A One-pot Ring-Closure and Ring-Opening Sequence for the Cascade Synthesis of Dihydrofurofurans and Functionalized Furan

Maruti B. Yadav, Yeon Tae Jeong*

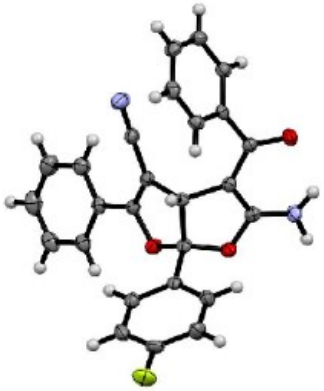
Department of Image Science and Engineering, Pukyong National University, Busan 608-737, Republic of Korea

Supporting Information

Table of contents

1) **Crystallographic Data**

a) 3m (CCDC no. 2077525):



3m

CCDC 2077525

Bond precision: C-C = 0.0021 A Wavelength=0.71073

Cell: a=6.8865(7) b=22.291(3) c=25.817(2)

alpha=90 beta=90 gamma=90

Temperature: 200 K

Calculated Reported

Volume 3963.1(7) 3963.1(7)

Space group P b c a P b c a

Hall group -P 2ac 2ab ?

Moiety formula C_{26} H_{17} F N_2 O_3 C_{26} H_{17} F N_2 O_3

Sum formula C_{26} H_{17} F N_2 O_3 C_{26} H_{17} F N_2 O_3

Mr 424.42 424.42

Dx,g cm-3 1.423 1.423

Z 8 8

Mu (mm-1) 0.100 0.100

F000 1760.0 1760.0

F000’ 1760.90

h,k,lmax 8,26,30 8,26,30

Nref 3513 3505

Tmin,Tmax 0.963,0.989 0.954,0.989, Tmin’ 0.954

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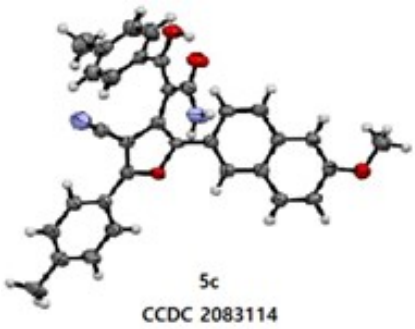
b) 5c (CCDC no. 2083114):



Bond precision: C-C = 0.0069 A Wavelength=0.71073

Cell: a=17.799(3) b=9.2371(19) c=18.139(3)

alpha=90 beta=114.941(4) gamma=90

Temperature: 200 K

Calculated Reported

Volume 2704.1(9) 2704.1(9)

Space group P 21/c P 21/c

Hall group -P 2ybc ?

Moiety formula C_{33} H_{26} N_2 O_4 C_{33} H_{26} N_2 O_4

Sum formula C_{33} H_{26} N_2 O_4 C_{33} H_{26} N_2 O_4

Mr 514.56 514.56

Dx,g cm-3 1.264 1.264

Z 4 4

Mu (mm-1) 0.084 0.084

F000 1080.0 1080.0

F000’ 1080.49

h,k,lmax 21,11,21 21,11,21

Nref 4816 4808

Tmin,Tmax 0.992,0.999 0.984,0.999

Tmin’ 0.984

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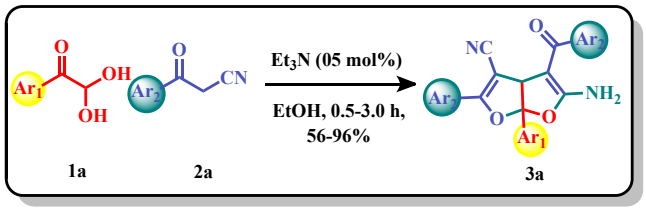
2) General Information

Chemical were purchased from Sigma Aldrich and Alfa Aesar chemical companies and used without further purification. NMR spectra were recorded in parts per million (ppm) in DMSO-d_6 and Chloroform on a Jeol JNM ECP 400 NMR instrument using TMS as internal standard abbreviation were used to denoted signals multiplicities (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplate). HRMS were obtained by EI on a double-focusing mass analyzer, ESI (positive ion mode) on TOF mass analyzer. All melting points were determined using open capillaries on an Electro thermal-9100(Japan) instrument and are uncorrected.

3) Experimental procedure-



General Procedure for the Synthesis of Aryl Dihydrofurofuran (**3**) - To a 50 mL round bottomed flask equipped with a magnetic bar, phenylglyoxal monohydrate **1a** (1.0 mmol) 4-methoxybenzoylacetonitrile **2a** (2.2 mmol), were dissolved in 4 mL of ethanol then added Et_3N (05 mol%). The reaction mixture was stirred at 50 ^oC for 3.0 h. To determine the status of the reaction, it was monitored by TLC. After completion, the reaction mixture turned to a white precipitate and showed a single spot in TLC. Then the precipitate was filtered and washed with 5*3 mL of cold ethanol solution. A white solid with a yield of 96 % (**3a**) was observed. The entire product was characterized by ^1H NMR, ^{13}C NMR and HRMS spectroscopy.

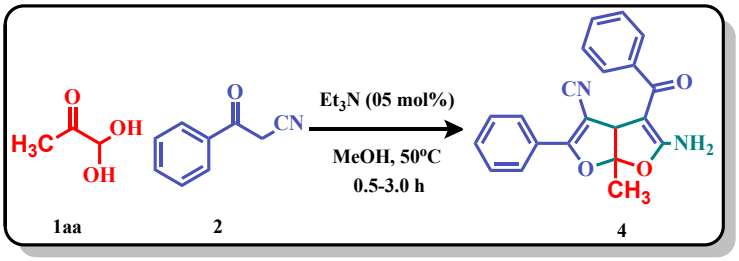


Table 1 Optimization of reaction conditions for **4a** compound [a]

Entry	Catalyst (mol %)	Solvent	Temp (°C)	Time (h)	Eq (2)	Yields (%)[b]
1	Et_3N (10)	EtOH	rt	12	2	60
2	Et_3N (05)	EtOH	50	03	2.2	72
3	**Et_3N (05)**	**MeOH**	**50**	**03**	**2.2**	**94**
4	Et_3N (05)	MeOH	60	03	2.2	92

[a]Reaction conditions: All of the reactions were run on a 1 mmol scale at open air atmosphere in 4.0 mL Solvent, base, [b] Isolated yield.

General Procedure for the Synthesis of Alkyl Dihydrofurofuran (**4**) - To a 50 mL round bottomed flask equipped with a magnetic bar, Methylglyoxal **1aa** (1.0 mmol, 40% aq. solution) benzoylacetonitrile **2** (2.2 mmol), were dissolved in 4 mL of methanol then added Et_3N (05 mol%). The reaction mixture was stirred at 50 °C for 3 h. To determine the status of the reaction, it was monitored by TLC. After completion, the reaction mixture turned to a white precipitate and showed a single spot in TLC. Then the precipitate was filtered and washed with 5*3 mL of cold MeOH solution. A white solid with a yield of 94 % (4a) was observed. The entire product was characterized by ^1H NMR, ^{13}C NMR and HRMS spectroscopy.

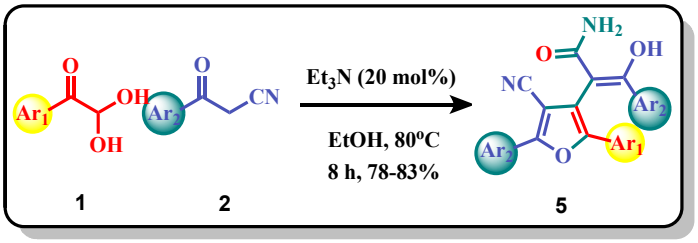
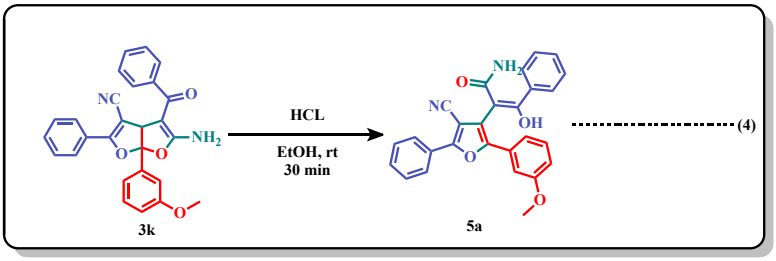


Table 2 Optimization of reaction conditions for **5a** compound

Entry	Catalyst (mol %)	Solvent	Temp (°C)	Time (h)	Eq (2)	Yields (%)[b]
1	Et_3N (05)	EtOH	70	03	2.2	36
2	Et_3N (05)	EtOH	70	06	2.2	59
3	Et_3N (10)	EtOH	80	08	2.2	77
4	**Et_3N (20)**	**EtOH**	**80**	**08**	**2.2**	**83**
5	Et_3N (30)	EtOH	80	08	2.2	81

[a]Reaction conditions: All of the reactions were run on a 1 mmol scale at open air atmosphere in 4.0 mL Solvent, base, [b] Isolated yield.

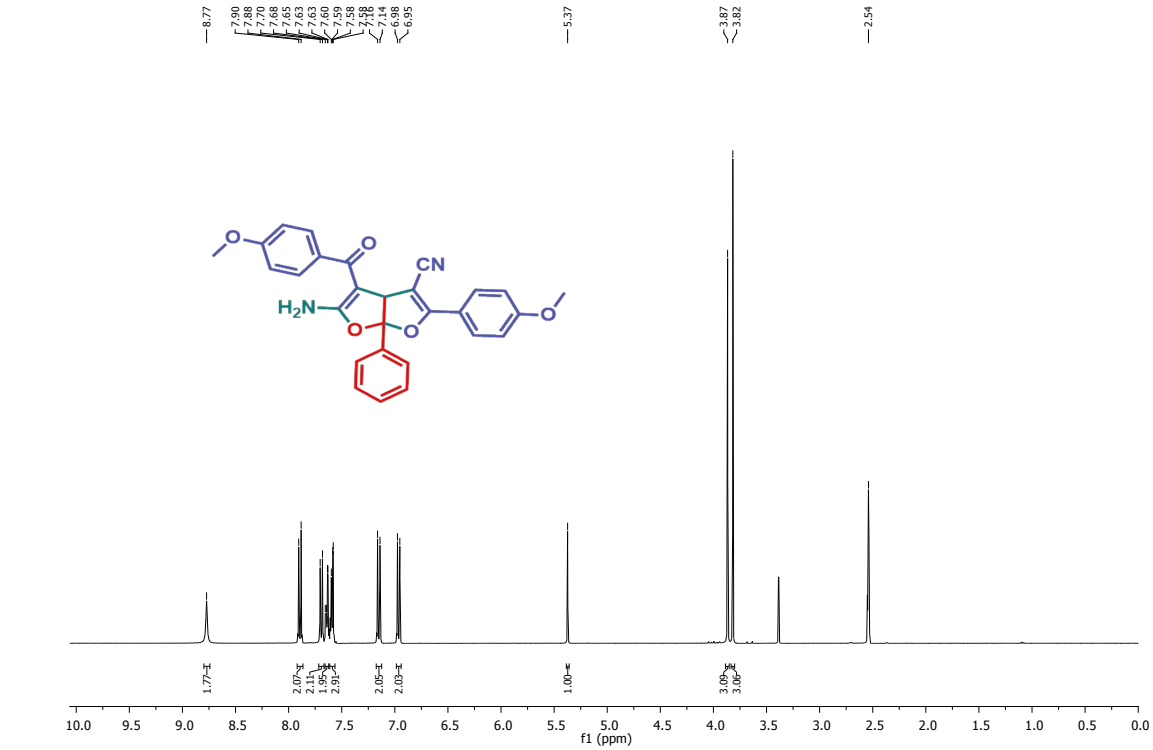
General Procedure for the Synthesis of functionalized Aryl furan **(5)**- To a 50 mL round bottomed flask equipped with a magnetic bar, 3-methoxyphenylglyoxal **1k** (1.0 mmol) benzoylacetonitrile **2** (2.2 mmol), were dissolved in 4 mL of Ethanol then added Et_3N (20 mol%). The reaction mixture was stirred at 80 °C for 8 h. To determine the status of the reaction, it was monitored by TLC. After completion, the reaction mixture turned to a white precipitate and showed a single spot in TLC. Then the precipitate was filtered and washed with 5*3 mL of cold EtOH solution. A white solid with a yield of 83 % (5a) was observed. The entire product was characterized by ^1H NMR, ^{13}C NMR and HRMS spectroscopy.

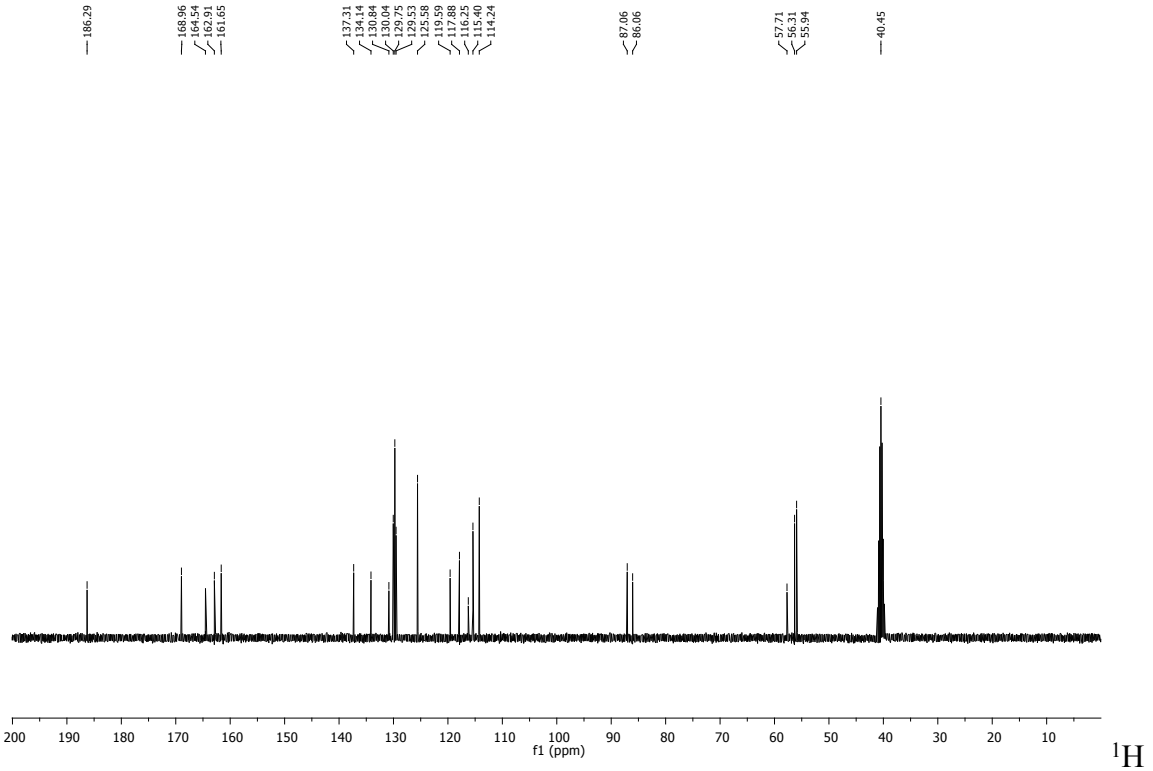


(E)-2-(4-cyano-2-(3-methoxyphenyl)-5-phenylfuran-3-yl)-3-hydroxy-3-phenylacrylamide **(5a)**- To a 50 mL round bottomed flask equipped with a magnetic bar, compound 3k (1.0 mmol) were dissolved in 5 mL of Ethanol then added con HCL (10 mol%). The reaction mixture was stirred at room temperature for 30 min. To determine the status of the reaction, it was monitored by TLC. After completion, the reaction mixture added 20 mL water to the mixture, extracted with EtOAc two times (2*20 mL). Dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc) to afford the desired product **5a.** The product was characterized by ^{1}H NMR, ^{13}C NMR and HRMS spectroscopy.

4) ^{1}H NMR and ^{13}C NMR spectra of the compounds

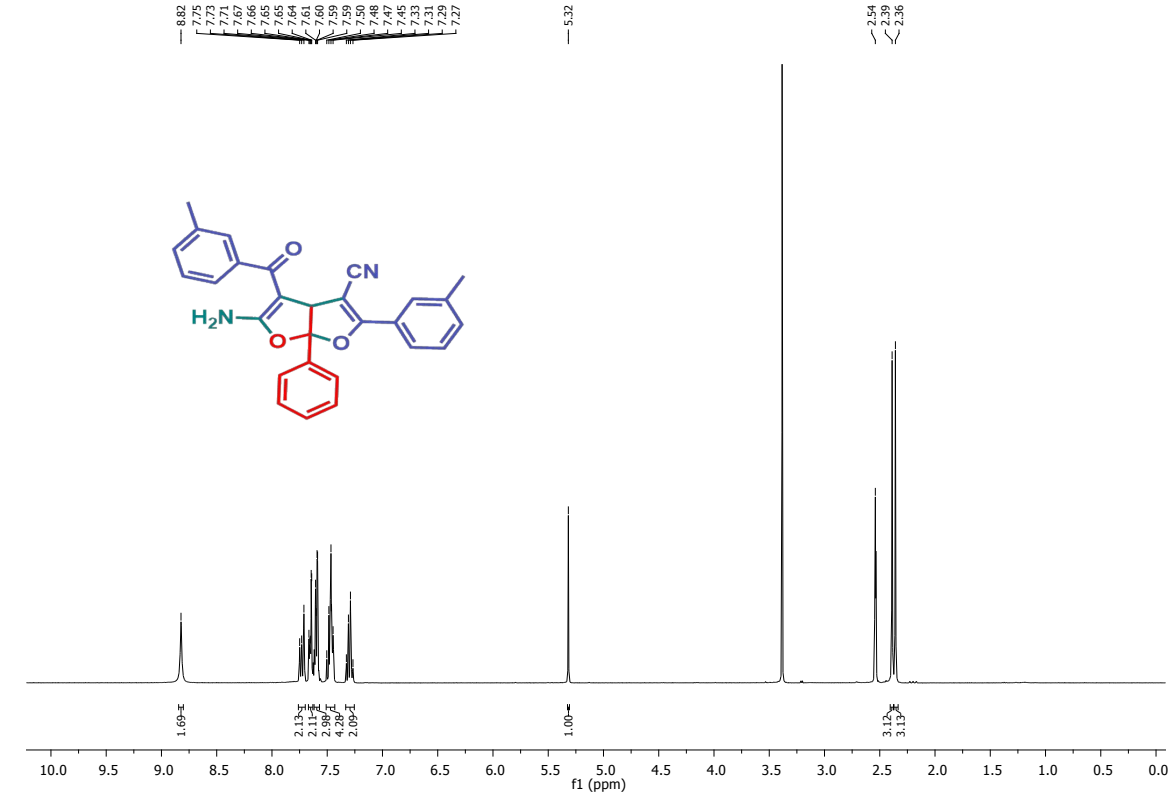
^{1}H NMR and ^{13}C NMR of compound (**3a)**

