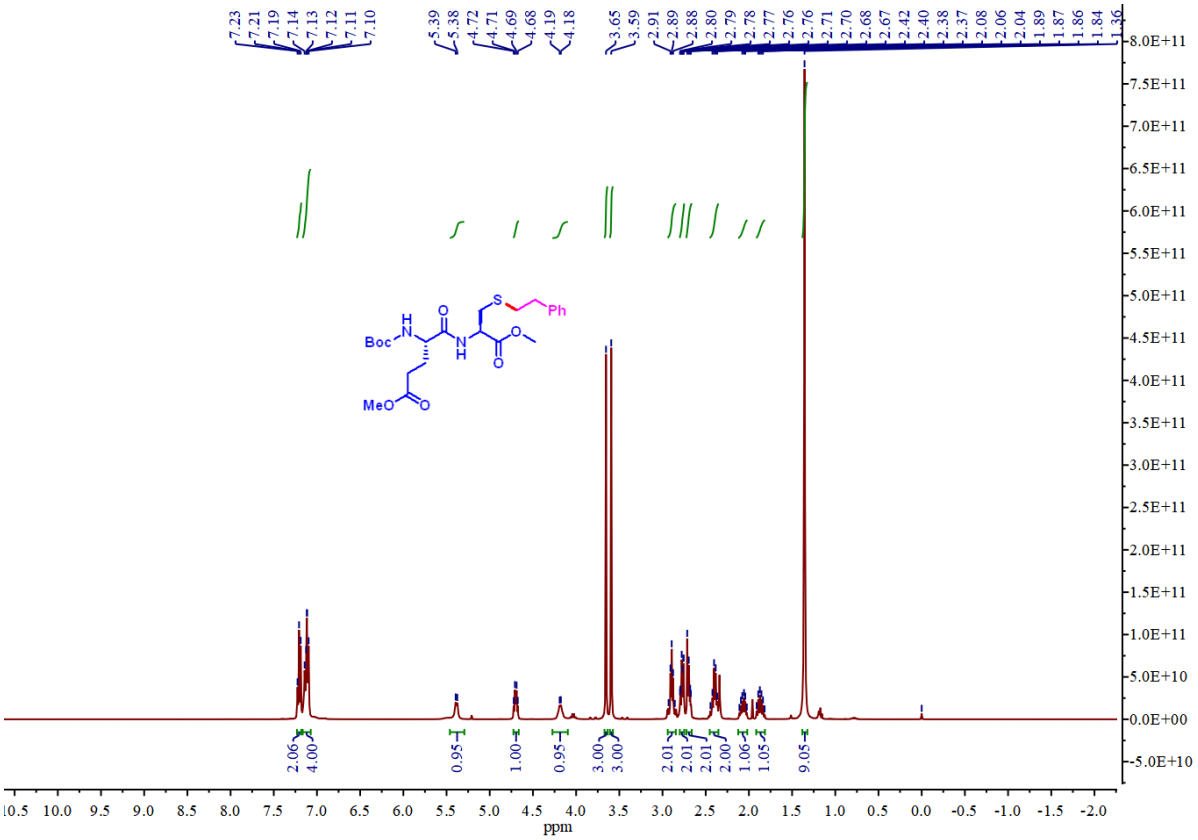
^{13}C NMR Spectrum of Compound **3f** (100 MHz, CDCl3)



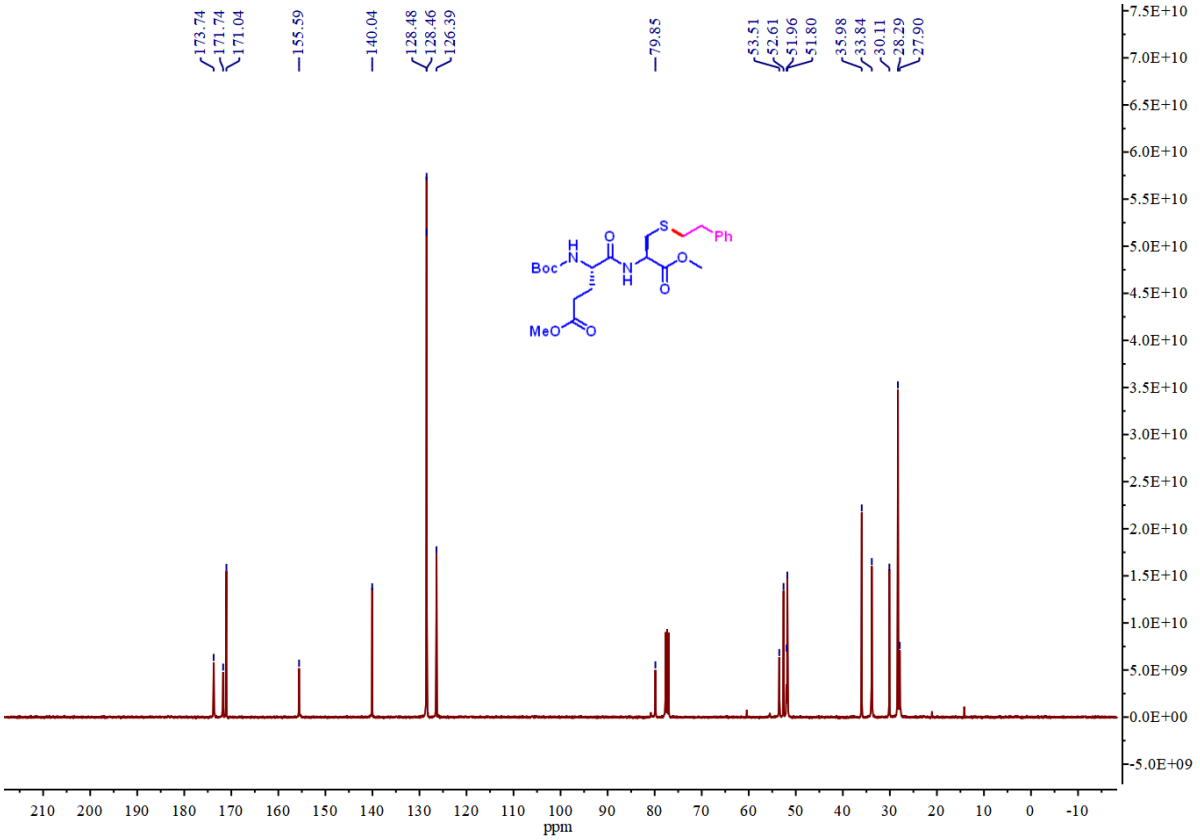
^{1}H NMR Spectrum of Compound **3g** (400 MHz, $CDCl_3$)



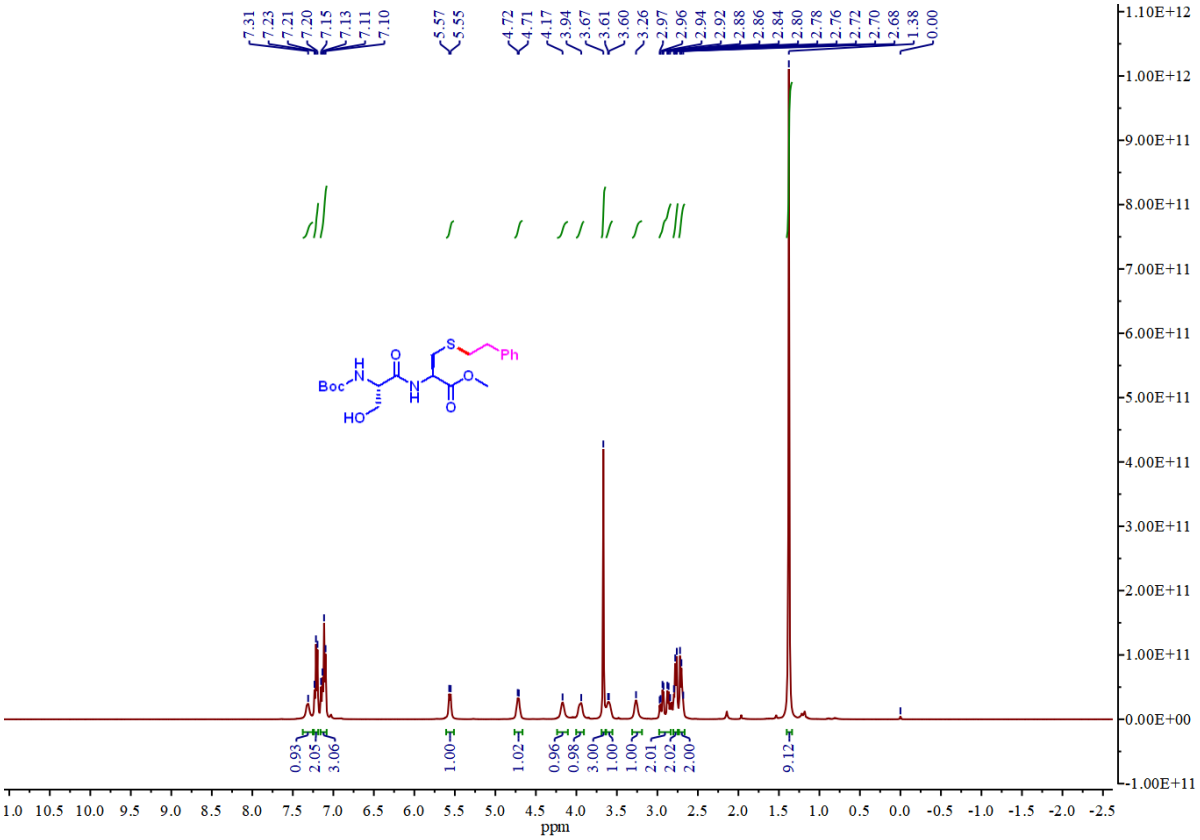
^{13}C NMR Spectrum of Compound **3g** (100 MHz, $CDCl_3$)



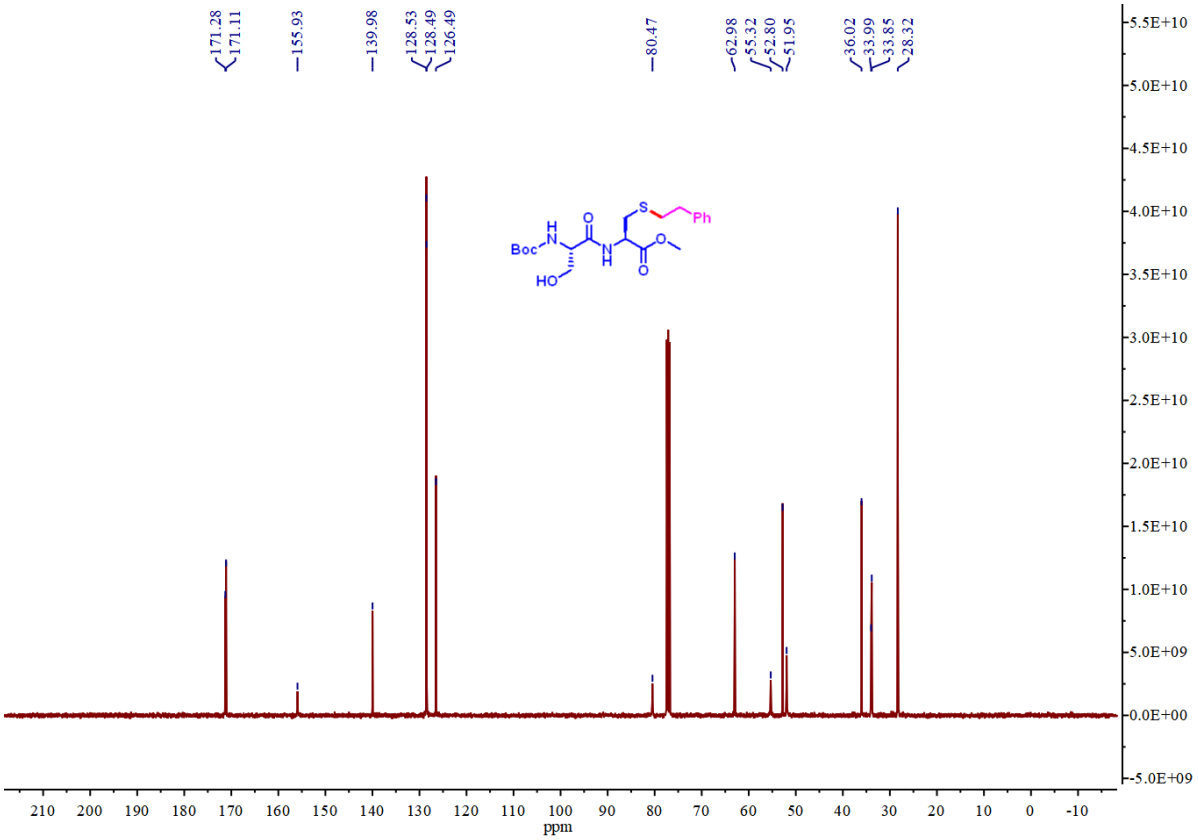
^{1}H NMR Spectrum of Compound **3h** (400 MHz, $CDCl_3$)



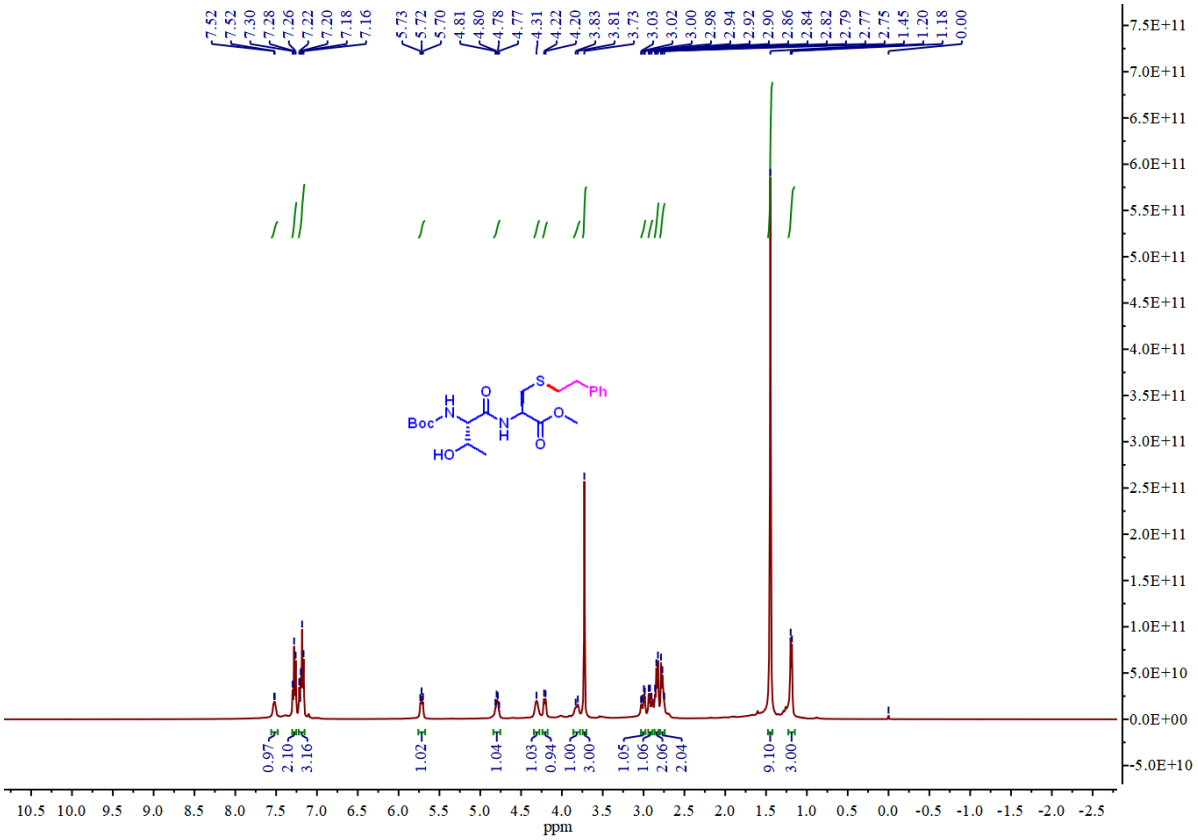
^{13}C NMR Spectrum of Compound **3h** (100 MHz, $CDCl_3$)



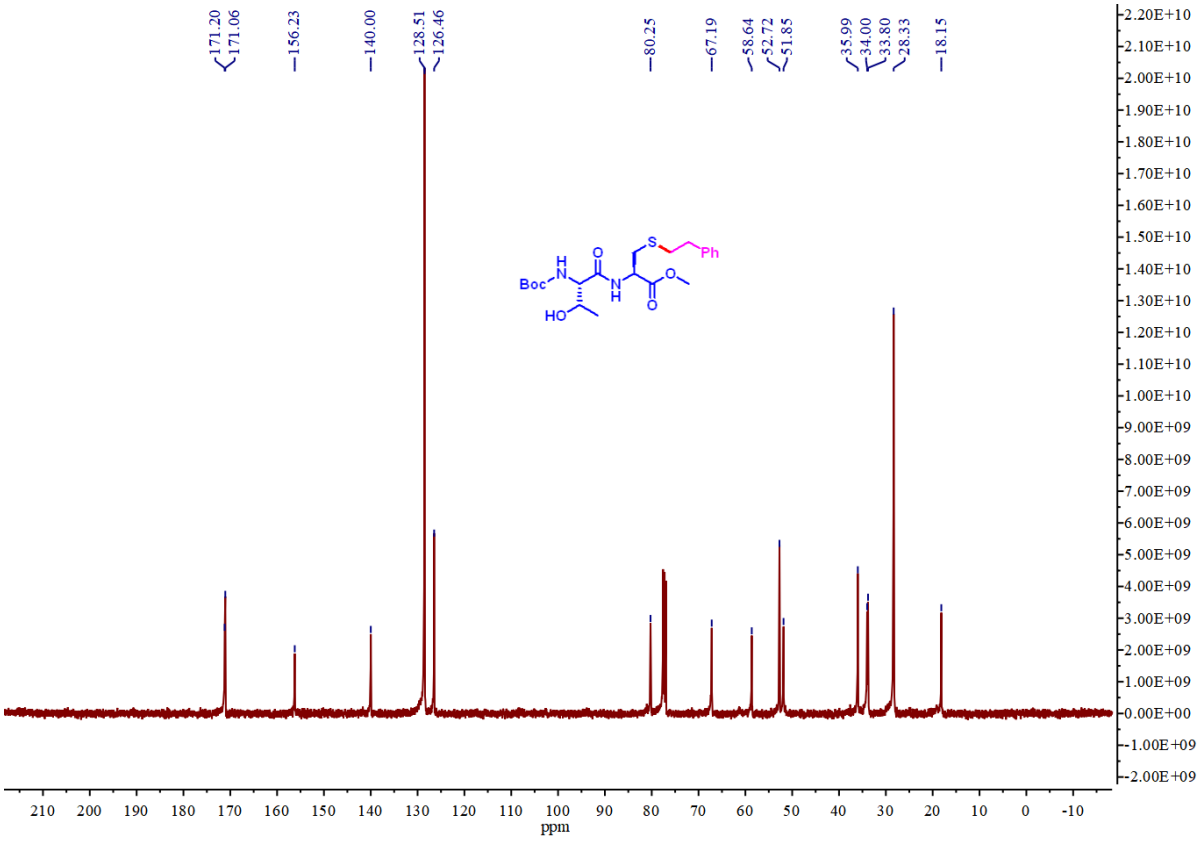
^{1}H NMR Spectrum of Compound **3i** (400 MHz, CDCl3)



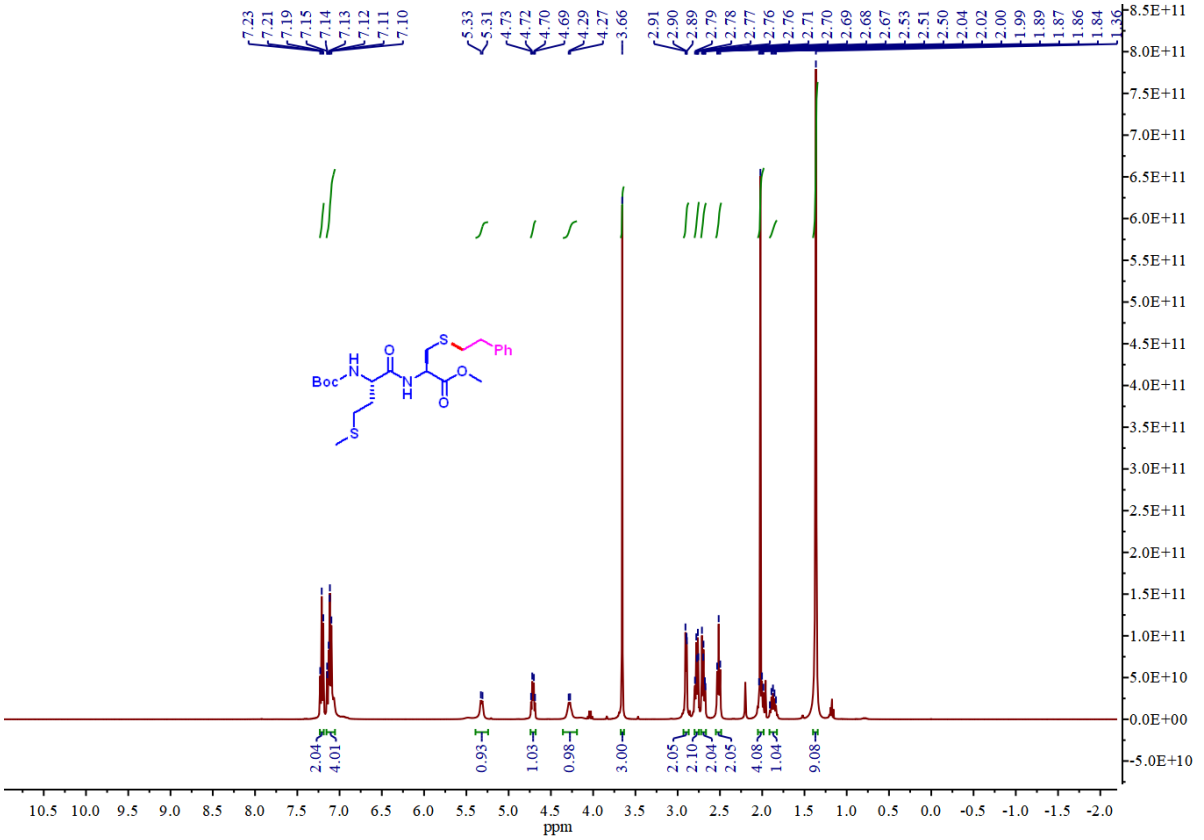
^{13}C NMR Spectrum of Compound **3i** (100 MHz, $CDCl_3$)



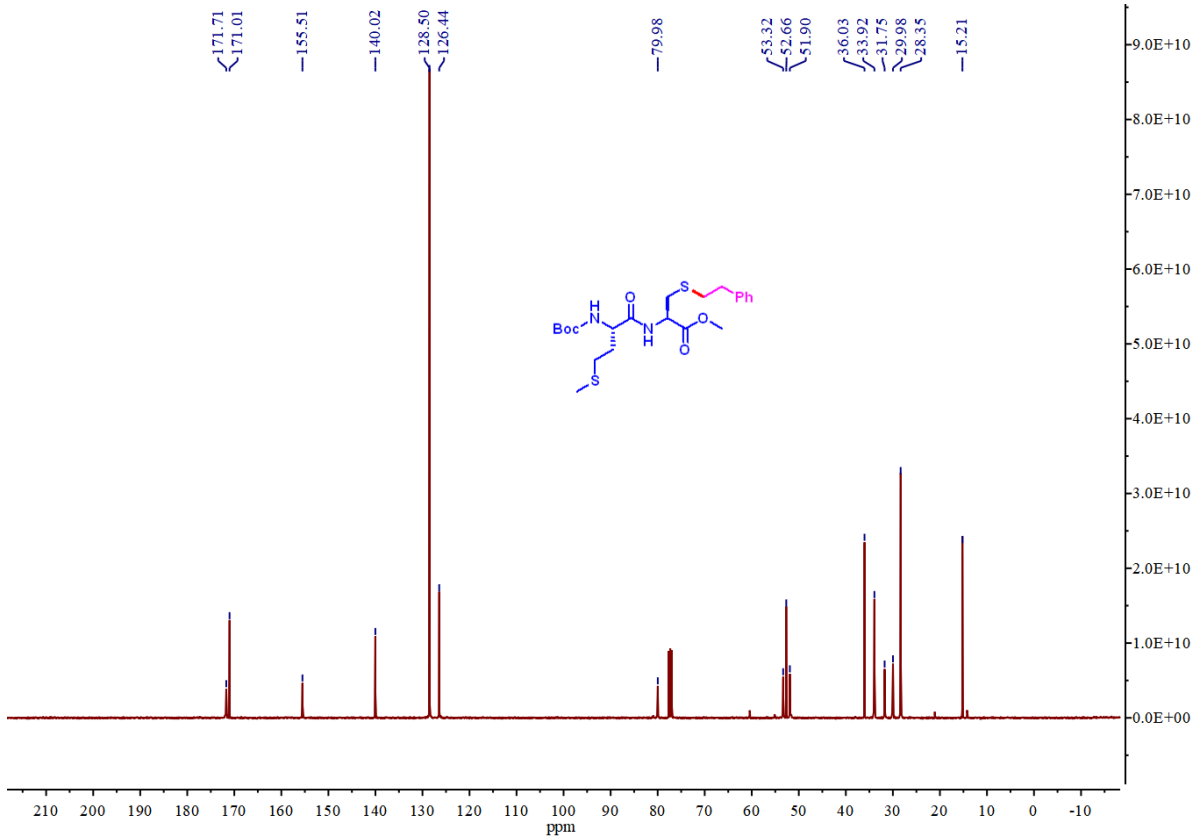
^{1}H NMR Spectrum of Compound **3j** (400 MHz, $CDCl_3$)



