Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting informations

Isothiocyanates (*in-situ*) and sulfonyl chlorides in water for N-functionalization of bicyclic amidines: Access to N-alkylated γ-/ω-lactam derivatized thiourea and sulfonamides

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1. General Information

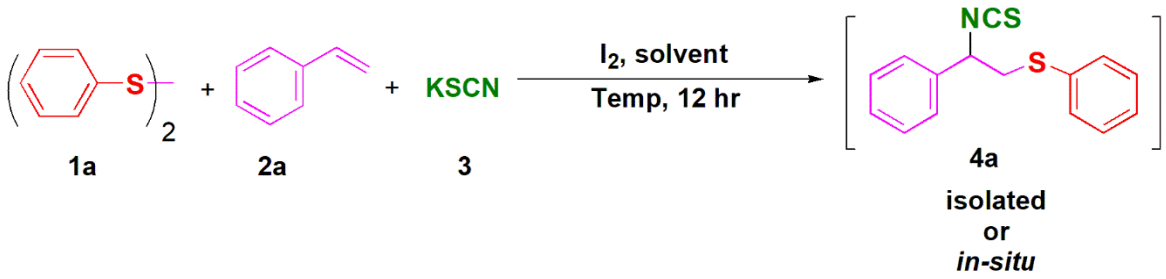
All reagents were used as supplied by commercial sources (Sigma-Aldrich, AVRA and TCI) without any further purification. Hexane and ethyl acetate required for column chromatography were dried using downward distillation assembly. 1, 2-dichloroethane (DCE) was dried by adding Phosphorous Pentoxide (P_2O_5) followed by upward distillation. All reactions were carried out in a 15 ml vial with magnetic stirring in an oil bath under open atmospheric conditions. ^{1}H NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 with a Bruker Avance NEO 500 NMR spectrometer operating at 500 MHz respectively. Proton-decoupled ^{13}C NMR spectra were also recorded in $CDCl_3$ and DMSO-d_6 with a Bruker Avance NEO 500 NMR spectrometer operating at 125.77 MHz respectively. Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane as an internal standard. Coupling constant (J) values are given in hertz (Hz). Multiplicity of the signal is defined as 's' (singlet), 'd' (doublet), 't' (triplet), 'q' (quartet), 'm' (multiplet). High resolution mass spectra (HRMS) were obtained with a Waters Q-TOF Micromass (YB361) spectrometer and XEVO G2-XS Q-TOF using ESI mode. Melting points were recorded in an open capillary sealed at one end using Perfit GSI-MP-3 melting point apparatus and are uncorrected. TLC analyses were performed using F254 aluminum backed plates pre-coated with silica gel containing fluorescent material from Merck followed by their examinations under 254 nm UV lamp. Column chromatography was performed by using Merck 60-120 mesh silica gel.

2. Optimization details

2.1 Synthesis of β-isothiocyanato sulfide 4a

To a 15 ml vial with a stir bar were added diphenyl disulphide **1a** (22 mg, 0.1 mmol, 0.5 equiv), styrene **2a** (0.24 mmol, 1.2 equiv), potassium thiocyanate and iodine. This was followed with the addition of solvent (1 ml) and the reaction mixture was stirred in open atmosphere at varied temperature. The reaction completion was monitored by TLC. However, based on data obtained the product formation ceased after 12 hr. After completion of reaction the saturated solution of sodium thiosulfate in water was added to the reaction mixture. The compound was extracted with ethyl acetate and dried over anhydrous sodium sulphate followed by filtration. Ethyl acetate was rota-evaporated under vacuum and the product of the reaction, β-isothiocyanato sulfide **4a** was purified using silica gel column chromatography with 2% ethyl acetate/hexane. The product was confirmed by NMR.

Table S1: Optimization of KSCN equiv, Iodine equiv, solvent and temperature conditions.



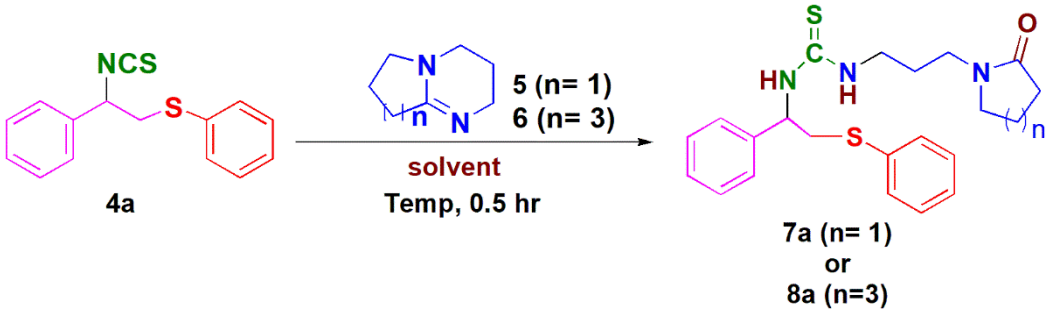
Sr No	KSCN equiv	I_2 equiv	Temp (^{0}C)	Solvent	Yield 4a (%)
1.	1.1	1	60	DMSO	15
2.	1.1	1	55	DMSO	trace
3.	1.1	1	50	DMSO	-
4.	1.1	1	65	DMSO	trace
5.	1.1	1	60	DMF	trace
6.	1.1	1	60	Acetonitrile	30
7.	1.1	1	60	1,4-dioxane	55
8.	1.1	1	60	Ethyl acetate	48
9.	1.1	1	60	THF	58
10.	1.1	1	60	DCE	59
11.	1.1	1	60	Toluene	58
12.	1.1	1	60	Ethanol	trace
13.	1.1	1	60	water	81
14.	1.2	1	60	water	80
15.	1.5	1	60	water	72
16.	1.1	0.5	60	water	30
17.	1.1	0.2	60	water	trace
18.	1.1	1	65	water	73
19.	1.1	1	55	water	68
20.	1.5	1	60	DCE	66
21.	2	1	60	DCE	79

Diphenyl disulphide **1a** (0.1 mmol, 0.5 equiv), styrene **2a** (1.2 equiv), Reaction time = 12 hr.

2.2 Synthesis of β-thiouredo sulfides 7a and 8a

In a 15 ml vial the mixture of β-isothiocyanato sulfide **4a** (27 mg, 0.1 mmol, 1 equiv) and nucleophile DBN **5** or DBU **6** (0.12 mmol, 1.2 equiv) was added in 1 ml of either water or DCE as solvent. The reaction completion was monitored with TLC. However, after 0.5 hr the reactant spot completely disappear and product formation stops. The reaction mixture was cooled to room temperature and the solvent was rota-evaporated in vacuo. Subsequently, the compound was washed with water and extracted with ethyl acetate. The ethyl acetate layer containing compound was dried over anhydrous Na_2SO_4 and filtered, followed by rotary evaporation under vacuo. The reaction product was purified with 60% (DBU as nucleophile) or 70% (DBN as nucleophile) ethyl acetate/hexane solvent using silica gel column chromatography. Finally, the compounds obtained were analysed by NMR and HRMS data.

Table S2: Optimization of temperature and solvent conditions for β-thiouredo sulfide derivatives 7a and 8a.



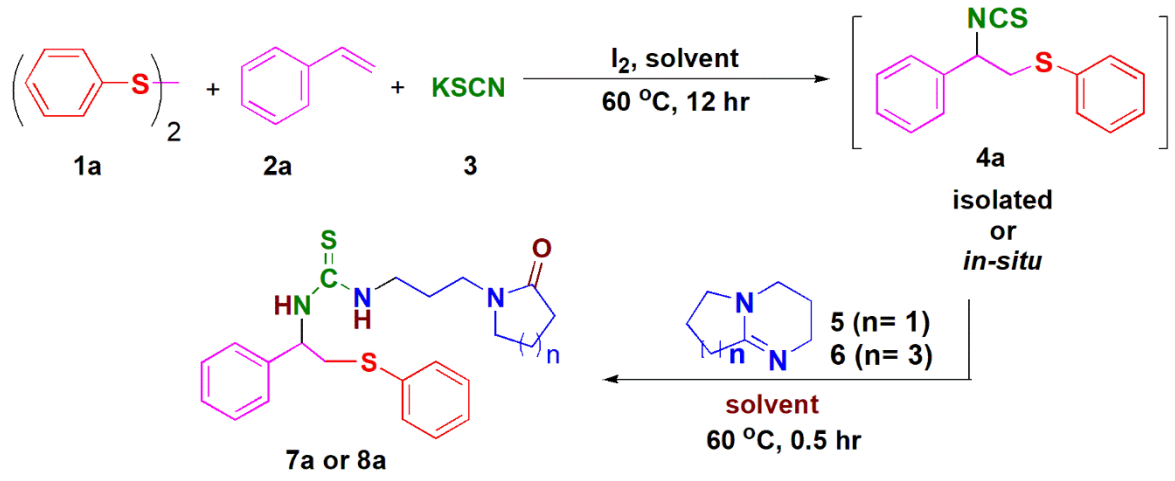
Sr. No.	Nucleophile (DBN or DBU)	Solvent	Temp (^{0}C)	%yield (7a or 8a)
1.	DBN	H_2O	60	7a (91)
2.	DBN	DCE	60	7a (88)
3.	DBN	H_2O	55	7a (78)
4.	DBN	H_2O	65	7a (90)
5.	DBN	DCE	55	7a (81)
6.	DBN	DCE	65	7a (89)
7.	DBU	H_2O	60	8a (94)
8.	DBU	DCE	60	8a (90)

4a (27 mg, 0.1 mmol, 1 equiv) and nucleophile DBN **5** or DBU **6** (0.12 mmol, 1.2 equiv), Reaction time= 0.5 hr.

2.3 One pot synthesis of β-thiouredo sulfide derivatives via *in-situ* trapping of β-isothiocyanato sulfides with bicyclic amidines.

After stirring the reaction mixture for 12 hr to afford β-isothiocyanato sulfide **4a** (as discussed in section 2.1), bicyclic amidines DBN **5** or DBU **6** was added. The reaction mixture was further stirred for another 0.5 hr. After completion the reaction was quenched with saturated solution of sodium thiosulfate in water. The compound was extracted with ethyl acetate and dried over anhydrous Na_2SO_4 followed by filtration. Ethyl acetate was rota-evaporated and the compound was purified with 60% (DBU as nucleophile) or 70% (DBN as nucleophile) ethyl acetate/hexane solvent using silica gel column chromatography.

Table S3: Optimization for *in-situ* trapping of β-isothiocyanto sulfides with bicyclic amidines.



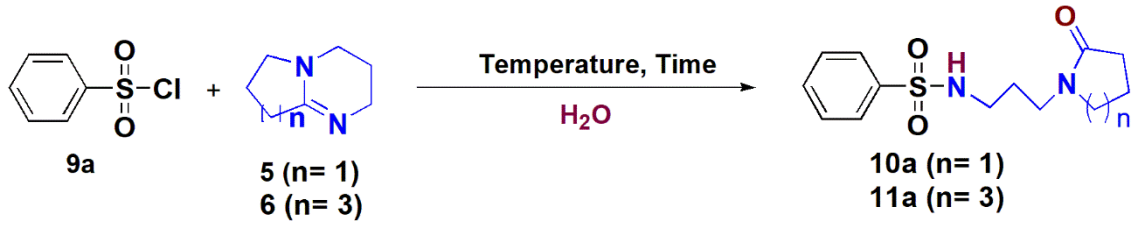
Sr. No.	Nucleophile equiv (DBN or DBU)	Solvent	% yield (8a or 9a)
1.	1.2 (DBN)	H_2O	30 (7a)
2.	1.2 (DBN)	DCE	33 (7a)
3.	1.5 (DBN)	H_2O	38 (7a)
4.	2.0 (DBN)	H_2O	64 (7a)
5.	2.5 (DBN)	H_2O	74 (7a)
6.	3.0 (DBN)	H_2O	74 (7a)
7.	2.5 (DBU)	H_2O	76 (8a)
8.	2.5 (DBU)	DCE	77 (8a)

1a (0.1 mmol, 0.5 equiv), **2a** (1.2 equiv), **3** (1.1 equiv when H_2O as solvent or 2 equiv when DCE as solvent), I_2 (0.2 mmol, 1 equiv), Reaction time= 12.5 hr.

2.4 One pot synthesis of sulfonamide derivatives via electrophilic reaction of sulfonyl chloride with bicyclic amidines.

To a stirred solution of DBN **5** or DBU **6** in water at various temperature was added sulfonyl chloride **9a** (0.1 mmol, 1 equiv) and continued to stir for 1 hr. After 1 hr the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and filtered. After rotary evaporation of ethyl acetate, the residue was purified using 70% (DBN as nucleophile) or 60% (DBU as nucleophile) ethyl acetate/hexane as mobile phase using silica gel column chromatography.

Table S4: Optimization for sulfonamide derivatives 7a and 8a via electrophilic reaction of sulfonyl chloride with bicyclic amidines.



9a

5 (n= 1)
6 (n= 3)

10a (n= 1)
11a (n= 3)

Sr. No.	Nucleophile equiv (DBN or DBU)	Solvent	Temperature (°C)	Time (hr)	% yield (10a or 11a)
1.	2..5 (DBN)	H_2O	60	1	Trace
2.	2.5 (DBN)	H_2O	65	1	28 (10a)
3.	2.5 (DBN)	H_2O	70	1	86 (10a)
4.	2.5 (DBN)	H_2O	75	1	85 (10a)
5.	2.5 (DBU)	H_2O	70	1	88 (11a)
6.	2.0 (DBN)	H_2O	70	1	86 (10a)
7.	2.0 (DBU)	H_2O	70	1	88 (11a)
8.	1.75 (DBN)	H_2O	70	1	72 (10a)
9.	2.0 (DBN)	H_2O	70	1.5	86(10a)
10.	2.0 (DBN)	H_2O	70	0.8	76(10a)

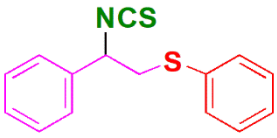
1a (0.1 mmol, 1 equiv)

3. General procedure for synthesis of β-isothiocyanato sulfides 4.

In a 15 ml vial with a stir bar were added disulphide **1** (0.1 mmol, 0.5 equiv), alkene source **2** (0.24 mmol, 1.2 equiv), potassium thiocyanate **3** (0.22 mmol, 1.1 equiv) and iodine (0.2 mmol,

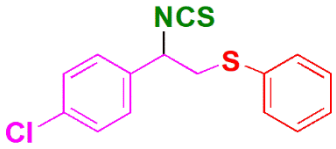
1 equiv) followed by the addition of water (1 ml). The reaction mixture was stirred for 12 hr at 60 ^{0}C. After completion of reaction the saturated solution of sodium thiosulfate in water was added to the reaction mixture. The compound was extracted with ethyl acetate and dried over anhydrous sodium sulphate. After filtration ethyl acetate was rota-evaporated under vacuum and synthesized β-isothiocyanato sulfides **4** were purified using silica gel column chromatography with 2% ethyl acetate/hexane. The synthesized derivatives were characterized with ^{1}HNMR and ^{13}CNMR spectroscopy, and that were further confirmed from earlier literature.[1]

1-(2-isothiocyanato-2-phenylethylthio)benzene (4a):



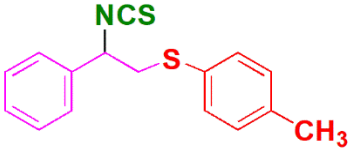
Yellow oil (44 mg, 81%). **^{1}H NMR (500 MHz, CDCl$_3$)** δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.41 (m, 2H), 7.39 – 7.31 (m, 5H), 7.28 – 7.26 (m, 3H), 4.82 (dd, *J* = 7.8, 6.0 Hz, 1H), 3.34 – 3.32 (m, 2H) . **^{13}C NMR (126 MHz, CDCl$_3$)** δ ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.63, 135.02, 134.21, 131.15, 129.33, 128.99, 128.76, 127.39, 126.12, 61.06, 43.44.

1-(2-(4-chlorophenyl)-2-isothiocyanatoethylthio)benzene (4c):



Yellow oil (45 mg, 74%). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.39 – 7.32 (m, 5H), 7.30 – 7.25 (m, 4H), 4.81 (dd, *J* = 7.4, 6.2 Hz, 1H), 3.31 – 3.29 (m, 2H). **^{13}C NMR (126 MHz, CDCl$_3$)** ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.44, 135.30, 133.59, 132.76, 132.56, 129.47, 129.04, 128.85, 126.10, 61.09, 43.66.

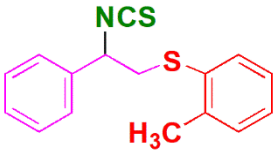
1-(2-isothiocyanato-2-phenylethylthio)-4-methylbenzene (4d):



Yellow oil (47 mg, 83%). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.38 – 7.32 (m, 5H), 7.26 – 7.25 (m, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 4.78 (dd, *J* = 8.0, 5.8 Hz, 1H), 3.28 – 3.26 (m, 2H), 2.35 (s, 3H).

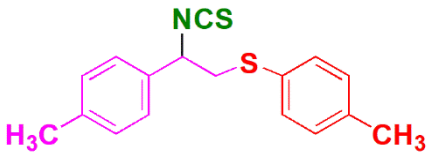
^{13}C NMR (126 MHz, $CDCl_3$) δ 137.73, 137.69, 134.85, 131.92, 130.36, 130.11, 128.95, 128.68, 126.11, 60.98, 44.07, 21.10.

1-(2-isothiocyanato-2-phenylethylthio)-2-methylbenzene (4g):



Yellow oil (46 mg, 81%).**^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.35 – 7.27 (m, 1H), 7.13 (d, *J* = 7.9 Hz, 1H), 4.68 (dd, *J* = 9.6, 3.4 Hz, 1H), 3.28 (dd, *J* = 13.8, 3.4 Hz, 1H), 3.03 (dd, *J* = 13.8, 9.6 Hz, 1H), 2.34 (s, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 141.28, 136.81, 134.56, 129.77, 129.31, 128.93, 128.85, 128.51, 128.02, 126.69, 125.94, 64.69, 41.66, 15.23.

1-(2-isothiocyanato-2-p-tolylethylthio)-4-methylbenzene (4i):



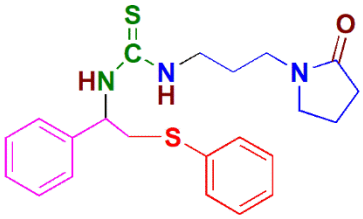
Yellow oil (53 mg, 88%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.35 – 7.32 (m, 2H), 7.17 – 7.13 (m, 6H), 4.75 – 4.72 (m, 1H), 3.26 – 3.24 (m, 2H), 2.34 (s, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 138.61, 137.66, 134.75, 131.86, 130.44, 130.09, 129.65, 129.60, 126.04, 60.78, 43.96, 21.15, 21.11.

4. General procedure for electrophilic reaction of β-isothiocyanato sulfides with bicyclic amidines to afford β-thiouredo sulfides 7a-7i and 8a-8i.

To a 15 ml vial with a stir bar were added diphenyl disulphide **1** (0.1 mmol, 0.5 equiv), styrene **2** (0.24 mmol, 1.2 equiv), potassium thiocyanate **3** (0.22 mmol,1.1 equiv and iodine (0.2 mmol, 1 equiv). This was followed with the addition of water (1 ml) and the reaction mixture was stirred in open atmosphere at 60 ^{0}C. The reaction was stirred for 12 hr to afford β-isothiocyanato sulfide **4**. Subsequently, bicyclic amidines DBN **5** or DBU **6** was added and the reaction mixture was further stirred for another 0.5 hr. After completion the reaction was quenched with saturated solution of sodium thiosulfate in water. The compound was extracted with ethyl acetate and dried over anhydrous Na_2SO_4 followed by filtration. The filtrate was concentrated using rotary evaporation under vacuum and the compound was purified with 50-

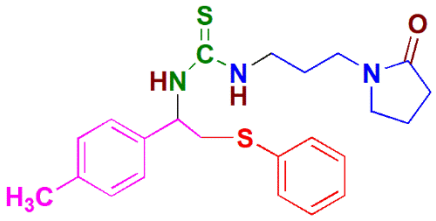
60% (DBU as nucleophile) or 50-70% (DBN as nucleophile) ethyl acetate/hexane solvent using silica gel column chromatography.

1-(3-(2-Oxopyrrolidin-1-yl)propyl)-3-(1-phenyl-2-(phenylthio)ethyl)thiourea (7a):



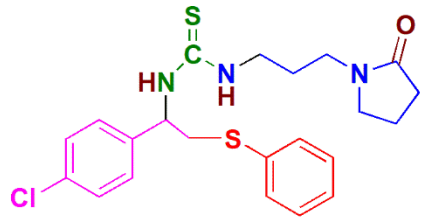
White semi solid (61 mg, 74%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.37 –7.34 (m, 4H), 7.32 – 7.29 (m, 2H), 7.25 – 7.24 (m, 3H), 7.19 – 7.16 (m, 1H), 7.02 (s, 1H), 6.82 (d, *J* = 6.45 Hz, 1H), 5.33 (s, 1H), 3.57 – 3.54 (m, 1H), 3.41 – 3.30 (m, 5H), 3.07 – 3.06 (m, 2H), 2.33 (t, *J* = 7.85 Hz, 2H), 2.03 – 1.97 (m, 2H), 1.74 – 1.70 (m, 1H), 1.66 – 1.60 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.42, 176.02, 139.83, 135.38, 130.26, 129.01, 128.72, 127.95, 126.77, 126.59, 56.67, 47.51, 41.20, 40.92, 39.55, 30.91, 25.97, 17.88, 14.20. **HRMS (ESI):** Mass calcd for $C_{22}H_{27}N_3OS_2H$ $[M+H]^+$: 414.1674; found: 414.1671.

1-(3-(2-Oxopyrrolidin-1-yl)propyl)-3-(2-(phenylthio)-1-p-tolylethyl)thiourea (7b):



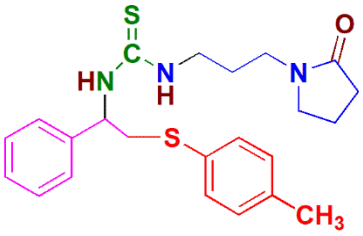
White semi solid (66 mg, 77%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.35 (d, *J* = 7.3 Hz, 2H), 7.27 – 7.22 (m, 4H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.11 (d, *J* = 7.85 Hz, 2H), 6.98 (s, 1H), 6.80 (d, *J* = 6.95 Hz, 1H), 5.29 (s, 1H), 3.54 – 3.50 (m, 1H), 3.44 – 3.30 (m, 5H), 3.10 – 3.08 (m, 2H), 2.33 (t, *J* = 7.9 Hz, 2H), 2.31 (s, 3H) 2.02 – 1.96 (m, 2H), 1.78 – 1.69 (m, 1H), 1.64 – 1.61 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.39, 175.96, 137.66, 136.79, 135.48, 130.15, 129.42, 128.98, 126.66, 126.48, 60.40, 56.44, 47.49, 41.24, 40.83, 39.59, 30.92, 26.00, 21.12, 17.89, 14.20. **HRMS (ESI):** Mass calcd for $C_{23}H_{29}N_3OS_2H$ $[M+H]^+$: 428.1830; found: 428.1827.

1-(1-(4-Chlorophenyl)-2-(phenylthio)ethyl)-3-(3-(2-oxopyrrolidin-1-yl)propyl)thiourea (7c):



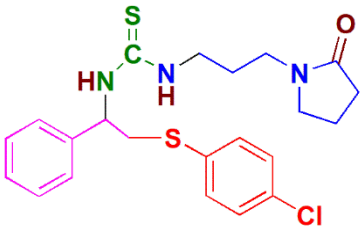
White semi solid (64 mg, 71%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.51 (s, 1H), 7.41 – 7.35 (m, 6H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.21 – 7.18 (m, 1H), 5.57 (s, 1H), 3.50 – 3.46 (m, 1H), 3.36 – 3.34 (m, 2H), 3.32 – 3.29 (m, 3H), 3.16 (m, 2H), 2.21 (t, *J* = 8.25 Hz, 2H), 1.93 – 1.87 (m, 2H) 1.66 – 1.63 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.39, 176.00, 139.76, 135.32, 130.33, 129.02, 128.74, 127.97, 126.75, 126.63, 56.64, 47.51, 41.17, 41.00, 39.49, 30.89, 29.69, 25.95, 17.89. **HRMS (ESI):** Mass calcd for $C_{22}H_{26}ClN_3OS_2H$ $[M+H]^+$: 448.1284; found: 448.1284.

1-(2-(*p*-Tolylthio)-1-phenylethyl)-3-(3-(2-oxopyrrolidin-1-yl)propyl)thiourea (7d):



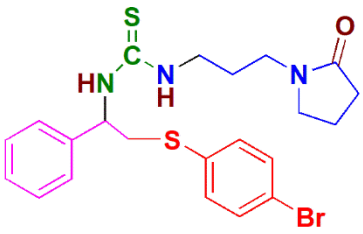
White semi solid (67 mg, 79%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.35 – 7.27 (m, 6H), 7.26 – 7.23 (m, 1H), 7.07 (d, *J* = 8 Hz, 2H), 6.95 (s, 1H), 6.73 (d, *J* = 5.9 Hz, 1H), 5.22 (s, 1H), 3.59 – 3.55 (m, 1H), 3.40 – 3.29 (m, 5H), 3.05 – 3.03 (m, 2H), 2.34 (t, *J* = 8.3 Hz, 2H), 2.30 (s, 3H), 2.03 – 1.97 (m, 2H), 1.74 – 1.67 (m, 1H), 1.62 – 1.59 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.33, 175.96, 139.83, 136.94, 131.38, 131.20, 129.85, 128.73, 127.92, 126.71, 56.62, 47.49, 41.81, 41.22, 39.45, 30.90, 25.98, 21.05, 17.90. **HRMS (ESI):** Mass calcd for $C_{23}H_{29}N_3OS_2H$ $[M+H]^+$: 428.1830; found: 428.1827.

1-(2-(4-Chlorophenylthio)-1-phenylethyl)-3-(3-(2-oxopyrrolidin-1-yl)propyl)thiourea (7e):



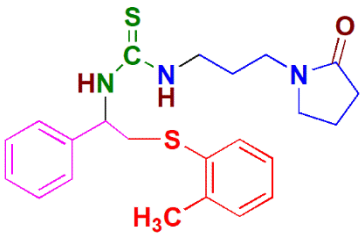
White semi solid (64 mg, 72%). **^{1}H NMR** (500 MHz, $CDCl_3$) d 7.34 (dt, *J* = 3.3, 1.9 Hz, 2H), 7.30 – 7.28 (m, 2H), 7.27 – 7.23 (m, 4H), 7.18 (ddd, *J* = 8.5, 2.4, 1.2 Hz, 1H), 7.14 (s, 1H), 6.96 (s, 1H), 5.39 (s, 1H), 3.55 – 3.52 (m, 1H), 3.44 – 3.21 (m, 5H), 3.15 – 3.09 (m, 2H), 2.35 (t, *J* = 8.55 Hz, 2H), 2.04 – 1.98 (m, 2H), 1.74 – 1.72 (m, 1H), 1.66 – 1.59 (m, 1H). **^{13}C NMR** ^{13}C NMR (126 MHz, DMSO) δ 181.49, 173.89, 140.34, 135.74, 131.68, 128.88, 128.70, 128.25, 128.10, 125.68, 59.62, 46.19, 38.15, 30.35, 26.37, 20.63, 17.40, 13.96. **HRMS (ESI)** Mass calcd for $C_{22}H_{26}ClN_3OS_2H$ $[M+H]^+$: 448.1284; found: 448.1287.

1-(2-(4-Bromophenylthio)-1-phenylethyl)-3-(3-(2-oxopyrrolidin-1-yl)propyl)thiourea (7f):



White semi solid (58 mg, 59%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.05 (s, 1H), 7.51 (s, 1H), 7.47 (dd, *J* = 6.8, 1.75 Hz, 2H), 7.35 – 7.31 (m, 6H), 7.29 – 7.25 (m, 1H), 5.58 (s, 1H), 3.52 – 3.48 (m, 1H), 3.39 – 3.35 (m, 3H), 3.32 – 3.30 (m, 2H), 3.15 (bs, 2H), 2.21 (t, *J* = 8.25 Hz, 2H), 1.94 – 1.87 (m, 2H) 1.65 – 1.63 (m, 2H). **^{13}C NMR (126 MHz, DMSO)** δ 181.85, 173.88, 141.05, 135.68, 131.59, 130.08, 128.22, 127.21, 126.80, 118.46, 59.63, 46.21, 38.16, 30.35, 26.40, 20.64, 17.40, 13.97. **HRMS (ESI):** Mass calcd for $C_{22}H_{26}BrN_3OS_2H$ $[M+H]^+$: 492.0779; found: 492.0780.

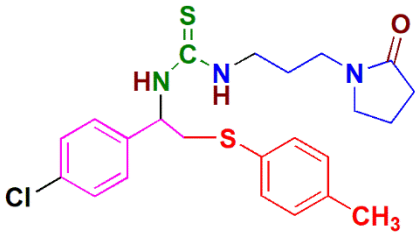
1-(2-(o-Tolylthio)-1-phenylethyl)-3-(3-(2-oxopyrrolidin-1-yl)propyl)thiourea (7g):



White semi solid (67 mg, 78%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.37 – 7.34 (m, 2H), 7.33 – 7.28 (m, 3H), 7.26 – 7.23 (m, 1H), 7.17 – 7.06 (m, 3H), 7.01 (s, 1H), 6.83 (d, *J* = 6.25 Hz, 1H), 5.29 (s, 1H), 3.58 – 3.54 (m, 1H), 3.41 – 3.27 (m, 5H), 3.05 (d, *J* = 4.5 Hz, 1H), 2.35 (s, 3H),

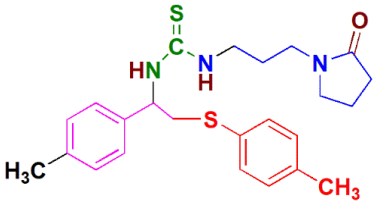
2.33-2.29 (m, 2H), 2.02 – 1.96 (m, 2H), 1.75 – 1.67 (m, 1H), 1.63 – 1.61 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.39, 175.98, 139.91, 138.54, 134.55, 130.25, 129.79, 128.72, 127.94, 126.73, 126.57, 126.53, 56.64, 47.49, 41.24, 40.27, 39.52, 30.90, 26.00, 20.59, 17.88. **HRMS (ESI):** Mass calcd for $C_{23}H_{29}N_3OS_2H$ $[M+H]^+$: 428.1830; found: 428.1829.

1-(2-(p-Tolylthio)-1-(4-chlorophenyl)ethyl)-3-(3-(2-oxopyrrolidin-1-yl)propyl)thiourea (7h):



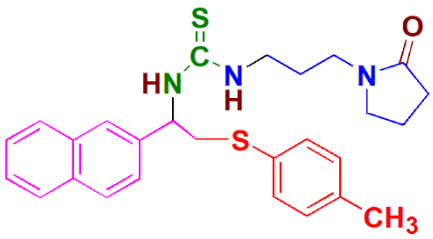
White semi solid (68 mg, 74%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.28 – 7.23 (m, 7H), 7.11 (s, 1H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.91 (s, 1H), 5.30 (s, 1H), 3.57 – 3.53 (m, 1H), 3.43-3.22 (m, 5H), 3.14 – 3.06 (m, 2H), 2.35 (t, *J* = 8.45 Hz, 2H), 2.30 (s, 3H), 2.03 – 1.98 (m, 2H), 1.77 – 1.70 (m, 1H), 1.65 – 1.62 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.43, 176.08, 138.64, 137.03, 133.52, 131.21, 129.85, 128.72, 128.24, 56.10, 47.54, 41.60, 41.12, 39.55, 30.93, 25.96, 21.05, 17.89. **HRMS (ESI):** Mass calcd for $C_{23}H_{28}ClN_3OS_2H$ $[M+H]^+$: 462.1441; found: 462.1443.

1-(2-(p-Tolylthio)-1-p-tolylethyl)-3-(3-(2-oxopyrrolidin-1-yl)propyl)thiourea (7i):



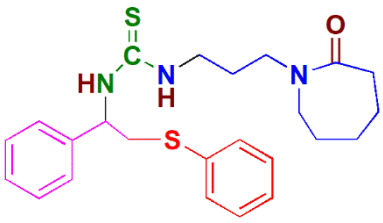
White semi solid (75 mg, 85%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.27 (d, *J* = 7.3 Hz, 2H), 7.21 (d, *J* = 8.05 Hz, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 7.06 (d, *J* = 7.95 Hz, 2H), 6.92 (s, 1H), 6.77 (d, *J* = 6.95 Hz, 1H), 5.20 (s, 1H), 3.55 – 3.51 (m, 1H), 3.44 – 3.37 (m, 1H), 3.36 – 3.24 (m, 4H), 3.11 – 3.06 (m, 2H), 2.33 (t, *J* = 8.45 Hz, 2H), 2.31 (s, 3H), 2.30 (s, 3H), 2.01 – 1.97 (m, 2H), 1.76 – 1.69 (m, 1H), 1.64 – 1.60 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.36, 175.93, 137.61, 136.85, 136.78, 131.53, 131.04, 129.80, 129.40, 126.62, 56.42, 47.48, 41.67, 41.27, 39.55, 30.92, 26.02, 21.12, 21.05, 17.90. **HRMS (ESI):** Mass calcd for $C_{24}H_{31}N_3OS_2H$ $[M+H]^+$: 442.1987; found: 442.1990.

1-(1-Naphthalen-2-yl-2-p-tolylsulfanyl-ethyl)-3-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-thio-urea (7j):



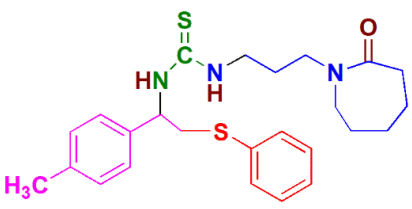
White semi solid (77 mg, 81%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.74 – 7.69 (m, 4H), 7.44 – 7.34 (m, 3H), 7.27 – 7.12 (m, 3H), 7.07 – 6.95 (m, 3H), 5.36 (s, 1H), 3.47 – 3.42 (m, 1H), 3.37 – 3.27 (m, 3H), 3.25 – 3.13 (m, 2H), 3.08 – 2.90 (m, 2H), 2.27 – 2.24 (m, 2H), 2.20 (s, 3H), 1.91 – 1.85 (m, 2H), 1.68 – 1.61 (m, 1H), 1.57 – 1.49 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 180.47, 174.99, 136.29, 135.88, 132.24, 131.98, 130.33, 130.21, 128.77, 127.55, 127.04, 126.58, 125.15, 124.99, 124.79, 123.61, 55.80, 46.44, 40.59, 40.24, 38.50, 29.86, 28.67, 24.89, 20.00, 16.82. Mass calcd for $C_{27}H_{32}N_3OS_2H$ $[M+H]^+$: 478.1987; found: 478.2005

1-(3-(2-Oxoazepan-1-yl)propyl)-3-(1-phenyl-2-(phenylthio)ethyl)thiourea (8a):



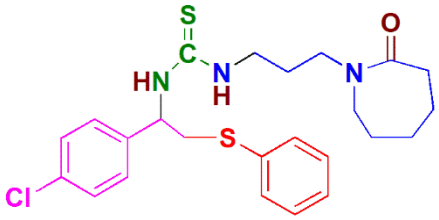
White semi solid (68 mg, 76%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.38 – 7.34 (m, 4H), 7.32 – 7.28 (m, 2H), 7.27 – 7.21 (m, 4H), 7.19 – 7.15 (m, 1H), 6.71 (d, *J* = 6.7 Hz, 1H), 5.34 (s, 1H), 3.58 – 3.55 (m, 1H), 3.42 – 3.32 (m, 3H), 3.28 – 3.26 (m, 2H), 3.14 (bs, 2H), 2.47 (t, *J* = 5.75 Hz, 2H), 1.74 – 1.67(m, 3H), 1.65 – 1.57 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.27, 176.94, 139.82, 135.43, 130.27, 128.99, 128.66, 127.90, 126.82, 126.55, 56.59, 49.72, 45.10, 41.11, 40.91, 37.10, 29.87, 28.36, 26.76, 23.30. **HRMS (ESI):** Mass calcd for $C_{24}H_{31}N_3OS_2H$ $[M+H]^+$: 442.1987; found: 442.2017.

1-(3-(2-Oxoazepan-1-yl)propyl)-3-(2-(phenylthio)-1-p-tolylethyl)thiourea (8b):



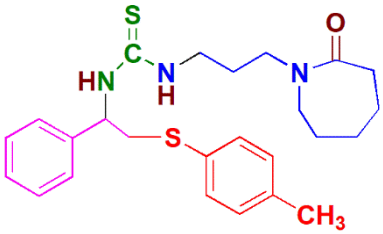
White semi solid (76 mg, 83%). **^{1}H NMR (500 MHz, $CDCl_3$)** d 7.35 – 7.34 (m, 2H), 7.31 – 7.22 (m, 5H), 7.17 (s, 1H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.77 (d, *J* = 6.95 Hz, 1H), 5.27 (s, 1H), 3.58 – 3.55 (m, 1H), 3.43 – 3.38 (m, 1H), 3.34-3.22 (m, 4H), 3.13 (bs, 2H), 2.46 (t, *J* = 5.75 Hz, 2H), 2.30 (s, 3H), 1.74-1.66 (m, 3H), 1.65 – 1.56 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.16, 176.88, 139.96, 136.80, 131.54, 131.11, 129.81, 128.63, 127.82, 126.80, 56.60, 49.71, 49.13, 45.09, 41.16, 37.10, 29.87, 28.36, 26.81, 23.37, 21.05. **HRMS (ESI):** Mass calcd for $C_{25}H_{33}N_3OS_2H$ $[M+H]^+$: 456.2143; found: 456.2159.

1-(1-(4-Chlorophenyl)-2-(phenylthio)ethyl)-3-(3-(2-oxoazepan-1-yl)propyl)thiourea (8c):



White semi solid (69 mg, 72%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.35 – 7.33 (m, 2H), 7.30 – 7.29 (m, 2H), 7.27 – 7.23 (m, 5H), 7.20 – 7.17 (m, 1H), 6.82 (s, 1H), 5.36 (s, 1H), 3.55 – 3.49 (m, 1H), 3.45 – 3.36 (m, 2H), 3.32 – 3.28 (m, 3H), 3.22 – 3.16 (m, 2H), 2.47 (t, *J* = 6.05 Hz, 2H), 1.74 – 1.68 (m, 3H), 1.66 – 1.58 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.23, 177.07, 138.55, 135.12, 133.54, 130.40, 129.03, 128.70, 128.32, 126.69, 56.00, 49.73, 45.10, 41.01, 40.84, 37.10, 29.86, 29.69, 28.31, 23.36. **HRMS (ESI):** Mass calcd for $C_{24}H_{30}ClN_3OS_2H$ $[M+H]^+$: 476.1597; found: 476.1611.

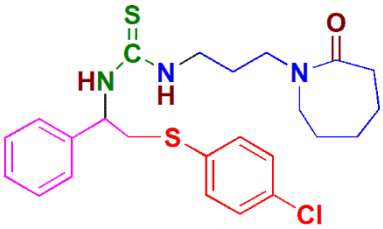
1-(2-(p-Tolylthio)-1-phenylethyl)-3-(3-(2-oxoazepan-1-yl)propyl)thiourea (8d):



White semi solid (76 mg, 83%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.26 (d, *J* = 7.25 Hz, 2H), 7.22 – 7.18 (m, 4H), 7.16 – 7.14 (m, 2H), 6.98 (d, *J* = 7.95 Hz, 2H), 6.89 (d, *J* = 7.25 Hz, 1H), 5.24 (bs, 1H), 3.48 – 3.47 (m, 1H), 3.35 – 3.24 (m, 2H), 3.22 – 3.17 (m, 3H), 3.07 (bs, 2H), 2.37 (t, *J* = 5.8 Hz, 2H), 2.22 (s, 3H), 1.65 – 1.57 (m, 3H), 1.55 – 1.48 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.25, 176.83, 140.09, 136.68, 131.66, 130.98, 129.78, 128.60, 127.76,

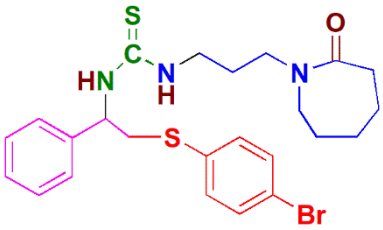
126.83, 56.67, 49.72, 45.21, 41.55, 41.23, 37.08, 29.84, 28.35, 26.90, 23.35, 21.04. **HRMS (ESI):** Mass calcd for $C_{25}H_{33}N_3OS_2H$ $[M+H]^+$: 456.2143; found: 456.2162.

1-(2-(4-chlorophenylthio)-1-phenylethyl)-3-(3-(2-oxoazepan-1-yl)propyl)thiourea (8e):



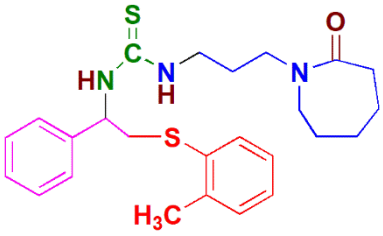
White semi solid (71 mg, 74%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.35 – 7.33 (m, 2H), 7.30 – 7.29 (m, 3H), 7.26 – 7.23 (m, 4H), 7.20 – 7.17 (m, 1H), 6.77 (s, 1H), 5.36 (s, 1H), 3.57 – 3.53 (m, 1H), 3.46 – 3.35 (m, 2H), 3.32 – 3.24 (m, 3H), 3.22 – 3.16 (m, 2H), 2.48 (t, *J* = 6.15 Hz, 2H), 1.76 – 1.68 (m, 3H), 1.67 – 1.59 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.22, 177.10, 138.54, 135.10, 133.55, 130.43, 129.04, 128.71, 128.31, 126.71, 56.00, 49.73, 45.08, 40.98, 40.87, 37.10, 29.87, 28.31, 26.67, 23.36. **HRMS (ESI):** Mass calcd for $C_{24}H_{30}ClN_3OS_2H$ $[M+H]^+$: 476.1597; found: 476.1612.

1-(2-(4-Bromophenylthio)-1-phenylethyl)-3-(3-(2-oxoazepan-1-yl)propyl)thiourea (8f):



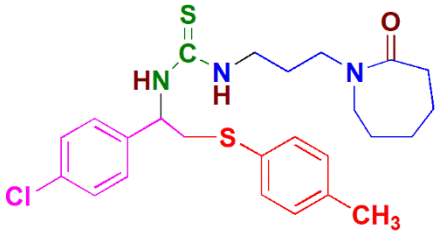
White semi solid (70 mg, 67%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.37 – 7.34 (m, 4H), 7.32 – 7.27 (m, 3H), 7.26 – 7.21 (m, 3H), 6.56 (s, 1H), 5.34 (s, 1H), 3.56 – 3.53 (m, 1H), 3.47 – 3.37 (m, 2H), 3.34 – 3.27 (m, 3H), 3.15 (bs, 2H), 2.48 (t, *J* = 5.75 Hz, 2H), 1.75 – 1.70 (m, 3H), 1.67 – 1.59 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.09, 177.06, 139.56, 134.58, 131.99, 131.84, 128.72, 128.01, 126.85, 120.50, 49.71, 45.00, 40.96, 40.62, 37.10, 29.88, 29.70, 28.32, 23.39. **HRMS (ESI):** Mass calcd for $C_{24}H_{30}BrN_3OS_2H$ $[M+H]^+$: 520.1092; found: 520.1058.