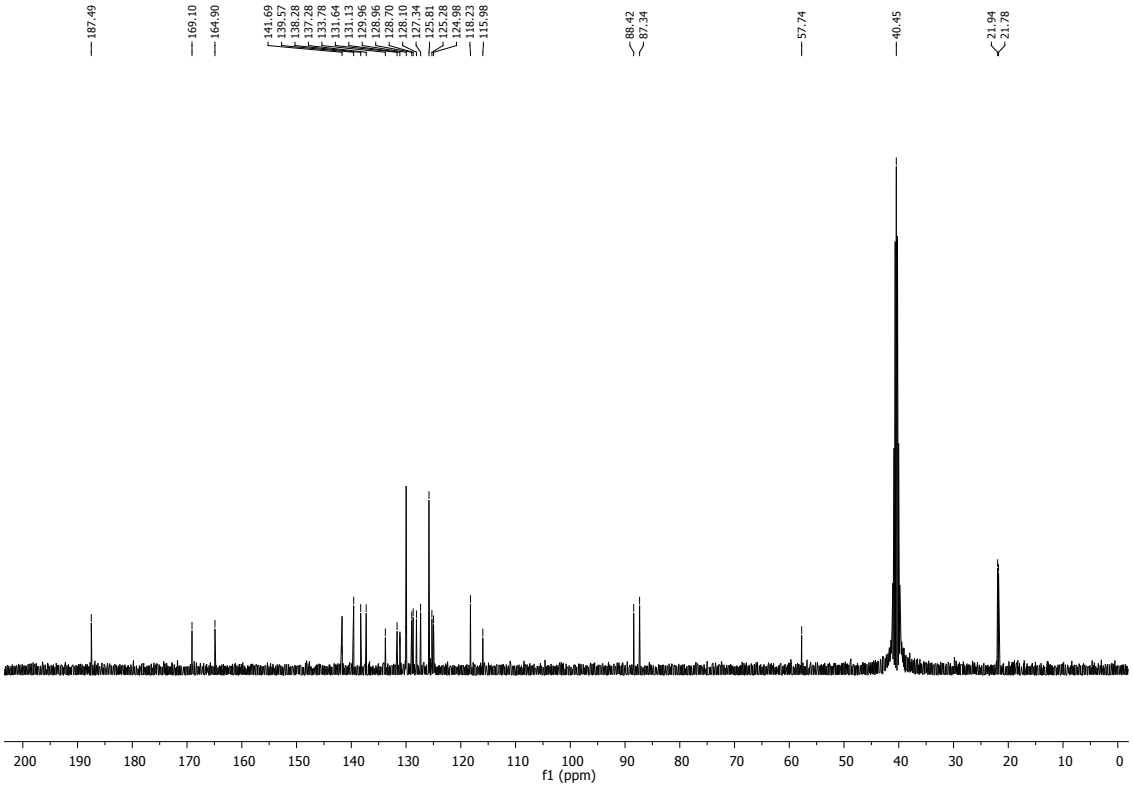




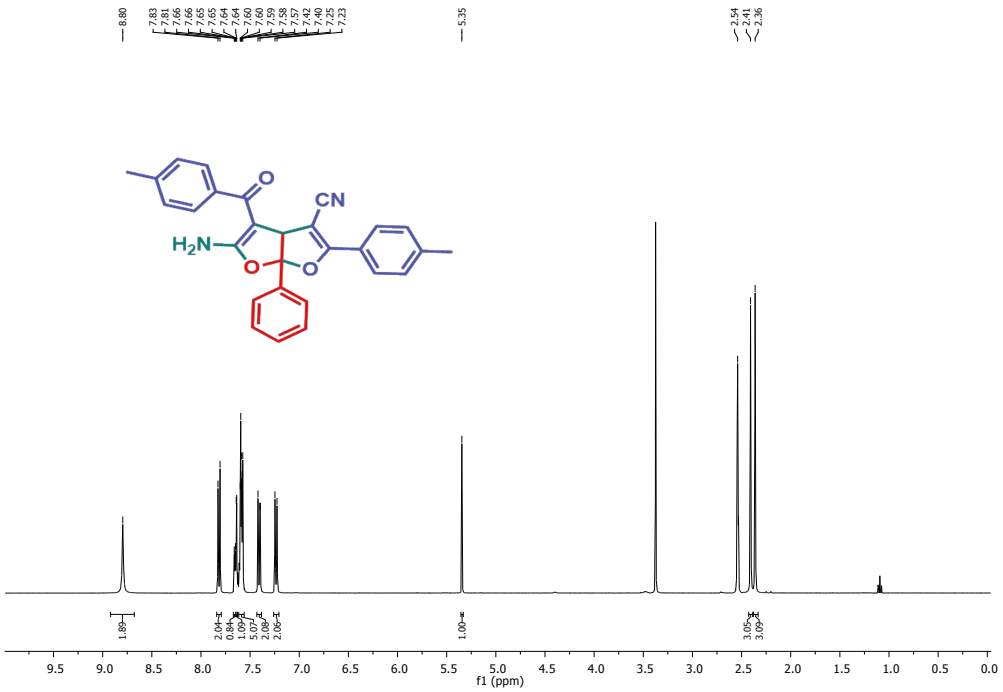
^{1}H

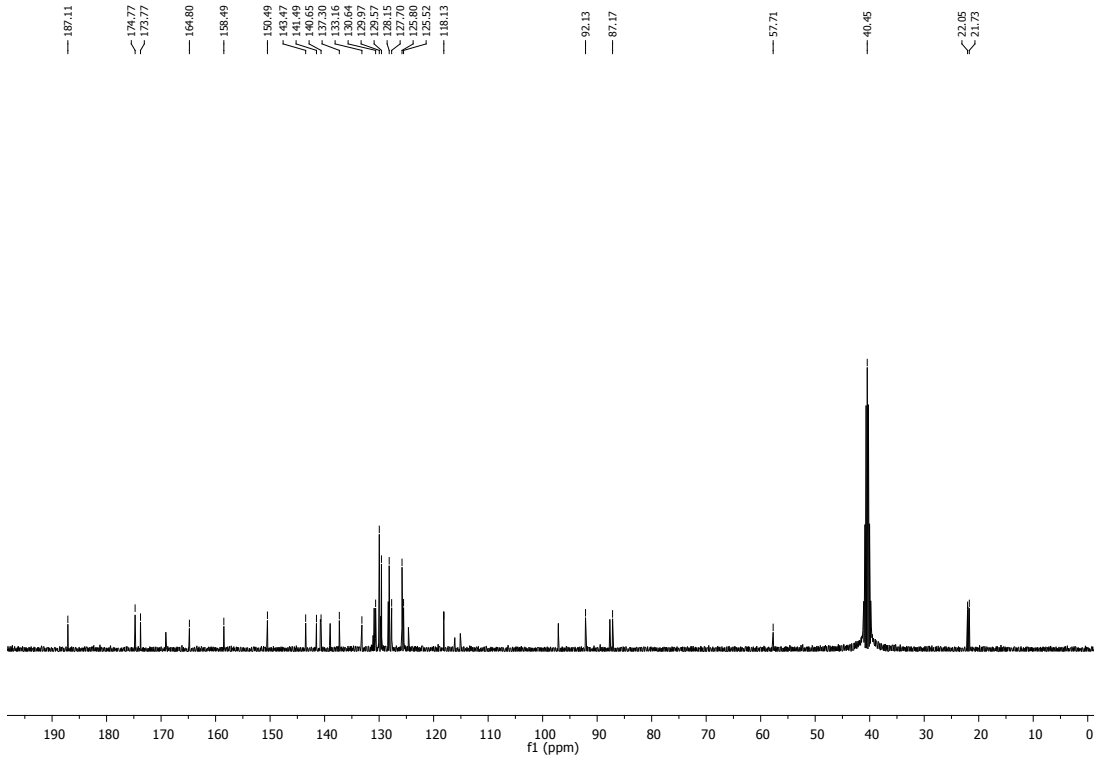
NMR and ^{13}C NMR of compound (**3b)**



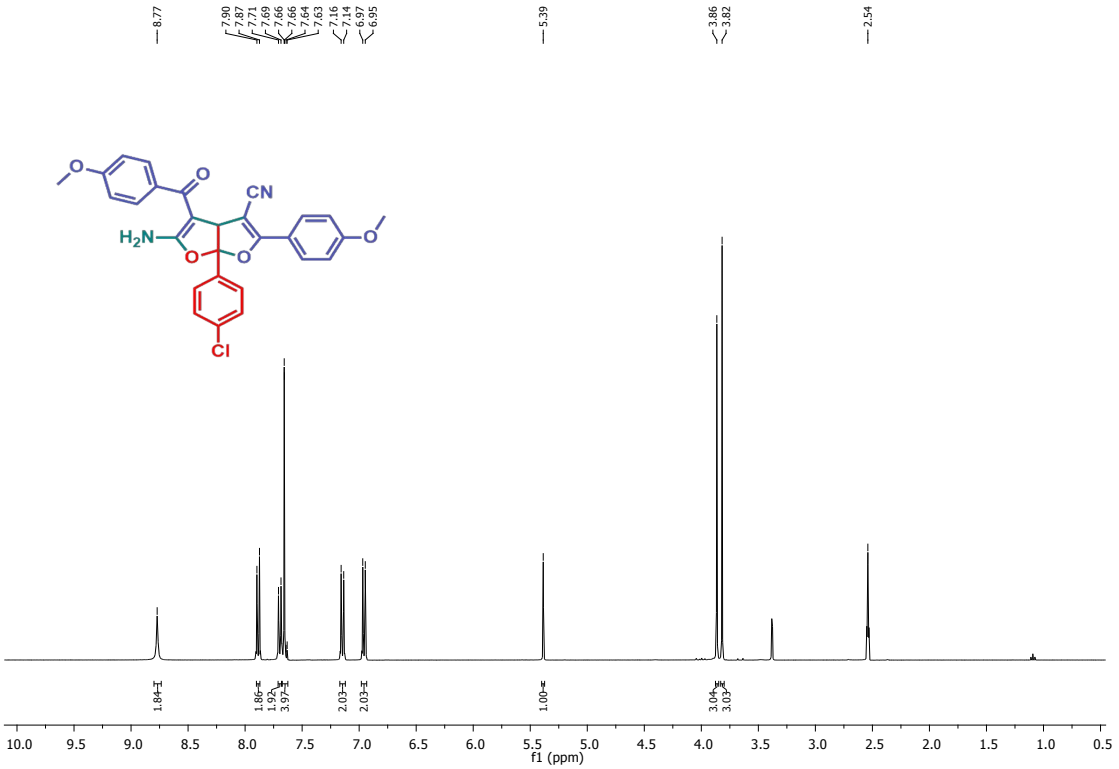


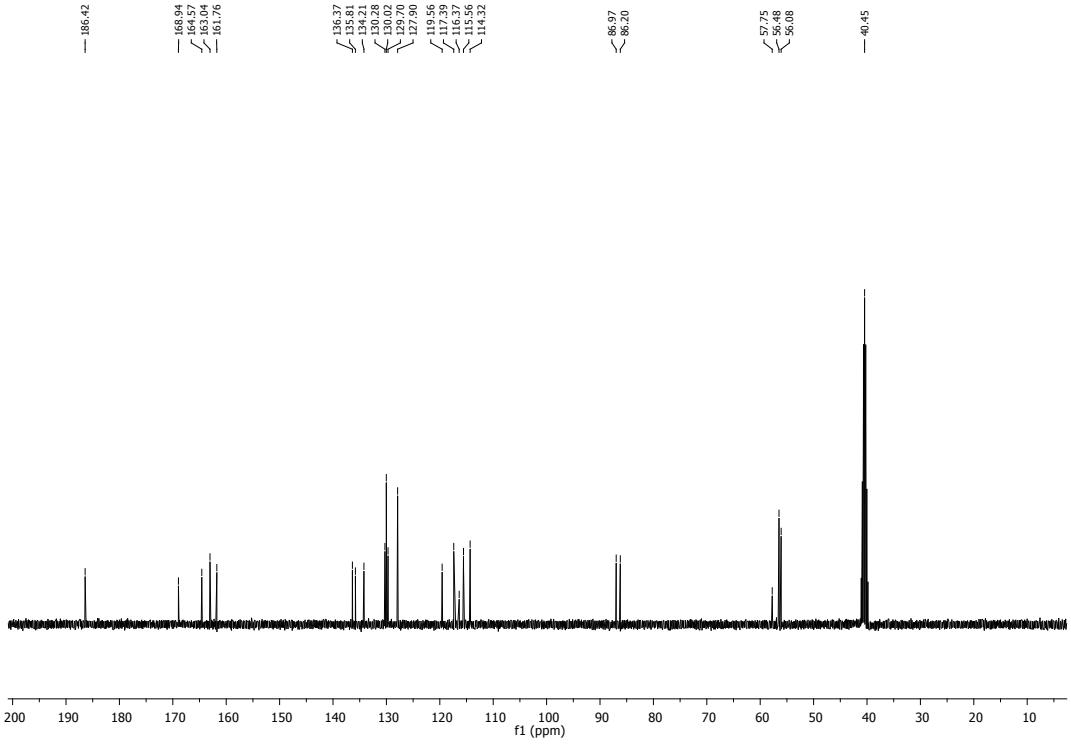
^{1}H NMR and ^{13}C NMR of compound (**3c)**



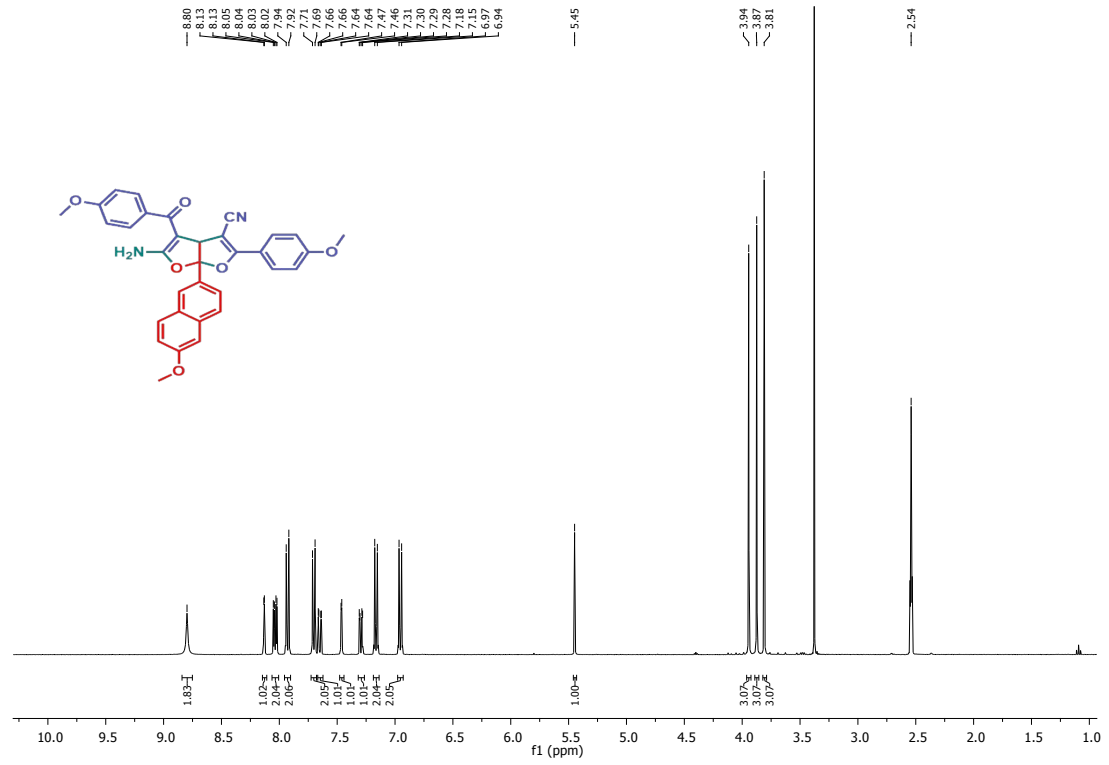


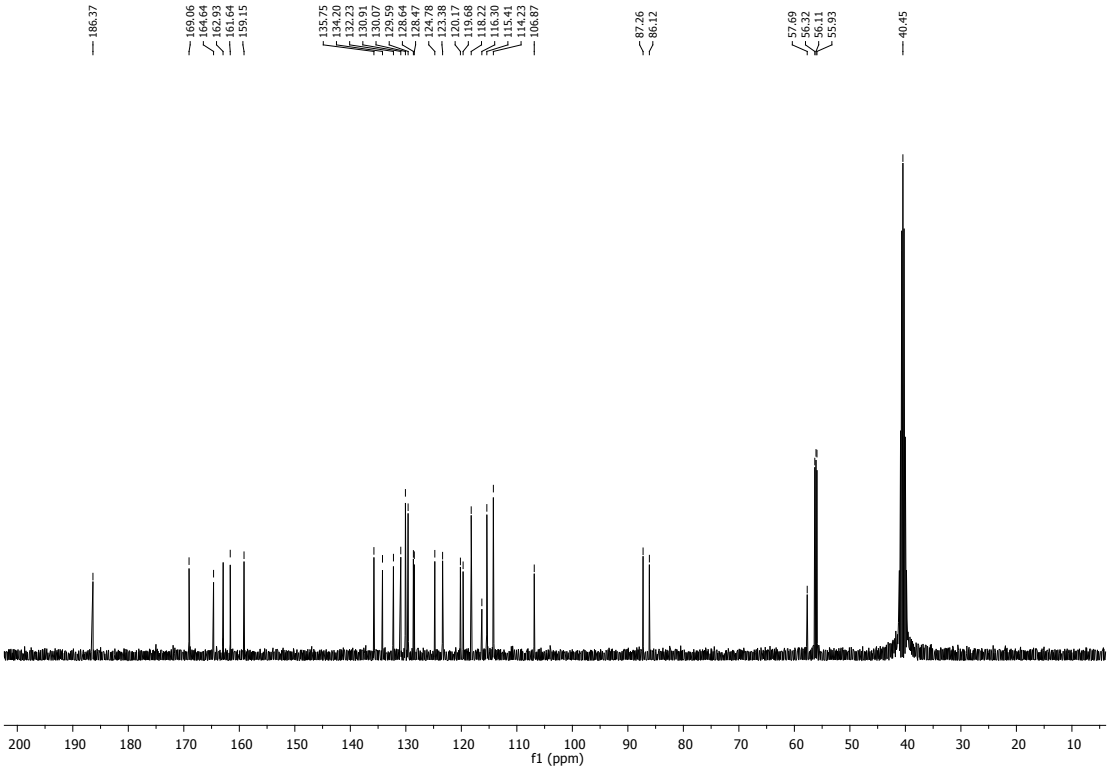
^{1}H NMR and ^{13}C NMR of compound (**3d)**