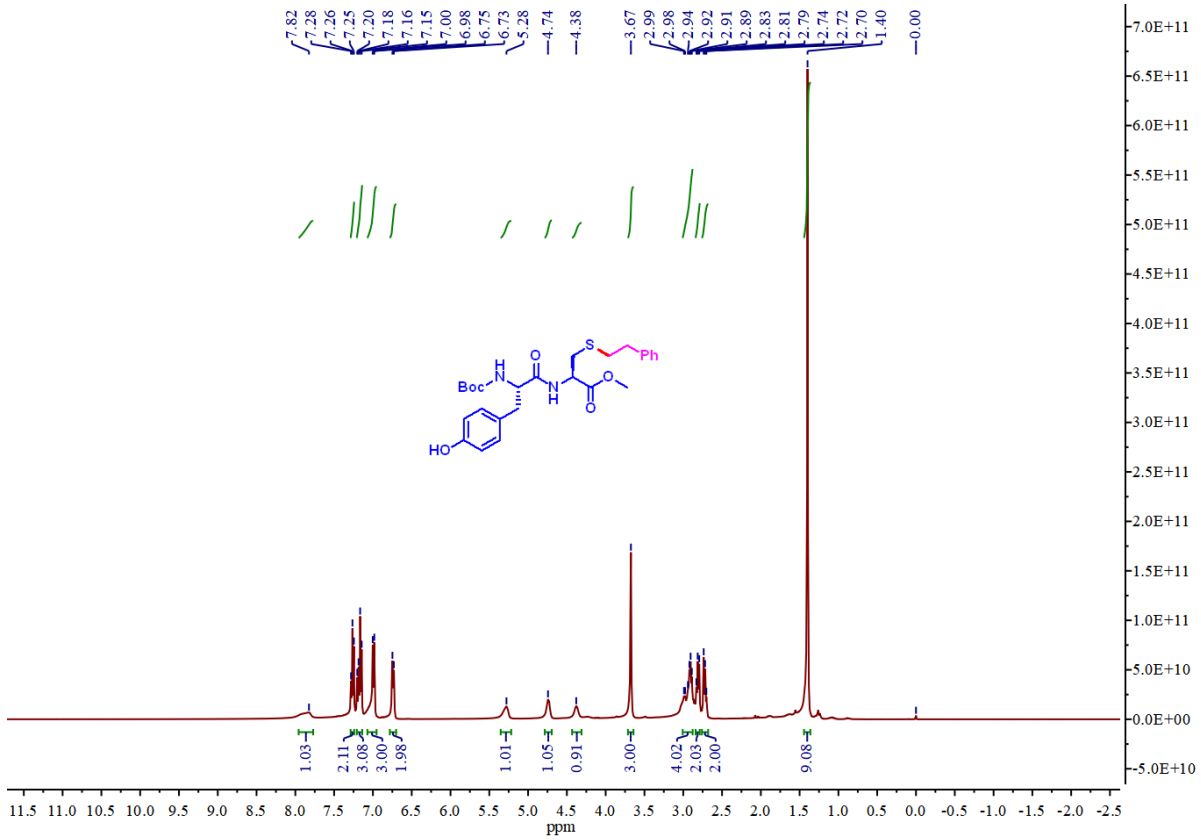
^{13}C NMR Spectrum of Compound **3j** (100 MHz, $CDCl_3$)



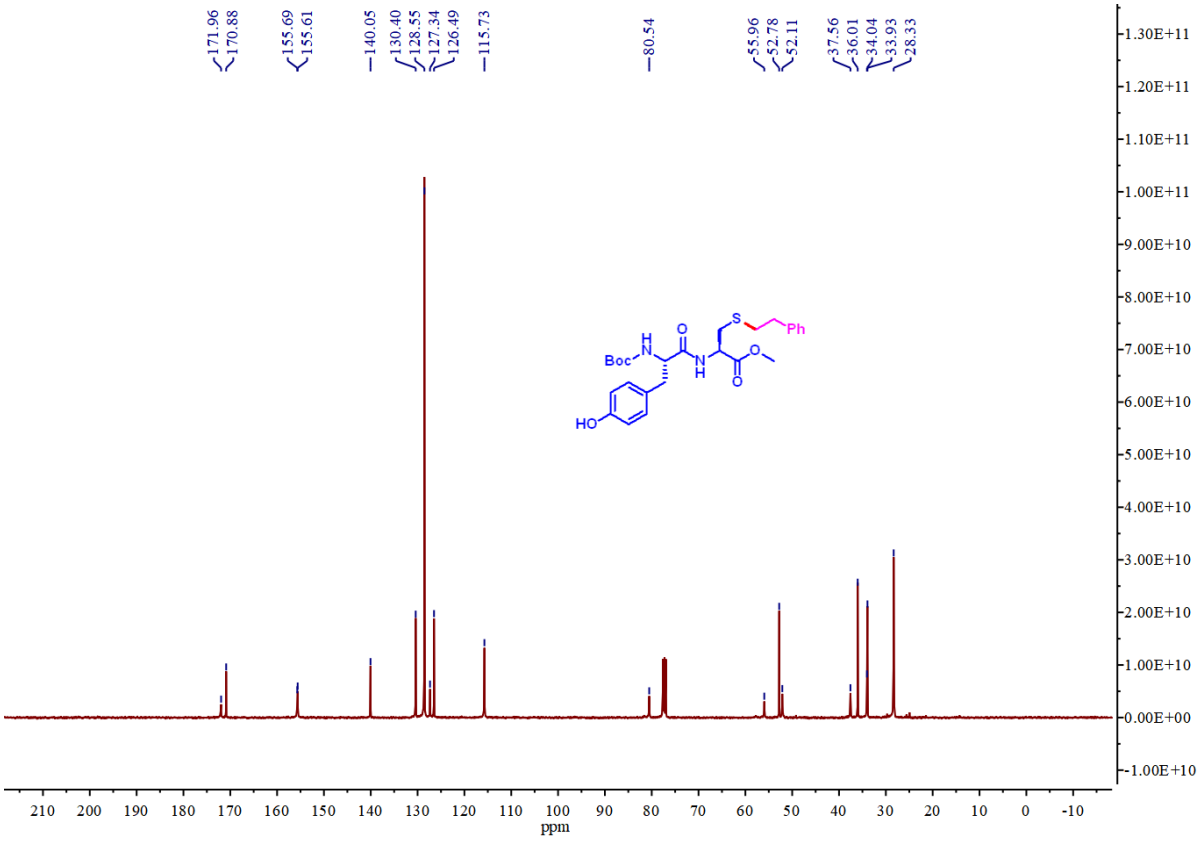
^{1}H NMR Spectrum of Compound **3k** (400 MHz, $CDCl_3$)



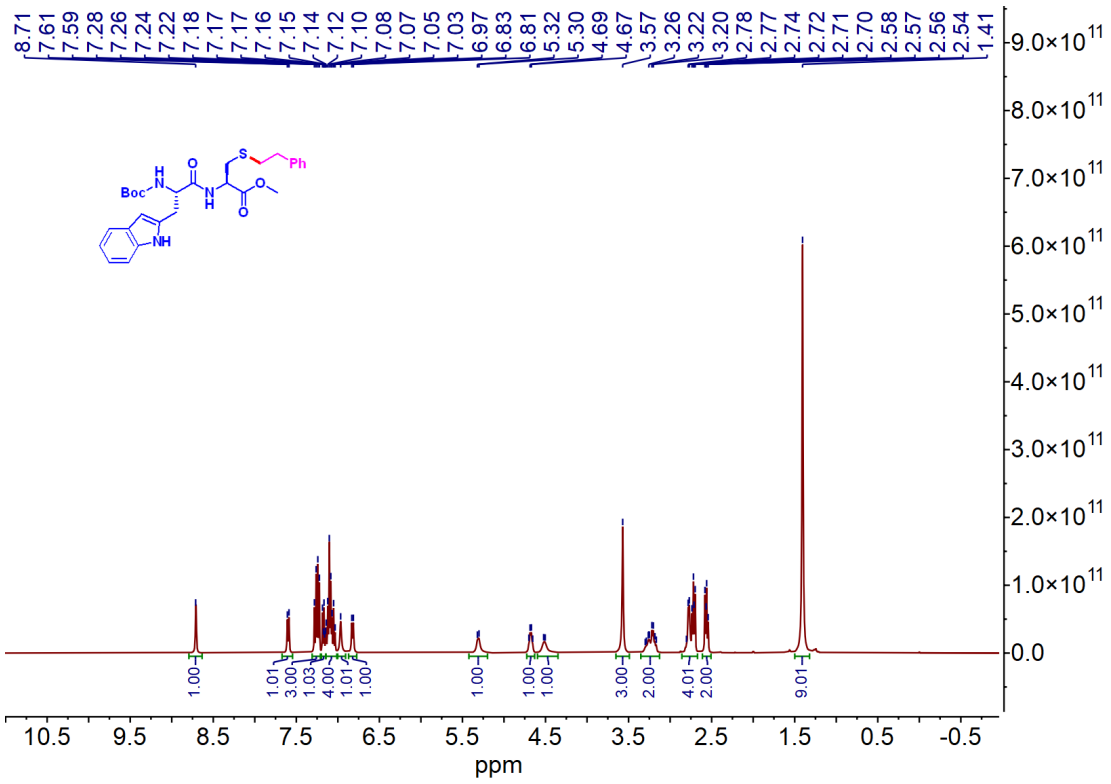
^{13}C NMR Spectrum of Compound **3k** (100 MHz, $CDCl_3$)



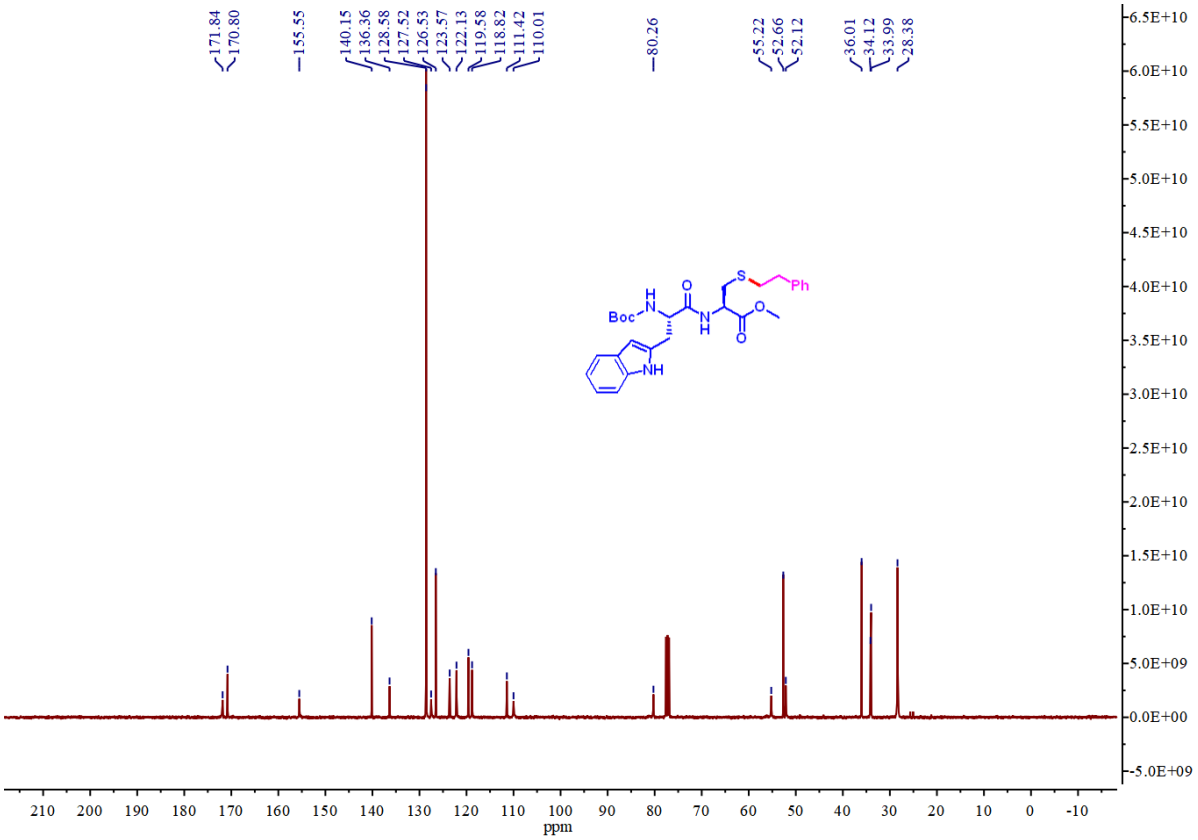
^{1}H NMR Spectrum of Compound **3l** (400 MHz, $CDCl_3$)



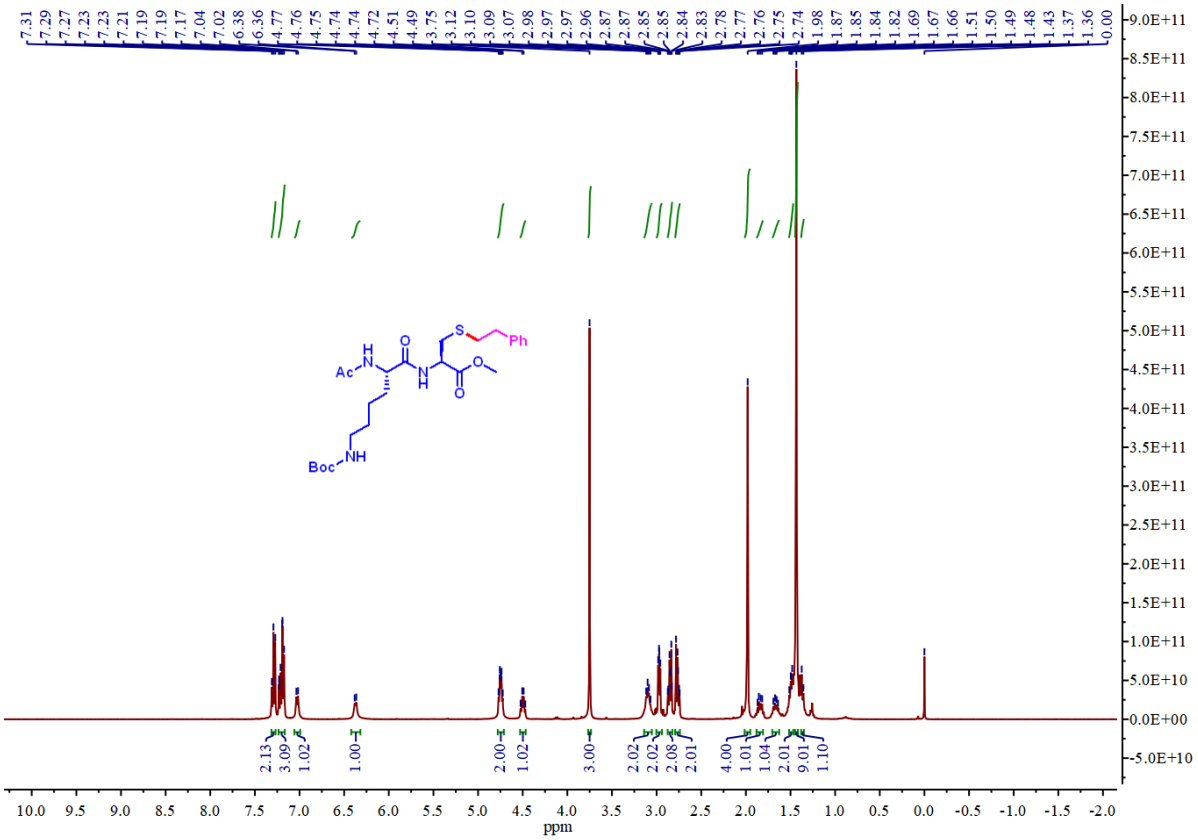
^{13}C NMR Spectrum of Compound **3l** (100 MHz, $CDCl_3$)



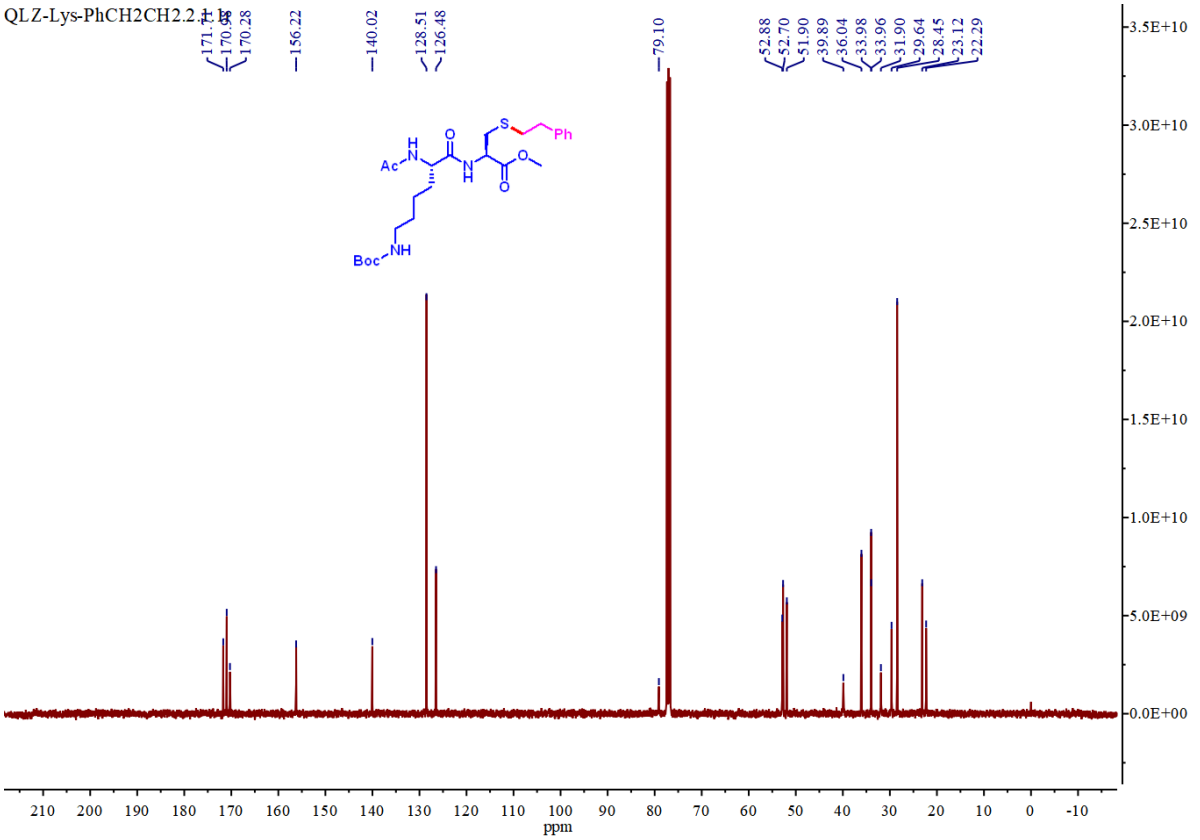
^{1}H NMR Spectrum of Compound **3m** (400 MHz, $CDCl_3$)



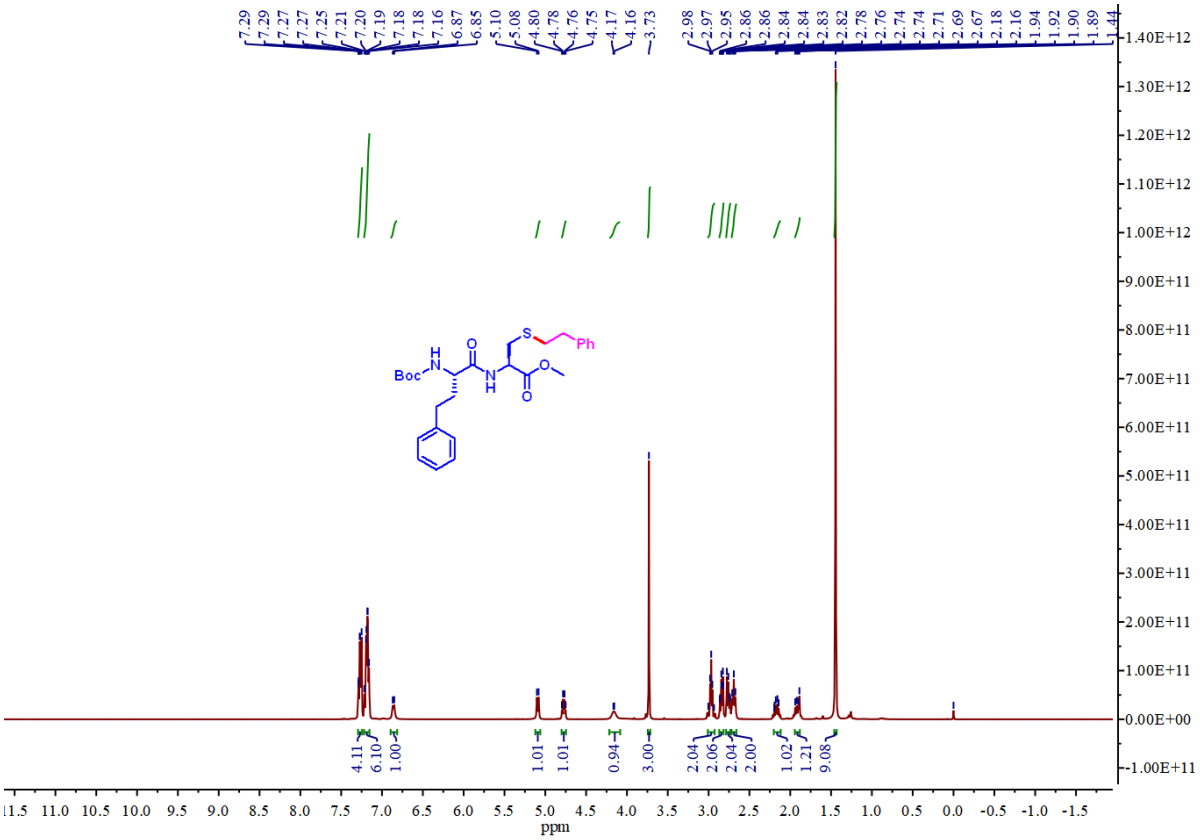
^{13}C NMR Spectrum of Compound **3m** (100 MHz, $CDCl_3$)



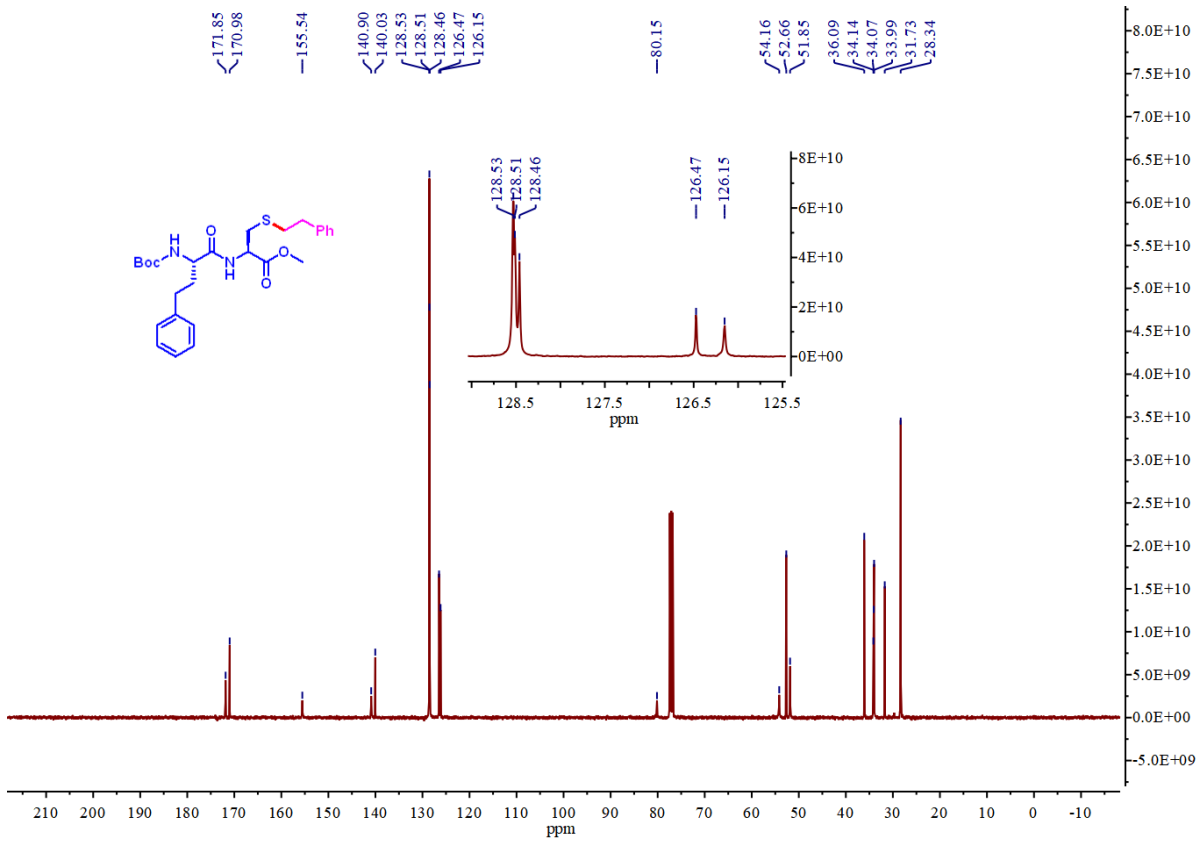
^{1}H NMR Spectrum of Compound **3n** (400 MHz, $CDCl_3$)