1-(2-(o-Tolylthio)-1-phenylethyl)-3-(3-(2-oxoazepan-1-yl)propyl)thiourea (8g):



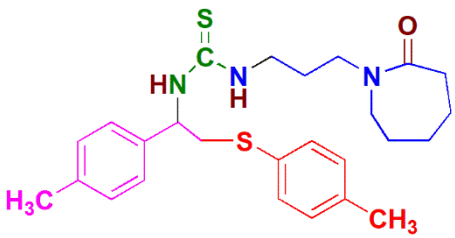
White semi solid (78 mg, 85%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.38 – 7.34 (m, 3H), 7.32 – 7.28 (m, 2H), 7.26 – 7.22 (m, 2H), 7.15 – 7.10 (m, 2H), 7.09 – 7.06 (m, 1H), 6.74 (d, *J* = 6.55 Hz, 1H), 5.29 (s, 1H), 3.58 – 3.56 (m, 1H), 3.44 – 3.38 (m, 1H), 3.36 – 3.25 (m, 4H), 3.12 (bs, 2H), 2.46 (t, *J* = 5.7 Hz, 2H), 2.35 (s, 3H), 1.74 – 1.66 (m, 3H), 1.65 – 1.56 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.12, 176.89, 139.92, 138.53, 134.62, 131.13, 130.22, 129.78, 128.66, 127.88, 126.79, 126.56, 56.56, 49.72, 45.09, 41.16, 40.28, 37.10, 29.87, 28.37, 26.80, 23.37, 20.59. **HRMS (ESI):** Mass calcd for $C_{25}H_{33}N_3OS_2H$ $[M+H]^+$: 456.2143; found: 456.2160.

1-(2-(p-Tolylthio)-1-(4-chlorophenyl)ethyl)-3-(3-(2-oxoazepan-1-yl)propyl)thiourea (8h):



White semi solid (76 mg, 78%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.28 – 7.27 (m, 3H), 7.26 – 7.22 (m, 4H), 7.05 (d, *J* = 7.9 Hz, 2H), 6.74 (s, 1H), 5.27 (s, 1H), 3.56 – 3.53 (m, 1H), 3.45 – 3.39 (m, 1H), 3.33 – 3.22 (m, 4H), 3.20 – 3.14 (m, 2H), 2.47 (t, *J* = 5.9 Hz, 2H), 2.30 (s, 3H), 1.77 – 1.68 (m, 3H), 1.67 – 1.57 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.17, 177.03, 138.60, 137.02, 133.49, 131.26, 131.19, 129.85, 128.67, 128.29, 55.98, 49.72, 45.05, 41.65, 41.04, 37.11, 29.87, 28.33, 26.70, 23.38, 21.06. **HRMS (ESI):** Mass calcd for $C_{25}H_{32}ClN_3OS_2H$ $[M+H]^+$: 490.1754; found: 490.1777.

1-(2-(p-Tolylthio)-1-p-tolylethyl)-3-(3-(2-oxoazepan-1-yl)propyl)thiourea (8i):

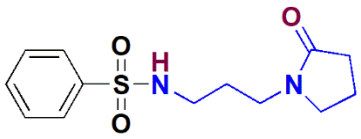


White semi solid (83 mg, 89%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.27 (dd, *J* = 6.7, 1.4 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 7.10 (d, *J* = 7.9 Hz, 2H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.82 (d, *J* = 7.3 Hz, 1H), 5.25 (s, 1H), 3.53 – 3.51 (m, 1H), 3.45 – 3.38 (m, 1H), 3.35 – 3.23 (m, 4H), 3.16 (d, *J* = 4.6 Hz, 2H), 2.48 – 2.44 (m, 2H), 2.30 (s, 6H), 1.73 – 1.66 (m, 3H), 1.65 – 1.56 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 181.17, 176.83, 137.47, 136.98, 136.65, 131.68, 130.96, 129.76, 129.31, 126.70, 56.41, 49.71, 45.17, 41.55, 41.20, 37.10, 29.86, 28.36, 26.85, 23.36, 21.12, 21.04, 14.20. **HRMS (ESI):** Mass calcd for $C_{26}H_{35}N_3OS_2H$ $[M+H]^+$: 470.2300; found: 470.2324.

5. General procedure for synthesis of sulphonamide derivatives 10a-10e and 11a-11e.

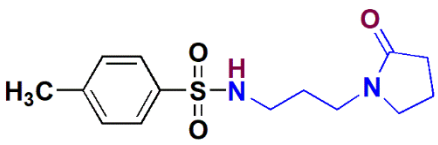
To a stirred solution of DBN **5** or DBU **6** (0.25 mmol, 2.0 equiv) in water at 70 °C was added sulfonyl chloride **9** (0.1 mmol, 1 equiv) and continued to stir for 1 hr. After 1 hr the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and filtered. After rotary evaporation of ethyl acetate, the residue was purified using 70% (DBN as nucleophile) or 60% (DBU as nucleophile) ethyl acetate/hexane as mobile phase using silica gel column chromatography.

N-(3-(2-oxopyrrolidin-1-yl)propyl)benzenesulfonamide (10a):



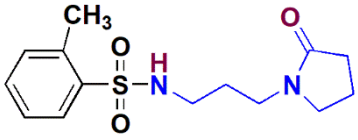
Transparent oil (48 mg, 86%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.88 – 7.86 (m, 2H), 7.57 – 7.53 (m, 1H), 7.51 – 7.48 (m, 2H), 6.25 (t, *J* = 6.5 Hz, 1H), 3.32 (td, *J* = 6.7, 3.1 Hz, 4H), 2.88 (dd, *J* = 12.6, 6.5 Hz, 2H), 2.34 – 2.31 (m, 2H), 1.99 (ddd, *J* = 15.5, 9.3, 5.5 Hz, 2H), 1.72 – 1.67 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 176.02, 140.30, 132.35, 128.99, 126.94, 47.39, 39.85, 39.38, 30.74, 26.91, 17.83. **HRMS (ESI):** Mass calcd for $C_{13}H_{18}N_2O_3SH$ $[M+H]^+$: 283.1116; found: 283.1133.

4-Methyl-N-(3-(2-oxopyrrolidin-1-yl)propyl)benzenesulfonamide (10b):



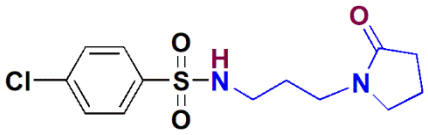
White solid (50 mg, 91%). Melting point: 124-125 °C **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.29 – 7.28 (m, 2H), 6.05 (t, *J* = 6.6 Hz, 1H), 3.32 (td, *J* = 6.7, 3.6 Hz, 4H), 2.86 (dd, *J* = 12.6, 6.5 Hz, 2H), 2.41 (s, 3H), 2.35 – 2.32 (m, 2H), 1.99 (ddd, *J* = 15.5, 9.4, 5.5 Hz, 2H), 1.72 – 1.657 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 175.96, 143.04, 137.39, 129.58, 127.02, 47.39, 39.82, 39.39, 30.74, 26.96, 21.47, 17.87. **HRMS (ESI):** Mass calcd for $C_{14}H_{20}N_2O_3SH$ $[M+H]^+$: 297.1273; found: 297.1281.

2-Methyl-N-(3-(2-oxopyrrolidin-1-yl)propyl)benzenesulfonamide (10c):



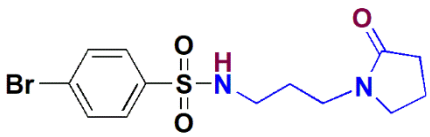
Transparent oil (48 mg, 89%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.44 – 7.41 (m, 1H), 7.30 – 7.27 (m, 2H), 6.23 (t, *J* = 6.5 Hz, 1H), 3.35 – 3.30 (m, 4H), 2.90 (dd, *J* = 12.5, 6.5 Hz, 2H), 2.67 (s, 3H), 2.39 – 2.32 (m, 2H), 2.04 – 1.98 (m, 2H), 1.70 – 1.64 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 176.12, 137.14, 132.51, 129.58, 129.00, 127.01, 125.98, 47.44, 39.64, 30.80, 27.29, 20.23, 17.87. **HRMS (ESI):** Mass calcd for $C_{14}H_{20}N_2O_3SH$ $[M+H]^+$: 297.1273; found: 297.1288.

4-Chloro-N-(3-(2-oxopyrrolidin-1-yl)propyl)benzenesulfonamide (10d):



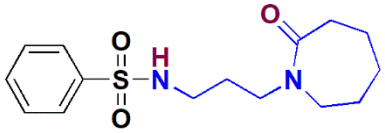
Transparent oil (52 mg, 82%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.75 – 7.72 (m, 2H), 7.64 – 7.62 (m, 2H), 6.31 (t, *J* = 6.5 Hz, 1H), 3.34 (t, *J* = 6.8 Hz, 4H), 2.87 (dd, *J* = 12.3, 6.4 Hz, 2H), 2.35 (t, *J* = 8.1 Hz, 2H), 2.04 – 1.98 (m, 2H), 1.73 – 1.68 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 176.18, 139.57, 132.22, 128.63, 127.16, 47.48, 39.71, 39.33, 30.72, 26.98, 17.88. **HRMS (ESI):** Mass calcd for $C_{13}H_{17}ClN_2O_3SH$ $[M+H]^+$: 317.0727; found: 317.0725.

4-Bromo-N-(3-(2-oxopyrrolidin-1-yl)propyl)benzenesulfonamide (10e):



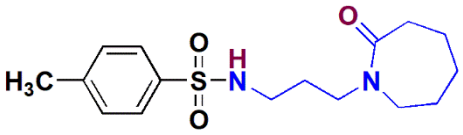
Transparent oil (56 mg, 78%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.75 – 7.72 (m, 2H), 7.64 – 7.62 (m, 2H), 6.23 (t, *J* = 6.6 Hz, 1H), 3.36 – 3.32 (m, 4H), 2.87 (dd, *J* = 12.2, 6.5 Hz, 2H), 2.35 (t, *J* = 8.1 Hz, 2H), 2.05 – 1.98 (m, 2H), 1.72 – 1.68 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 176.23, 139.61, 132.22, 128.63, 127.16, 47.49, 39.63, 39.29, 30.69, 27.01, 17.90. **HRMS (ESI):** Mass calcd for $C_{13}H_{17}BrN_2O_3SH$ $[M+H]^+$: 361.0222; found: 361.0236.

N-(3-(2-oxoazepan-1-yl)propyl)benzenesulfonamide (11a):



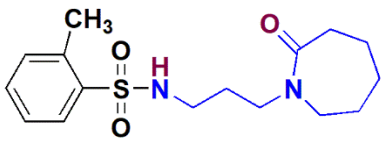
White solid (54 mg, 88%). Melting point: 110-112 °C **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.89 – 7.87 (m, 2H), 7.54 – 7.47 (m, 3H), 6.29 (t, *J* = 6.5 Hz, 1H), 3.43 – 3.41 (m, 2H), 3.26 – 3.24 (m, 2H), 2.87 (dd, *J* = 12.0, 6.5 Hz, 2H), 2.46 – 2.44 (m, 2H), 1.70 – 1.65 (m, 4H), 1.59 – 1.53 (m, 4H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 177.02, 140.47, 132.21, 128.88, 127.07, 49.65, 44.82, 39.57, 36.91, 29.86, 28.36, 27.54, 23.27. **HRMS (ESI):** Mass calcd for $C_{15}H_{22}N_2O_3SH$ $[M+H]^+$: 311.1429; found: 311.1437.

4-Methyl-N-(3-(2-oxoazepan-1-yl)propyl)benzenesulfonamide (11b):



White solid (60 mg, 93%). Melting point: 75-76 °C **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.69 – 7.68 (m, 2H), 7.21– 7.20 (m, 2H), 6.11 (t, *J* = 6.6 Hz, 1H), 3.35 – 3.33 (m, 2H), 3.20 – 3.18 (m, 2H), 2.80 – 2.76 (dd, *J* = 12.1, 6.5 Hz, 2H), 2.40 – 2.37 (m, 2H), 2.34 (s, 3H), 1.63 – 1.57 (m, 4H), 1.52 – 1.47 (m, 4H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 176.95, 142.88, 137.49, 129.48, 127.12, 49.65, 44.87, 39.59, 36.92, 29.87, 28.36, 27.54, 23.24, 21.47. **HRMS (ESI):** Mass calcd for $C_{16}H_{24}N_2O_3SH$ $[M+H]^+$: 325.1586; found: 325.1605.

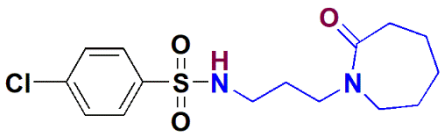
2-Methyl-N-(3-(2-oxoazepan-1-yl)propyl)benzenesulfonamide (11c):



Transparent oil (59 mg, 91%). **^{1}H NMR (500 MHz, $CDCl_3$)** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.86 (m, 1H), 7.34 (td, *J* = 7.5, 1.3 Hz, 1H), 7.22 – 7.20 (m, 2H), 6.25 (t, *J* = 6.6 Hz, 1H), 3.36 – 3.33 (m, 2H), 3.21 – 3.19 (m, 2H), 2.85 – 2.81 (m, 2H), 2.62 (s, 3H), 2.43 – 2.41

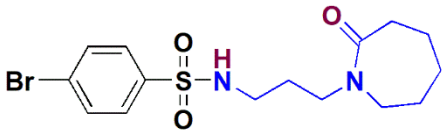
(m, 2H), 1.66 – 1.59 (m, 3H), 1.57 – 1.51 (m, 5H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 177.08, 138.87, 137.24, 132.28, 129.02, 127.12, 125.91, 49.63, 44.87, 39.43, 36.98, 29.89, 28.36, 27.93, 23.33, 20.29. **HRMS (ESI):** Mass calcd for $C_{16}H_{24}N_2O_3SH$ $[M+H]^+$: 325.1586; found: 325.1607.

4-Chloro-N-(3-(2-oxoazepan-1-yl)propyl)benzenesulfonamide (11d):



Transparent oil (58 mg, 85%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.69 – 7.67 (m, 2H), 7.57 – 7.54 (m, 2H), 6.37 (t, *J* = 6.5 Hz, 1H), 3.37 – 3.35 (m, 2H), 3.21 – 3.19 (m, 2H), 2.80 – 2.76 (m, 2H), 2.40 – 2.38 (m, 2H), 1.65 – 1.60 (m, 4H), 1.53 – 1.48 (m, 4H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 177.25, 139.58, 132.12, 128.74, 127.06, 49.72, 44.83, 39.49, 36.87, 29.86, 28.33, 27.50, 23.24. **HRMS (ESI):** Mass calcd for $C_{15}H_{21}ClN_2O_3SH$ $[M+H]^+$: 345.1040; found: 345.1057.

4-Bromo-N-(3-(2-oxoazepan-1-yl)propyl)benzenesulfonamide (11e):



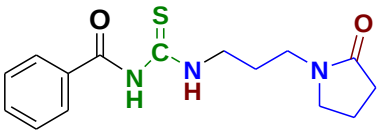
Transparent oil (63 mg, 81%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.76 – 7.73 (m, 2H), 7.63 – 7.61 (m, 2H), 6.45 (t, *J* = 6.6 Hz, 1H), 3.44 – 3.41 (m, 2H), 3.27 – 3.25 (m, 2H), 2.87 – 2.83 (m, 2H), 2.47 – 2.45 (m, 2H), 1.72 – 1.66 (m, 4H), 1.60 – 1.54 (m, 4H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 177.19, 139.59, 132.11, 128.74, 127.05, 49.70, 44.79, 39.47, 36.90, 29.86, 28.35, 27.49, 23.25. **HRMS (ESI):** Mass calcd for $C_{15}H_{21}BrN_2O_3SH$ $[M+H]^+$: 389.0535; found: 389.0561.

6. General procedure for synthesis of aroyl thiourea (14) and amides (15, 16) derivatives with distal cyclic amides functionality.

To a 15 ml vile, aroyl chloride **12** (0.5 mmol, 1 equiv) and KSCN **3** (1.2 equiv) was added and stirred at RT for 1 h. After 1 hr the temperature was increased to 60 °C with subsequent addition of DBN **5** or DBU **6** (1.2 equiv). The reaction mixture was stirred for another 15 minutes and cooled. The compound was extracted with ethyl acetate after washing with water. After drying the organic layer and rotary evaporation the target compounds were purified with column chromatography with 80-90% (DBN as nucleophile) and 80% (DBU as nucleophile) ethyl

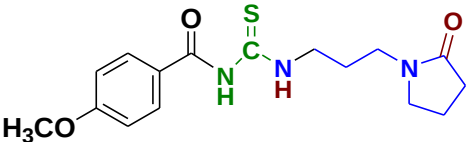
acetate/hexane as mobile phase. All the new compounds were characterized via ^{1}HNMR, ^{13}CNMR and HRMS spectroscopy (Note: Compound 16b is earlier reported and only ^{1}HNMR and ^{13}CNMR spectra were attached.[2])

1-Benzoyl-3-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-thiourea (14a):



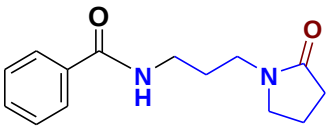
Transparent viscous oil (65 mg, 43%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 10.95 (s, 1H), 9.02 (s, 1H), 7.87 – 7.85 (m, 2H), 7.63 – 7.60 (m, 1H), 7.52 – 7.44 (m, 2H), 3.74 (q, *J* = 6.7 Hz, 2H), 3.46 – 3.39 (m, 4H), 2.43 (t, *J* = 8.2 Hz, 2H), 2.09 – 2.03 (m, 2H), 1.96 (dd, *J* = 13.3, 6.7 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 180.01, 175.73, 166.47, 133.48, 131.82, 129.08, 127.51, 47.37, 43.04, 40.06, 30.85, 25.90, 18.01. Mass calcd for $C_{15}H_{19}N_3O_2SNa$ $[M+Na]^+$: 328.1096; found: 328.1123.

1-(4-Methoxy-benzoyl)-3-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-thiourea (14b):



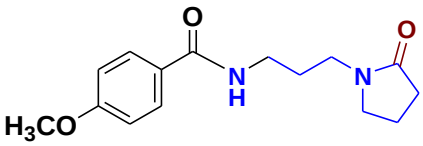
Transparent viscous oil (70 mg, 42%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 10.99 (s, 1H), 8.96 (s, 1H), 7.84 – 7.81 (m, 2H), 6.99 – 6.96 (m, 2H), 3.88 (s, 3H), 3.73 (q, *J* = 6.7 Hz, 2H), 3.46 – 3.39 (m, 4H), 2.43 (t, *J* = 8.1 Hz, 2H), 2.05 (dd, *J* = 15.3, 7.6 Hz, 2H), 1.96 – 1.94 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 180.16, 175.68, 165.92, 163.83, 129.68, 123.74, 114.33, 55.59, 47.36, 43.01, 40.07, 30.86, 25.95, 18.01. Mass calcd for $C_{16}H_{21}N_3O_3SNa$ $[M+Na]^+$: 358.1201; found: 358.1232.

N-[3-(2-Oxo-pyrrolidin-1-yl)-propyl]-benzamide (15a):



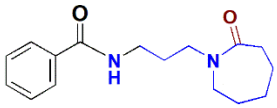
White semisolid (55 mg, 45%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.94 – 7.92 (m, 2H), 7.81 (s, 1H), 7.49 – 7.42 (m, 3H), 3.44 – 3.39 (m, 6H), 2.46 – 2.43 (m, 2H), 2.11 – 2.06 (m, 2H), 1.80 – 1.77 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 176.35, 167.09, 134.35, 131.28, 128.49, 127.09, 47.47, 39.58, 35.57, 30.90, 26.21, 17.95. Mass calcd for $C_{14}H_{18}N_2O_2Na$ $[M+Na]^+$: 269.1266; found: 269.1295.

4-Methoxy-N-[3-(2-oxo-pyrrolidin-1-yl)-propyl]-benzamide (15b):



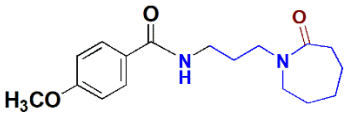
White semisolid (59 mg, 43%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.91 – 7.88 (m, 2H), 7.70 (s, 1H), 6.95 – 6.92 (m, 2H), 3.84 (s, 3H), 3.44 – 3.38 (m, 6H), 2.45 (t, *J* = 8.1 Hz, 2H), 2.10 – 2.04 (m, 2H), 1.78 (dq, *J* = 12.0, 6.0 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 176.31, 166.70, 162.04, 128.90, 126.78, 113.67, 55.35, 47.45, 39.58, 35.49, 30.92, 26.21, 17.95. Mass calcd for $C_{15}H_{20}N_2O_2Na$ $[M+Na]^+$: 299.1372; found: 299.1400.

N-[3-(2-Oxo-azepan-1-yl)-propyl]-benzamide (16a):



White semisolid (122 mg, 87%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.97 (s, 1H), 7.94 – 7.91 (m, 2H), 7.48 – 7.41 (m, 3H), 3.53 – 3.50 (m, 2H), 3.42 (dd, *J* = 11.9, 6.1 Hz, 2H), 3.37 – 3.35 (m, 2H), 2.60 – 2.57 (m, 2H), 1.77 – 1.66 (m, 8H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 176.36, 167.07, 134.37, 131.27, 128.49, 127.09, 47.46, 44.25, 39.55, 35.52, 30.90, 29.70, 26.19, 17.97. **HRMS (ESI):** Mass calcd for $C_{16}H_{23}N_2O_2H$ $[M+H]^+$: 275.1760; found: 275.1774.

4-Methoxy-N-[3-(2-oxo-azepan-1-yl)-propyl]-benzamide (16b):



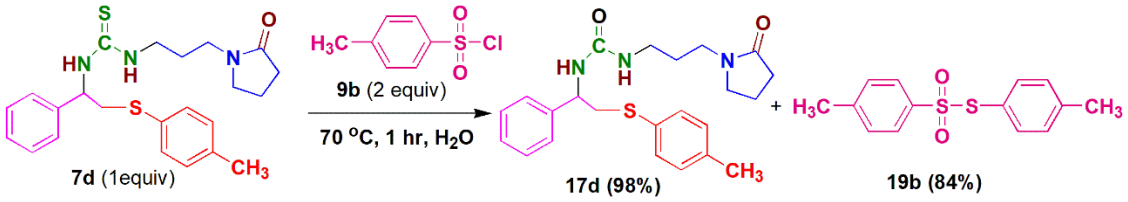
White semisolid (131 mg, 86%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.84 – 7.80 (m, 3H), 6.86 – 6.84 (m, 2H), 3.75 (s, 3H), 3.44 – 3.41 (m, 2H), 3.32 (dd, *J* = 11.9, 6.1 Hz, 2H), 3.28 – 3.26 (m, 2H), 2.51 – 2.48 (m, 2H), 1.68 – 1.58 (m, 8H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 177.26, 166.56, 161.92, 128.85, 126.95, 113.61, 55.31, 49.55, 44.99, 37.10, 35.31, 29.89, 28.33, 27.09, 23.41.

7. Conversion of β-thiouredo sulfides to β-uredo sulfide derivatives.

In a 15 ml vial containing β-thiouredo sulfide **7d** (43 mg, 0.1 mmol, 1 equiv) was added tosyl chloride **9b**. Further varied solvents were evaluated for β-thiouredo sulfide to β-uredo sulfide

transformation by stirring at different temperature conditions. Completion of reaction was confirmed from TLC. After completion of reaction the solvent was rotary-evaporated and the compound was extracted with ethyl acetate upon washing with water. The organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure. The compound was then purified with 75% ethyl acetate/hexane solvent using silica gel column chromatography. The product was elucidated with NMR and HRMS spectroscopy.

Table S5: Evaluation of sulfonyl chloride equivalents, solvent, temperature and reaction time conditions for β-thiouredo sulfides to β-uredo sulfides transformations



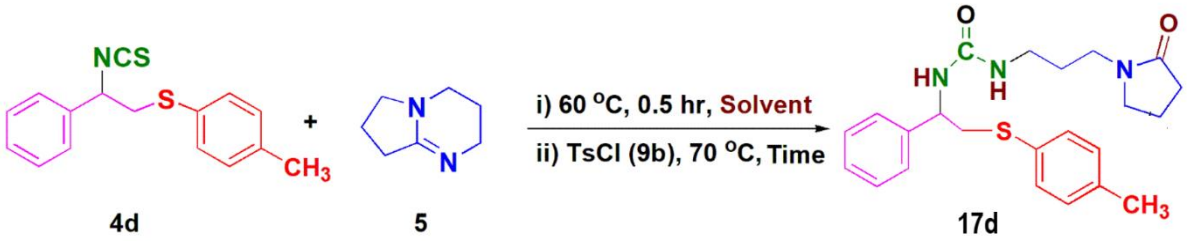
Sr. No.	Tosyl chloride (9b) equiv	Solvent	Temp (°C)	Time (hr)	% Yield 17d	% Yield 19b
1.	1	H_2O	60	3	20	Trace
2.	1	THF	60	3	No conversion	No conversion
3.	1	Ethyl acetate	60	3	No conversion	No conversion
4.	1	Toluene	60	3	No conversion	No conversion
5.	1	DCE	60	7	22	trace
6.	1	H_2O	65	3	32	trace
7.	1	H_2O	70	2	43	20
8.	1	H_2O	75	2	43	18
9.	1.2	H_2O	70	2	44	20
10.	1.5	H_2O	70	2	62	45
11.	2.0	H_2O	70	1	98	84
12.	2.5	H_2O	70	1	97	84
13.	2	DCE	70	10	94	81

7d (0.1 mmol, 1equiv), Note-The reaction was stirred till the reactant conversion ceased or reactant spot completely disappears from TLC.

8. One pot approach for β-uredo sulfide 17d from β-isothiocyanato sulfide 4d.

β-isothiocyanato sulfide **4d** (29 mg, 0.1 mmol, 1 equiv) containing in a 15 ml vial was added DBN (0.12 mmol, 1.2 equiv) solution in 1 ml water or DCE. Then the reaction mixture was stirred at 60 °C for 0.5 hr. After this tosyl chloride (0.2 mmol, 2 equiv) was added and the temperature of reaction was increased to 70 °C. Subsequent stirring with constant monitoring using TLC results in reaction completion. The reaction mixture was cooled to room temperature. Later the product was washed with water and extracted with ethyl acetate. The ethyl acetate containing product was dried over anhydrous sodium sulphate and filtered. After rota evaporating the ethyl acetate, the product was extracted using silica gel chromatography with 75% ethyl acetate/hexane as mobile phase.

Table S6: Evaluation of solvent and reaction time for *in-situ* conversion of β-thiouredo sulfides to β-uredo sulfides.



4d 5 17d

Sr. No.	Solvent	Temp (°C)	Time (hr)	% Yield 17d
1.	H_2O	70	1.5	94
2.	DCE	70	10	92

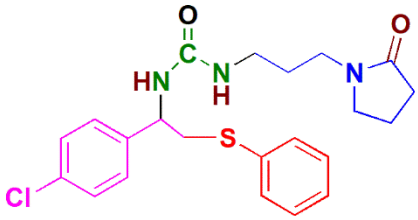
4b (0.1 mmol, 1 equiv), **5** (1.2 equiv), **9b** (2 equiv)

9. General procedure for β-uredo sulfides derivatives 17 and 18 from β-isothiocyanato sulfides 4.

In a 15 ml vial containing β-isothiocyanato sulfide **4** (0.1 mmol, 1 equiv) and stir bar was added DBN or DBU (0.12 mmol, 1.2 equiv) solution in 1 ml water. Then the reaction mixture was stirred at 60 °C for 0.5 hr. After this tosyl chloride (0.2 mmol, 2 equiv) was added and the temperature of reaction was increased to 70 °C with constant stirring for 1 hr. After completion the reaction mixture was cooled to room temperature. This was followed with the extraction of

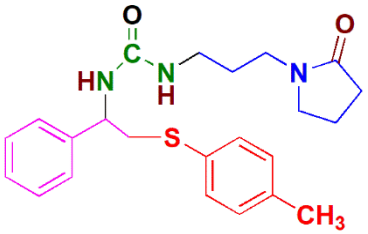
product was with ethyl acetate and washing with water. The organic layer was collected and dried over anhydrous sodium sulphate. After filtration and rota evaporating the ethyl acetate, the product was extracted using silica gel chromatography with 75% or 85% ethyl acetate/hexane solution.

1-(1-(4-Chlorophenyl)-2-(phenylthio)ethyl)-3-(3-(2-oxopyrrolidin-1-yl)propyl)urea (17c):



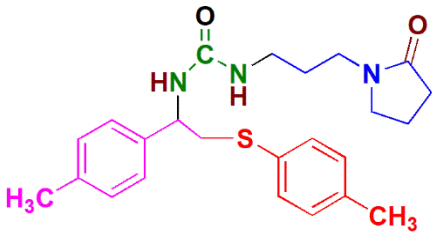
White semisolid (39 mg, 90%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.34 – 7.32 (m, 2H), 7.28 – 7.27 (m, 1H), 7.26-7.25 (m, 3H), 7.24 – 7.22 (m, 2H), 7.19 – 7.16 (m, 1H), 5.61 (s, 1H), 5.29 (d, *J* = 6.05 Hz, 1H), 4.95 (q, *J* = 6.5 Hz, 1H), 3.37 – 3.34 (m, 2H), 3.33 – 3.31 (m, 1H), 3.28 (t, *J* = 6.2 Hz, 2H), 3.25-3.21 (m, 1H), 3.14-3.06 (m, 2H), 2.39 (td, *J* = 7.8, 1.9 Hz, 2H), 2.06 – 2.01 (m, 2H), 1.66 – 1.60 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 175.90, 157.37, 140.20, 135.50, 133.24, 129.92, 129.03, 128.71, 128.04, 126.46, 53.19, 47.35, 40.79, 39.51, 36.32, 30.97, 26.85, 17.88. **HRMS (ESI):** Mass calcd for $C_{22}H_{26}ClN_3O_2SH$ $[M+H]^+$: 432.1513; found: 432.1516.

1-(2-(p-Tolylthio)-1-phenylethyl)-3-(3-(2-oxopyrrolidin-1-yl)propyl)urea (17d):



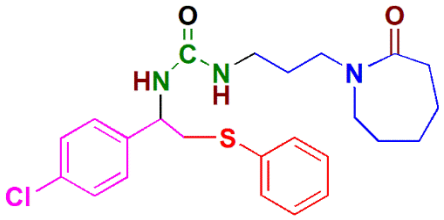
White semisolid (39 mg, 94%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.32 – 7.27 (m, 5H), 7.25 – 7.22 (m, 2H), 7.07 (d, *J* = 7.95 Hz, 2H), 5.46 (s, 1H), 5.11 (d, *J* = 6.05 Hz, 1H), 4.91 (q, *J* = 6.6 Hz, 1H), 3.35 (t, *J* = 7.1 Hz, 2H), 3.31 – 3.21 (m, 4H), 3.15 – 3.07 (m, 2H), 2.38 (td, *J* = 7.9, 2.6 Hz, 2H), 2.30 (s, 3H), 2.02 (tt, *J* = 13.9, 6.9 Hz, 2H), 1.63 – 1.60 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 176.09, 157.91, 141.06, 135.70, 129.87, 129.00, 128.70, 127.76, 126.65, 126.37, 54.16, 47.59, 40.80, 39.73, 36.95, 30.98, 29.70, 27.22, 17.89. **HRMS (ESI):** Mass calcd for $C_{23}H_{29}N_3O_2SH$ $[M+H]^+$: 412.2059; found: 412.2077.

1-(2-(p-Tolylthio)-1-p-tolylethyl)-3-(3-(2-oxopyrrolidin-1-yl)propyl)urea (17i):



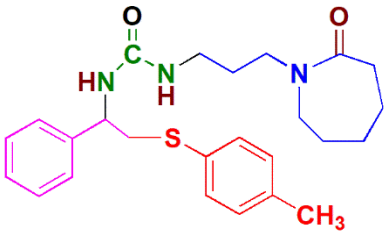
White semisolid (41 mg, 96%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.27 (d, *J* = 1.8 Hz, 1H), 7.25 (d, *J* = 2.2 Hz, 1H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 7.9 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 5.43 (s, 1H), 5.12 (d, *J* = 6.2 Hz, 1H), 4.87 (q, *J* = 6.5 Hz, 1H), 3.35 (t, *J* = 7.1 Hz, 2H), 3.31 – 3.25 (m, 3H), 3.22 – 3.18 (m, 1H), 3.11 – 3.10 (m, 2H), 2.40 – 2.36 (m, 2H), 2.31 (s, 3H), 2.30 (s, 3H), 2.04 – 1.98 (m, 2H), 1.63 – 1.59 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 175.77, 157.47, 138.57, 137.22, 136.42, 132.02, 130.51, 129.75, 129.32, 126.49, 53.53, 47.32, 41.55, 39.57, 36.47, 30.96, 26.94, 21.10, 21.02, 17.90. **HRMS (ESI):** Mass calcd for $C_{24}H_{31}N_3O_2SH$ $[M+H]^+$: 426.2215; found: 426.2231.

1-(1-(4-Chlorophenyl)-2-(phenylthio)ethyl)-3-(3-(2-oxoazepan-1-yl)propyl)urea (18c):



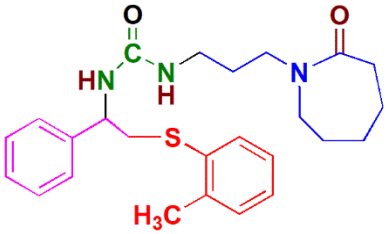
White semisolid (42 mg, 91%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.34 –7.33 (m, 2H), 7.27 – 7.22 (m, 6H), 7.19 – 7.16 (m, 1H), 5.81 (s, 1H), 5.17 (s, 1H), 4.95 (d, *J* = 5.0 Hz, 1H), 3.39 – 3.36 (m, 2H), 3.34 – 3.29 (m, 3H), 3.24 – 3.20 (m, 1H), 3.15 – 3.08 (m, 2H), 2.52 – 2.50 (m, 2H), 1.76 – 1.72 (m, 2H), 1.67 – 1.57 (m, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 174.44, 157.11, 142.55, 135.11, 132.40, 129.55, 128.72, 128.12, 126.89, 126.54, 52.56, 48.40, 44.82, 36.70, 36.45, 29.12, 28.51, 28.26, 22.95, 20.40. **HRMS (ESI):** Mass calcd for $C_{24}H_{30}ClN_3O_2SH$ $[M+H]^+$: 460.1826; found: 460.1838.

1-(2-(p-Tolylthio)-1-phenylethyl)-3-(3-(2-oxoazepan-1-yl)propyl)urea (18d):



White semisolid (41 mg, 93%). **^{1}H NMR (500 MHz, DMSO)** δ 7.34 – 7.28 (m, 4H), 7.26 – 7.23 (m, 3H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.61 (d, *J* = 8.3 Hz, 1H), 5.93 (t, *J* = 5.8 Hz, 1H), 4.79 (q, *J* = 7.65 Hz, 1H), 3.32 – 3.30 (m, 2H), 3.29 – 3.23 (m, 3H), 3.21 – 3.17 (m, 1H), 2.98 – 2.91 (m, 2H), 2.42 – 2.38 (m, 2H), 2.27 (s, 3H), 1.65 – 1.62 (m, 2H), 1.55 – 1.47 (m, 6H). **^{13}C NMR (126 MHz, DMSO)** δ 176.75, 157.47, 138.62, 137.16, 136.35, 132.10, 130.47, 129.73, 129.29, 126.54, 53.50, 49.53, 45.04, 41.48, 37.20, 36.23, 29.94, 28.40, 27.73, 23.41, 21.10. **HRMS (ESI):** Mass calcd for $C_{25}H_{33}N_3O_2SH$ $[M+H]^+$: 440.2372; found: 440.2378.

1-(2-(o-Tolylthio)-1-phenylethyl)-3-(3-(2-oxoazepan-1-yl)propyl)urea (18g):



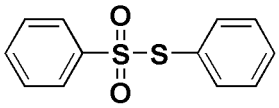
White semisolid (42 mg, 95%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.37 (d, *J* = 7.7 Hz, 1H), 7.31 – 7.27 (m, 4H), 7.26 – 7.22 (m, 1H), 7.13 (d, *J* = 7.1 Hz, 1H), 7.09 – 7.06 (m, 1H), 5.71 (t, *J* = 5.9 Hz, 1H), 5.17 (d, *J* = 6.8 Hz, 1H), 4.97 (q, *J* = 6.9 Hz, 1H), 3.38 – 3.34 (m, 2H), 3.33 – 3.28 (m, 3H), 3.25 – 3.21 (m, 1H), 3.17 – 3.09 (m, 2H), 2.52 – 2.50 (m, 2H), 2.32 (s, 3H), 1.74 – 1.72 (m, 3H), 1.68 – 1.66 (m, 2H), 1.64 – 1.58 (m, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 176.86, 157.47, 141.64, 138.07, 135.17, 130.11, 129.09, 128.59, 127.54, 126.65, 126.55, 126.09, 53.77, 49.54, 45.06, 40.17, 37.17, 36.20, 29.70, 28.38, 27.70, 23.40, 20.50. **HRMS (ESI):** Mass calcd for $C_{25}H_{33}N_3O_2SH$ $[M+H]^+$: 440.2372; found: 440.2390.

10. General procedure for β-thiouredo sulfide (7d) mediated transformation of sulfonyl chloride to thiosulfonates.

The mixture of sulfonyl chloride **9** (0.2 mmol, 2 equiv) and β-thiouredo sulfide **7d** (0.1 mmol, 1 equiv) in a 15 ml vial was added 1 ml water and stirred for 1 hr at 70 °C. After completion the reaction mixture was cooled and compound was extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated under vacuum. Finally, the

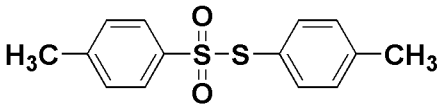
residue was purified with 8% ethyl acetate/hexane solvent system with silica gel column chromatography. All the synthesized derivatives **19a-e** were characterized via ^{1}H and ^{13}C NMR spectroscopy and their data were further reconfirmed from previous literature.[3]

S-phenyl benzenesulfonothioate (19a):



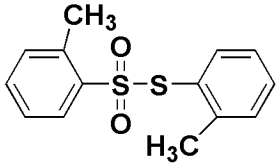
Transparent oil (22 mg, 87%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.79 – 7.77 (m, 1H), 7.71 – 7.69 (m, 1H), 7.57 (dd, *J* = 7.0, 1.7 Hz, 2H), 7.47 (ddt, *J* = 8.7, 6.9, 1.8 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.37 – 7.32 (m, 4H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 136.61, 133.62, 132.58, 131.41, 129.44, 129.32, 128.80, 127.58.

S-p-tolyl 4-methylbenzenesulfonothioate (19b):



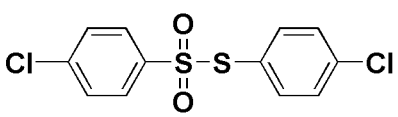
White solid (23 mg, 84%). Melting point: 74-76 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.46 (d, *J* = 8.3 Hz, 2H), 7.25 – 7.20 (m, 4H), 7.14 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H), 2.38 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 144.56, 142.04, 140.51, 136.51, 130.20, 129.36, 127.62, 124.63, 21.65, 21.48.

S-o-tolyl 2-methylbenzenesulfonothioate (19c):



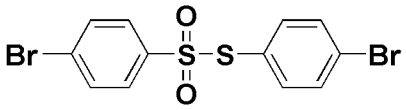
Transparent oil (22 mg, 83%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.47 – 7.46 (m, 2H), 7.25 – 7.21 (m, 4H), 7.14 (d, *J* = 7.9 Hz, 2H), 2.42 (s, 3H), 2.38 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 144.61, 144.56, 142.04, 140.52, 136.51, 130.70, 130.20, 129.94, 129.36, 129.07, 127.62, 124.63, 21.65, 21.47.

S-4-chlorophenyl 4-chlorobenzenesulfonothioate (19d):



White solid (27 mg, 84%). Melting point: 134-135 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.61 – 7.59 (m, 2H), 7.54 – 7.50 (m, 2H), 7.47 – 7.43 (m, 2H), 7.25 – 7.23 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 137.84, 132.94, 132.30, 129.20, 128.96, 127.04, 126.63, 124.32.

S-4-bromophenyl 4-bromobenzenesulfonothioate (19e):



White solid (34 mg, 83%). Melting point: 148-149 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.59 – 7.56 (m, 2H), 7.49 – 7.45 (m, 1H), 7.43 – 7.40 (m, 2H), 7.37 – 7.32 (m, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 143.00, 136.61, 133.62, 131.41, 129.44, 128.80, 127.87, 127.58.

11. Mechanistic studies:

11.1 Radical trapping experiment with TEMPO: To a 15 ml vial with a stir bar were added diphenyl disulphide **1** (0.1 mmol, 0.5 equiv), styrene **2a** (0.24 mmol, 1.2 equiv), potassium thiocyanate **3** (0.22 mmol,1.1 equiv), iodine (0.2 mmol, 1 equiv) and TEMPO (0.6 mmol, 3 equiv). This was followed with the addition of water (1 ml) and the reaction mixture was stirred in open atmosphere at 60 ^{0}C. The reaction was stirred and monitored with TLC. However constant TLC monitoring revealed no product formation till 5 hr. After completion the reaction mixture was submitted for HRMS and TEMPO adduct 20 was confirmed. **HRMS (ESI):** Mass calcd for $C_{24}H_{33}NOSH$ $[M+H]^+$: 384.2361; found: 384.2383.

11.2 Radical scavenging experiment with BHT: To a 15 ml vial with a stir bar were added diphenyl disulphide **1** (0.1 mmol, 0.5 equiv), styrene **2a** (0.24 mmol, 1.2 equiv), potassium thiocyanate **3** (0.22 mmol,1.1 equiv), iodine (0.2 mmol, 1 equiv) and BHT (0.4 mmol, 2 equiv). This was followed with the addition of water (1 ml) and the reaction mixture was stirred in open atmosphere at 60 ^{0}C. The reaction was stirred and monitored with TLC. After completion of reaction the saturated solution of sodium thiosulfate in water was added to the reaction mixture. The compound was extracted with ethyl acetate and dried over anhydrous sodium sulphate followed by filtration. Ethyl acetate was rota-evaporated under vacuum and the product of the reaction, β-isothiocyanato sulfide **4d** was purified using silica gel column chromatography with 2% ethyl acetate/hexane. The product was confirmed by NMR and HRMS spectroscopy.

11.3 Investigation for H_2O mediated ring opening of DBN: A two necked RBF containing stir bar was vacuum dried and N_2 was flushed in the system. β-isothiocyanato sulfide **4d** (0.1 mmol, 1 equiv) and DBN (0.12 mmol, 1.2 equiv) was added in the presence of N_2. Further, dried DCE (2 ml) was added to the RBF and stirred at 60 °C. The reaction progress was monitored with TLC. However, the reaction yields no poduct.

11.4 Investigation for role of H_2O in β-thiouredo sulfide to β-uredo sulfide conversion: Thiourea 7d (0.1 mmol, 1 equiv) was added to a vacuum dried two necked RBF containing stir bar. N_2 was flushed in the system followed by the addition of tosyl chloride **9b** (0.2 mmol, 2 equiv), dried DCE (2 ml) and stirred at 70 °C. The reaction progress was monitored with TLC. However, no transformation was obtained.

