10.1071/CH11015_AC

Australian Journal of Chemistry, 2011, 64(5), 638–646

SUPPORTING INFORMATION

Novel synthesis of 2-thienylcarbonyl-cyclohexane-1,3-dione as building block for indazolones and isoxazolones

Guillermo M. Chans, Elizabeth L. Moyano and Gloria I. Yranzo

INFIQC - Departamento de Química Orgánica - Facultad de Ciencias Químicas - Universidad Nacional de Córdoba - Ciudad Universitaria - 5016 - Córdoba, Argentina.

Table of Contents

General:

All chemicals were of reagent grade and were used without further purification. All solvents were distilled. Melting points were determined in open capillary tubes and are uncorrected. FT-IR spectra were obtained with a Nicolet 55XC-FTIR. Mass spectra were measured at an ionizing voltage of 70 eV. All ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded at 400.16, 376.48 and 100.56 MHz respectively (Bruker Avance II, BBI probe, *Z*-gradient spectrometer). Chemical shifts (δ) are reported in ppm values and coupling constants (*J*) in Hz. The internal standard was TMS. ^{13}C and ^{1}H assignments were made using 2D HSQC and HMBC experiments.

Preparative thin-layer chromatography was carried out with Merck silica-gel (60 DGF_{254}) and column chromatography with Merck silica gel (70-230 mesh).

Computational Methods:

All geometries and energy calculations were performed at the HF/6-31+G(d,p) level of theory by using the Gaussian 03[32] suite of programs. All stationary points were confirmed as true minima by harmonic vibrational frequency calculations at the same computational level.

Synthesis of 3-oxocyclohex-1-en-1-yl thiophene-2-carboxylate (3) and 3-hydroxy-2-(2-thienylcarbonyl)cyclohex-2-en-1-one (5) (Pathway A): Thiophene-2-carbonyl chloride **1** (0.304 g, 2.0 mmol) was added dropwise to a cooled (-10 °C) stirred solution of cyclohexane-1,3-dione **2** (0.300 g, 2.7 mmol) and triethylamine (0.35 mL) in anhydrous CH_2Cl_2 (12 mL). The mixture is left for 10 minutes at -10 °C and then for another 12 h at room temperature.

A solution of **3** (0.250 g, 1.126 mmol), triethylamine (0.34 mL), potassium cyanide (1.1 mg, 16.9 µmol, 1.5 % mol) in acetonitrile (2.8 mL) was stirred for 12 h at room temperature. The solution was concentrated in vacuo and the residue was partitioned between ethyl acetate and 1M HCl. The triketone **5** was then extracted from the organic layer into aqueous sodium bicarbonate. Neutralization and extraction with ether gave, after drying and concentration, the crude product that was chromatographed.[10]

Synthesis of 3-hydroxy-2-(2-thienylcarbonyl)cyclohex-2-en-1-one (5) (Pathway B): A mixture of thiophene-2-carbonyl chloride **1** (0.5 g; 3.4 mmol), potassium cyanide (dried at 150 °C in vacuo and powdered), (0.245 g, 3.75 mmol), and acetonitrile (5 mL) is placed in a 100 mL round-bottom flask which is immersed in a laboratory ultrasonic cleaner (TestLab, 80 W, 40 KHz) thermostated at 50 °C. After ultrasonic treatment for 3 h, anhydrous Et_3N (1 mL) and cyclohexane-1,3-dione (0.420 g, 3.75 mmol) were added and the mixture was stirred at room temperature overnight. Isolation methodology used was identical to Pathway A, nevertheless, no further purification was needed.

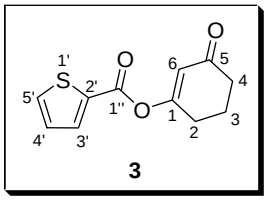
Synthesis of 3-(2-thienyl)-1,5,6,7-tetrahydro-4*H*-indazol-4-ones (7a,c): A mixture of 3-hydroxy-2-(2-thienylcarbonyl)cyclohex-2-en-1-one **5** (0.318 g, 1.436 mmol) and the corresponding hydrazine in DMF (3 mL) was heated to reflux for 5 h. The reaction progress was monitored by TLC. Water was added dropwise to the mixture; after cooling, the precipitate was collected by filtration. The mother liquor was further purified by extraction with ether (3×10 mL), the combined organic extracts were dried with anhydrous $MgSO_4$ and evaporated. The residue (**7c**) was purified by column chromatography with ether as eluent and then recristallized from acetone/water.

Synthesis of 1-(4-fluorophenyl)-3-(2-thienyl)-1,5,6,7-tetrahydro-4*H*-indazol-4-one (7b): Compound **5** (0.105 g, 0.475 mmol) was dissolved in ethanol (2 mL) and 4-fluorophenylhydrazine hydrochloride **6d** (0.080 mg, 0.493 mmol) and NaOH (0.0221 g, 0.552 mmol) were added. The reaction mixture was heated at reflux temperature for 6 h. The residue was evaporated to dryness under reduced pressure, dissolved with $CHCl_3$ (10 mL) and extracted with HCl 0.1 M (3×10 mL). The organic layer was dried ($MgSO_4$), filtered and evaporated. The solid residue obtained was purified by column chromatography with $CHCl_3$:Hexane:EtOH [3.5:0.1:0.05] as eluent.

Synthesis of 3-(2-thienyl)-6,7-dihydro-1,2-benzisoxazol-4(5*H*)-one (11): To a solution of **5** (0.1 g, 0.45 mmol) in ethanol (3 mL), hydroxylamine hydrochloride (0.344 g, 0.495 mmol) and pyridine (0.1 mL) were added. The mixture was heated to reflux in a water bath for 6 h. The solvent was evaporated to dryness, and the residue was dissolved with water, extracted with ethyl acetate and dried with anhydrous $MgSO_4$. The residue was purified by thin-layer chromatography with $CHCl_3$:Hexane:EtOH [3:1:0.05] as eluent.

General characterization of products

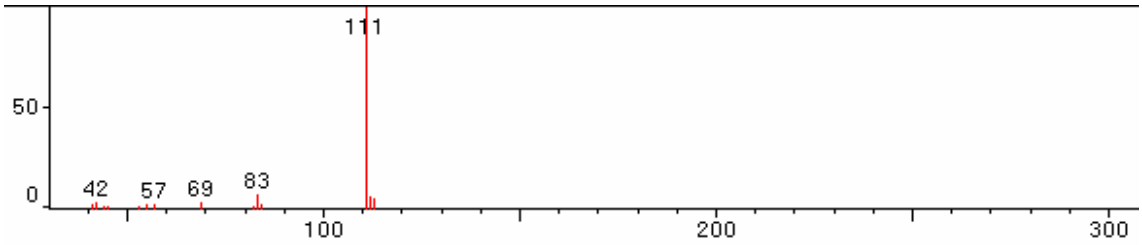
3-oxocyclohex-1-en-1-yl thiophene-2-carboxylate (3): White crystals, m.p. 41–44 ºC. Yield 55.7 % (0.3352 g). ^{1}H NMR ($CDCl_3$), δ = 2.12 (quintuplet, J = 6.2 Hz, 2 H, H-3), 2.46 (t, J = 6.2 Hz, 2 H, H-2), 2.68 (t, J = 6.2 and 1.1 Hz, 2 H, H-4), 6.06 (t, J = 1.1 Hz, 1 H, H-6), 7.17 (dd, J = 5.0 and 3.8 Hz, 1 H, H-4´), 7.69 (dd, J = 5.0 and 1.2 Hz, 1 H, H-5´), 7.91 (dd, J = 3.8 and 1.2 Hz, 1 H, H-3´) ppm. ^{13}C NMR ($CDCl_3$), δ = 21.45 (C-3), 28.54 (C-2), 36.92 (C-4), 117.85 (C-6), 128.39 (C-4´), 132.02 (C-2´), 134.54 (C-5´), 135.48 (C-3´), 158.63 (C-1´´), 169.75 (C-1), 199.59 (C-5) ppm. IR (KBr): ν = 3092, 2951, 2886, 2866, 1733, 1674, 1410, 1249, 1123, 735 cm^{-1}. MS: m/z (%) = 113 (5), 112 (6), 111 [M-111]$^{+}$ (100), 83 (7), 69 (3), 57 (2), 42 (3).



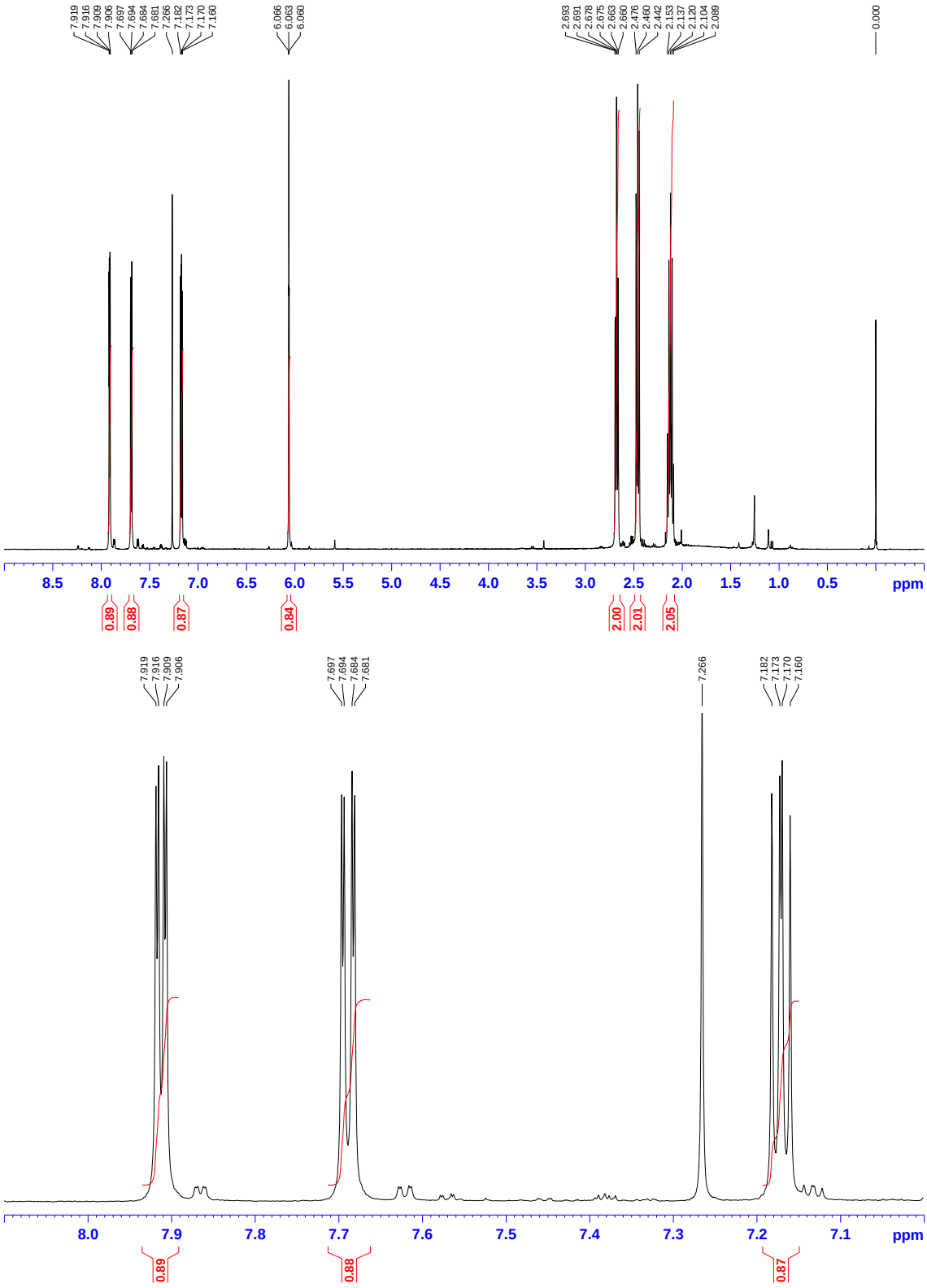
3

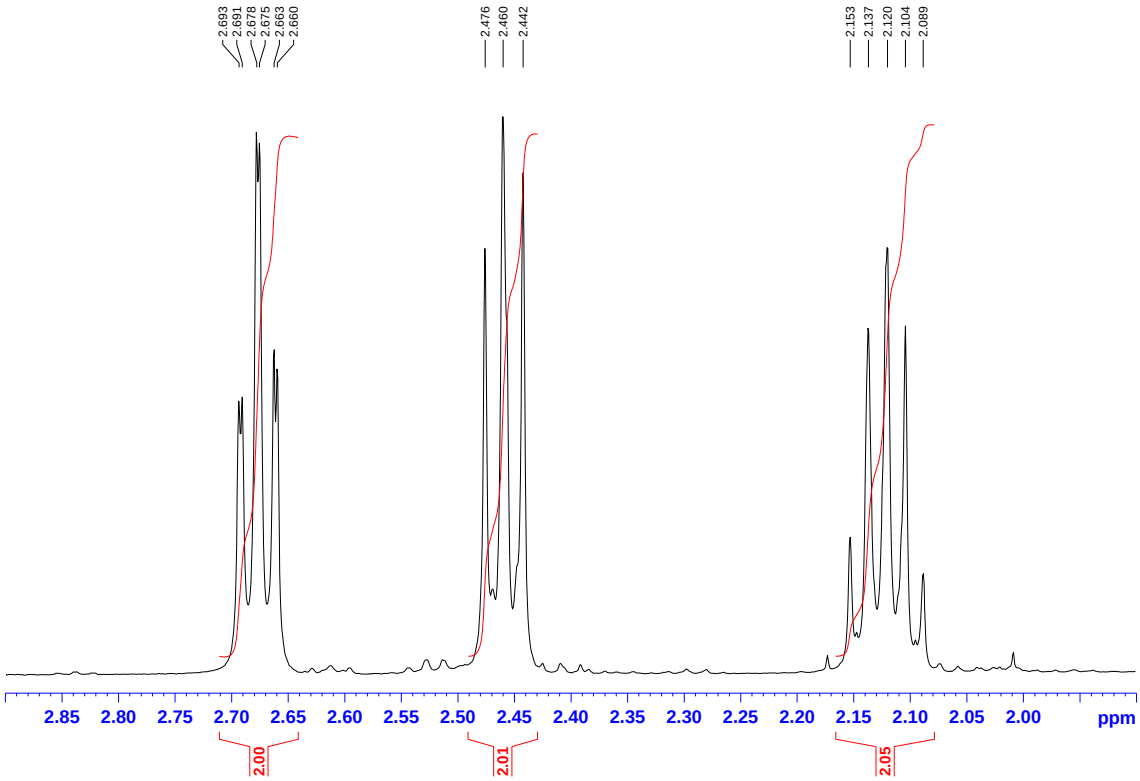
Carbon Number	δH (ppm) (*J* in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.69, dd (5.0, 1.2), 1 H	134.54	3', 4'	1'', 2', 3', 4'	
4'	7.17, dd (5.0, 3.8), 1 H	128.39	3', 5'	2', 3', 5'	
3'	7.91, dd (3.7, 1.2), 1 H	135.48	4', 5'	1'', 2', 4', 5'	
2'		132.02			
1''		158.63			
6	6.06, t (1.1)	117.85	4	1, 2, 4	
1		169.75			
2	2.46, t (6.2), 2 H	28.54	3, 4	1, 3, 4, 5, 6	
3	2.12, quintuplet (6.2), 2 H	21.45	2, 4	1, 2, 4, 5	
4	2.68, t (6.2), 2 H	36.92	2, 3, 6	2, 3, 5, 6	
5		199.59			