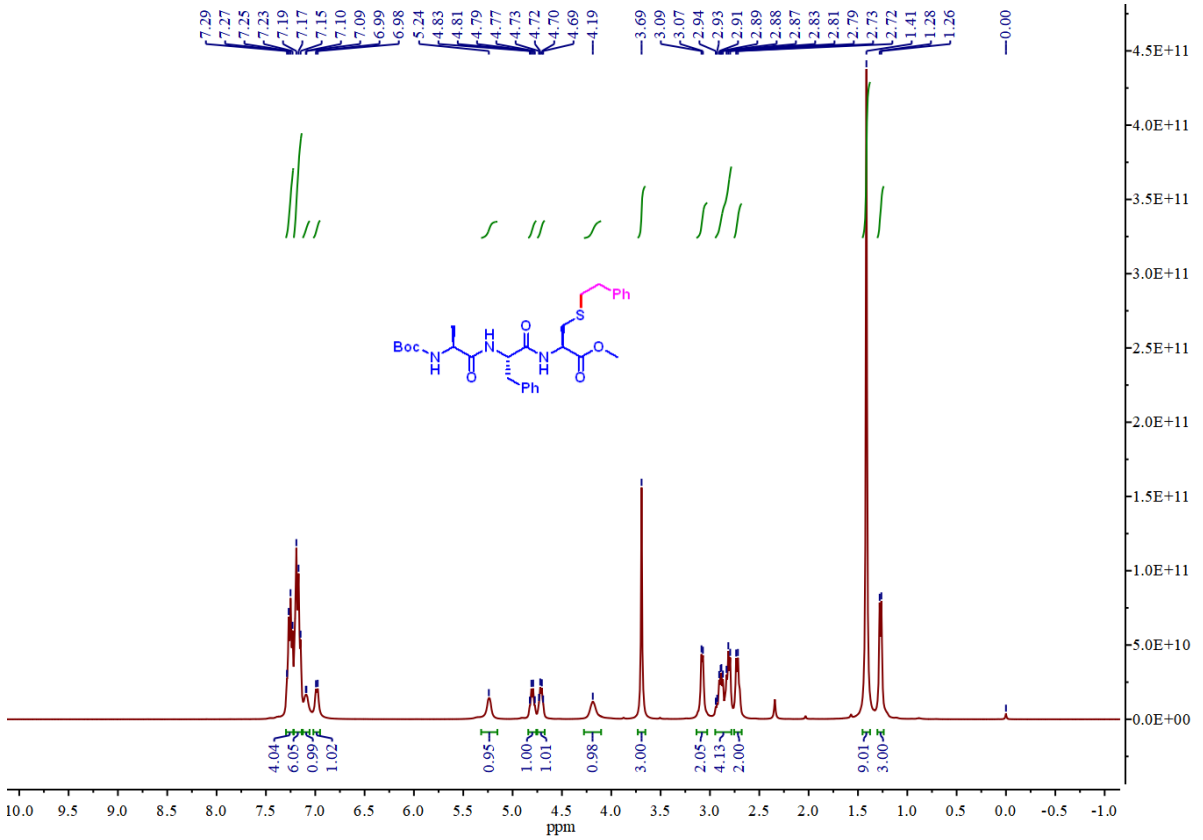
^{13}C NMR Spectrum of Compound **3n** (100 MHz, $CDCl_3$)



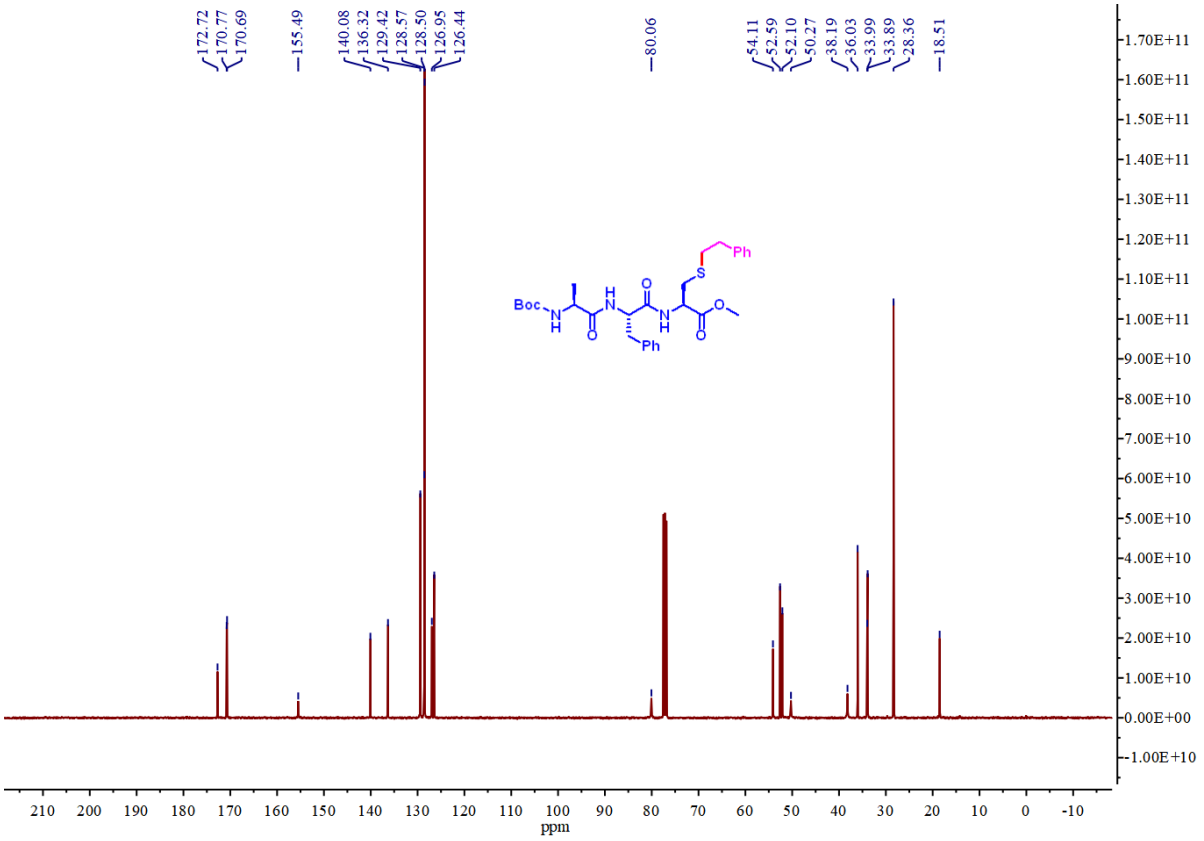
^{1}H NMR Spectrum of Compound **3o** (400 MHz, $CDCl_3$)



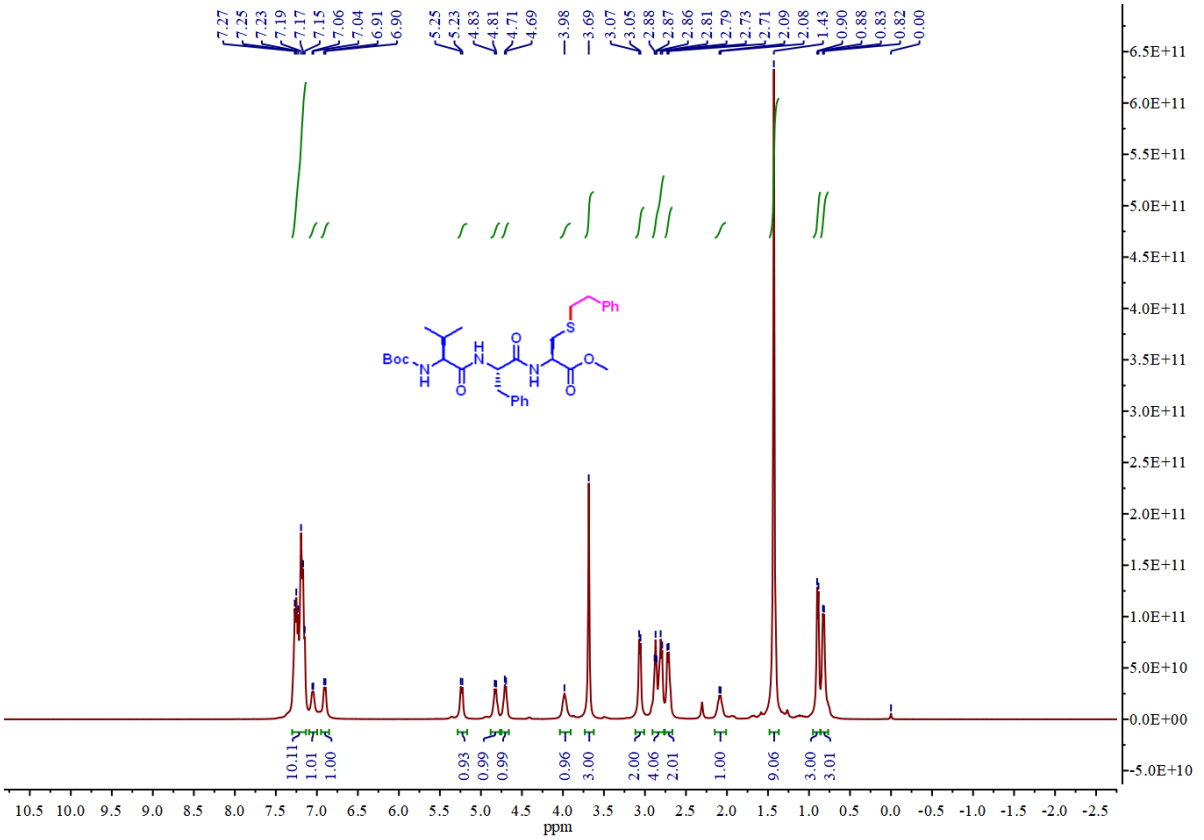
^{13}C NMR Spectrum of Compound **3o** (100 MHz, $CDCl_3$)



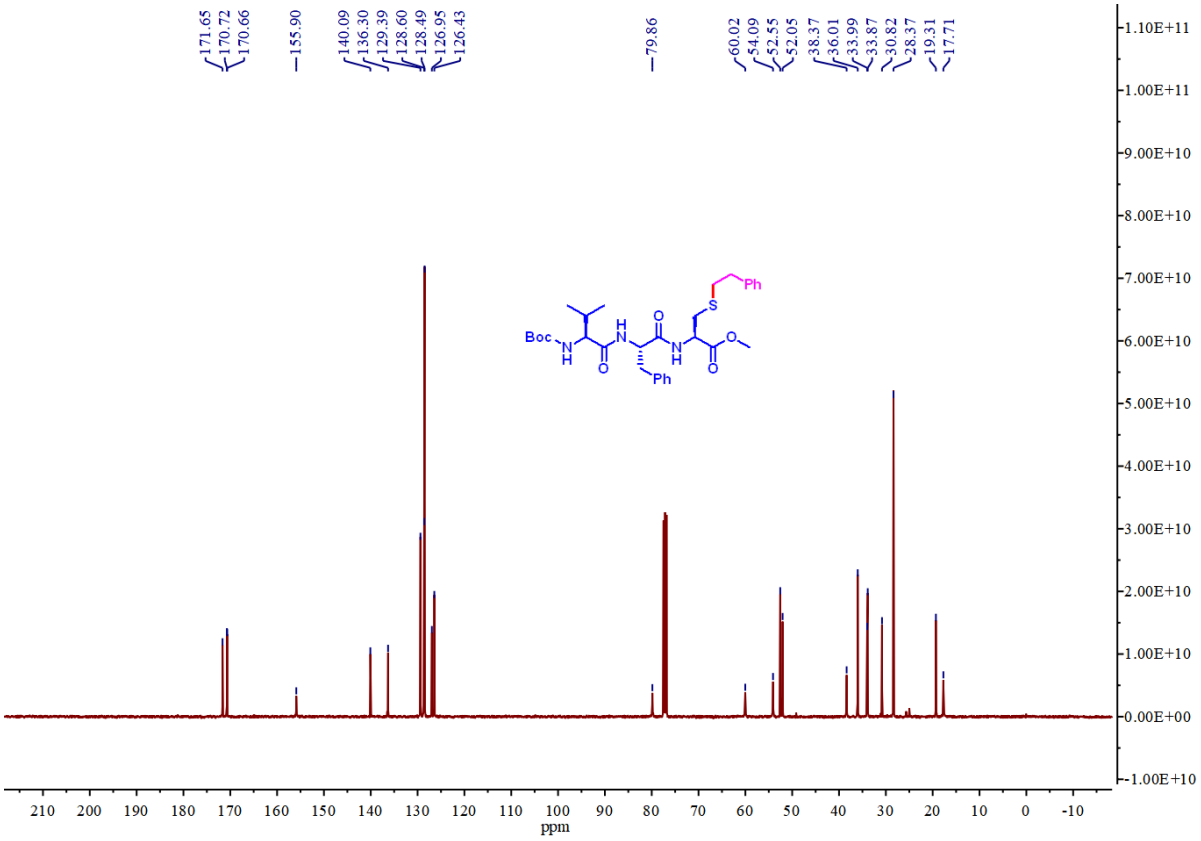
^{1}H NMR Spectrum of Compound **4a** (400 MHz, $CDCl_3$)



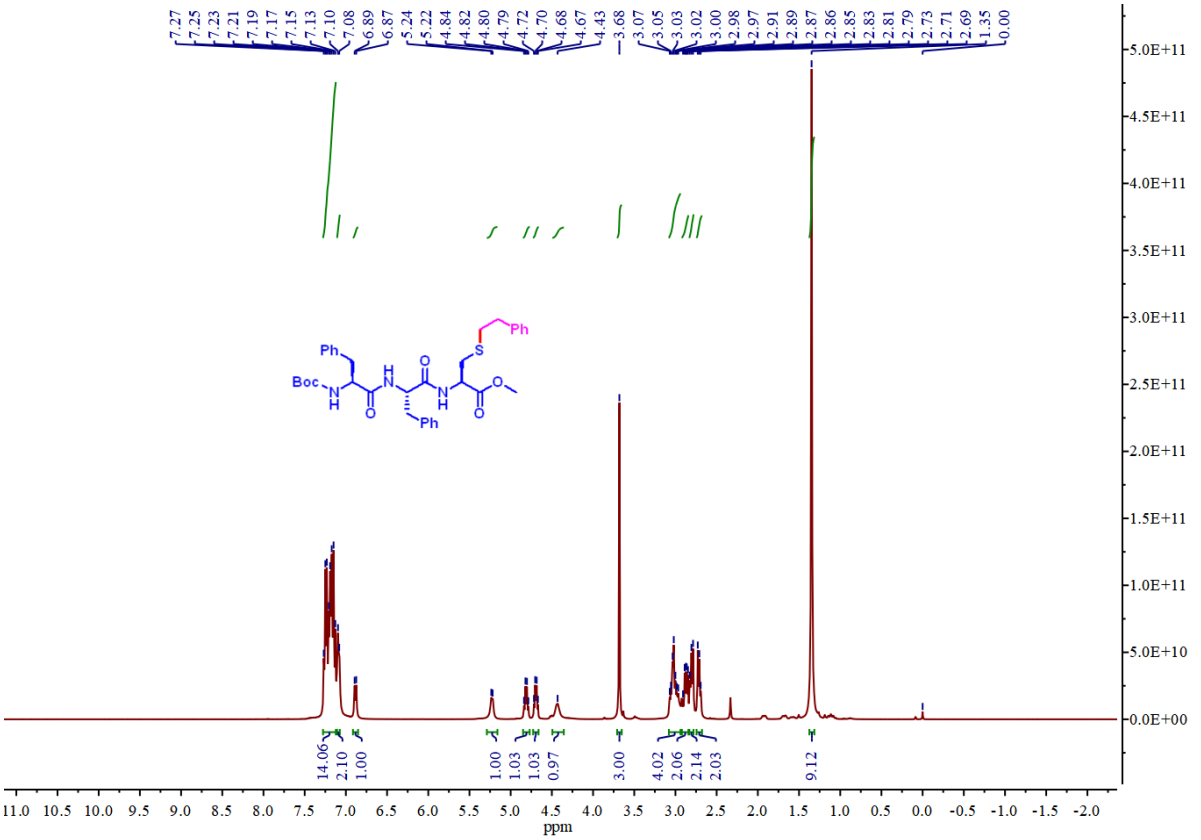
^{13}C NMR Spectrum of Compound **4a** (100 MHz, $CDCl_3$)



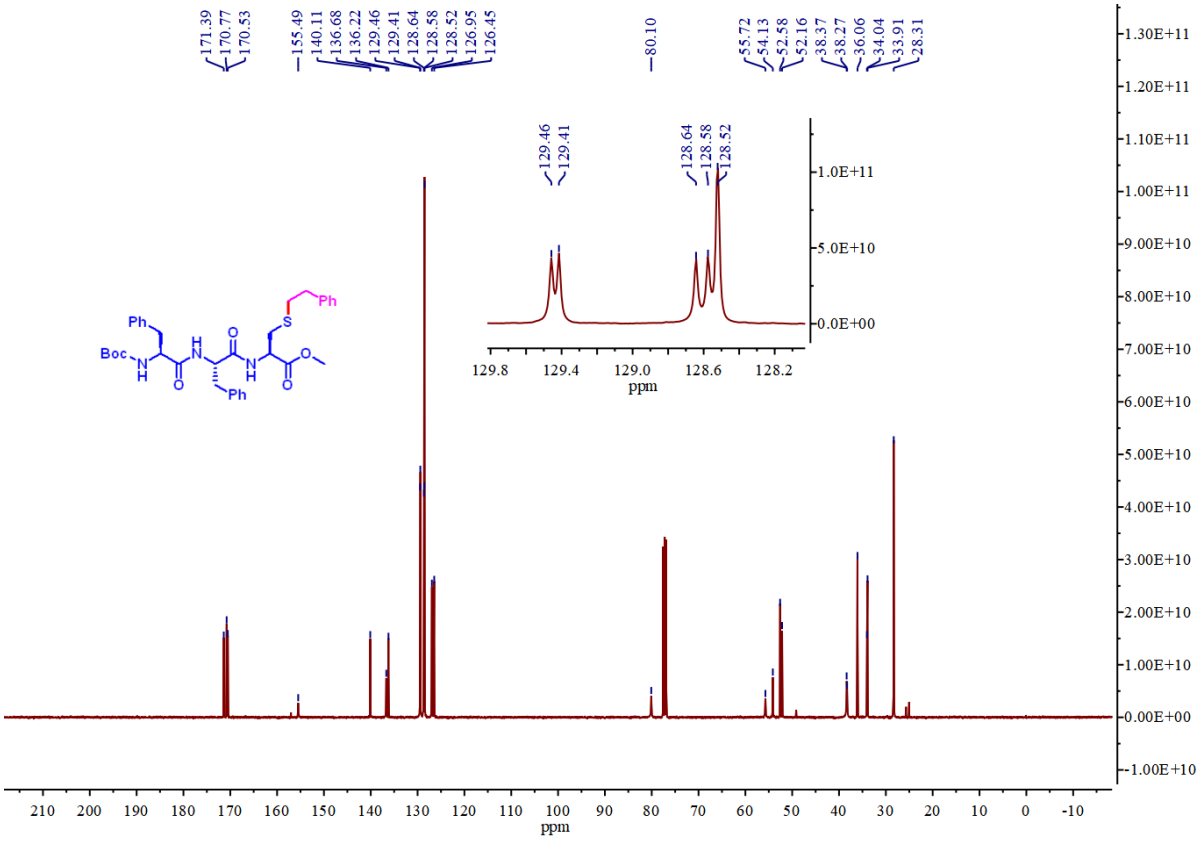
^{1}H NMR Spectrum of Compound **4b** (400 MHz, $CDCl_3$)



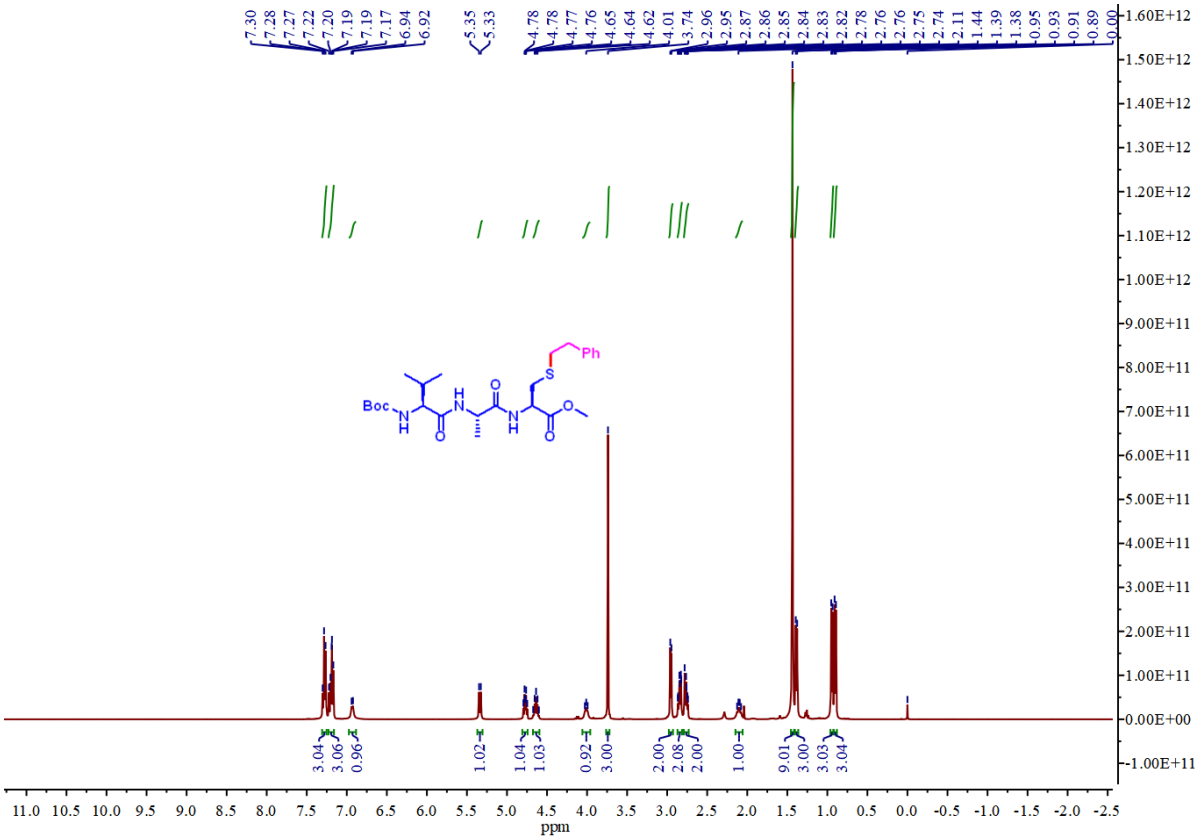
^{13}C NMR Spectrum of Compound **4b** (100 MHz, $CDCl_3$)



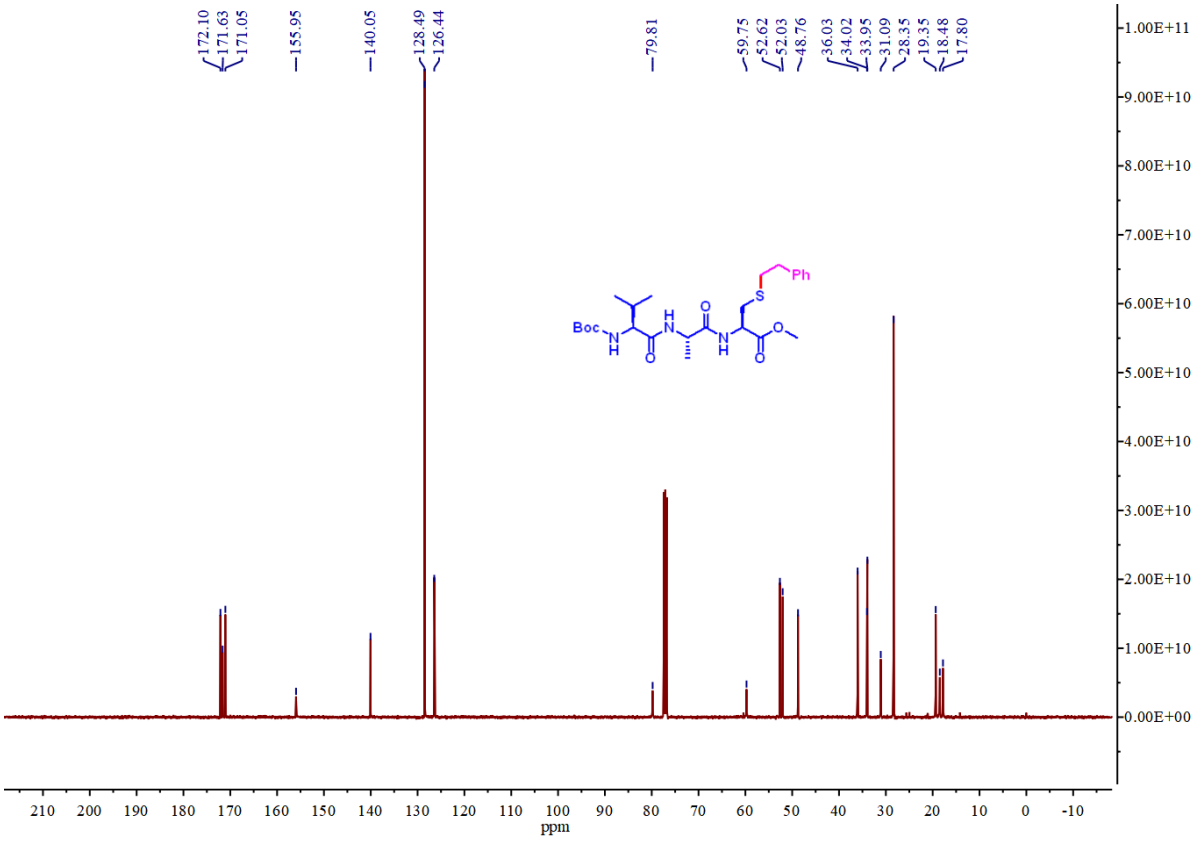
^{1}H NMR Spectrum of Compound **4c** (400 MHz, $CDCl_3$)