11.5 Investigations for β-thiouredo sulfide to β-uredo sulfide conversion in other sulfonyl sources

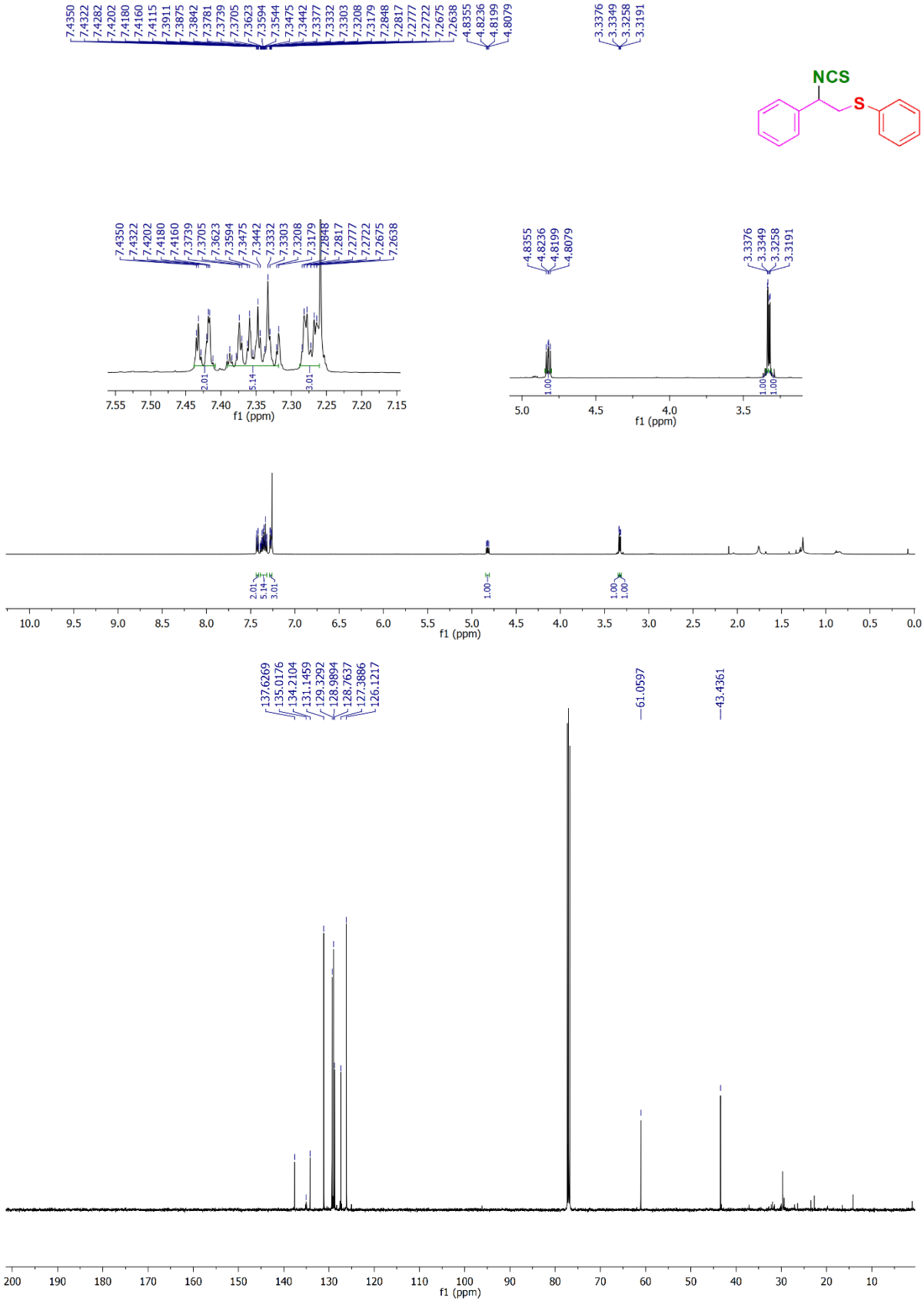
In a 15 ml vial containing thiourea 7d (0.1 mmol, 1 equiv) in 1 ml H_2O was added DMSO (SO_2Cl_2) or benzyl sulfonyl chloride ($PhCH_2SO_2Cl$) (0.2 mmol, 2 equiv). The reaction was stirred at 70 °C and progress of reaction was monitored by TLC. However, no product was obtained.

11.6 Investigations for β-thiouredo sulfide to β-uredo sulfide conversion in other sulfonyl sources

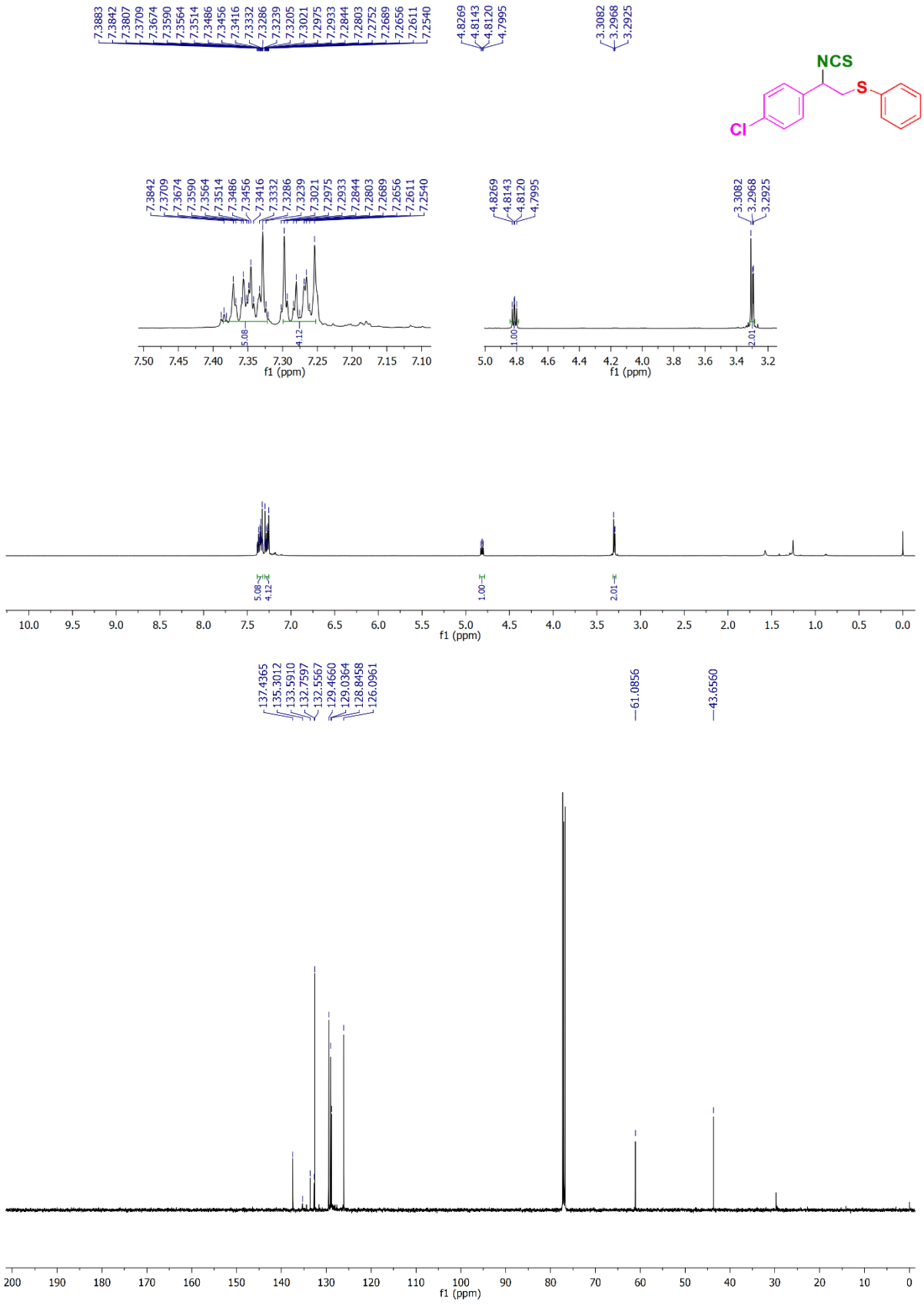
β-thiouredo sulfides **21** (0.1 mmol, 1 equiv) and tosyl chloride (0.2 mmol, 2 equiv) contained in 15 ml vial with magnetic stirred bar was added 1 ml H_2O. The reaction was stirred at 70 °C. However, TLC revealed no transformation till 5 hr.