MS **(3)**

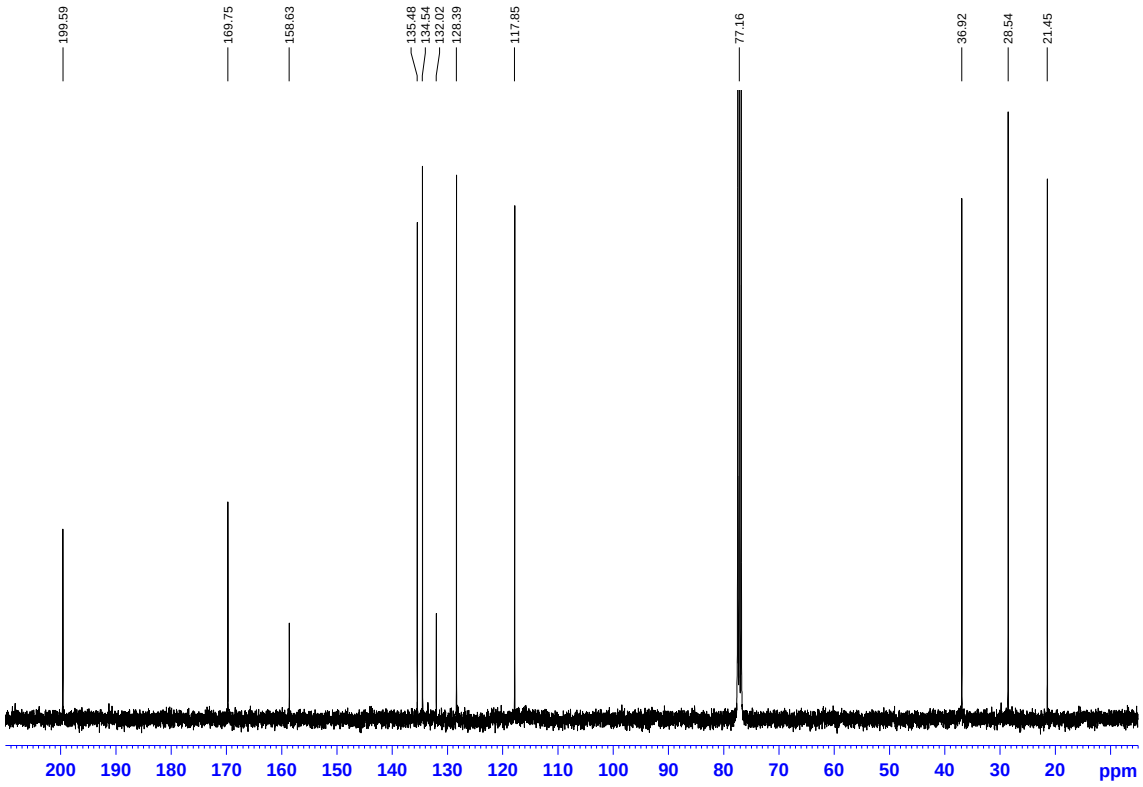


^{1}H **(3)**

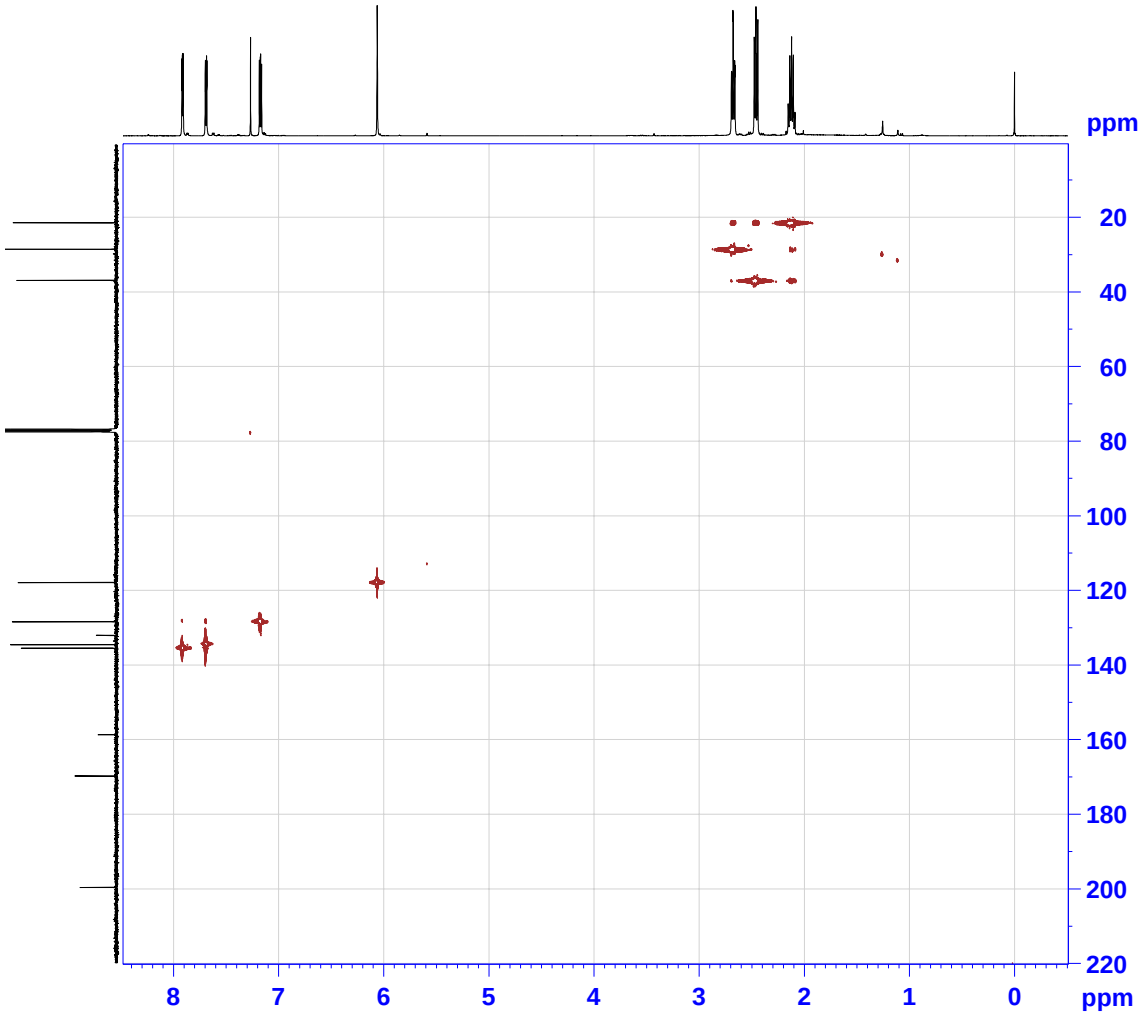

7.919
7.916
7.909
7.906
7.697
7.694
7.684
7.681
7.266
7.182
7.173
7.170
7.160
6.066
6.063
6.060
2.693
2.691
2.678
2.675
2.663
2.660
2.476
2.460
2.442
2.153
2.137
2.120
2.104
2.089
0.000
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.89
0.88
0.87
0.84
2.00
2.01
2.05
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 ppm
0.89
0.88
0.87


2.693
2.691
2.678
2.675
2.663
2.660
2.476
2.460
2.442
2.153
2.137
2.120
2.104
2.089
2.85 2.80 2.75 2.70 2.65 2.60 2.55 2.50 2.45 2.40 2.35 2.30 2.25 2.20 2.15 2.10 2.05 2.00 ppm
2.00
2.01
2.05

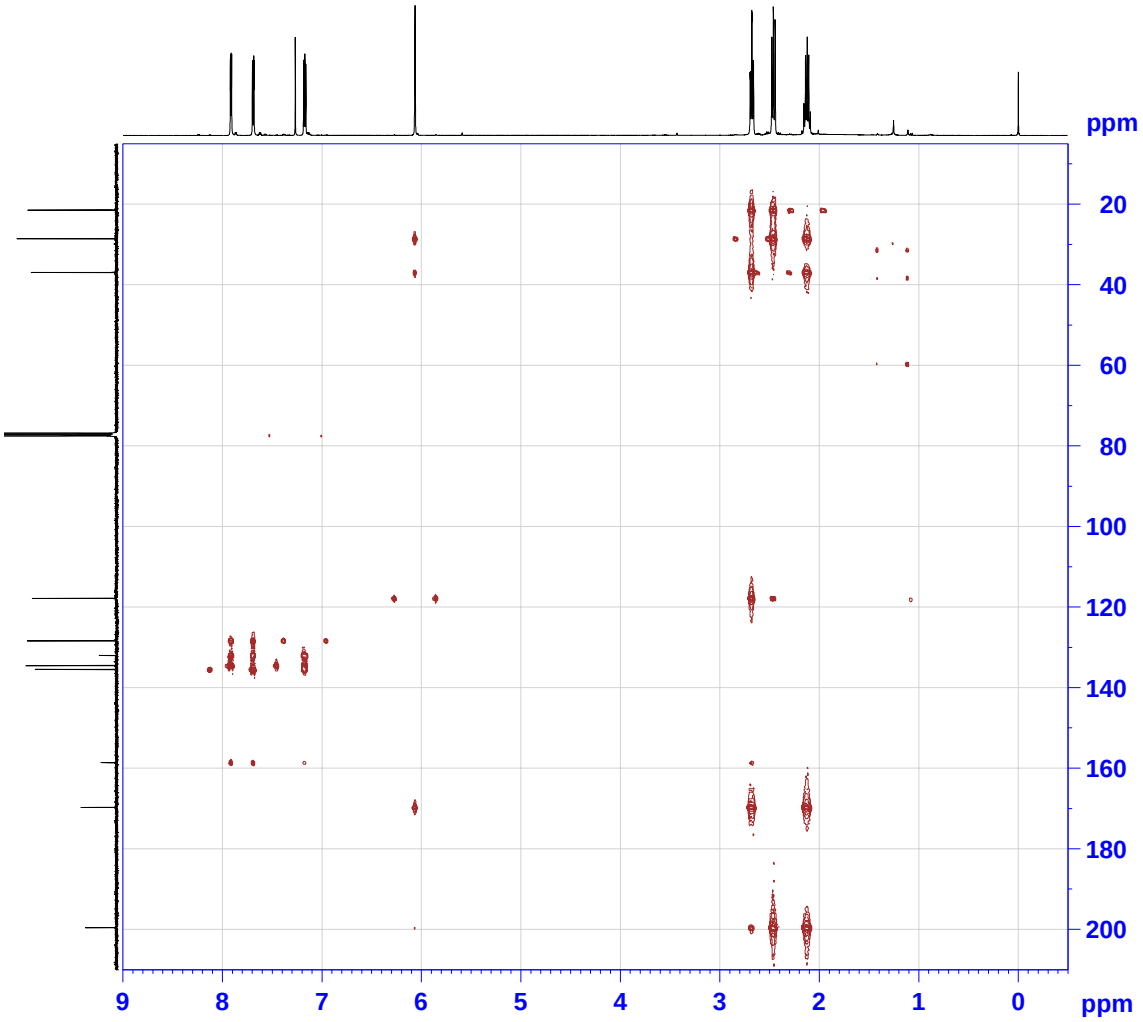
^{13}C **(3)**


199.59
169.75
158.63
135.48
134.54
132.02
128.39
117.85
77.16
36.92
28.54
21.45
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

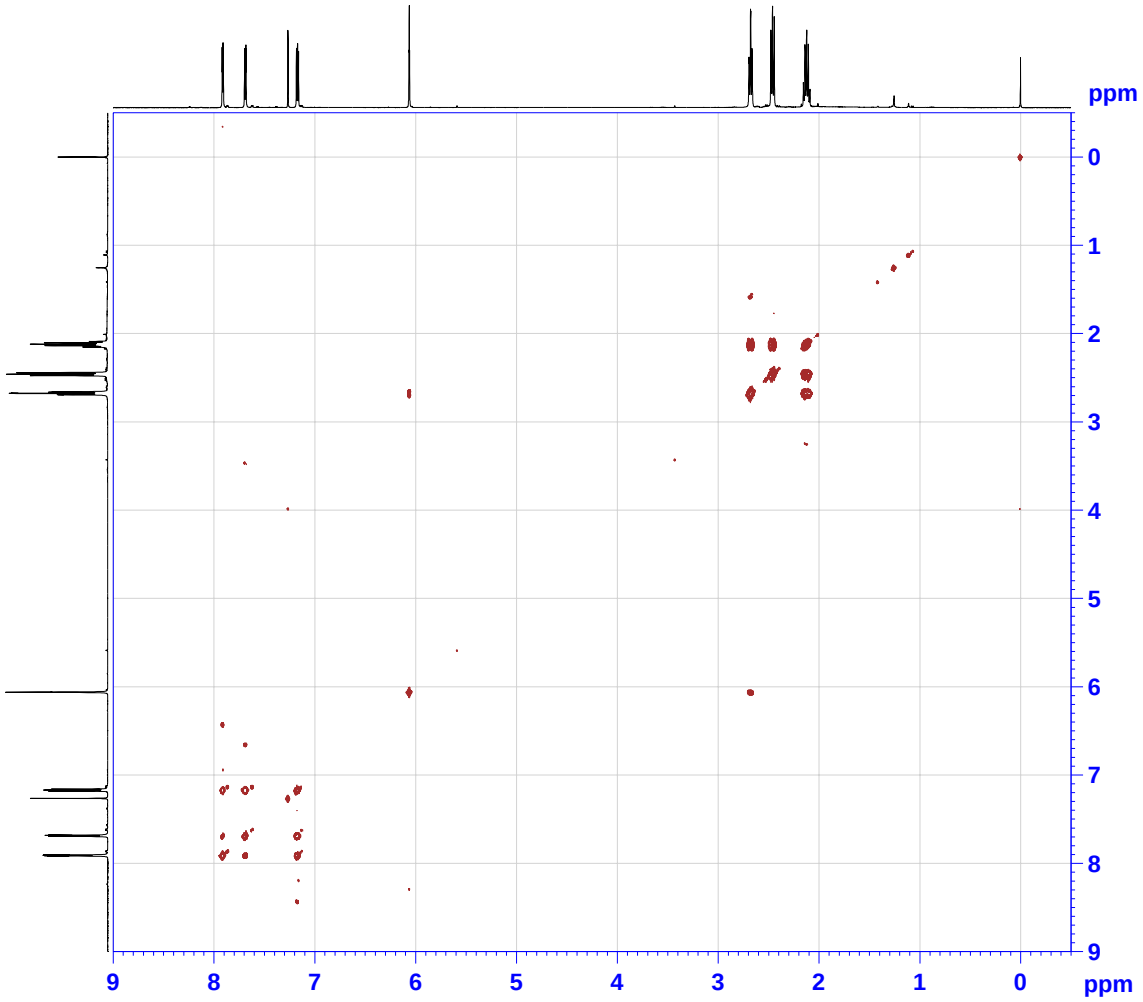
HSQC **(3)**



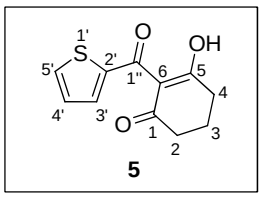
HMBC **(3)**



COSY **(3)**



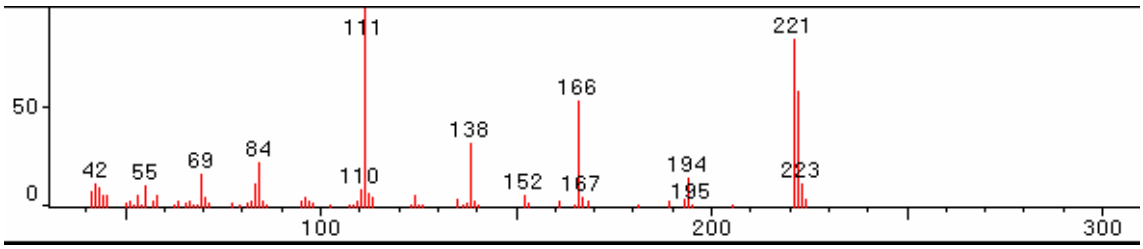
3-hydroxy-2-(2-thienylcarbonyl)cyclohex-2-en-1-one (5): Yellow crystals. Yield 88.5 % (0.6766 g). ^{1}H NMR ($CDCl_3$): δ = 2.05 (quintuplet, J = 6.2 Hz, 2 H, H-3), 2.57 (t, J = 6.2 Hz, 2 H, H-2), 2.72 (t, J = 6.2 Hz, 2 H, H-4), 7.11 (dd, J = 5.0 and 4.0 Hz, 1 H, H-4´), 7.70 (dd, J = 5.0 and 1.1 Hz, 1 H, H-5´), 8.08 (dd, J = 4.0 and 1.1 Hz, 1 H, H-3´), 17.28 (s, 1H, OH-5) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.02 (C-3), 32.97 (C-4), 38.45 (C-2), 112.78 (C-6), 127.63 (C-4´), 135.49 (C-5´), 136.38 (C-3´), 141.07 (C-2´), 187.37 (C-1´´), 194.48 (C-1), 196.44 (C-5) ppm. IR (KBr): $\tilde{\nu}$ = 3092, 2952, 2925, 2861, 1666, 1555, 1406, 1351, 1255, 721 cm^{-1}. MS: *m/z* (%) = 223 (12), 222 [M]$^{+}$ (62), 221 (89), 194 (15), 166 (57), 138 (31), 111 (100), 84 (19), 83 (11), 69 (16), 42 (11).



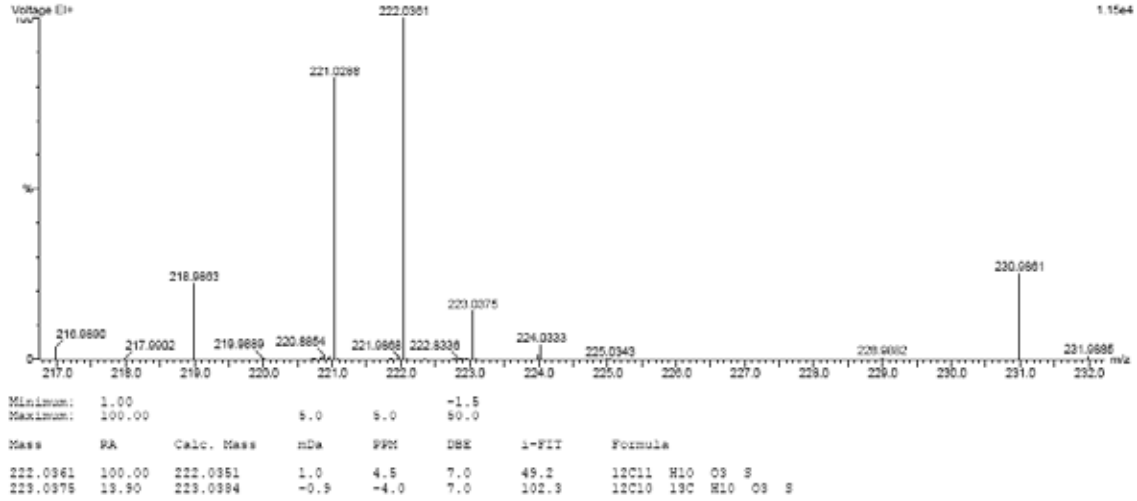
5

Carbon Number	δH (ppm) (*J* in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.70, dd (5.0, 1.1), 1 H	135.49	3', 4'	2', 3', 4'	
4'	7.11, dd (5.0, 4.0), 1 H	127.63	3', 5'	2', 3', 5'	
3'	8.08, dd (4.0, 1.1), 1 H	136.38	4', 5'	1'', 2', 4', 5'	
2'		141.07			
1''		187.37			
6		112.78			
1		194.48			
2	2.57, t (6.2), 2 H	38.45	3, 4	1, 3, 4	
3	2.05, quintuplet (6.2), 2 H	19.02	2, 4	1, 3, 4, 5	
4	2.72, t (6.2), 2 H	32.97	2, 3	2, 3, 5, 6	
5 (OH)	17.28, s, 1 H (OH)	196.44			