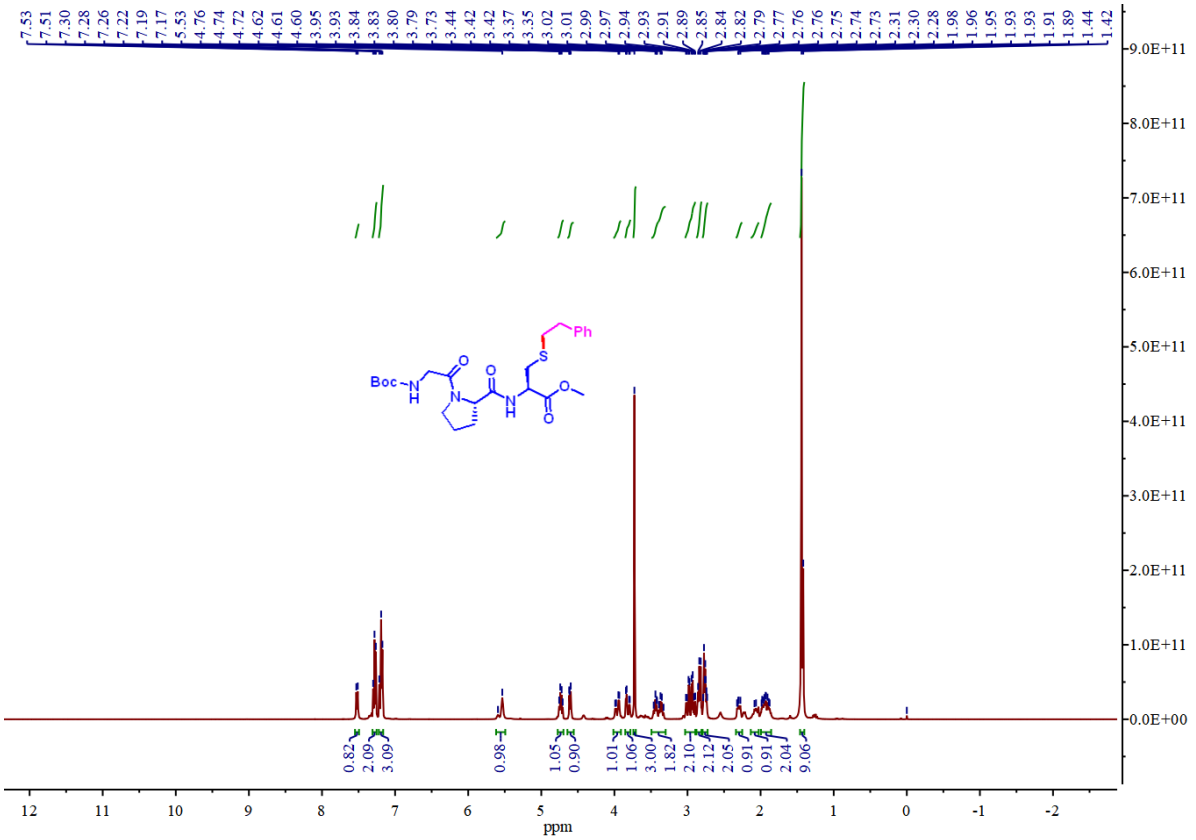
^{13}C NMR Spectrum of Compound **4c** (100 MHz, $CDCl_3$)



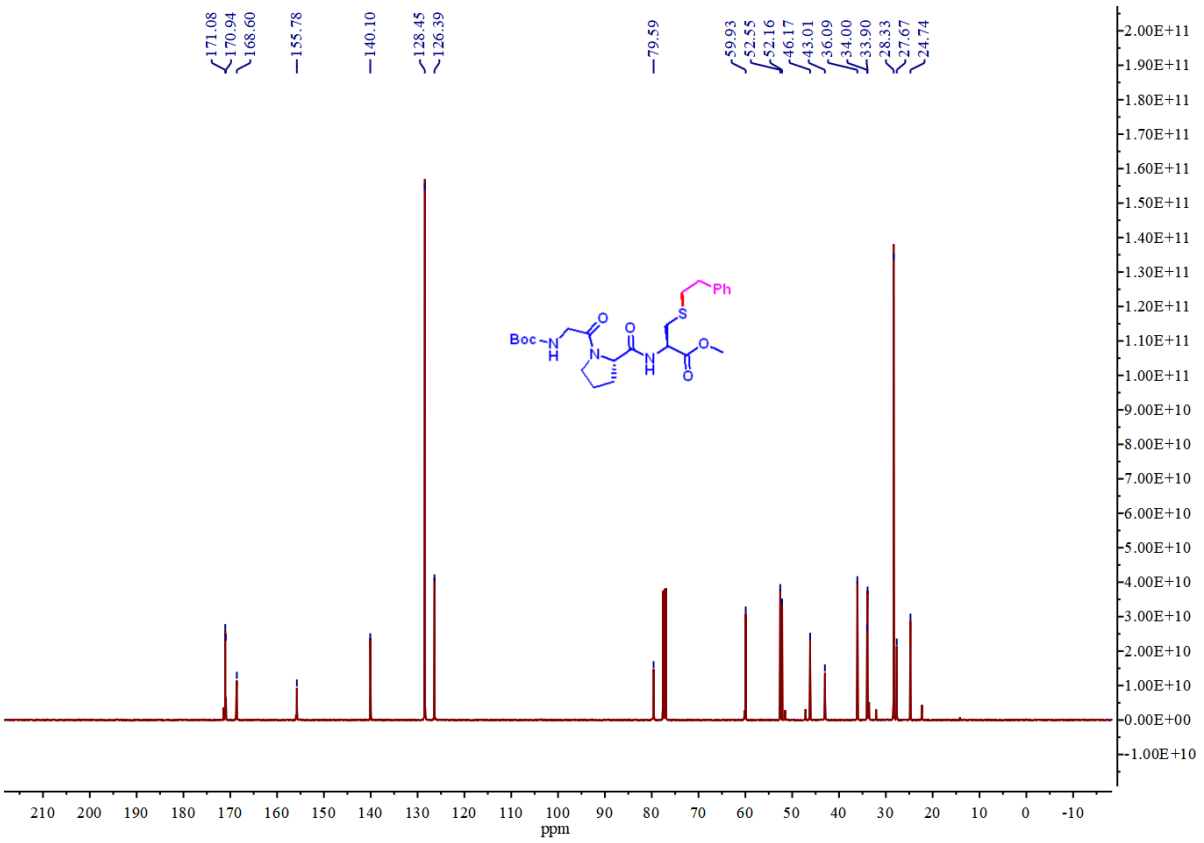
^{1}H NMR Spectrum of Compound **4d** (400 MHz, $CDCl_3$)



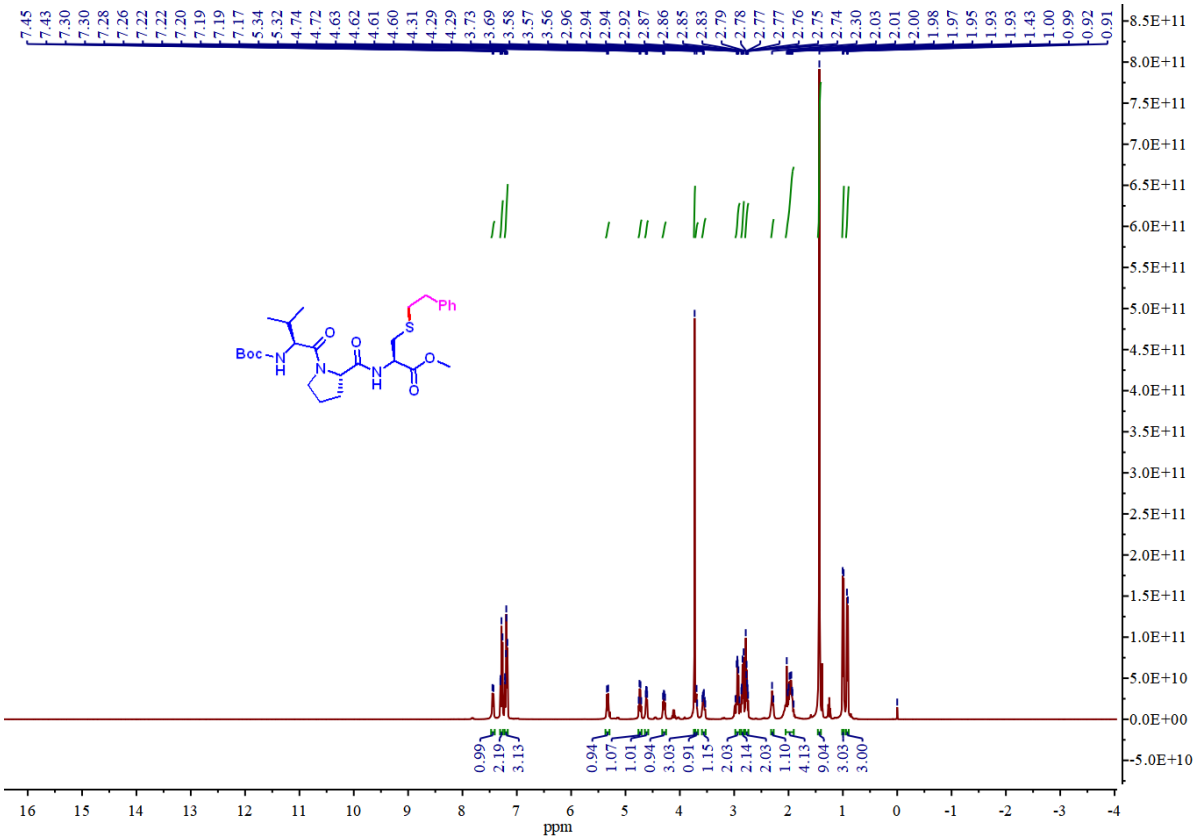
^{13}C NMR Spectrum of Compound **4d** (100 MHz, $CDCl_3$)



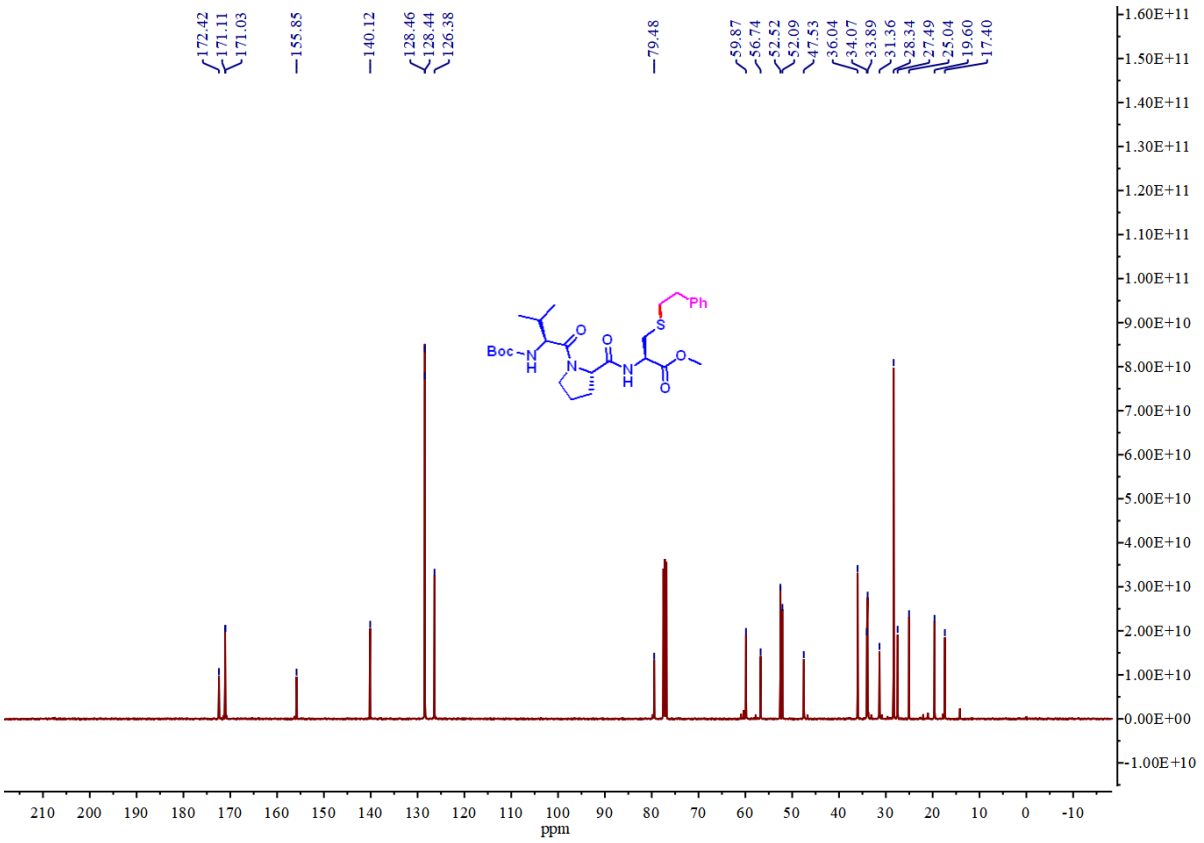
^{1}H NMR Spectrum of Compound **4e** (400 MHz, $CDCl_3$)



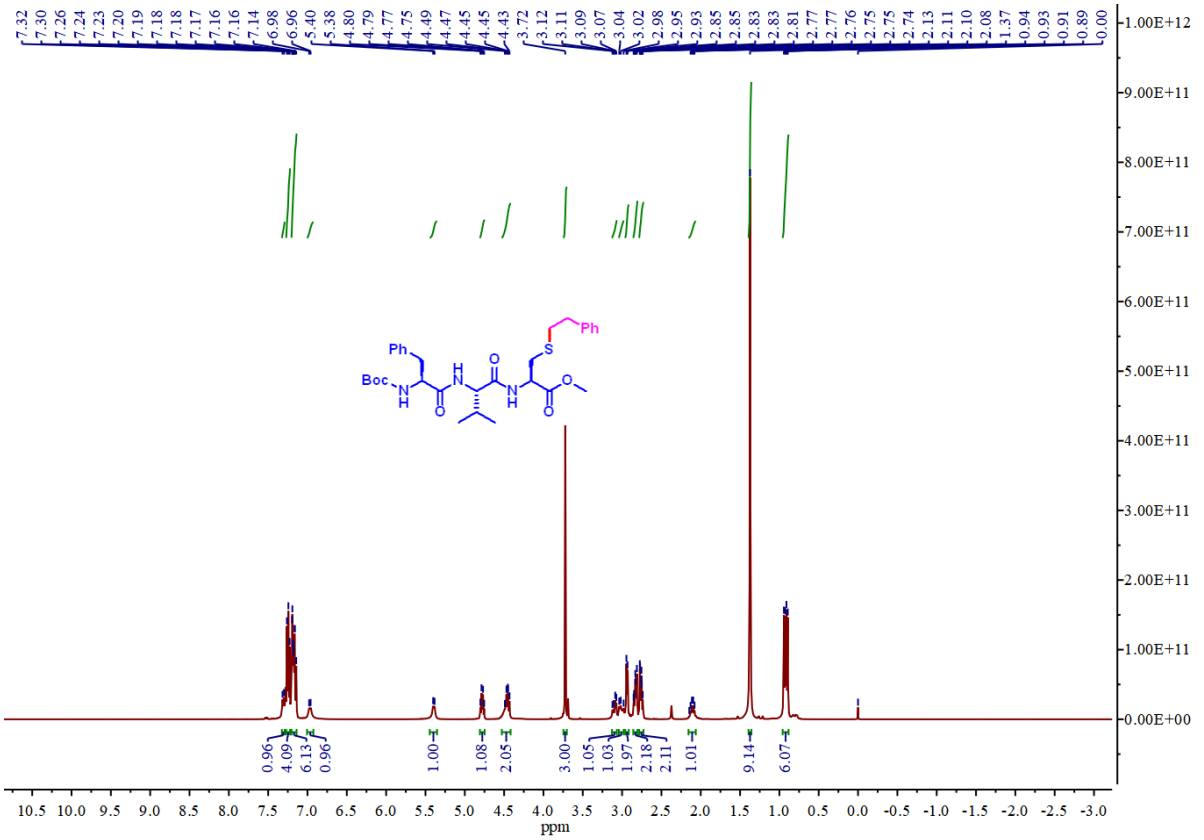
^{13}C NMR Spectrum of Compound **4e** (100 MHz, $CDCl_3$)



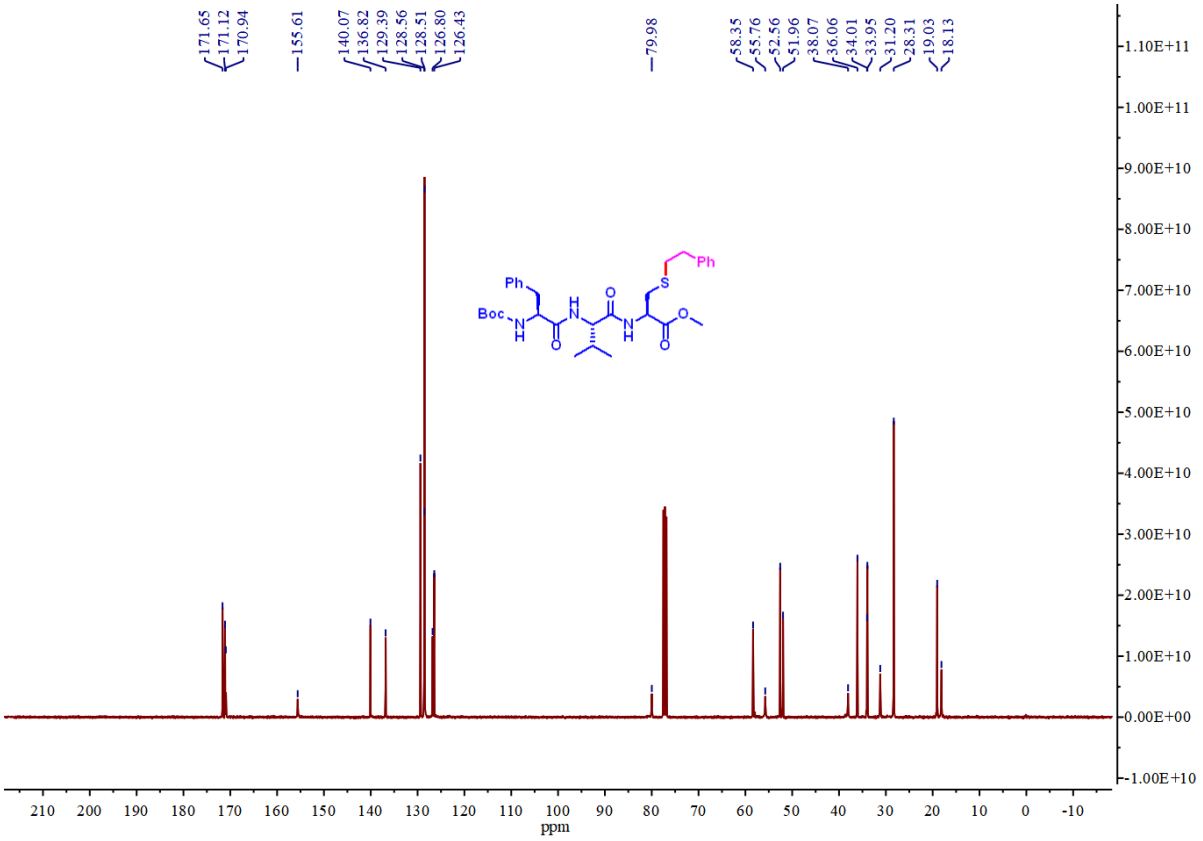
^{1}H NMR Spectrum of Compound **4f** (400 MHz, $CDCl_3$)



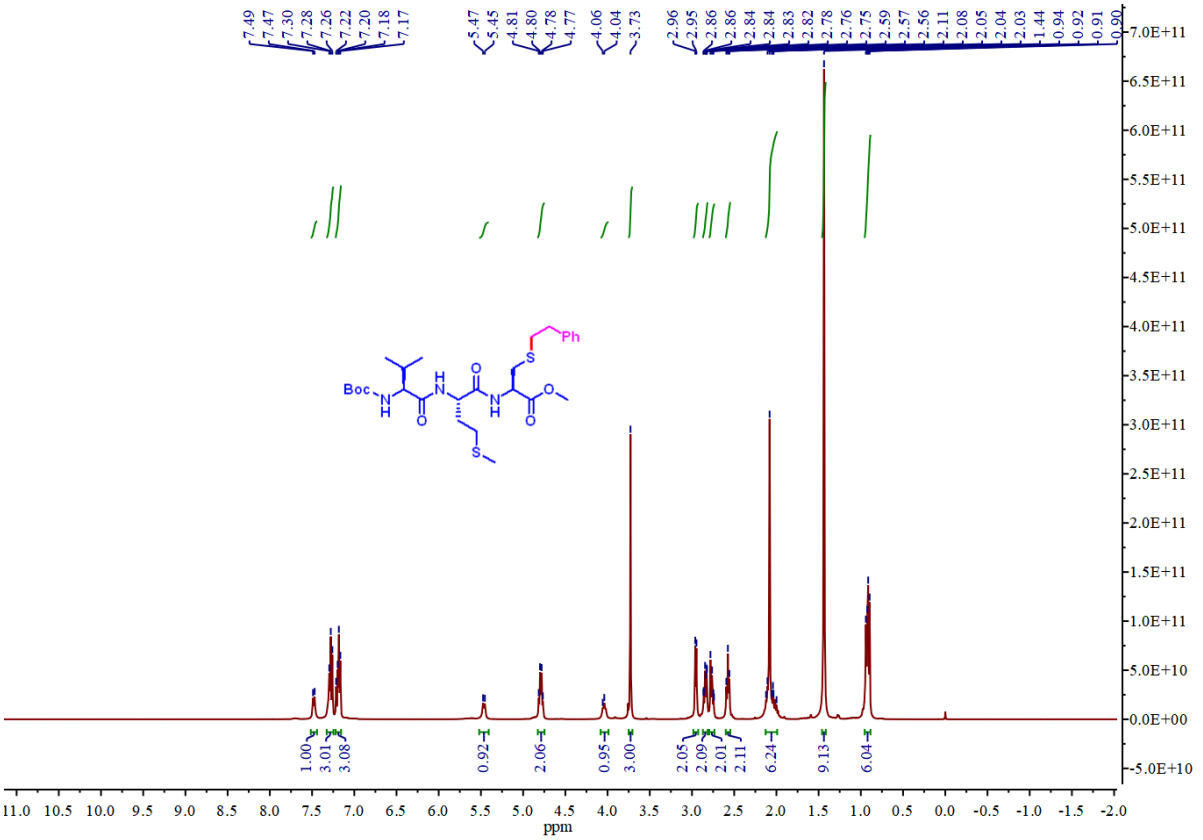
^{13}C NMR Spectrum of Compound **4f** (100 MHz, $CDCl_3$)



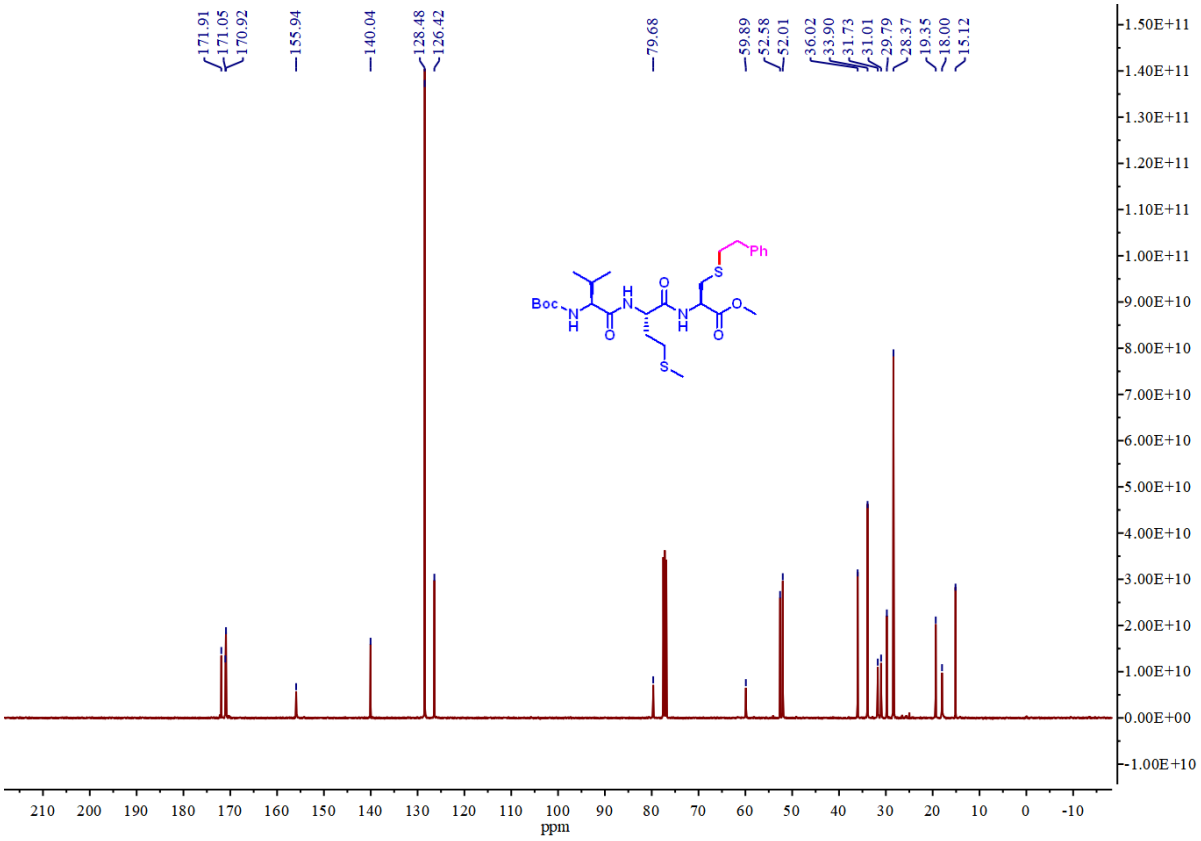
^{1}H NMR Spectrum of Compound **4g** (400 MHz, $CDCl_3$)