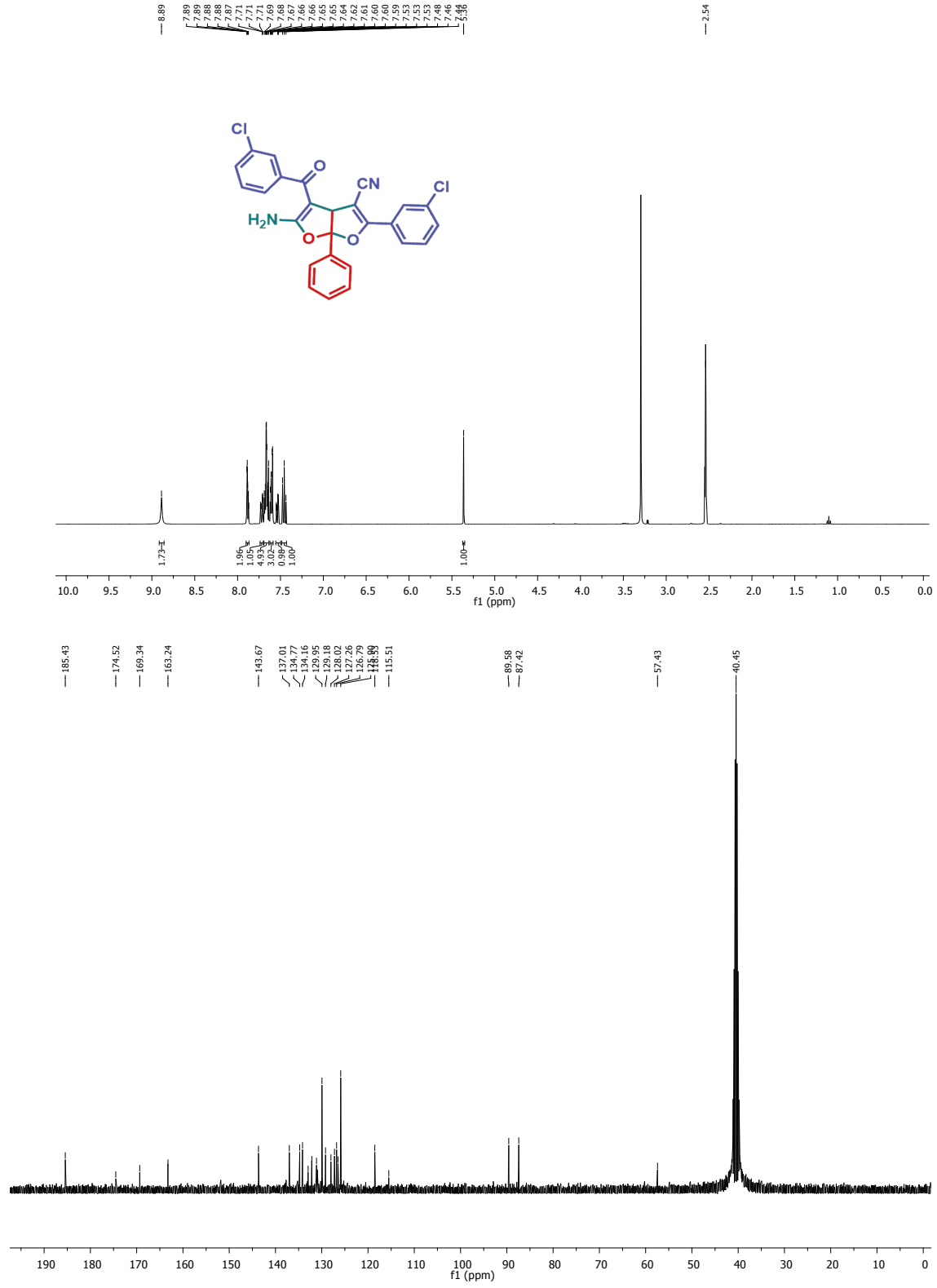


^{1}H NMR and ^{13}C NMR of compound (**3e)**

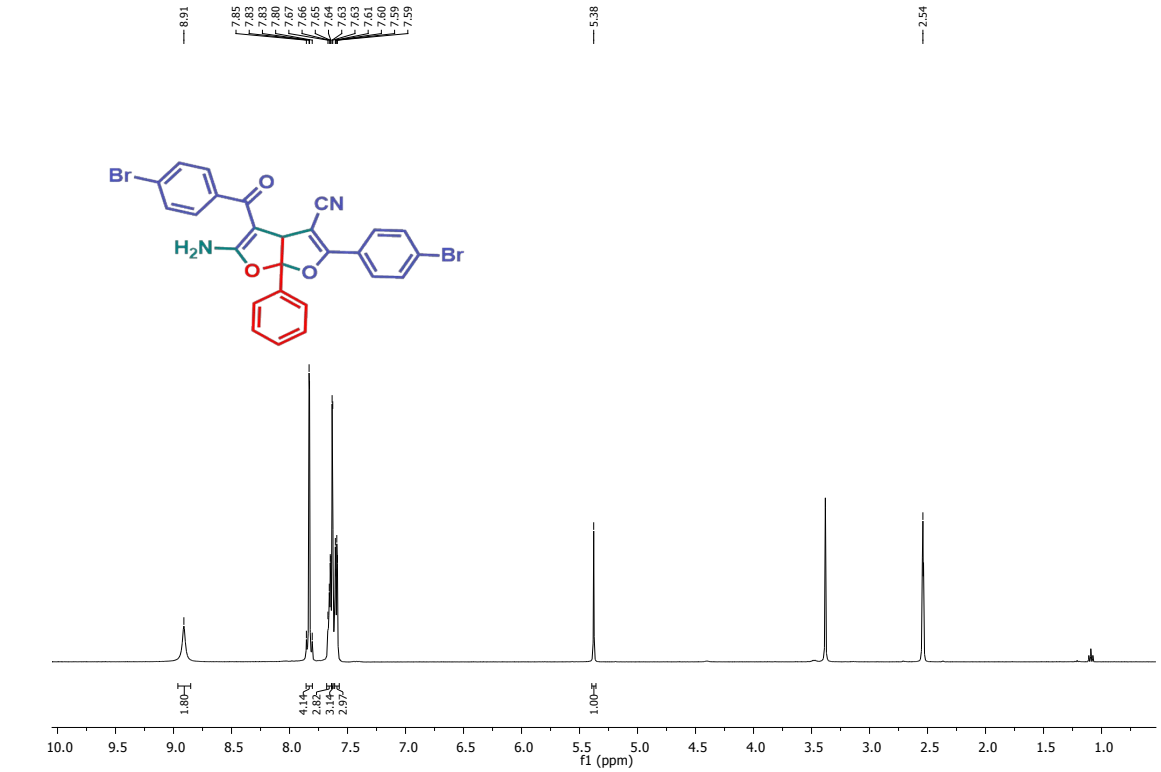


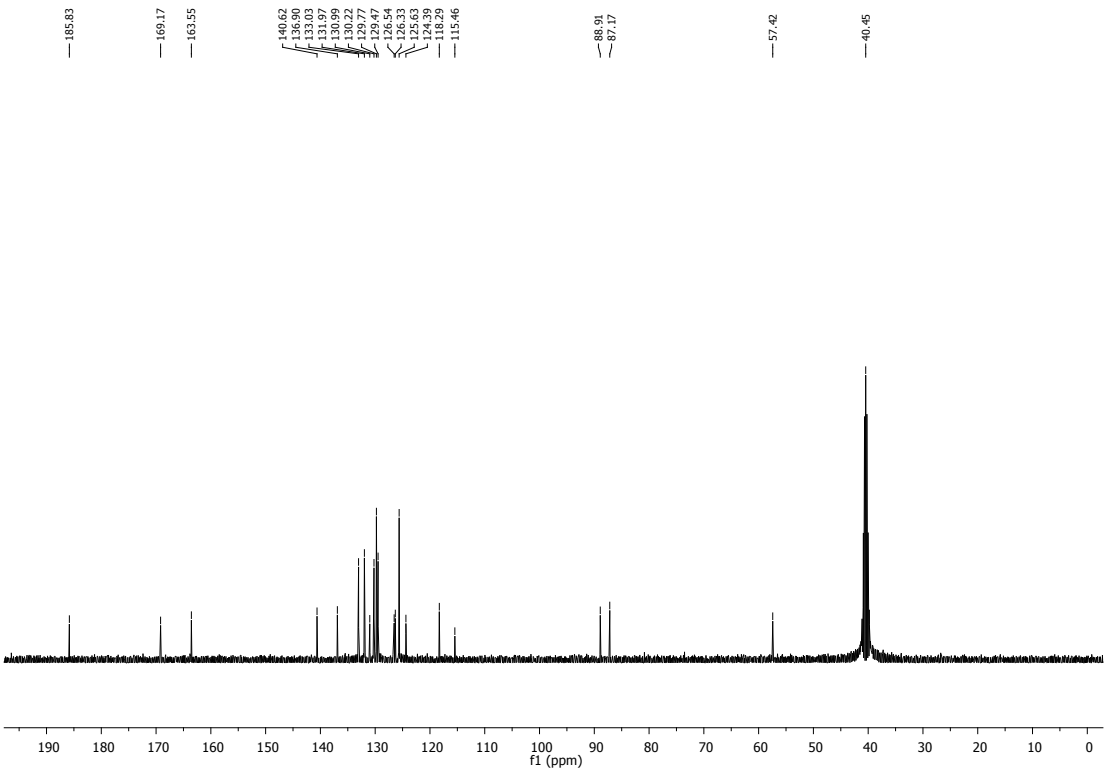


^{1}H NMR and ^{13}C NMR of compound (**3f)**

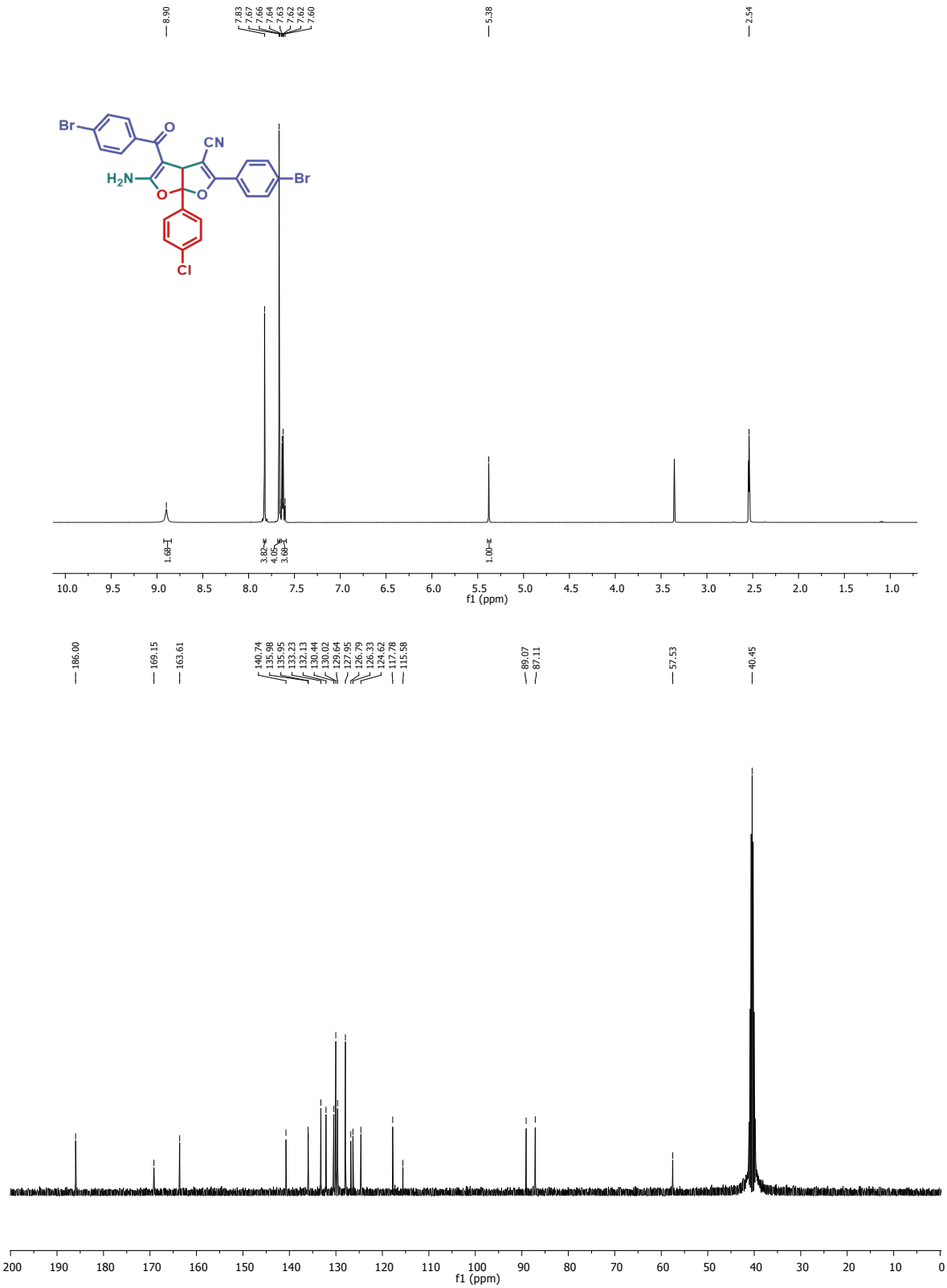


^{1}H NMR and ^{13}C NMR of compound (**3g)**

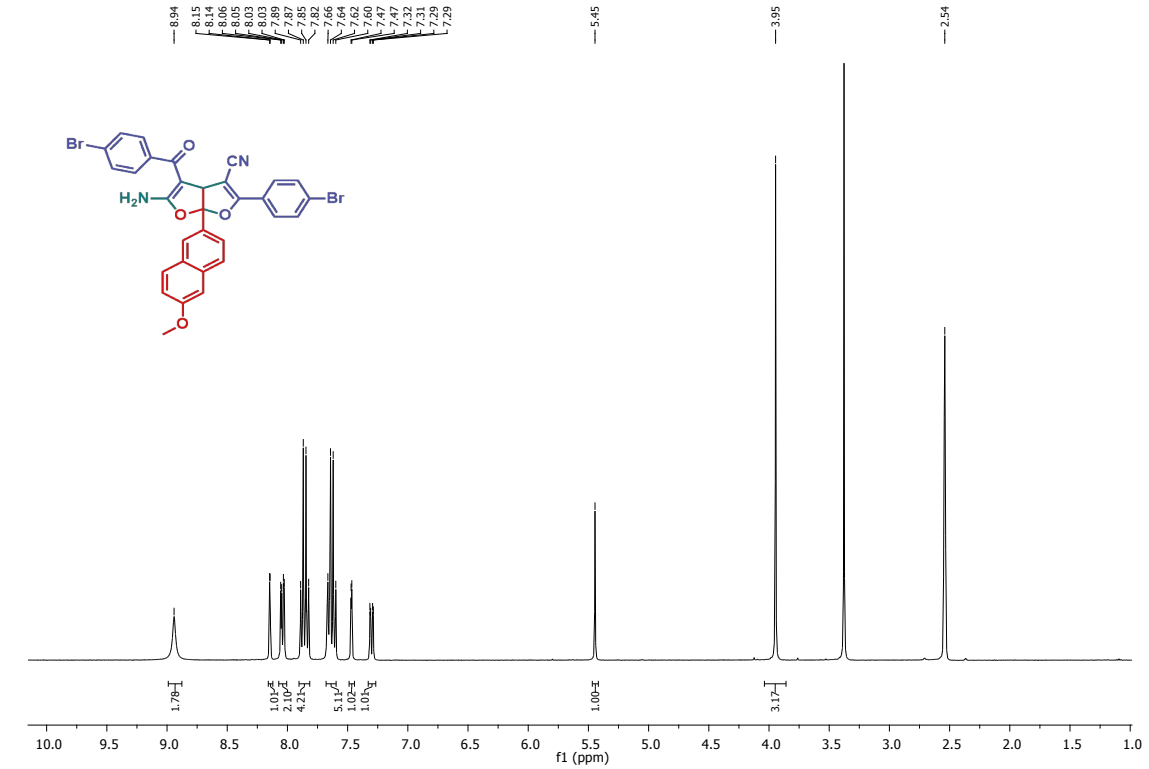


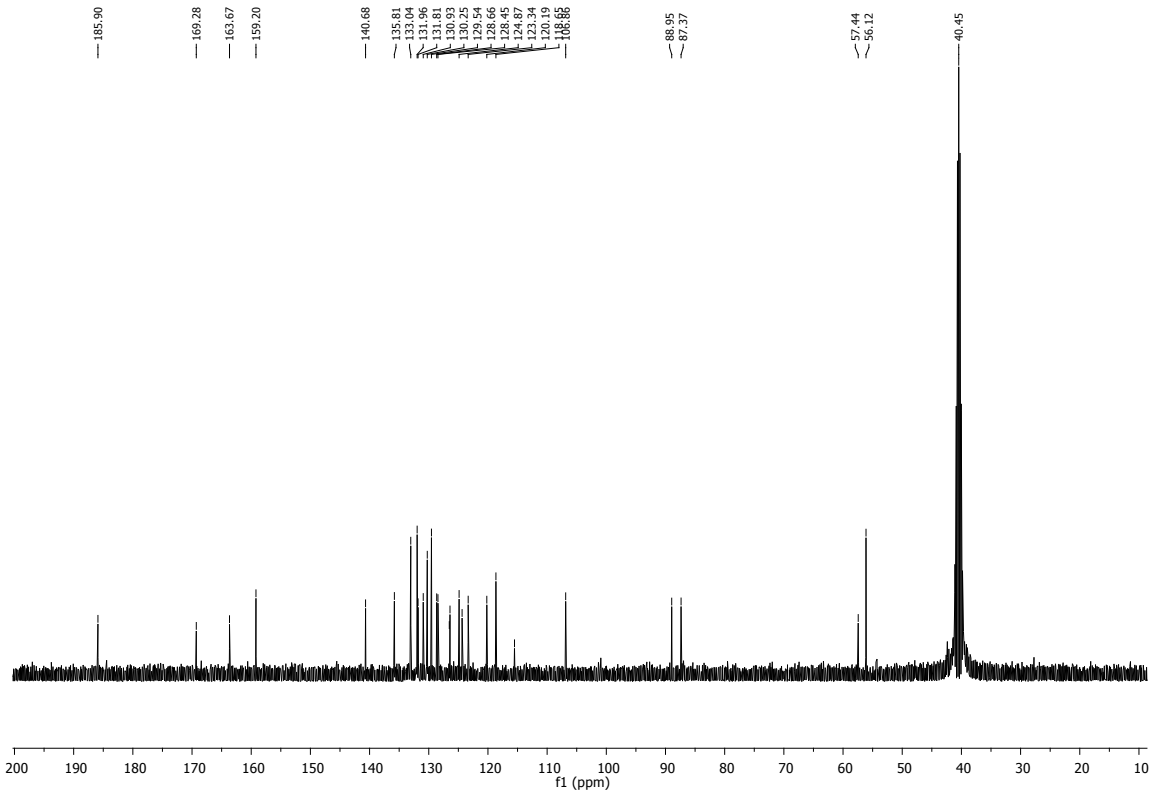


^{1}H NMR and ^{13}C NMR of compound (**3h)**

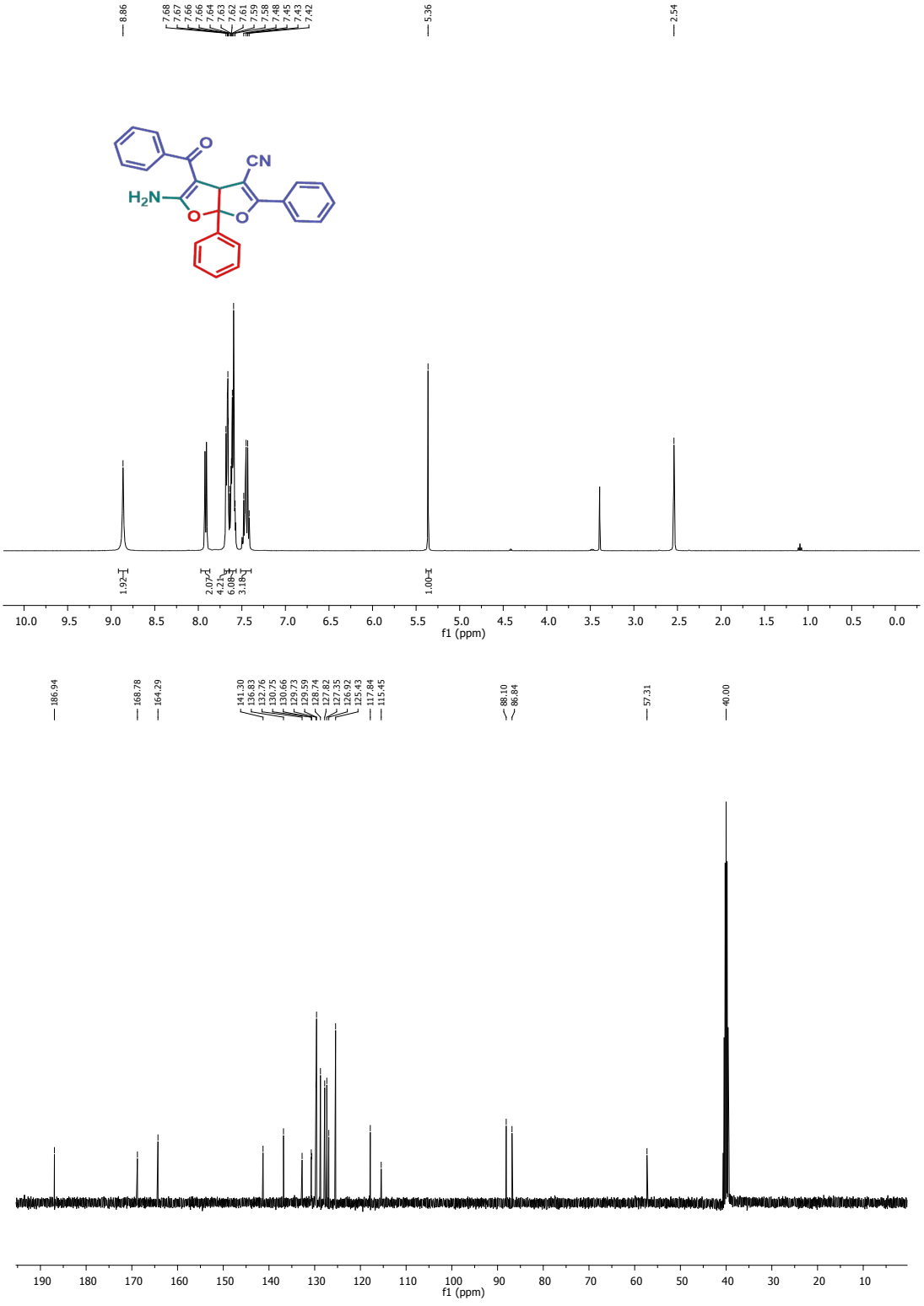


^{1}H NMR and ^{13}C NMR of compound (**3i)**

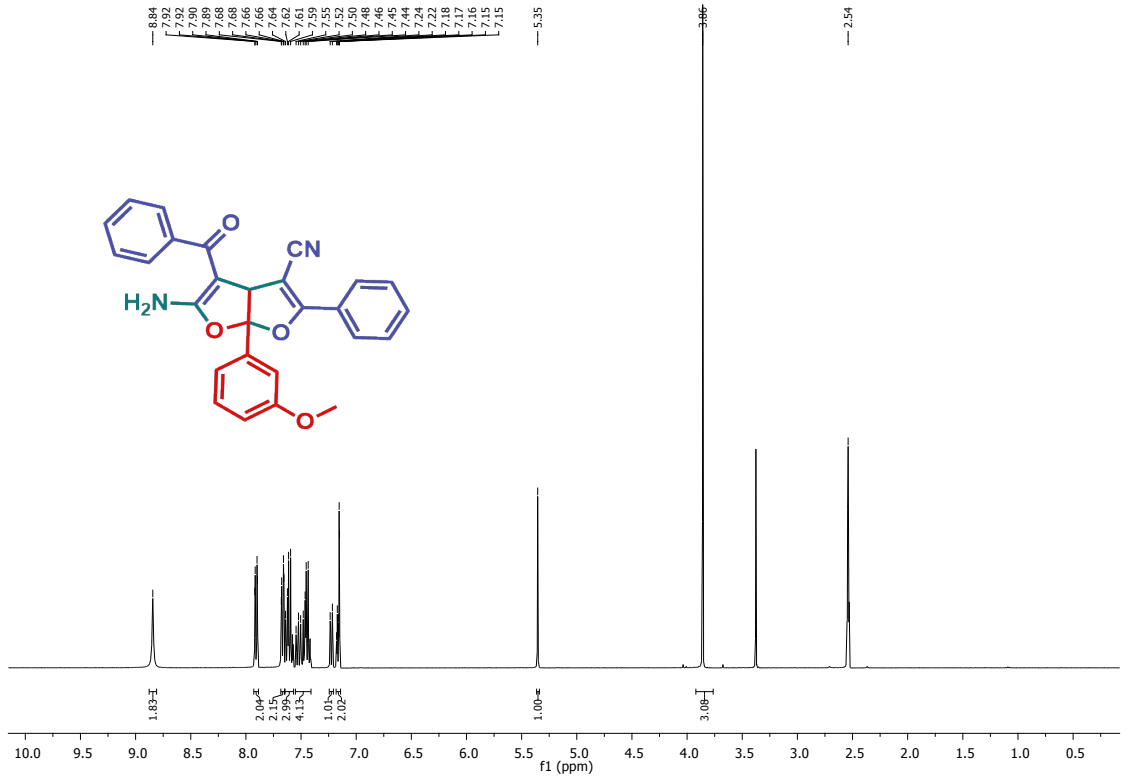


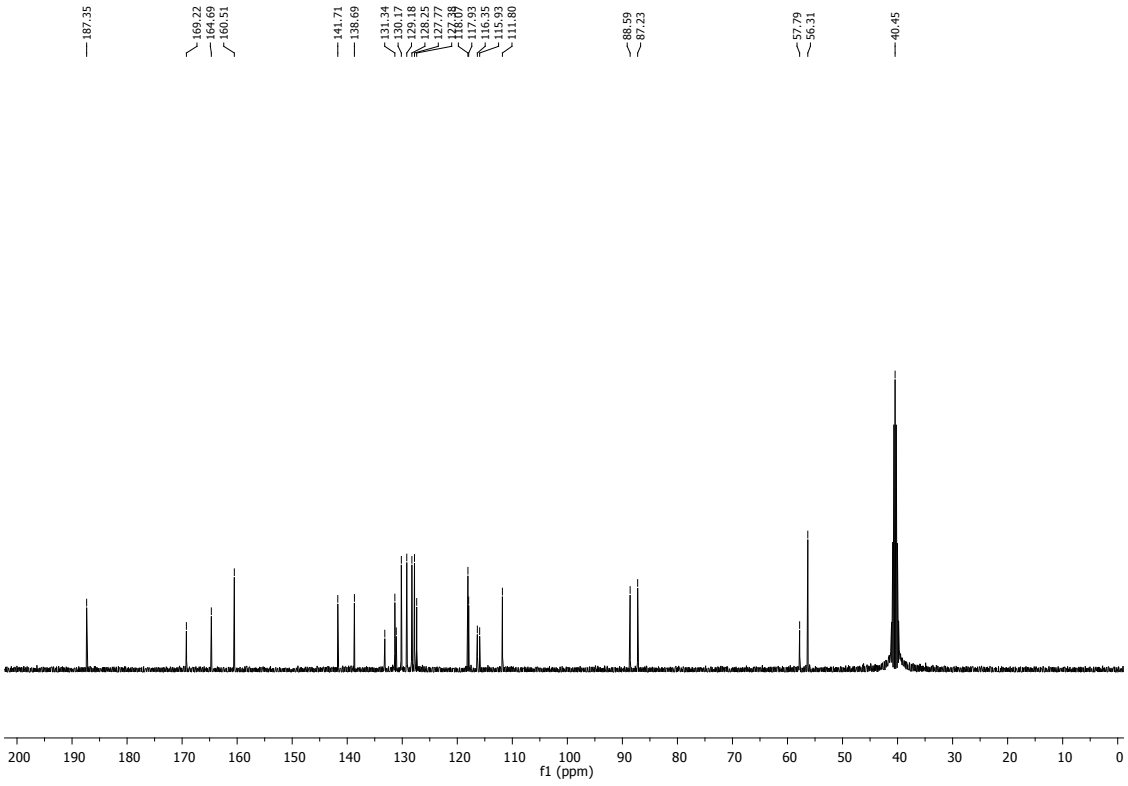