12. ^{1}H and ^{13}C NMR Spectra

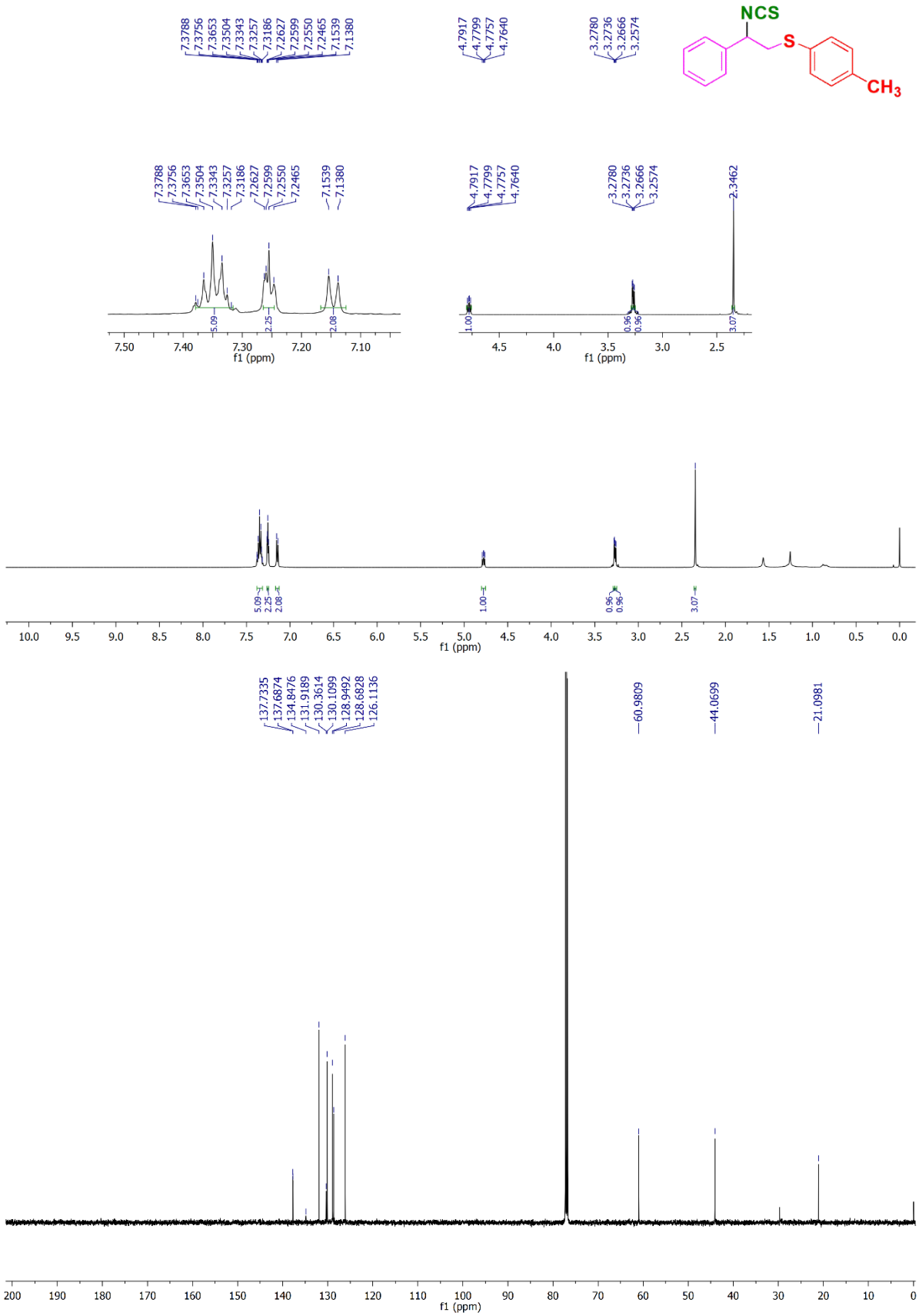
^{1}H and ^{13}C NMR for 4a



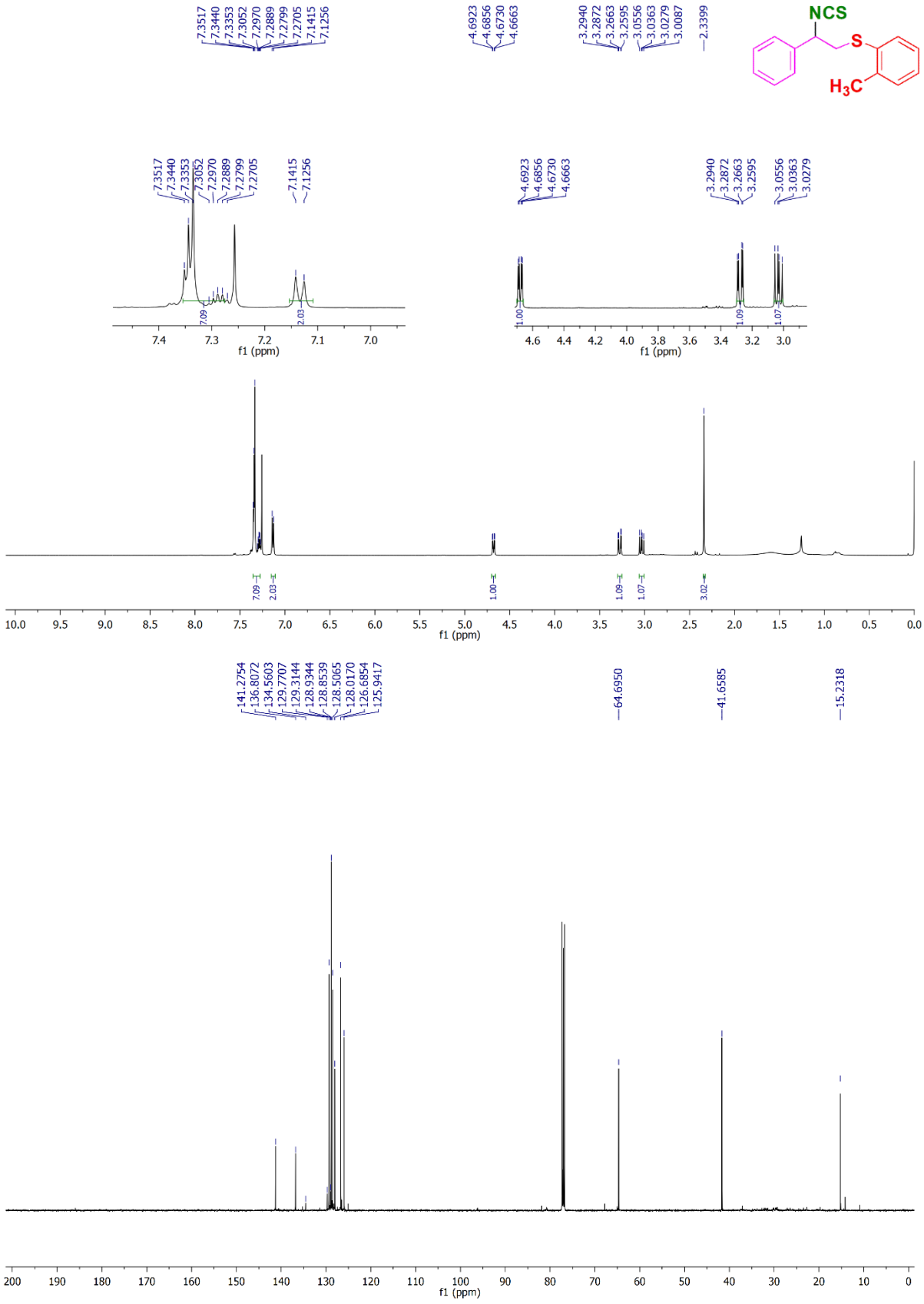
^{1}H and ^{13}C NMR for 4c



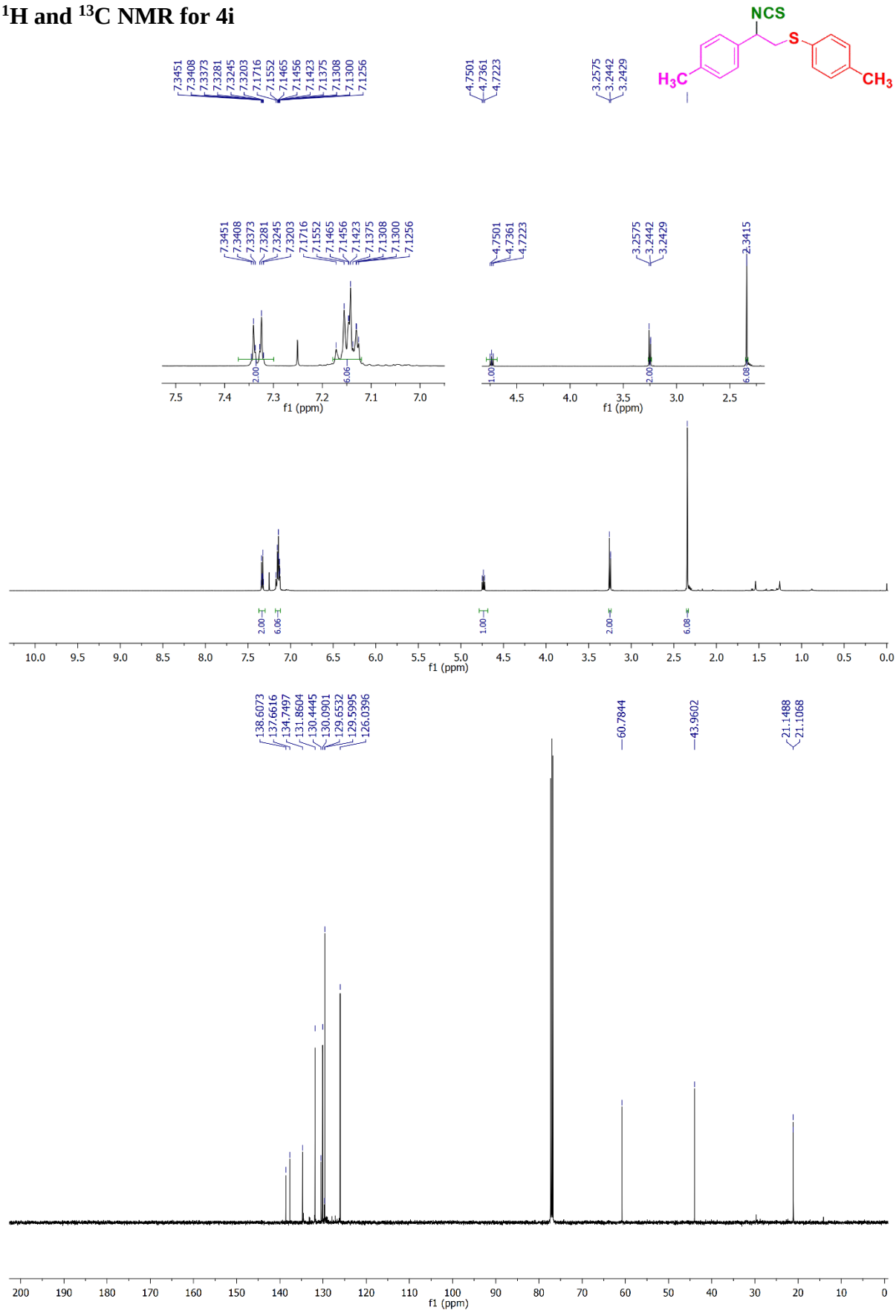
^{1}H and ^{13}C NMR for 4d



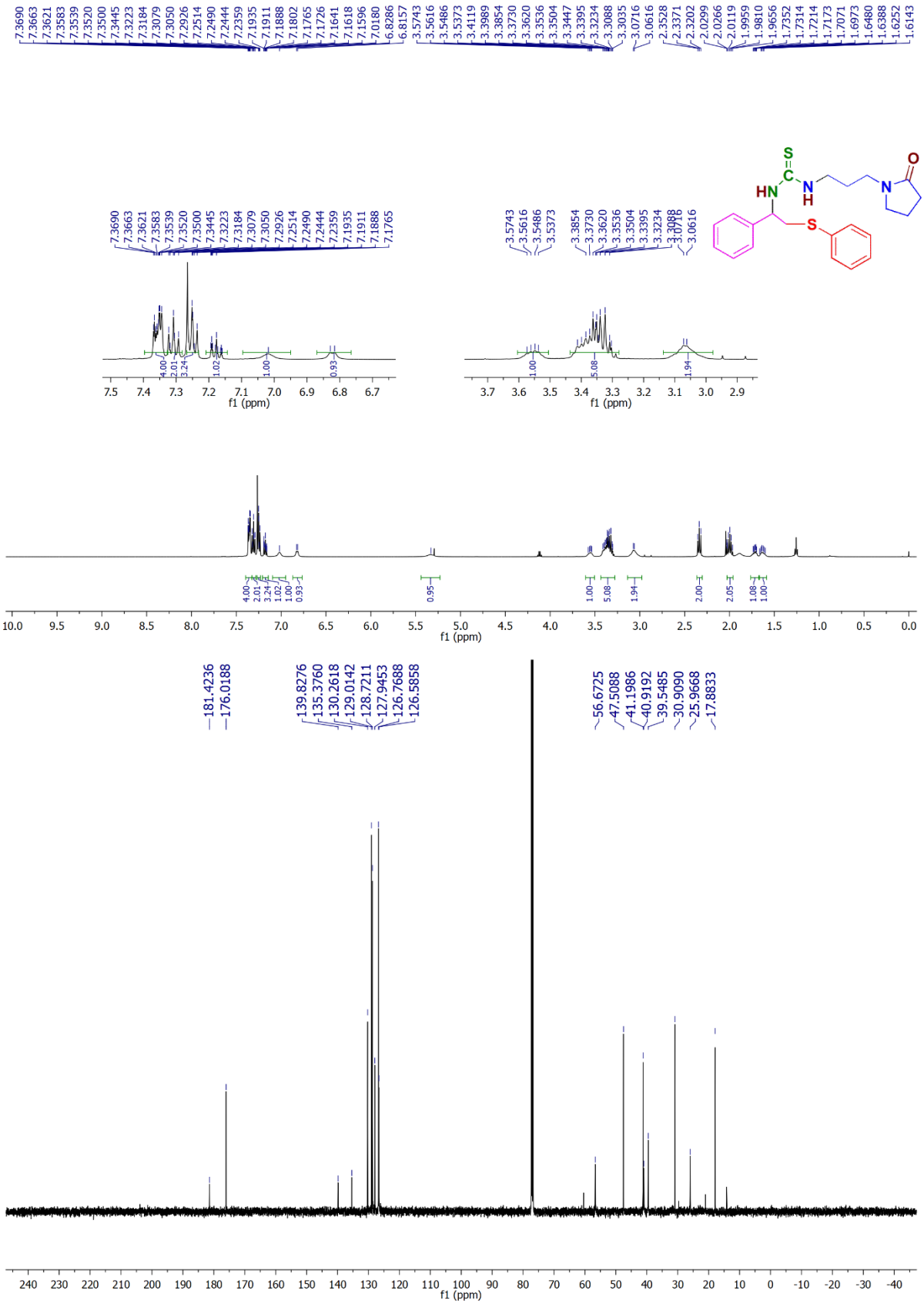
^{1}H and ^{13}C NMR for 4g



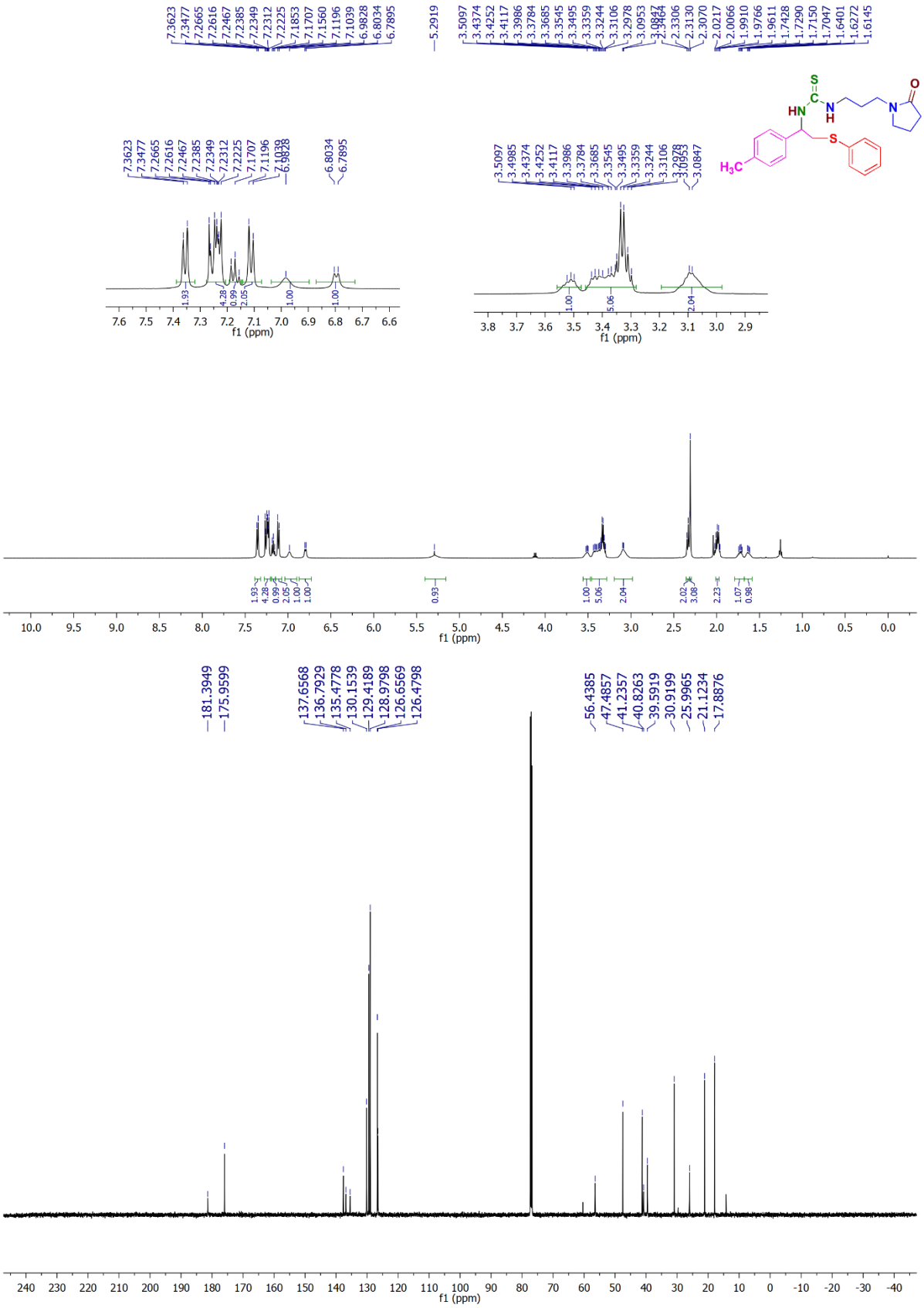
^{1}H and ^{13}C NMR for 4i



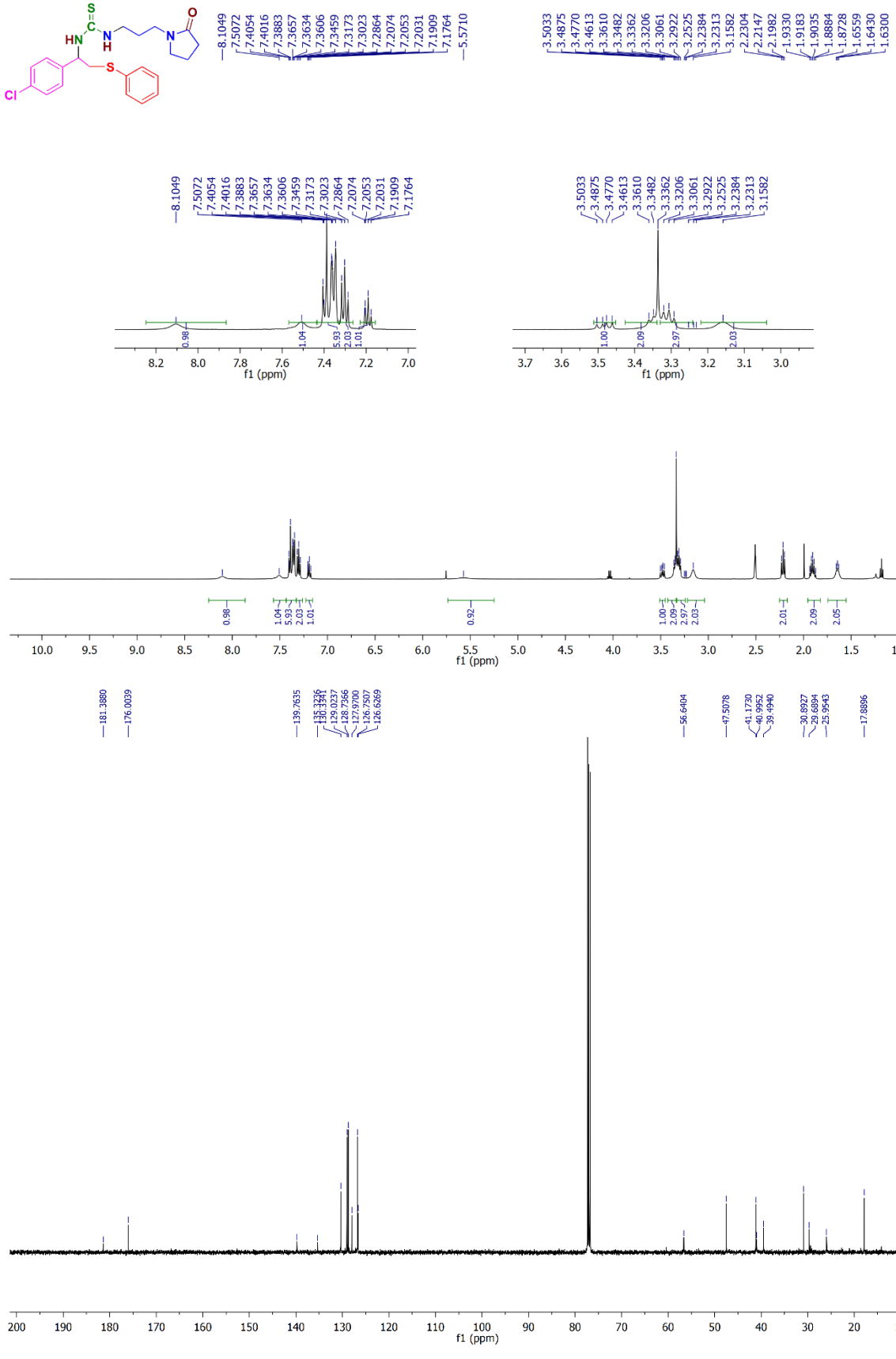
^{1}H and ^{13}C NMR for 7a



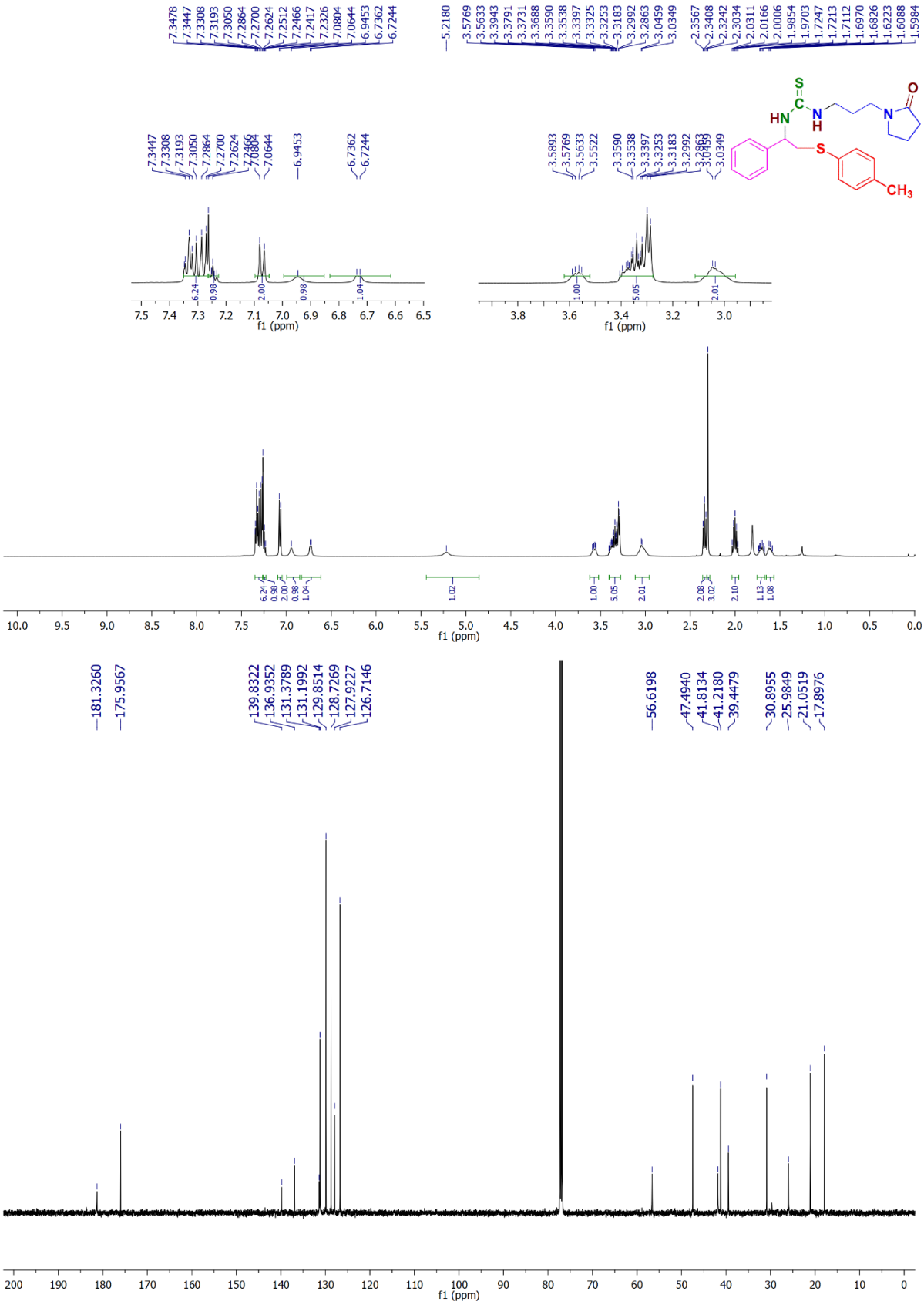
^{1}H and ^{13}C NMR for 7b



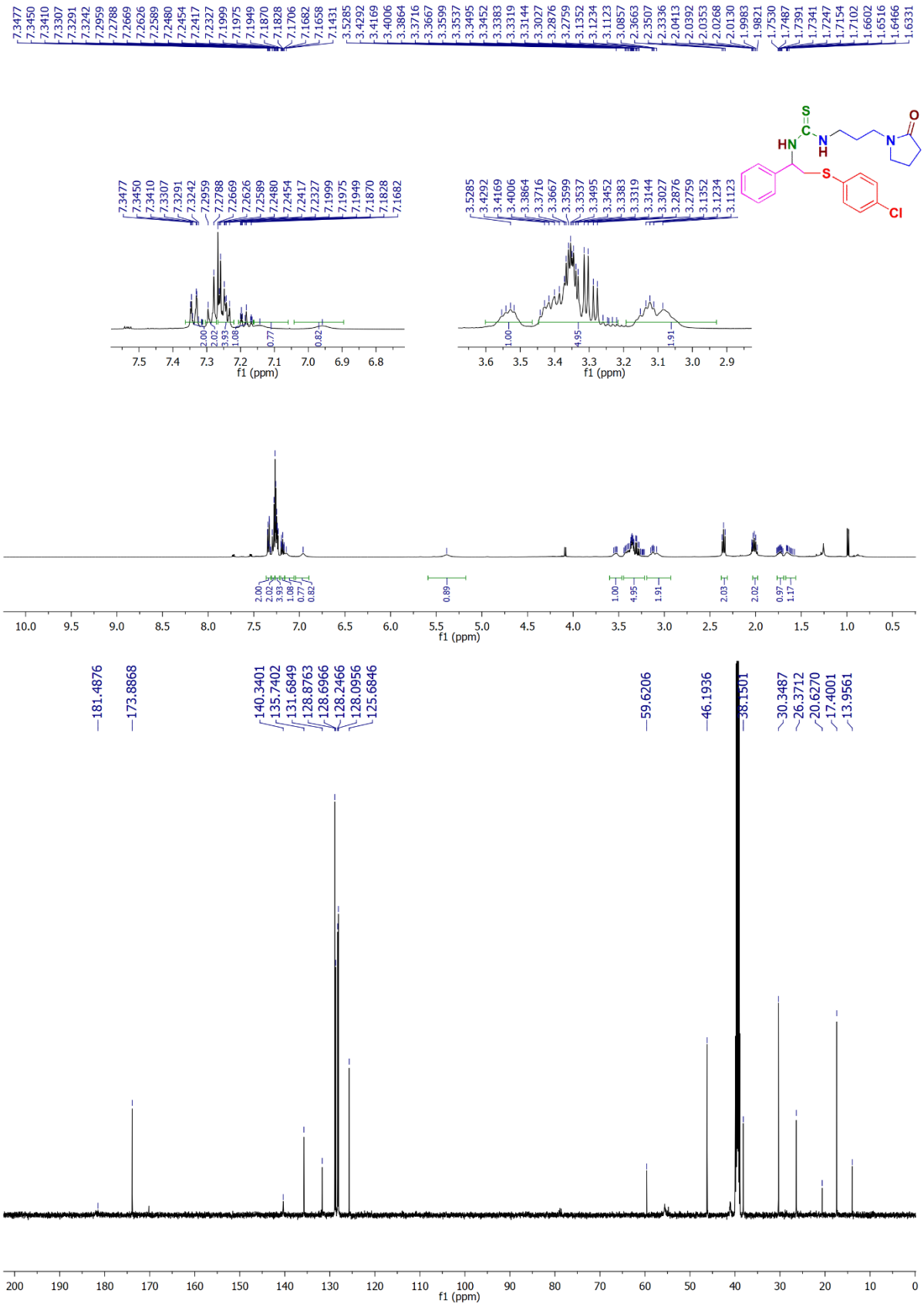
^{1}H and ^{13}C NMR for 7c



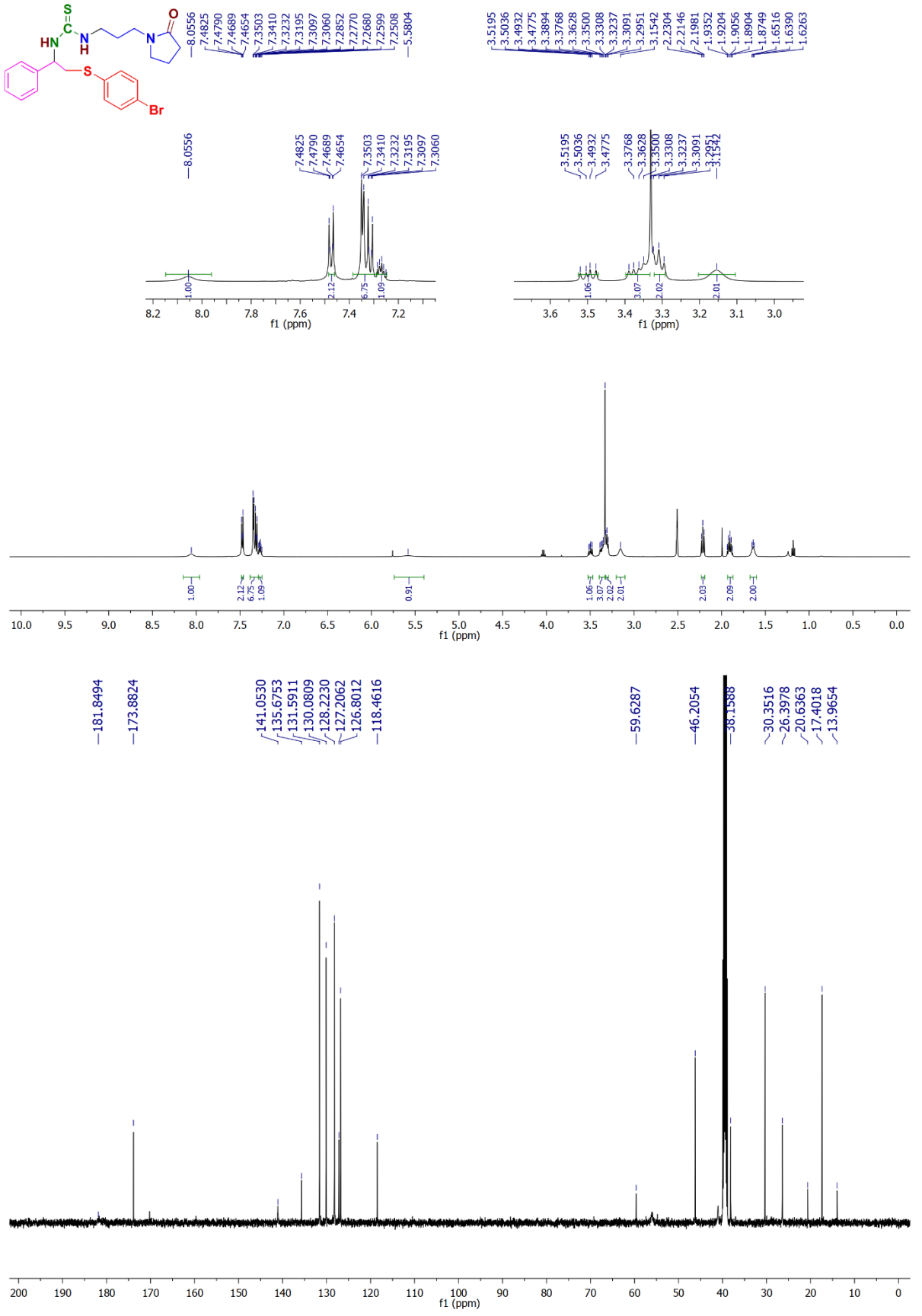
^{1}H and ^{13}C NMR for 7d



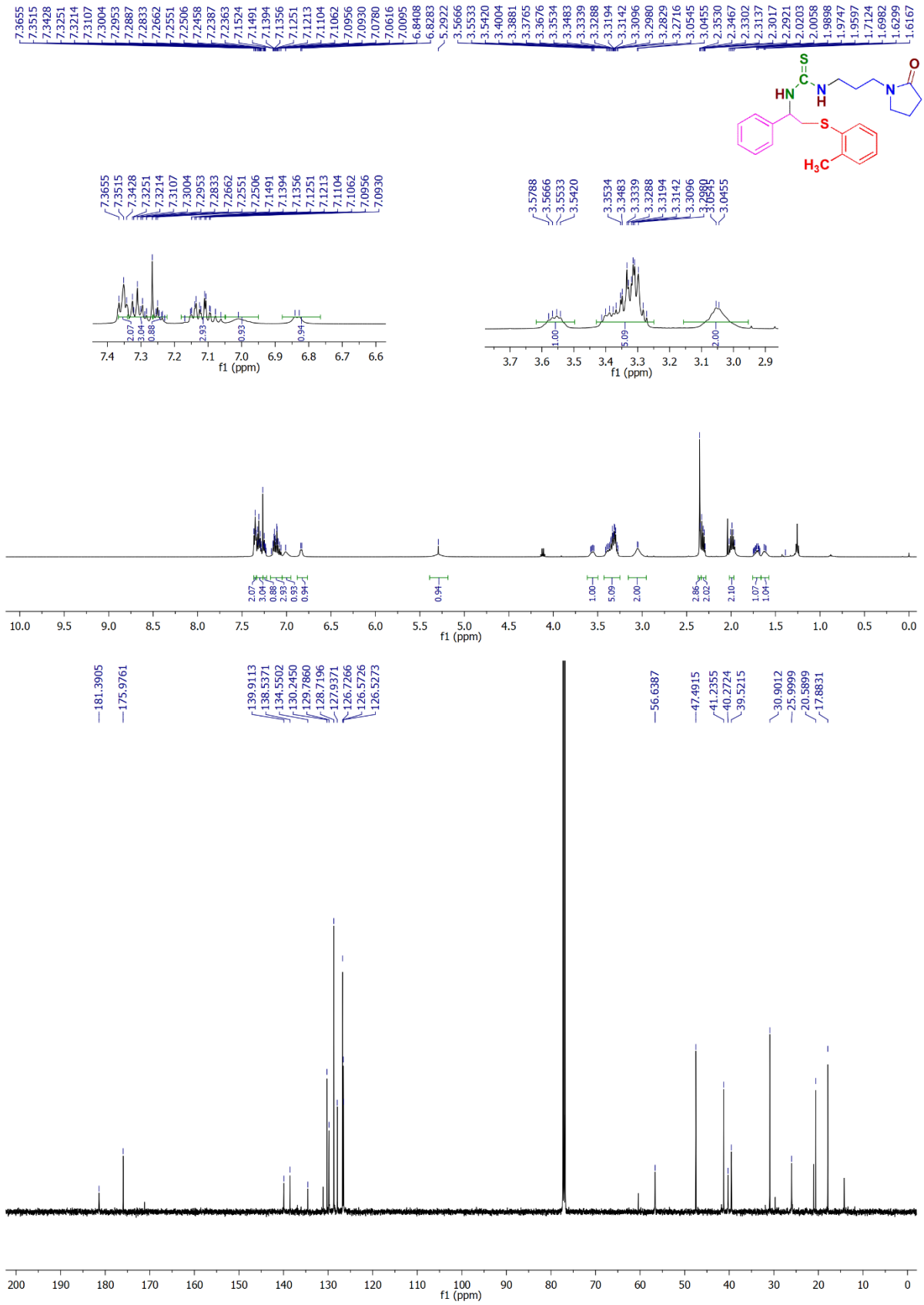
^{1}H and ^{13}C NMR for 7e



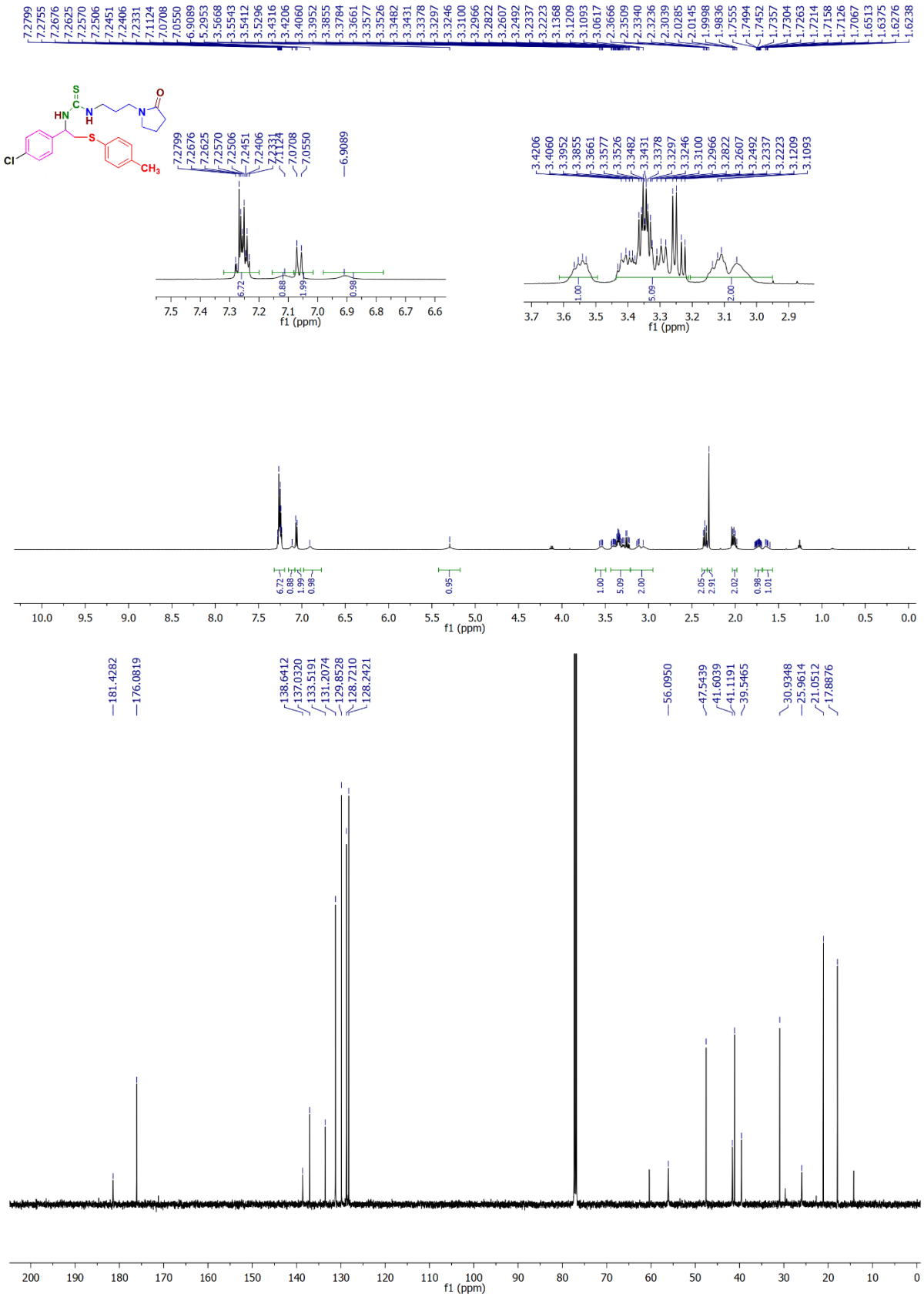
^{1}H and ^{13}C NMR for 7f



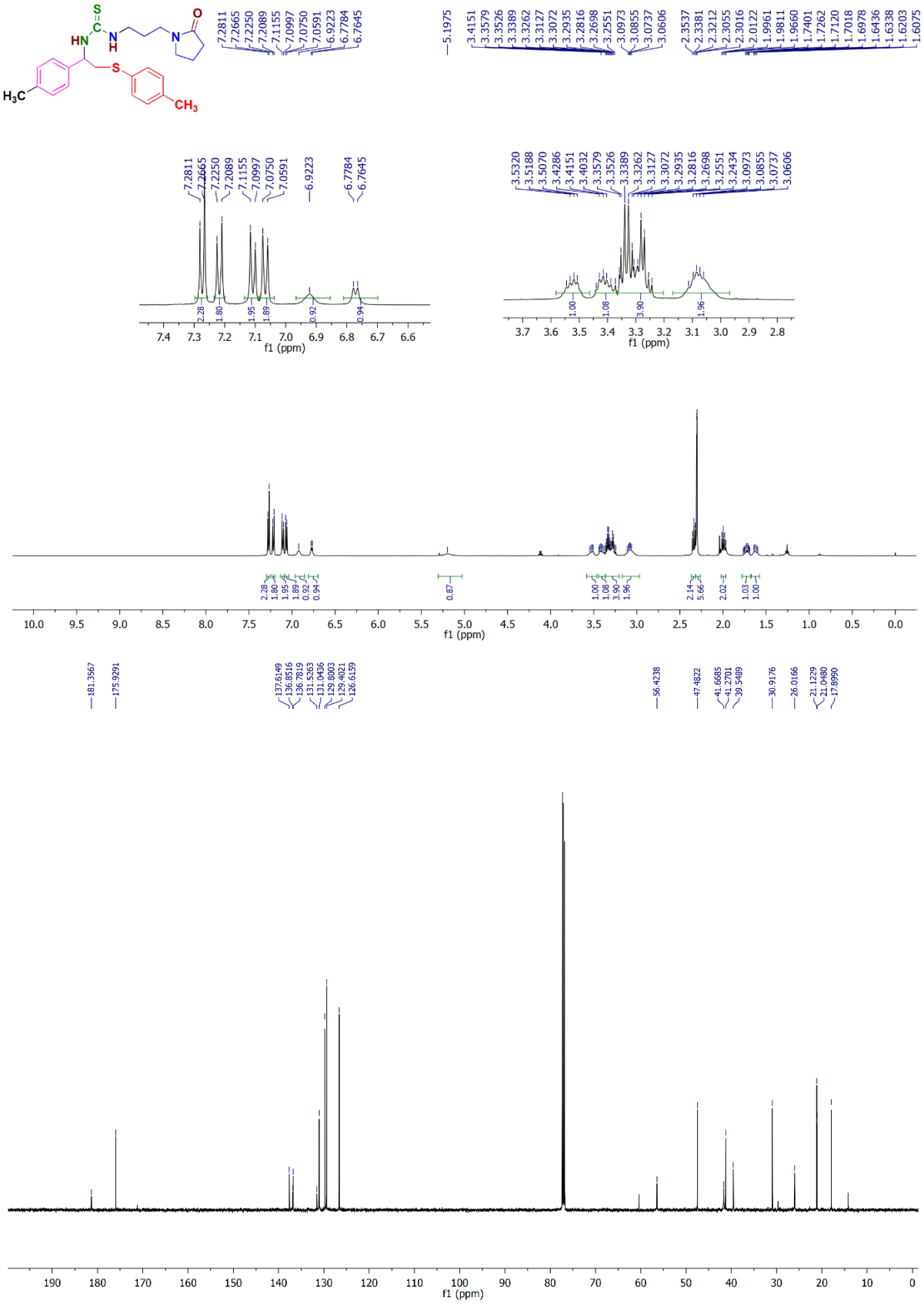
^{1}H and ^{13}C NMR for 7g



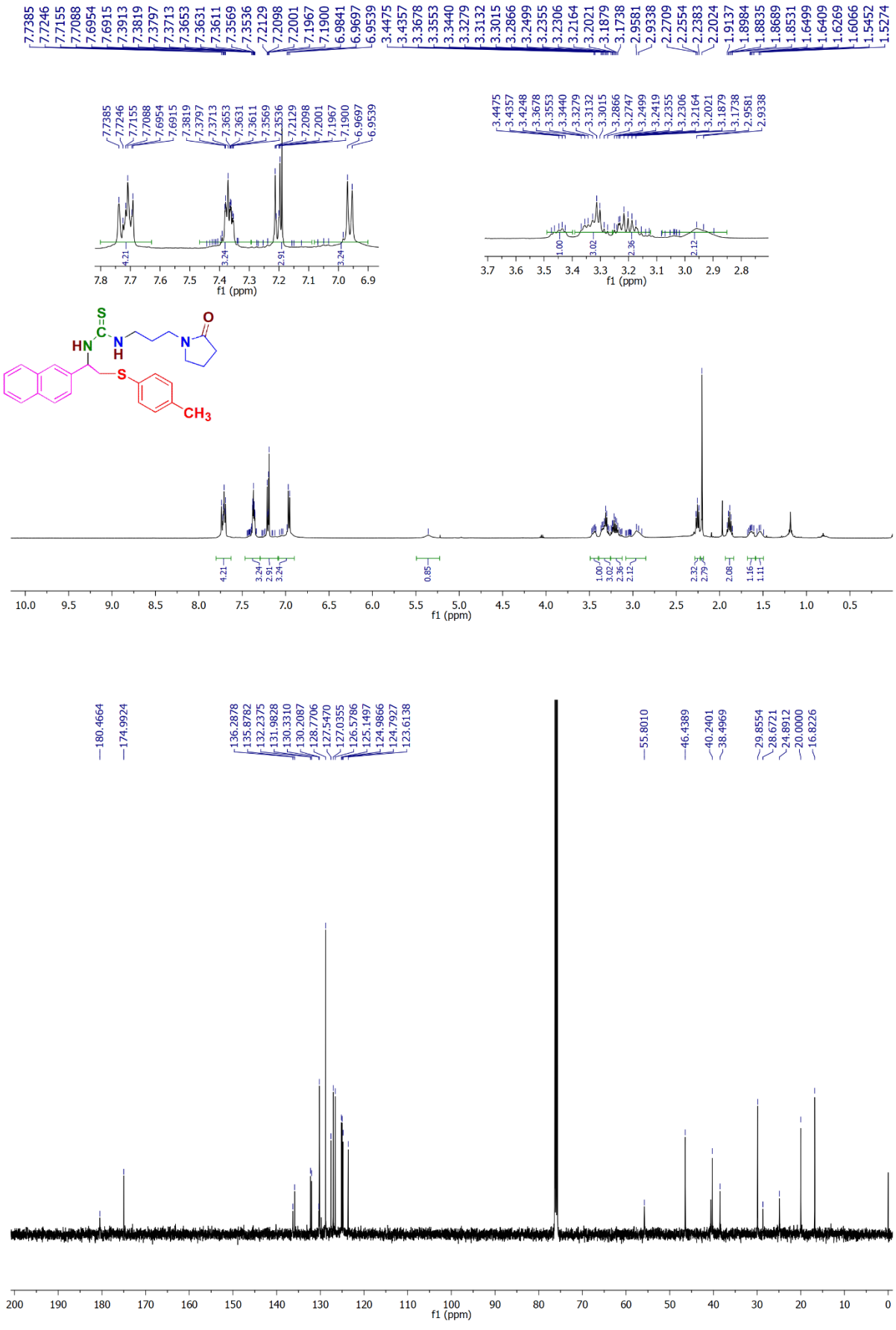
^{1}H and ^{13}C NMR for 7h



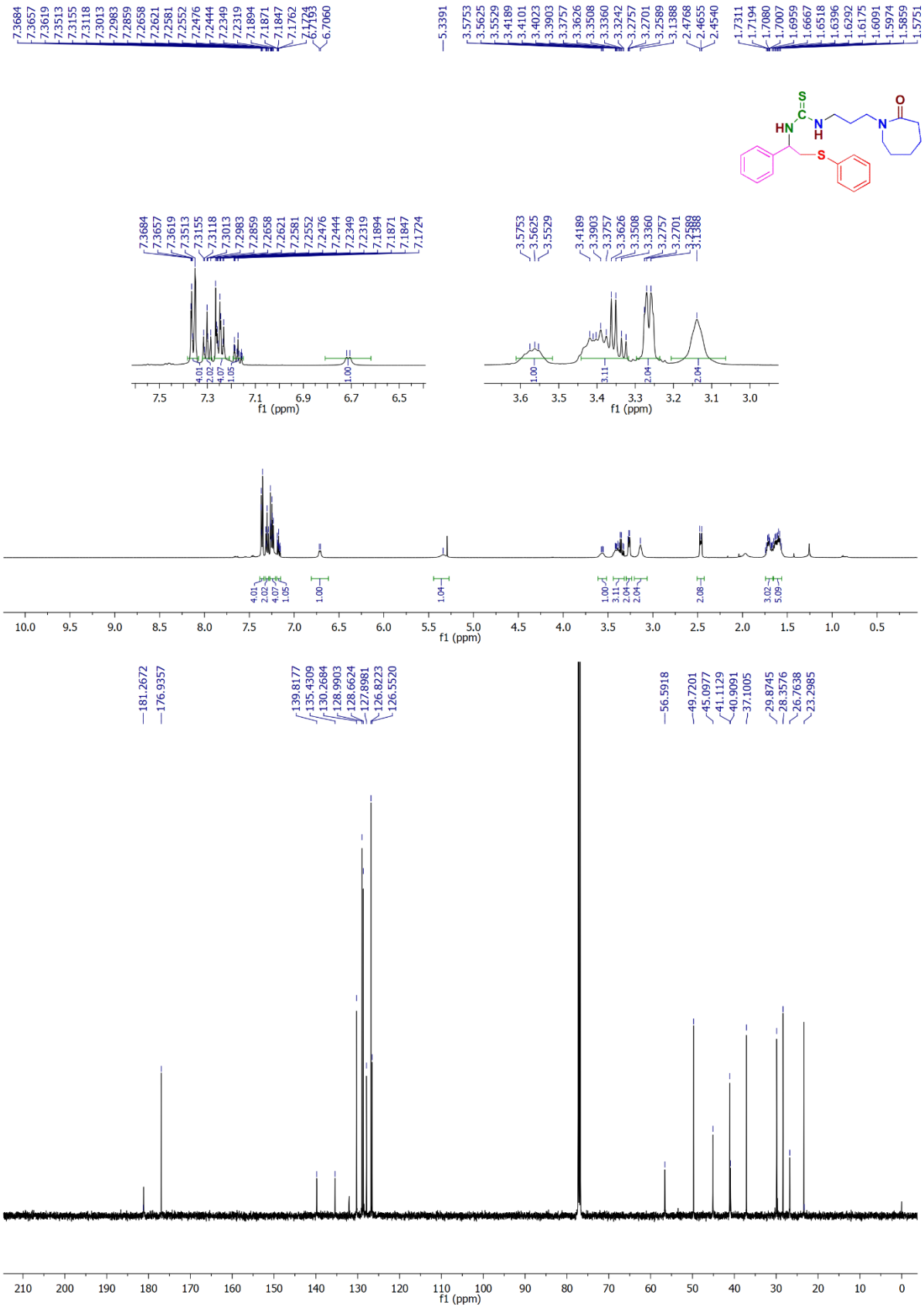
^{1}H and ^{13}C NMR for 7i



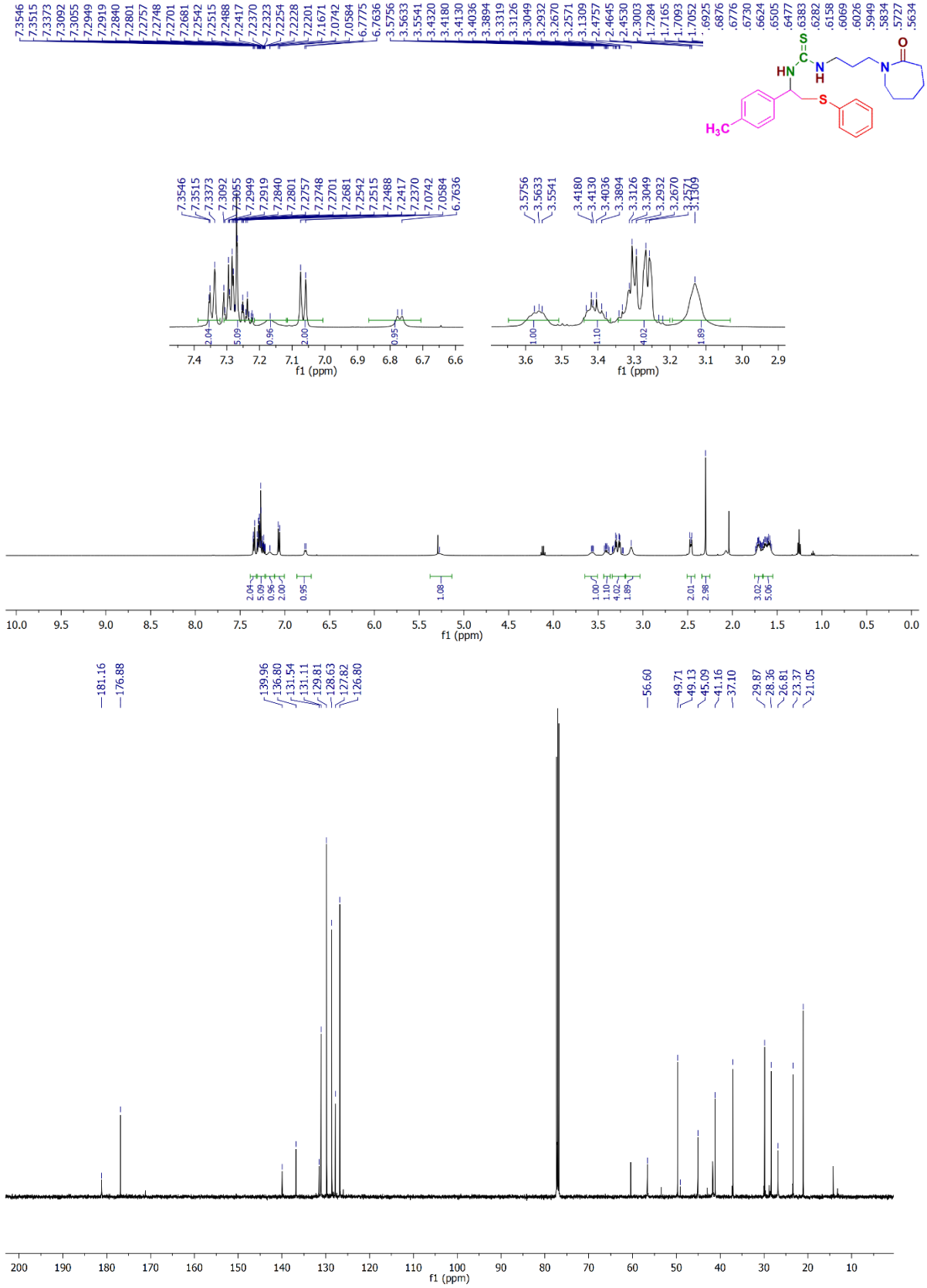
^{1}H and ^{13}C NMR for 7j



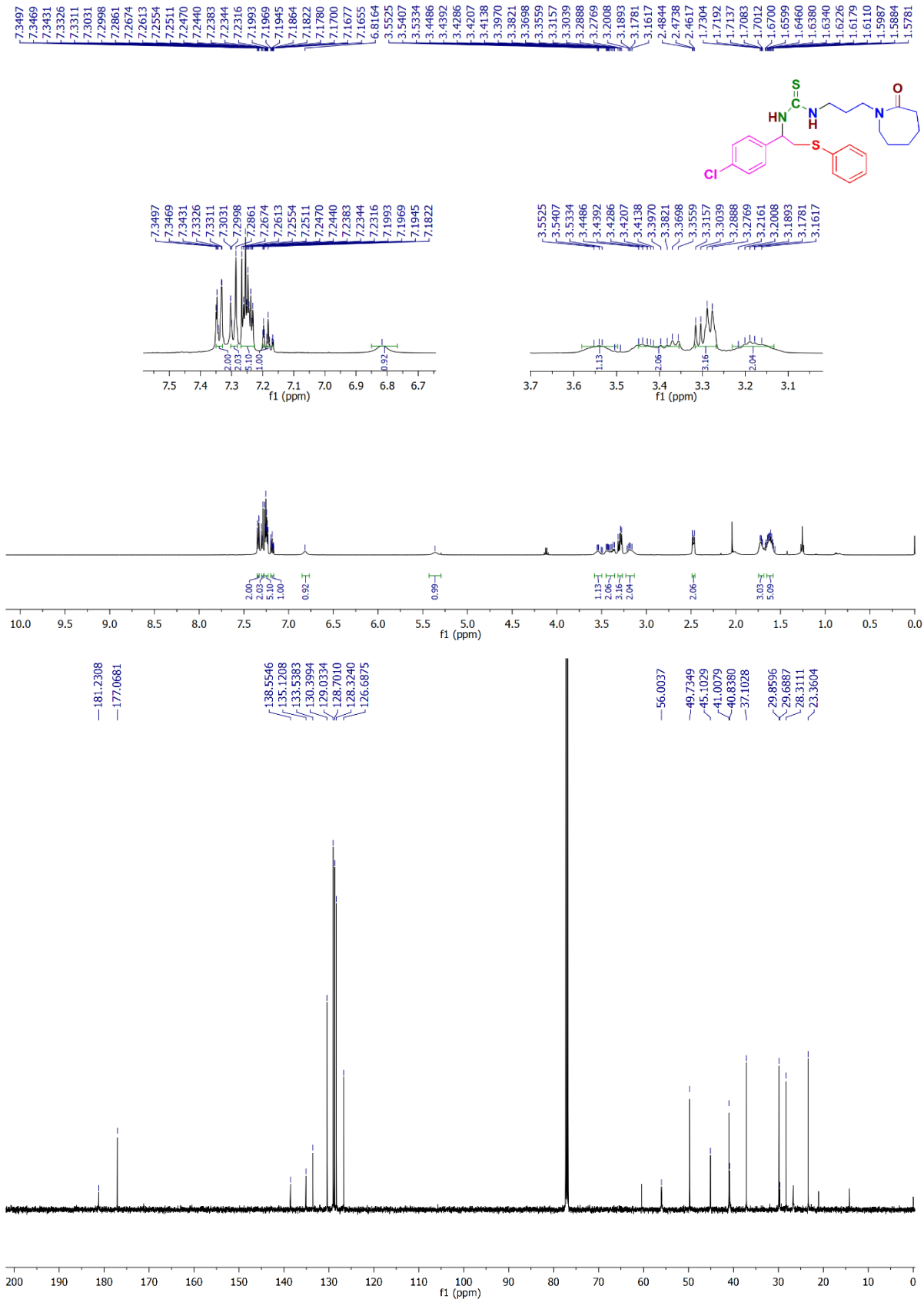
^{1}H and ^{13}C NMR for 8a



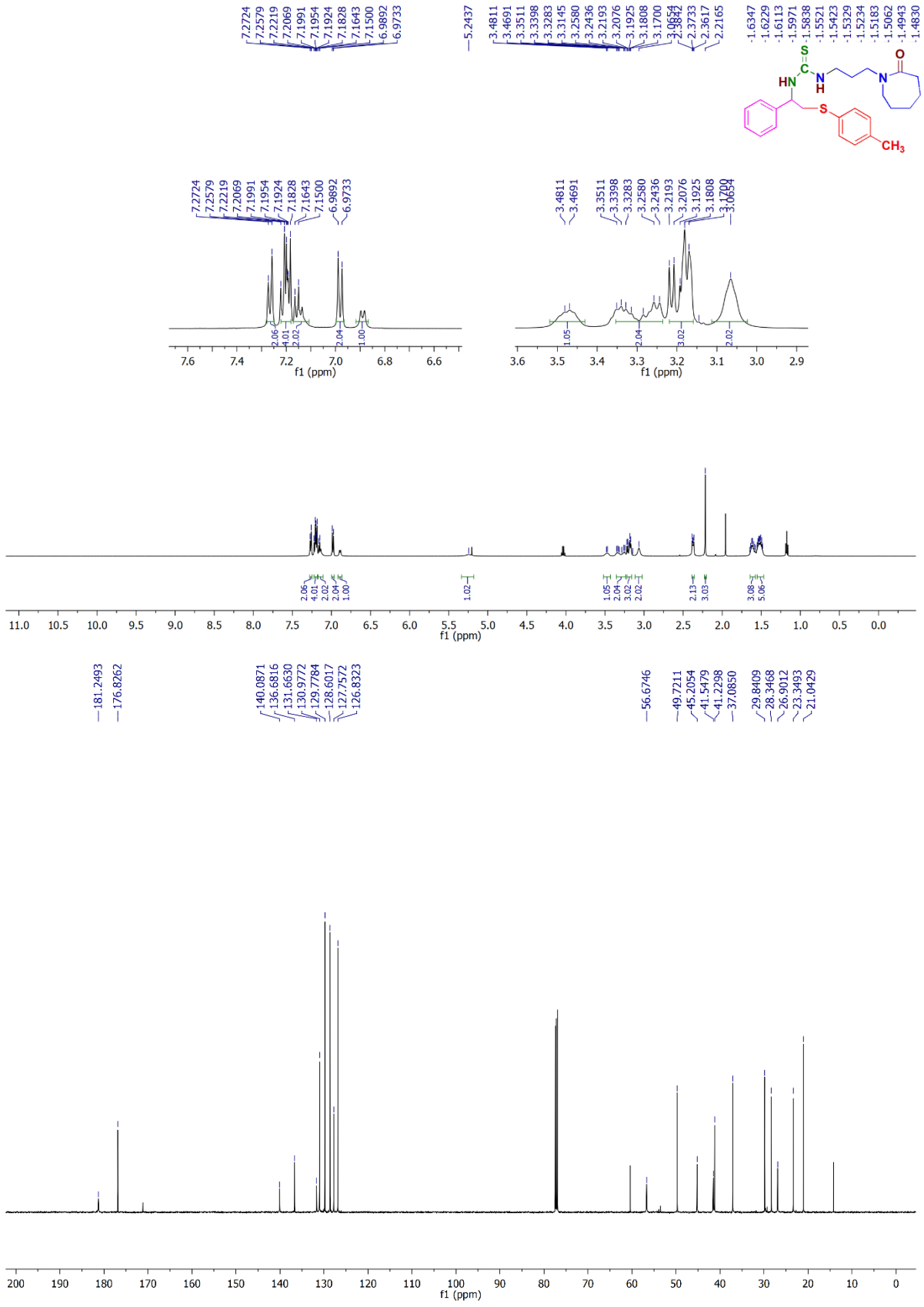
^{1}H and ^{13}C NMR for 8b



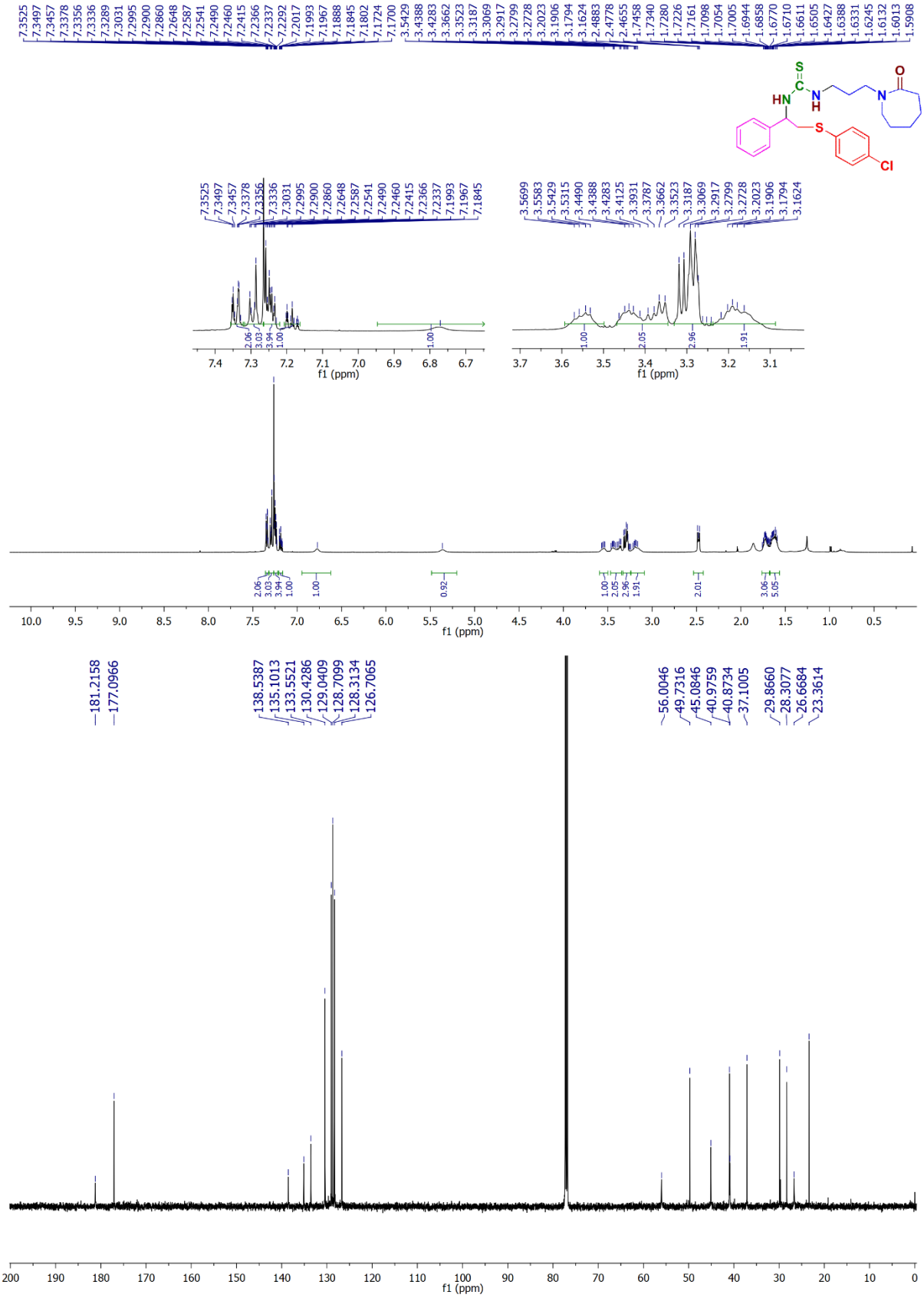
^{1}H and ^{13}C NMR for 8c



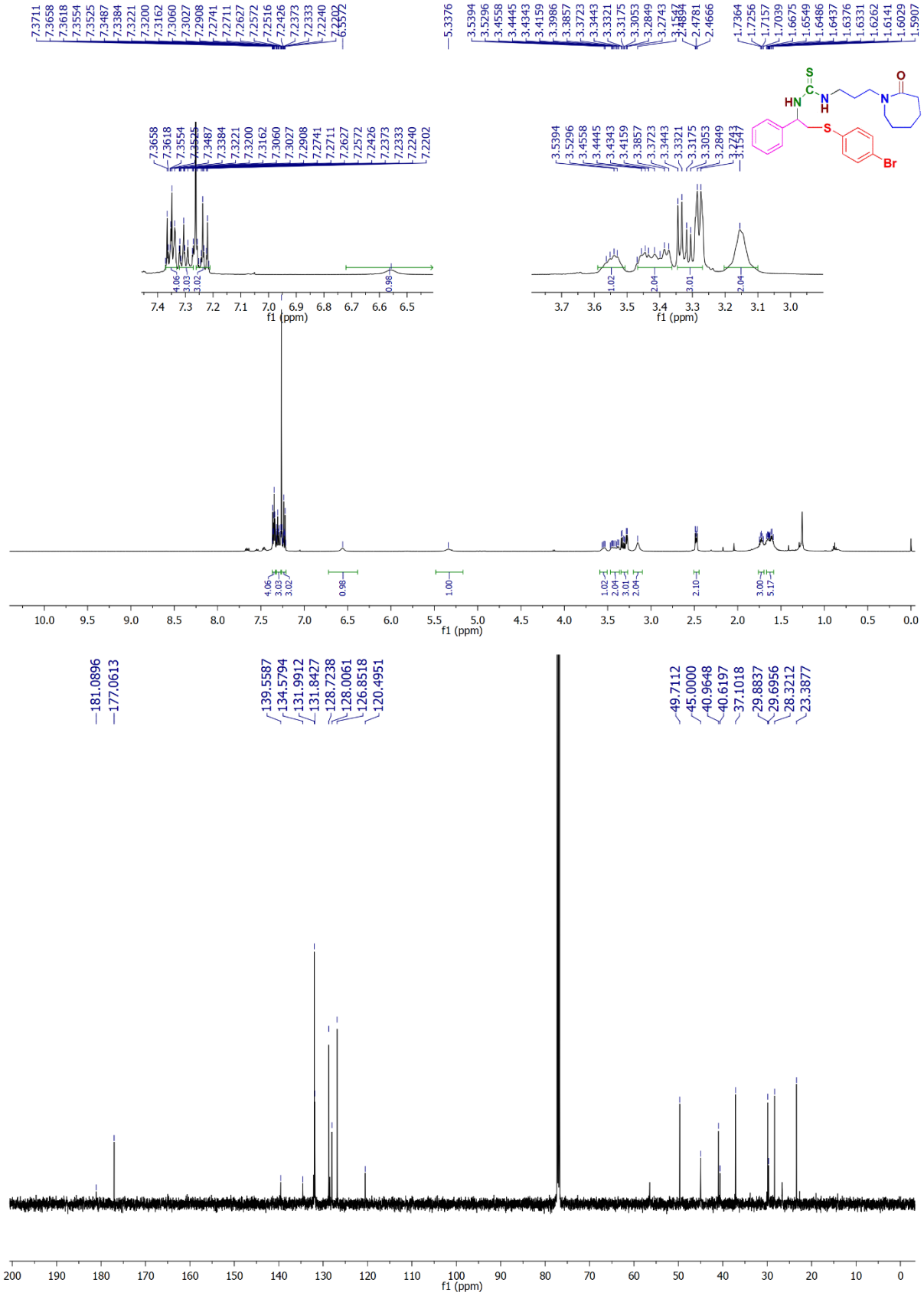
^{1}H and ^{13}C NMR for 8d



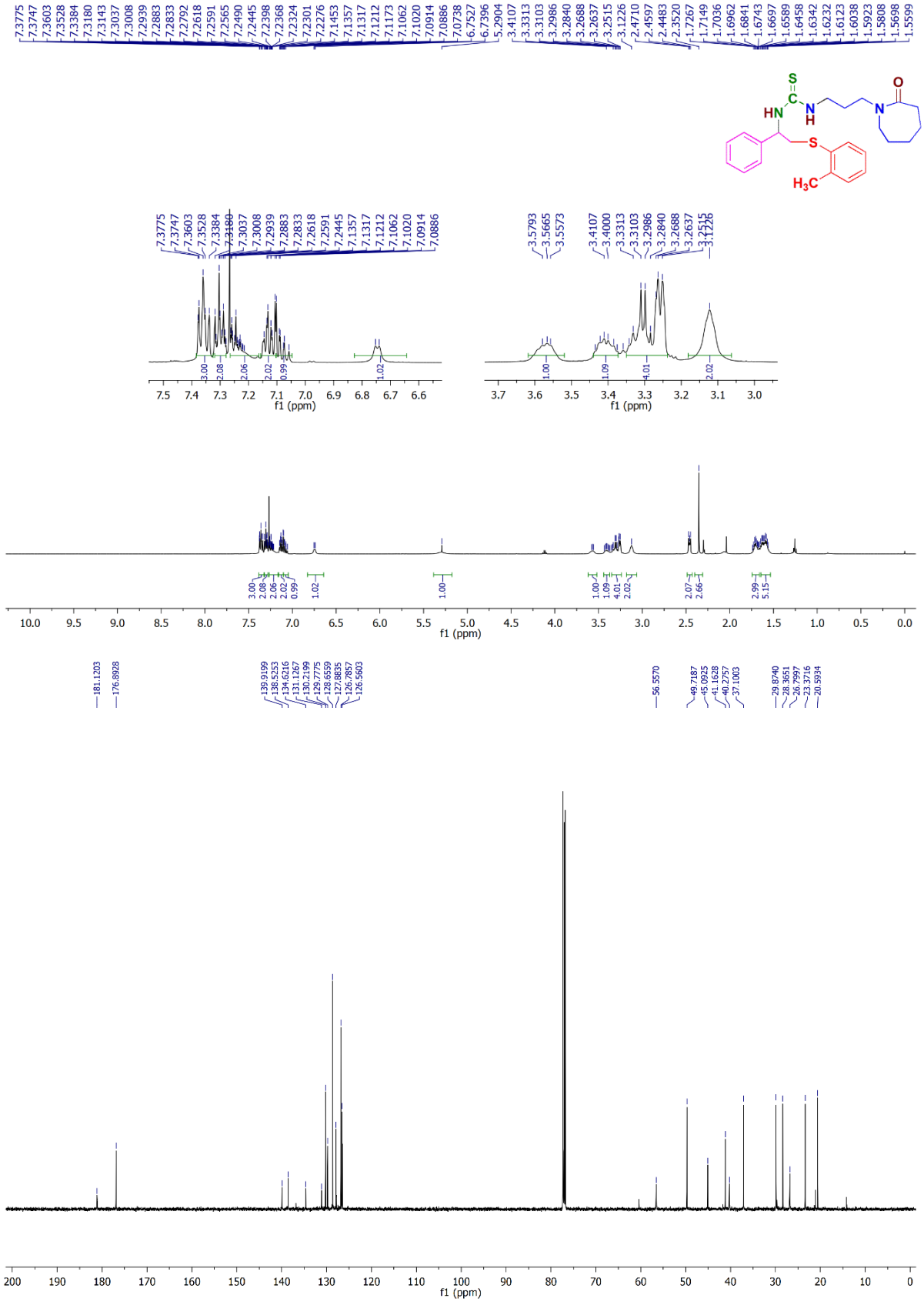
^{1}H and ^{13}C NMR for 8e