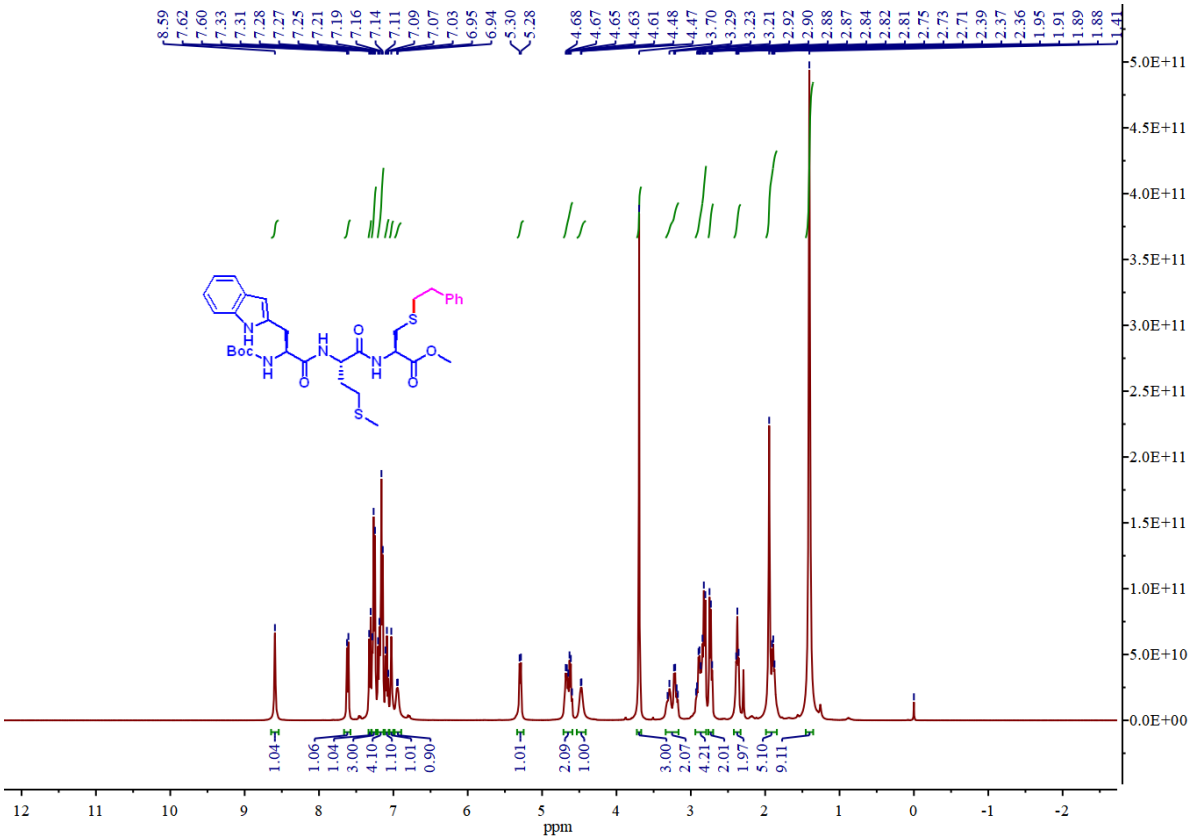
^{13}C NMR Spectrum of Compound **4g** (100 MHz, $CDCl_3$)



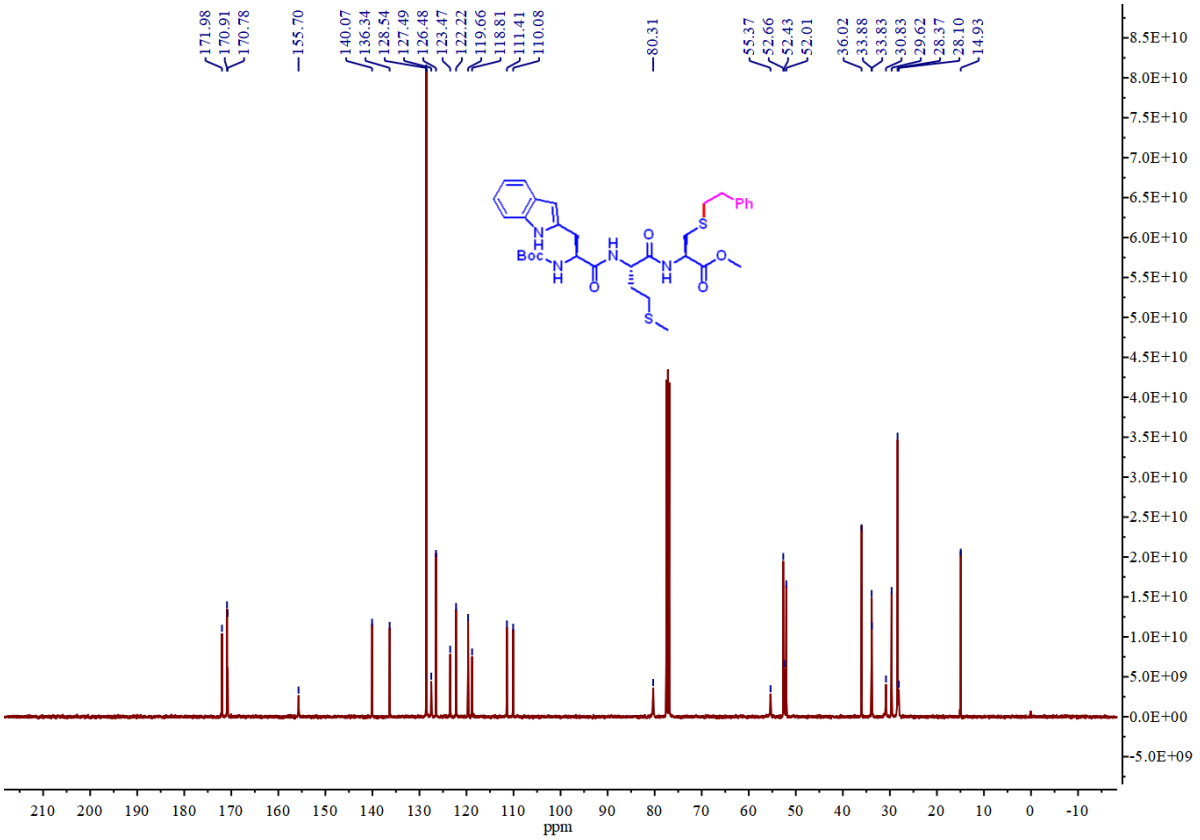
^{1}H NMR Spectrum of Compound **4h** (400 MHz, $CDCl_3$)



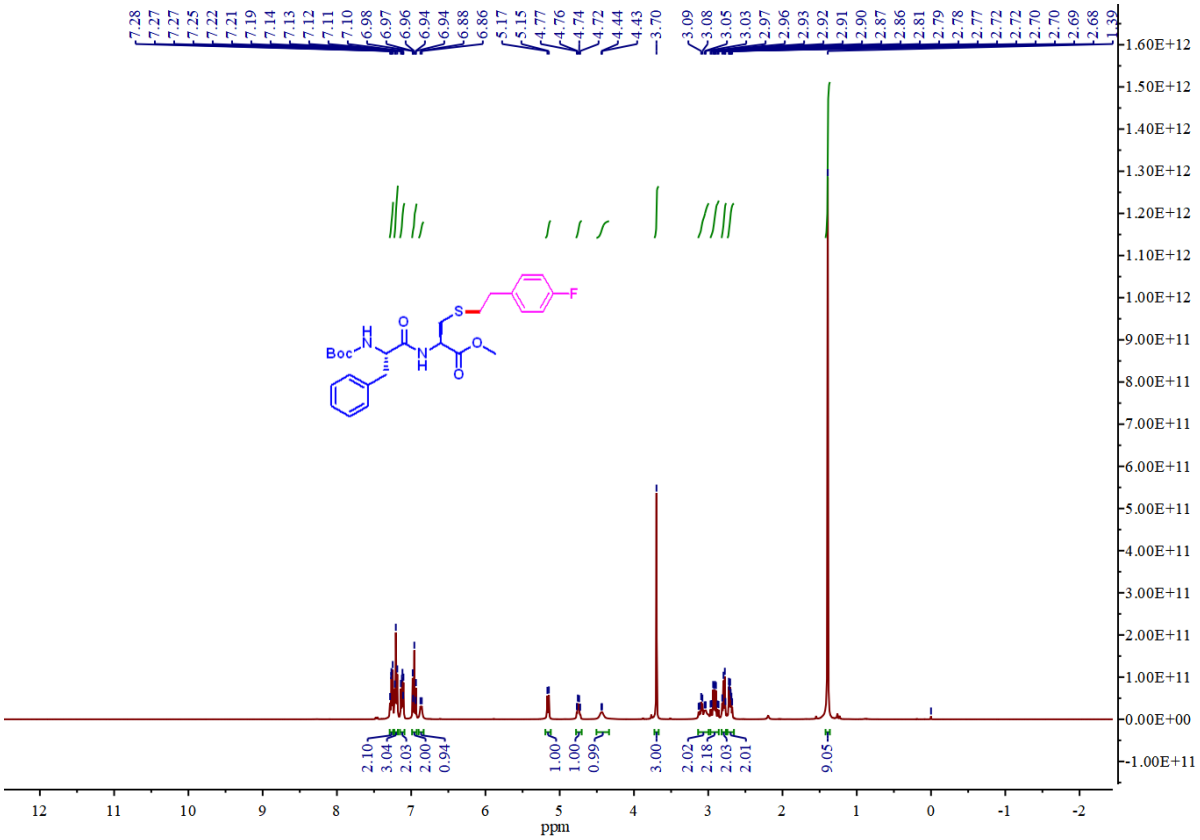
^{13}C NMR Spectrum of Compound **4h** (100 MHz, $CDCl_3$)



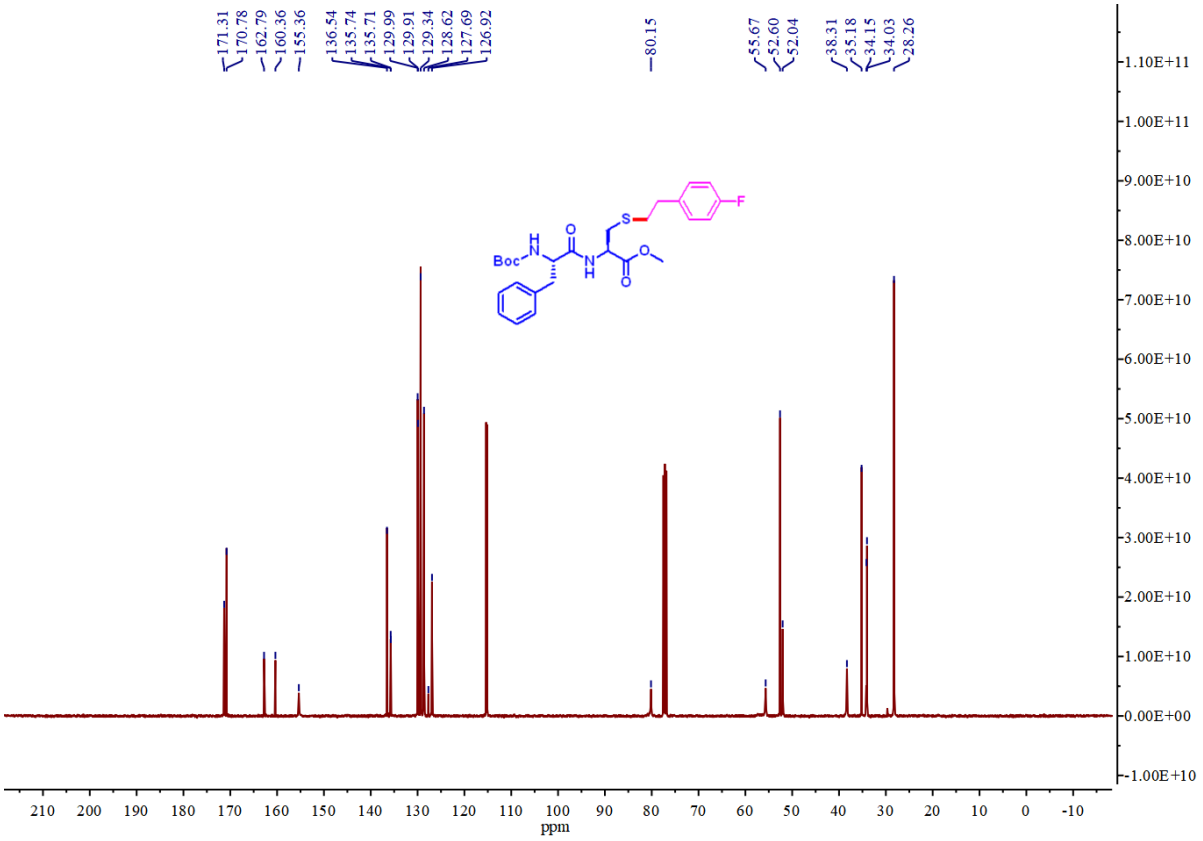
^{1}H NMR Spectrum of Compound **4i** (400 MHz, $CDCl_3$)



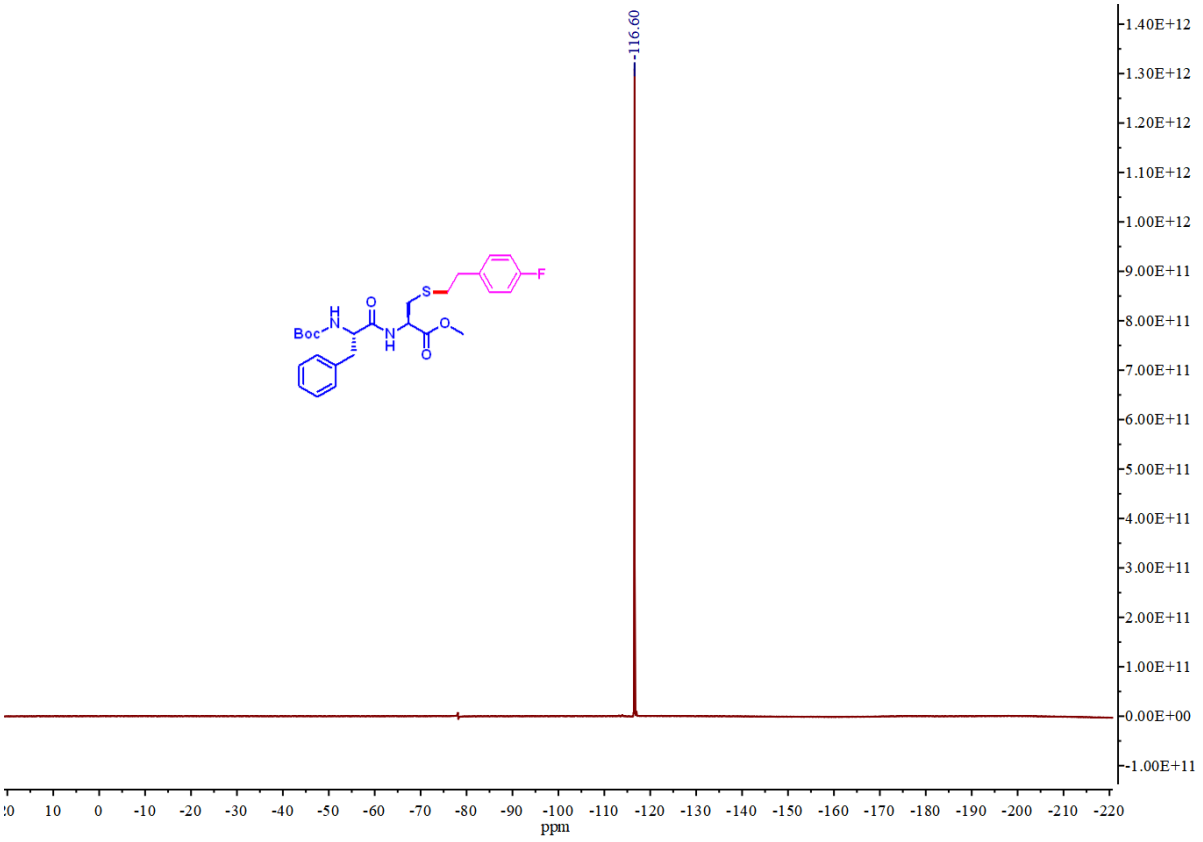
^{13}C NMR Spectrum of Compound **4i** (100 MHz, $CDCl_3$)



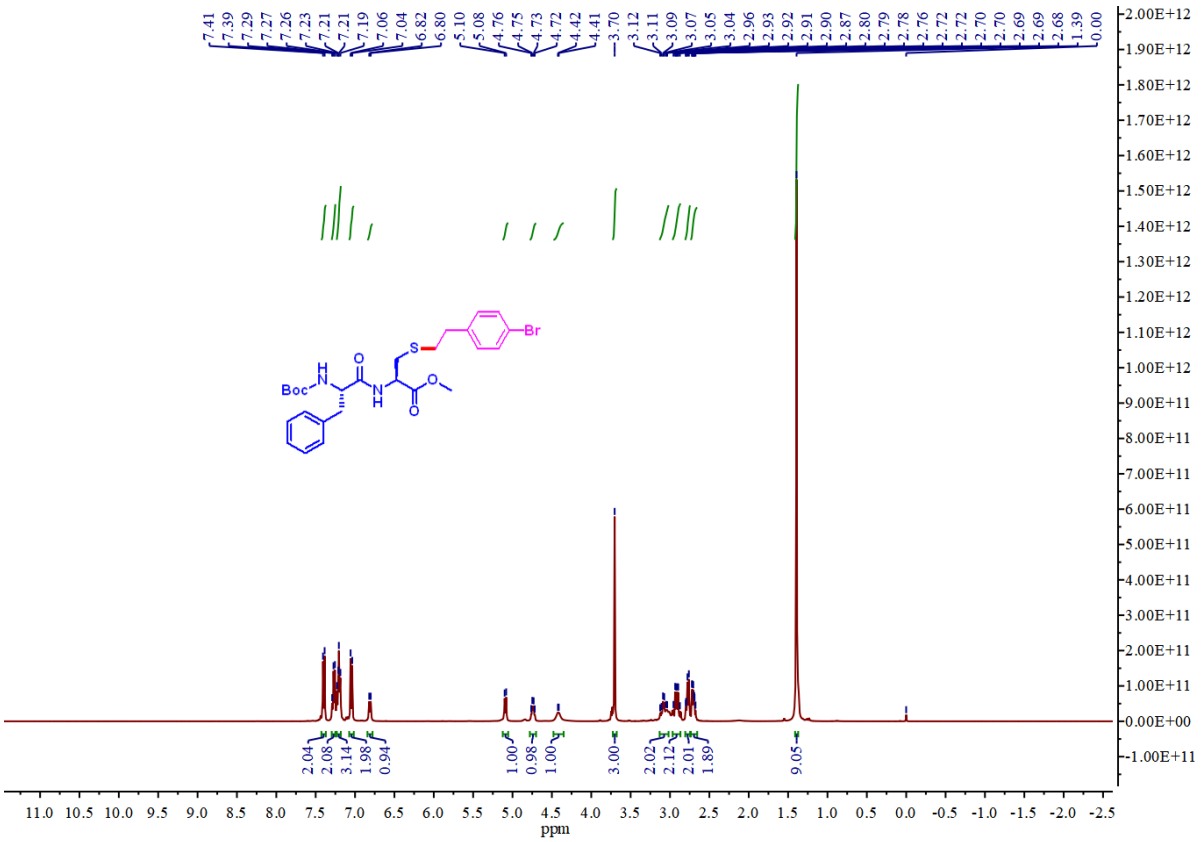
^{1}H NMR Spectrum of Compound **5a** (400 MHz, $CDCl_3$)



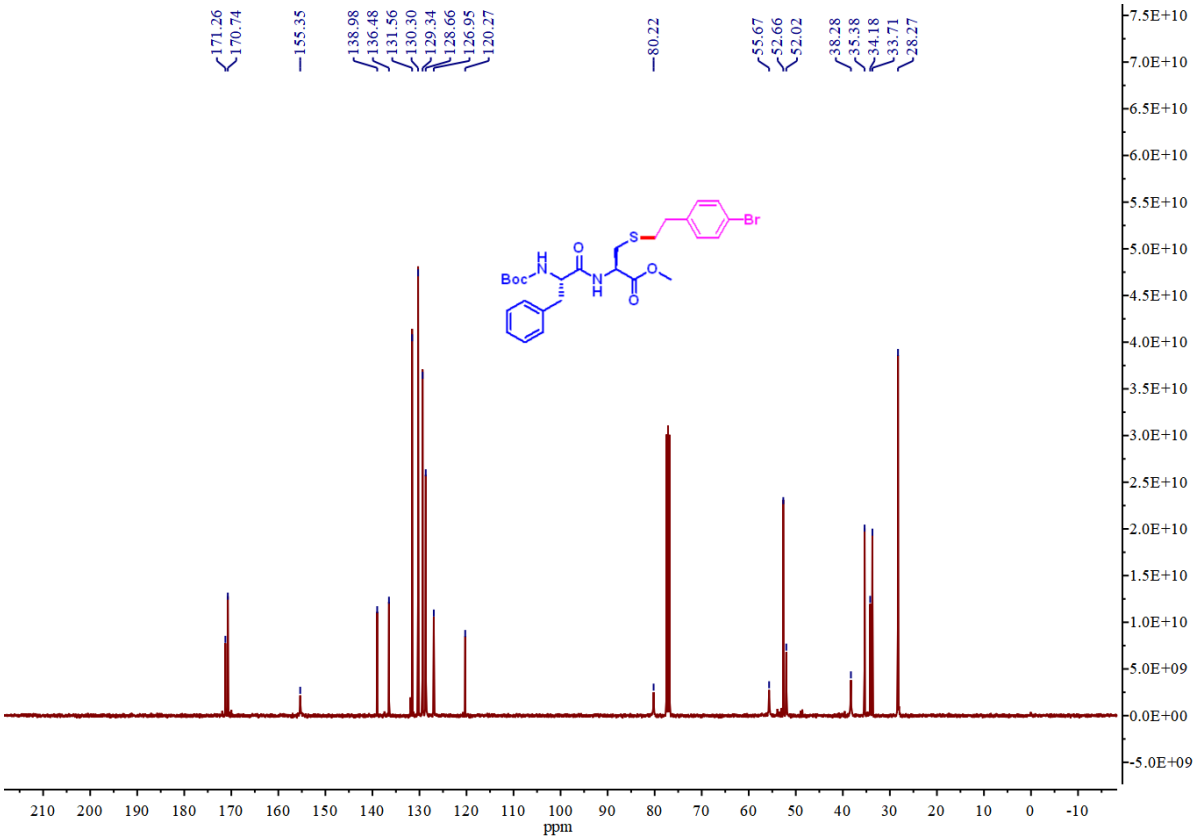
^{13}C NMR Spectrum of Compound **5a** (100 MHz, $CDCl_3$)