^{1}H NMR and ^{13}C NMR of compound (**3j)**

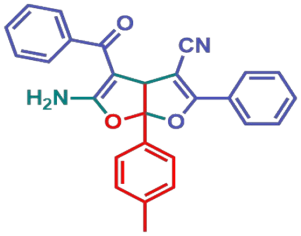


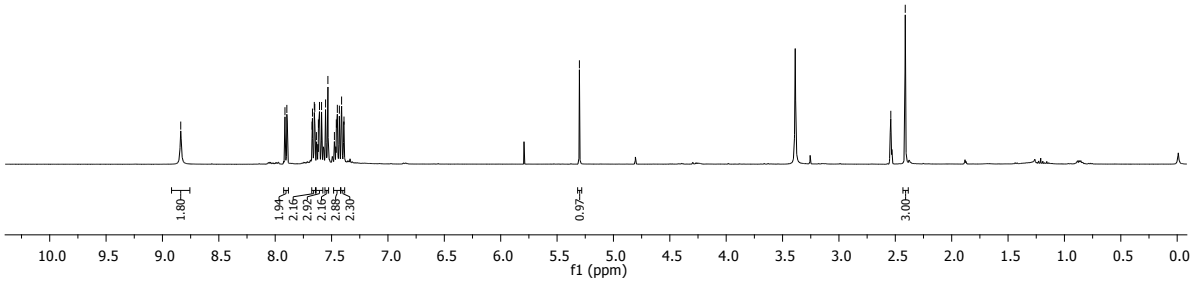
^{1}H NMR and ^{13}C NMR of compound (3**k**)

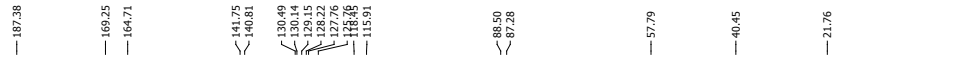


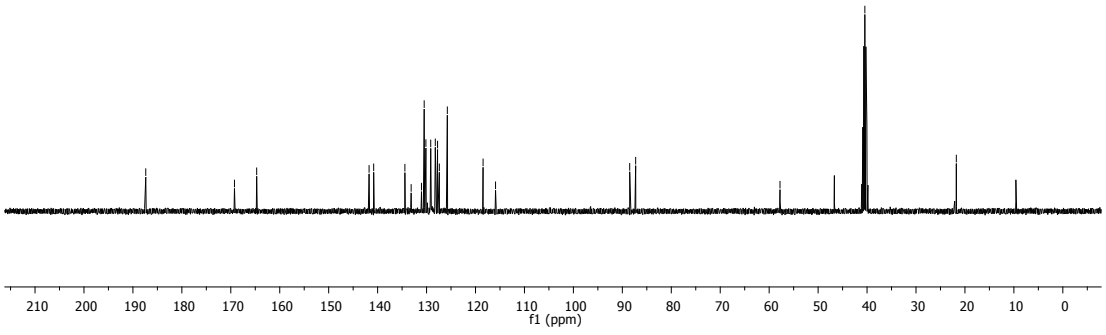


^{1}H NMR and ^{13}C NMR of compound (**3l**)

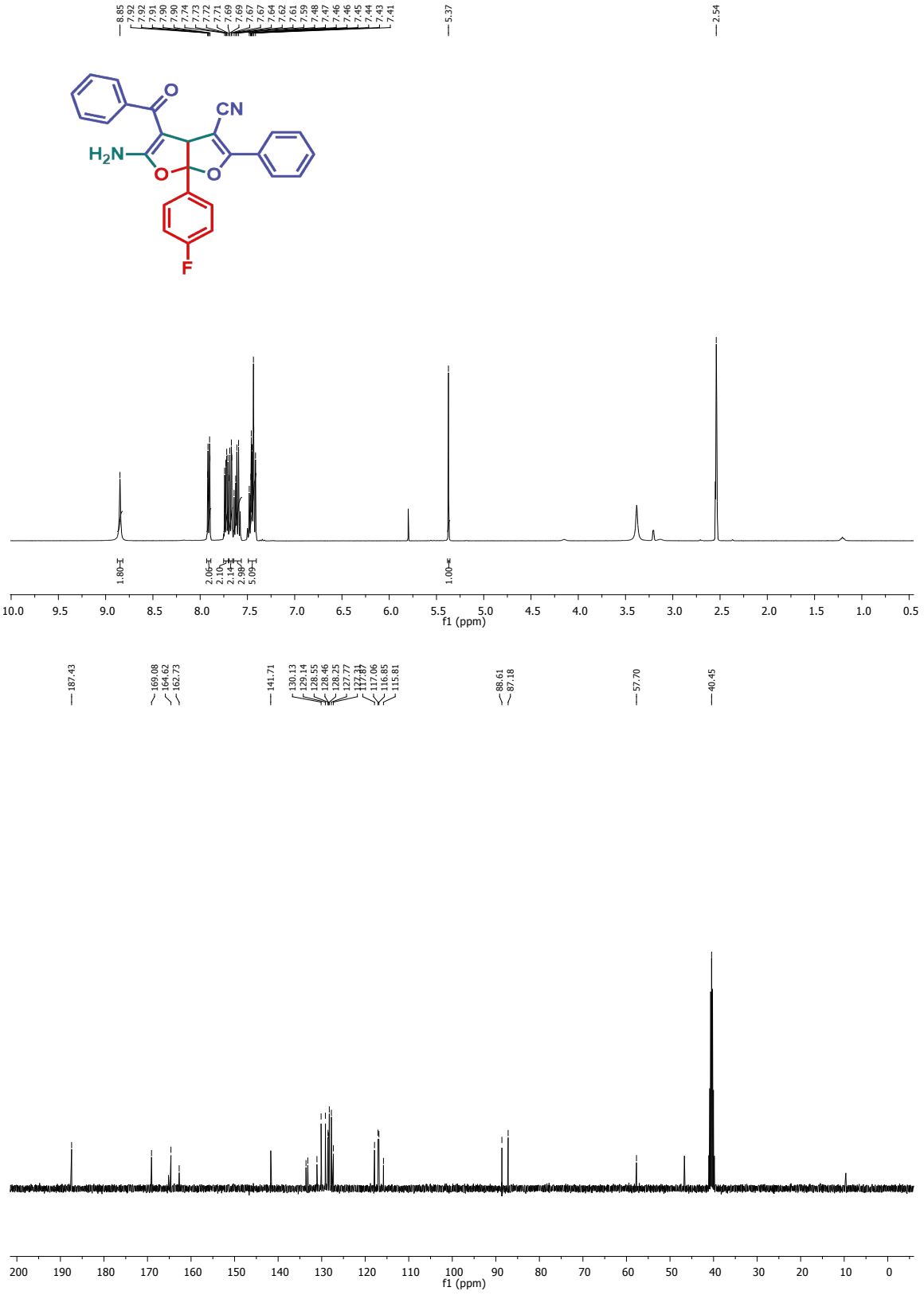


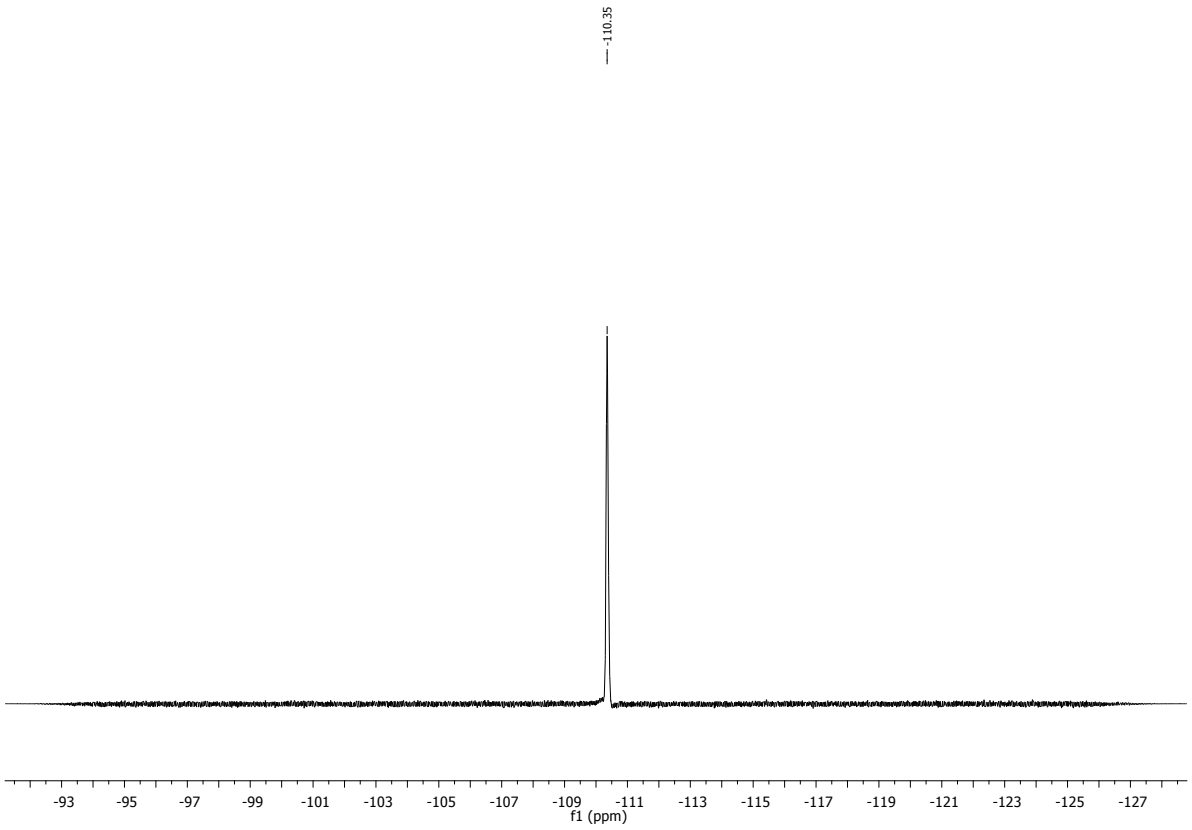






^{1}H NMR, ^{13}C NMR and ^{19}F NMR of compound (**3m)**

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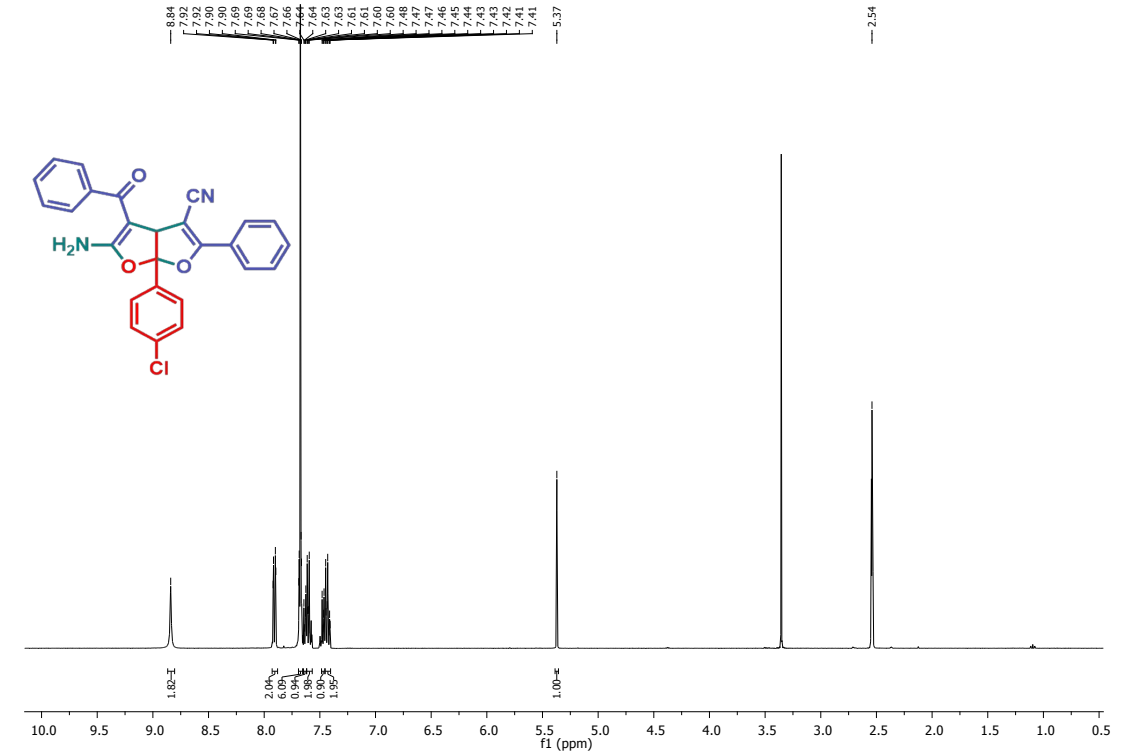
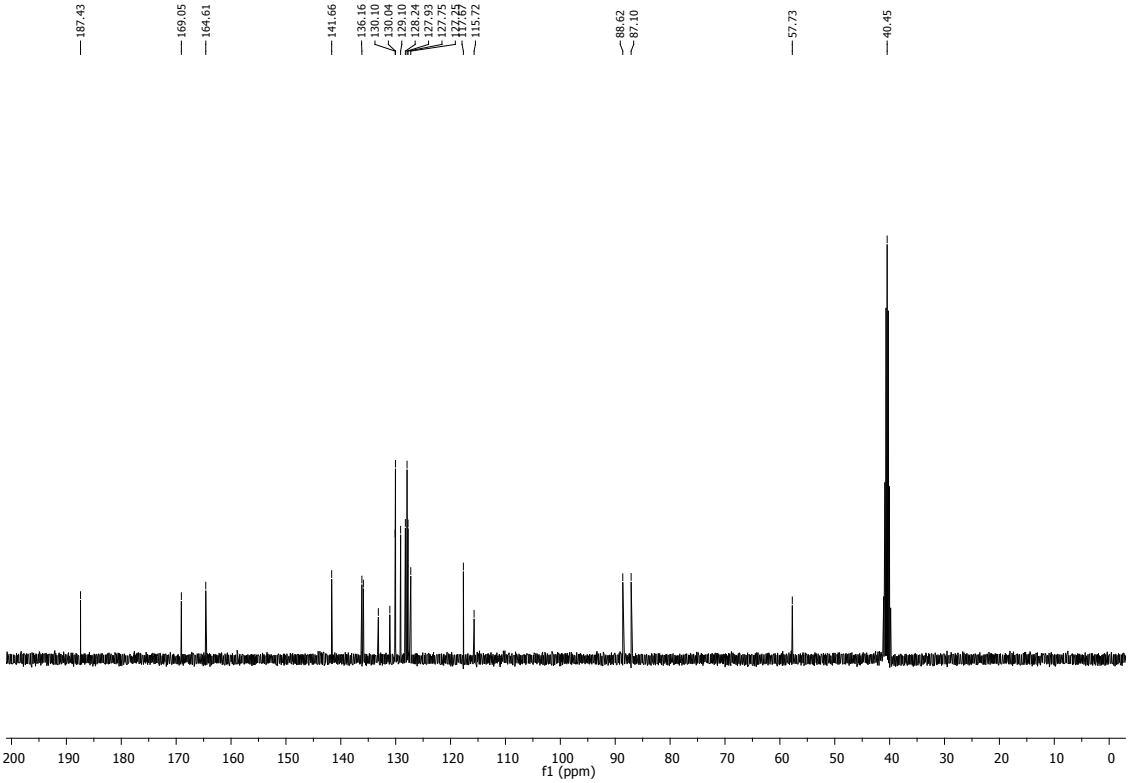
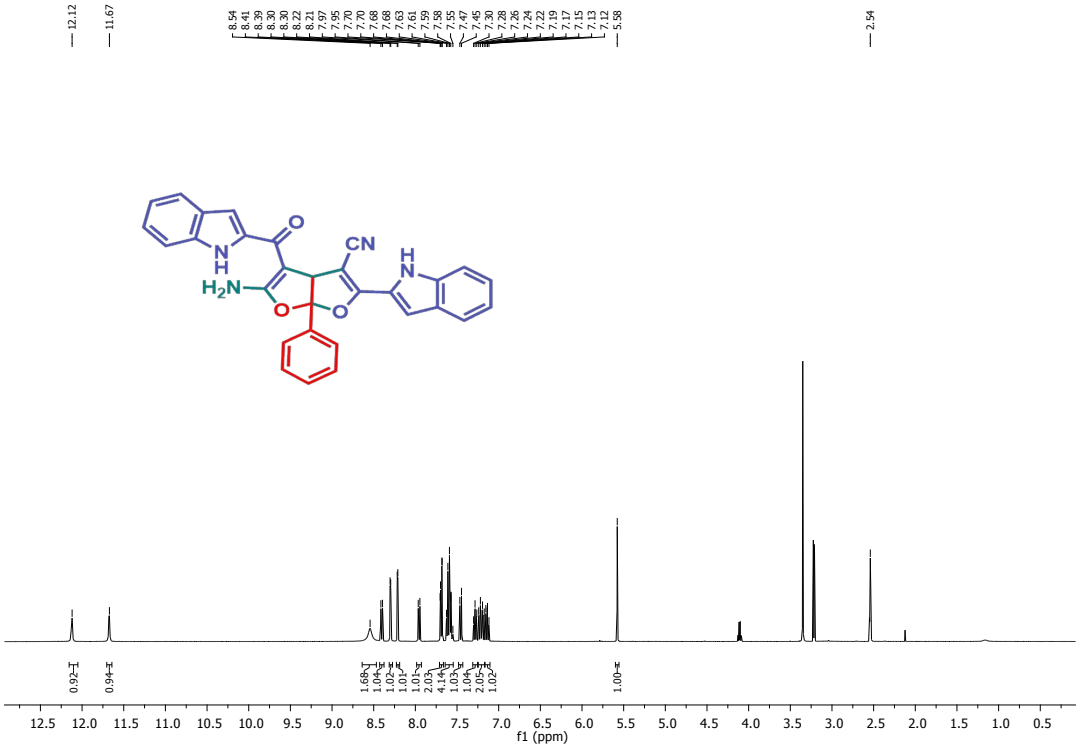
-125
-127
f1 (ppm)