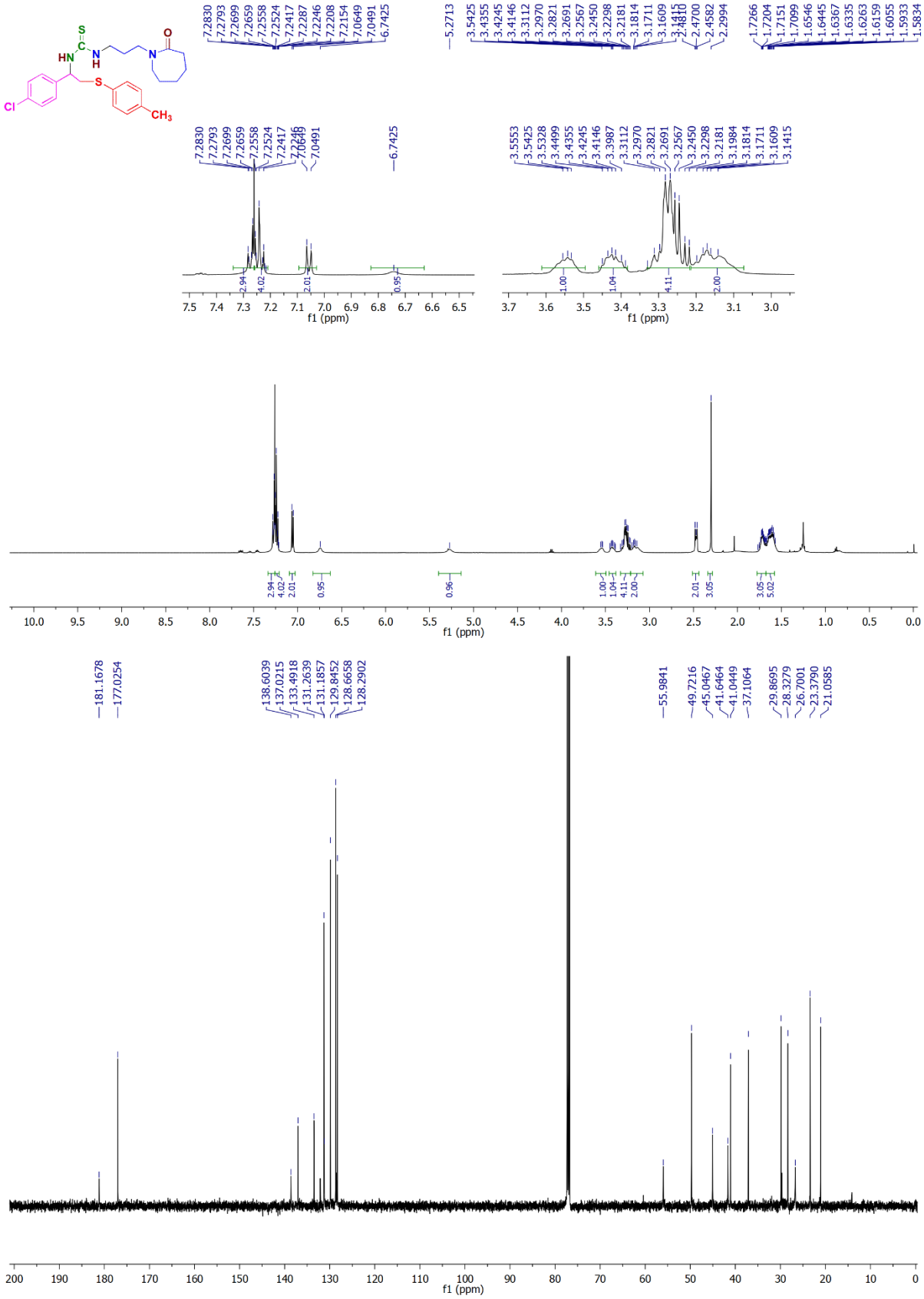
^{1}H and ^{13}C NMR for 8f



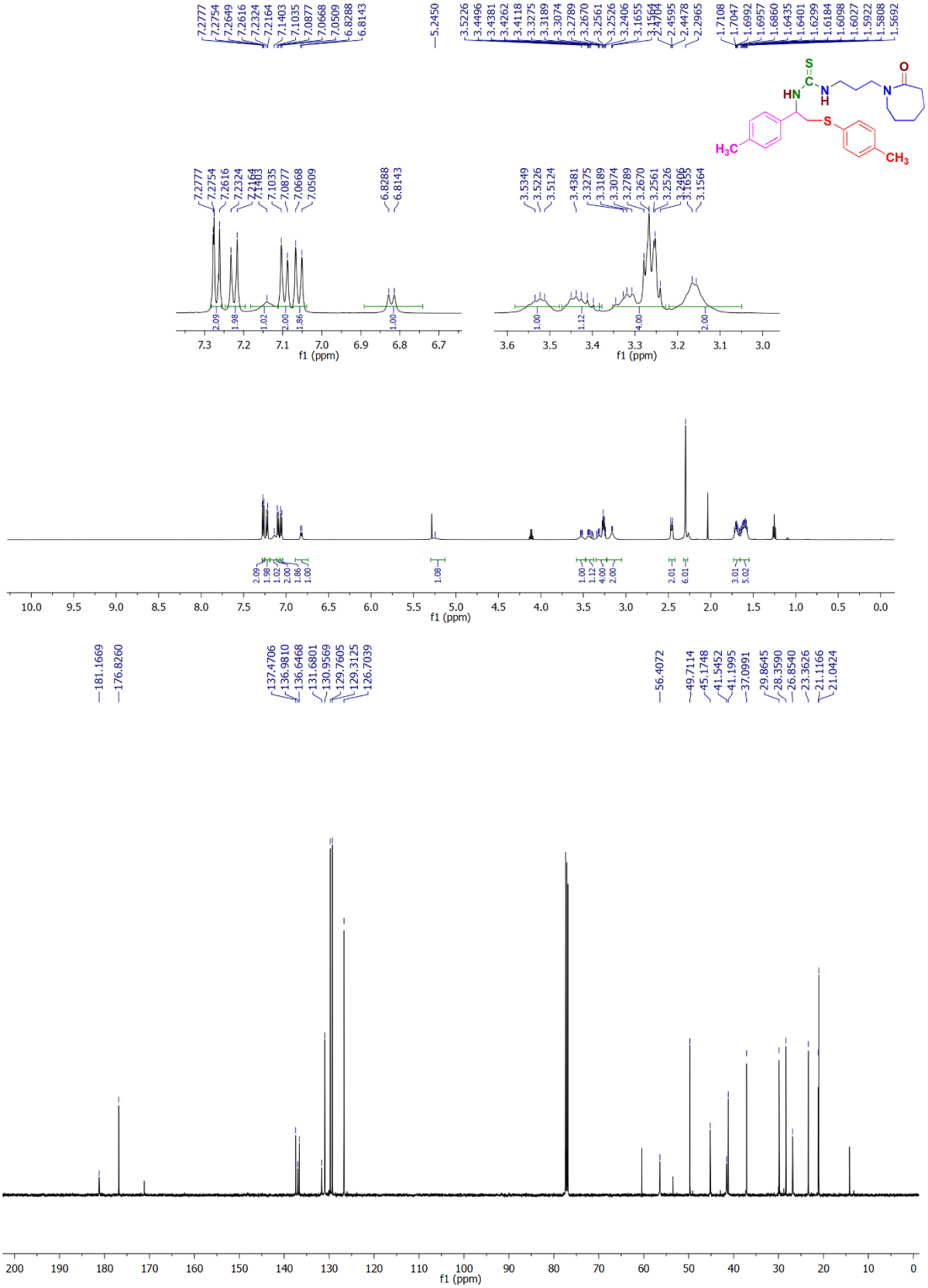
^{1}H and ^{13}C NMR for 8g



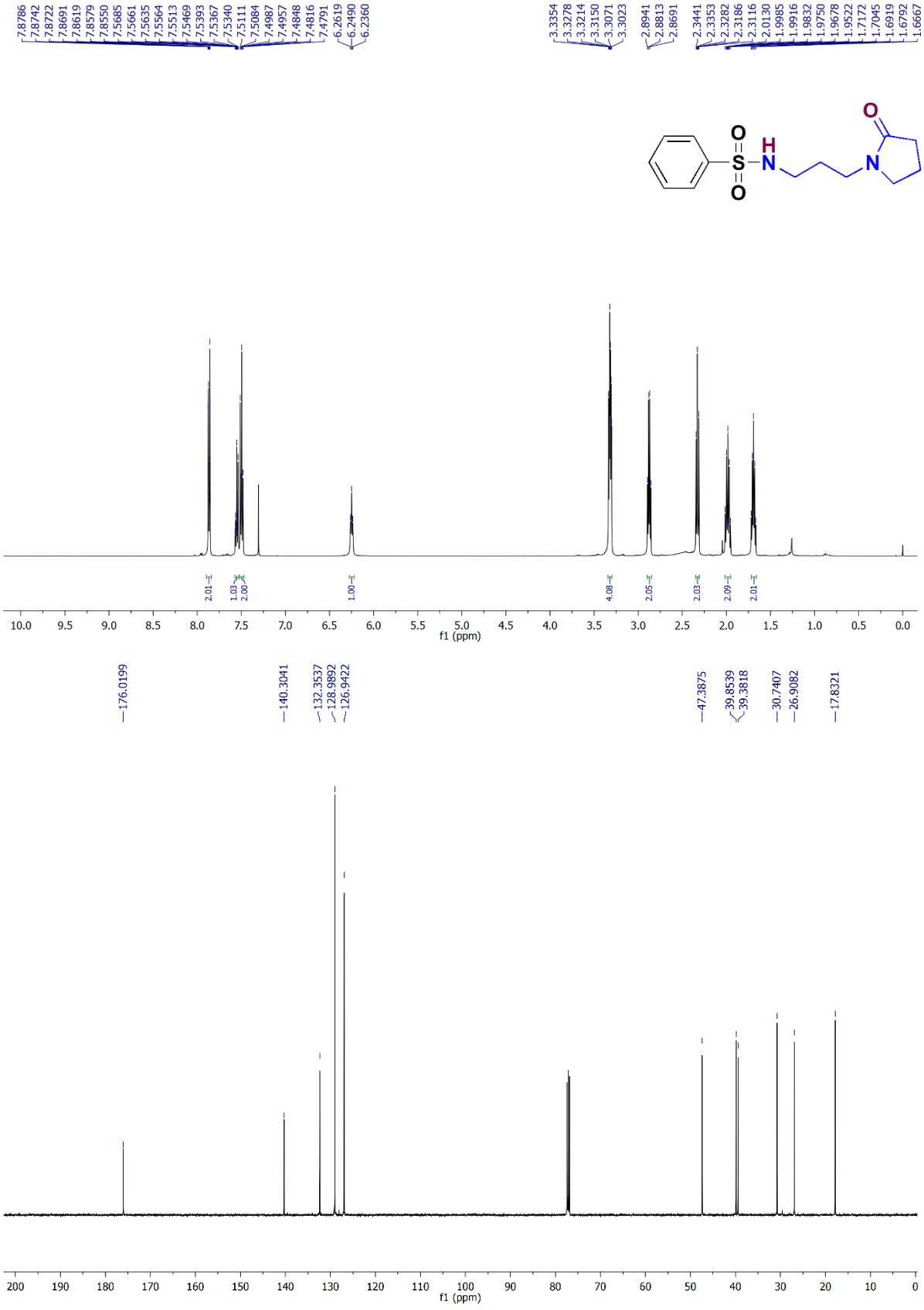
^{1}H and ^{13}C NMR for 8h



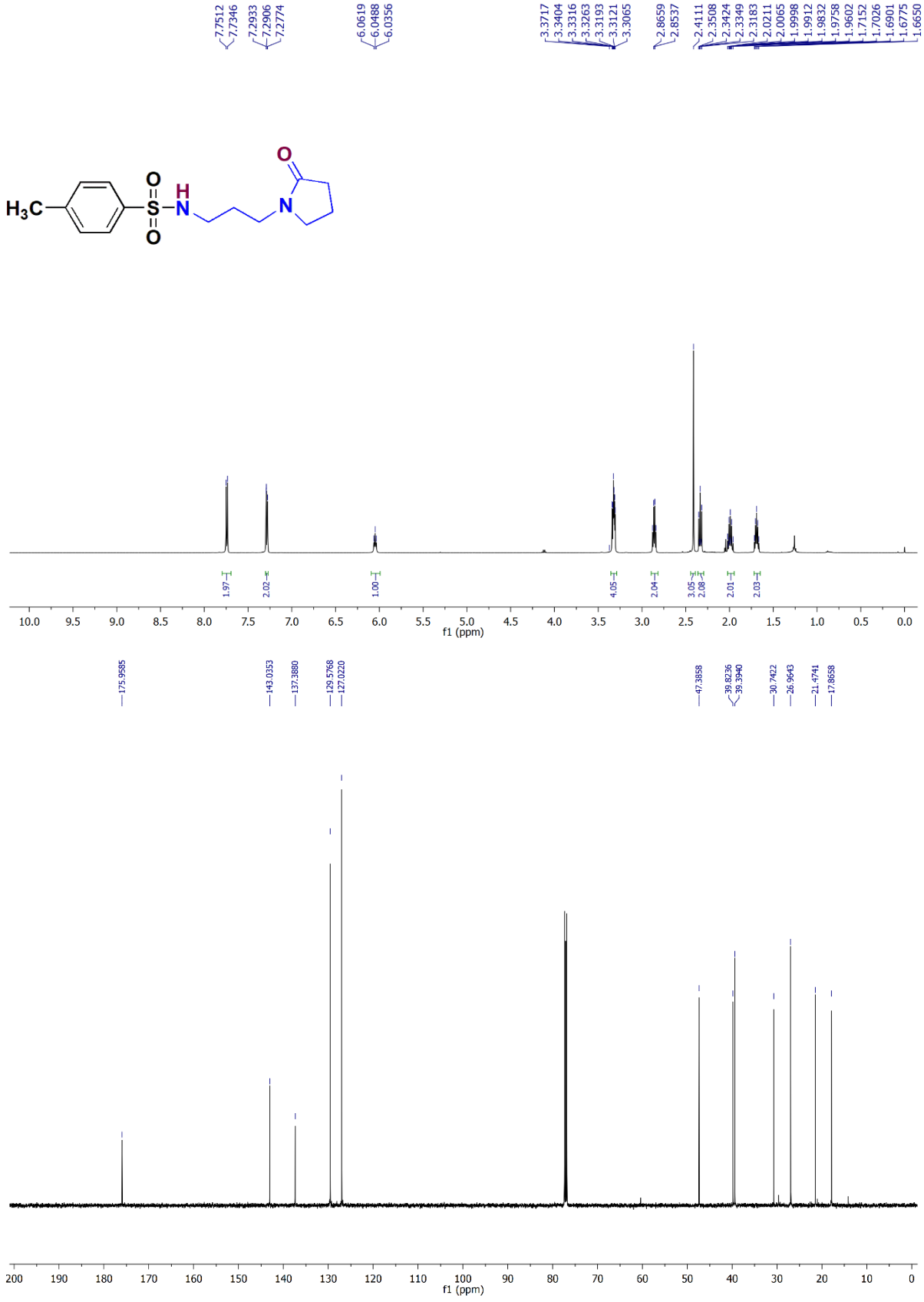
^{1}H and ^{13}C NMR for 8i



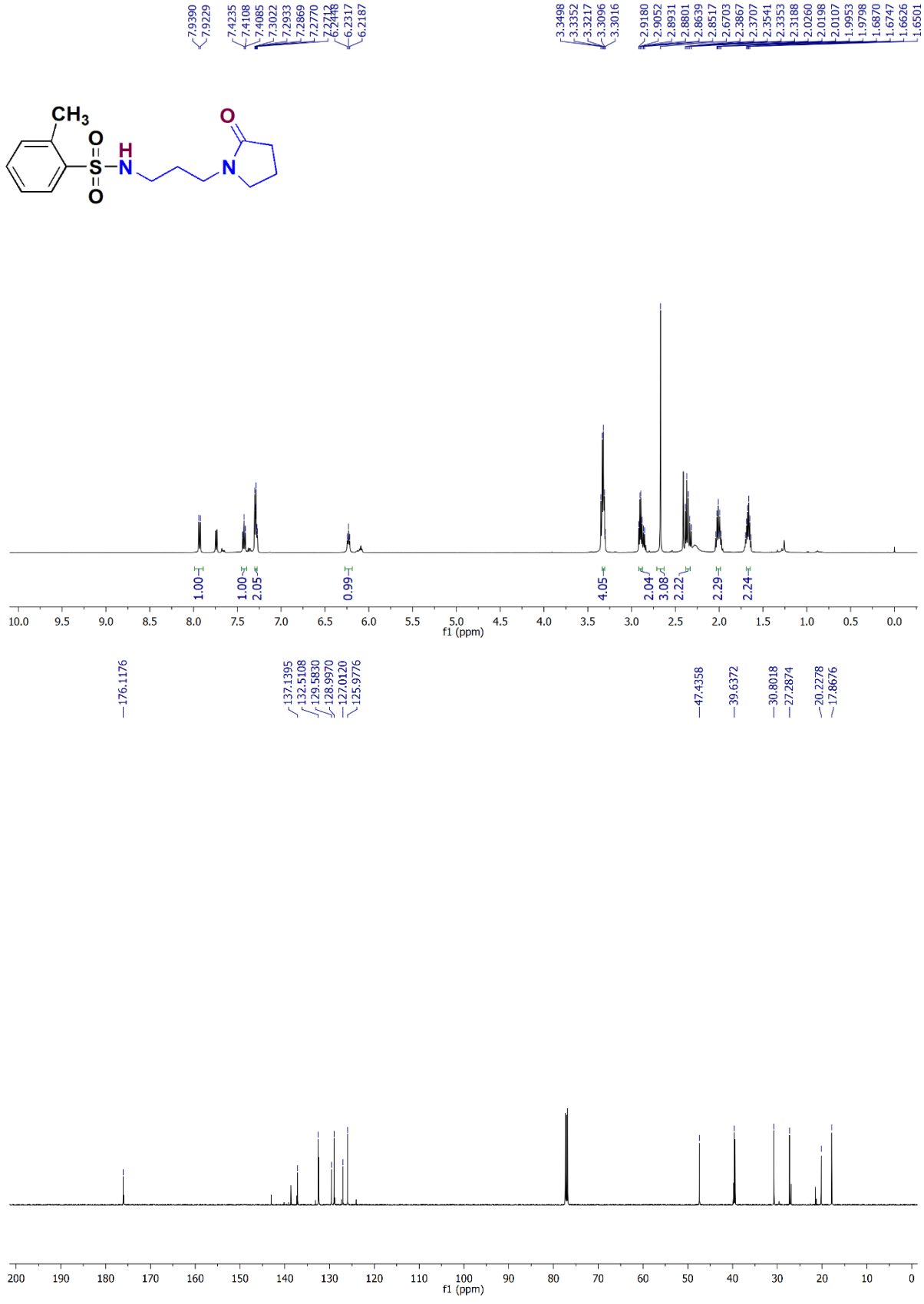
^{1}H and ^{13}C NMR for 10a



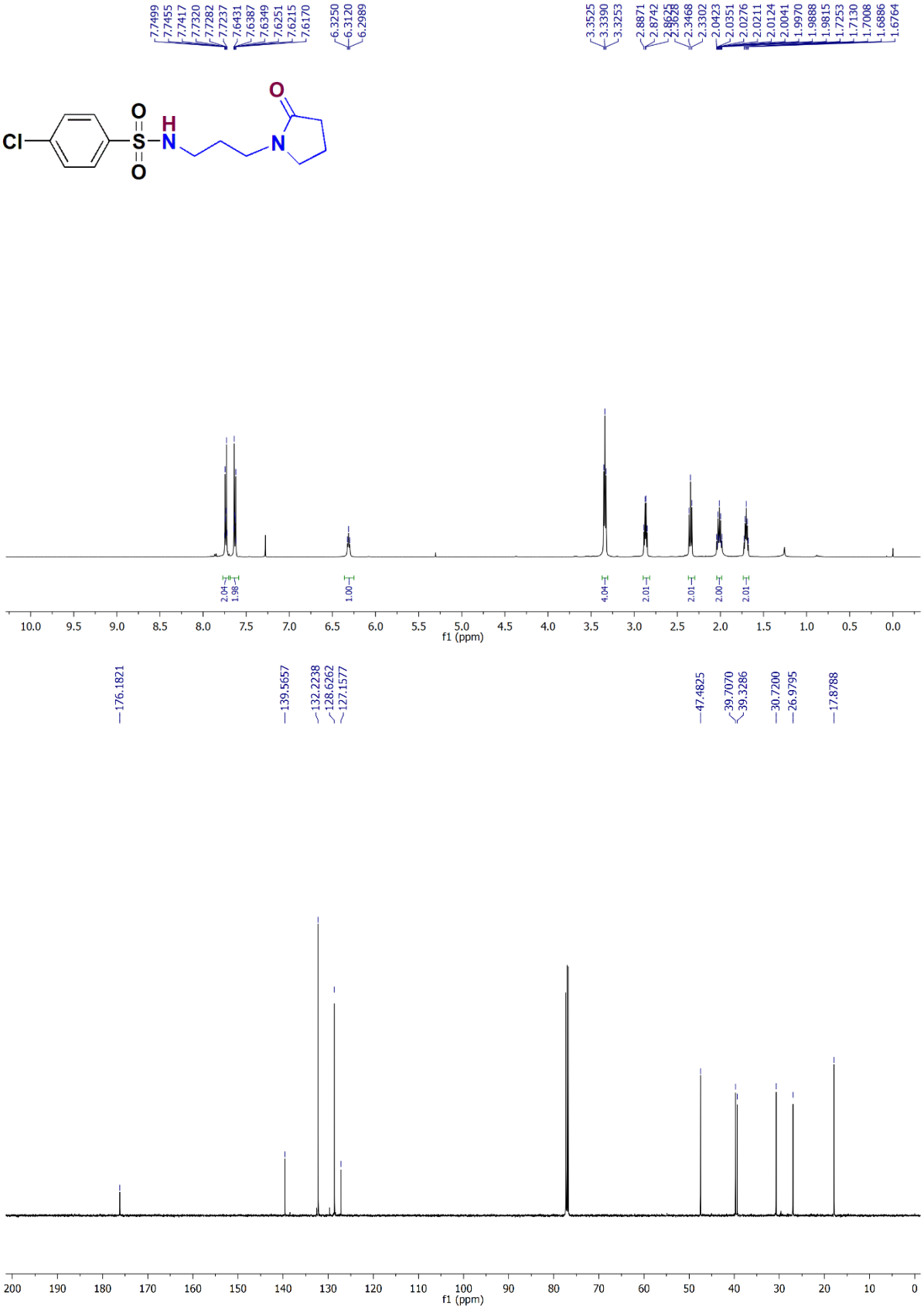
^{1}H and ^{13}C NMR for 10b



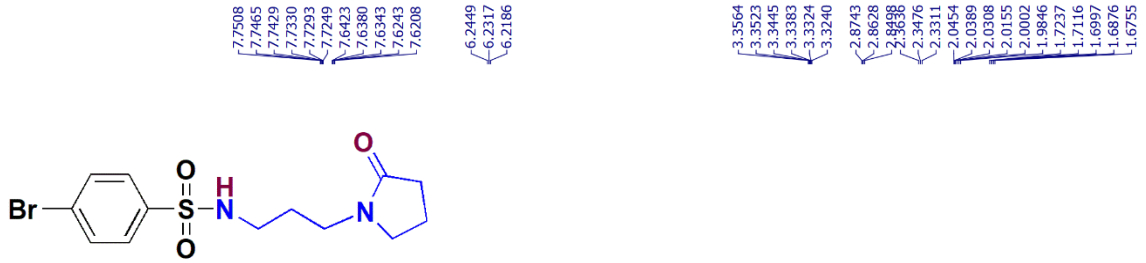
^{1}H and ^{13}C NMR for 10c

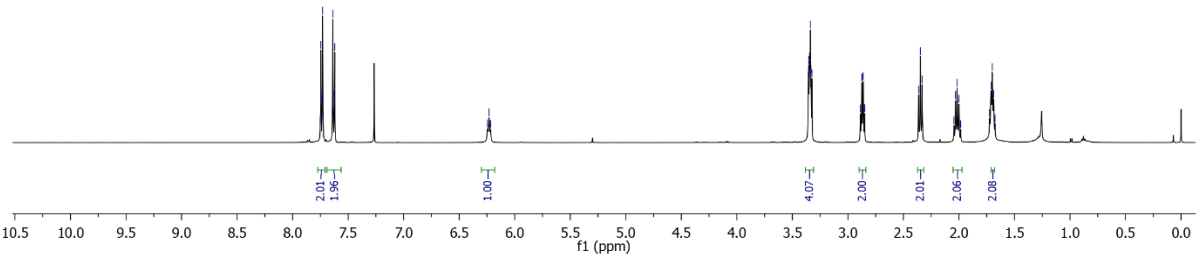


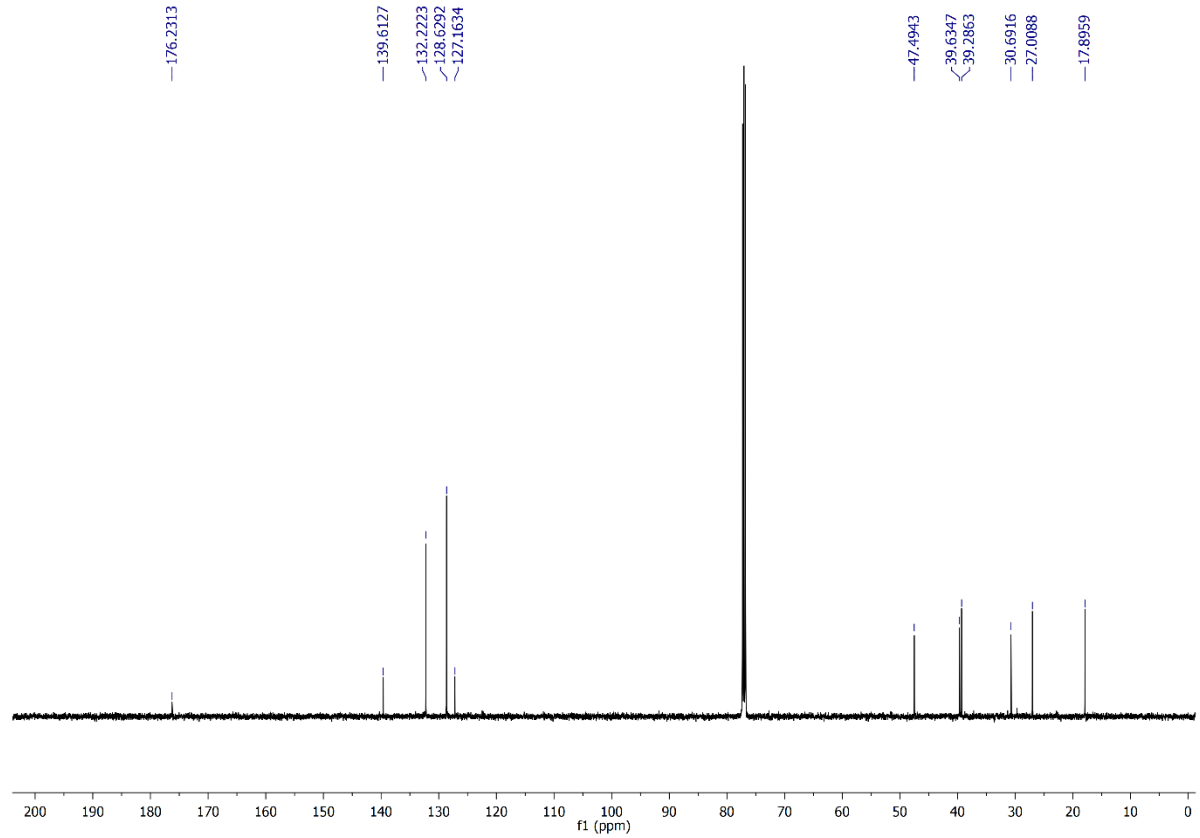
^{1}H and ^{13}C NMR for 10d



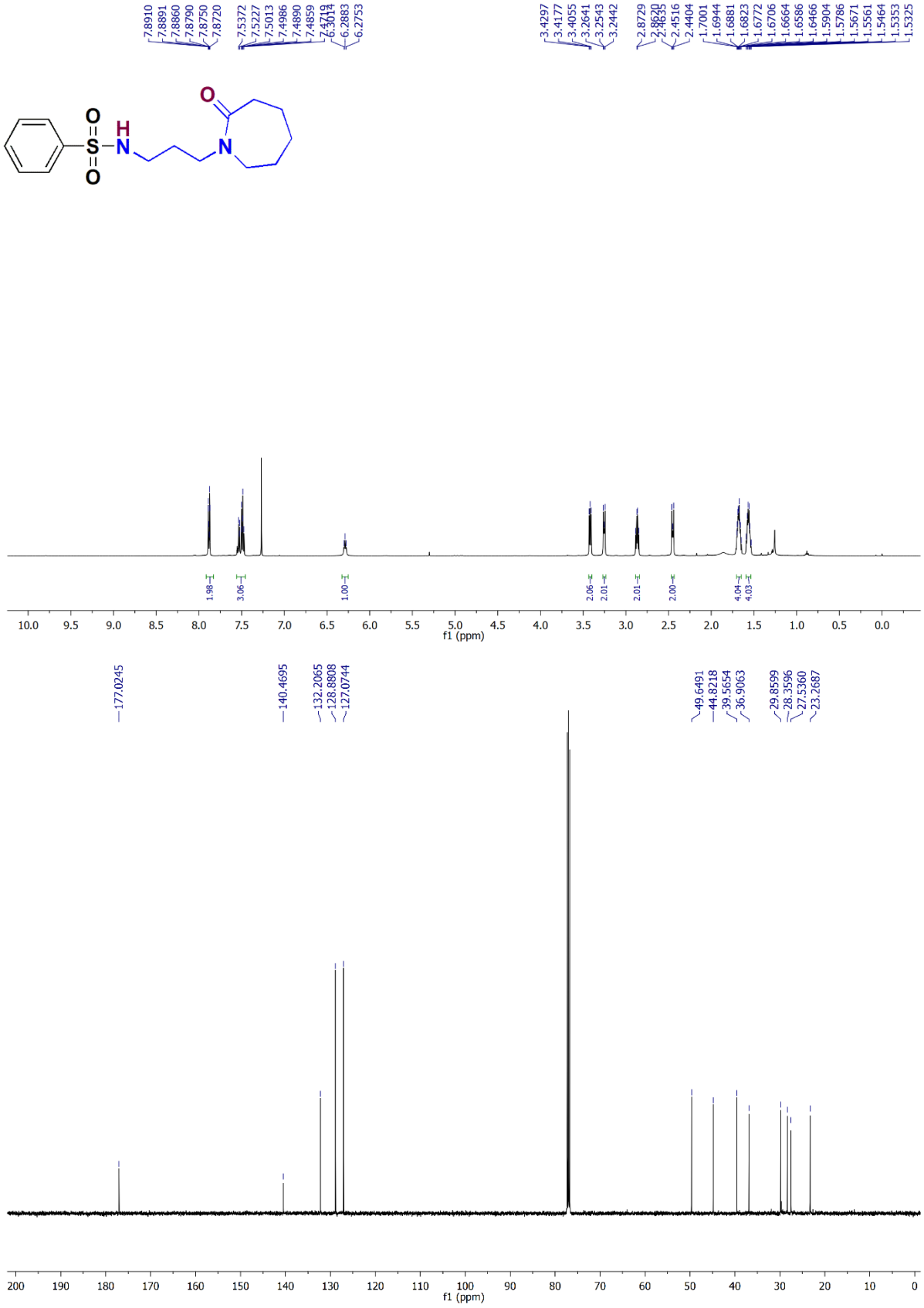
^{1}H and ^{13}C NMR for 10e



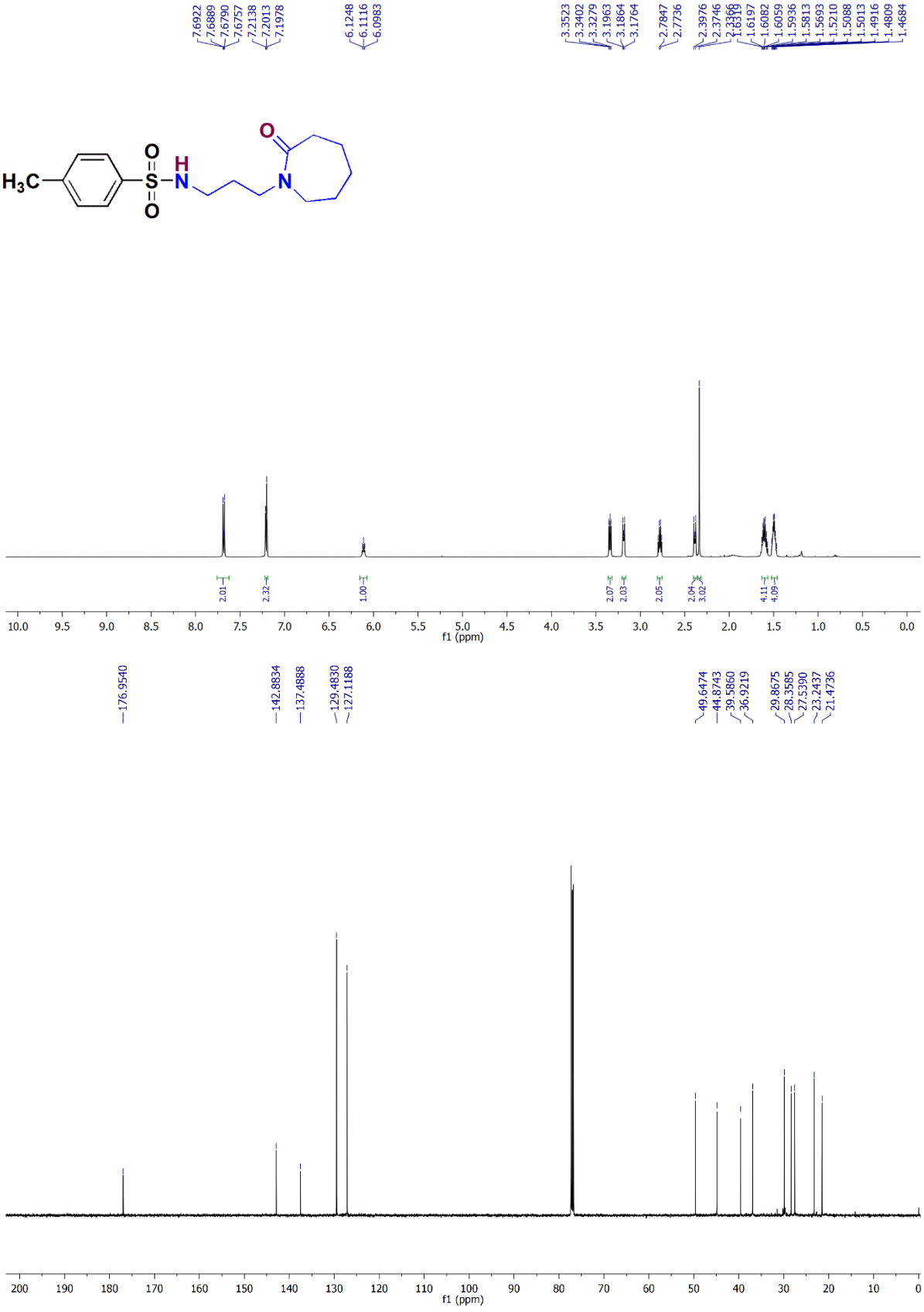




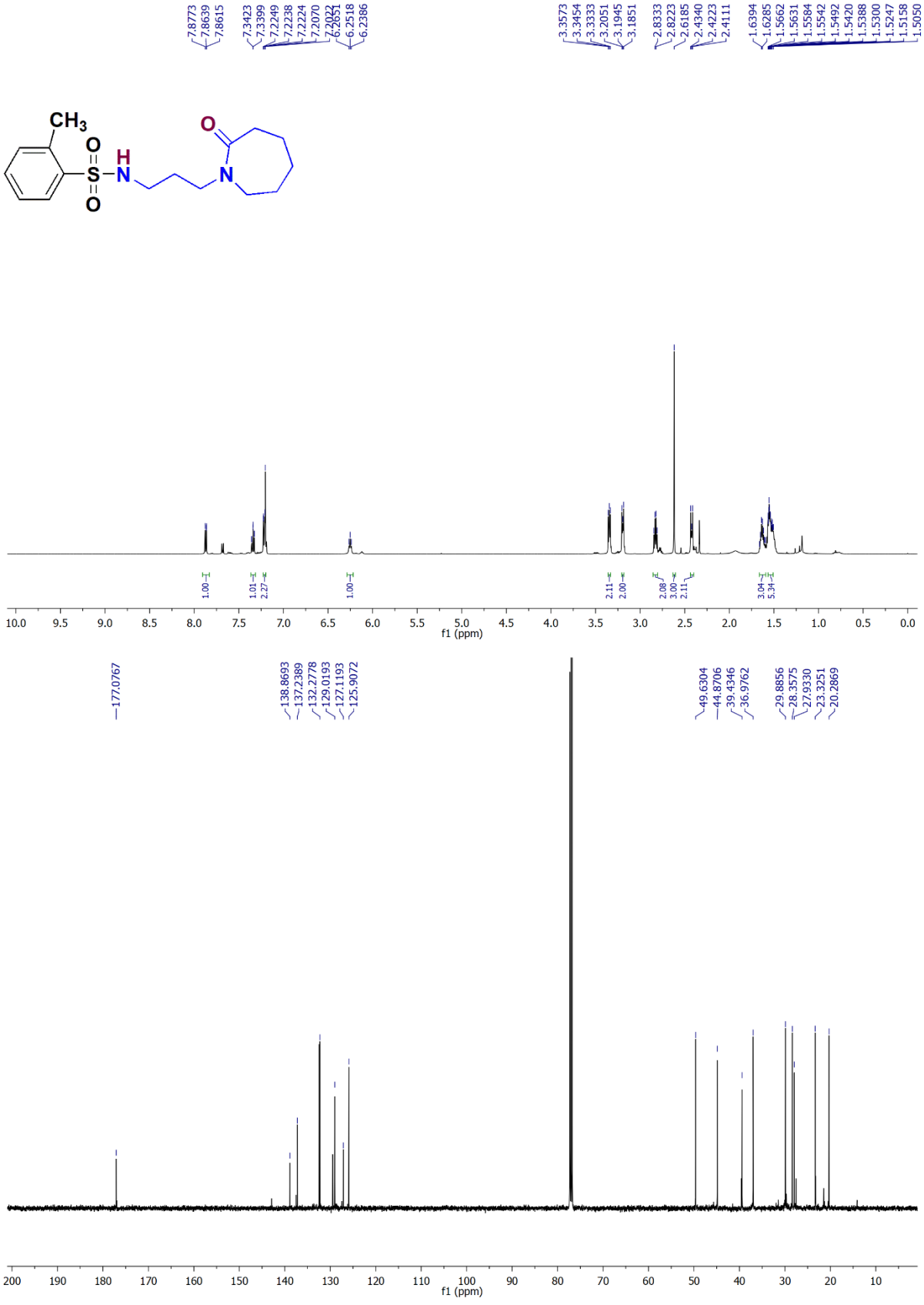
^{1}H and ^{13}C NMR for 11a



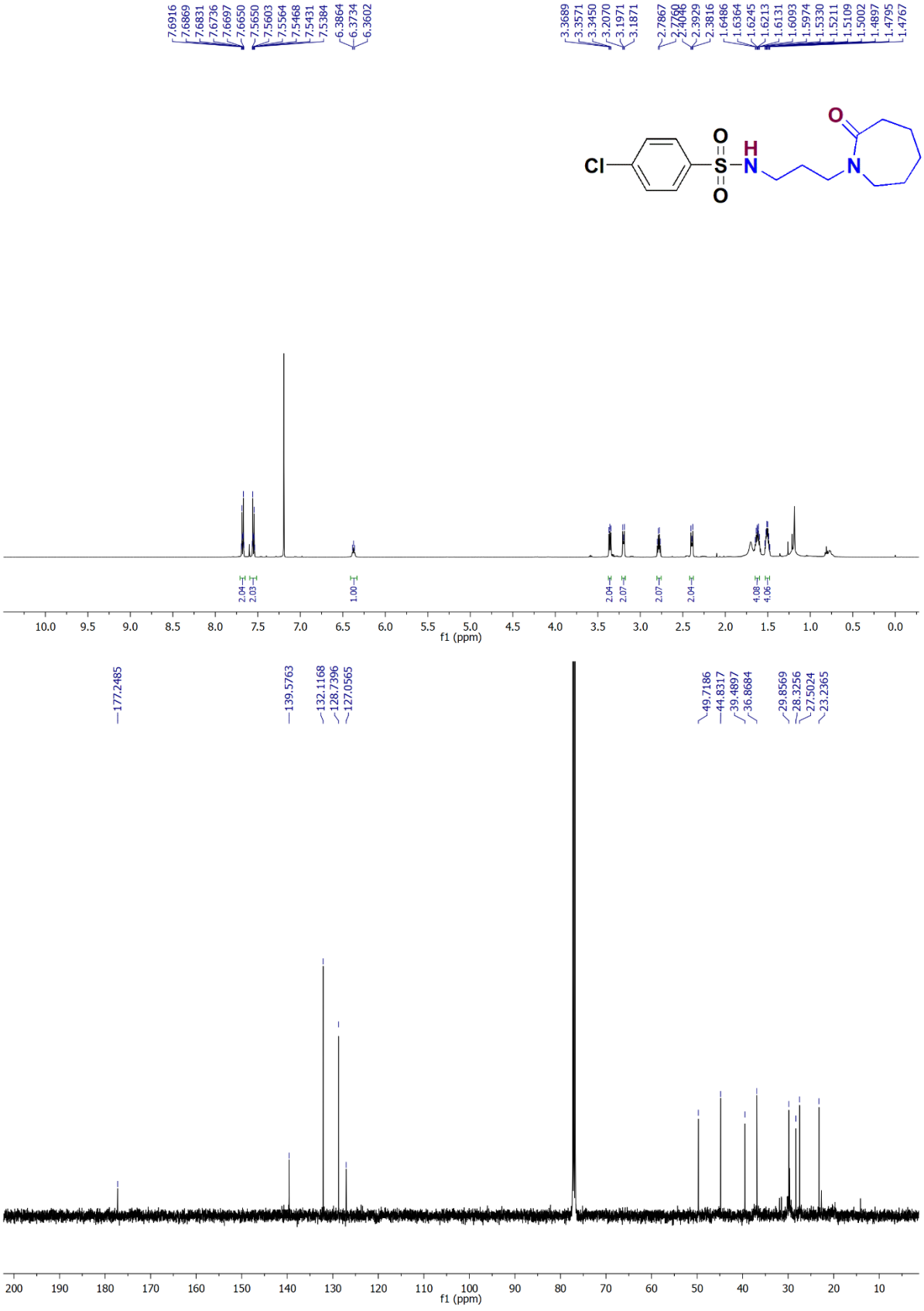
^{1}H and ^{13}C NMR for 11b



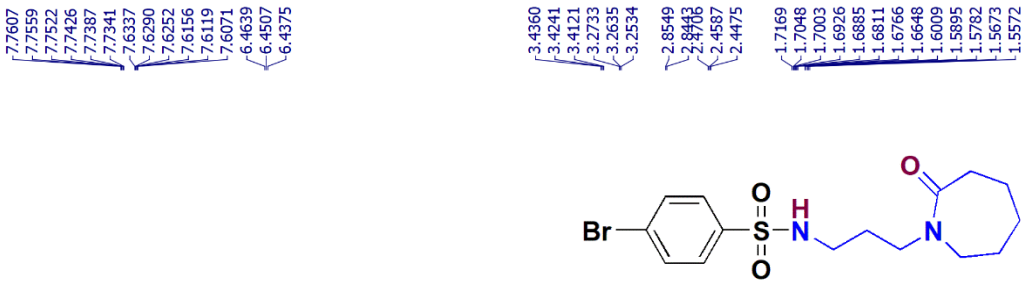
^{1}H and ^{13}C NMR for 11c

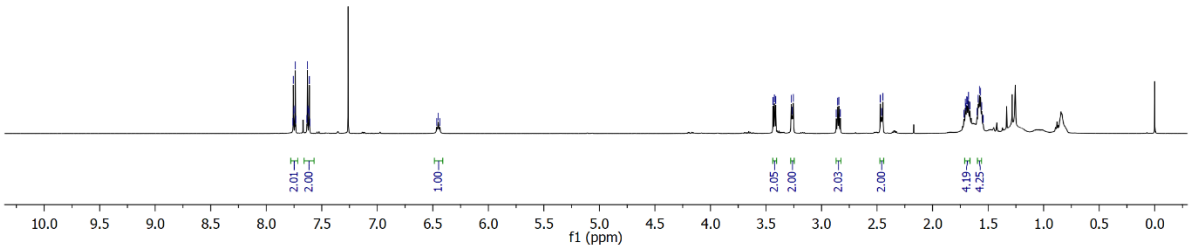


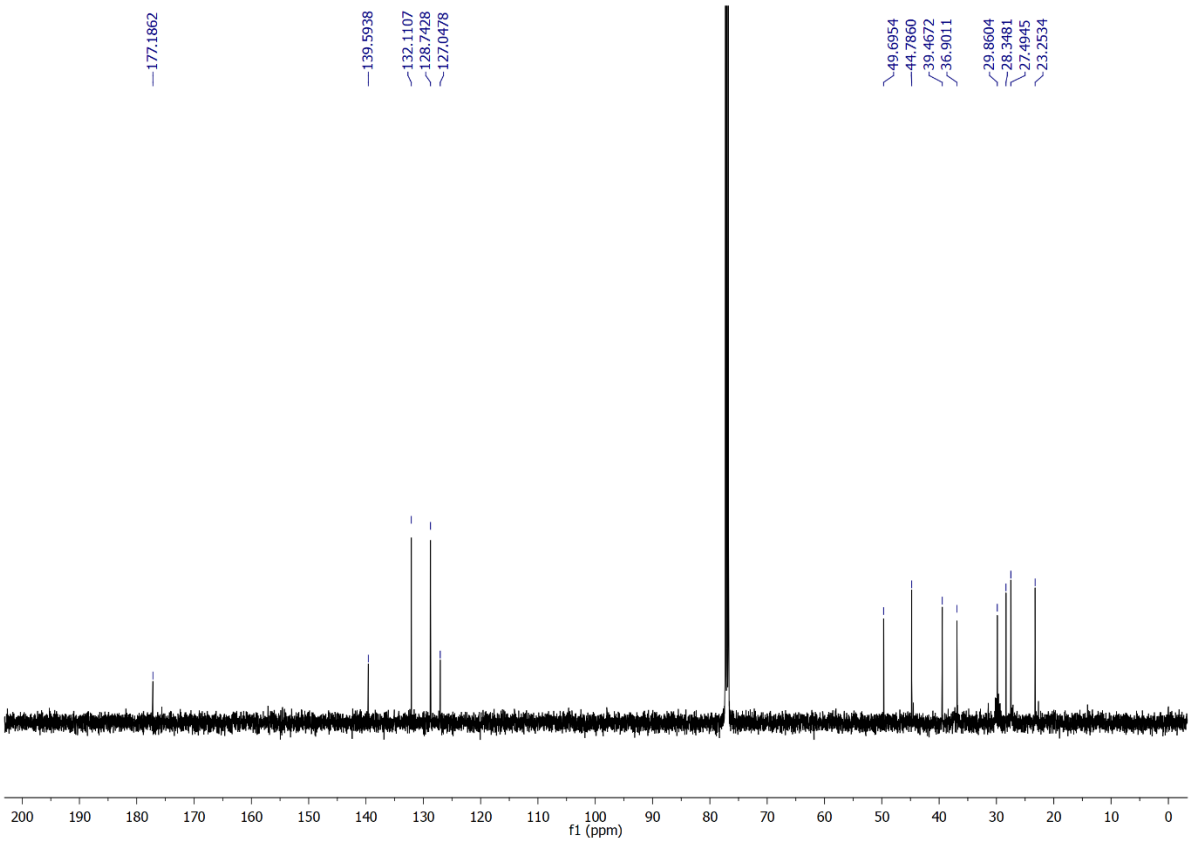
^{1}H and ^{13}C NMR for 11d



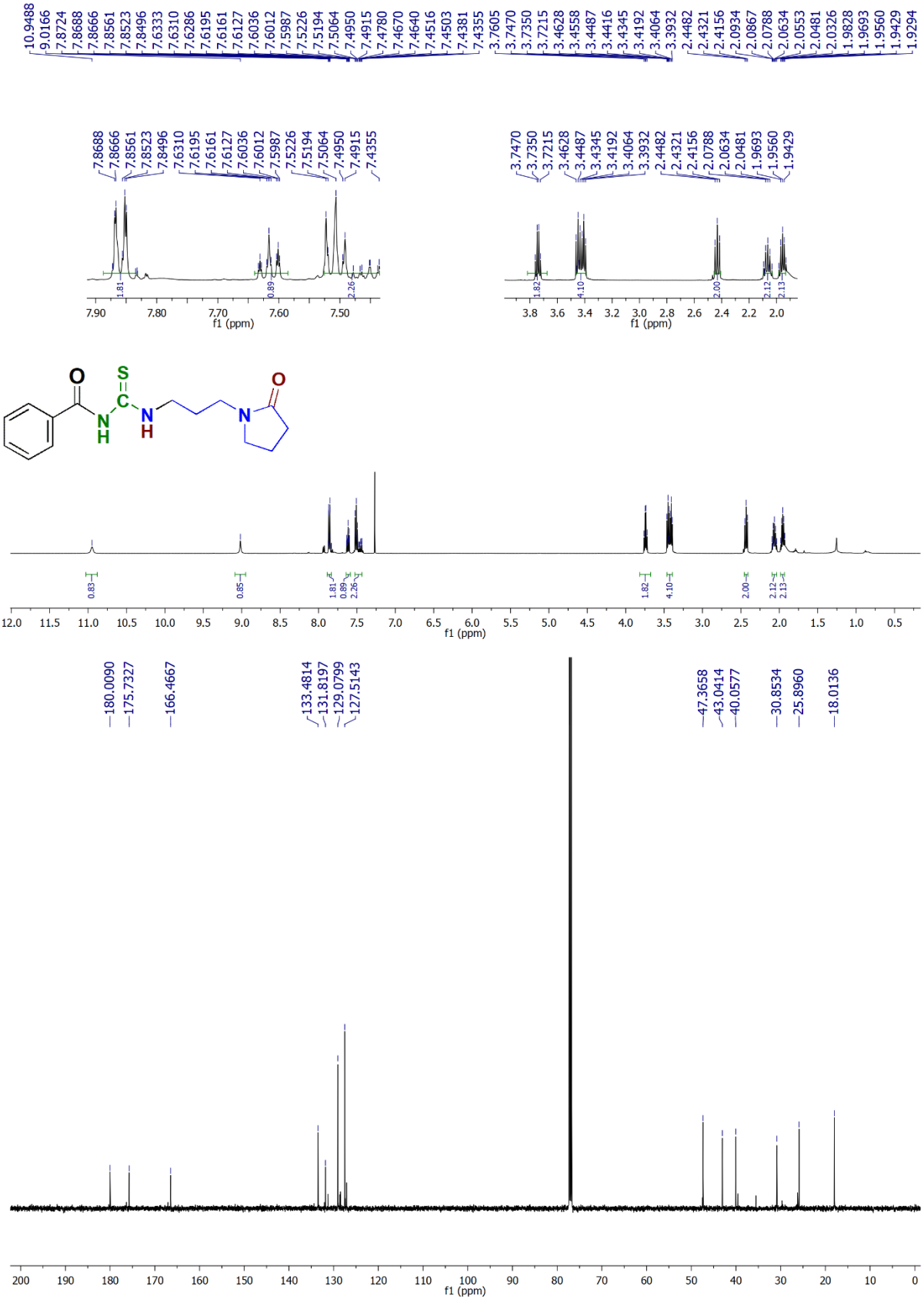
^{1}H and ^{13}C NMR for 11e



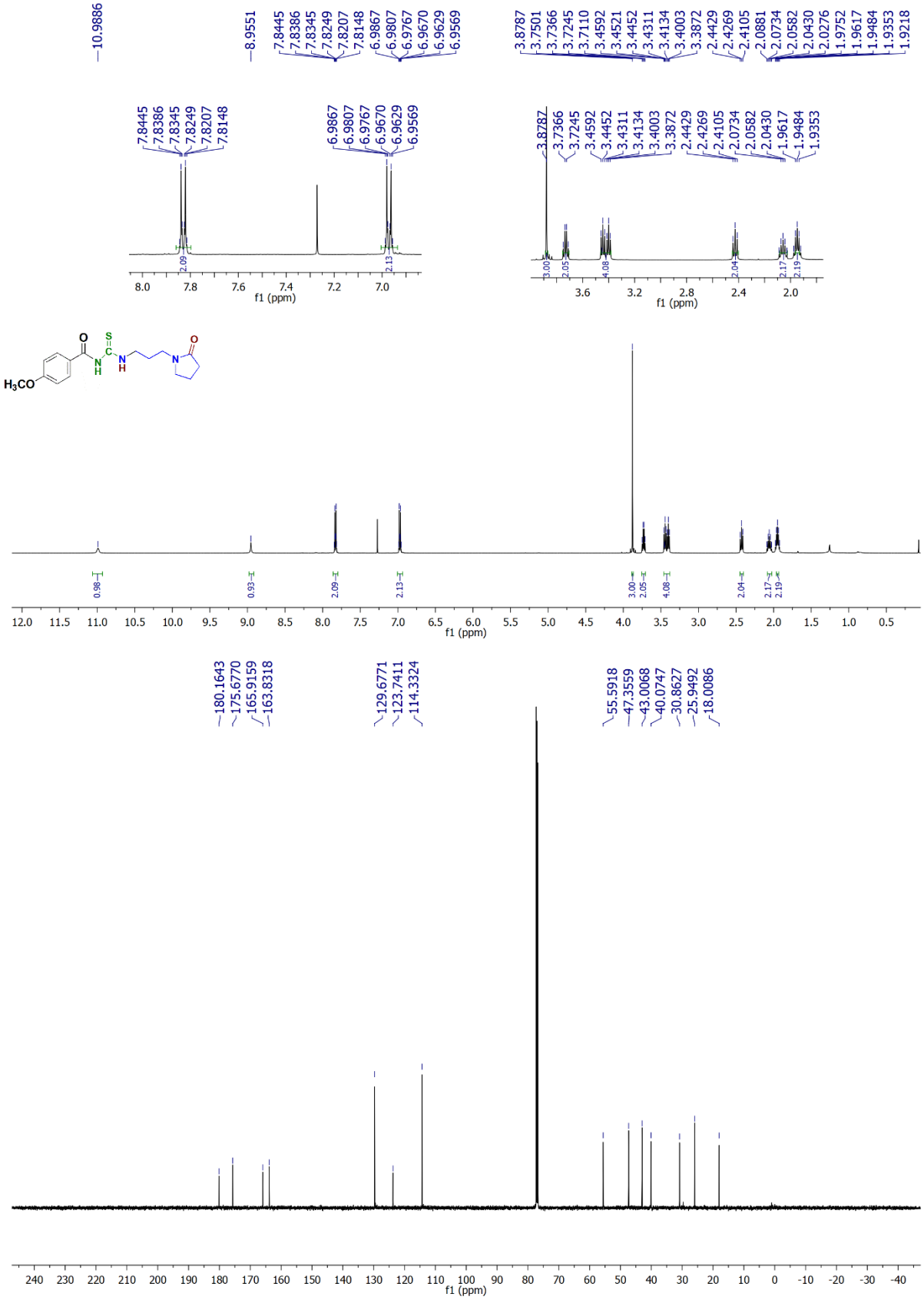




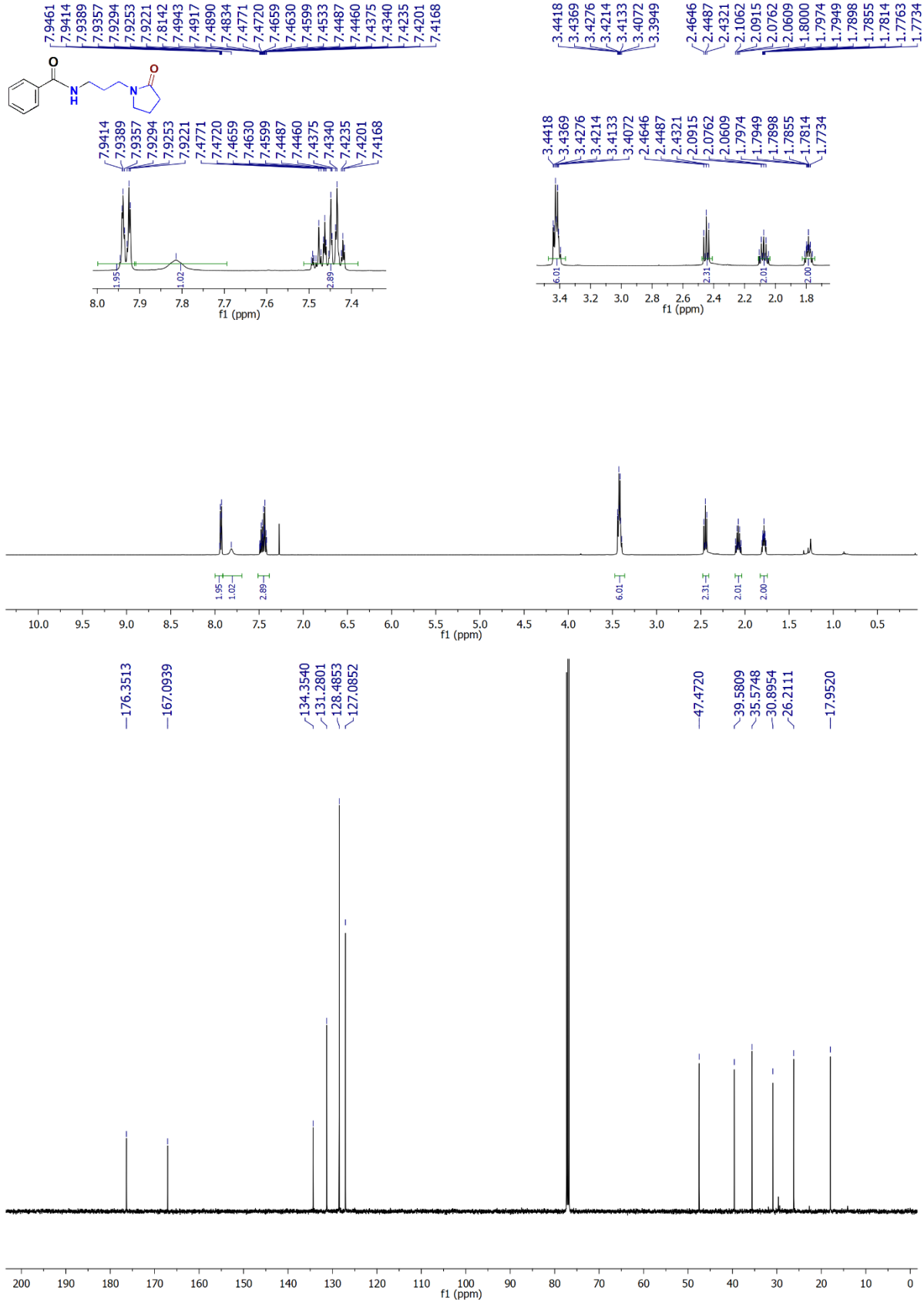
^{1}H and ^{13}C NMR for 14a



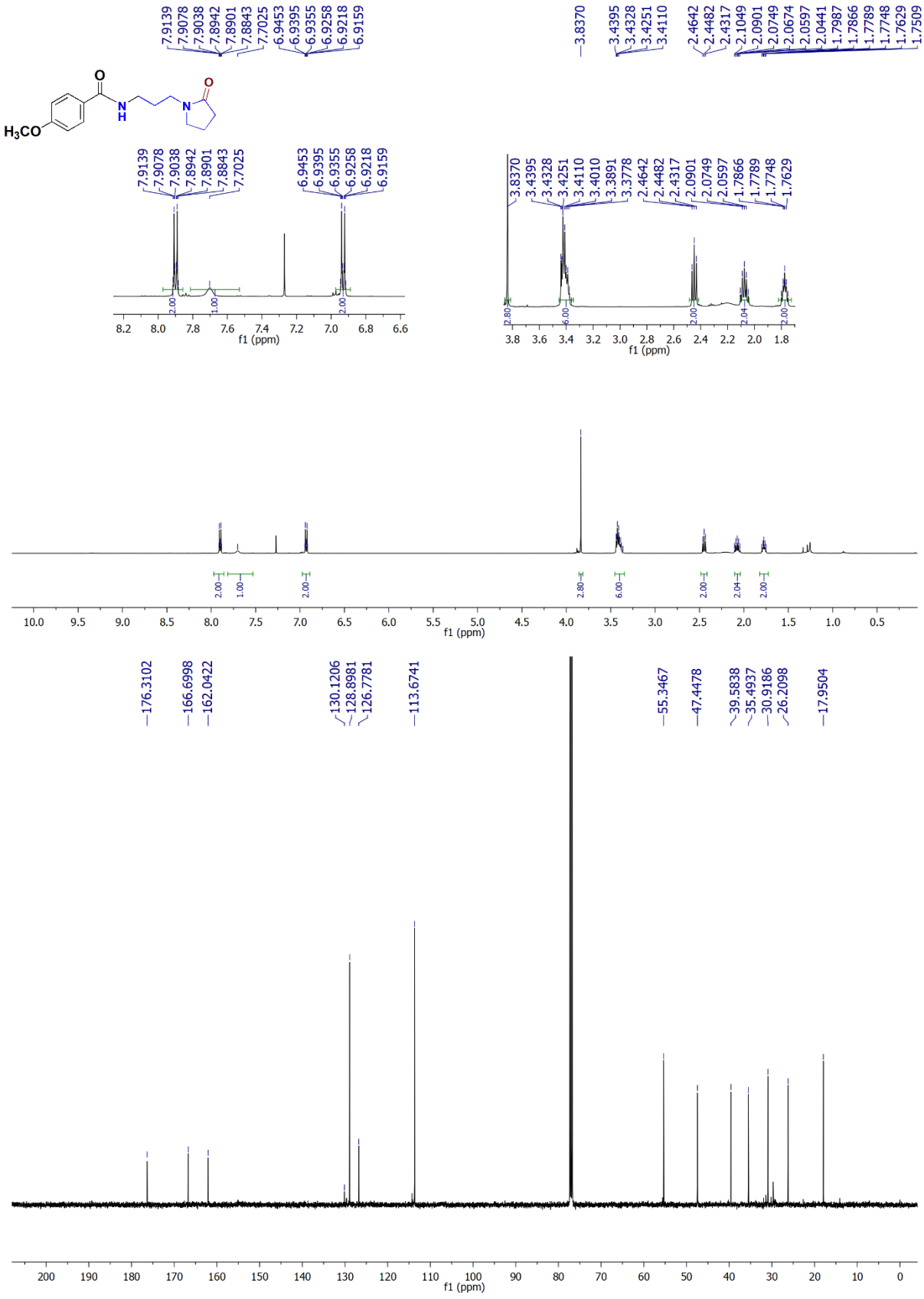
^{1}H and ^{13}C NMR for 14b



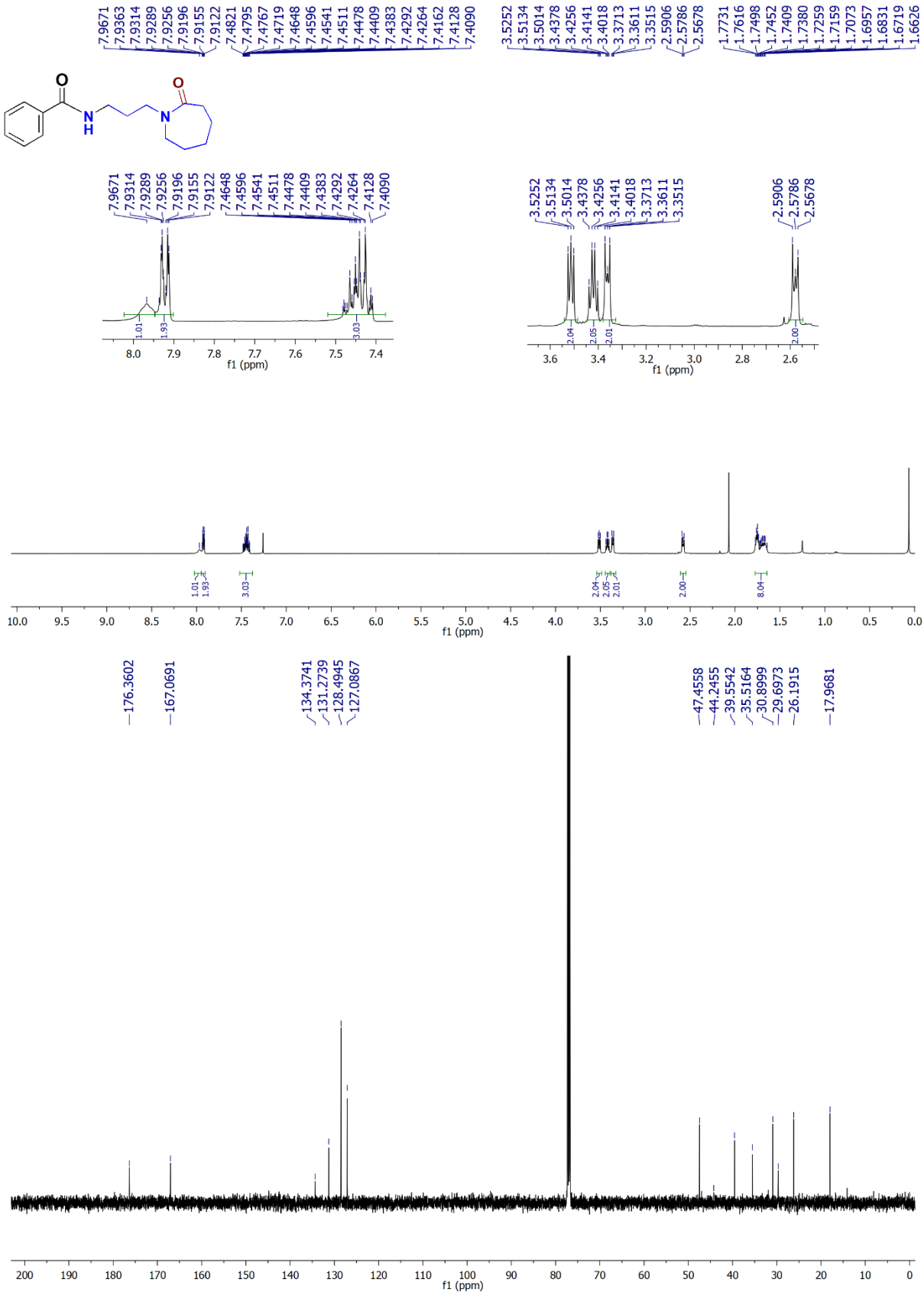
^{1}H and ^{13}C NMR for 15a



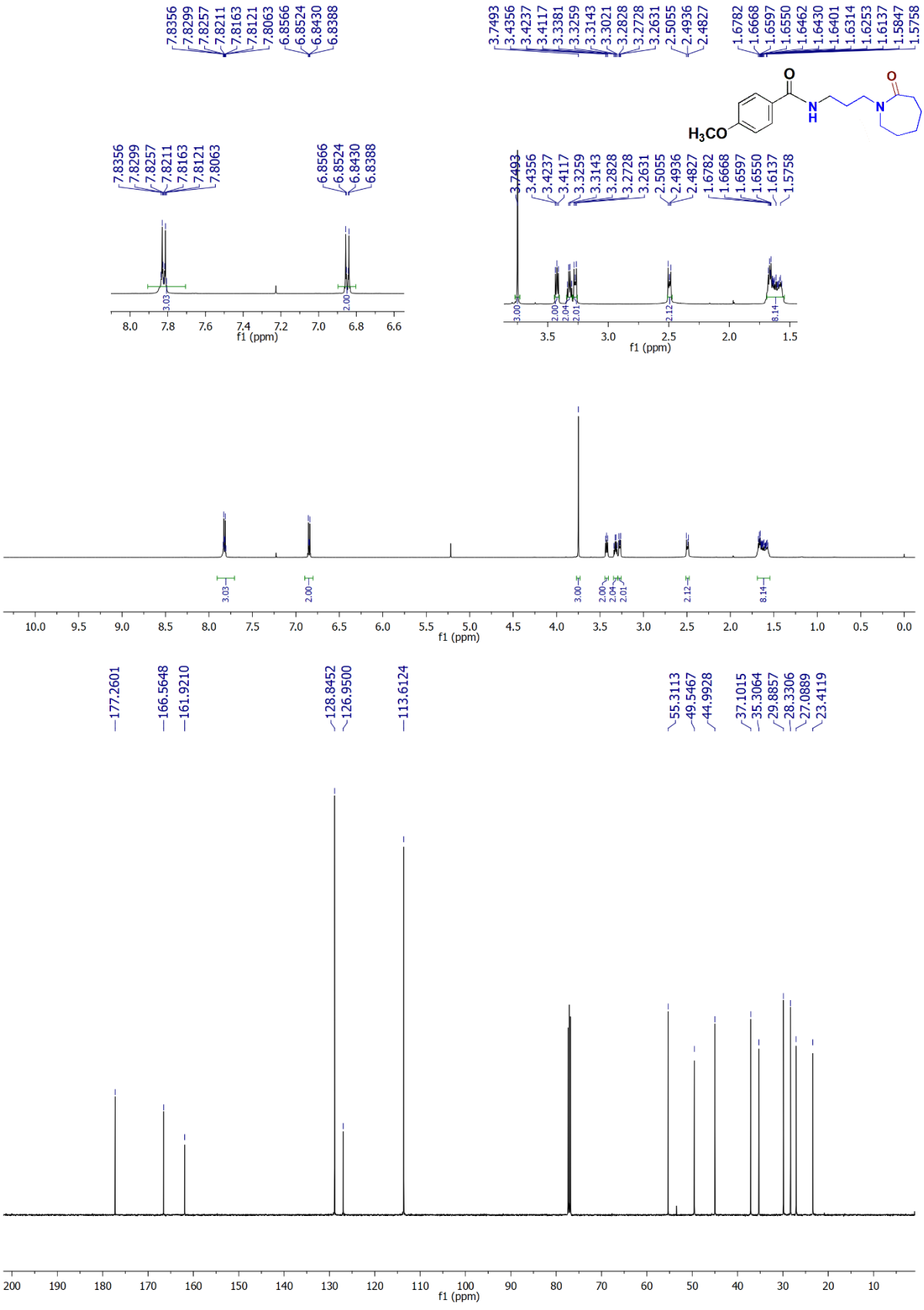
^{1}H and ^{13}C NMR for 15b