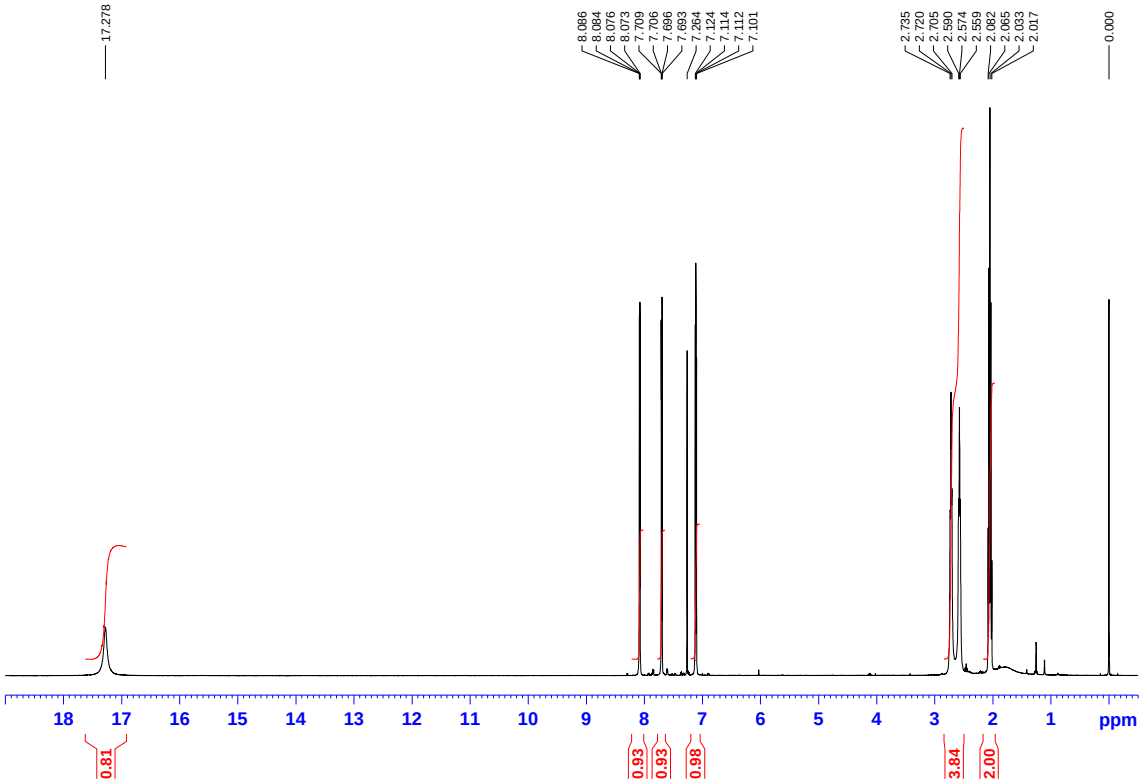
MS **(5)**

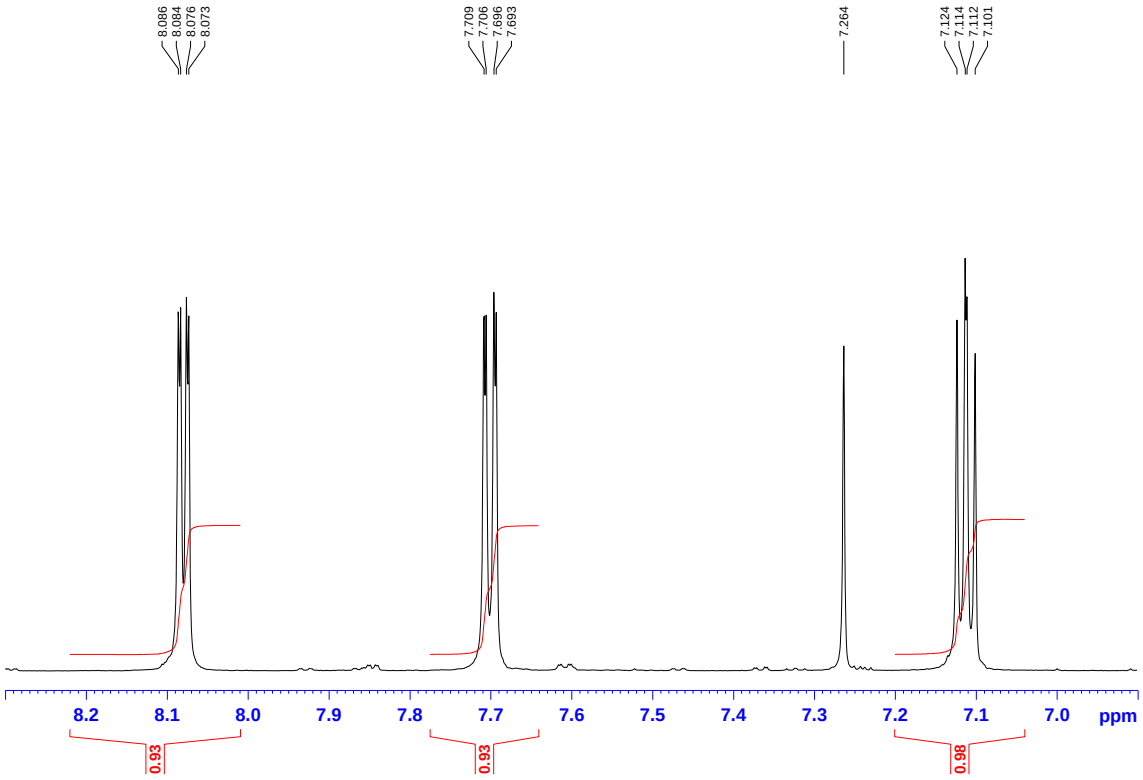


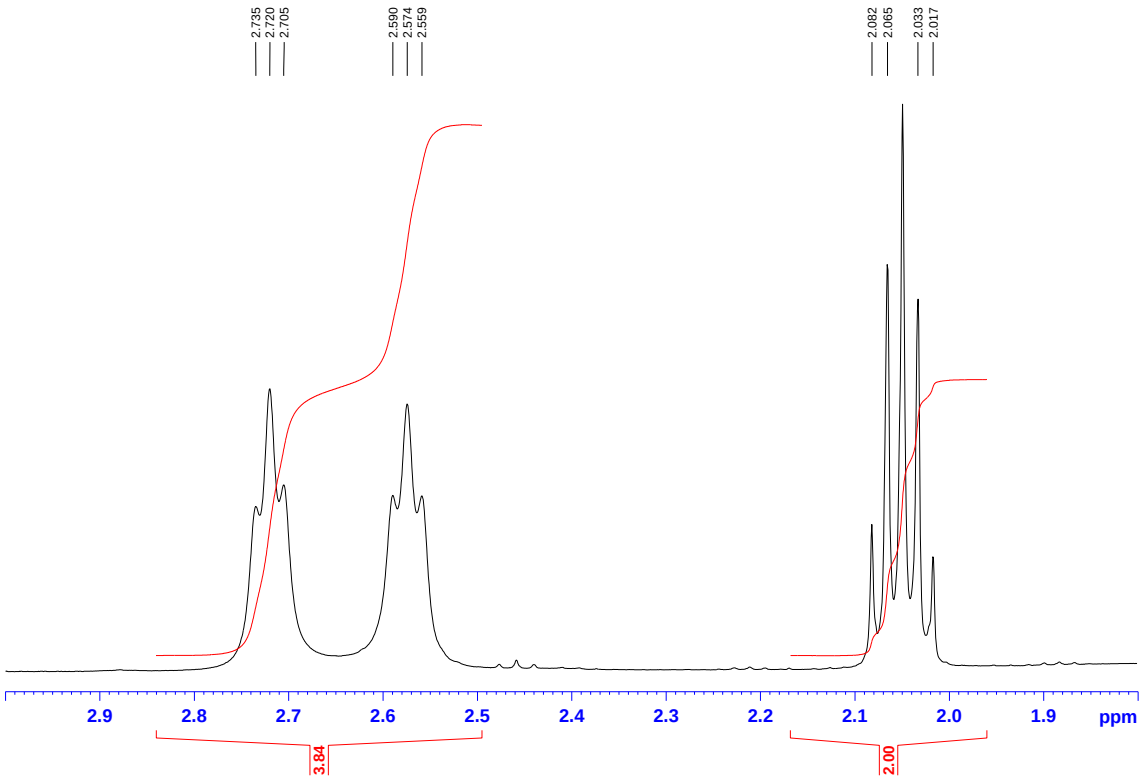
HRMS **(5)**


Voltage EI+
1.15e4
%
222.0361
221.0288
218.9803
230.0661
220.0375
216.0800
217.0002
219.9889
220.8854
221.0868
222.8336
224.0333
225.0343
228.9882
231.0886
m/z
Minimum: 1.00 -1.5
Maximum: 100.00 5.0 5.0 50.0
Mass RA Calc. Mass mDa PPM DBE i-FIT Formula
222.0361 100.00 222.0351 1.0 4.5 7.0 49.2 12C11 H10 O3 S
223.0375 13.90 223.0394 -0.9 -4.0 7.0 102.3 12C10 13C H10 O3 S

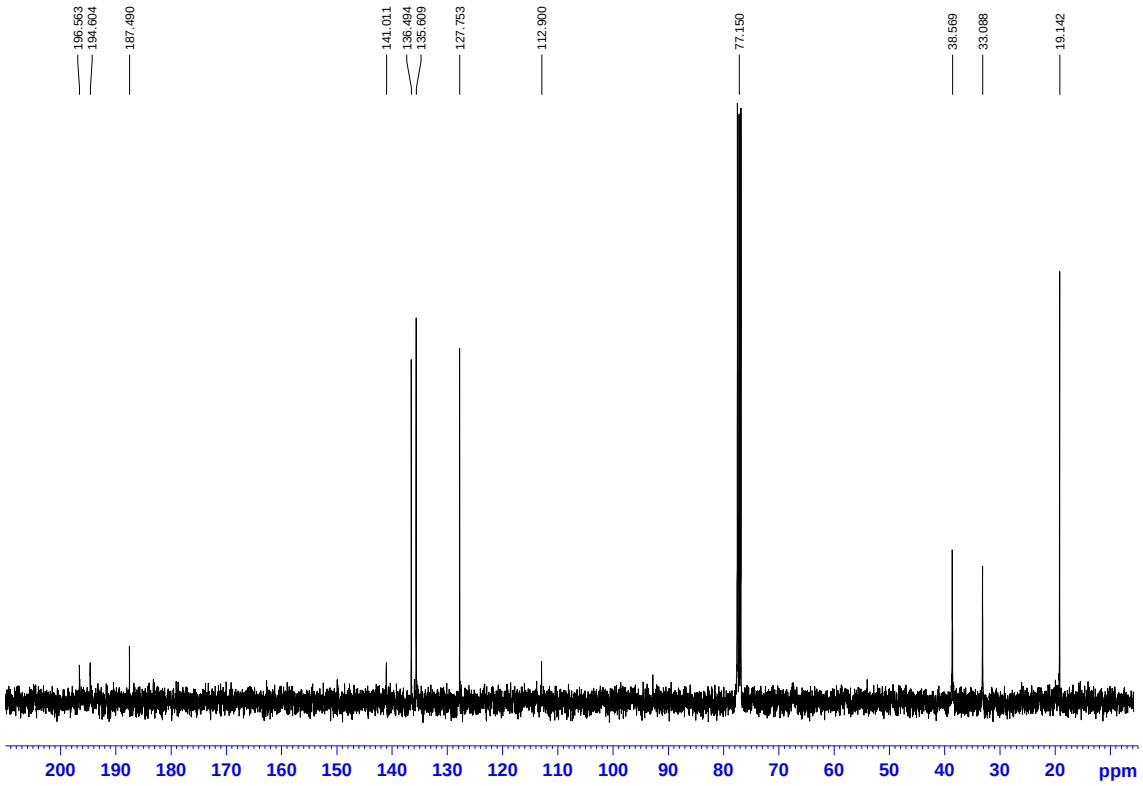
^{1}H **(5)**


17.278
8.086
8.084
8.076
8.073
7.709
7.706
7.696
7.693
7.264
7.124
7.114
7.112
7.101
2.735
2.720
2.705
2.590
2.574
2.559
2.082
2.065
2.033
2.017
0.000
18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.81
0.93
0.93
0.98
3.84
2.00

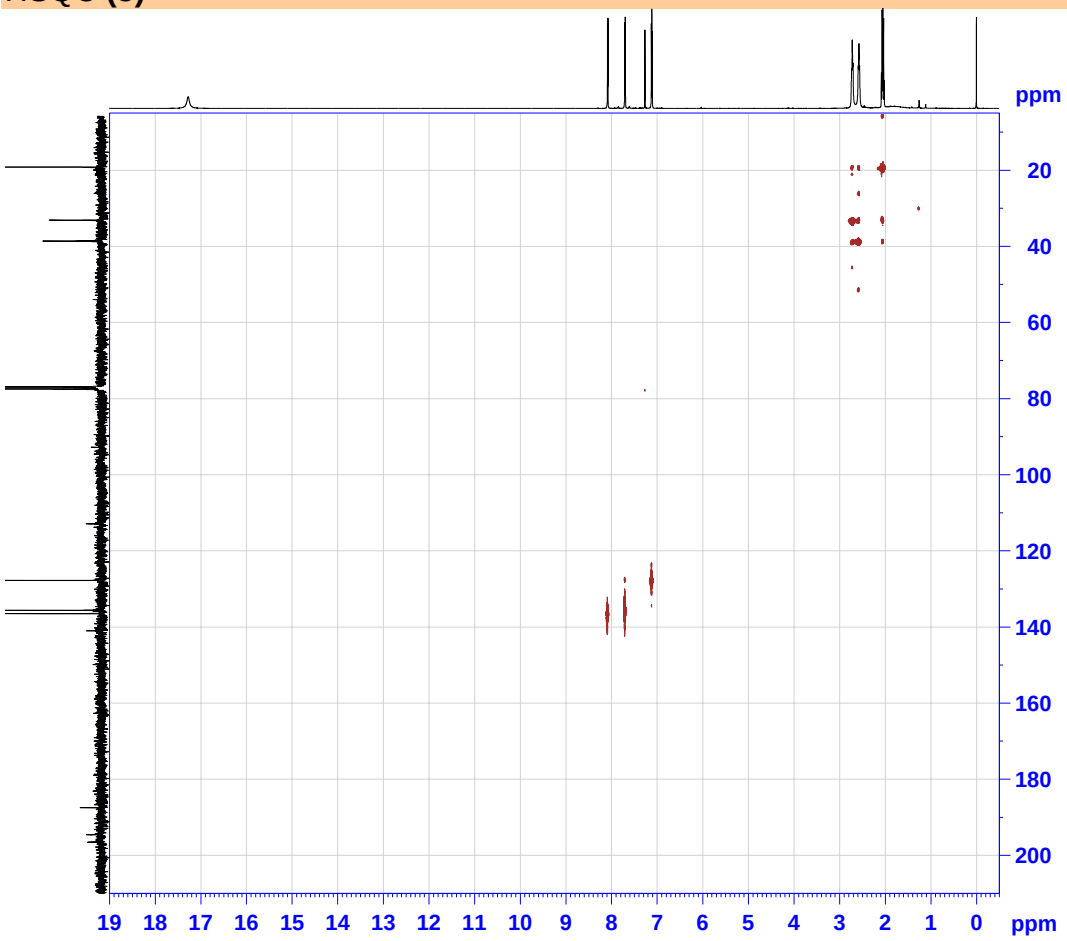

8.086
8.084
8.076
8.073
7.709
7.706
7.696
7.693
7.264
7.124
7.114
7.112
7.101
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
ppm
0.93
0.93
0.98


2.735
2.720
2.705
2.590
2.574
2.559
2.082
2.065
2.033
2.017
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
ppm
3.84
2.00

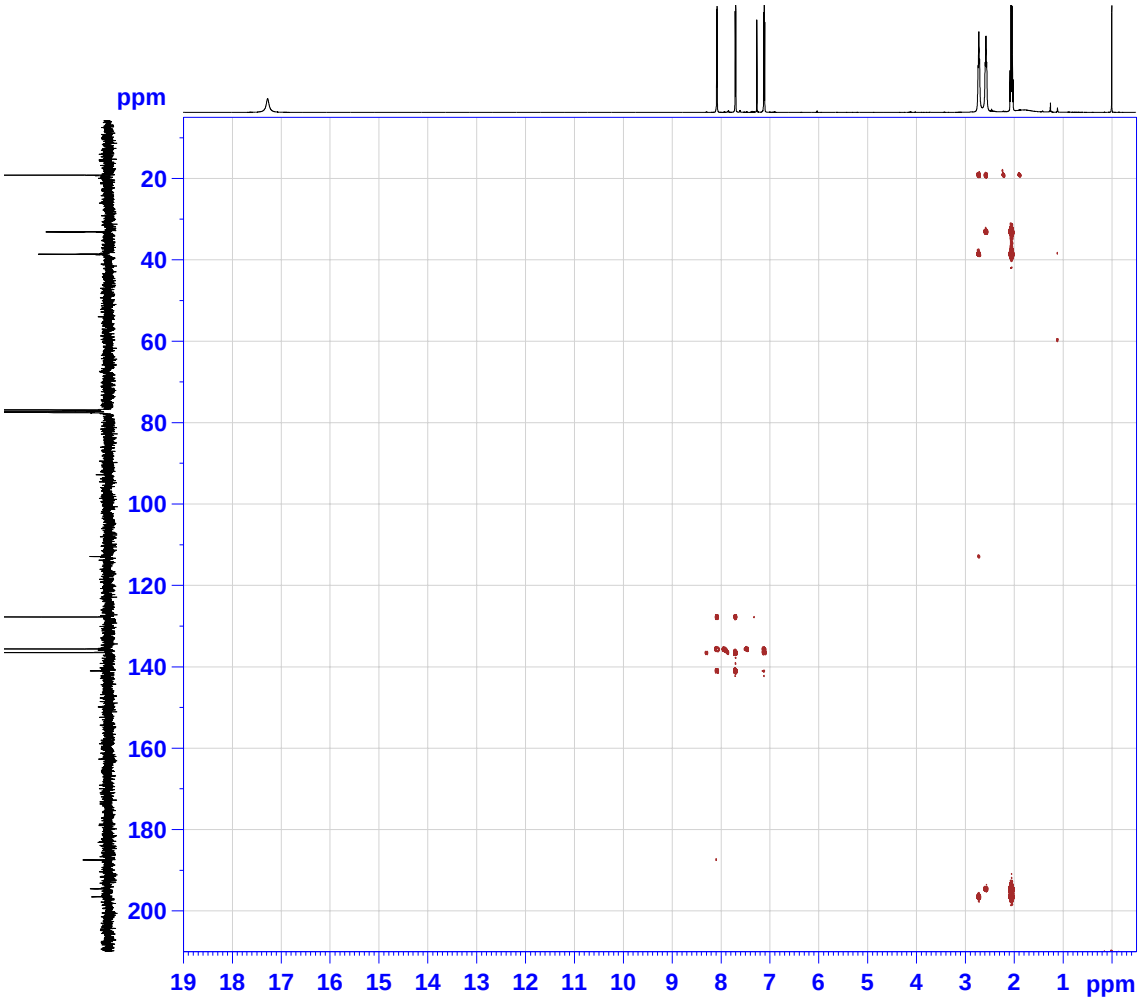
^{13}C **(5)**


196.563
194.604
187.490
141.011
136.494
135.609
127.753
112.900
77.150
38.569
33.088
19.142
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

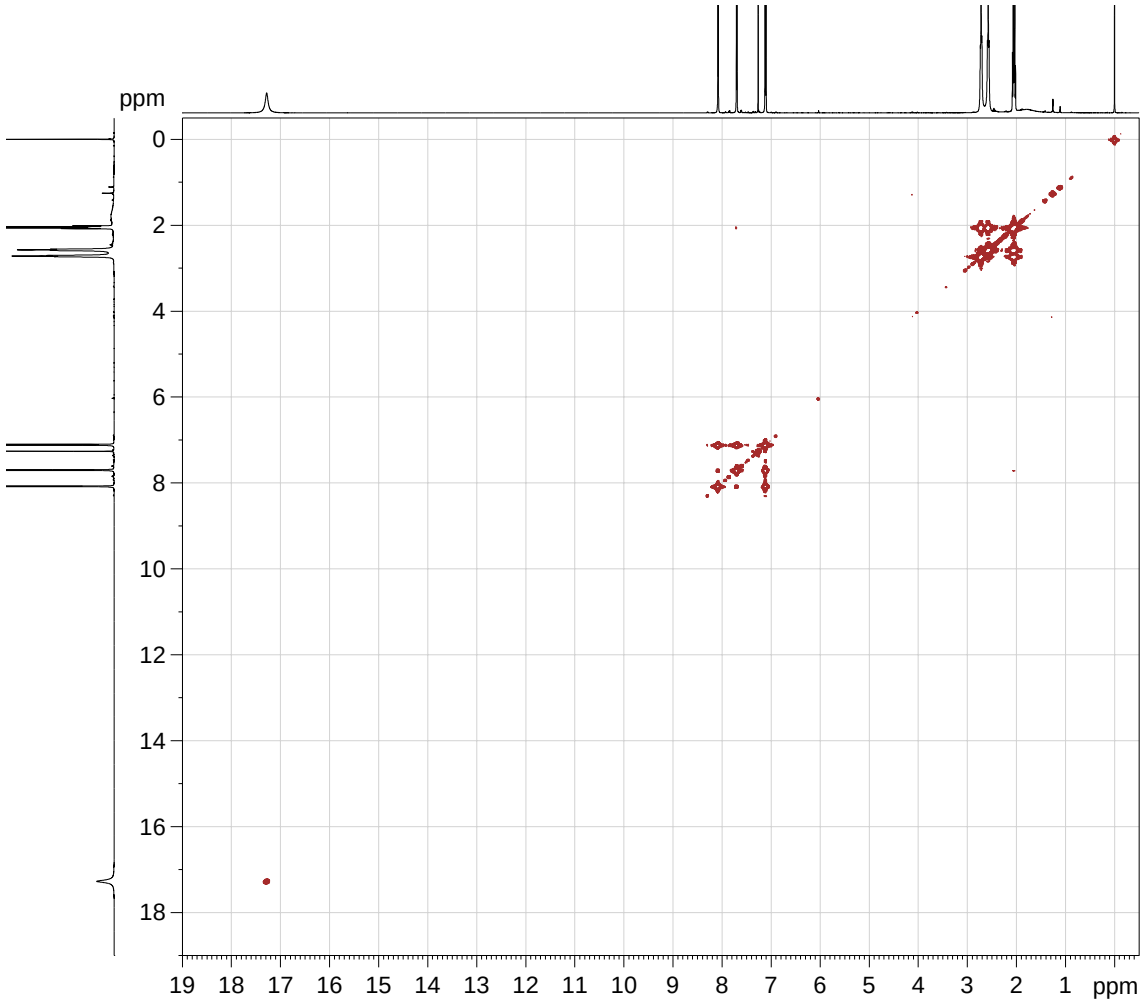
HSQC **(5)**


ppm
20
40
60
80
100
120
140
160
180
200
19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm