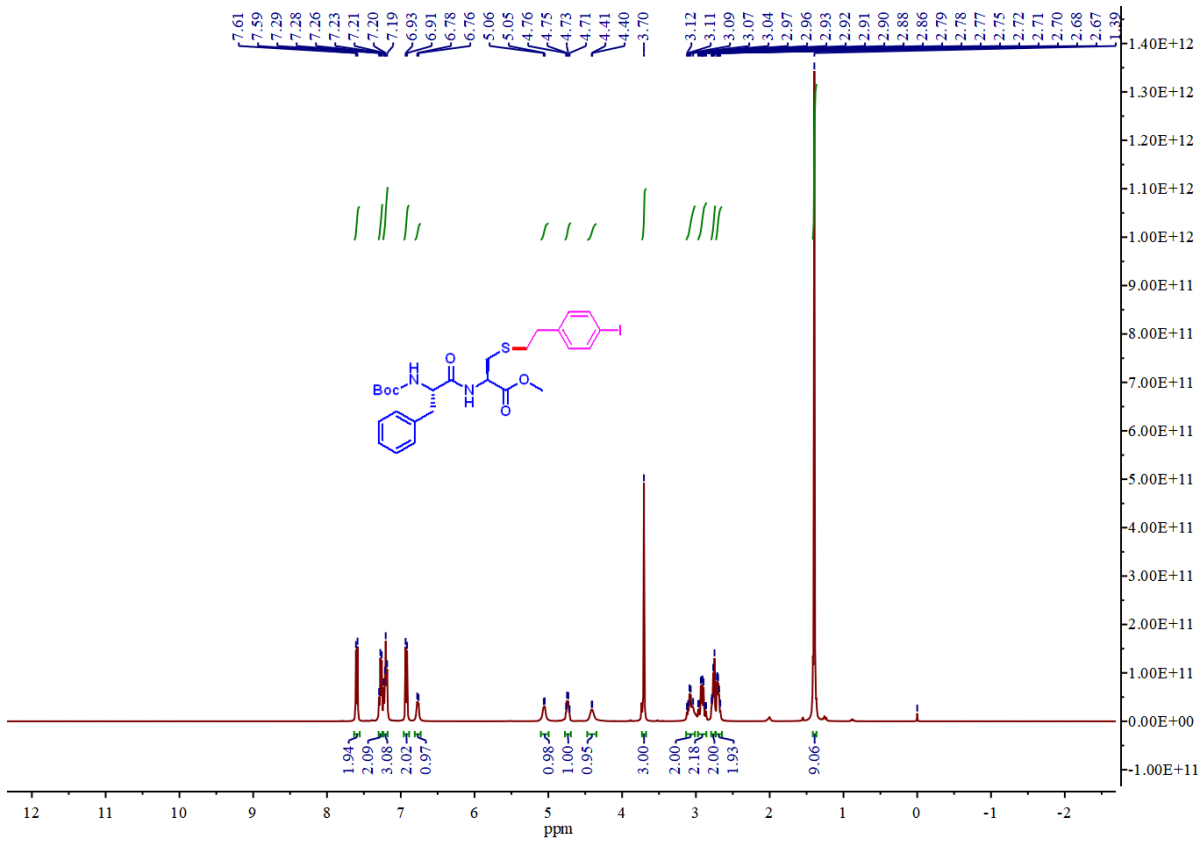
^{19}F NMR Spectrum of Compound **5a** (376 MHz, $CDCl_3$)



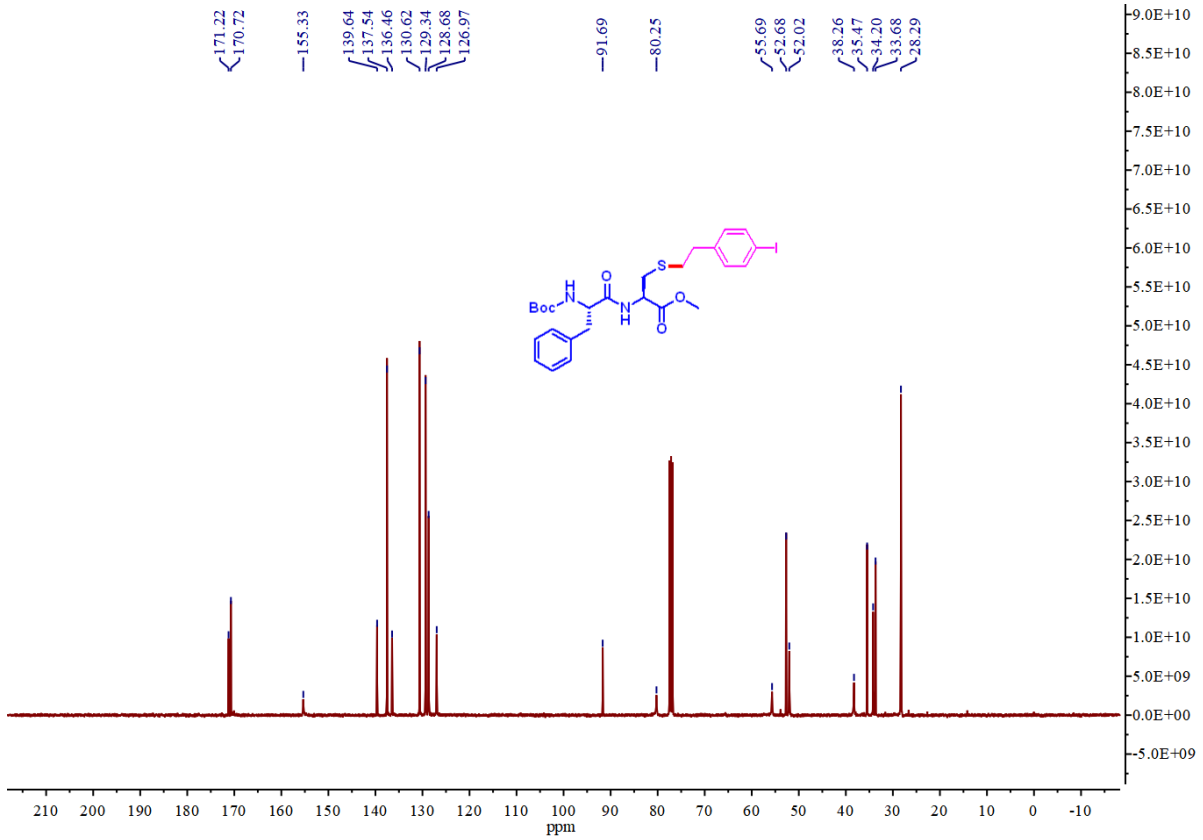
^{1}H NMR Spectrum of Compound **5b** (400 MHz, $CDCl_3$)



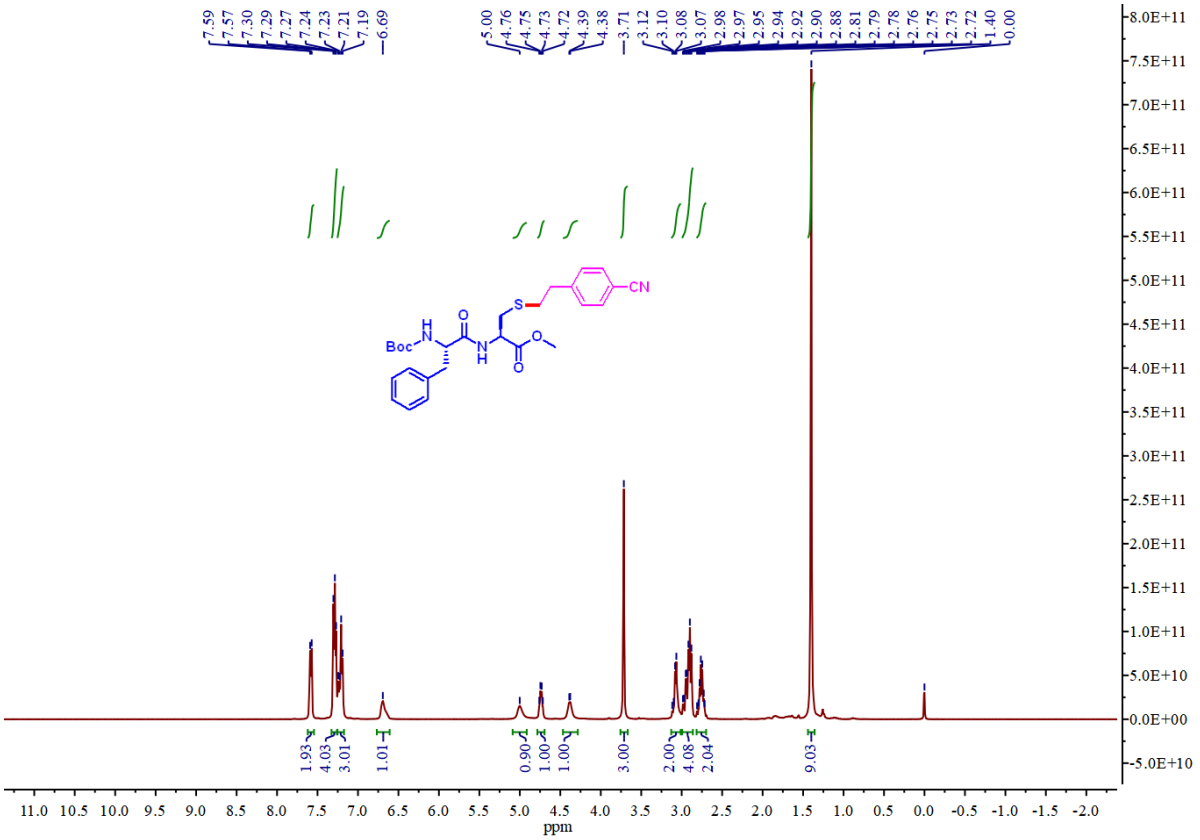
^{13}C NMR Spectrum of Compound **5b** (100 MHz, $CDCl_3$)



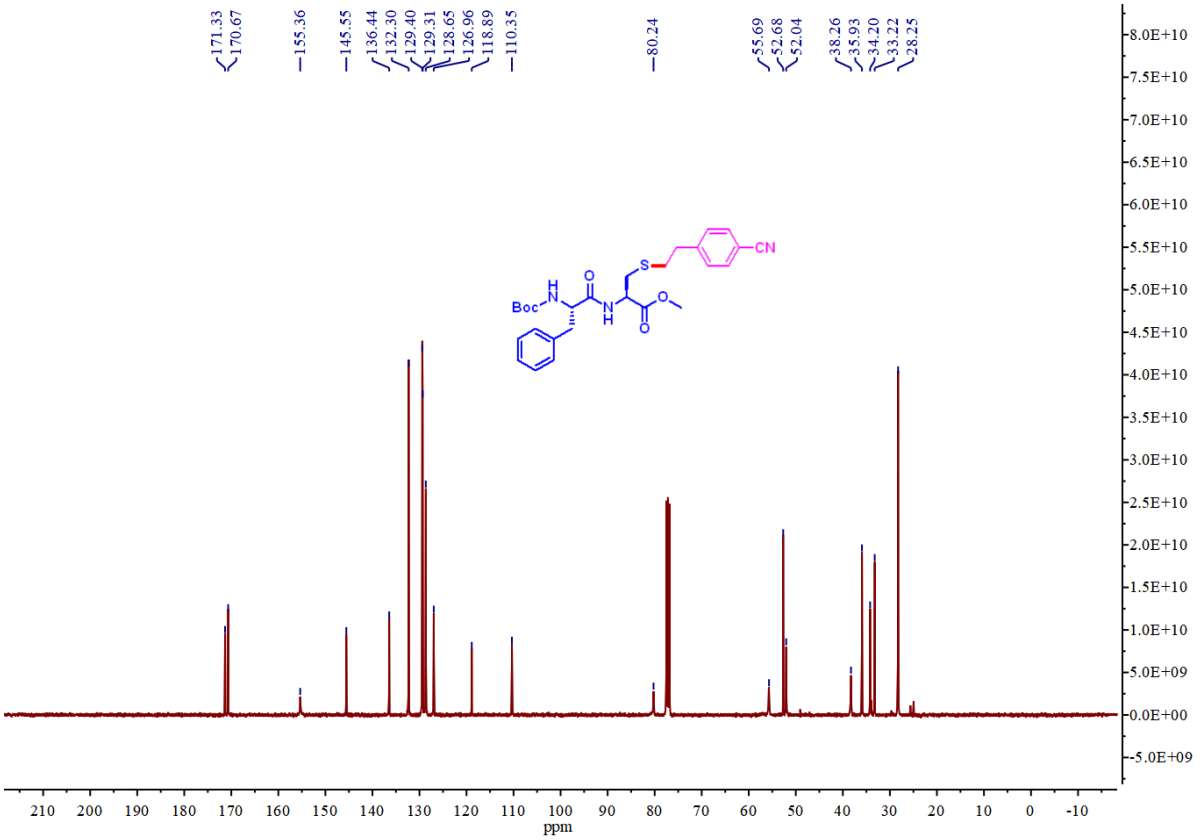
^{1}H NMR Spectrum of Compound **5c** (400 MHz, $CDCl_3$)



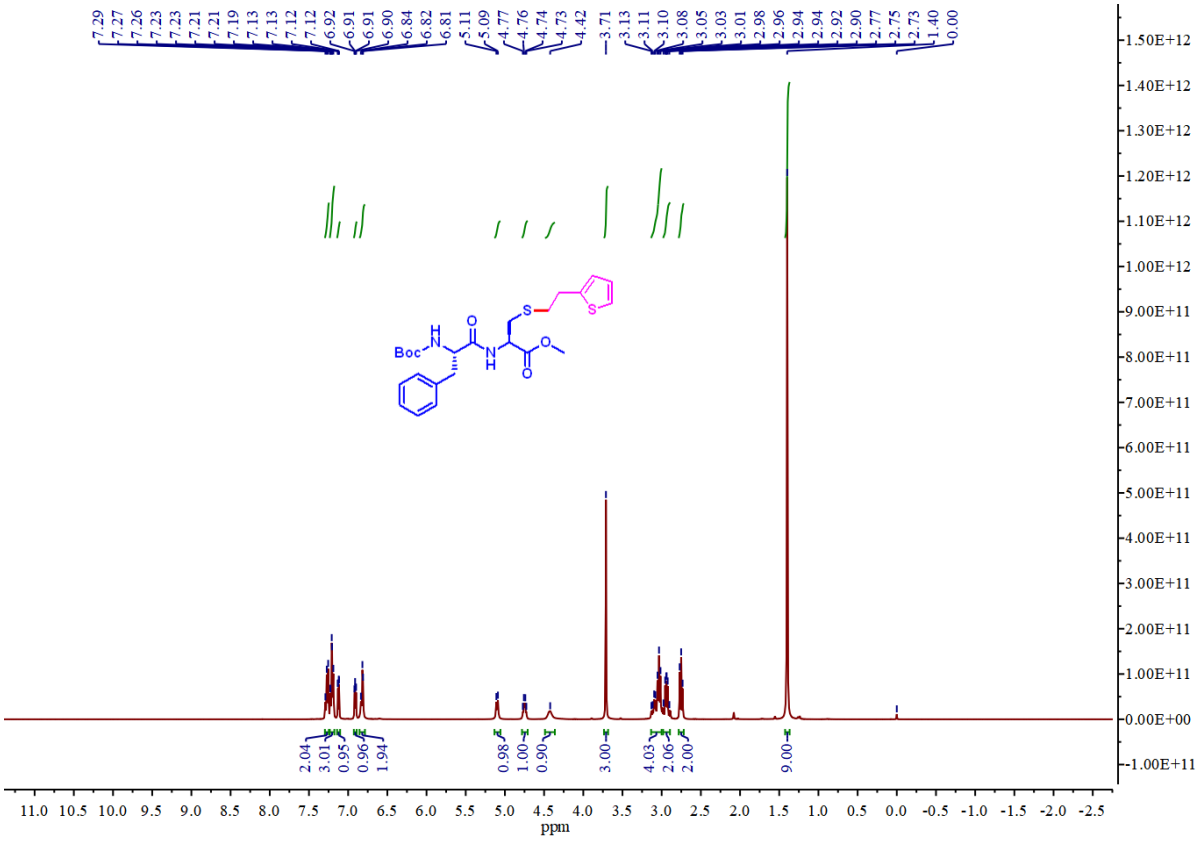
^{13}C NMR Spectrum of Compound **5c** (100 MHz, $CDCl_3$)



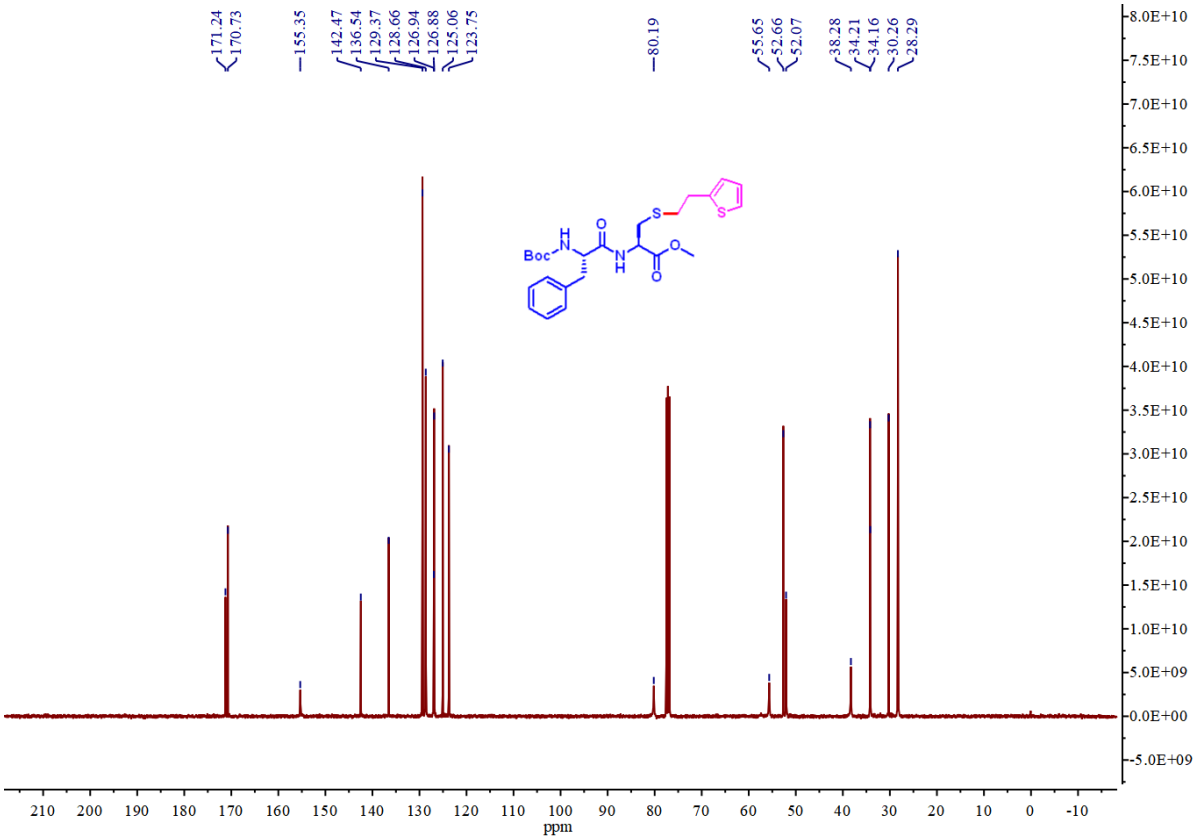
^{1}H NMR Spectrum of Compound **5d** (400 MHz, $CDCl_3$)



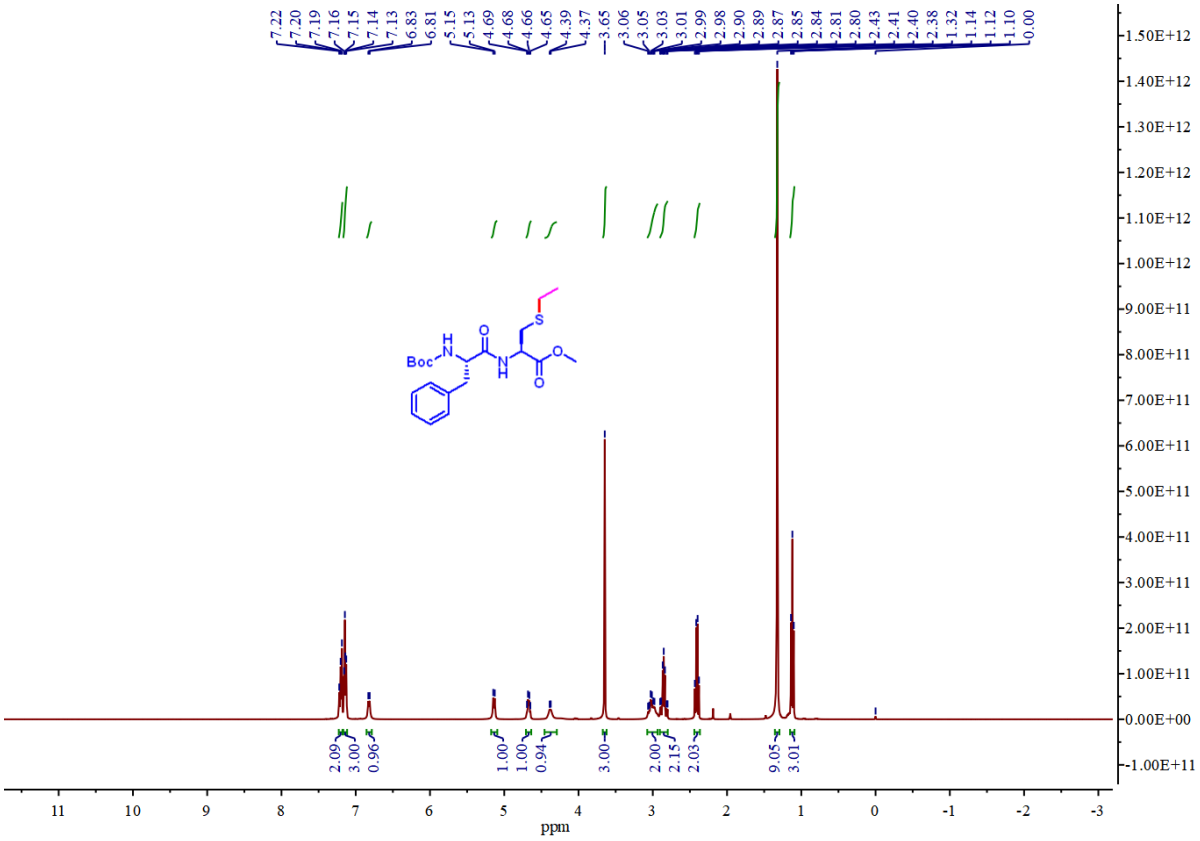
^{13}C NMR Spectrum of Compound **5d** (100 MHz, $CDCl_3$)



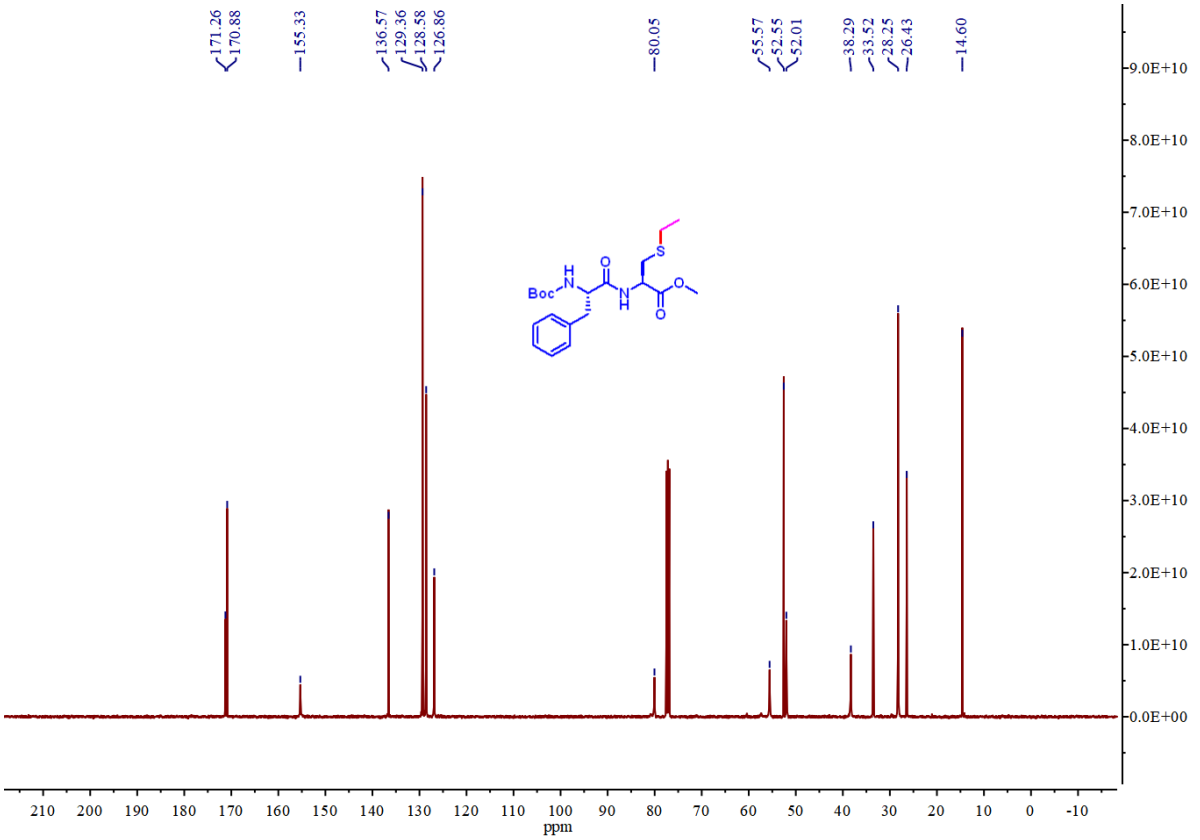
^{1}H NMR Spectrum of Compound **5e** (400 MHz, $CDCl_3$)