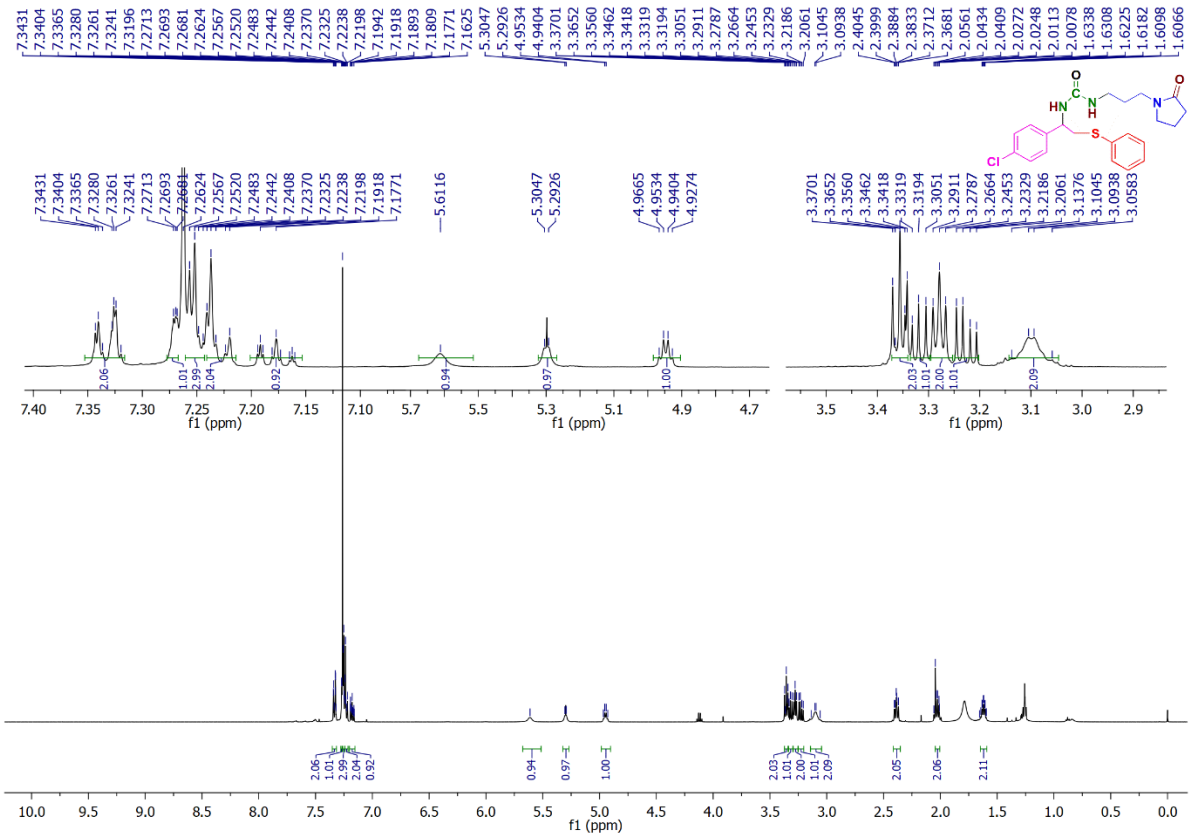
^{1}H and ^{13}C NMR for 16a

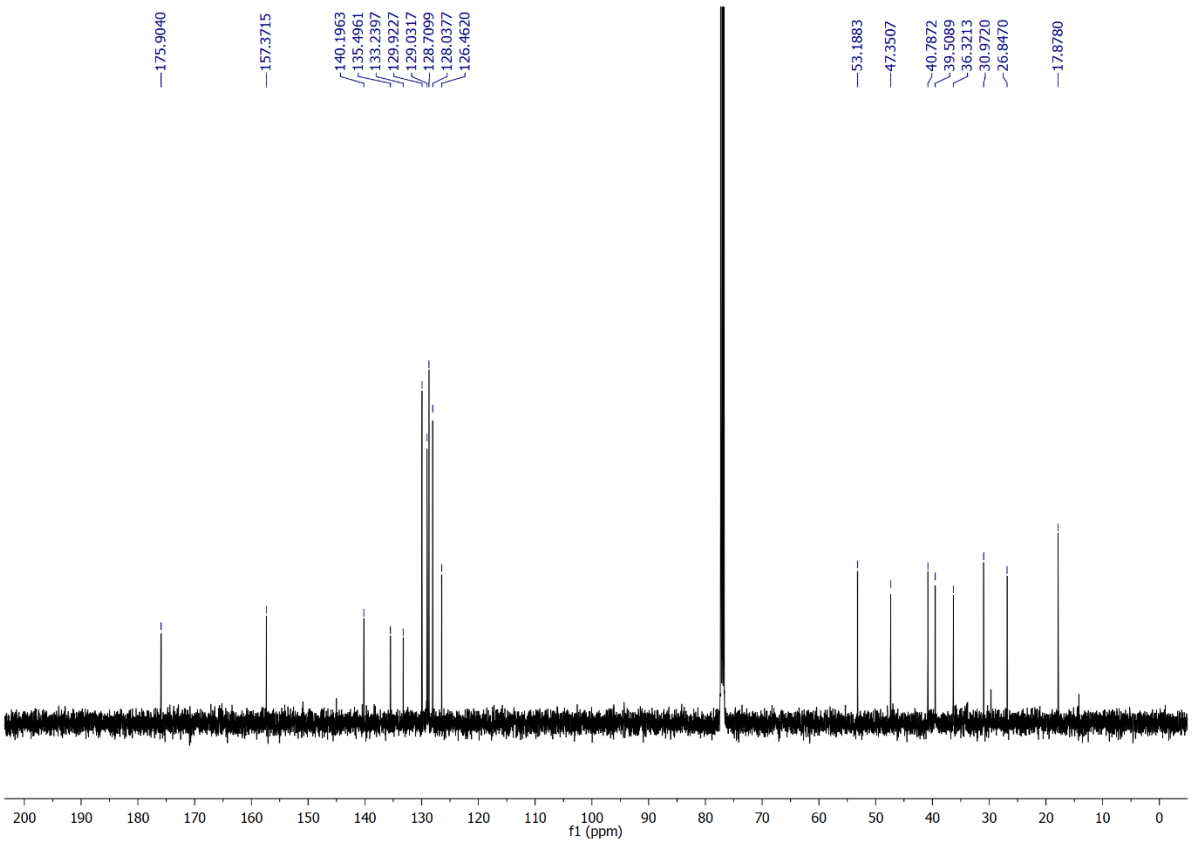


^{1}H and ^{13}C NMR for 16b

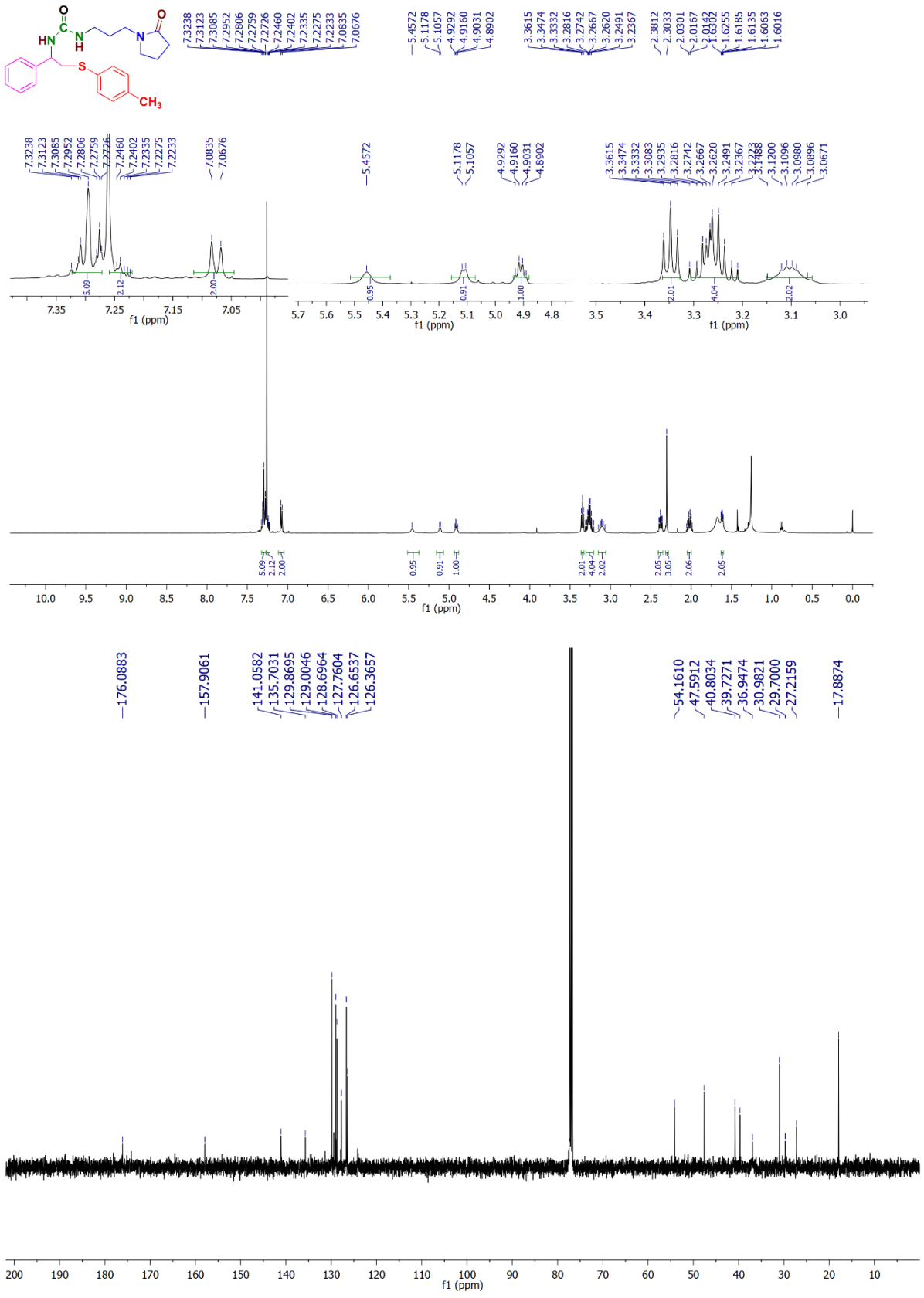


^{1}H and ^{13}C NMR for 17c

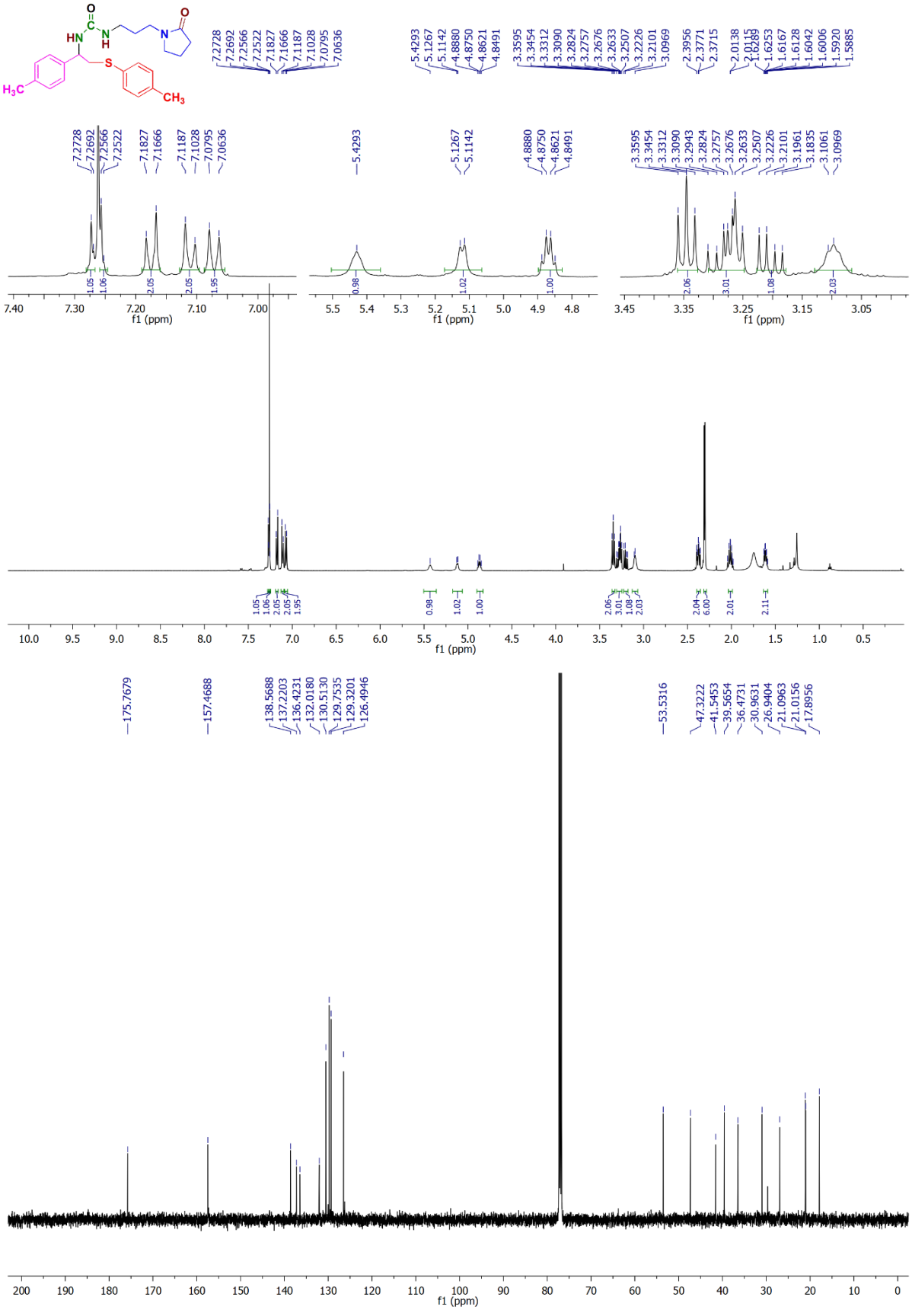




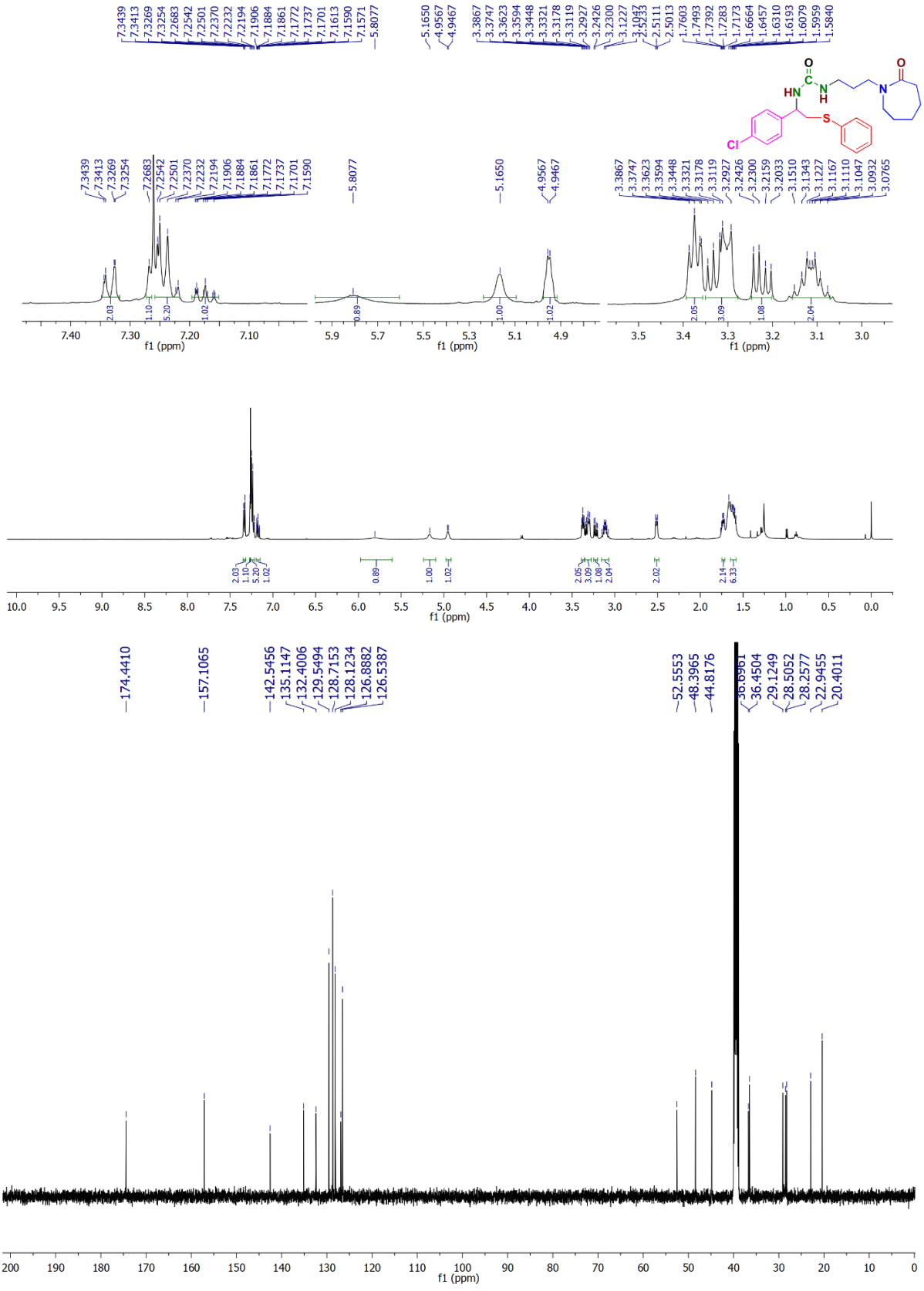
^{1}H and ^{13}C NMR for 17d



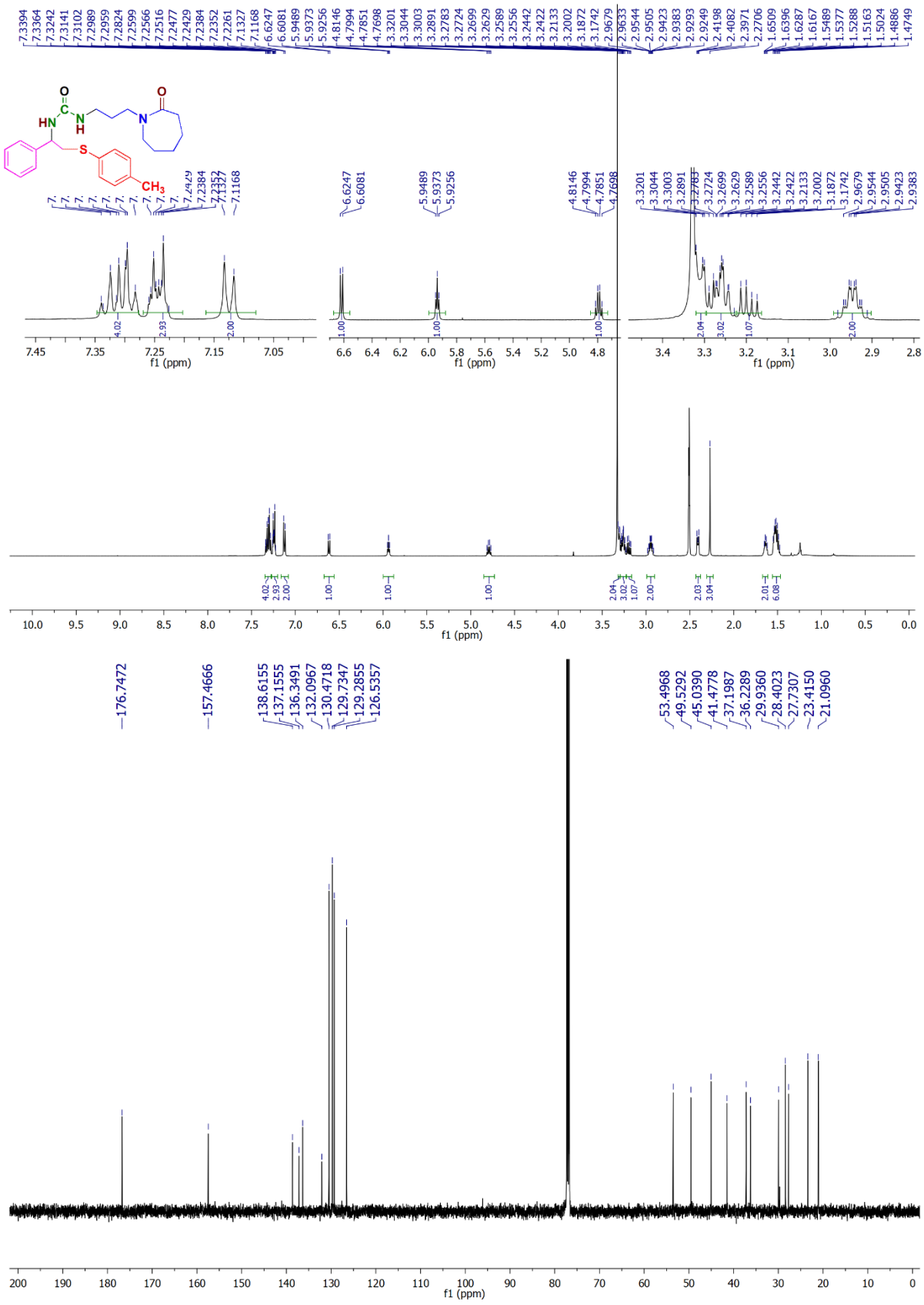
^{1}H and ^{13}C NMR for 17i



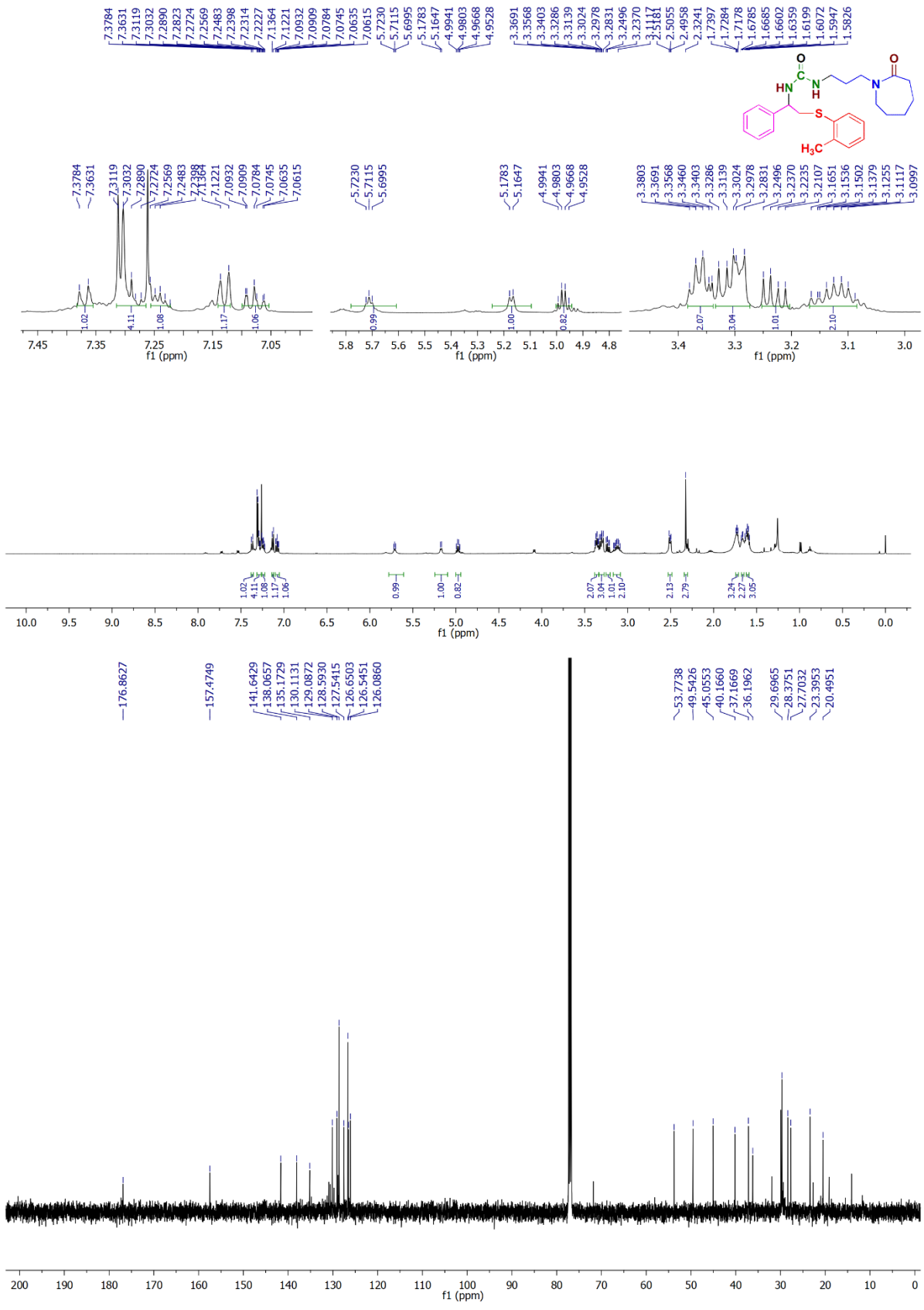
^{1}H and ^{13}C NMR for 18c



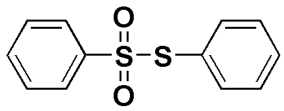
^{1}H and ^{13}C NMR for 18d

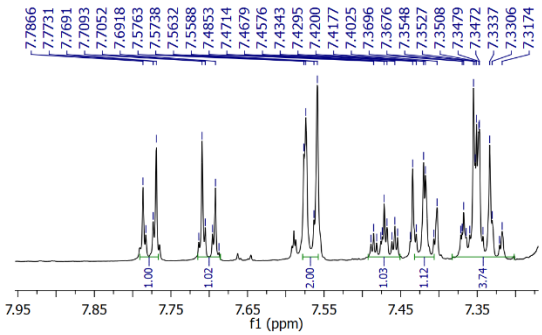


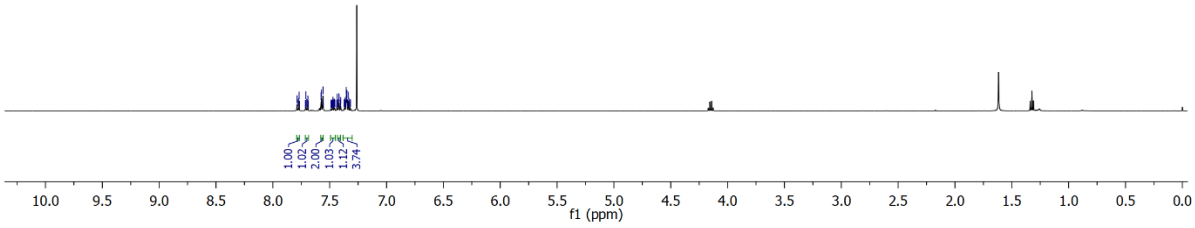
^{1}H and ^{13}C NMR for 18g

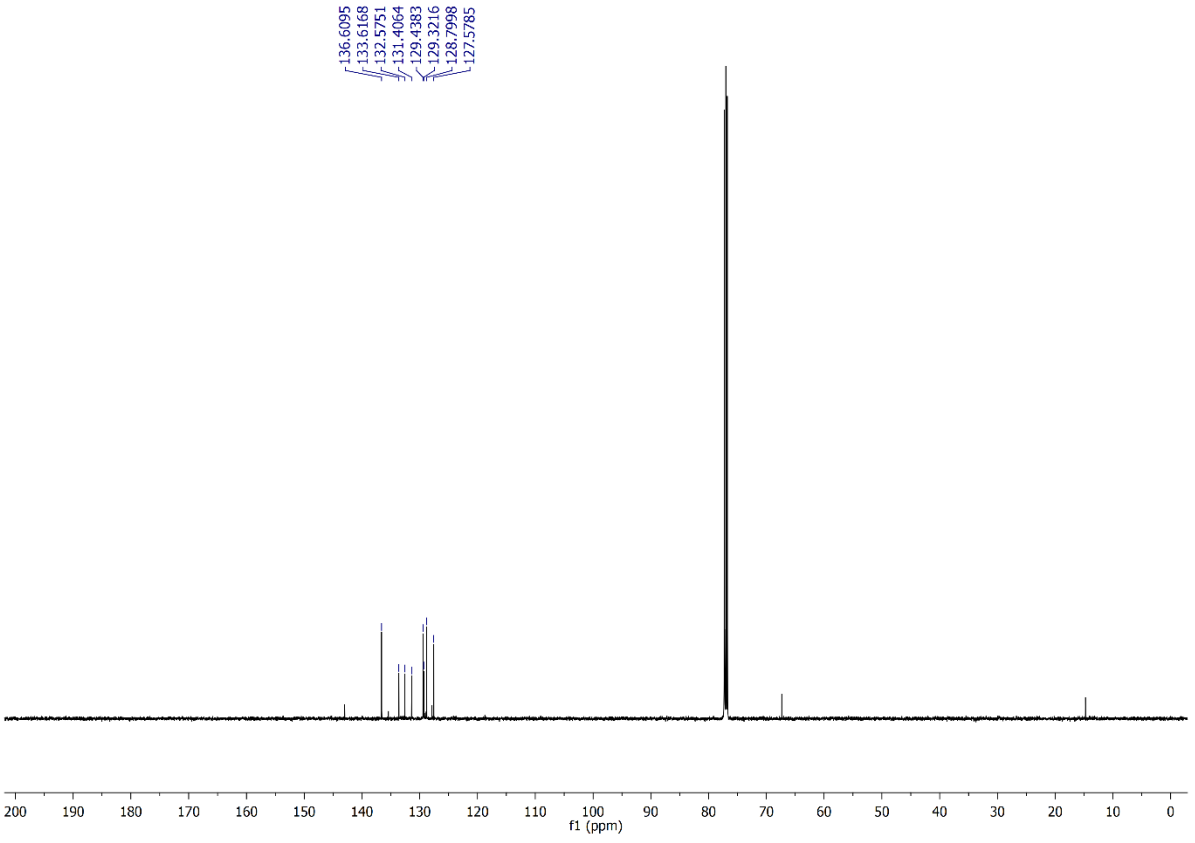


^{1}H and ^{13}C NMR for 19a

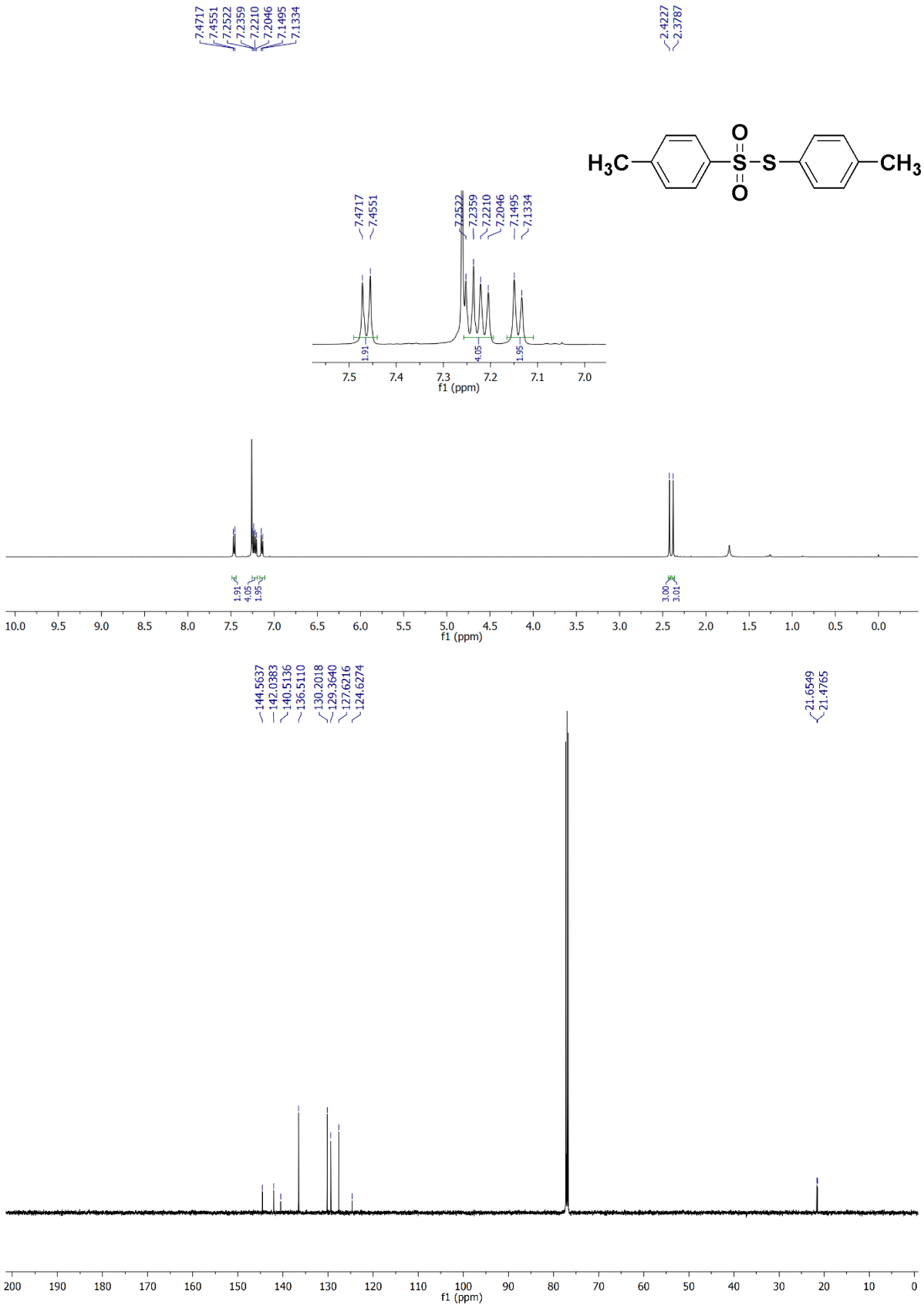




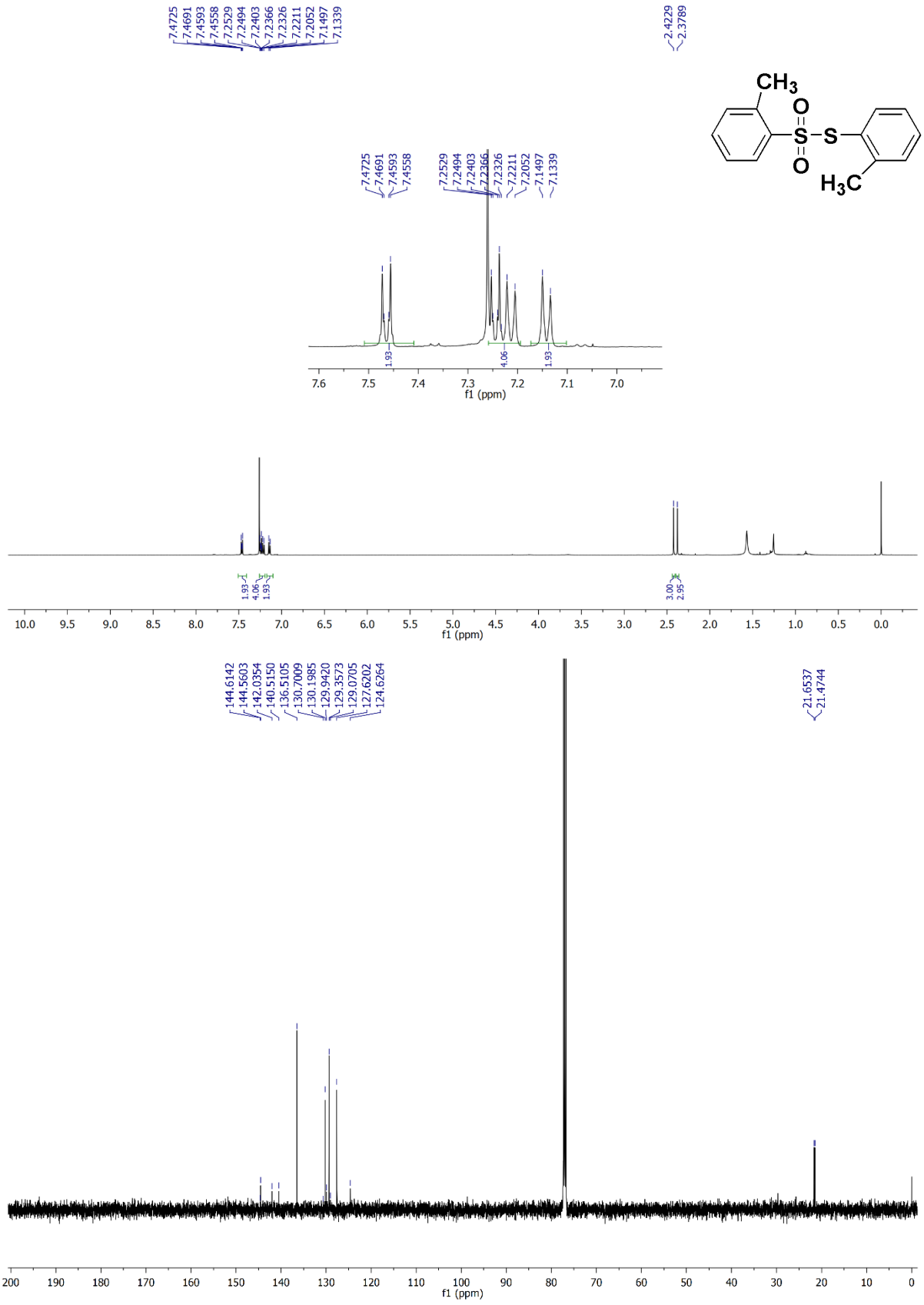




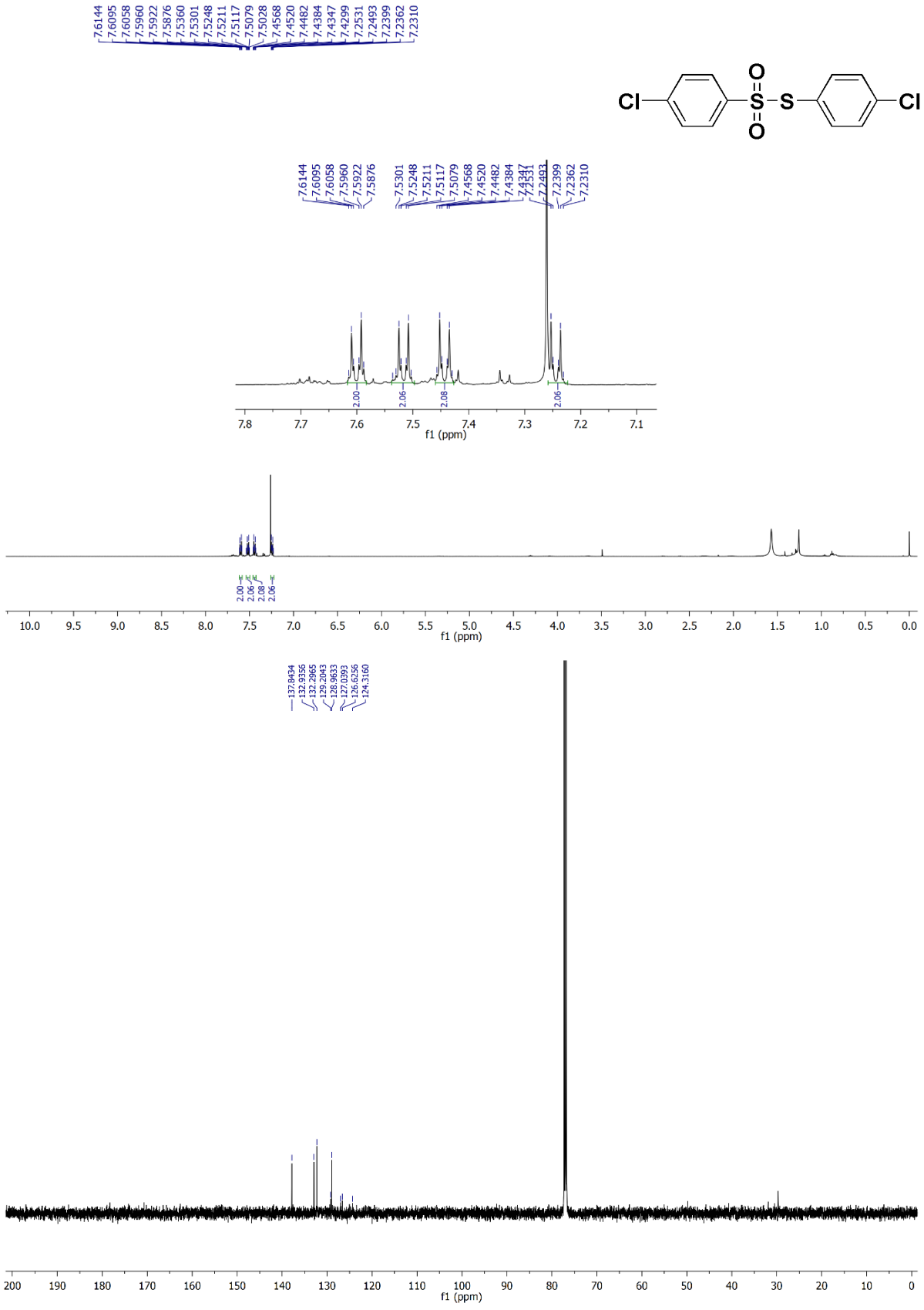
^{1}H and ^{13}C NMR for 19b



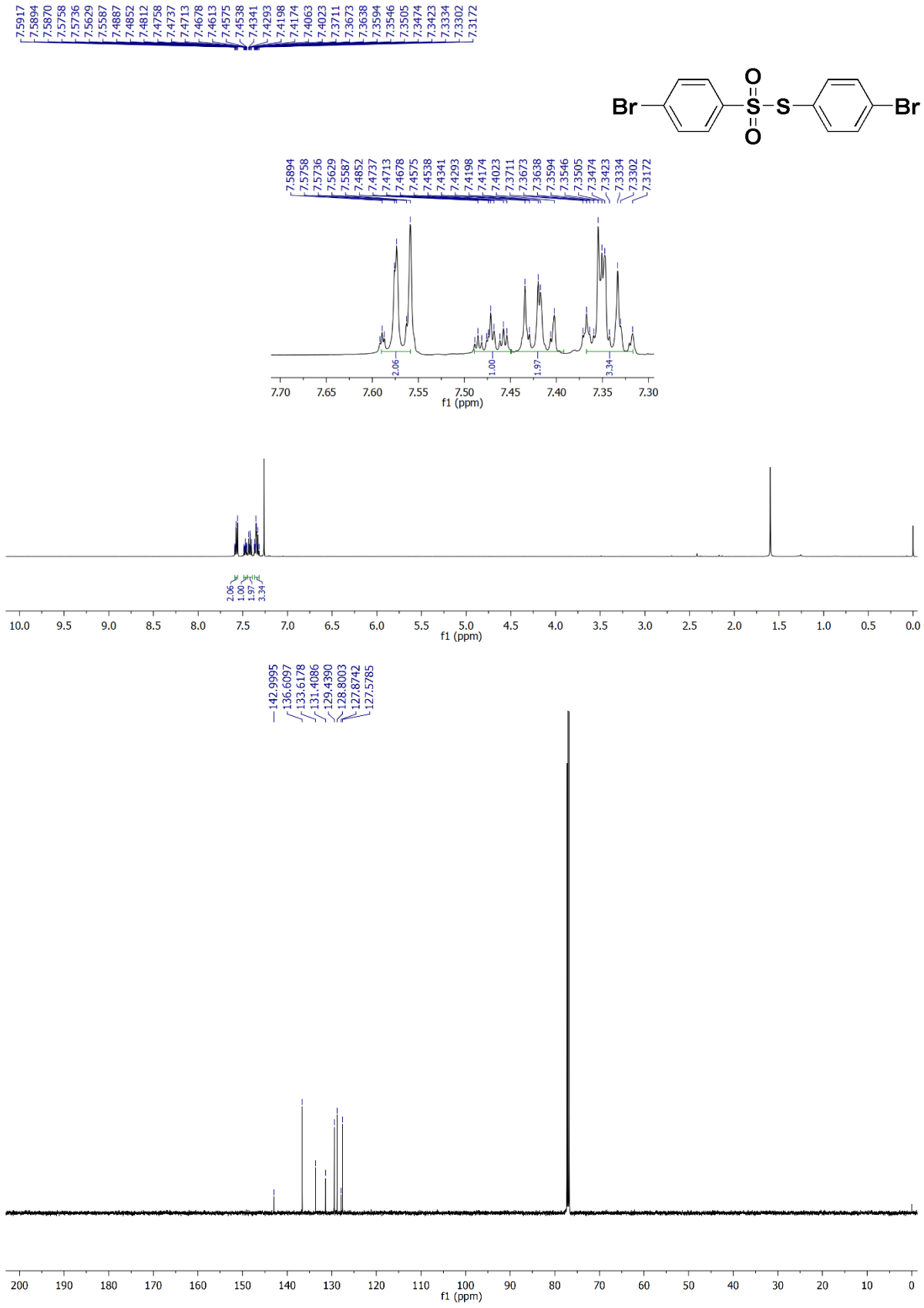
^{1}H and ^{13}C NMR for 19c



^{1}H and ^{13}C NMR for 19d

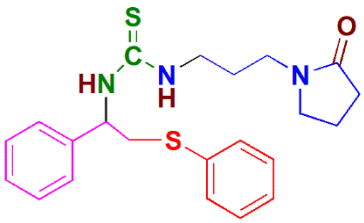


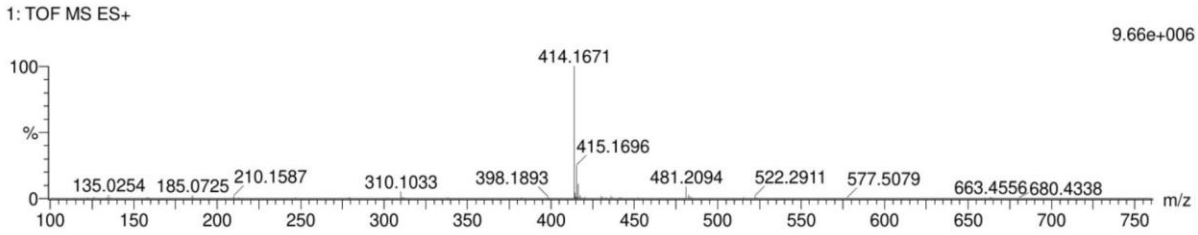
^{1}H and ^{13}C NMR for 19e



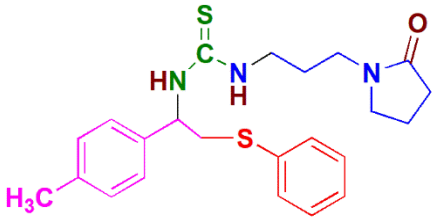
13. HRMS

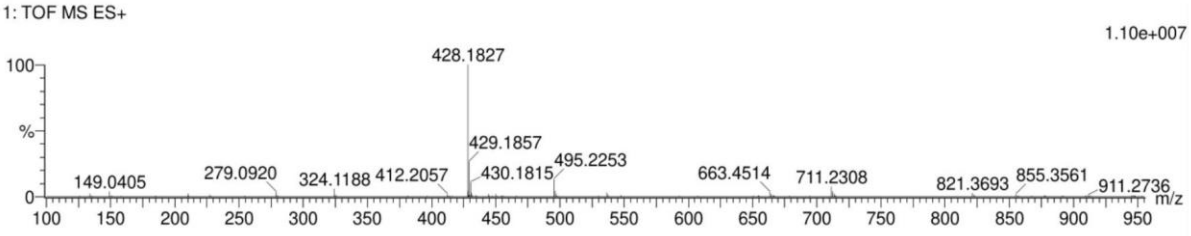
HRMS 7a





HRMS 7b





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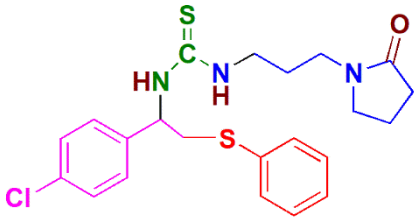

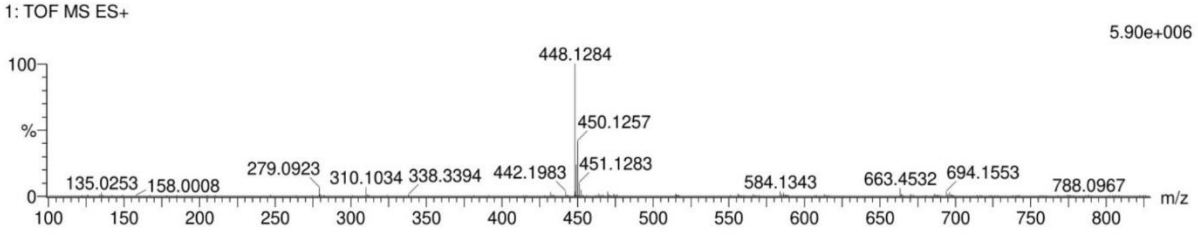

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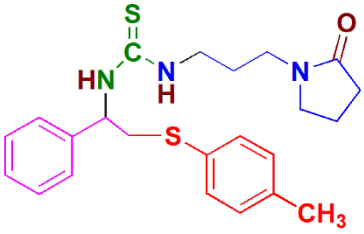

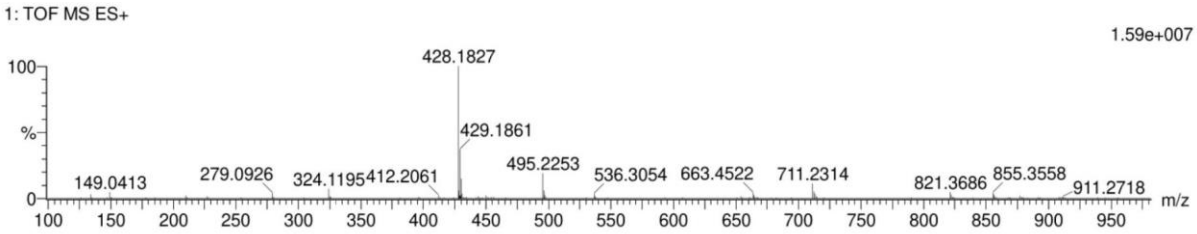