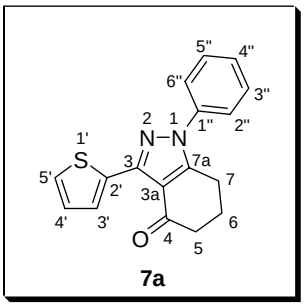
HMBC **(5)**


ppm
20
40
60
80
100
120
140
160
180
200
19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm

COSY **(5)**


ppm
0
2
4
6
8
10
12
14
16
18
19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm

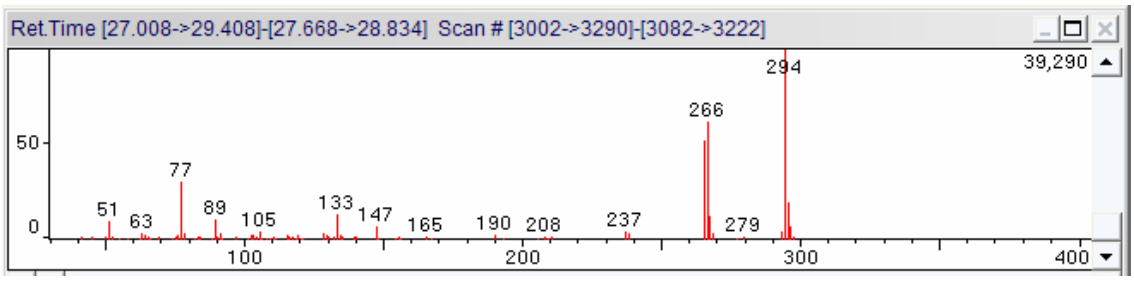
1-phenyl-3-(2-thienyl)-1,5,6,7-tetrahydro-4*H*-indazol-4-one (7a): Pale yellow solid, m.p. 146.8–147.5 ºC. Yield 87.0 % (0.3674 g) ^{1}H NMR ($CDCl_3$): δ = 2.17 (quintuplet, J = 6.2 Hz, 2 H, H-6), 2.63 (t, J = 6.2 Hz, 2 H, H-5), 2.97 (t, J = 6.2 Hz, 2 H, H-7), 7.12 (dd, J = 5.0 and 3.7 Hz, 1 H, H-4´), 7.33 (dd, J = 5.0 and 1.0 Hz, 1 H, H-5´), 7.43 (tt, J = 7.0 and 1.7 Hz, 1 H, H-4´´), 7.52–7.59 (m, 2 H, H-2´´,6´´), 7.52–7.59 (m, 2 H, H-3´´,5´´), 8.49 (dd, J = 3.7 and 1.0 Hz, 1 H, H-3´) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.23 (C-6), 23.82 (C-7), 38.98 (C-5), 116.18 (C-3a), 124.19 (C-3´´,5´´), 126.55 (C-5´), 127.62 (C-4´), 128.43 (C-4´´), 129.41 (C-2´´,6´´), 129.91 (C-3´), 134.44 (C-2´), 138.41 (C-1´´), 146.49 (C-3), 150.78 (C-7a), 192.65 (C-4) ppm. IR (KBr): ν = 3092, 3071, 2941, 2923, 2846, 1665, 1497, 1468, 948, 698 cm^{-1}. MS: *m/z* (%) = 295 (20), 294 [M]$^{+}$ (100), 267 (12), 266 (61), 265 (52), 133 (13), 89 (10), 77 (30), 51 (9).



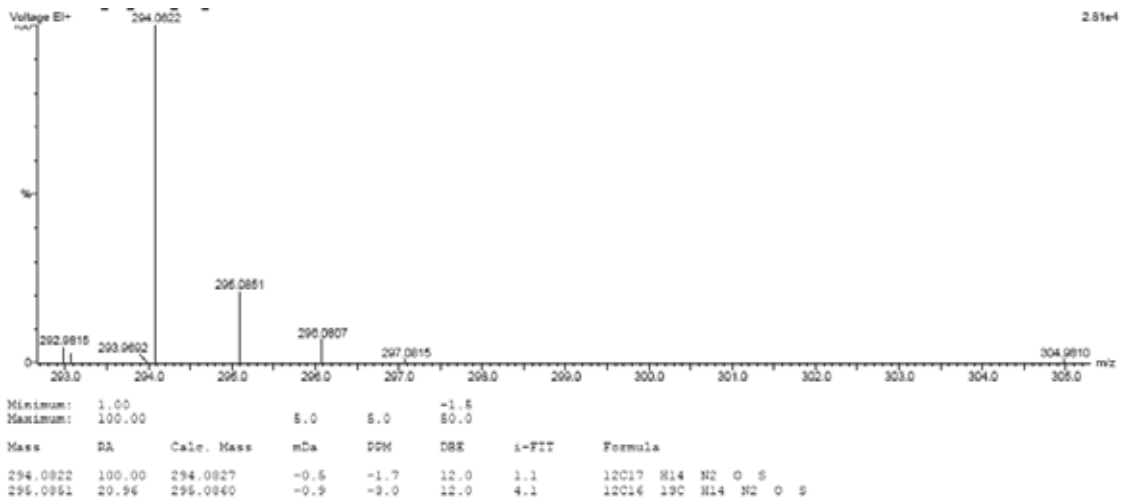
7a

Carbon Number	δH (ppm) (*J* in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.33, dd (5.0, 1.0), 1 H	126.55	3', 4'	2', 3', 4'	
4'	7.12, dd (5.0, 3.7), 1 H	127.62	3', 5'	2', 3', 5'	
3'	8.49, dd (3.7, 1.0), 1 H	129.91	4', 5'	2', 4', 5', 3	
2'		134.44			
3		146.49			
3a		116.18			
4		192.65			
5	2.63, t (6.2), 2 H	38.98	6, 7	3a, 4, 6, 7	
6	2.17, quintuplet (6.2), 2 H	23.23	5, 7	4, 5, 7, 7a	
7	2.97, t (6.2), 2 H	23.82	5, 6	3a, 5, 6, 7a	2'', 6''
7a		150.78			
1''		138.41			
2''/6''	7.52-7.59, m, 2 H	129.41	3'', 4'', 5''	1'', 3'', 4'', 5''	7
3''/5''	7.52-7.59, m, 2 H	124.19	2'', 4'', 6''	1'', 2'', 4'', 6''	
4''	7.43, tt (7.0,1.7), 2 H	128.43	3'', 5''	2'', 3'', 5'', 6''	

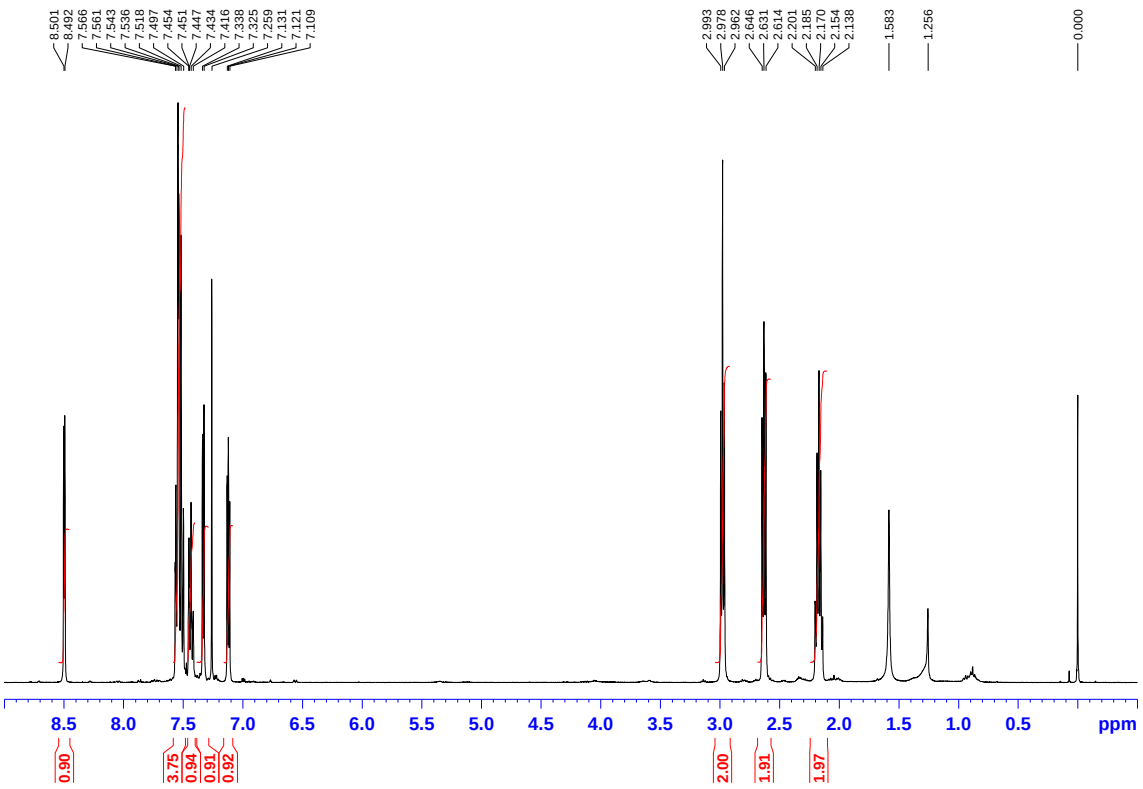
MS **(7a)**

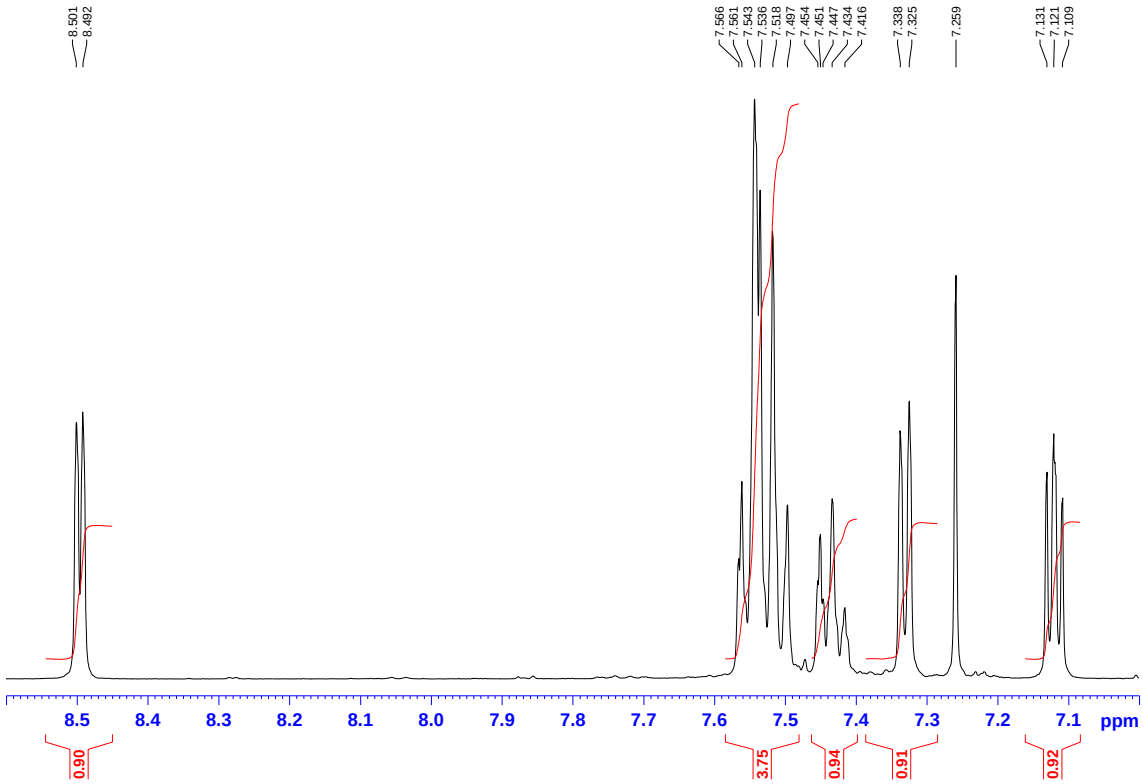


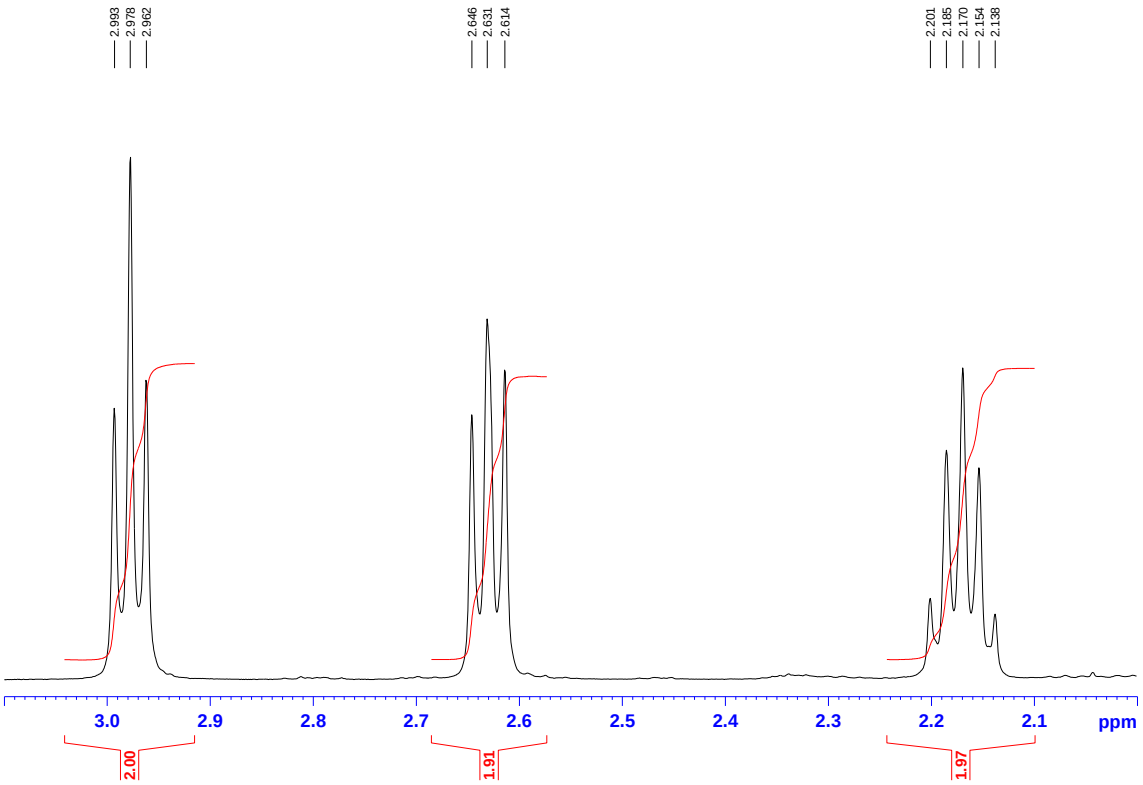
HRMS **(7a)**


Voltage El+
294.0822
2.81e4
296.0851
296.0807
292.9815
293.9802
297.0815
304.9810
m/z
Minimum: 1.00
Maximum: 100.00 5.0 5.0 50.0
Mass PA Calc. Mass mDa PPM DBE i-FIT Formula
294.0822 100.00 294.0827 -0.5 -1.7 12.0 1.1 12C17 H14 N2 O S
296.0851 20.96 296.0860 -0.9 -3.0 12.0 4.1 12C16 13C H14 N2 O S

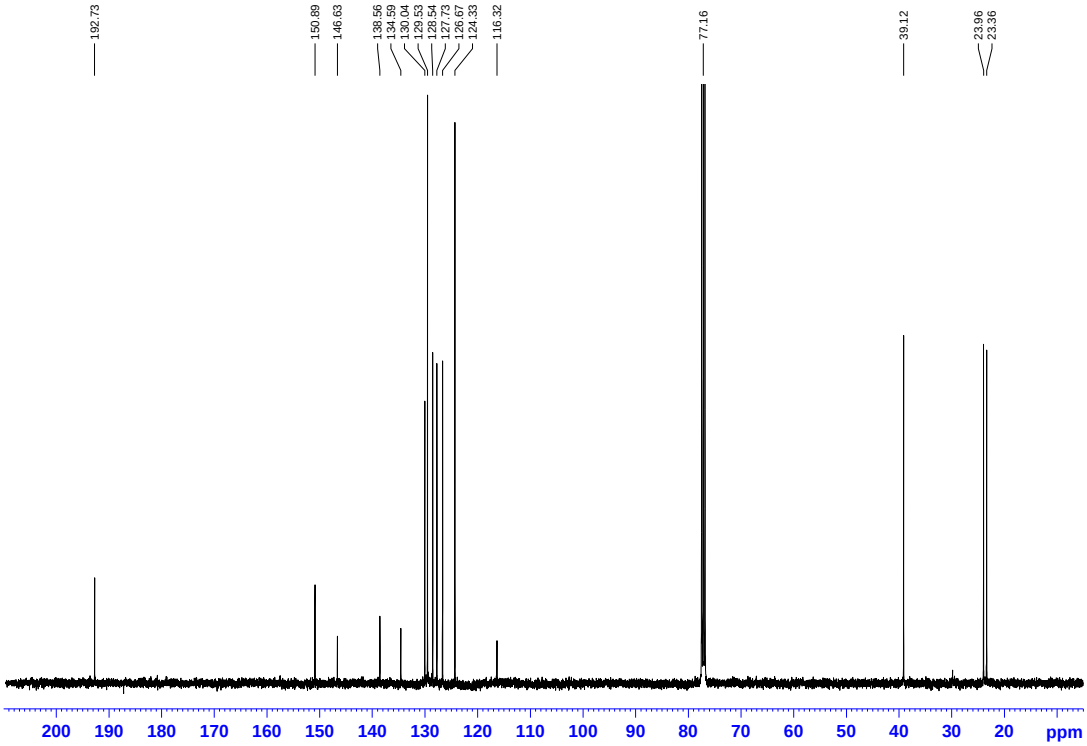
^{1}H **(7a)**


8.501
8.492
7.566
7.561
7.543
7.536
7.518
7.497
7.454
7.451
7.447
7.434
7.416
7.338
7.325
7.259
7.131
7.121
7.109
2.993
2.978
2.962
2.646
2.631
2.614
2.201
2.185
2.170
2.154
2.138
1.583
1.256
0.000
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 ppm
0.90
3.75
0.94
0.91
0.92
2.00
1.91
1.97