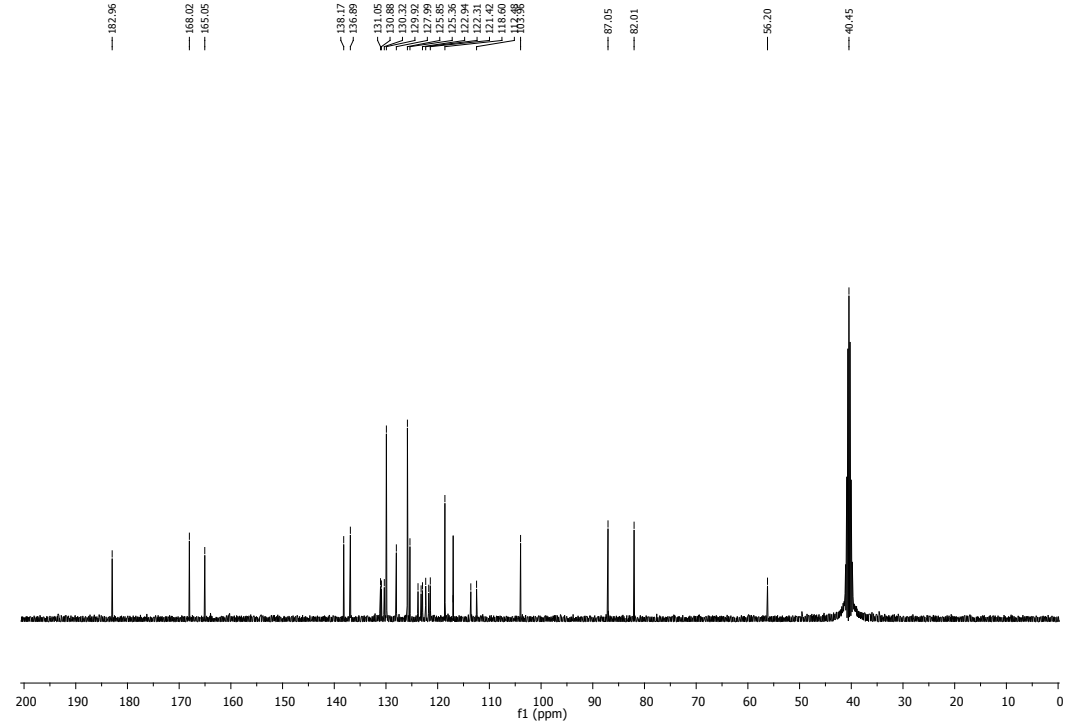
^{1}H NMR and ^{13}C NMR of compound (**3n)**



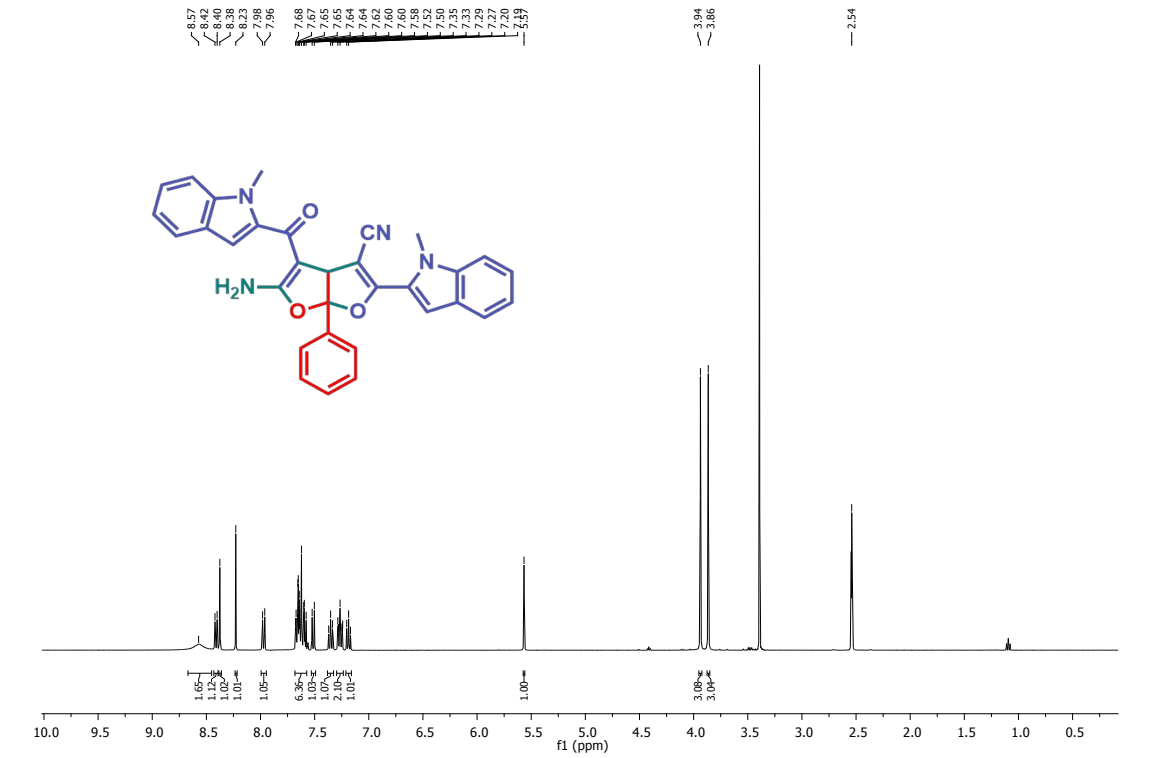


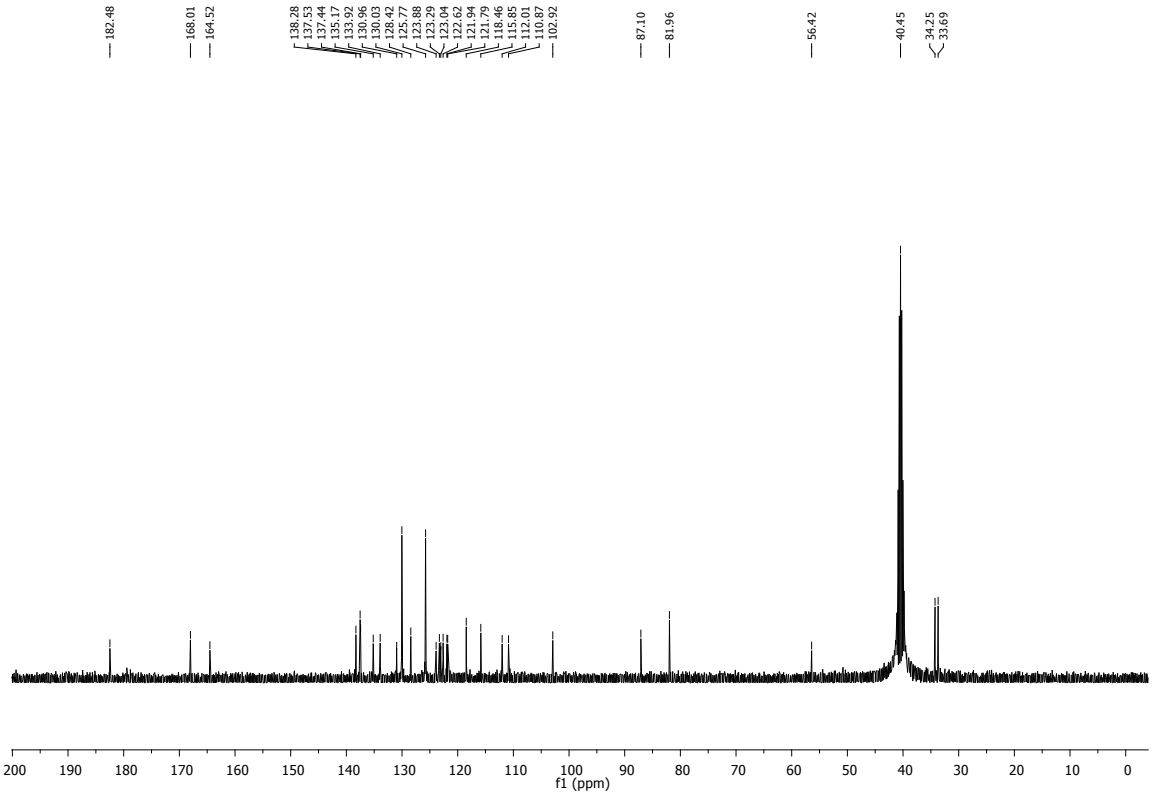
^{1}H NMR and ^{13}C NMR of compound (**3o)**



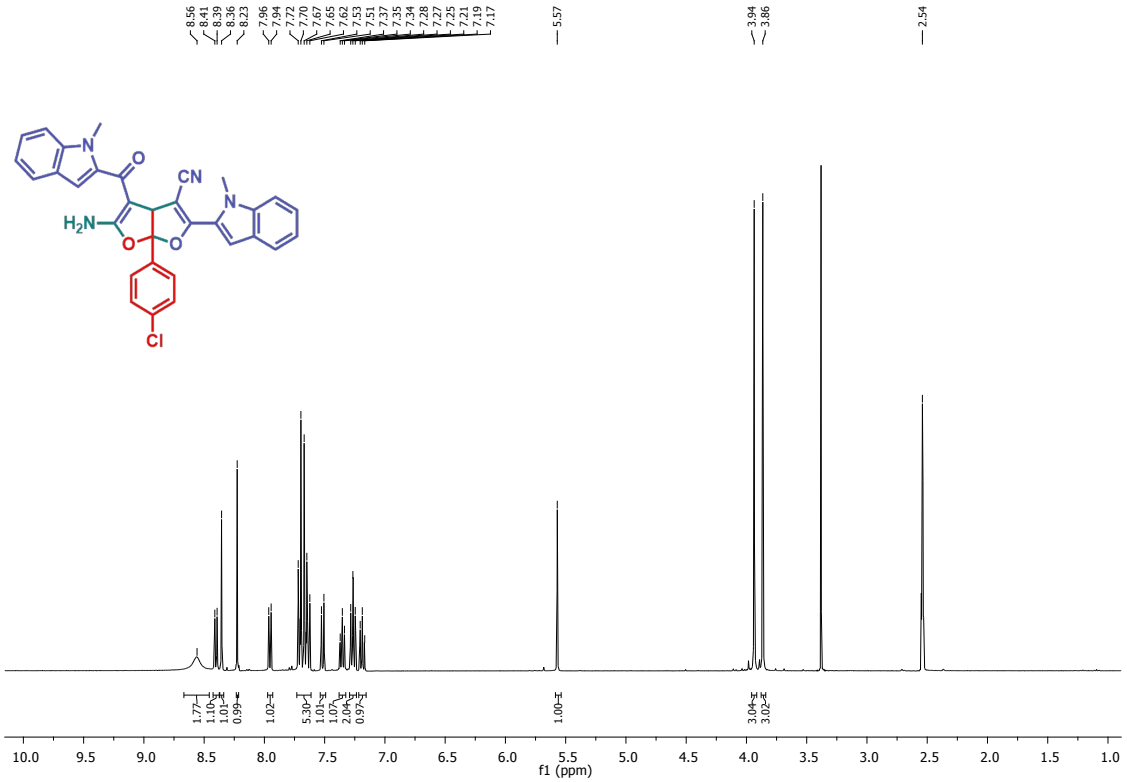


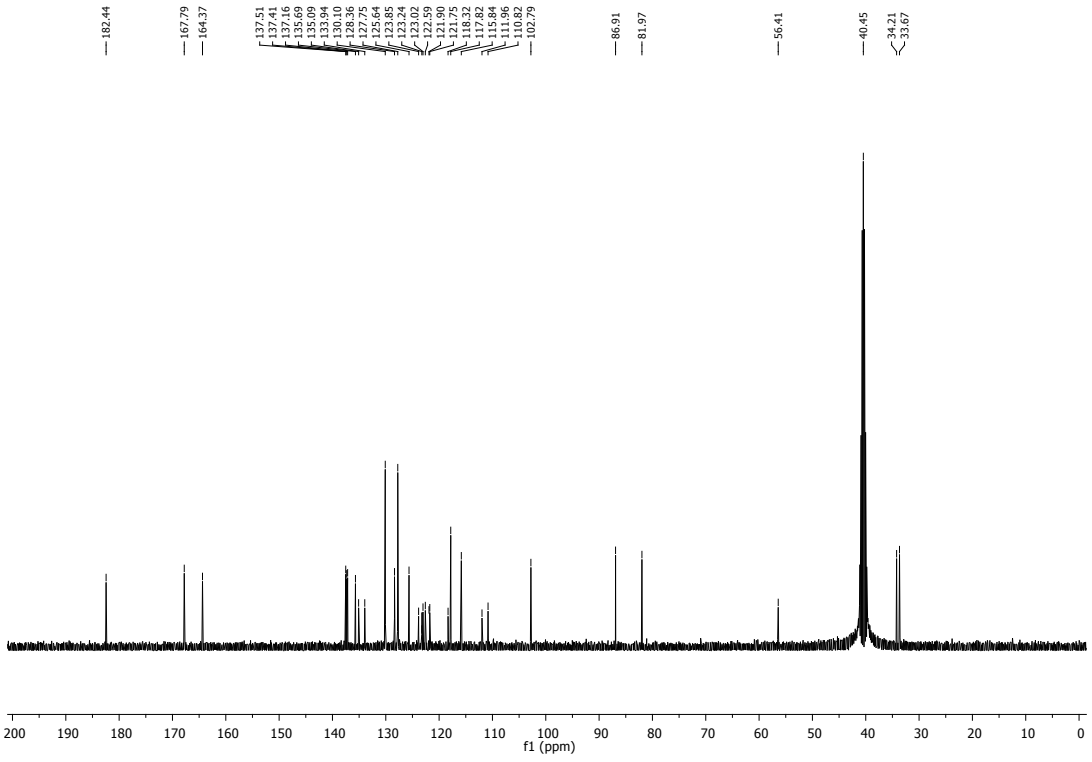
^{1}H NMR and ^{13}C NMR of compound (**3p)**