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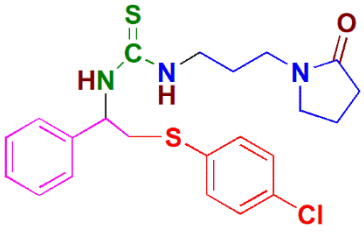

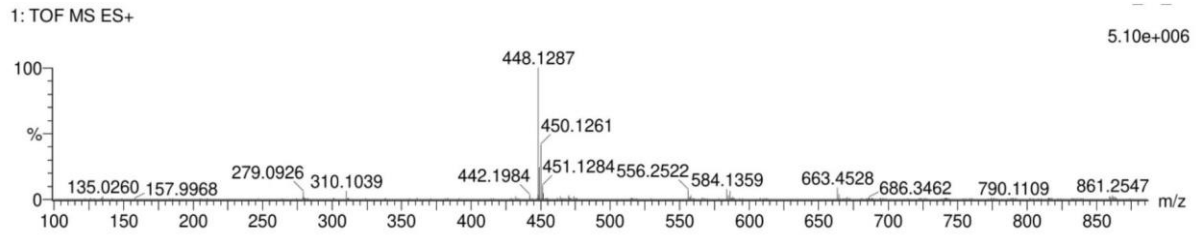

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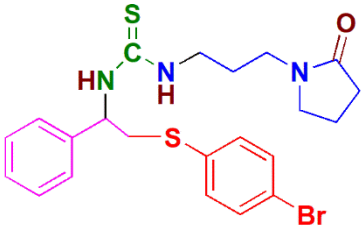

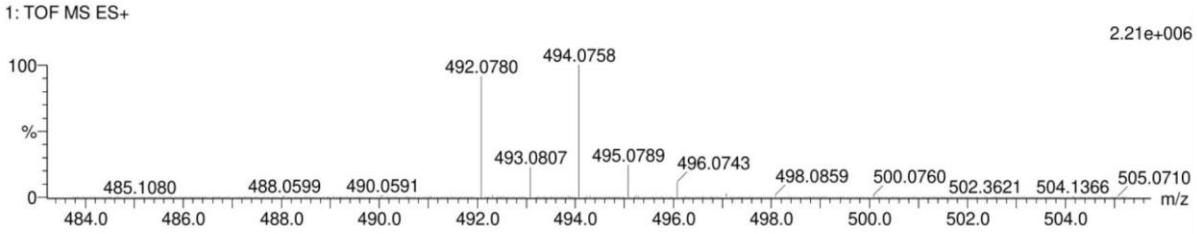

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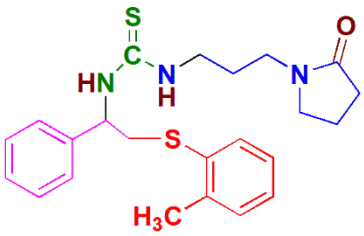

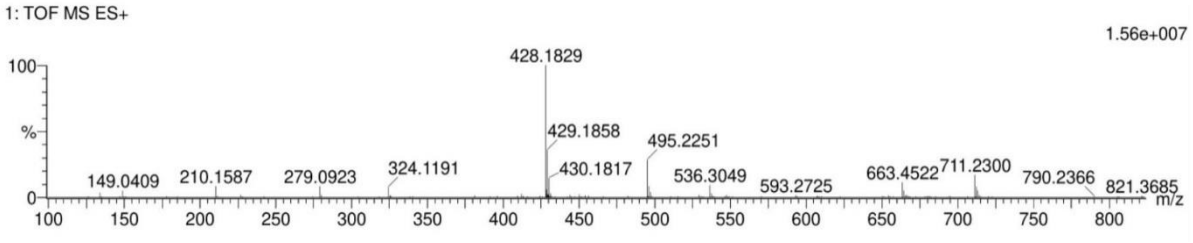

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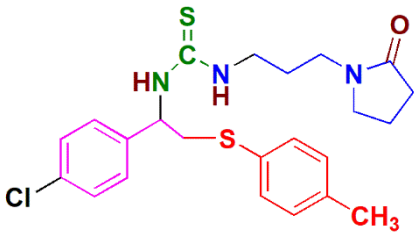

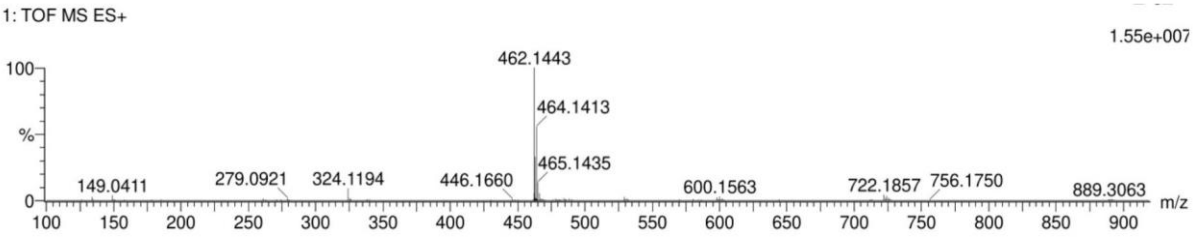

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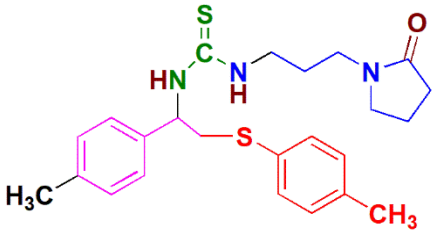

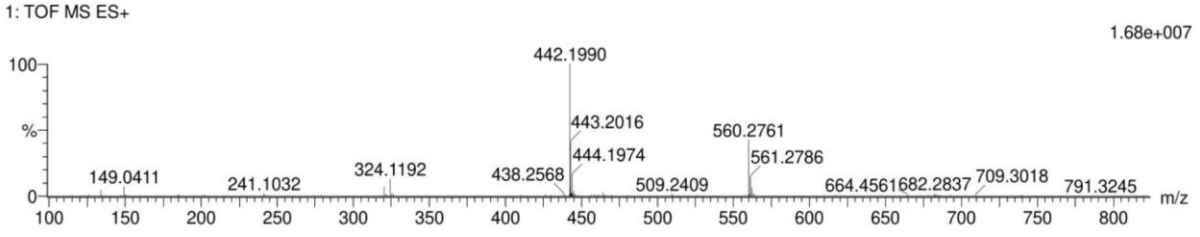

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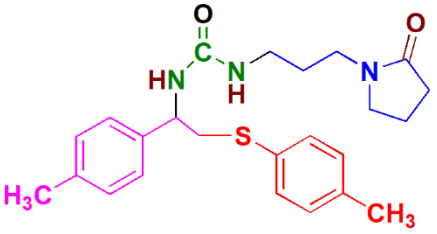

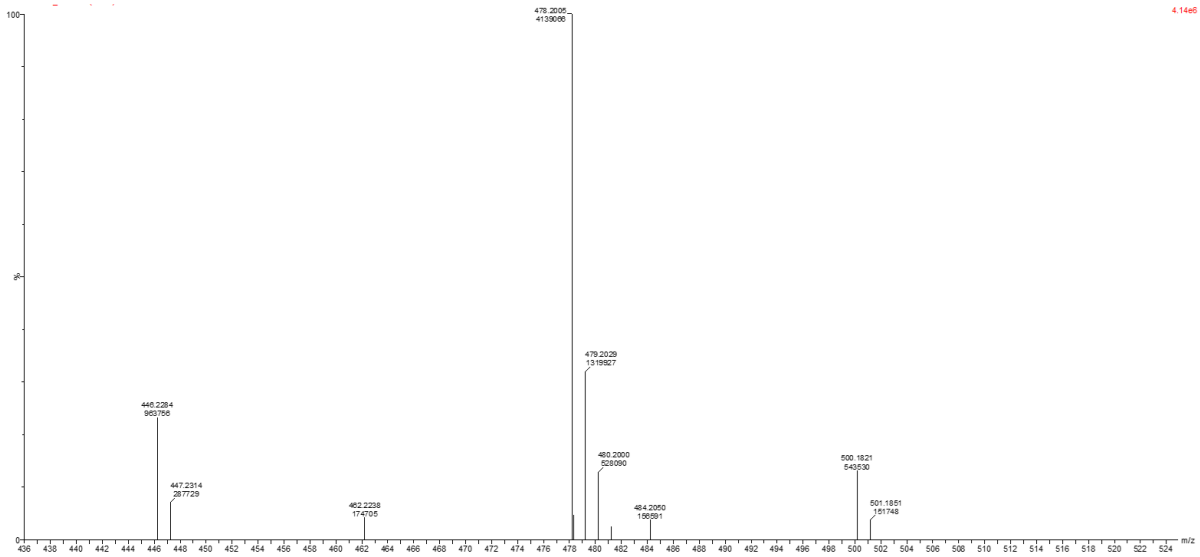

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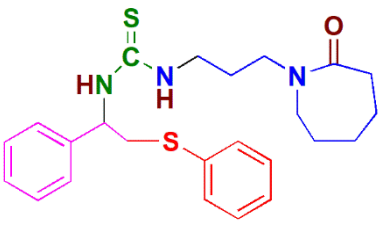

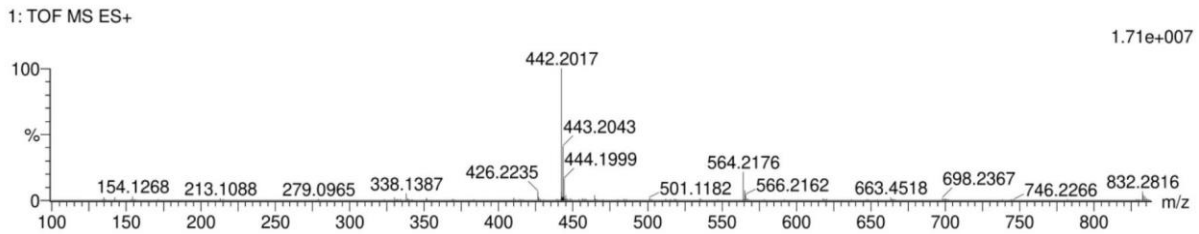

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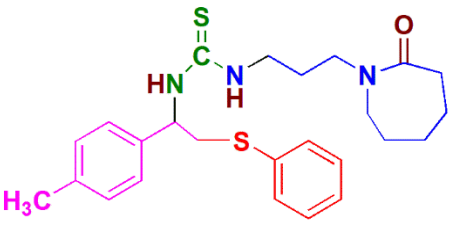

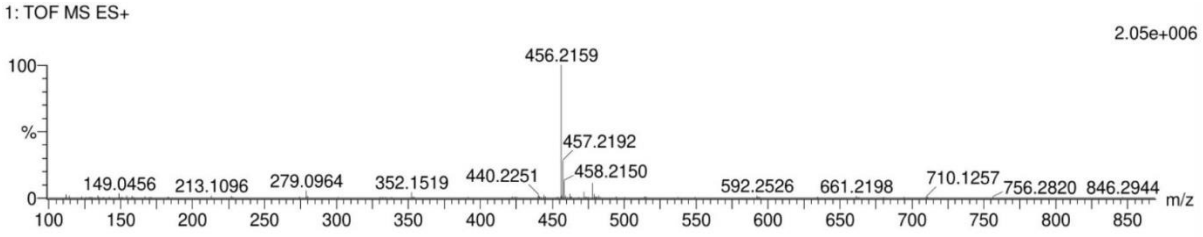

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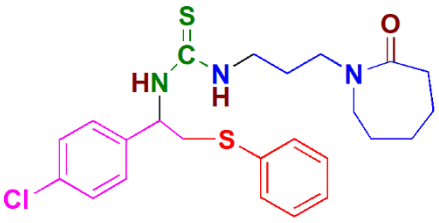

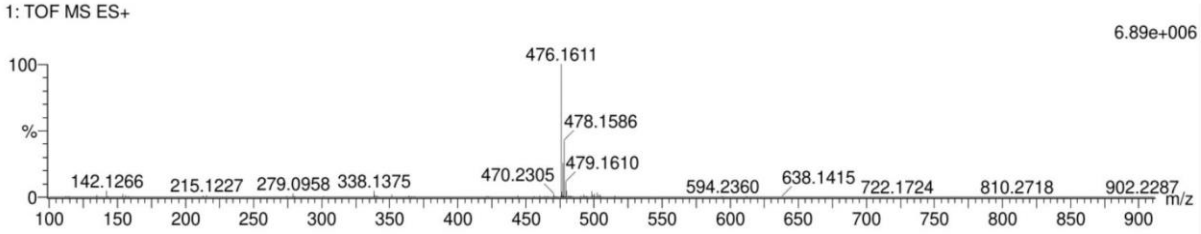

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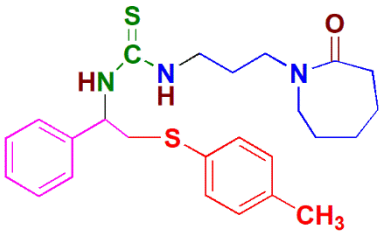

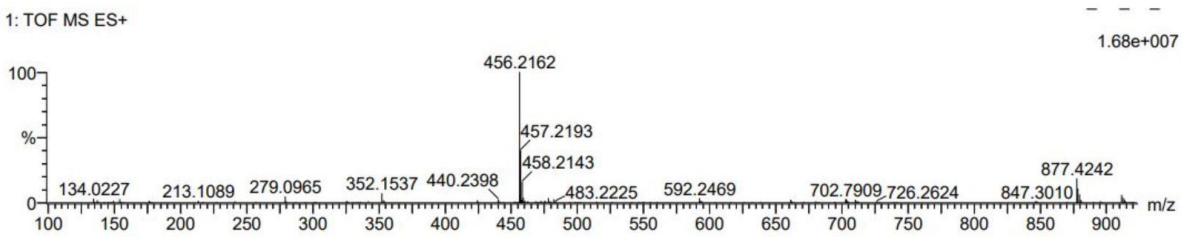

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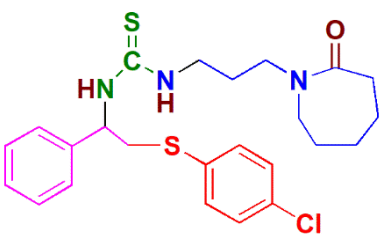