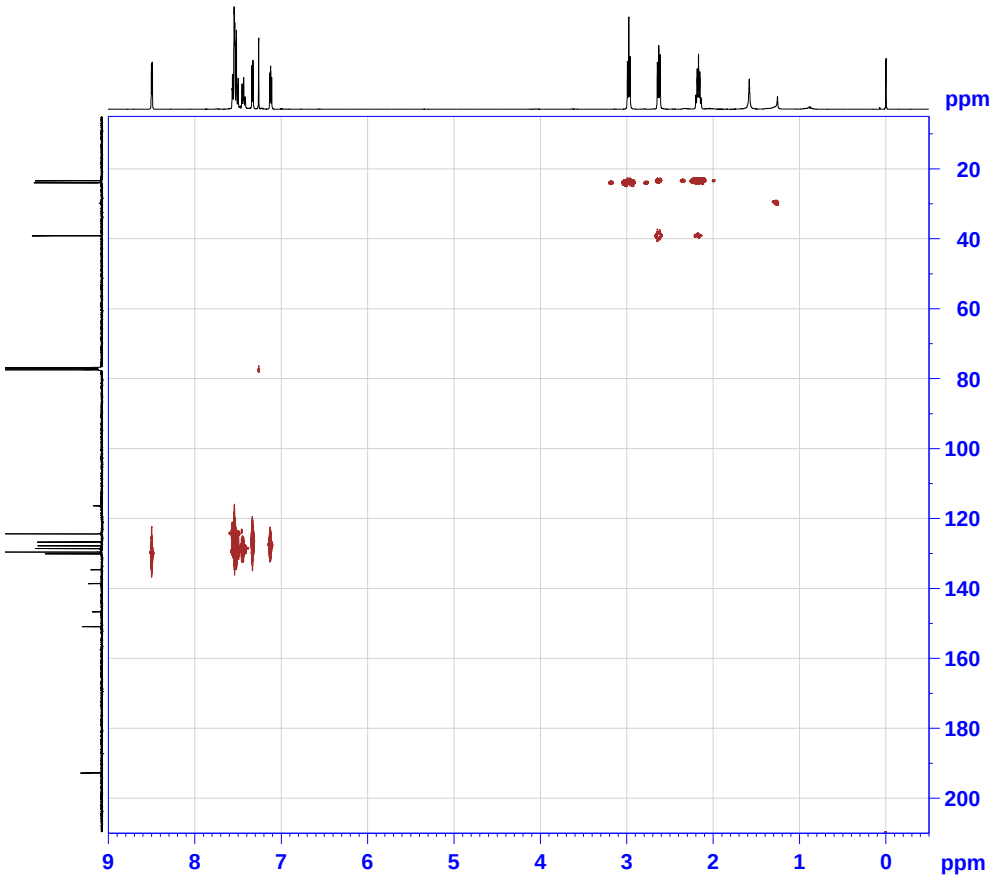

8.501
8.492
7.566
7.561
7.543
7.536
7.518
7.497
7.454
7.451
7.447
7.434
7.416
7.338
7.325
7.259
7.131
7.121
7.109
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
ppm
0.90
3.75
0.94
0.91
0.92


2.993
2.978
2.962
2.646
2.631
2.614
2.201
2.185
2.170
2.154
2.138
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
ppm
2.00
1.91
1.97

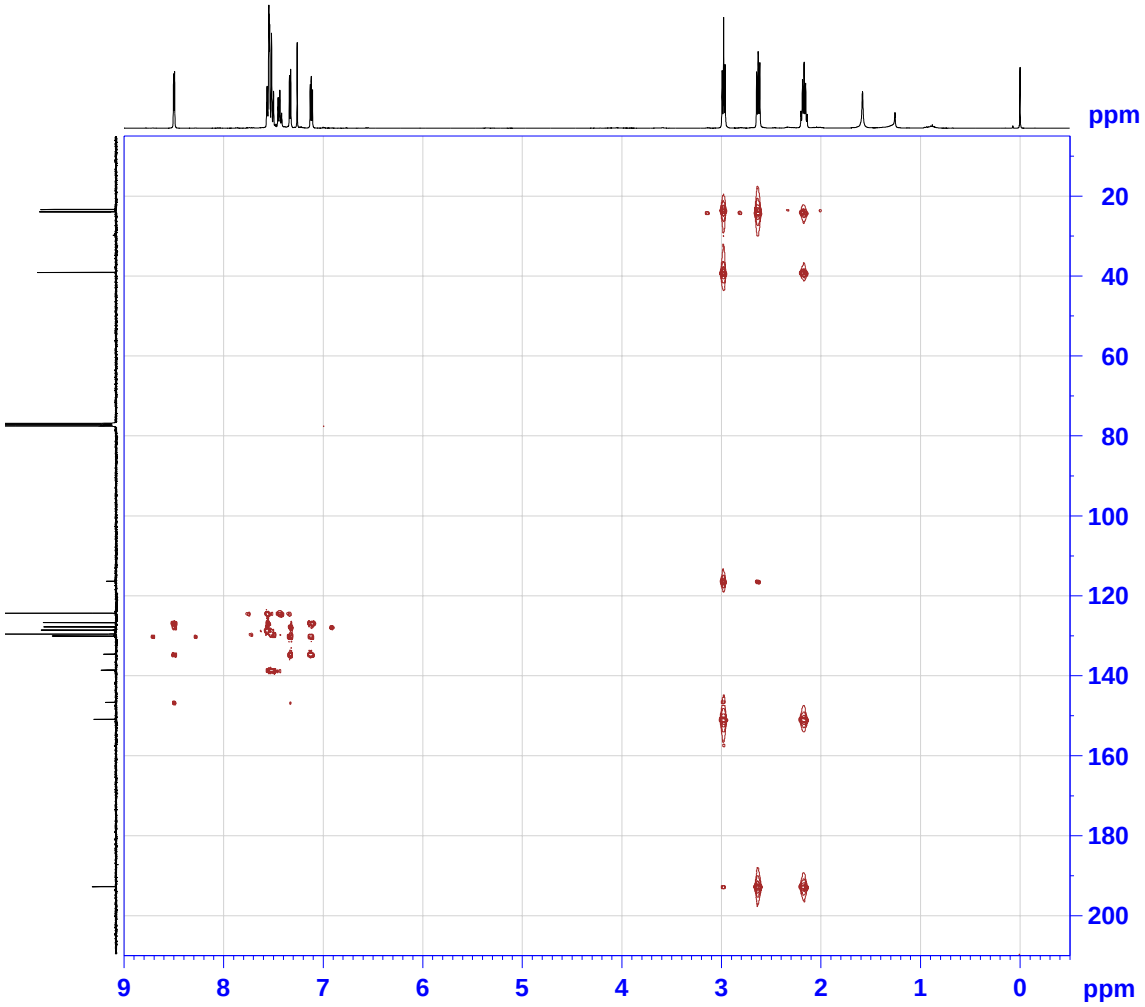
^{13}C **(7a)**



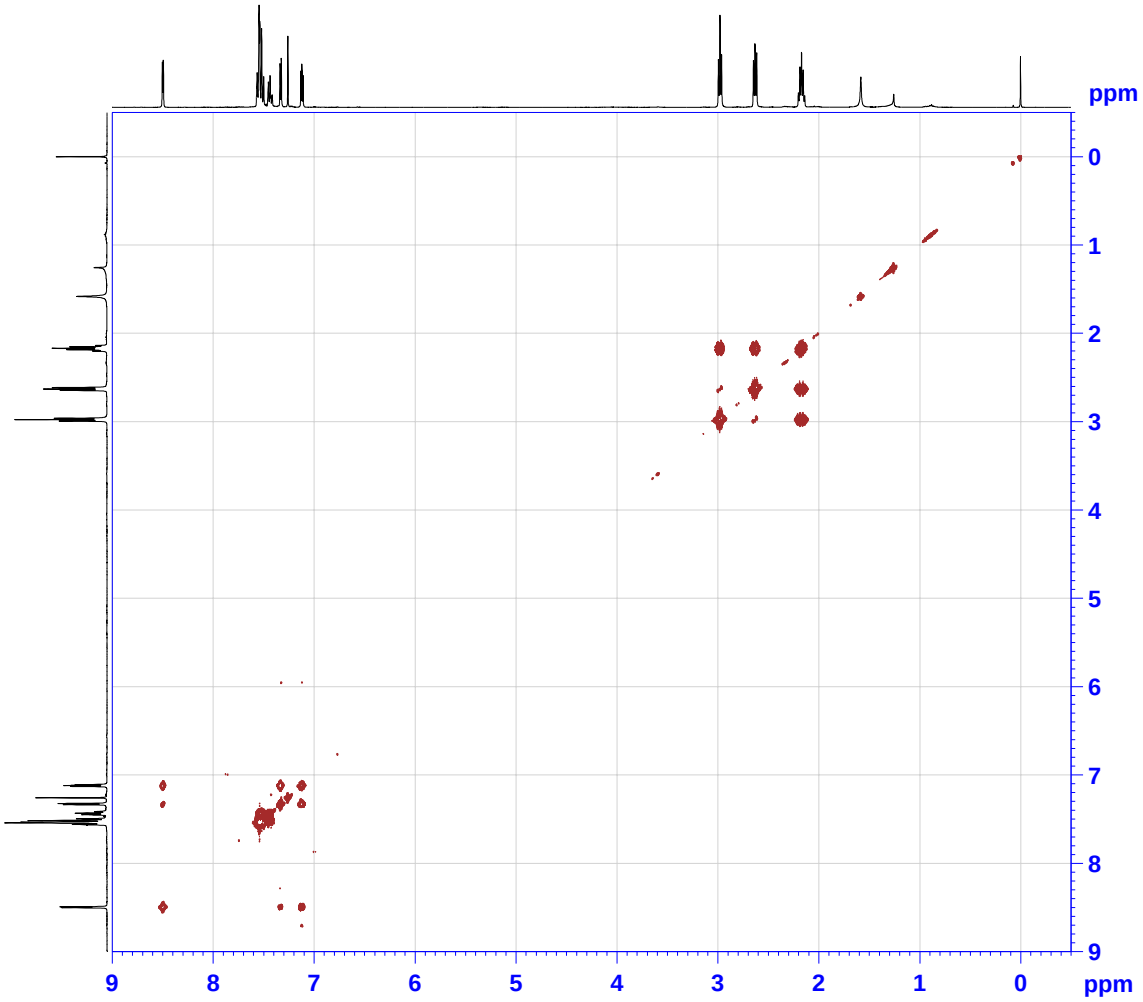
HSQC **(7a)**



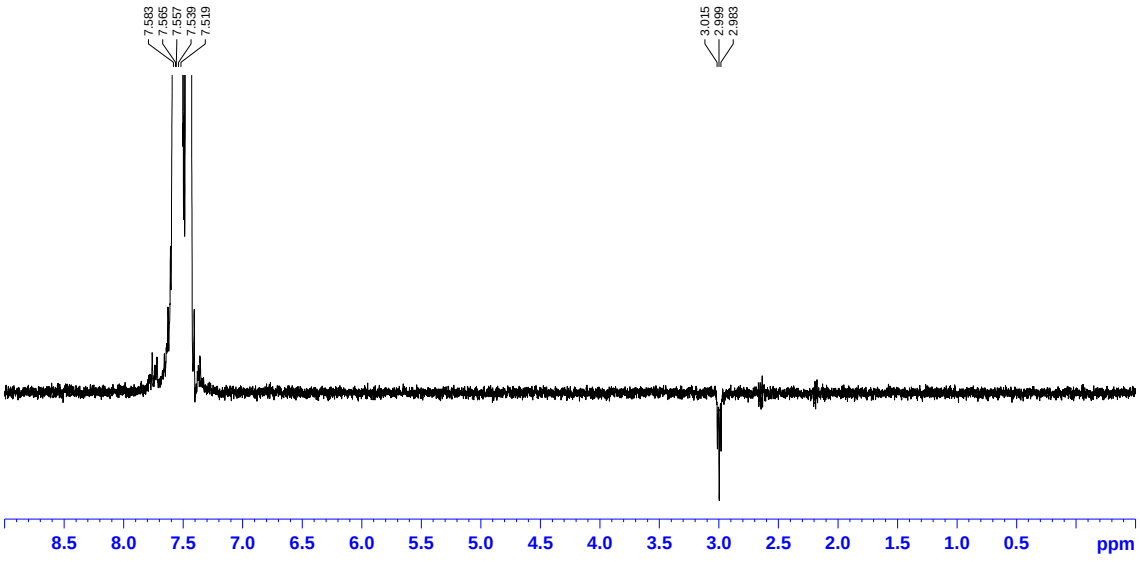
HMBC **(7a)**

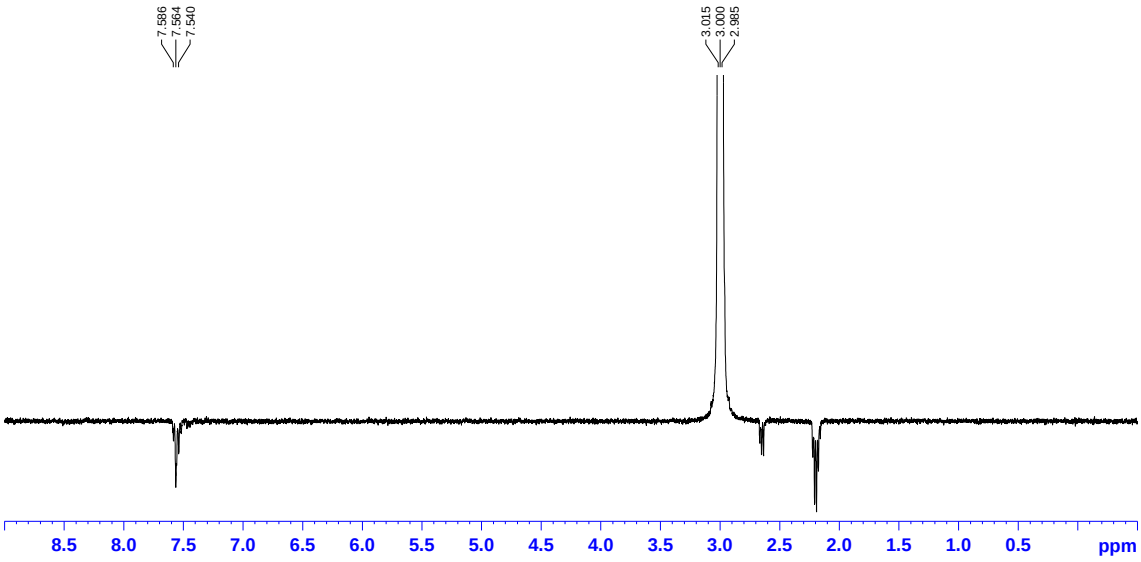


COSY **(7a)**

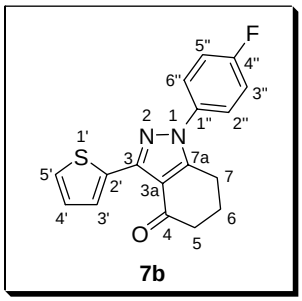


ROESY **(7a)**




7.586
7.564
7.540
3.015
3.000
2.985
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
ppm

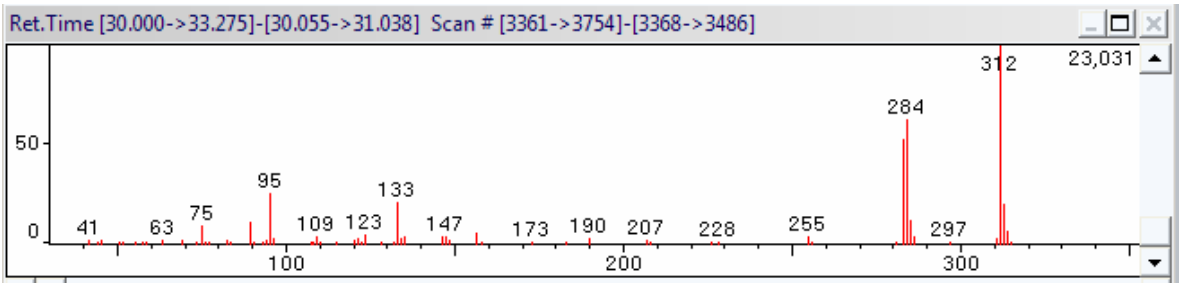
1-(4-fluorophenyl)-3-(2-thienyl)-1,5,6,7-tetrahydro-4*H*-indazol-4-one (7b): Pale yellow solid. Yield 39.4 % (0.0553 g) ^{1}H NMR ($CDCl_3$): δ = 2.17 (quintuplet, J = 6.3 Hz, 2 H, H-6), 2.62 (t, J = 6.3 Hz, 2 H, H-5), 2.93 (t, J = 6.3 Hz, 2 H, H-7), 7.12 (dd, J = 5.1 and 3.7 Hz, 1 H, H-4´), 7.21 (m, 2 H, H-3´´,5´´), 7.33 (dd, J = 5.1 and 1.1 Hz, 1 H, H-5´), 7.52 (m, 2 H, H-2´´,6´´), 8.49 (dd, J = 3.7 and 1.1 Hz, 1 H, H-3´) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.27 (C-6), 23.77 (C-7), 39.03 (C-5), 116.27 (C-3a), 116.50 (J_{CF} = 22.9 Hz, C-3´´,5´´), 126.24 (J_{CF} = 8.8 Hz, C-2´´,6´´), 126.75 (C-5´), 127.77 (C-4´), 130.13 (C-3´), 134.38 (C-2´), 134.64 (J_{CF} = 3.2 Hz, C-1´´), 146.66 (C-3), 150.93 (C-7a), 162.32 (J_{CF} = 248.7 Hz, C-4´´), 192.62 (C-4) ppm. ^{19}F NMR ($CDCl_3$): δ = -112.27 ppm (ddd, J = 12.4, 7.9 and 4.8 Hz, F-4´´) MS: m/z (%) = 313 (20), 312 $[M]^+$ (100), 285 (13), 284 (62), 283 (53), 133 (20), 95 (26), 89 (11), 75 (9).