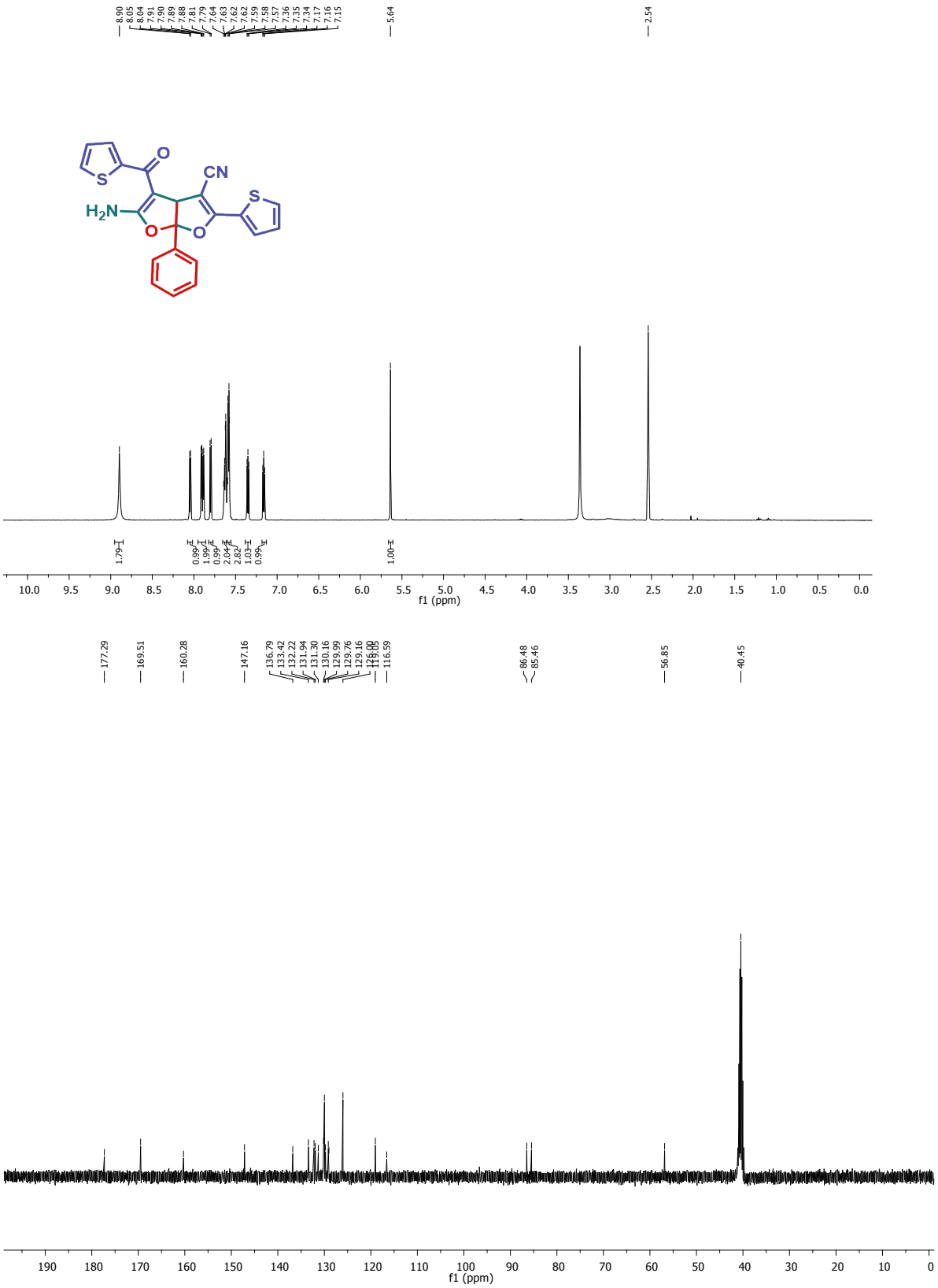


^{1}H NMR and ^{13}C NMR of compound (**3q)**

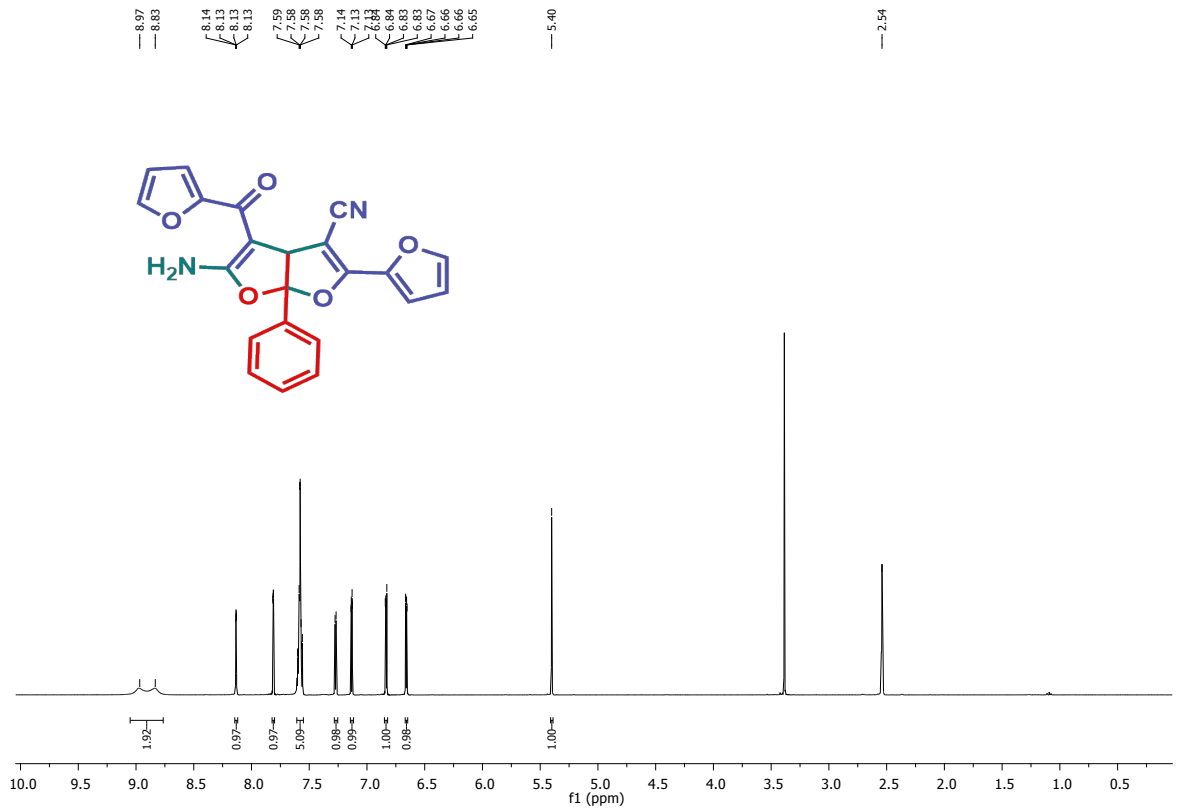


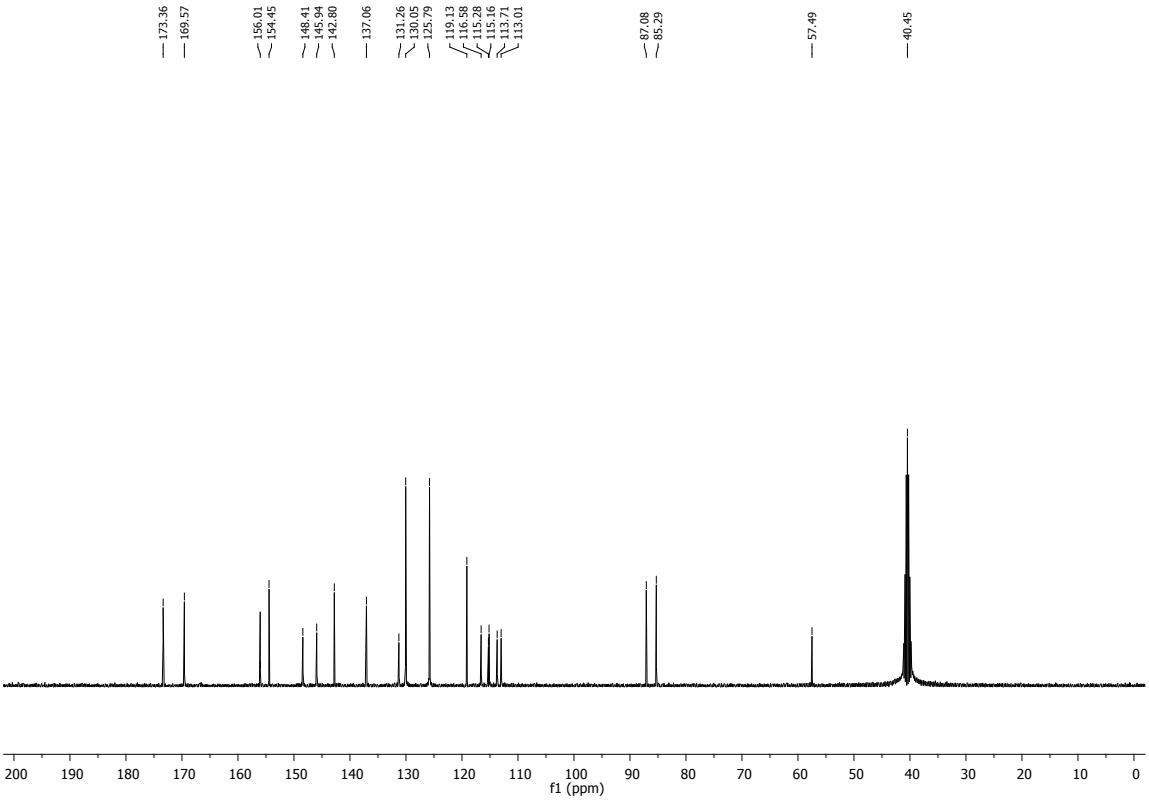


^{1}H NMR and ^{13}C NMR of compound (**3r)**

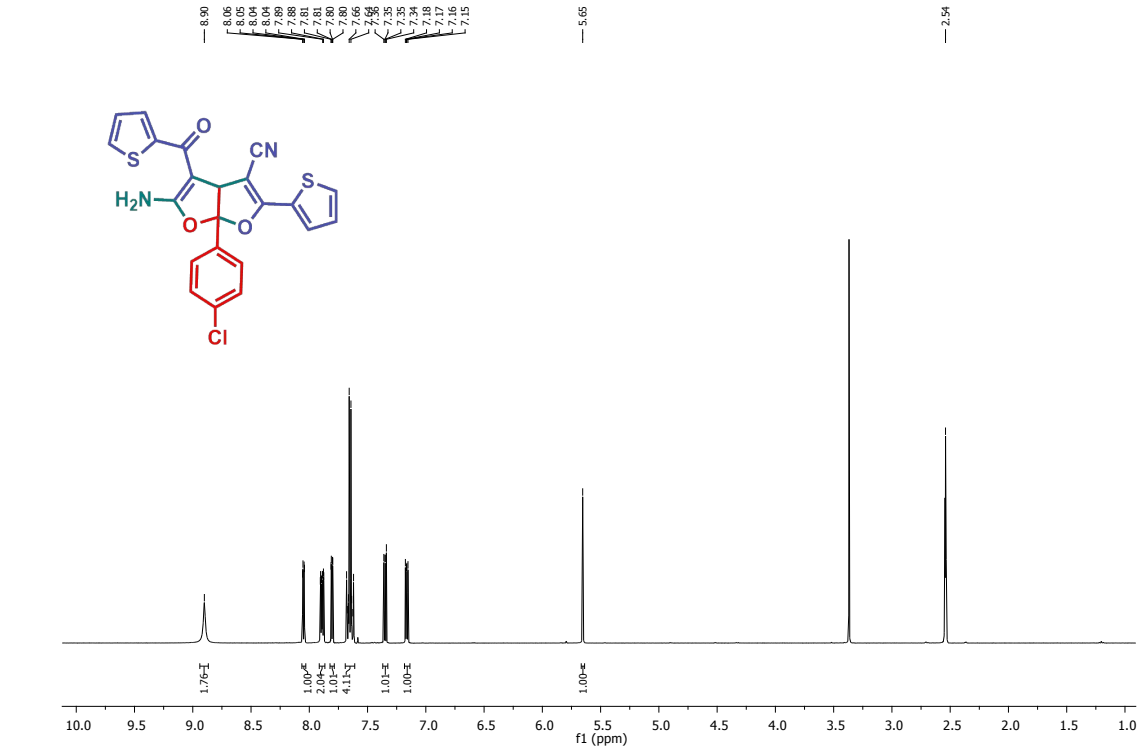


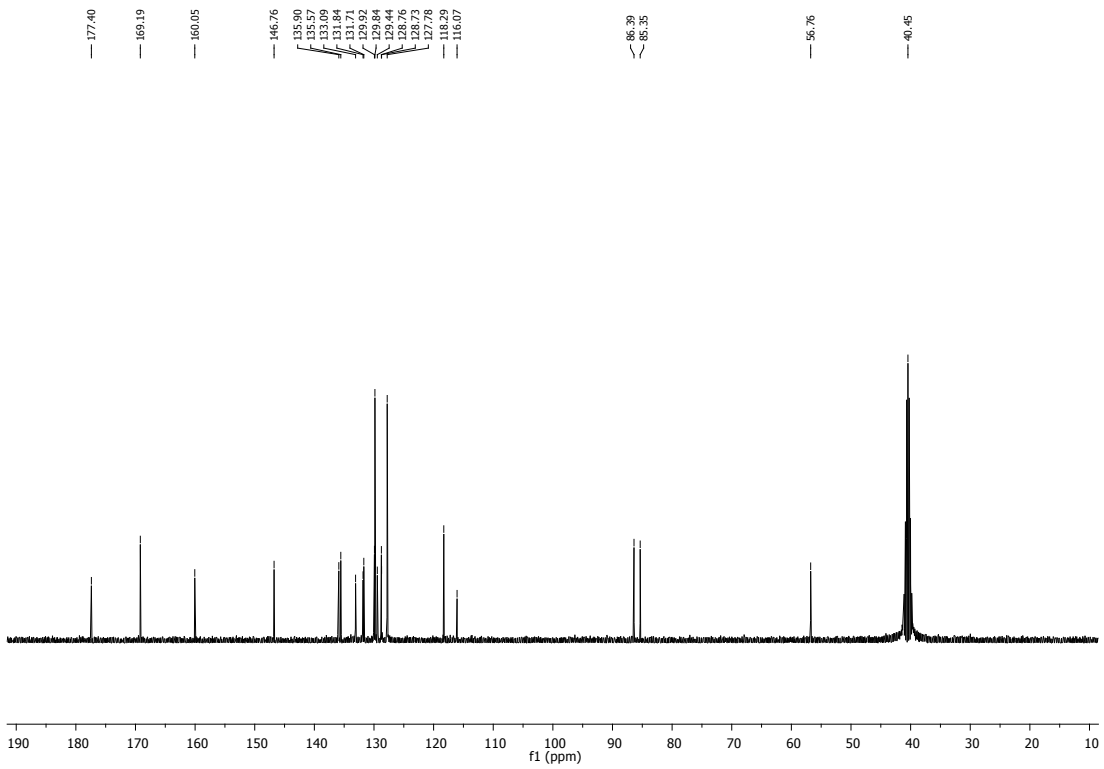
^{1}H NMR and ^{13}C NMR of compound (**3s)**



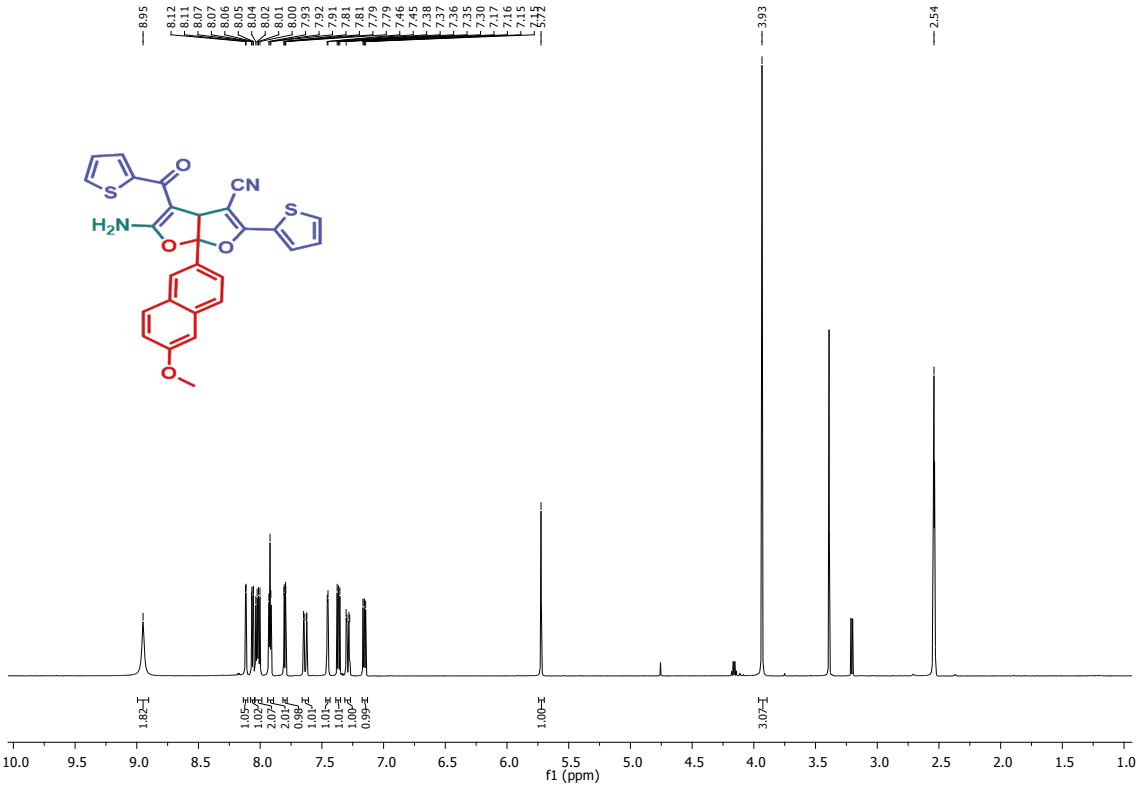


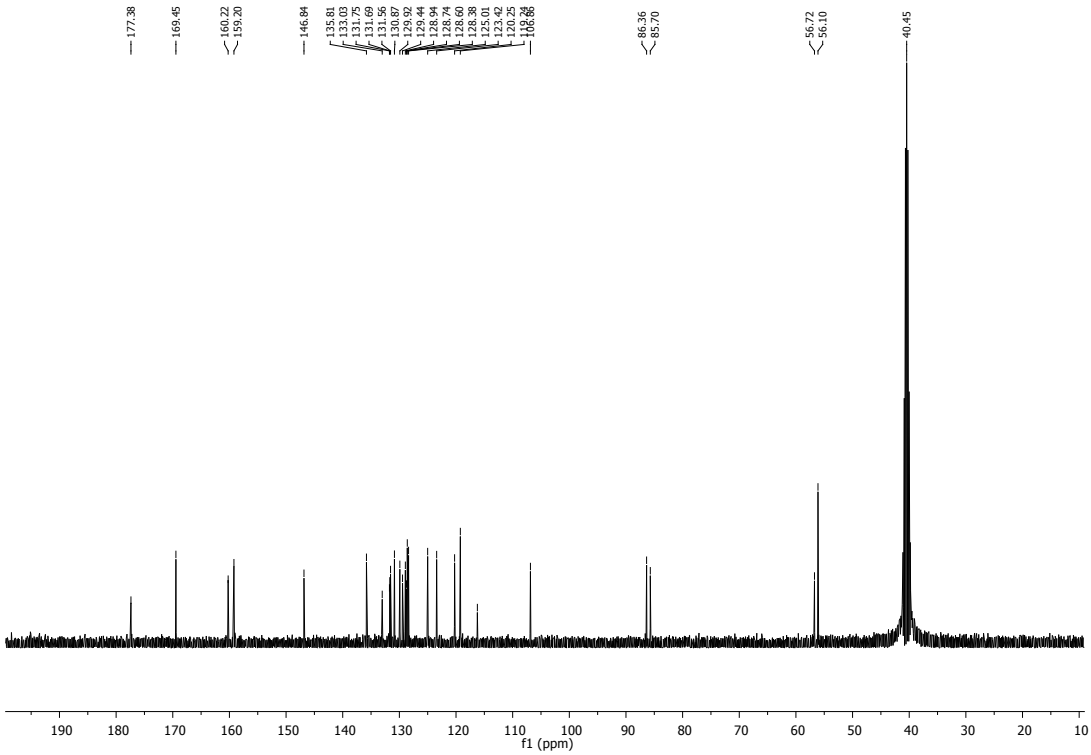
^{1}H NMR and ^{13}C NMR of compound (**3t)**