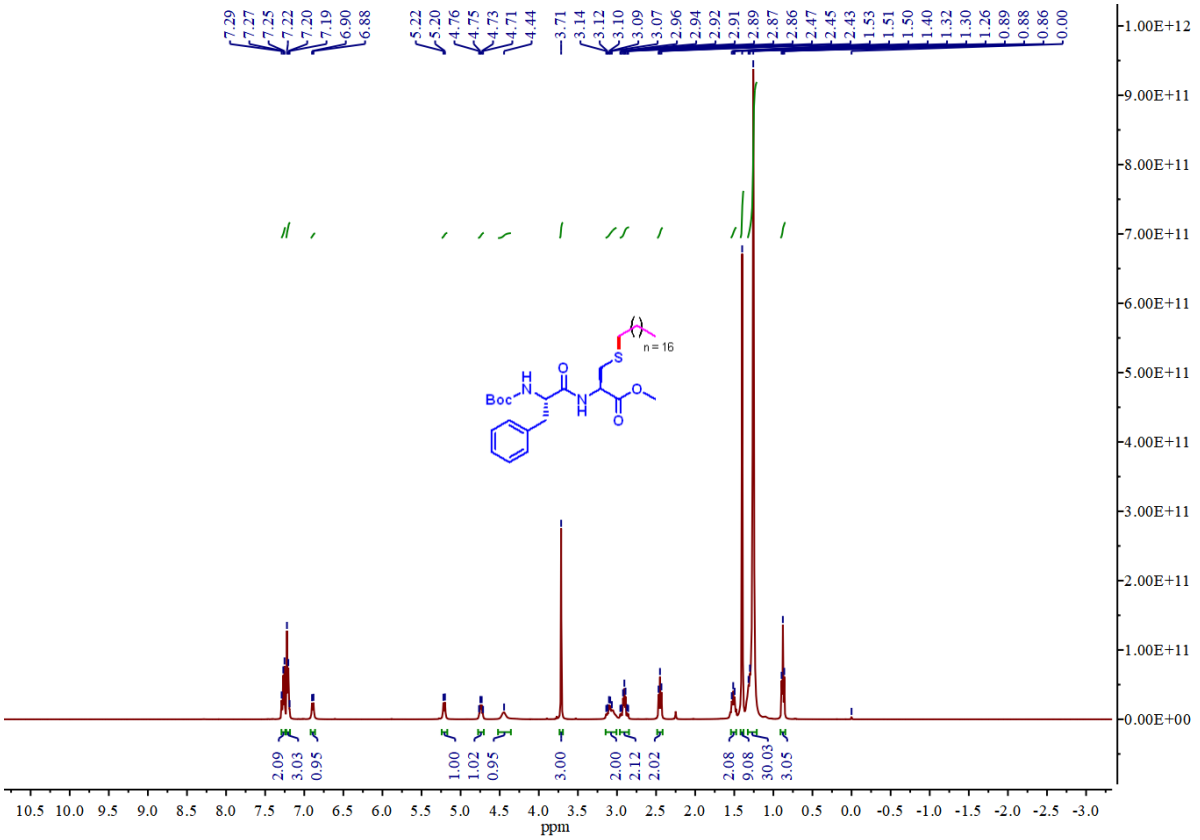
^{13}C NMR Spectrum of Compound **5e** (100 MHz, $CDCl_3$)



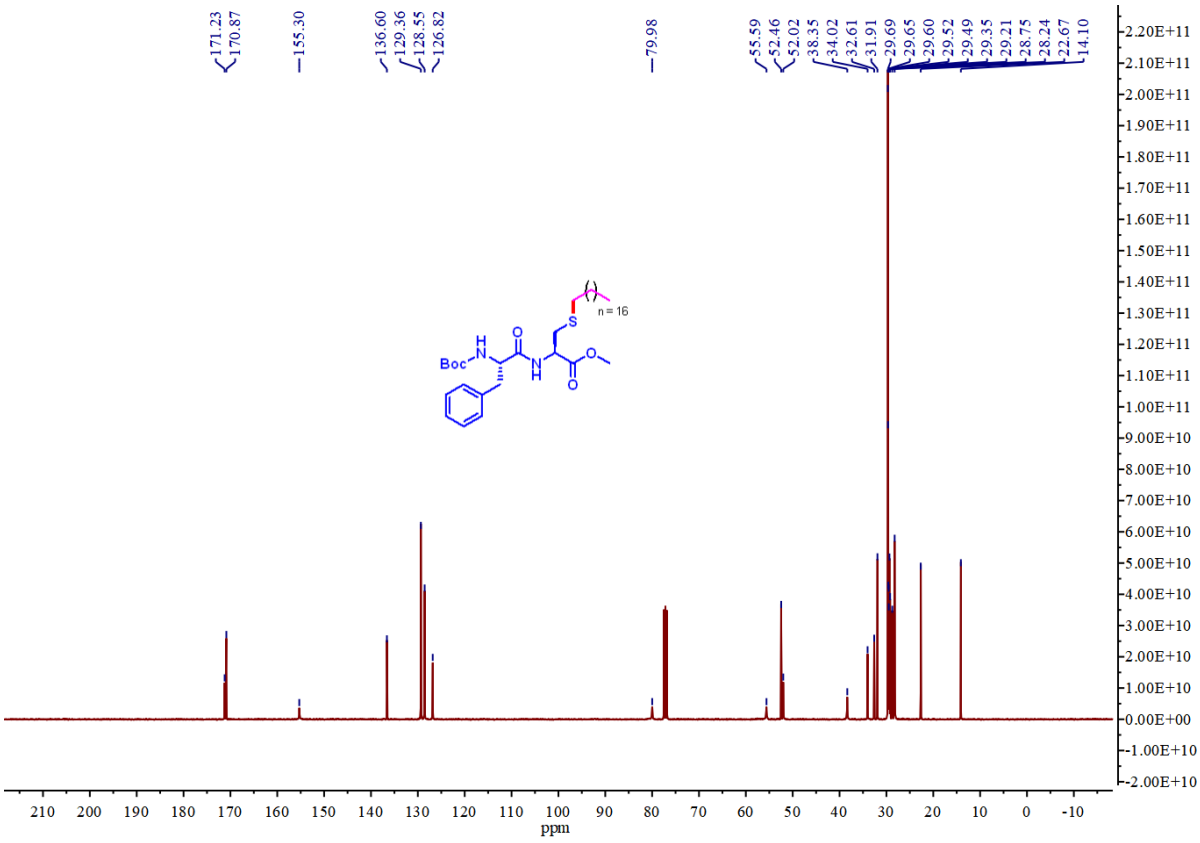
^{1}H NMR Spectrum of Compound **5f** (400 MHz, $CDCl_3$)



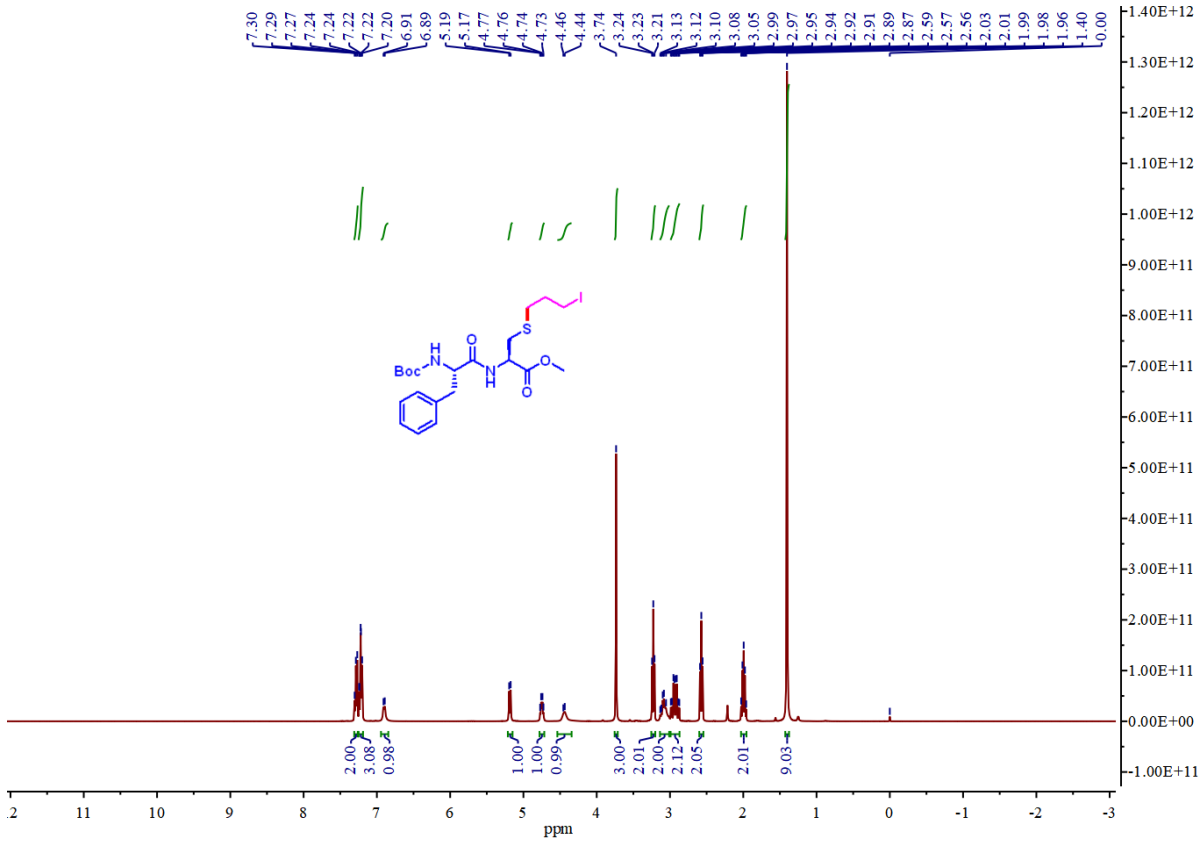
^{13}C NMR Spectrum of Compound **5f** (100 MHz, $CDCl_3$)



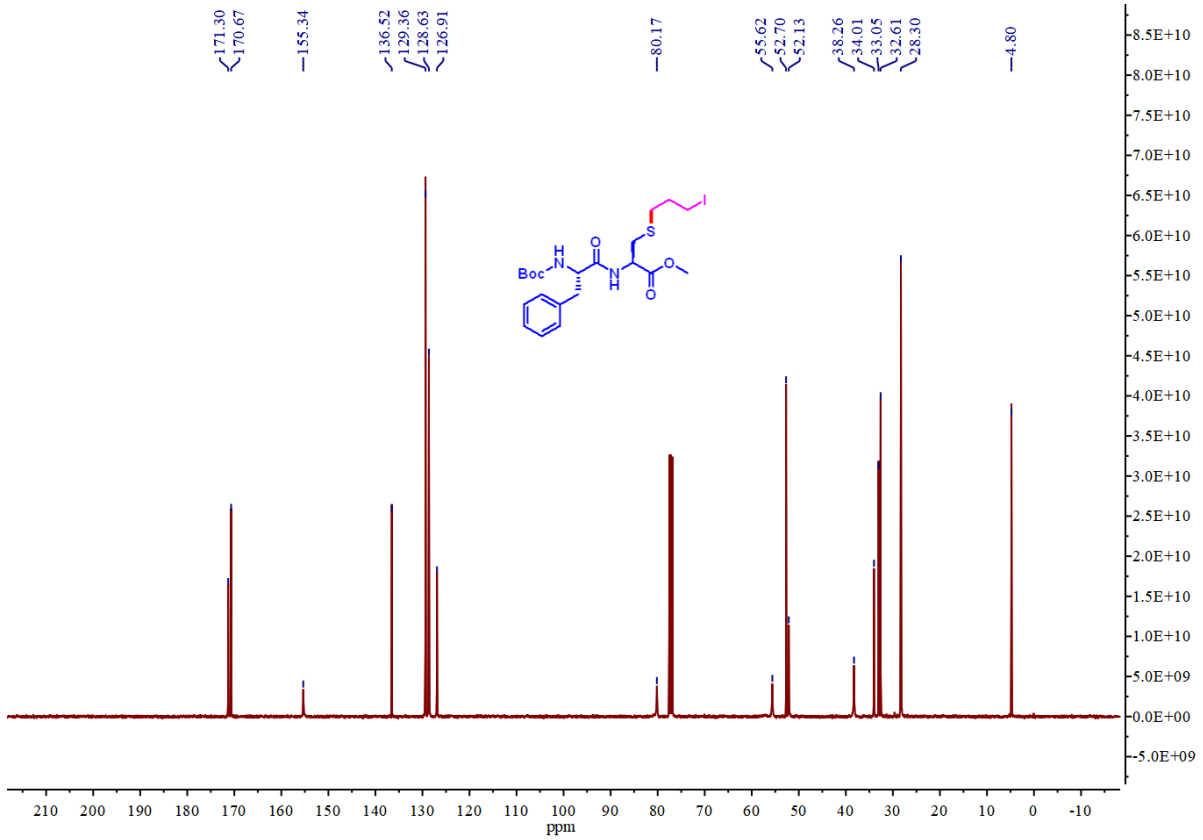
^{1}H NMR Spectrum of Compound **5g** (400 MHz, $CDCl_3$)



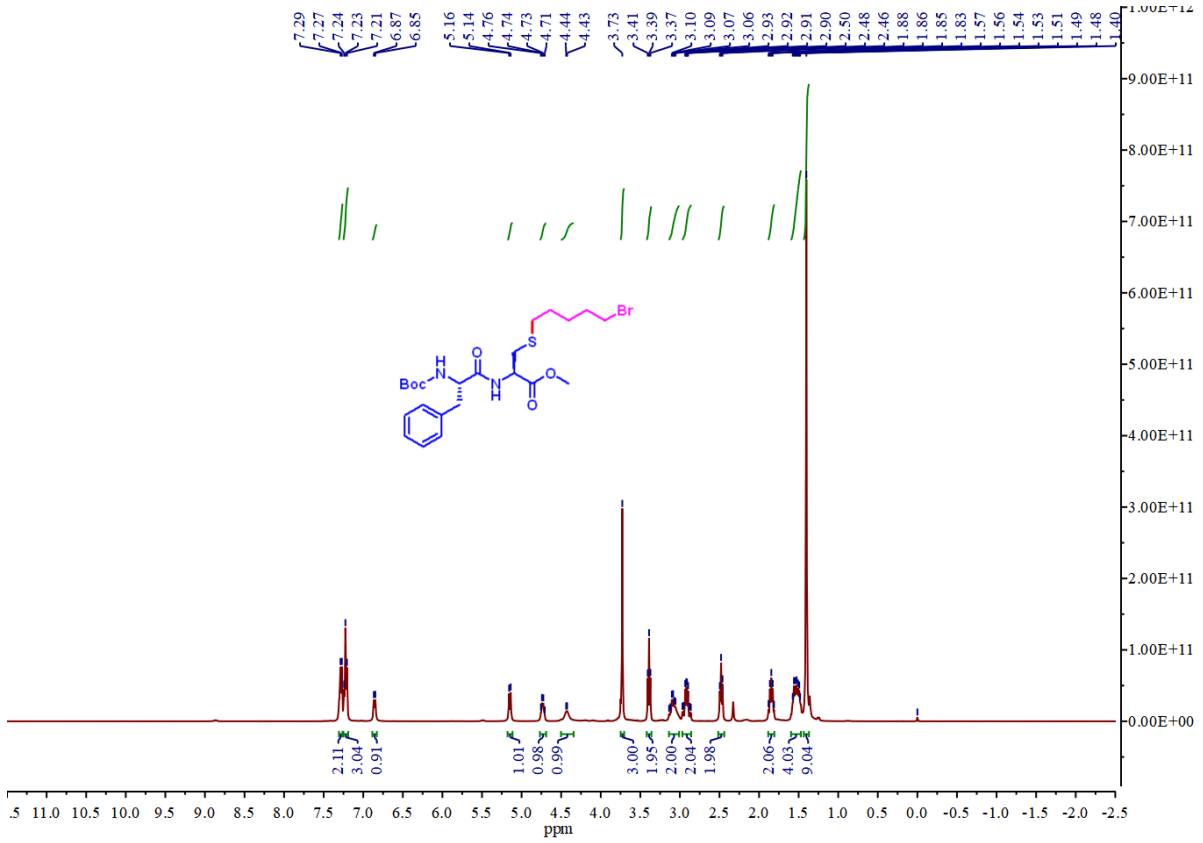
^{13}C NMR Spectrum of Compound **5g** (100 MHz, $CDCl_3$)



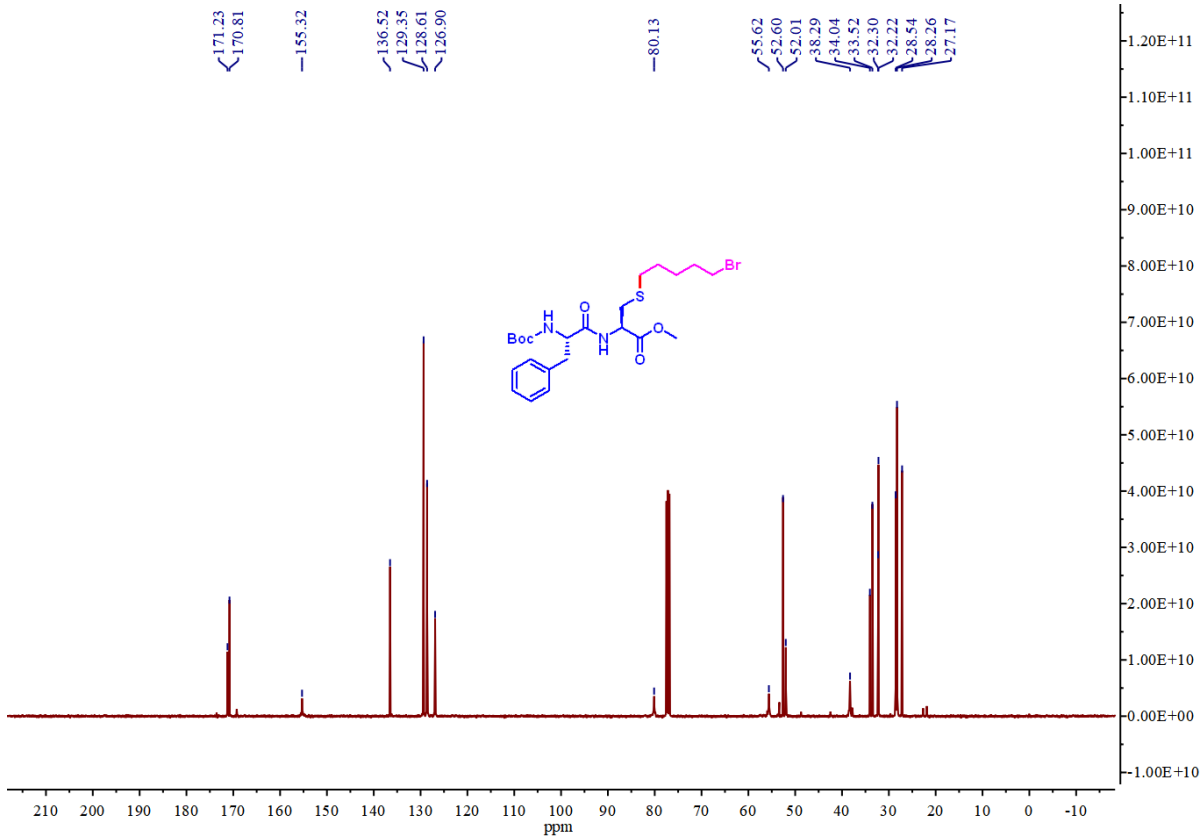
^{1}H NMR Spectrum of Compound **5h** (400 MHz, $CDCl_3$)



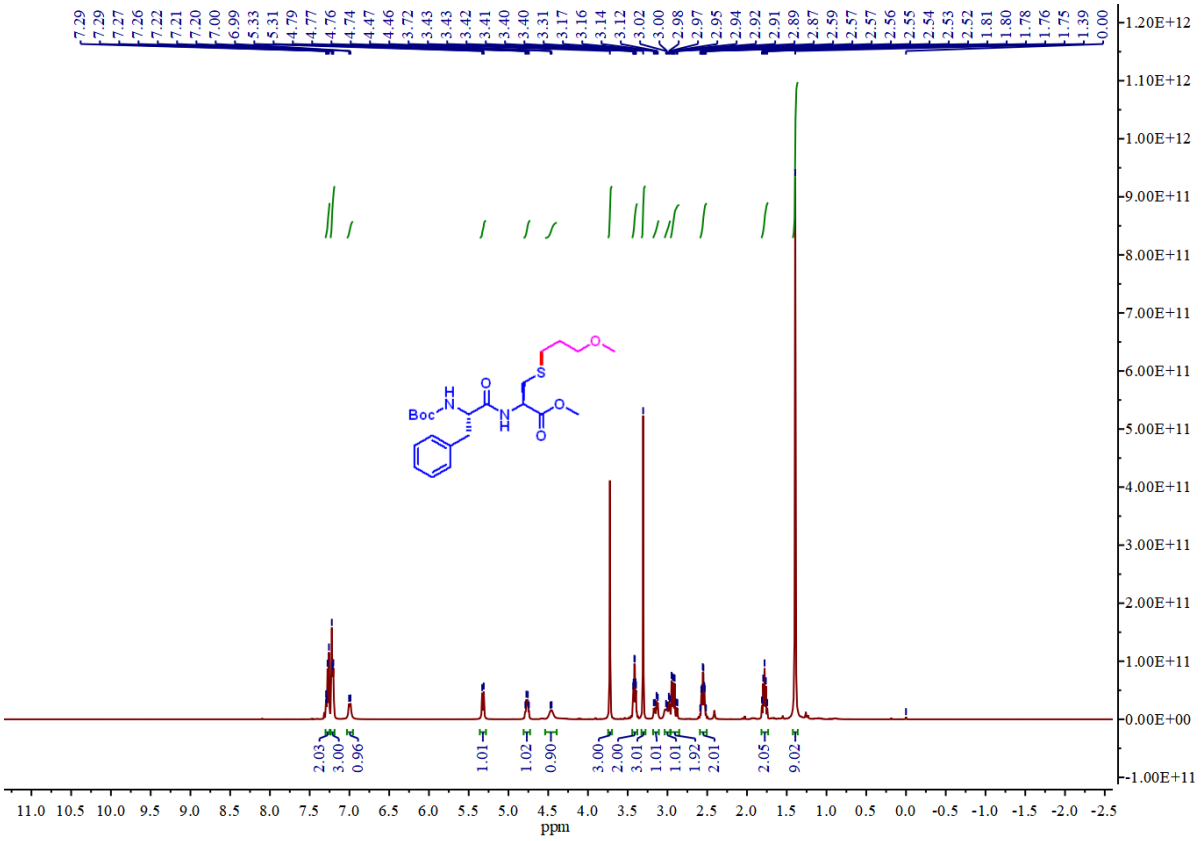
^{13}C NMR Spectrum of Compound **5h** (100 MHz, $CDCl_3$)



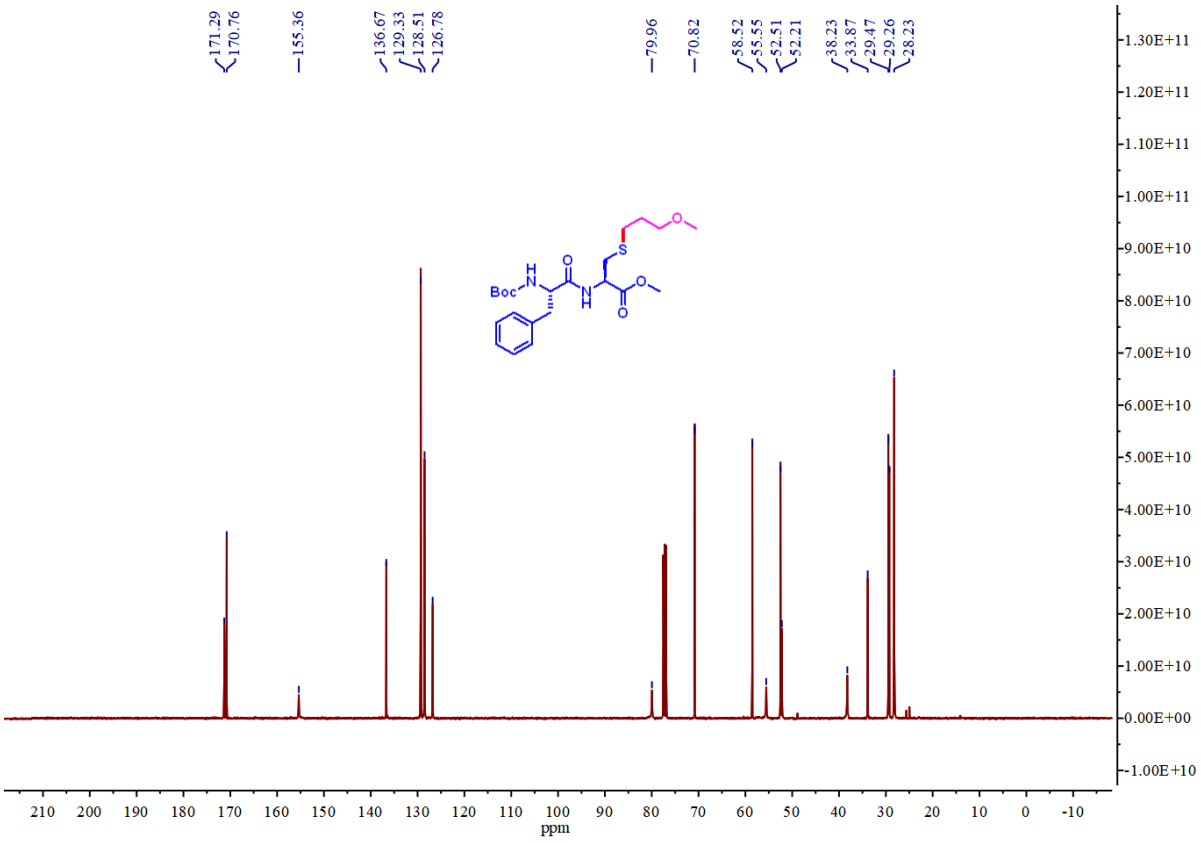
^{1}H NMR Spectrum of Compound **5i** (400 MHz, $CDCl_3$)