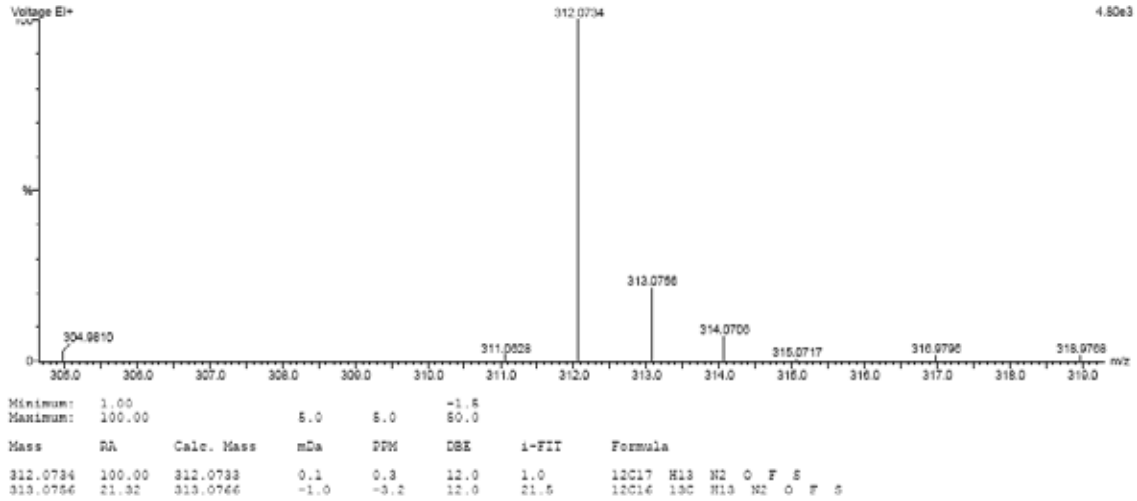
7b

Carbon Number	δH (ppm) (*J* in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.33, dd (5.1, 1.1), 1 H	126.75	3', 4'	2', 3', 4', 3	
4'	7.12, dd (5.1, 3.7), 1 H	127.77	3', 5'	2', 3', 5'	
3'	8.49, dd (3.7, 1.1), 1 H	130.13	4', 5'	2', 4', 5', 3	
2'		134.38			
3		146.66			
3a		116.27			
4		192.62			
5	2.62, t (6.3), 2 H	39.03	6, 7	3a, 4, 6, 7	
6	2.17, quintuplet (6.3), 2 H	23.27	5, 7	4, 5, 7, 7a	
7	2.93, t (6.3), 2 H	23.77	5, 6	3, 3a, 4, 5, 6, 7a	2''
7a		150.93			
1''		134.64 J_{C-F}=3.2 Hz		2'', 3'', 5'', 6''	
2''/6''	7.50-7.54, m, 2 H	126.24 J_{C-F}=8.8 Hz	3'', 5''	1'', 2'', 3'', 4'', 5'', 6''	7
3''/5''	7.18-7.23, m, 2 H	116.50 J_{C-F}=22.9 Hz	2'', 6''	1'', 2'', 3'', 4'', 5'', 6''	
4''		162.32 J_{C-F}=248.7 Hz		2'', 3'', 5'', 6''	
^{19}F	-112.27	J_{C-F}= (12.4, 7.9, 4.8) Hz			

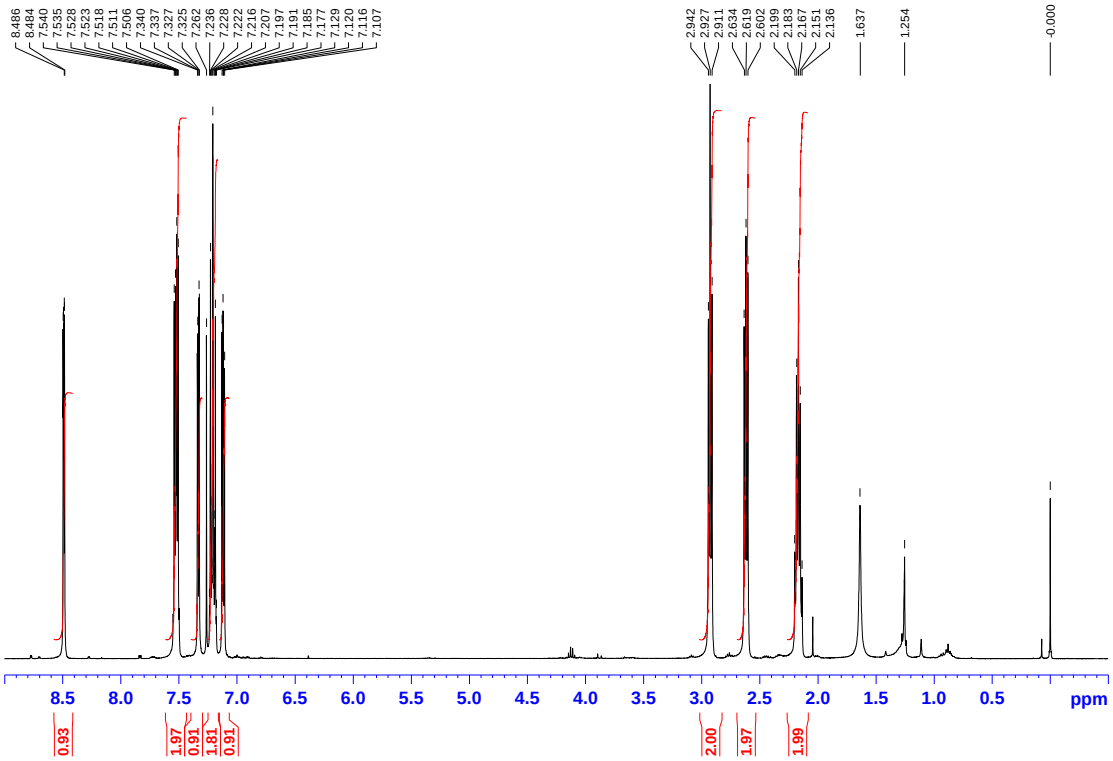
MS **(7b)**

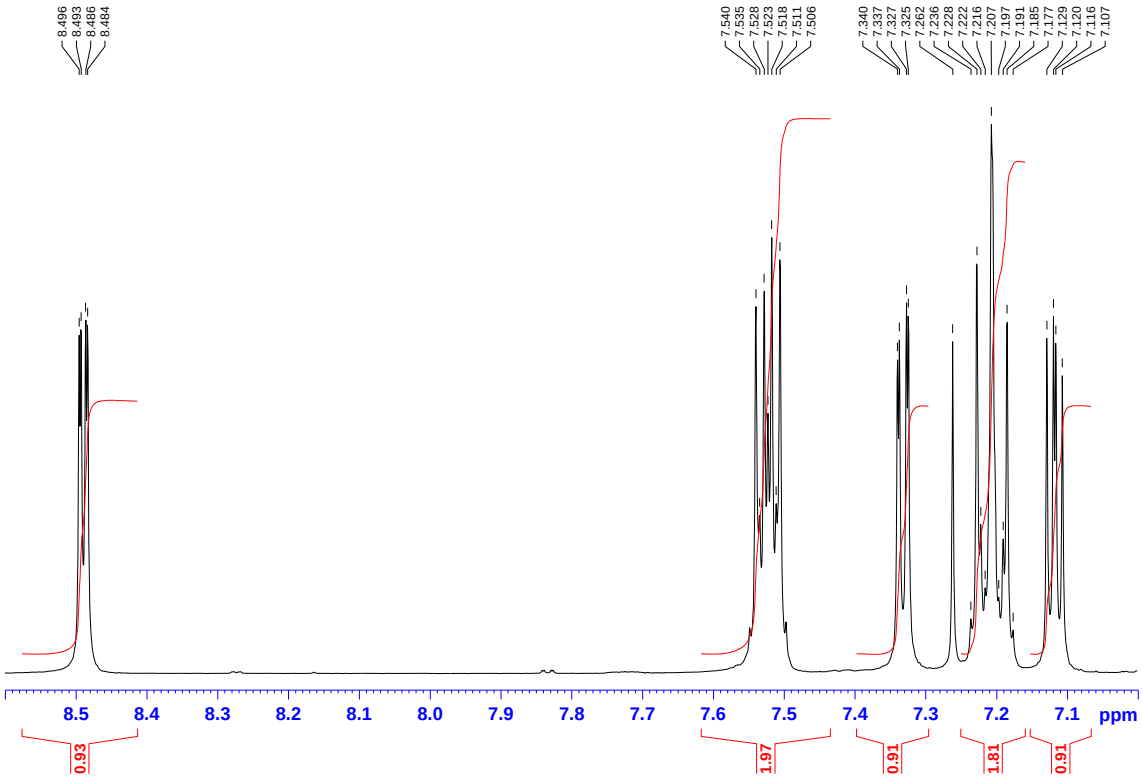


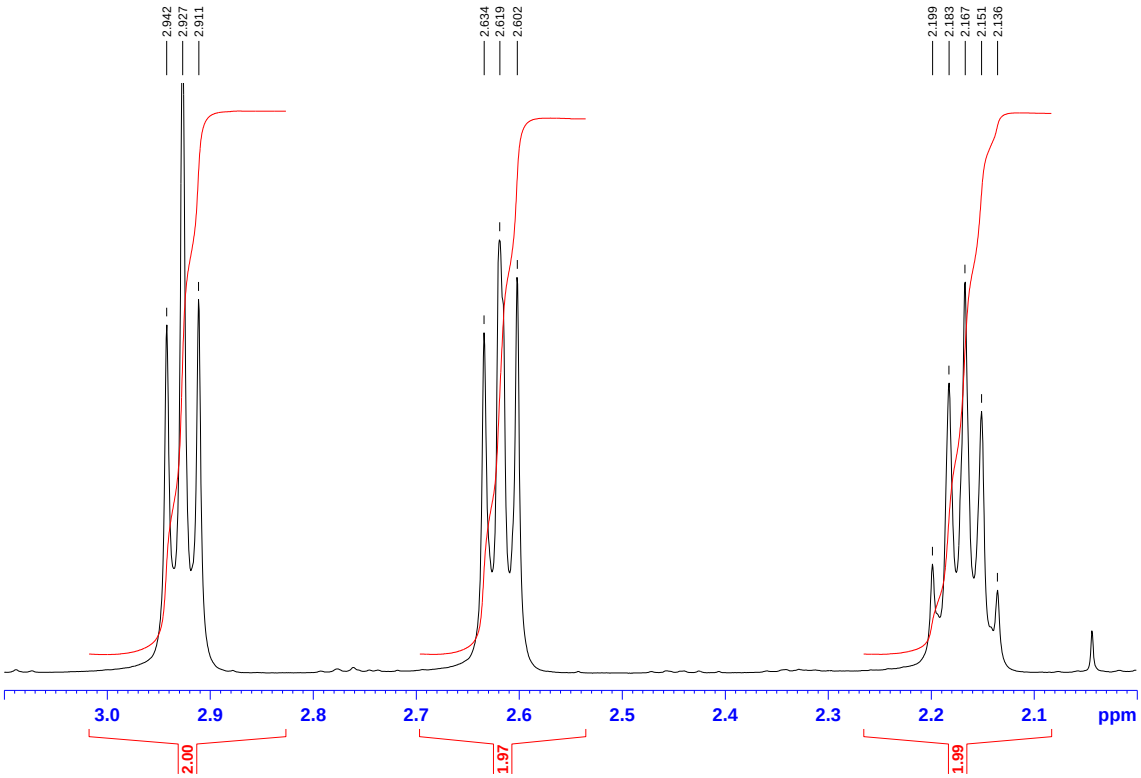
HRMS **(7b)**



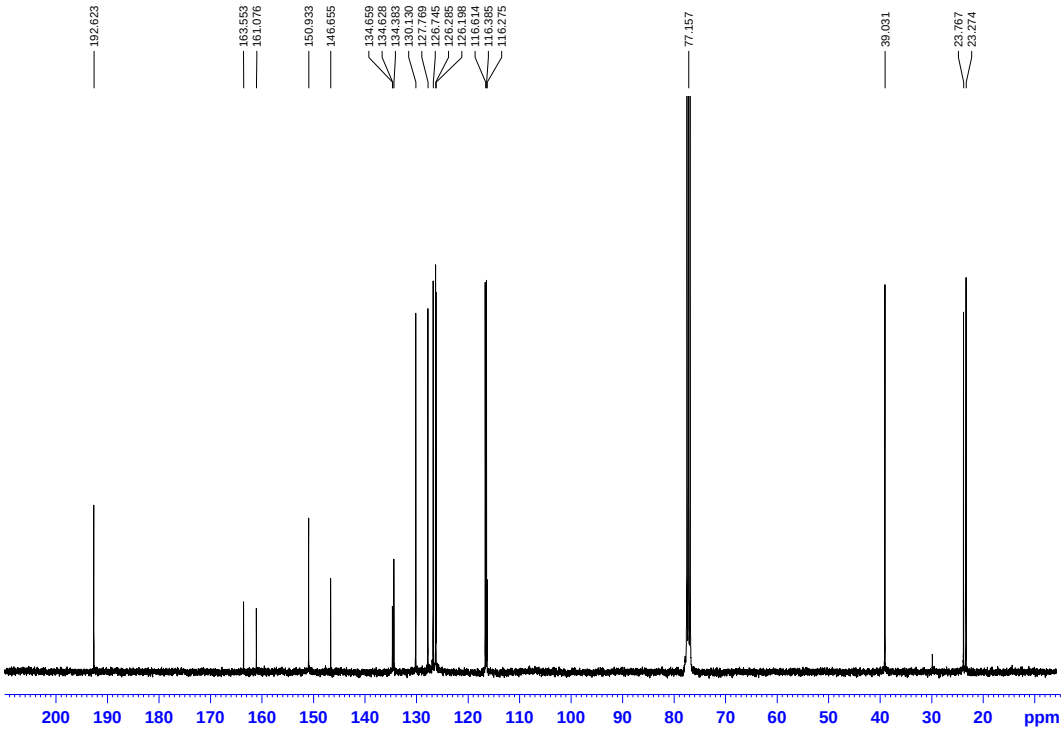
^{1}H **(7b)**



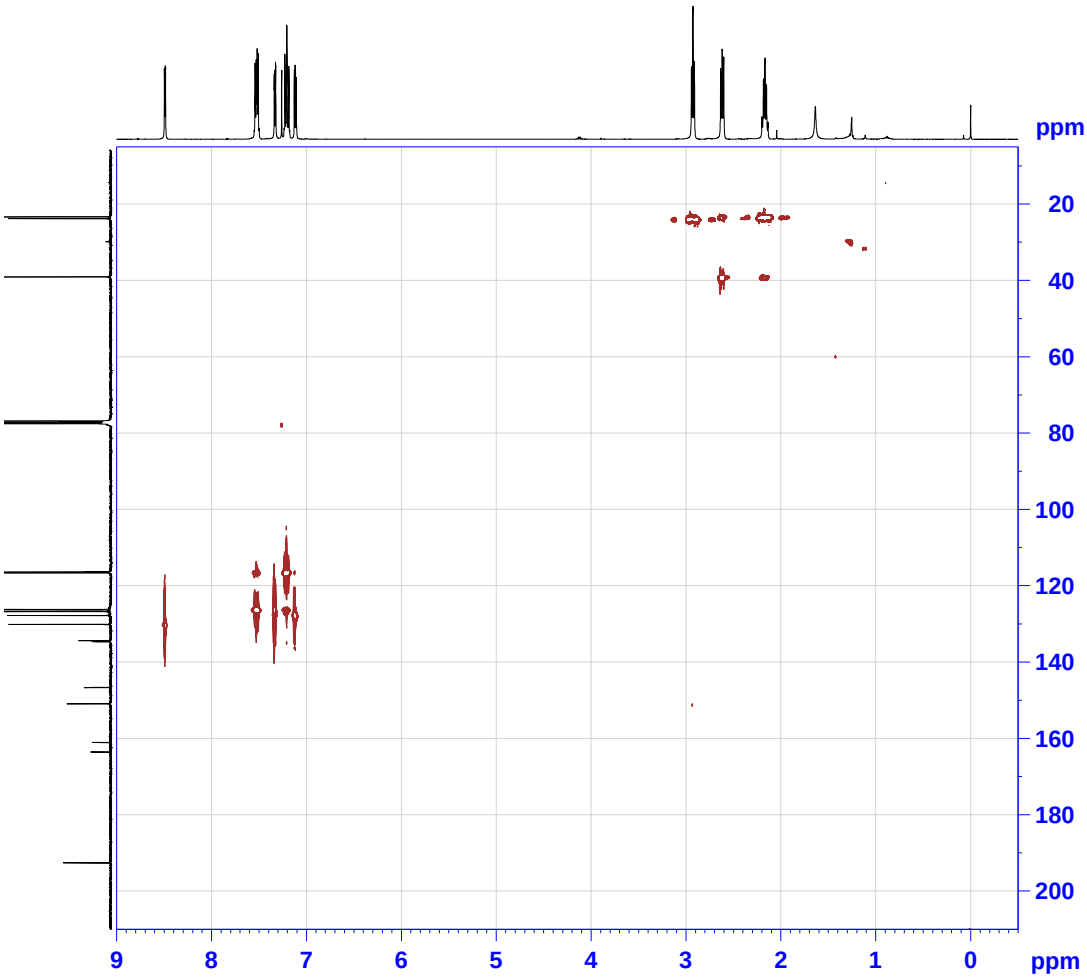

8.496
8.493
8.486
8.484
7.540
7.535
7.528
7.523
7.518
7.511
7.506
7.340
7.337
7.327
7.325
7.262
7.236
7.228
7.222
7.216
7.207
7.197
7.191
7.185
7.177
7.129
7.120
7.116
7.107
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
ppm
0.93
1.97
0.91
1.81
0.91


2.942
2.927
2.911
2.634
2.619
2.602
2.199
2.183
2.167
2.151
2.136
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
ppm
2.00
1.97
1.99