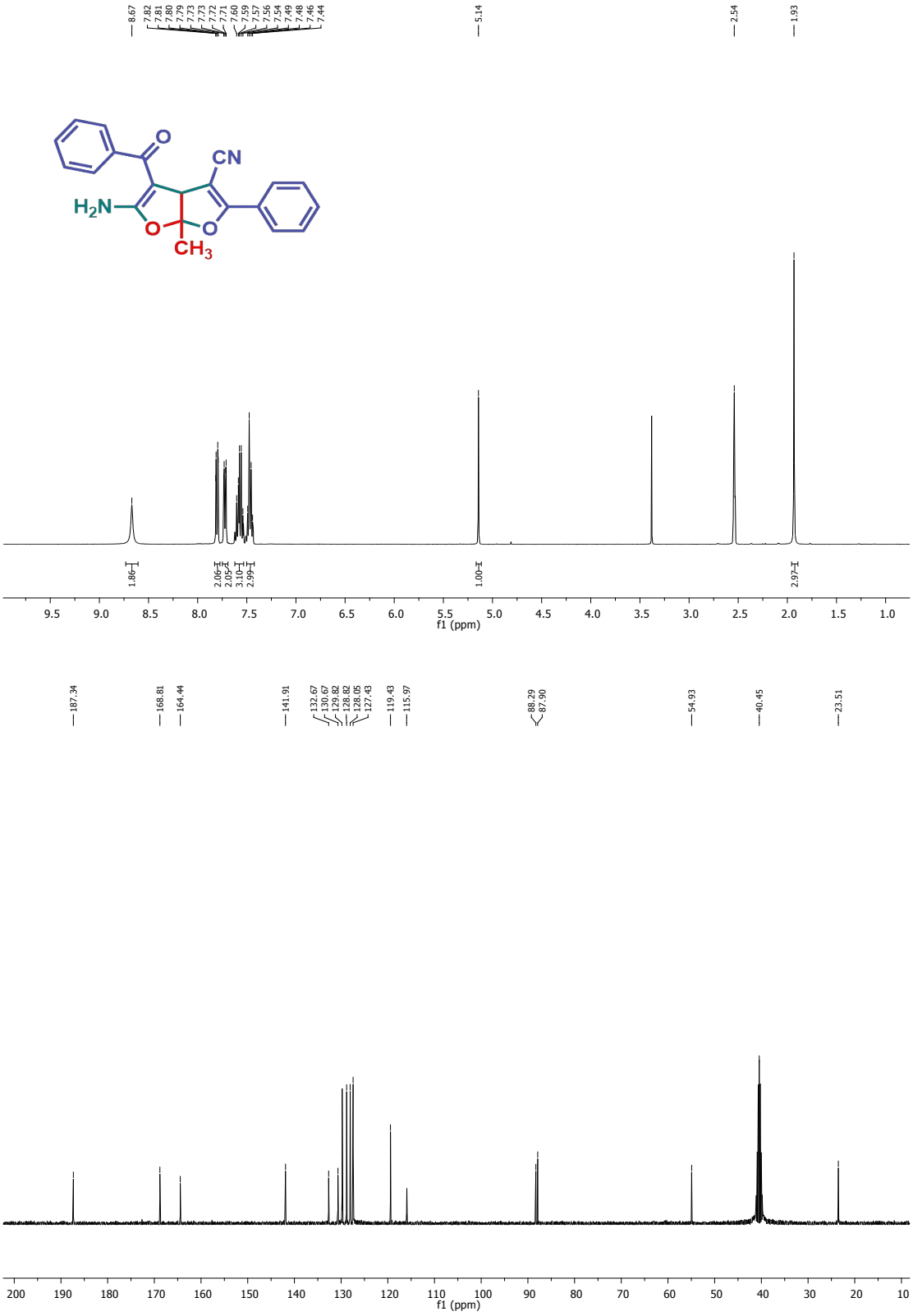


^{1}H NMR and ^{13}C NMR of compound (**3u)**

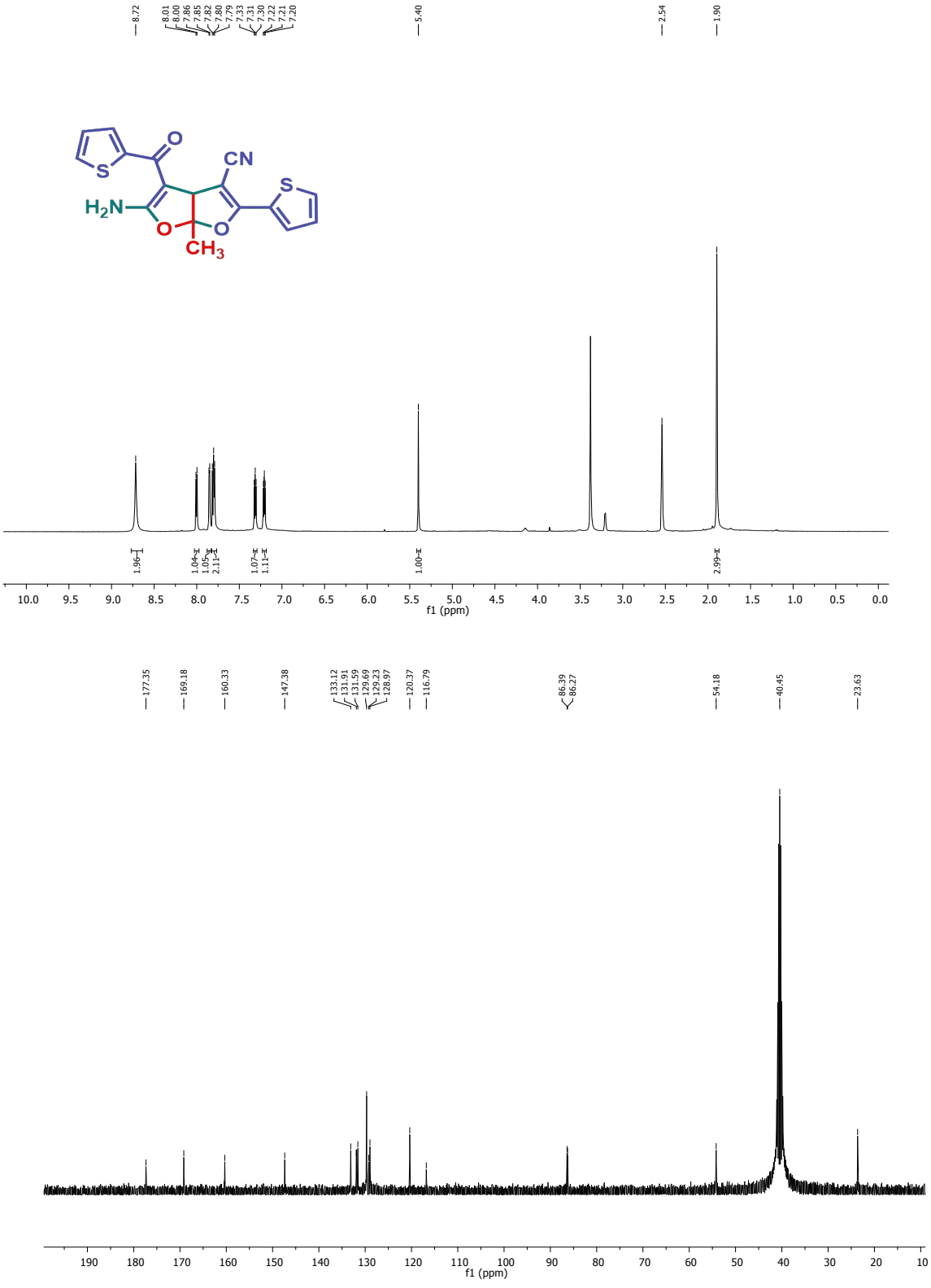




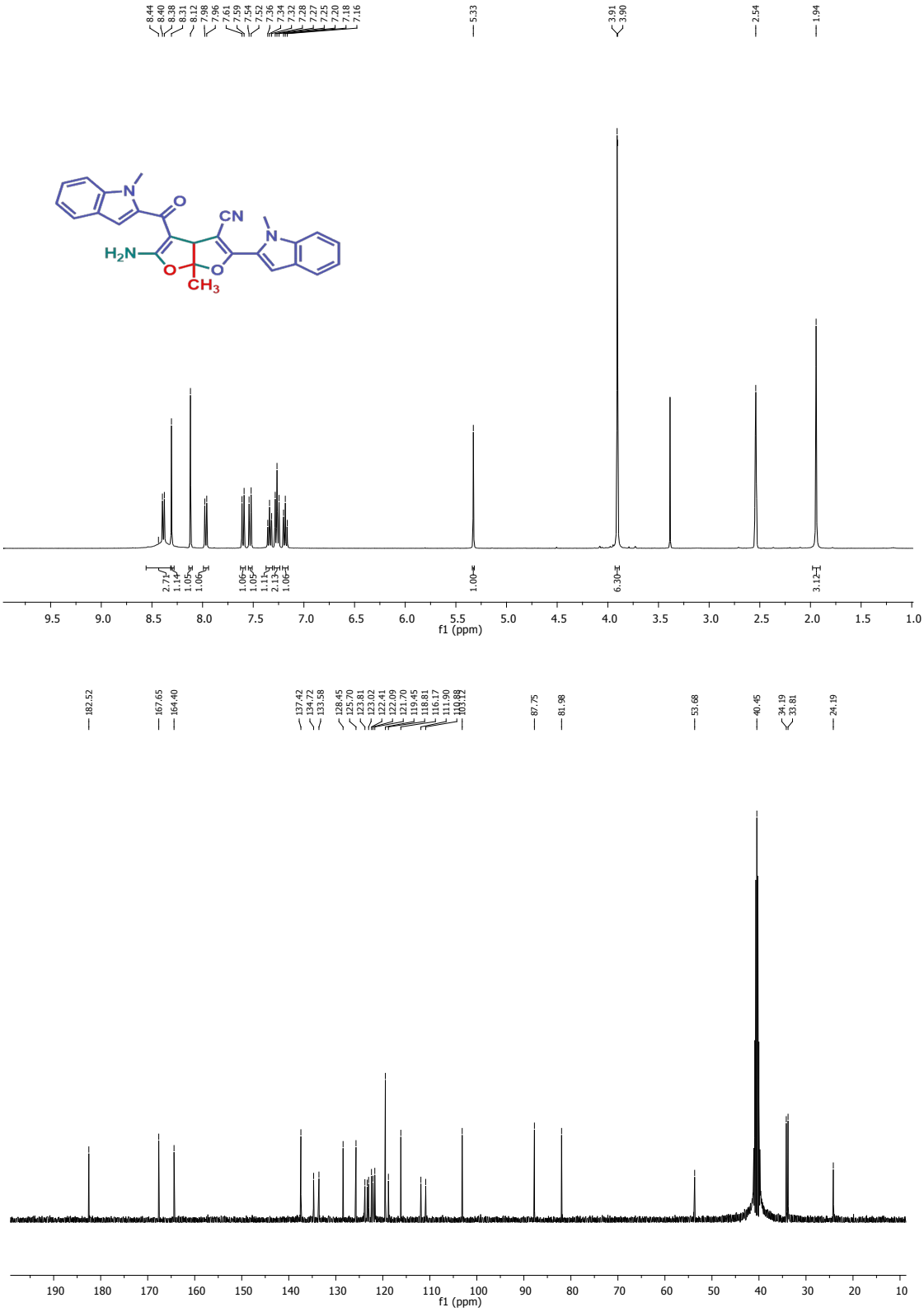
^{1}H NMR and ^{13}C NMR of compound (**4a)**



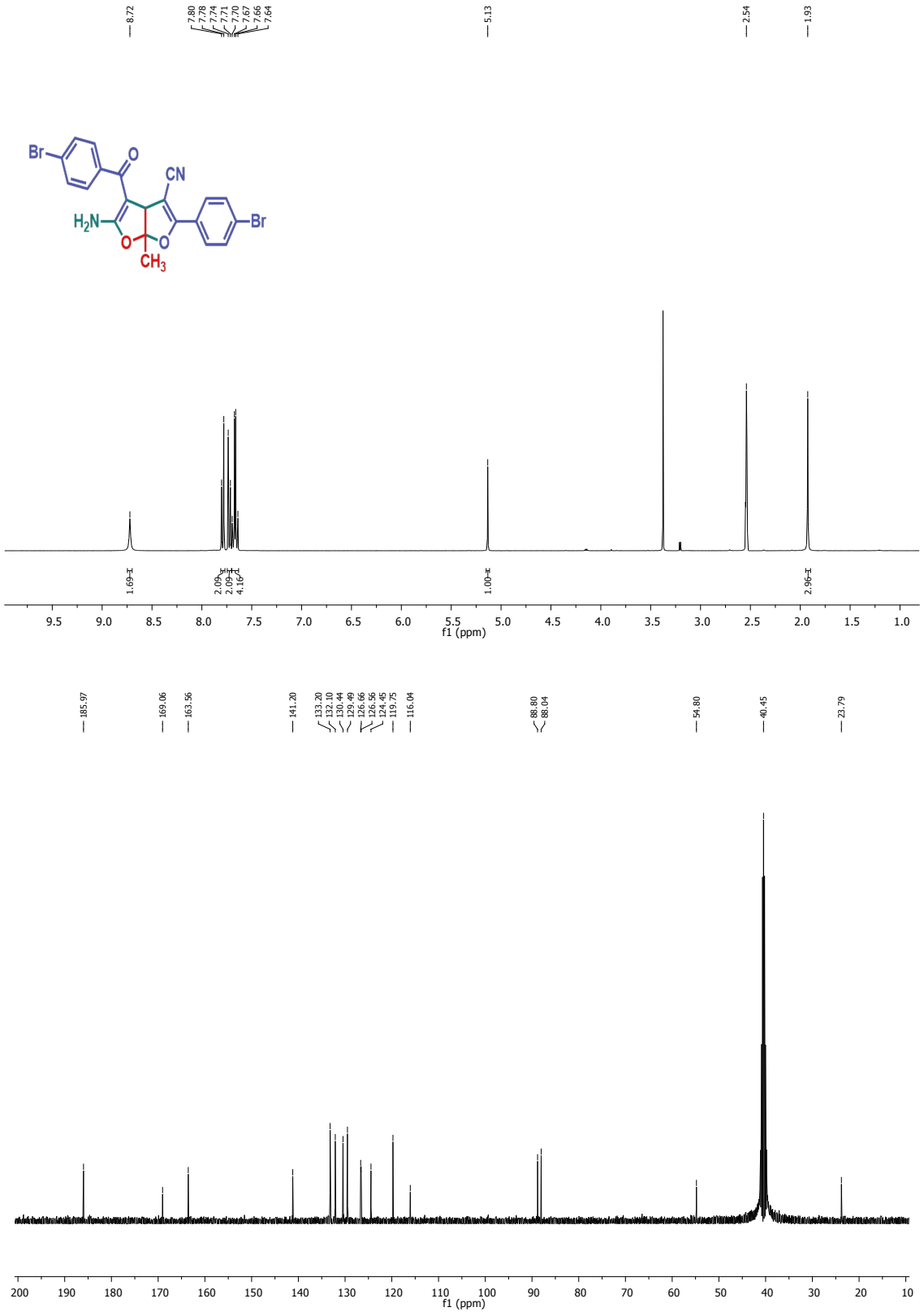
^{1}H NMR and ^{13}C NMR of compound (**4b)**



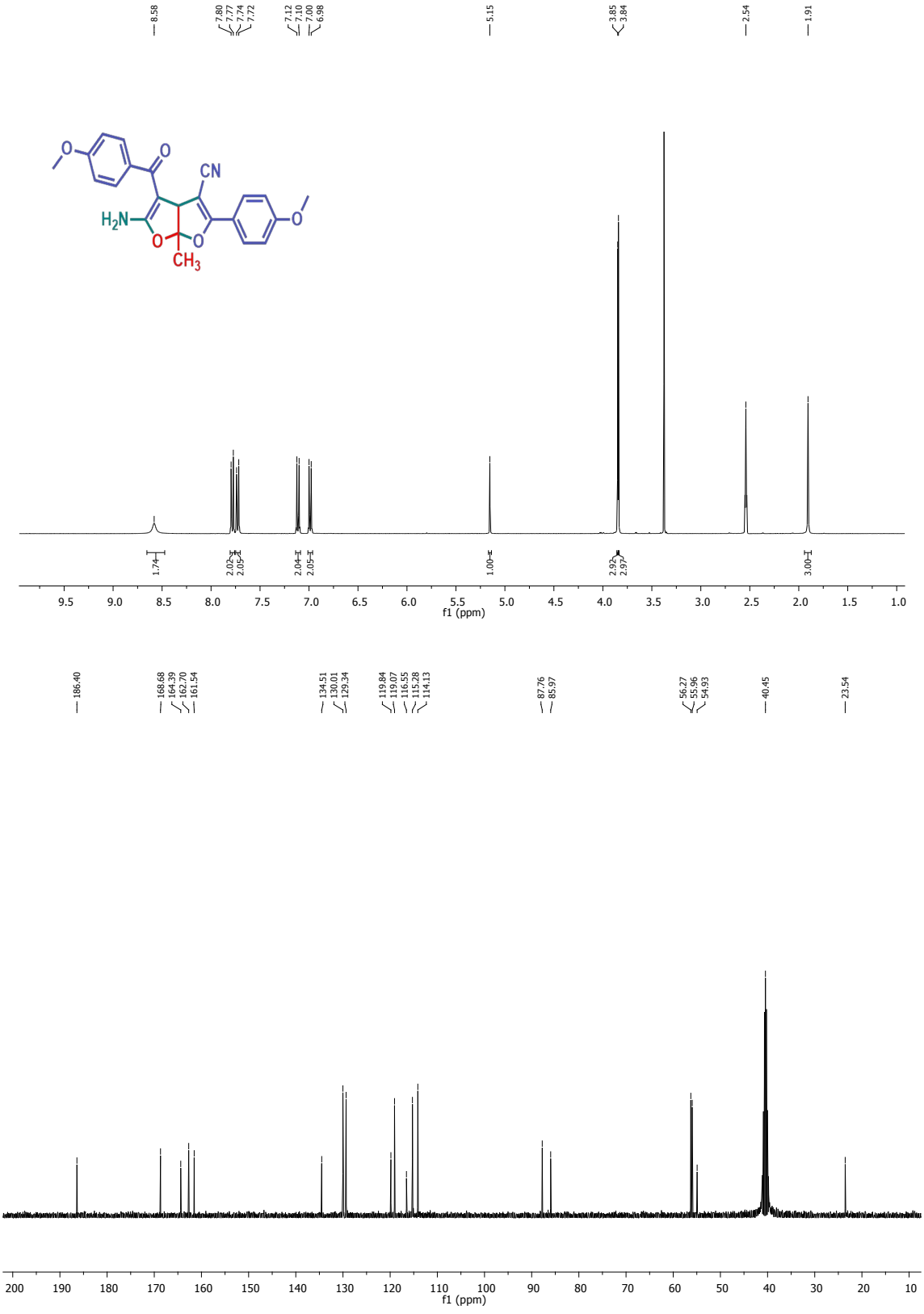
^{1}H NMR and ^{13}C NMR of compound (**4c)**



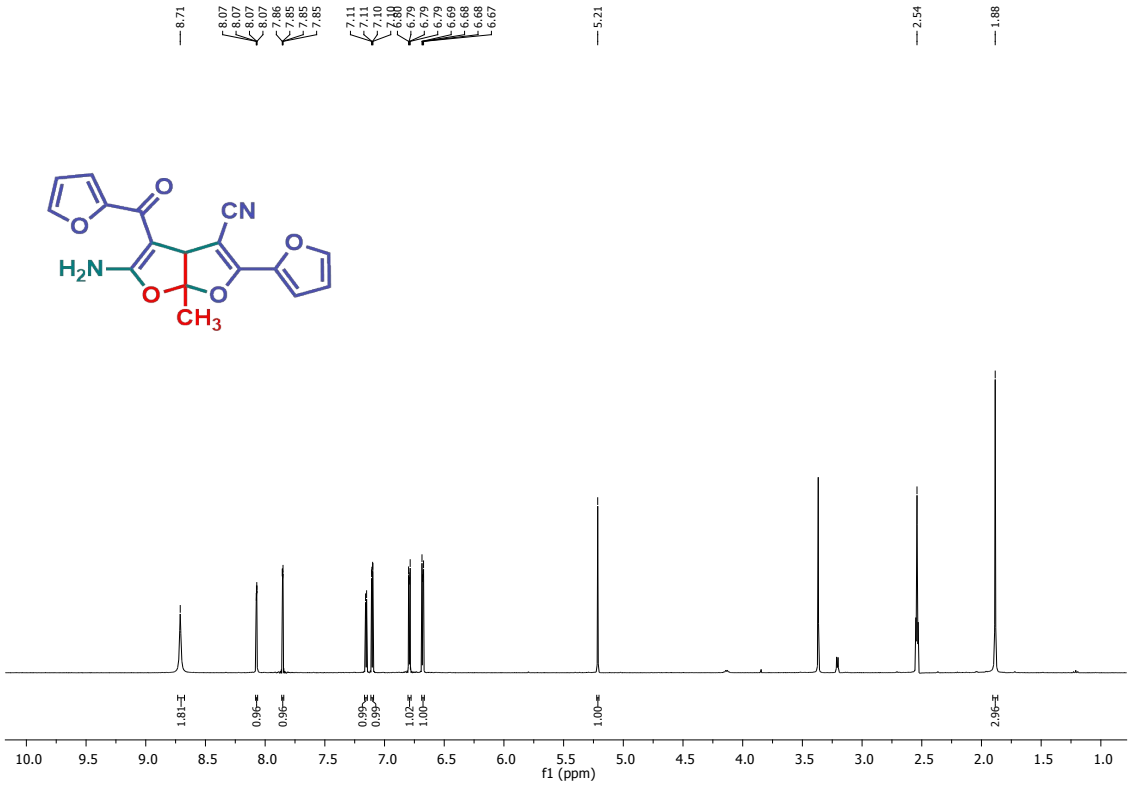
^{1}H NMR and ^{13}C NMR of compound (**4d)**