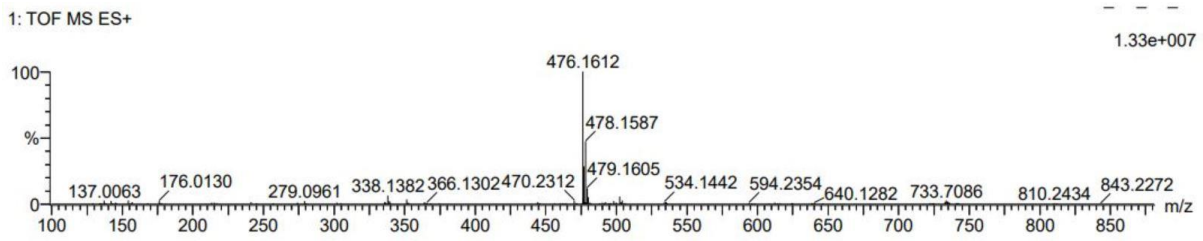

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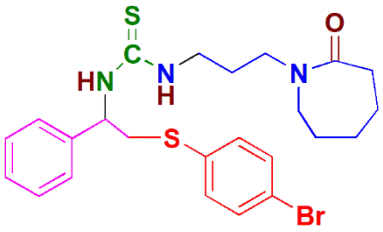

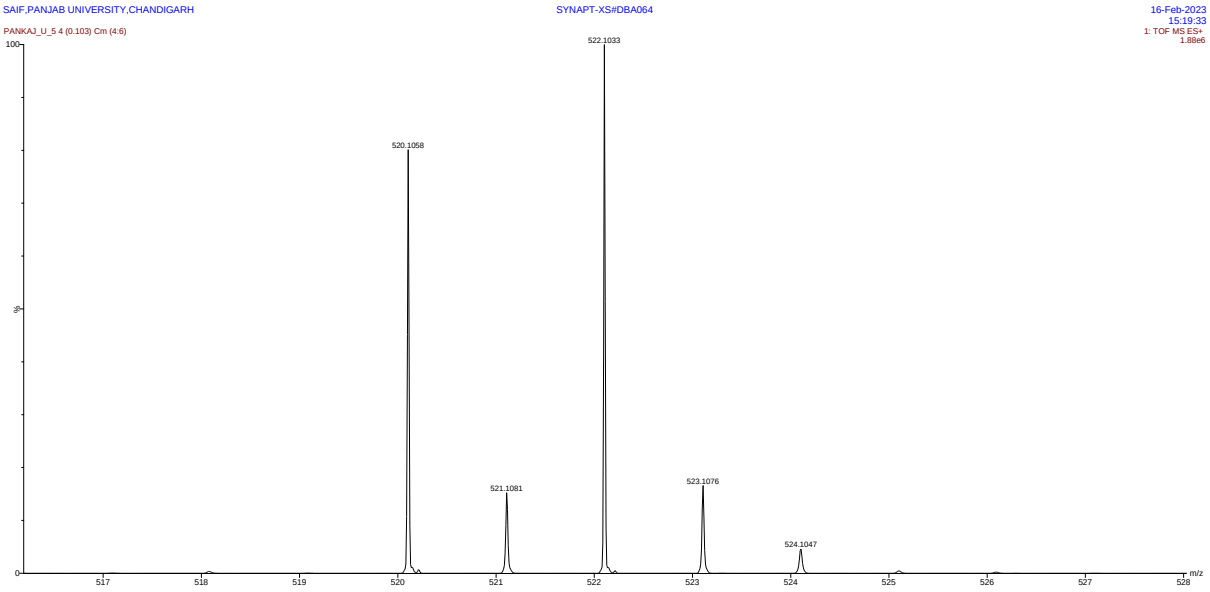

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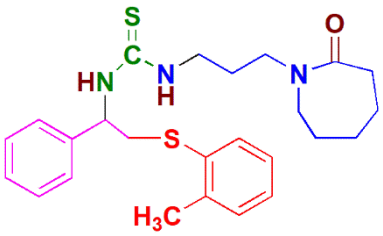

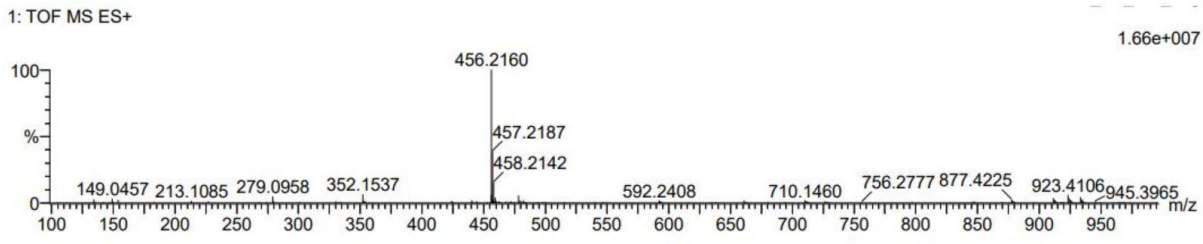

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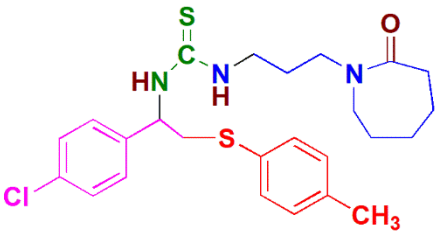

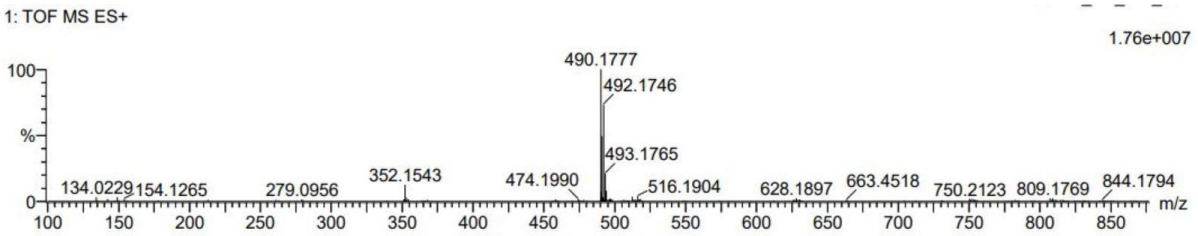

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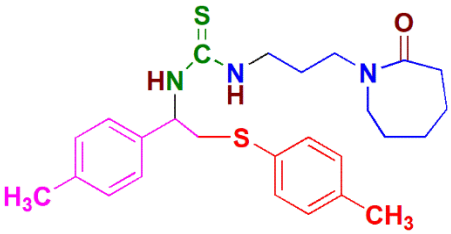

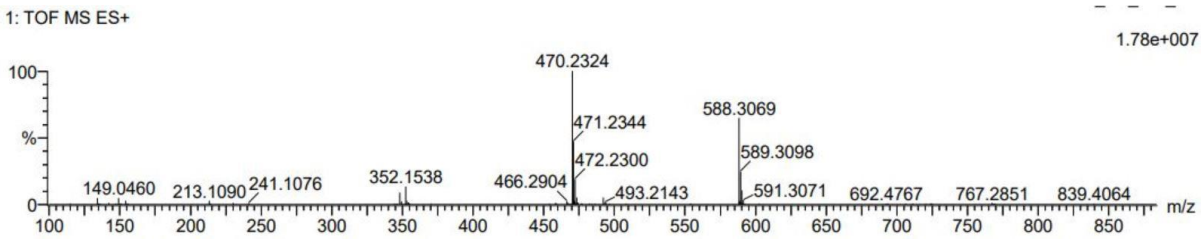

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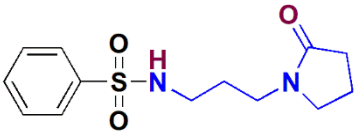

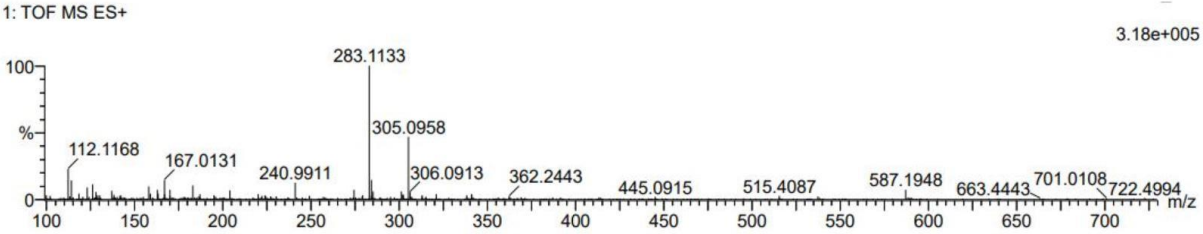

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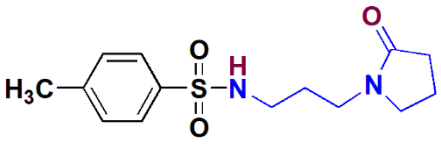

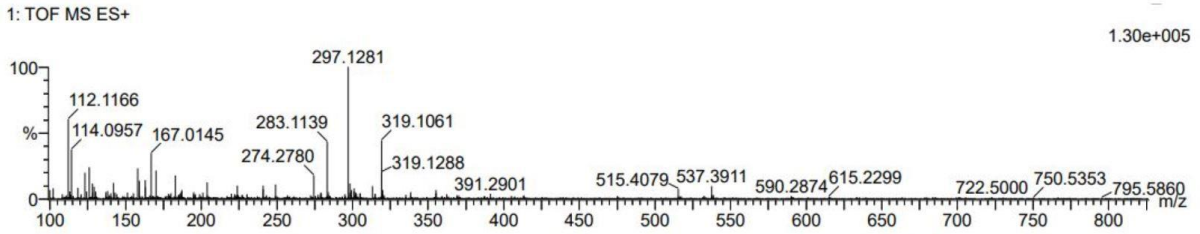

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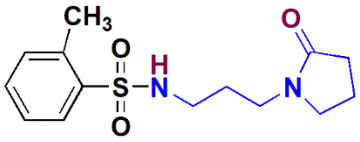

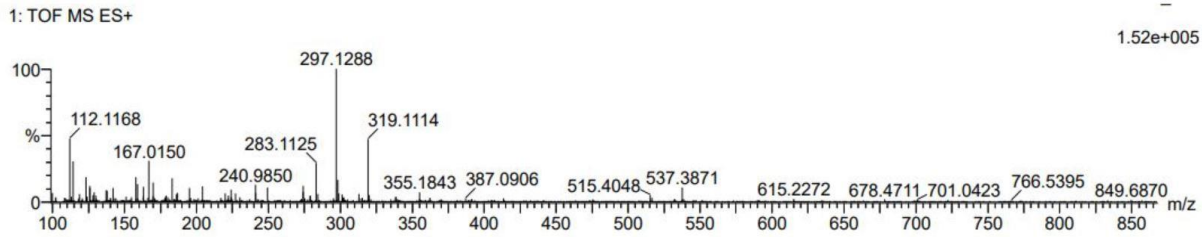

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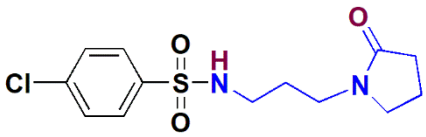

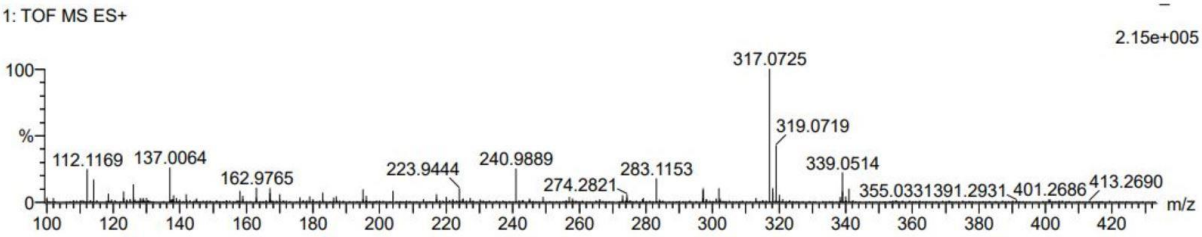

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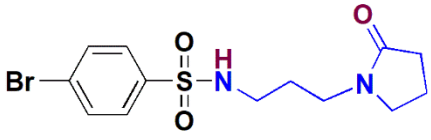

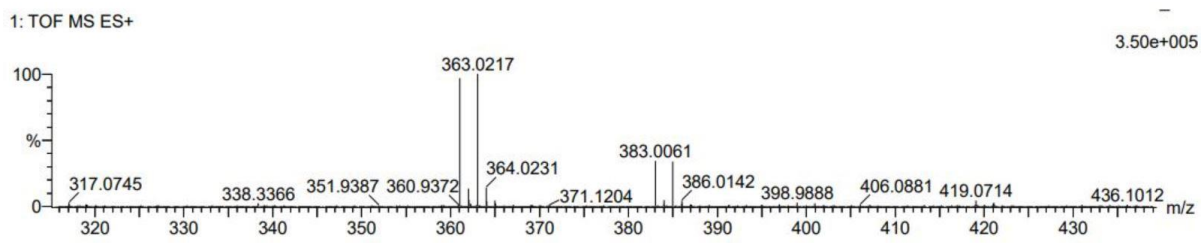

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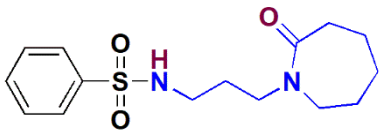

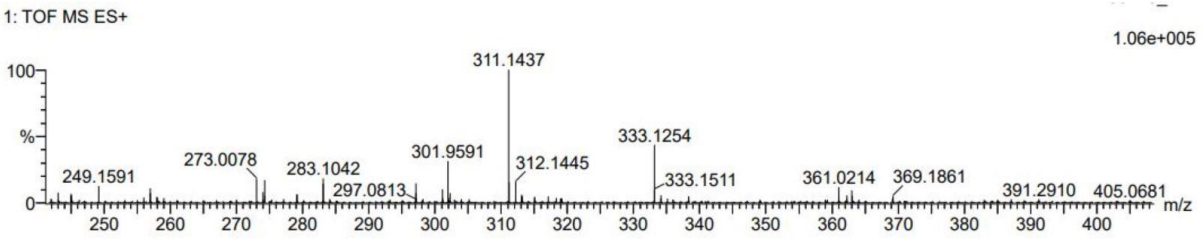

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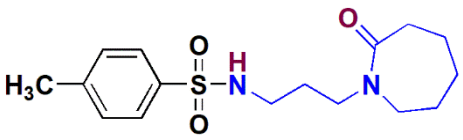

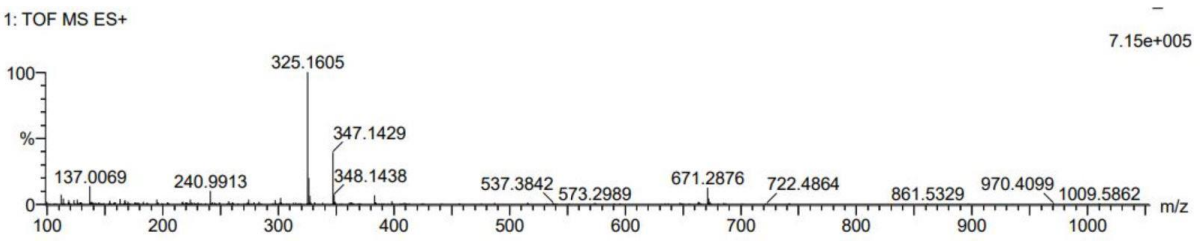

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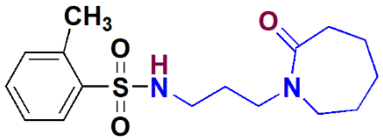

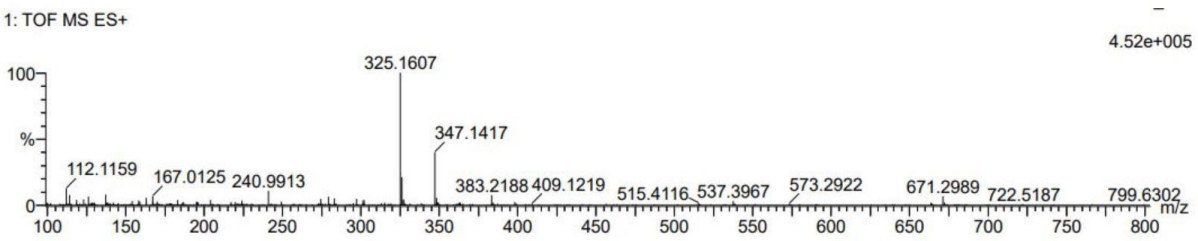

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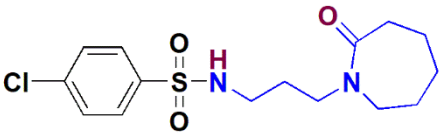

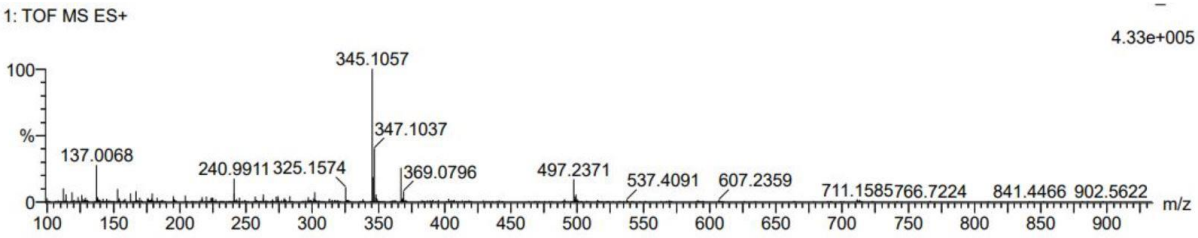

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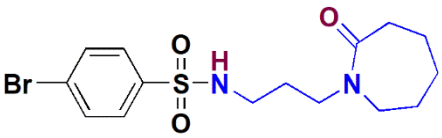

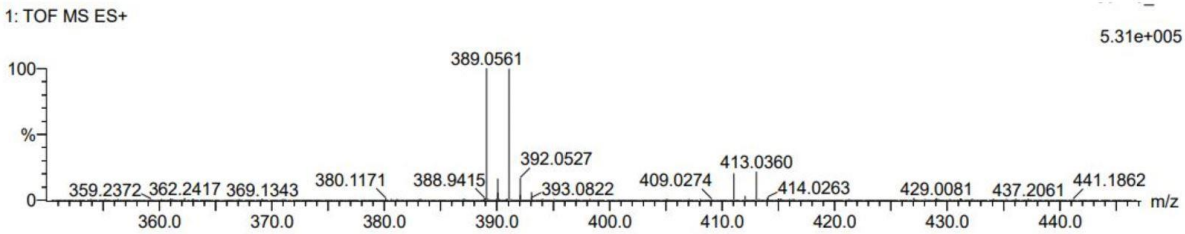

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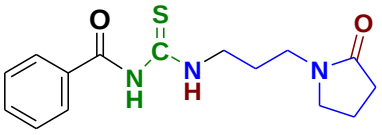

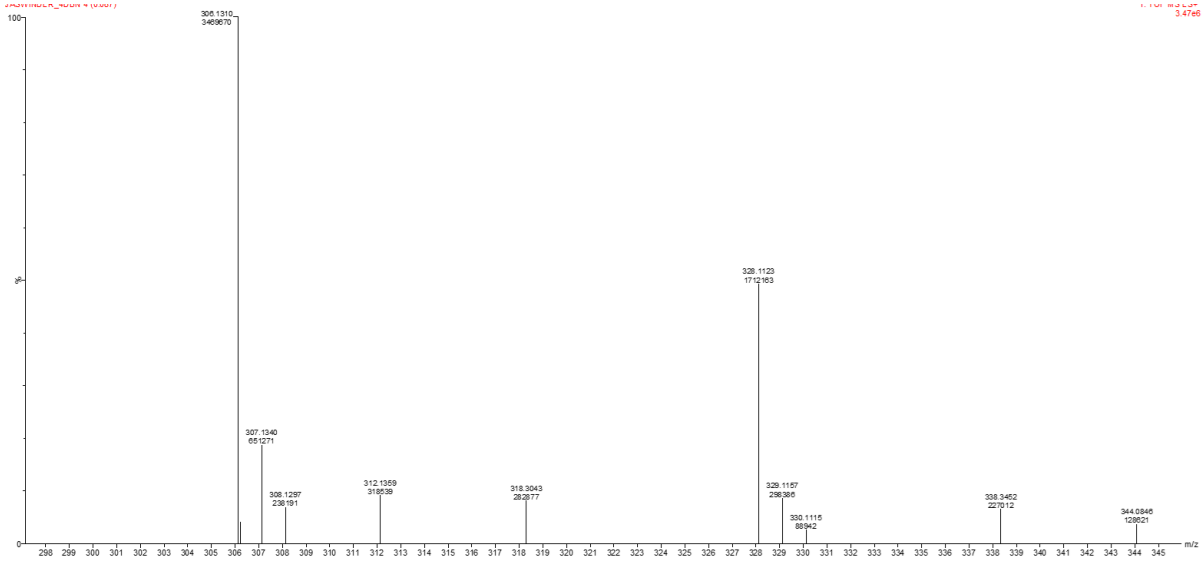

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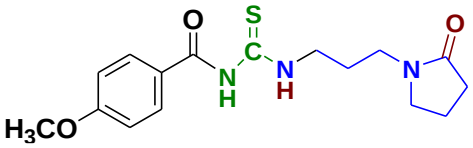
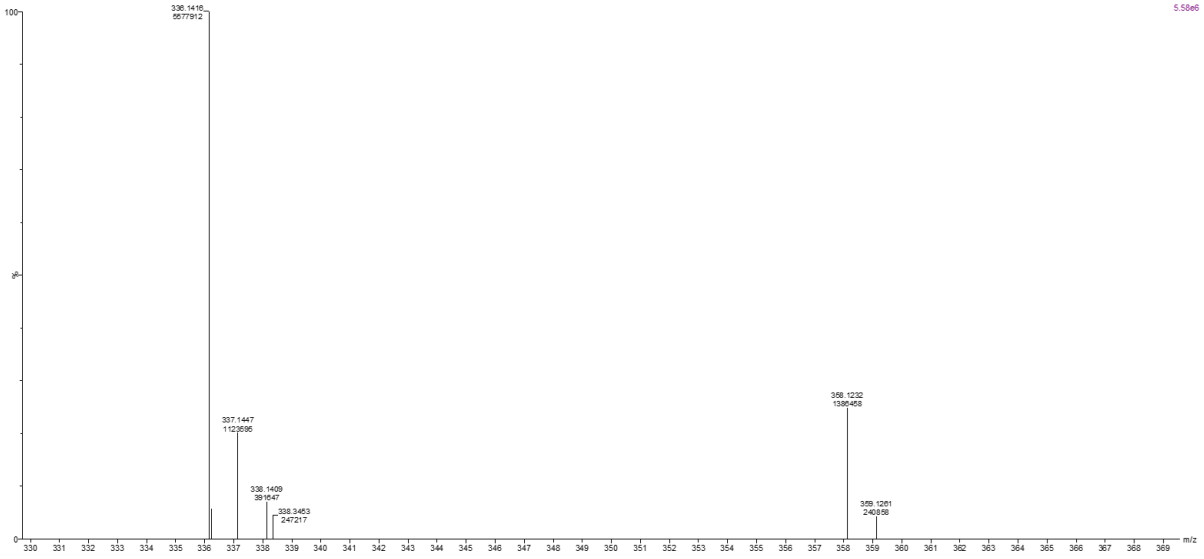
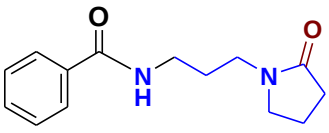
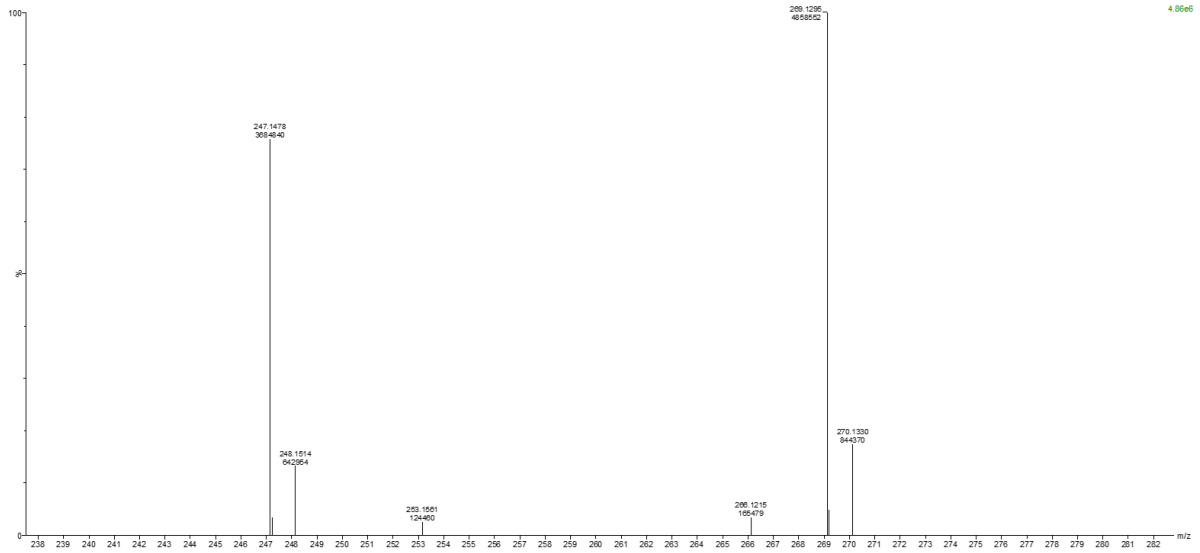


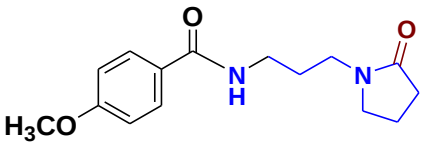


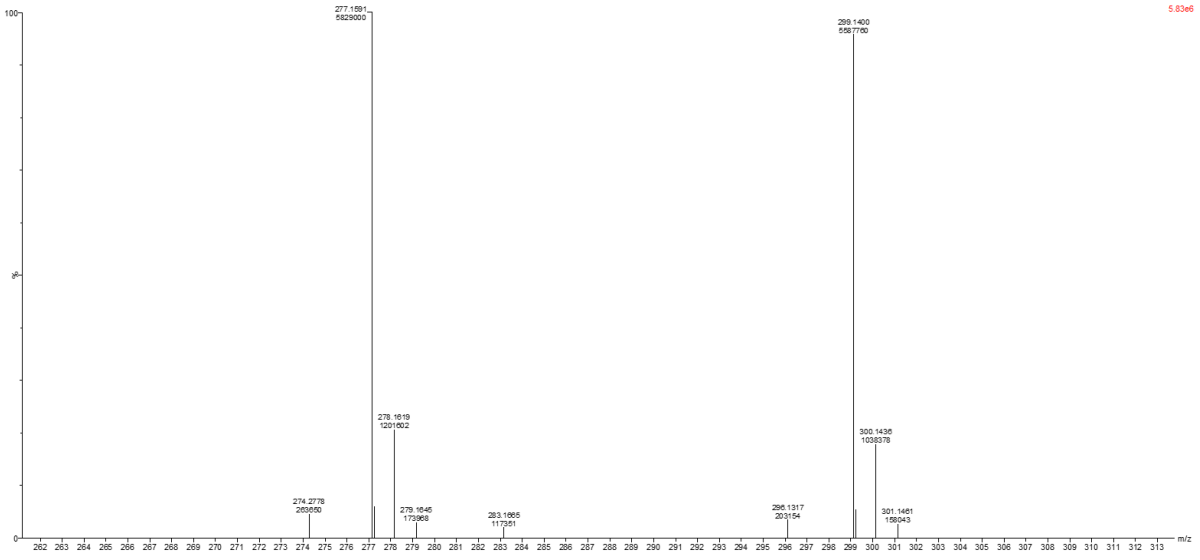
HRMS 15a



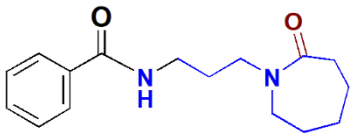


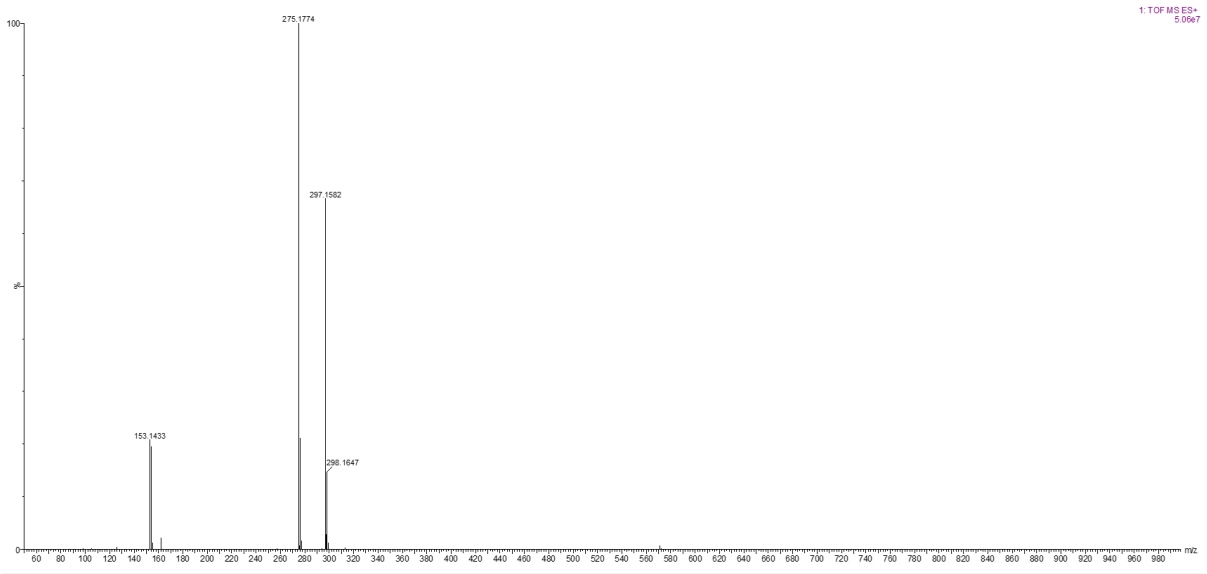
HRMS 15b



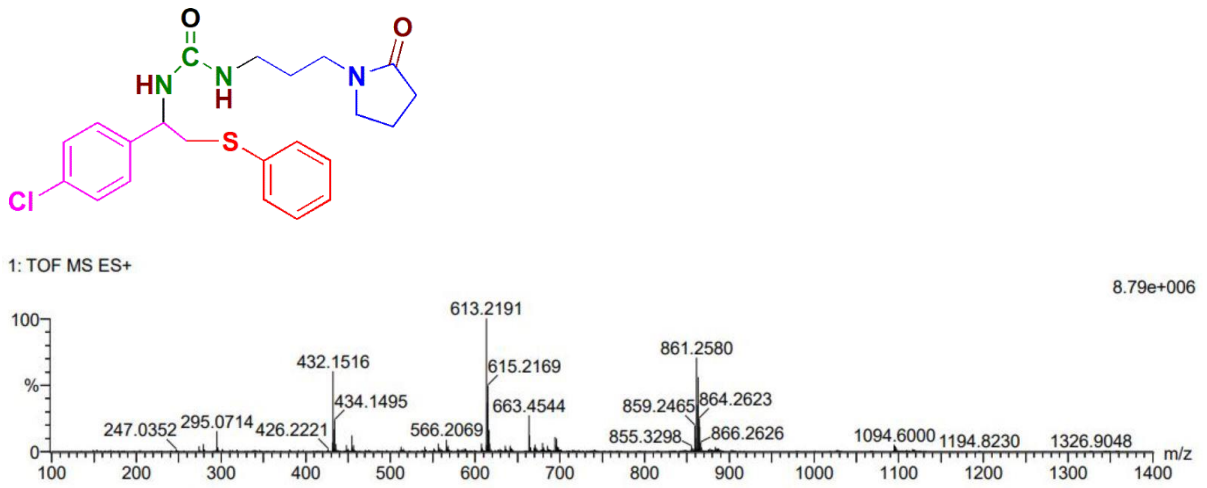


HRMS 16a





HRMS 17c



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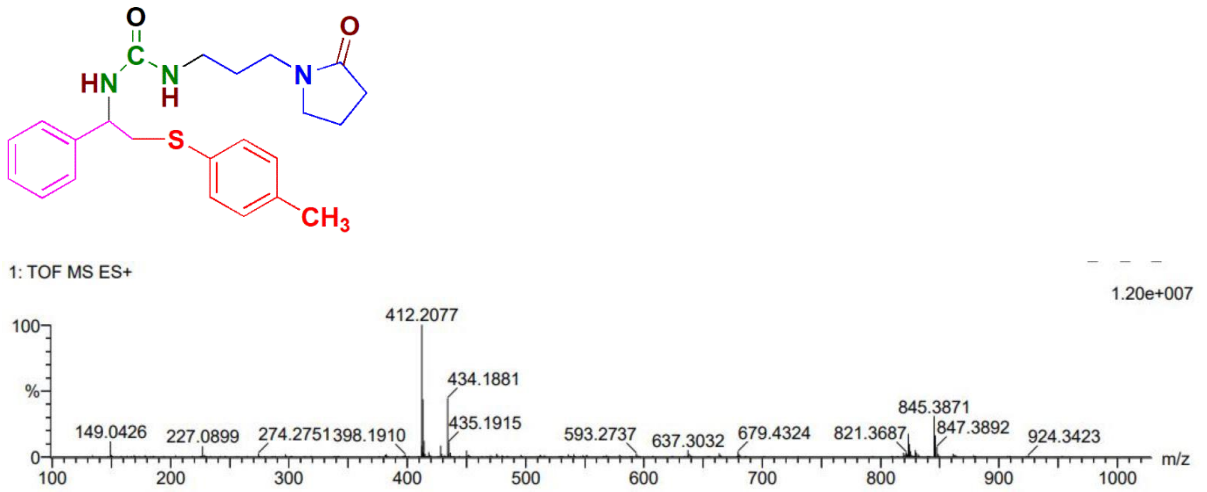
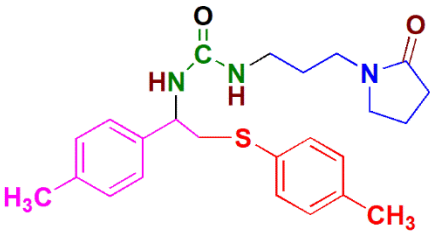
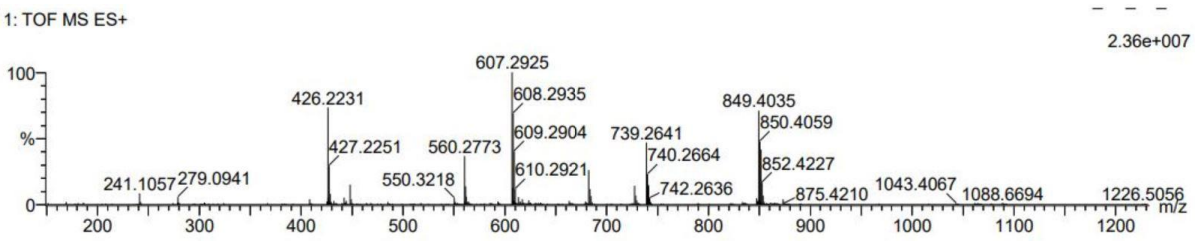
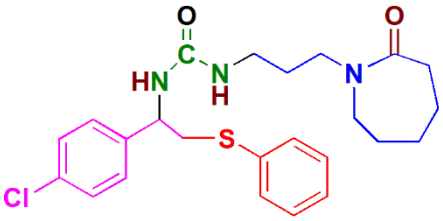


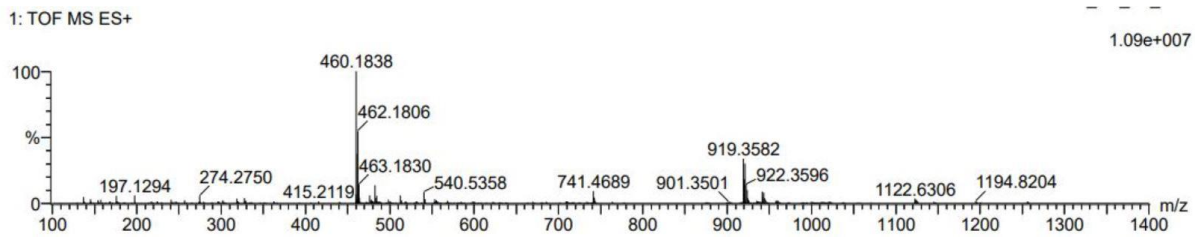
HRMS 17i



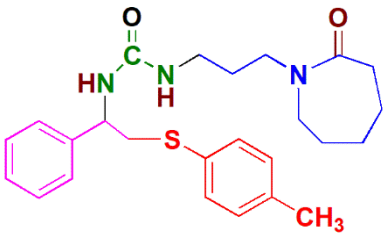


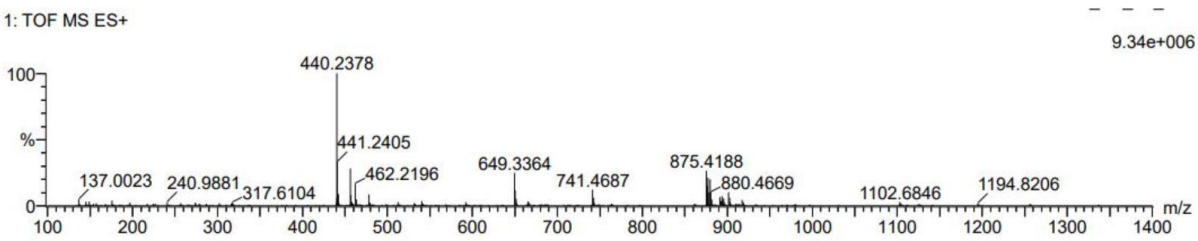
HRMS 18c



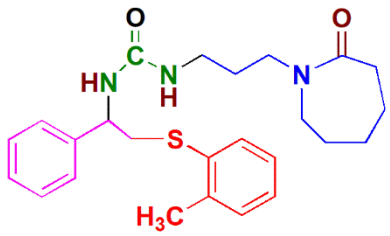


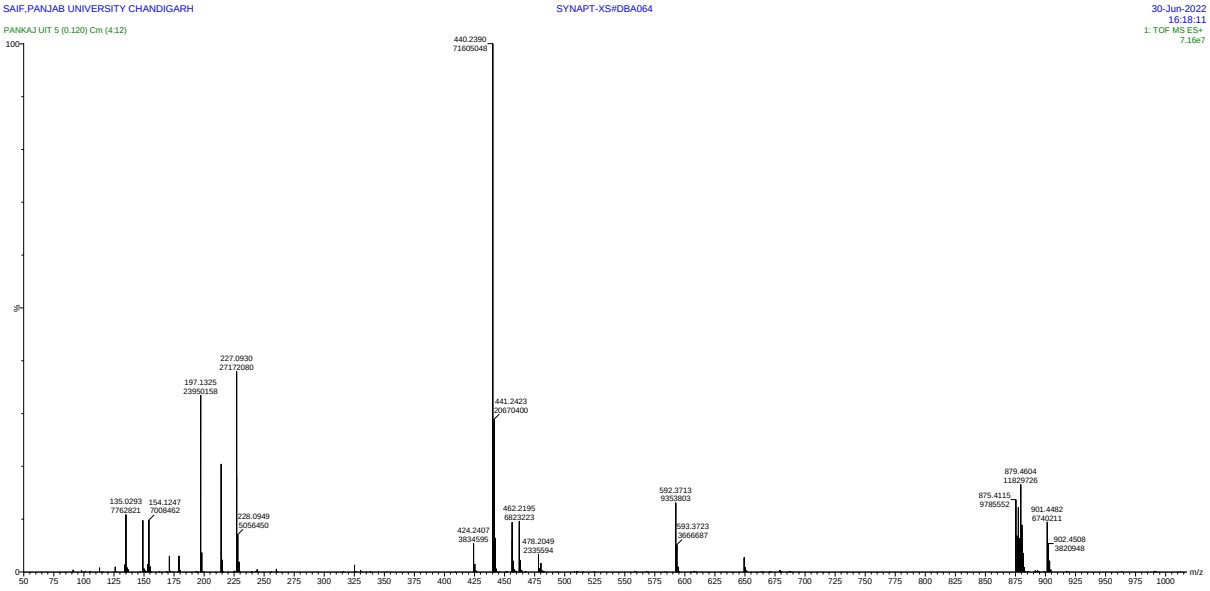
HRMS 18d



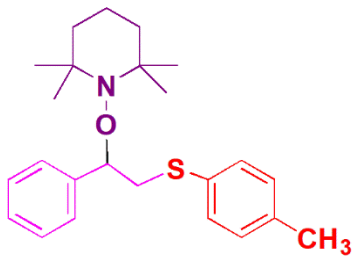


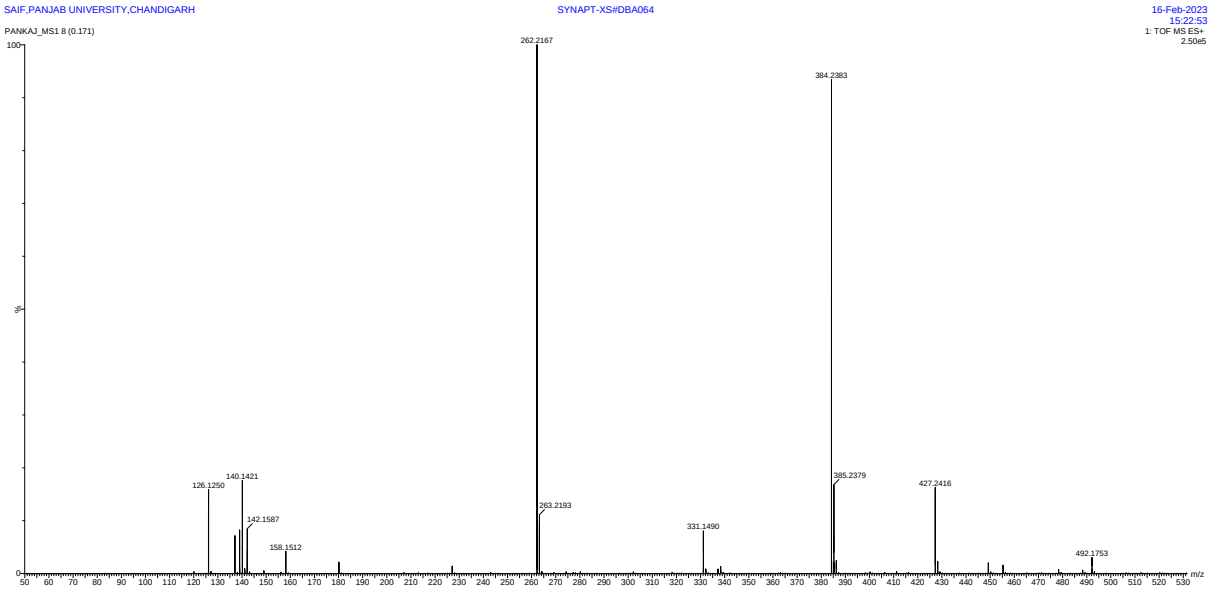
HRMS 18g





HRMS TEMPO-Adduct 20





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2. J. Chen, K. Natte. X. F. Wu. *Tetrahedron lett.*, 2015, ***56***, 342.
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