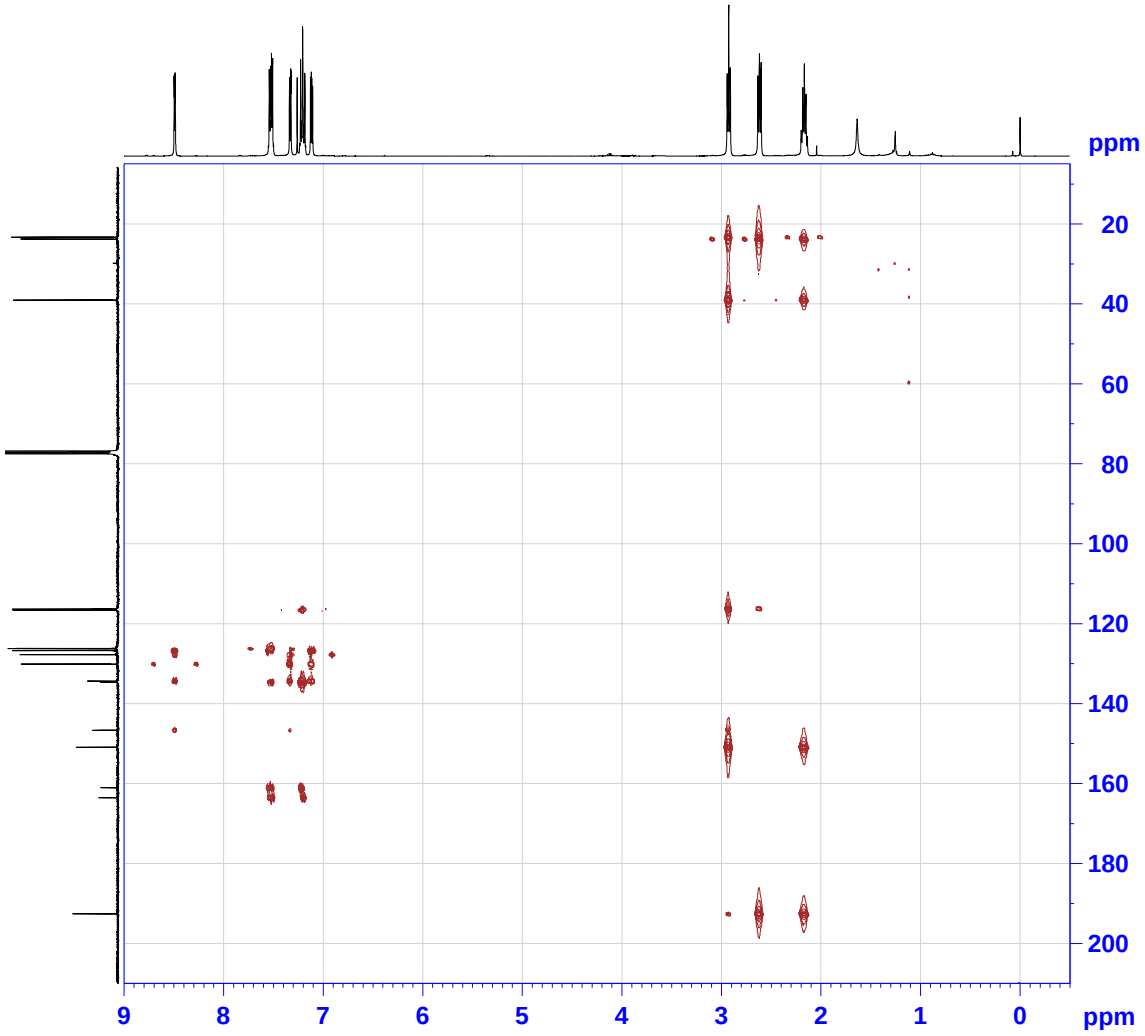
^{13}C **(7b)**



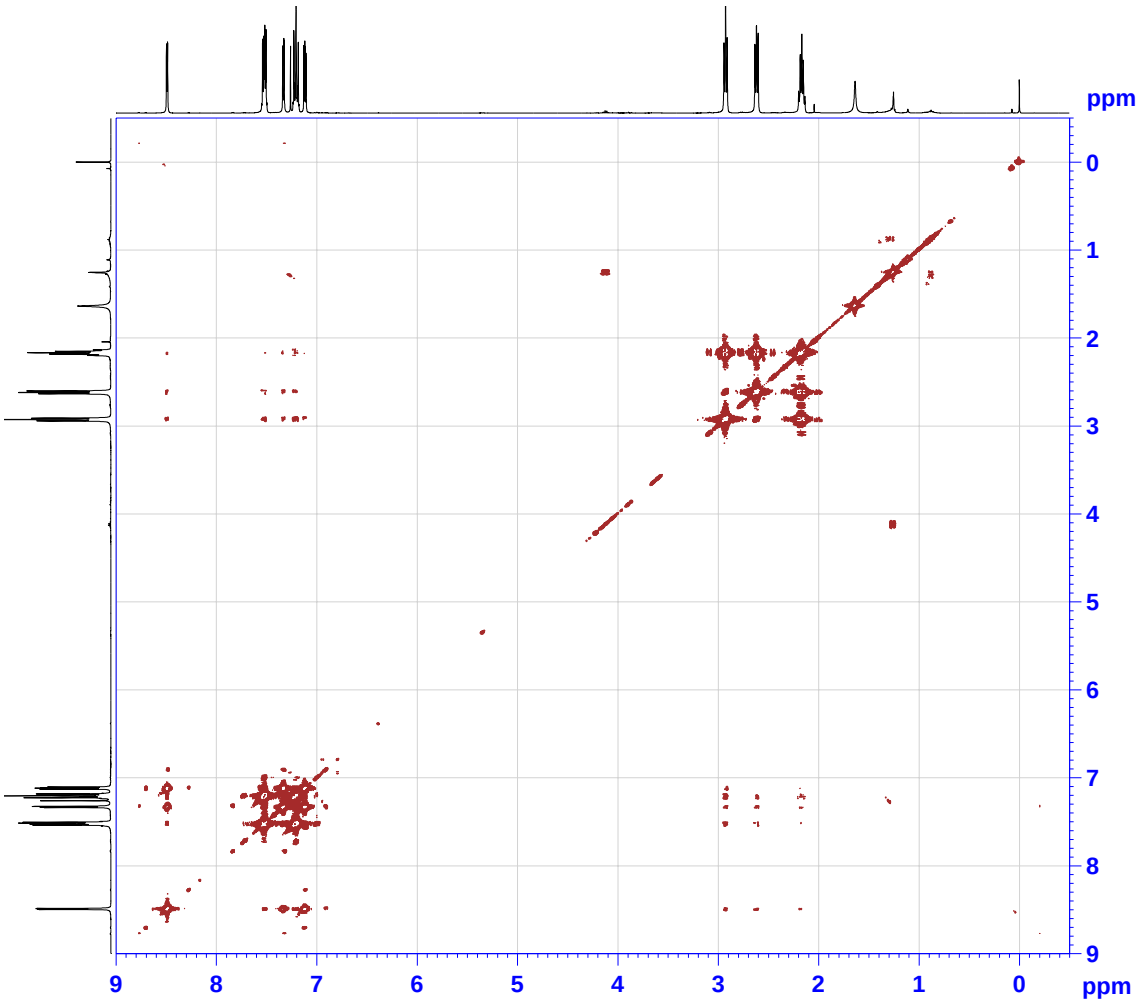
HSQC **(7b)**



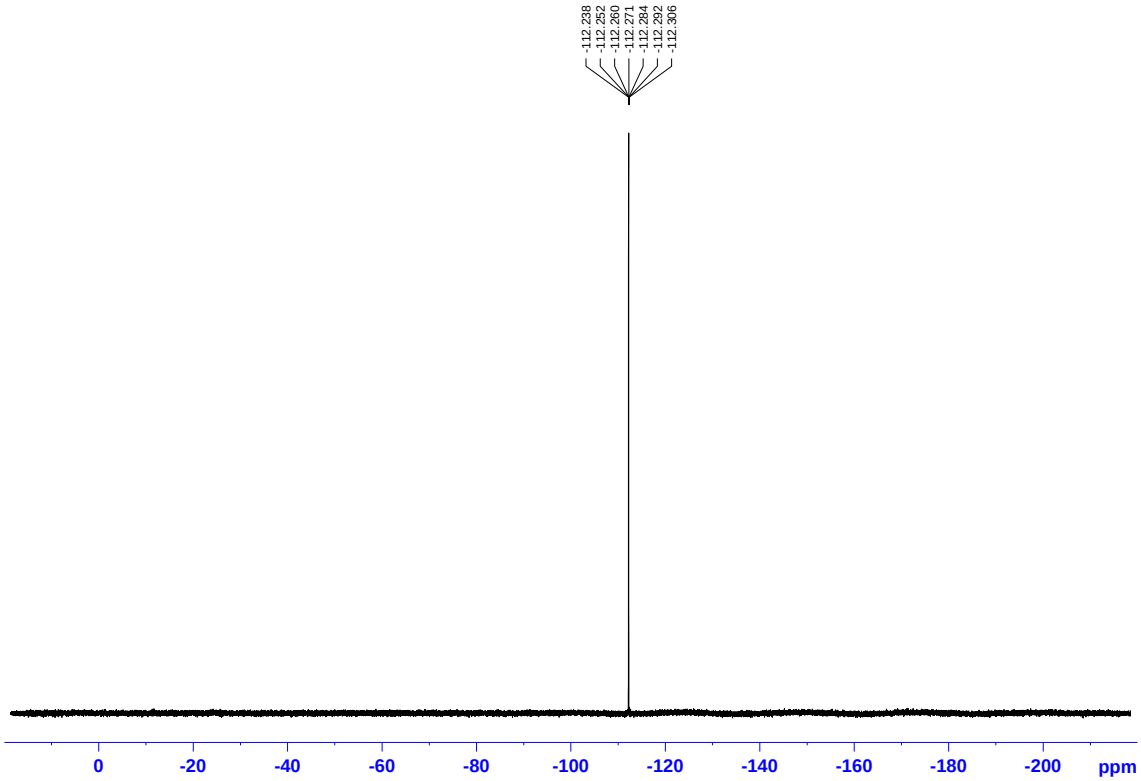
HMBC **(7b)**



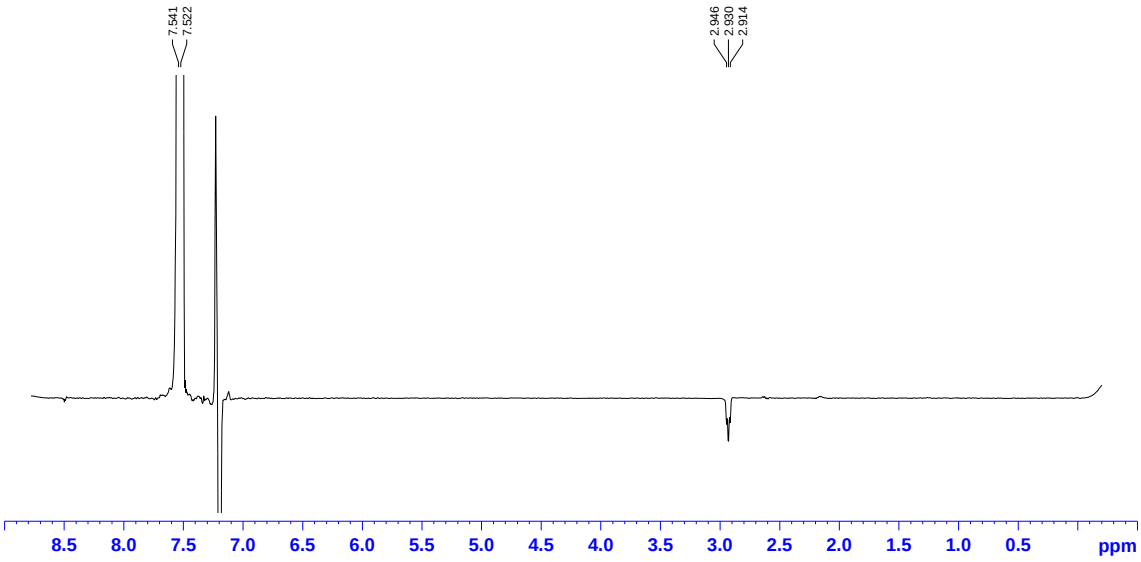
COSY **(7b)**

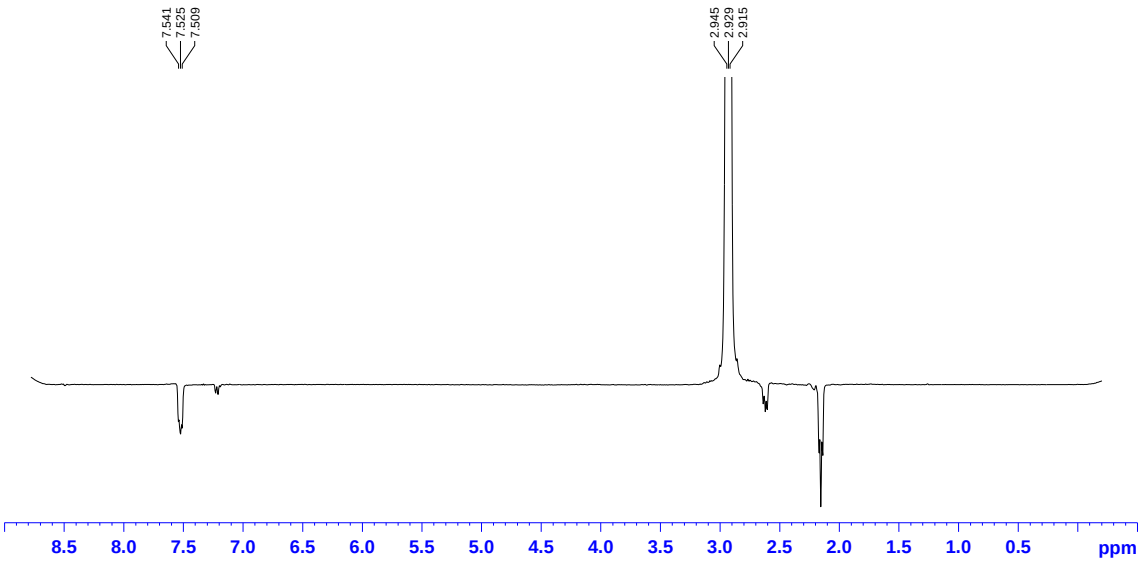


^{19}F **(7b)**

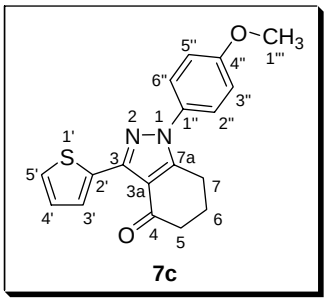


ROESY **(7b)**




7.541
7.525
7.509
2.945
2.929
2.915
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
ppm

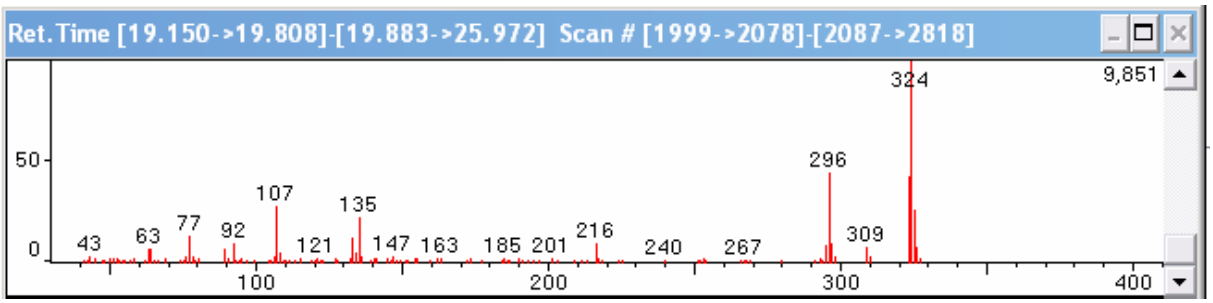
1-(4-methoxyphenyl)-3-(2-thienyl)-1,5,6,7-tetrahydro-4*H*-indazol-4-one (7c): Pale brown solid, m.p. 160.7-162.6 ºC. (Dec.) Yield 41.1 % (0.0609 g) ^{1}H NMR ($CDCl_3$): δ = 2.15 (quintuplet, J = 6.2 Hz, 2 H, H-6), 2.61 (t, J = 6.2 Hz, 2 H, H-5), 2.90 (t, J = 6.2 Hz, 2 H, H-7), 3.86 (s, 3 H, H-1´´´), 7.00 (m, 2 H, H-3´´,5´´), 7.11 (dd, J = 5.0 and 3.7 Hz, 1 H, H-4´), 7.31 (dd, J = 5.0 and 1.0 Hz, 1 H, H-5´), 7.43 (m, 2 H, H-2´´,6´´), 8.48 (dd, J = 3.7 and 1.0 Hz, 1 H, H-3´) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.29 (C-6), 23.68 (C-7), 39.10 (C-5), 55.77 (C-1´´´), 114.63 (C-3´´,5´´), 115.93 (C-3a), 125.86 (C-2´´,6´´), 126.53 (C-5´), 127.71 (C-4´), 129.89 (C-3´), 131.59 (C-1´´), 134.68 (C-2´), 146.29 (C-3), 150.87 (C-7a), 159.71 (C-4´´), 192.71 (C-4) ppm. MS: *m/z* (%) = 325 (29), 324 [M]$^{+}$ (100), 323 (47), 297 (10), 296 (50), 216 (10), 135 (26), 133 (12), 107 (29), 77 (15).



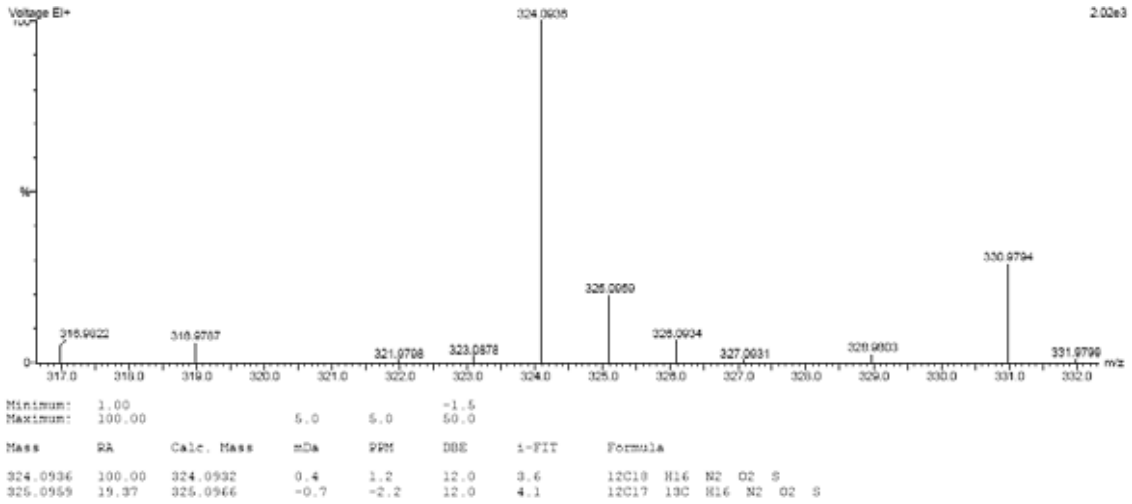
7c

Carbon Number	δH (ppm) (*J* in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.31, dd (5.0,1.0), 1 H	126.53	3', 4'	2', 3', 4'	
4'	7.11, dd (5.0,3.7), 1 H	127.71	3', 5'	2', 3', 5'	
3'	8.48, dd (3.7,1.0), 1 H	129.89	4', 5'	2', 4', 5', 3	
2'		134.68			
3		146.29			
3a		115.93			
4		192.71			
5	2.61, t (6.2), 2 H	39.10	6, 7	3a, 4, 6, 7	
6	2.15, quintuplet (6.2), 2 H	23.29	5, 7	4, 5, 7, 7a	
7	2.90, t (6.2), 2 H	23.68	5, 6	3a, 5, 6, 7a	2''
7a		150.87			
1''		131.59			
2''/6''	7.43, m, 2 H	125.86	3'', 5''	1'', 2'', 3'', 4'', 5'', 6''	7
3''/5''	7.00, m, 2 H	114.63	2'', 6''	1'', 2'', 3'', 4'', 5'', 6''	1'''
4''		159.71			
1''	3.86, s, 3 H	55.77	2'', 3'', 5'', 6''	4''	3'', 5''