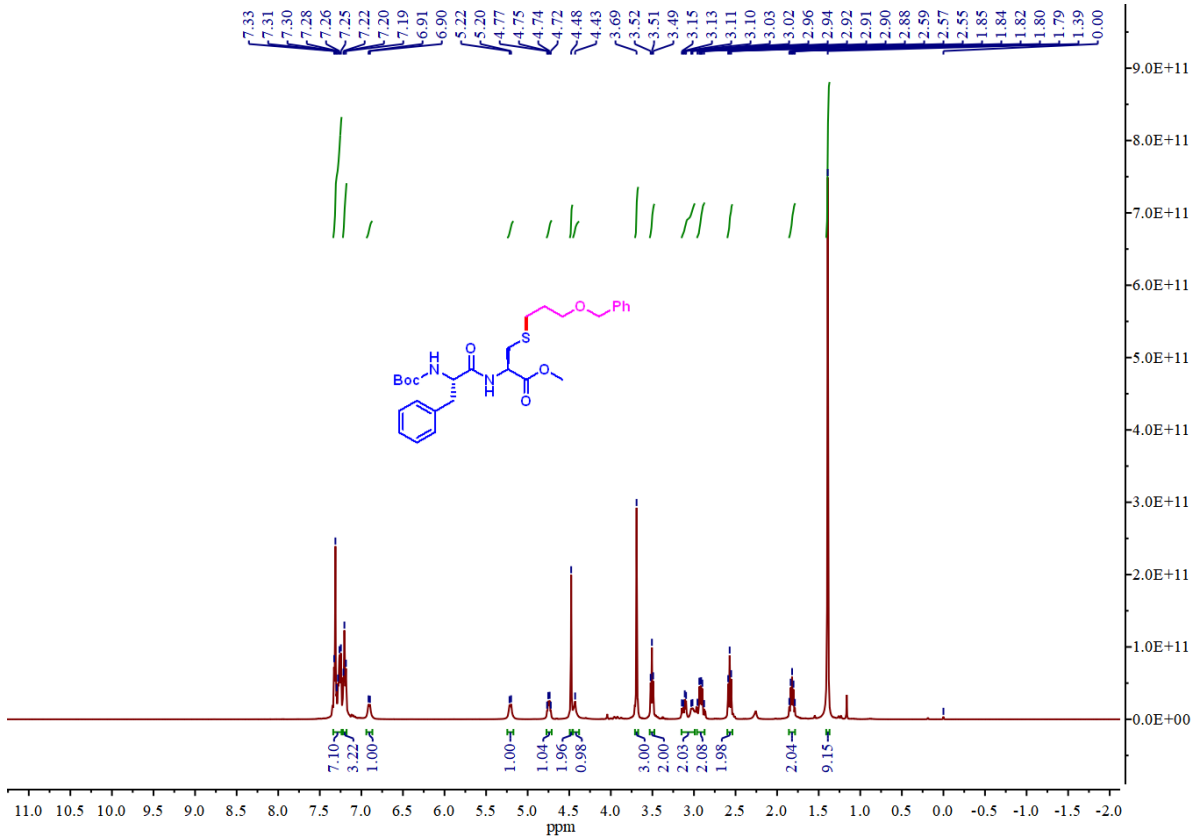
^{13}C NMR Spectrum of Compound **5i** (100 MHz, $CDCl_3$)



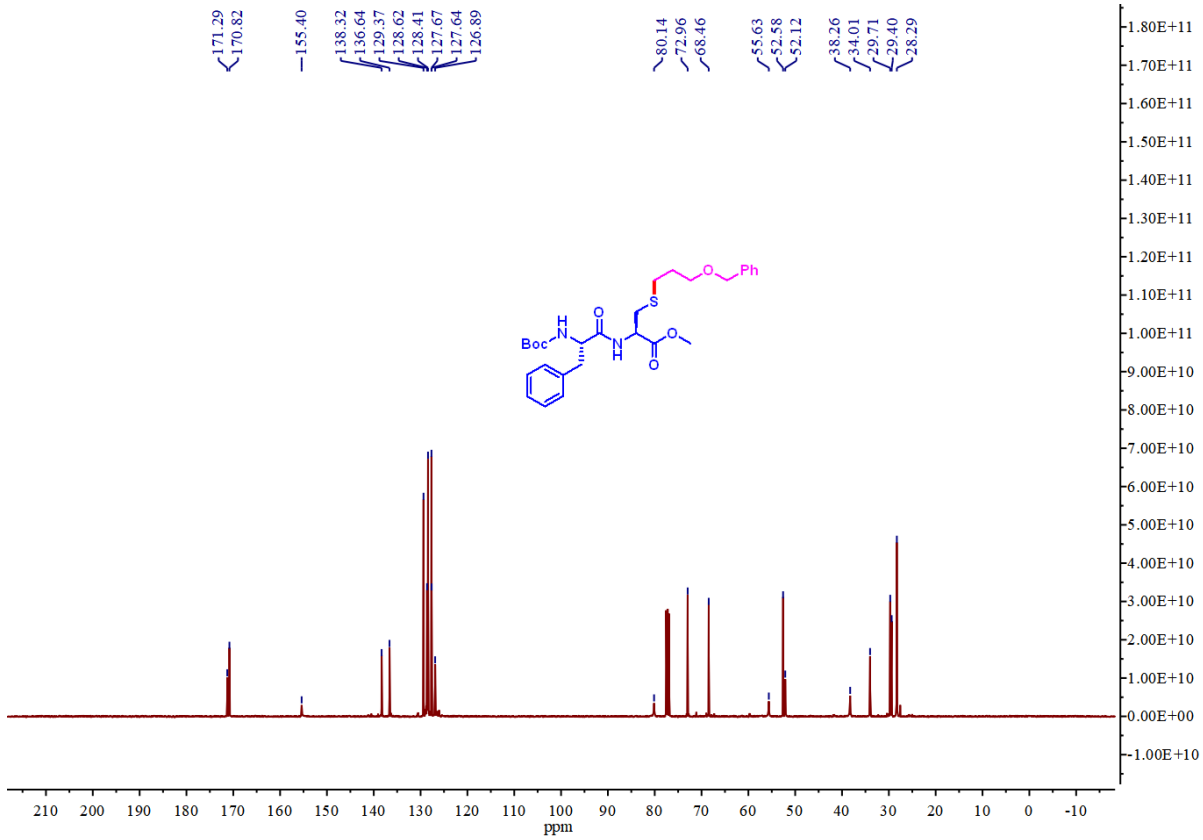
^{1}H NMR Spectrum of Compound **5j** (400 MHz, $CDCl_3$)



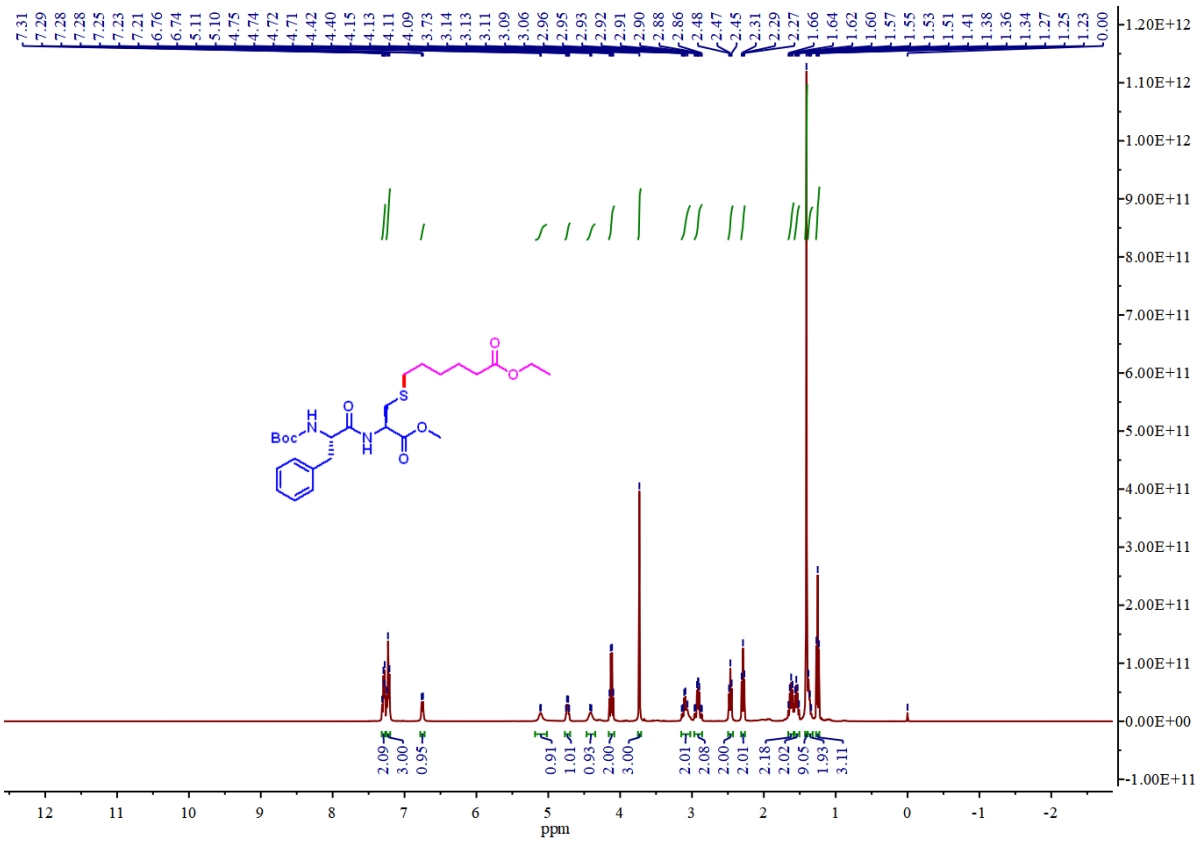
^{13}C NMR Spectrum of Compound **5j** (100 MHz, $CDCl_3$)



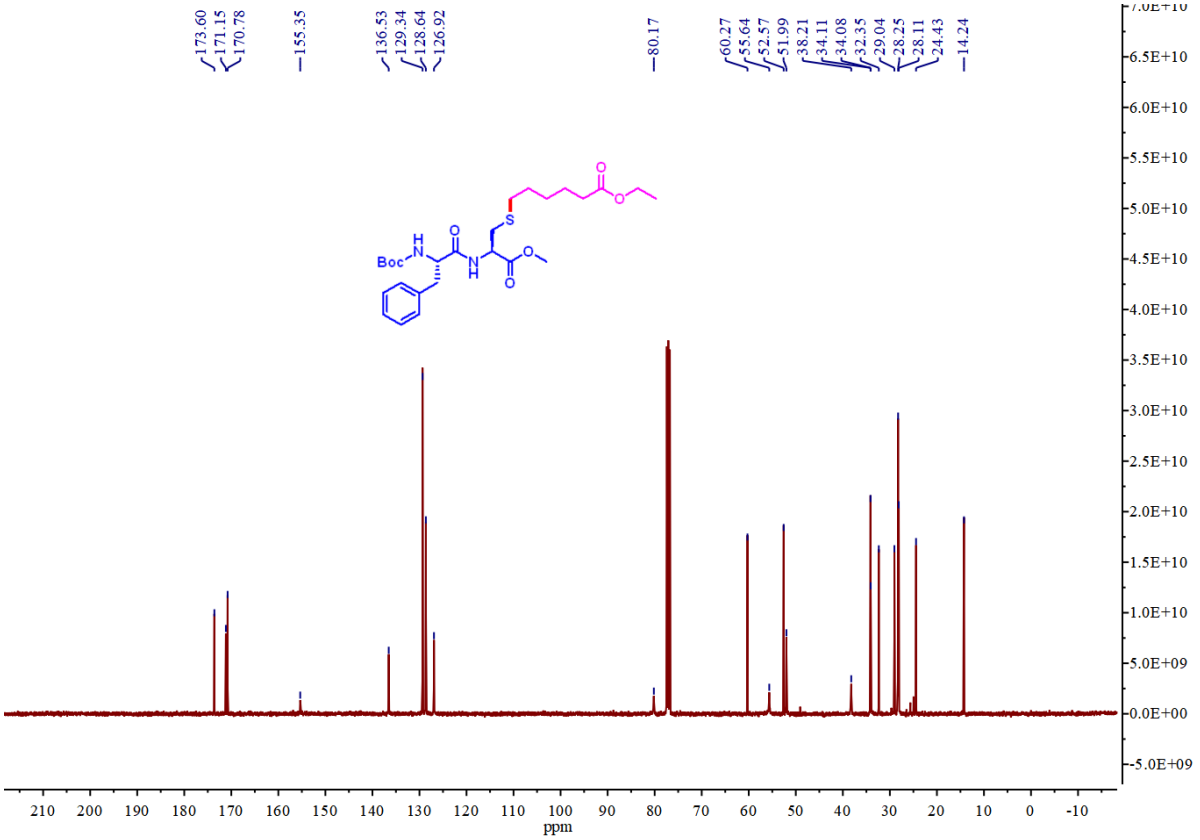
^{1}H NMR Spectrum of Compound **5k** (400 MHz, $CDCl_3$)



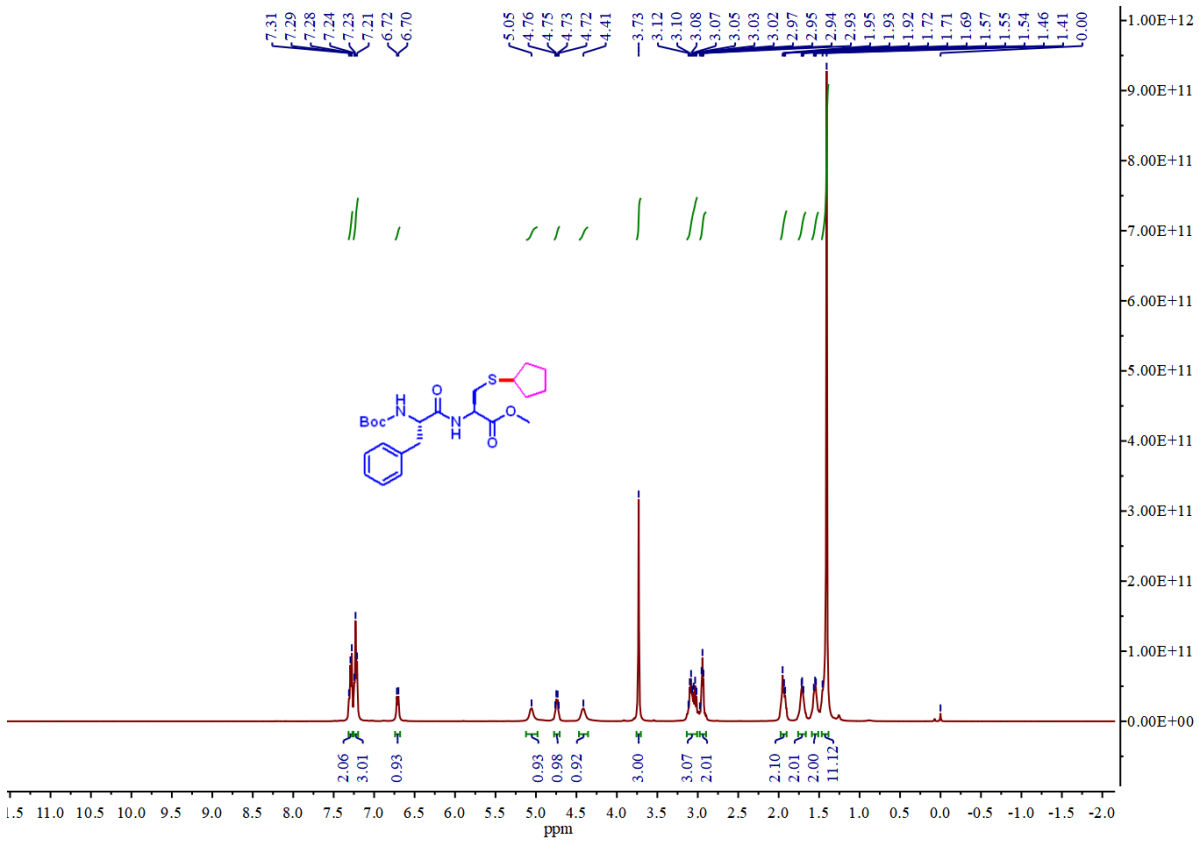
^{13}C NMR Spectrum of Compound **5k** (100 MHz, $CDCl_3$)



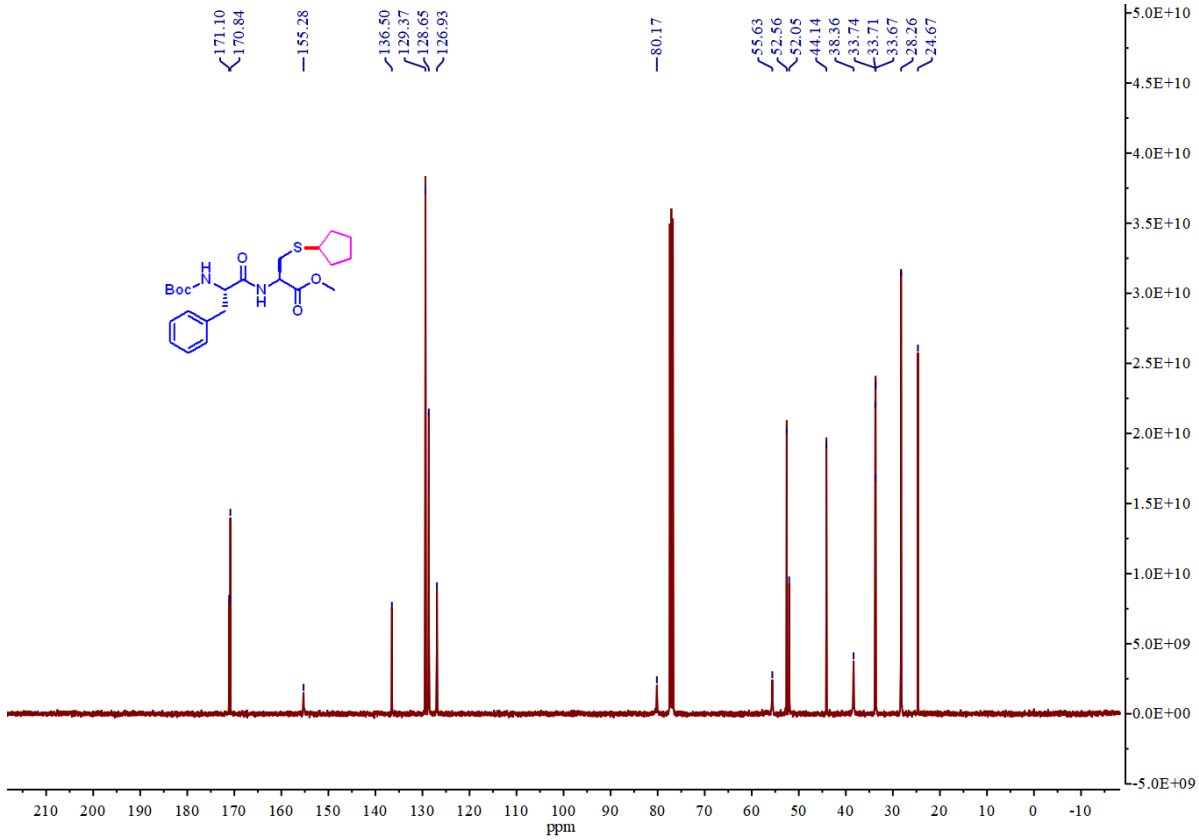
^{1}H NMR Spectrum of Compound **5l** (400 MHz, $CDCl_3$)



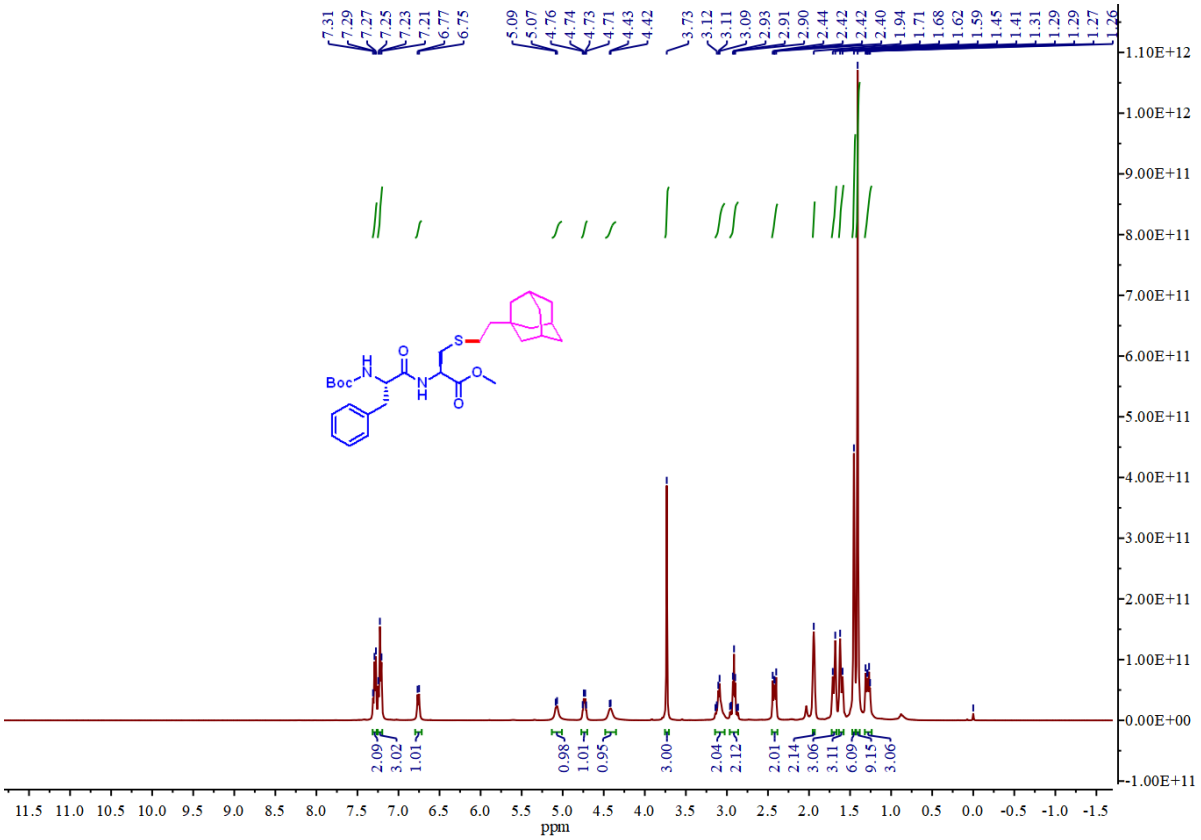
^{13}C NMR Spectrum of Compound **5l** (100 MHz, $CDCl_3$)



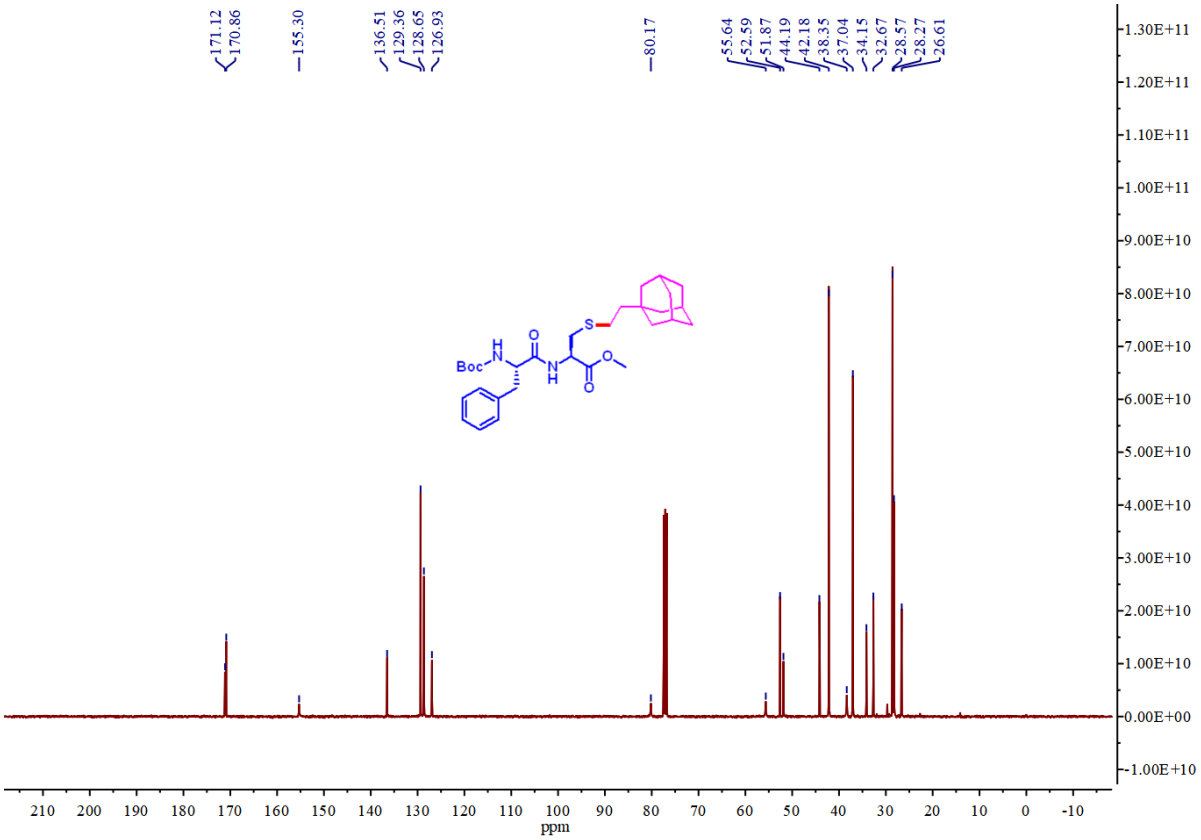
^{1}H NMR Spectrum of Compound **5m** (400 MHz, $CDCl_3$)



^{13}C NMR Spectrum of Compound **5m** (100 MHz, $CDCl_3$)



^{1}H NMR Spectrum of Compound **5n** (400 MHz, $CDCl_3$)



^{13}C NMR Spectrum of Compound **5n** (100 MHz, $CDCl_3$)