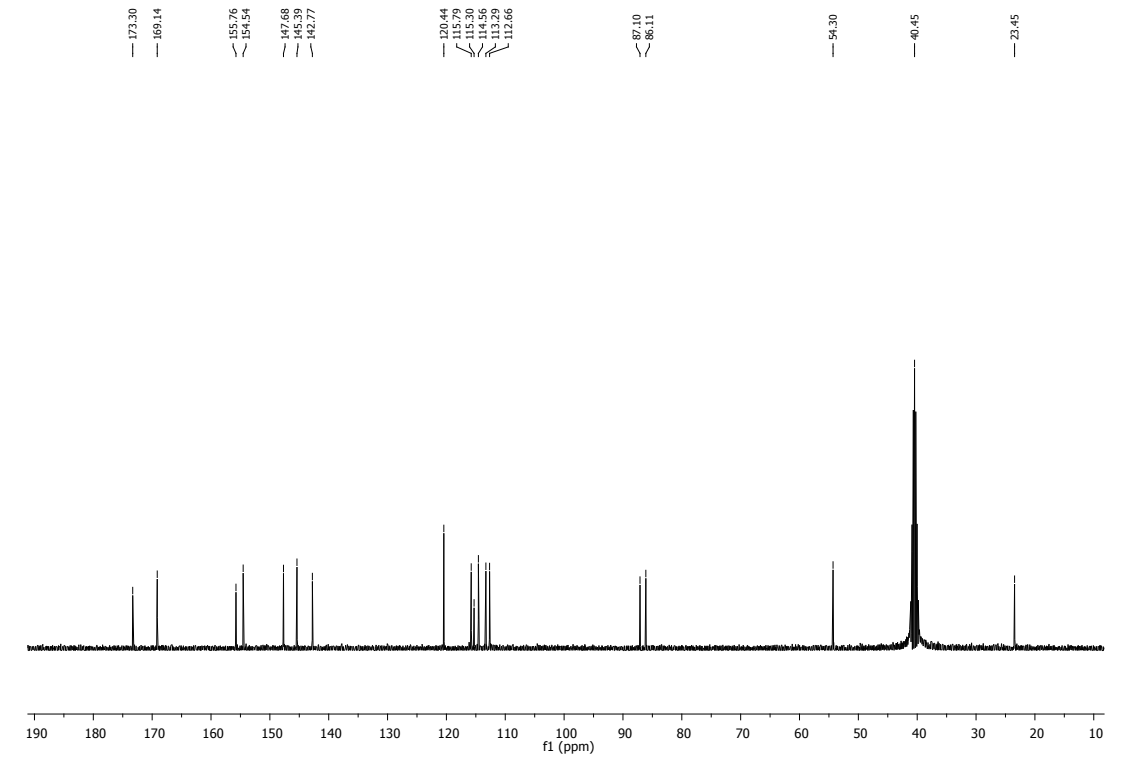


^{1}H NMR and ^{13}C NMR of compound (**4e)**

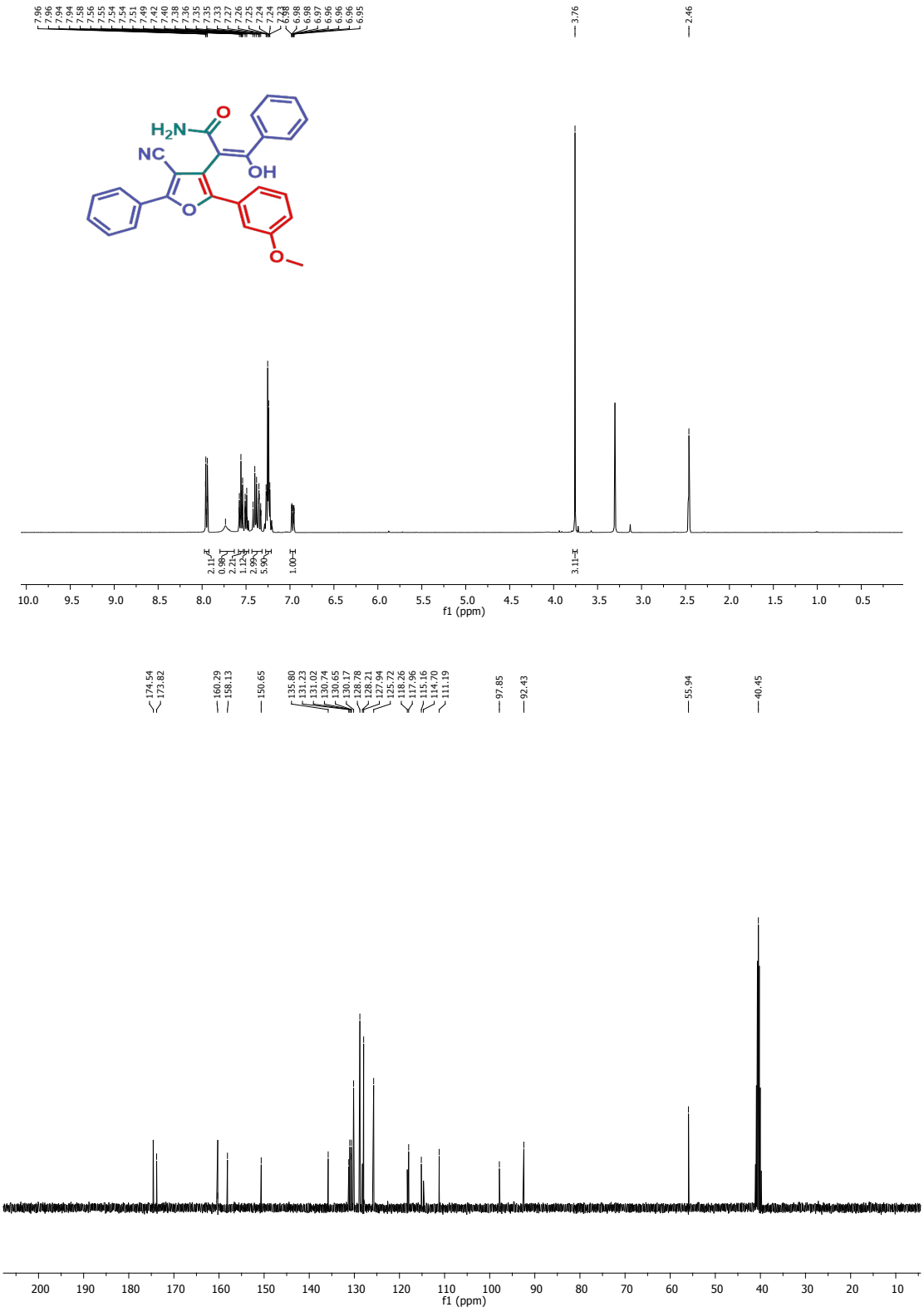


^{1}H NMR and ^{13}C NMR of compound (**4f)**

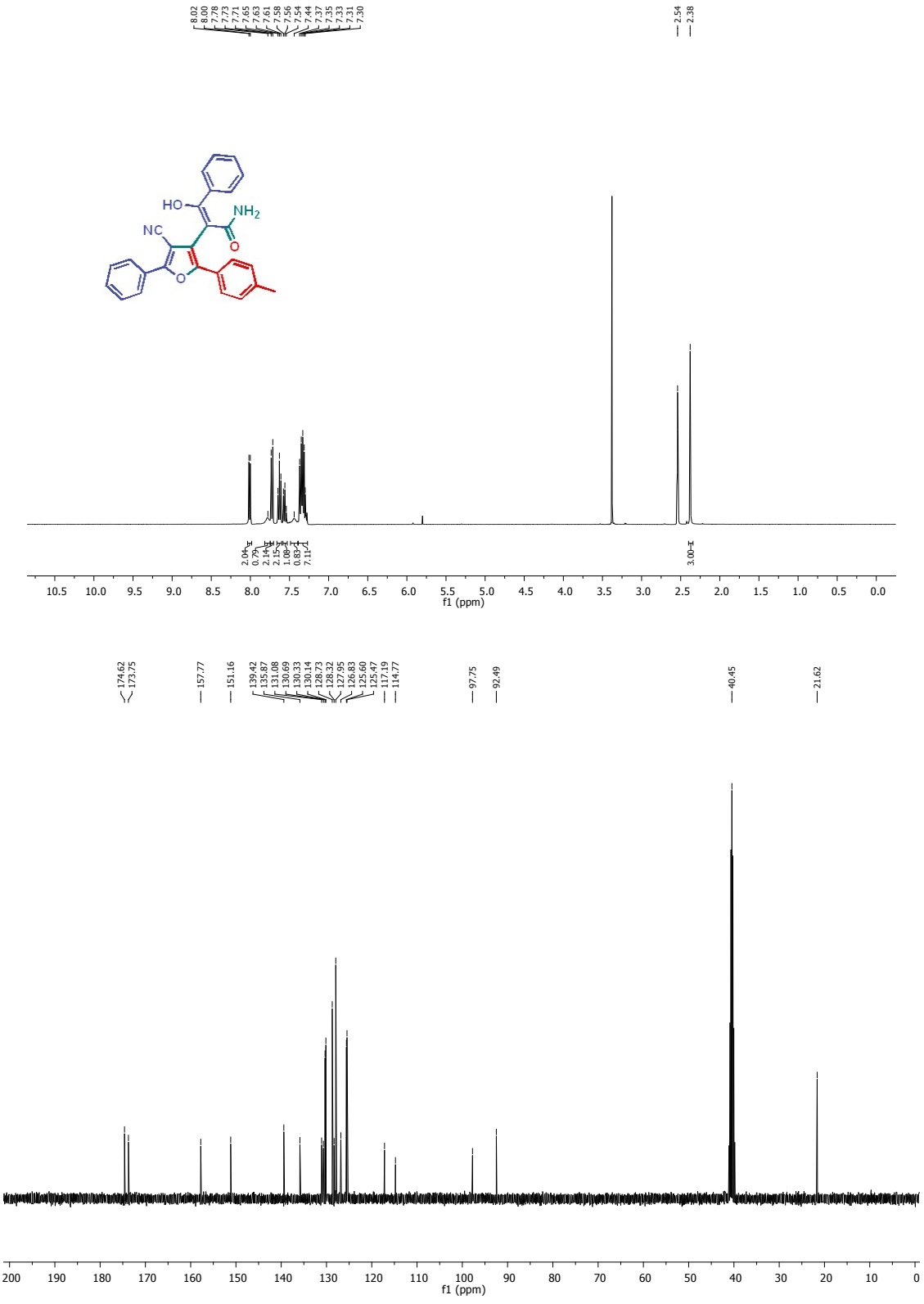




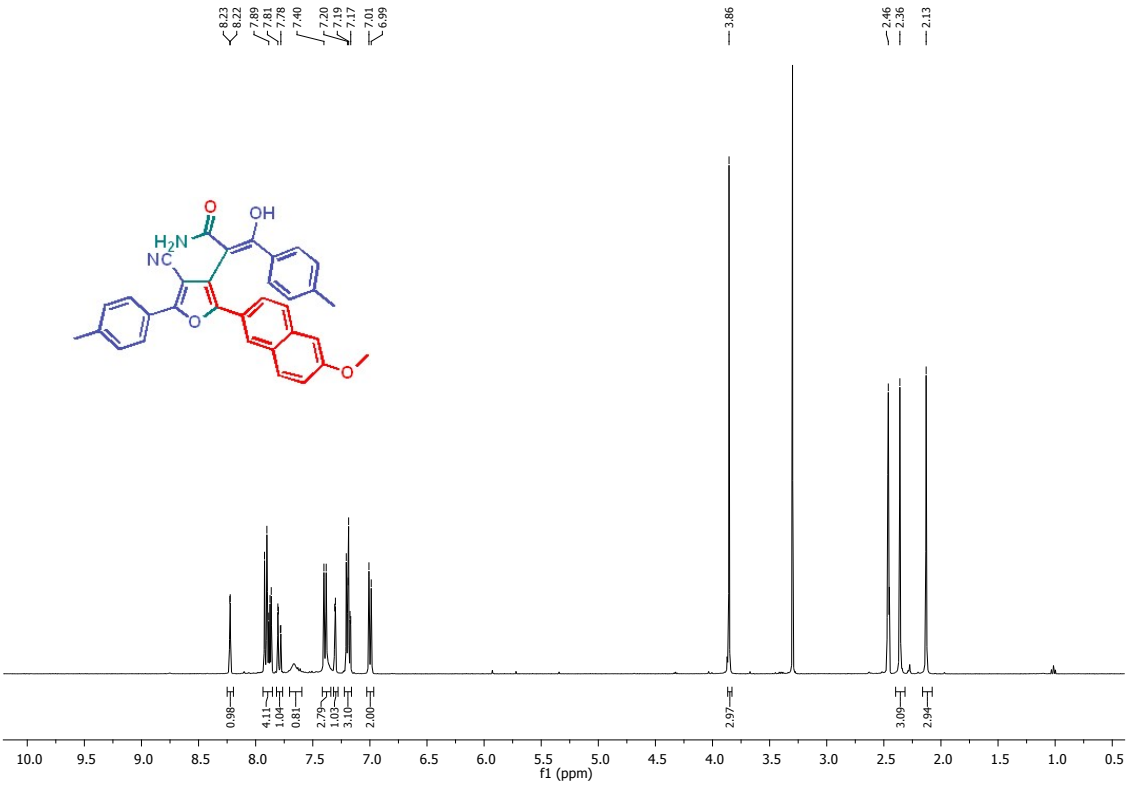
^{1}H NMR and ^{13}C NMR of compound (**5a)**

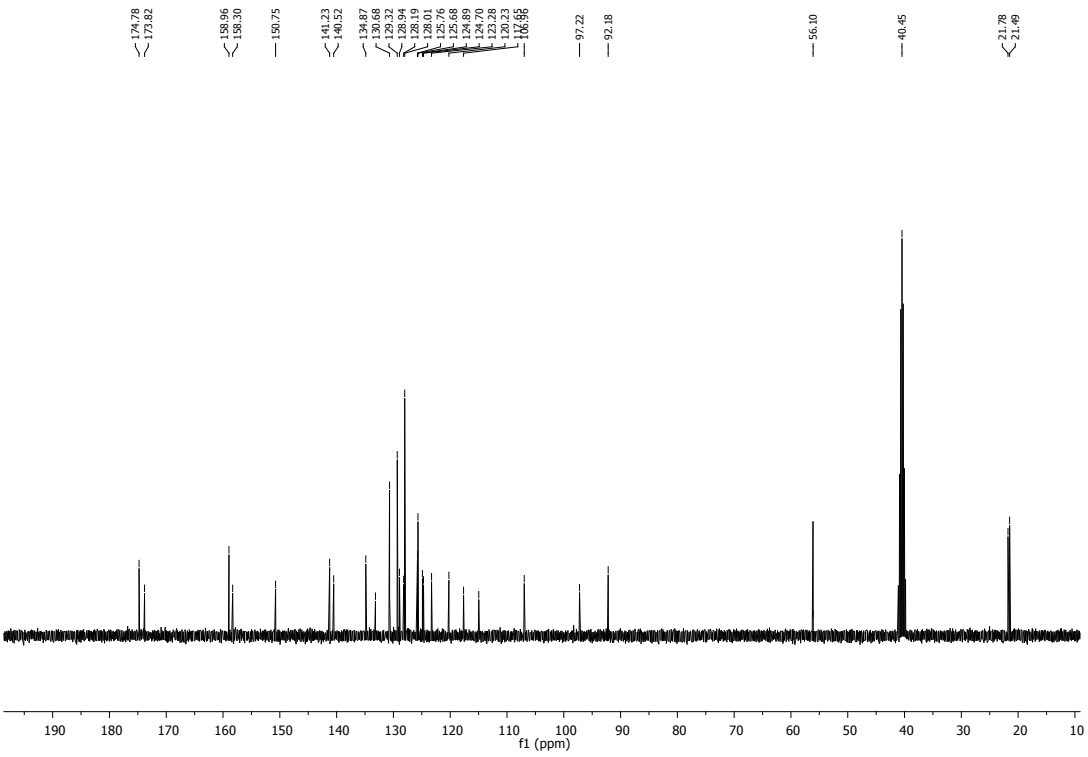


^{1}H NMR and ^{13}C NMR of compound (**5b)**

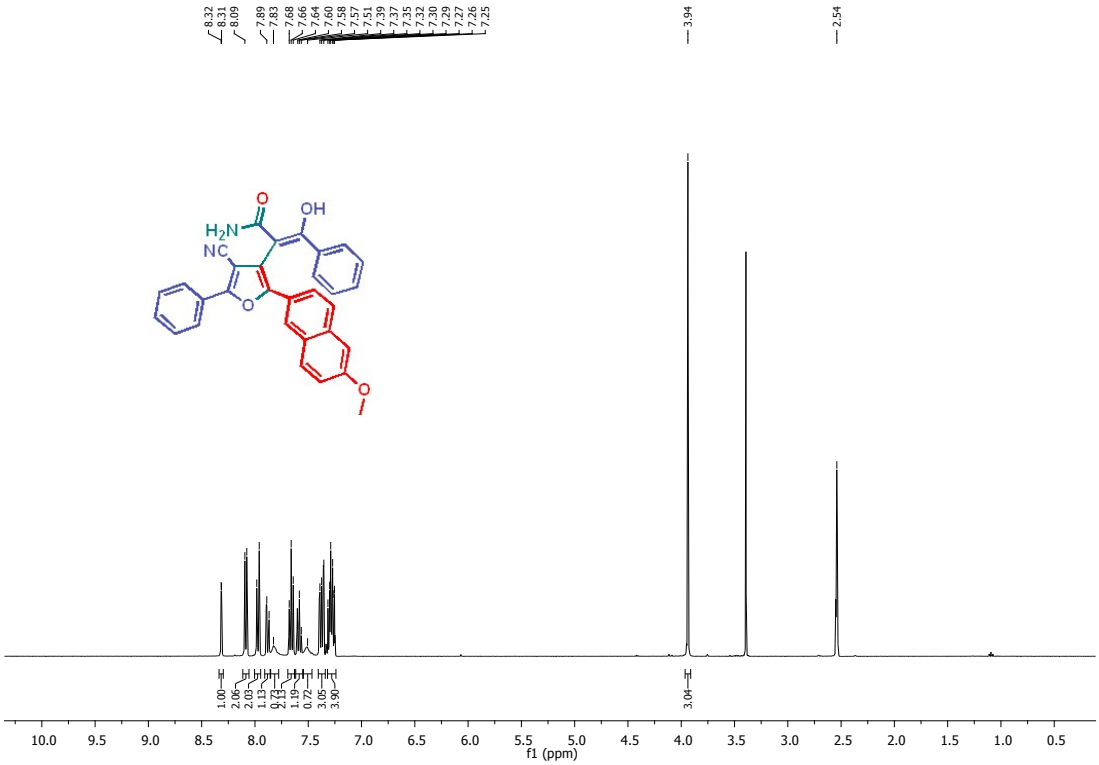


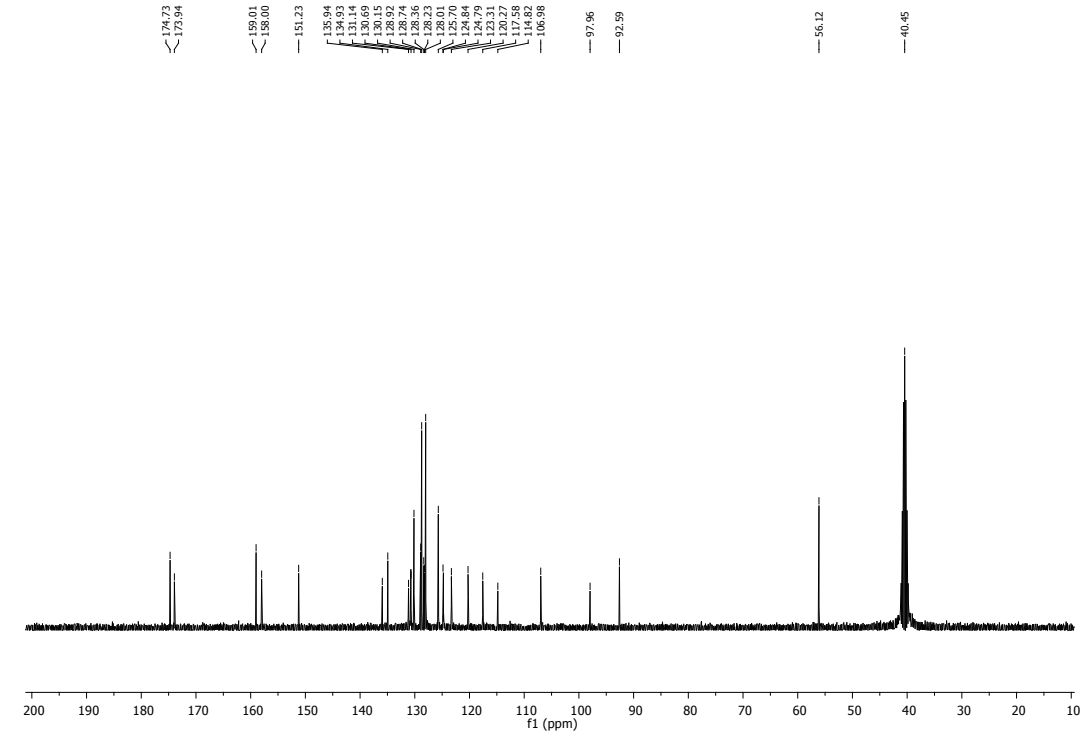
^{1}H NMR and ^{13}C NMR of compound (**5c)**



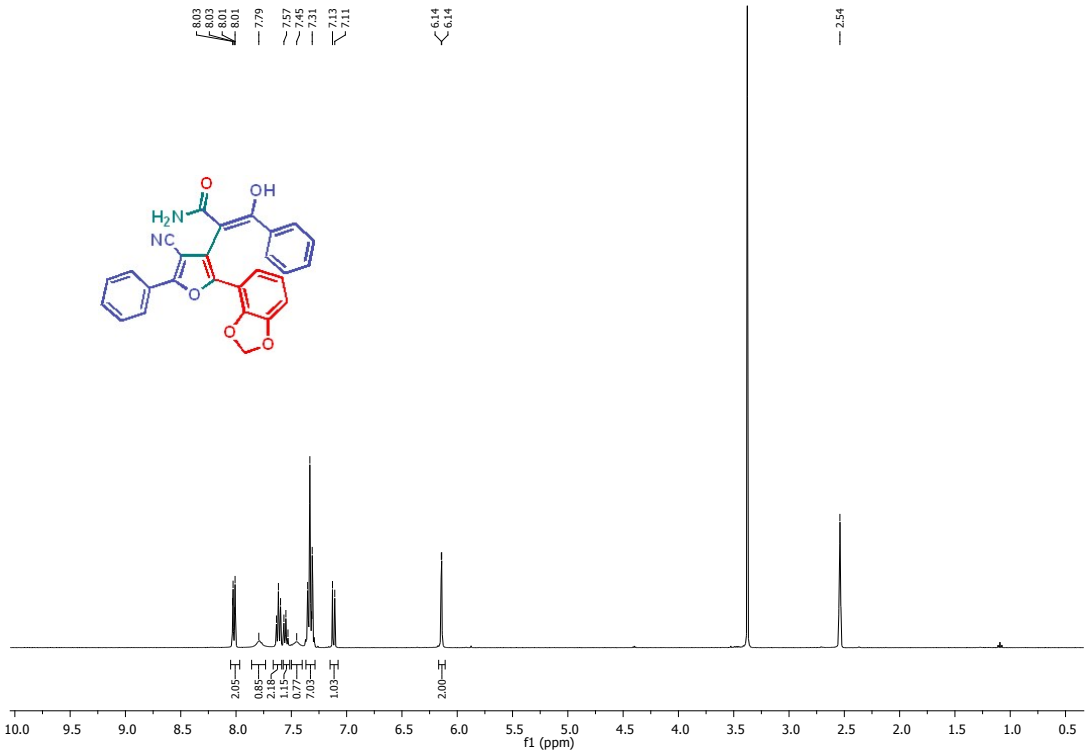


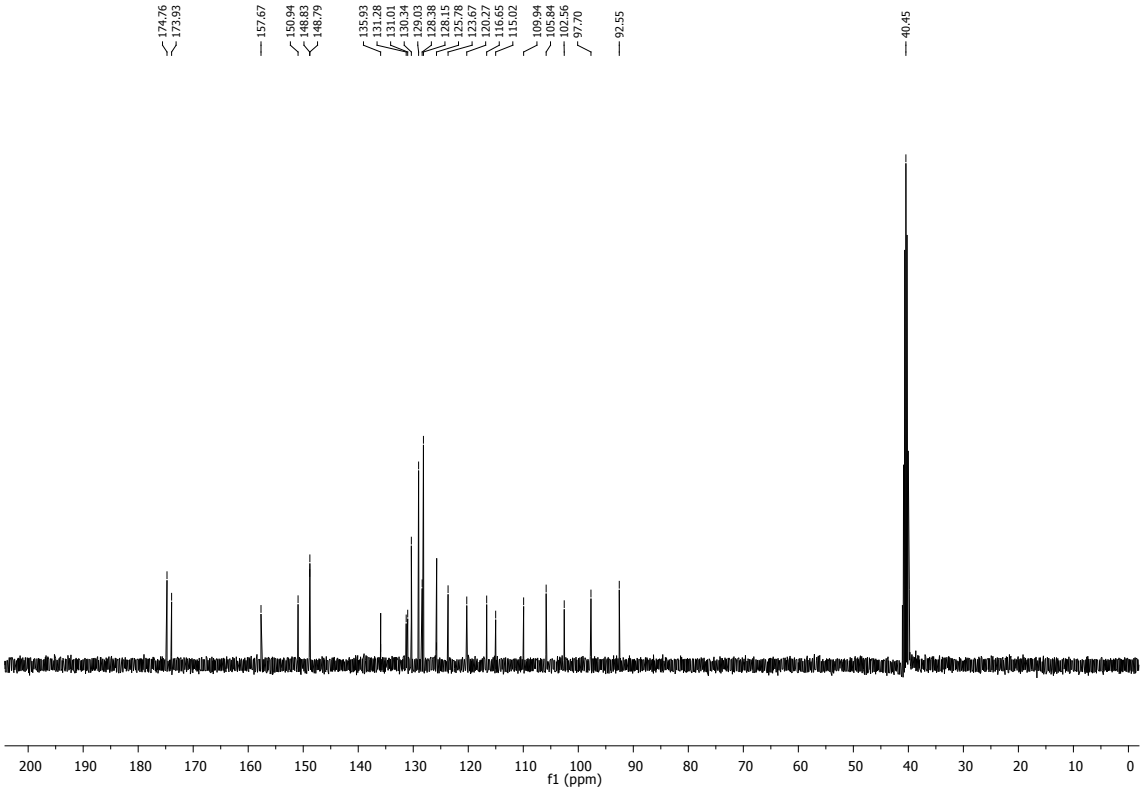
^{1}H NMR and ^{13}C NMR of compound (**5d)**





^{1}H NMR and ^{13}C NMR of compound (**5e)**


8.03
8.03
8.01
8.01
7.79
7.57
7.45
7.31
7.13
7.11
6.14
6.14
2.54
O
OH
H2N
NC
O
O
O
2.05
0.85
2.16
1.15
0.77
7.03
1.03
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


174.76
173.93
157.67
150.94
148.83
148.79
135.93
131.28
131.01
130.34
129.03
128.38
128.15
125.78
123.67
120.27
116.65
115.02
109.94
105.84
102.56
97.70
92.55
40.45
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)