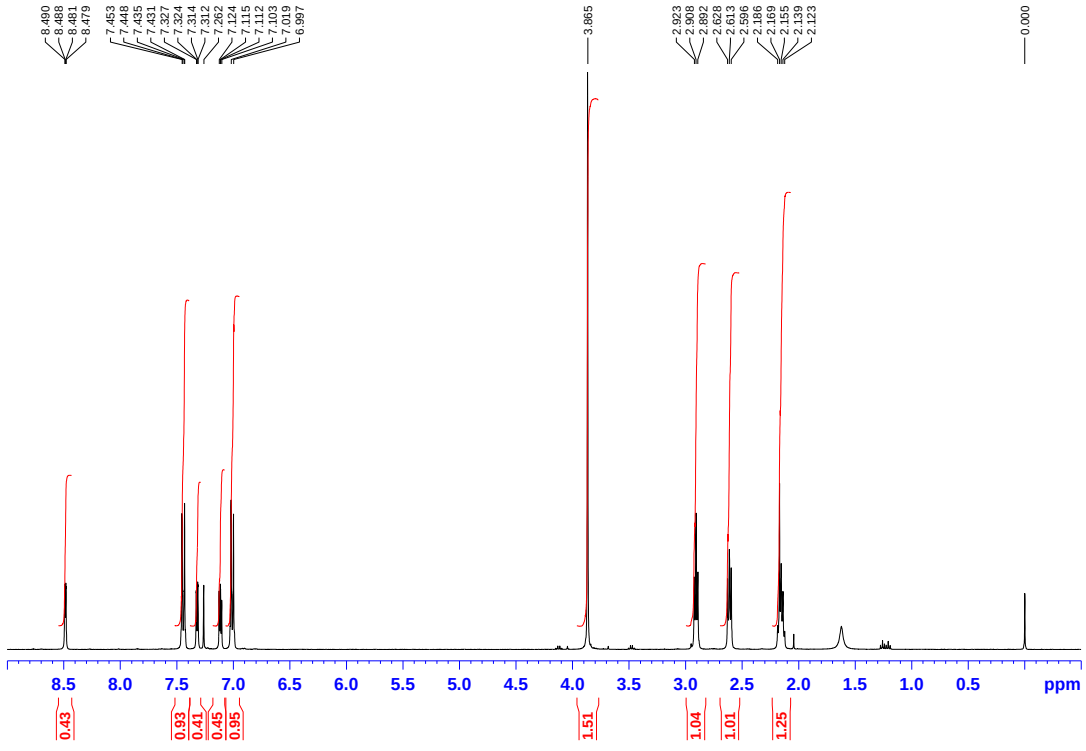
MS **(7c)**

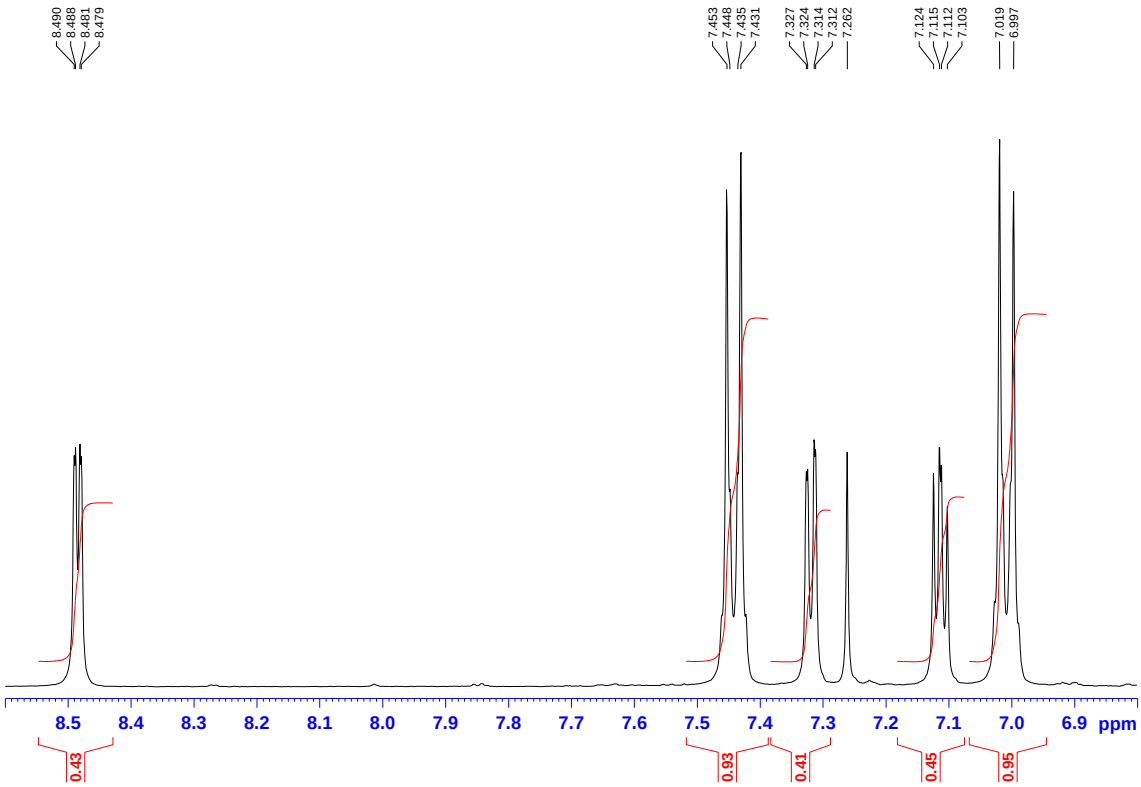


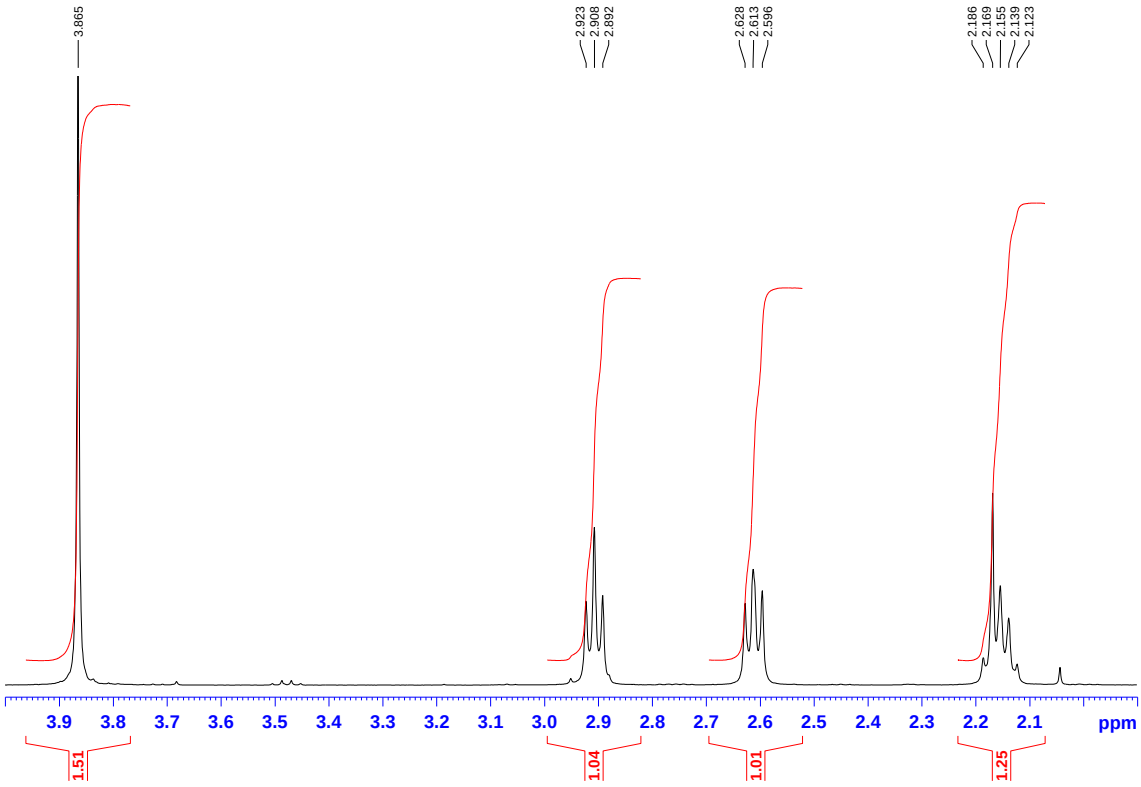
HRMS **(7c)**



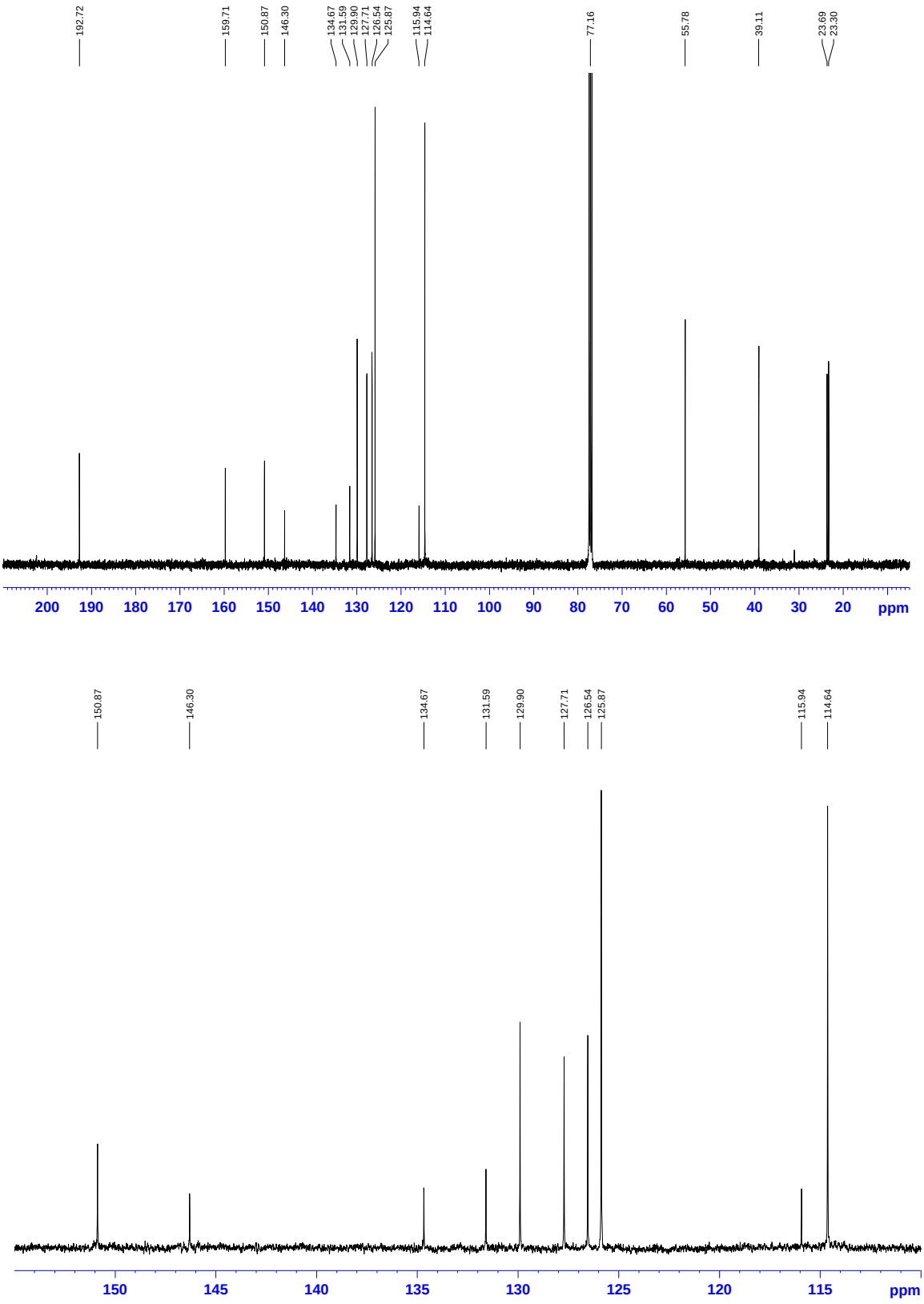
^{1}H **(7c)**



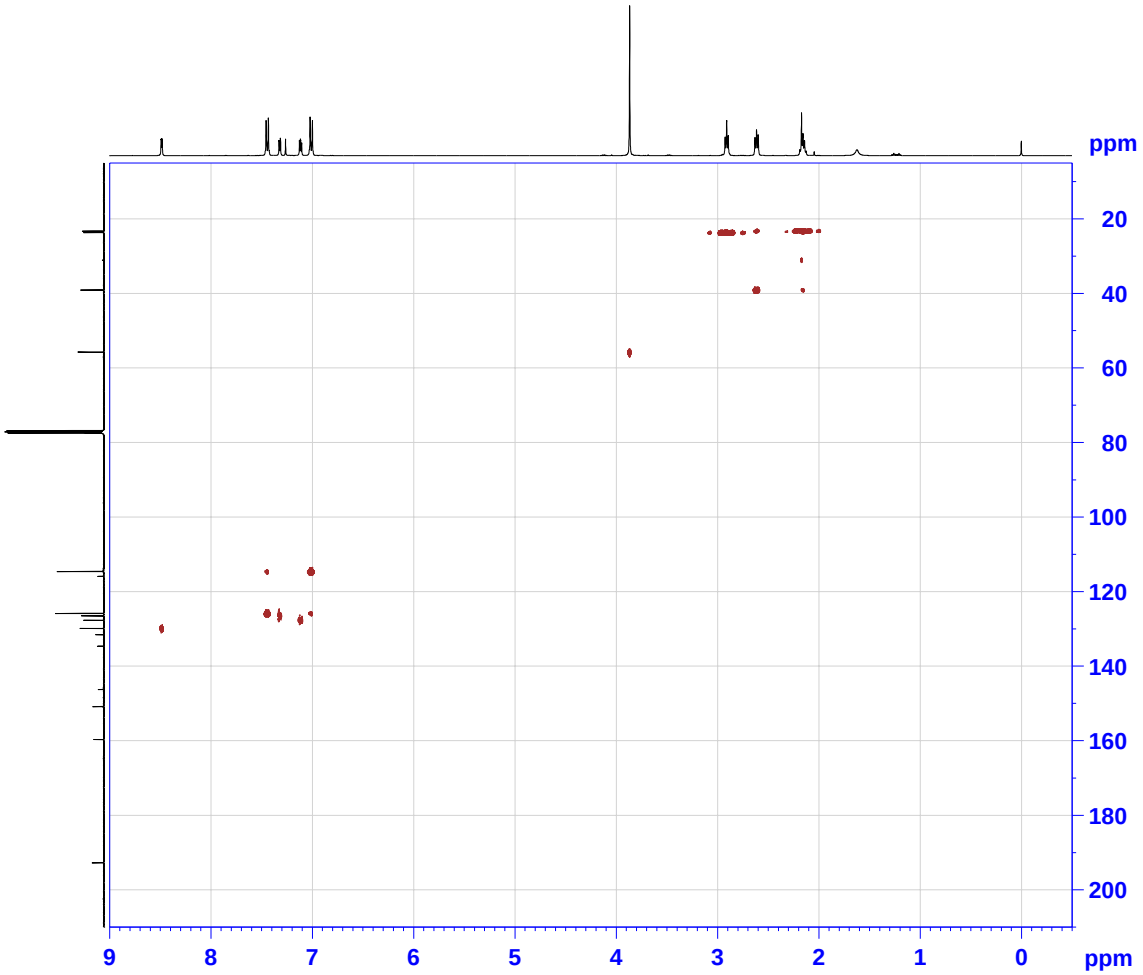

8.490
8.488
8.481
8.479
7.453
7.448
7.435
7.431
7.327
7.324
7.314
7.312
7.262
7.124
7.115
7.112
7.103
7.019
6.997
8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 ppm
0.43
0.93
0.41
0.45
0.95


3.865
2.923
2.908
2.892
2.628
2.613
2.596
2.186
2.169
2.155
2.139
2.123
3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 ppm
1.51
1.04
1.01
1.25

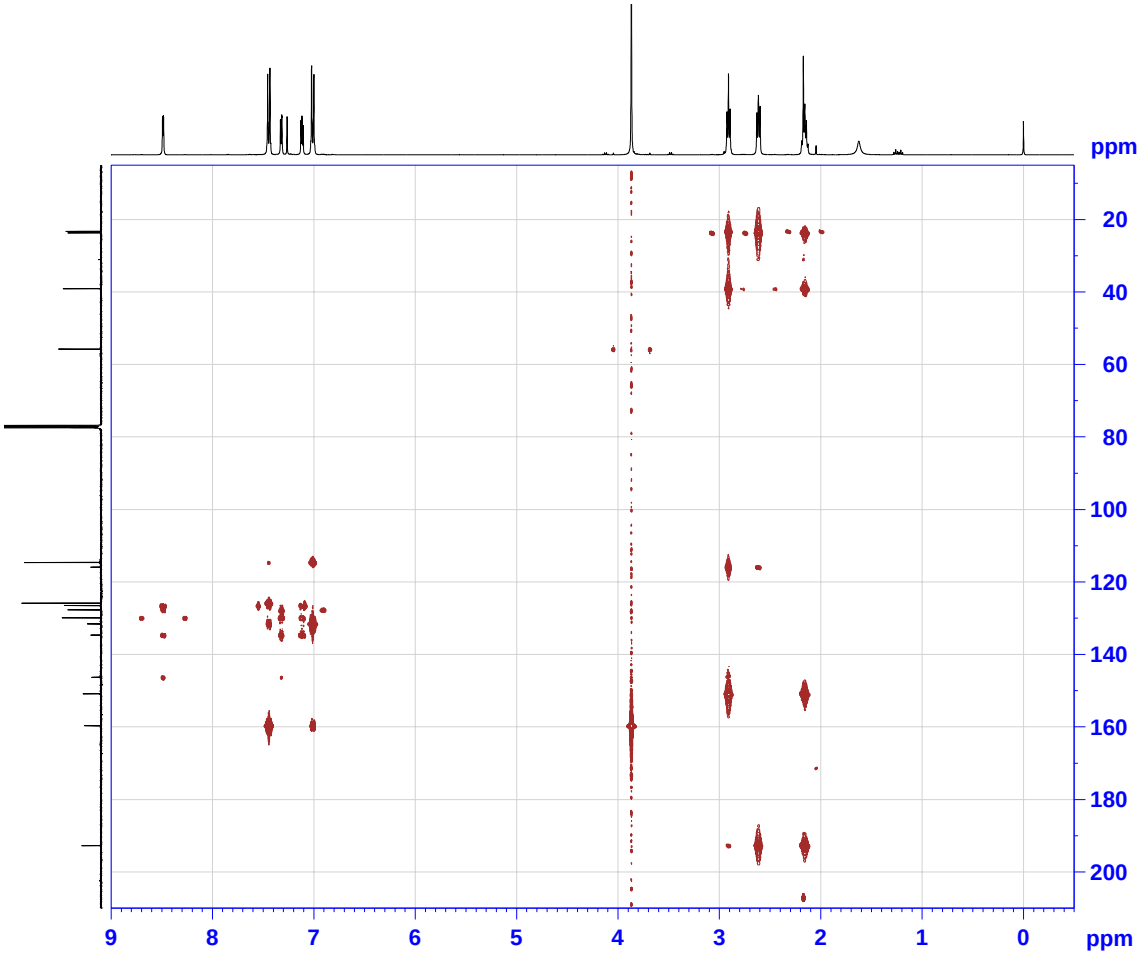
^{13}C **(7c)**


192.72
159.71
150.87
146.30
134.67
131.59
129.90
127.71
126.54
125.87
115.94
114.64
77.16
55.78
39.11
23.69
23.30
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm
150.87
146.30
134.67
131.59
129.90
127.71
126.54
125.87
115.94
114.64
150 145 140 135 130 125 120 115 ppm

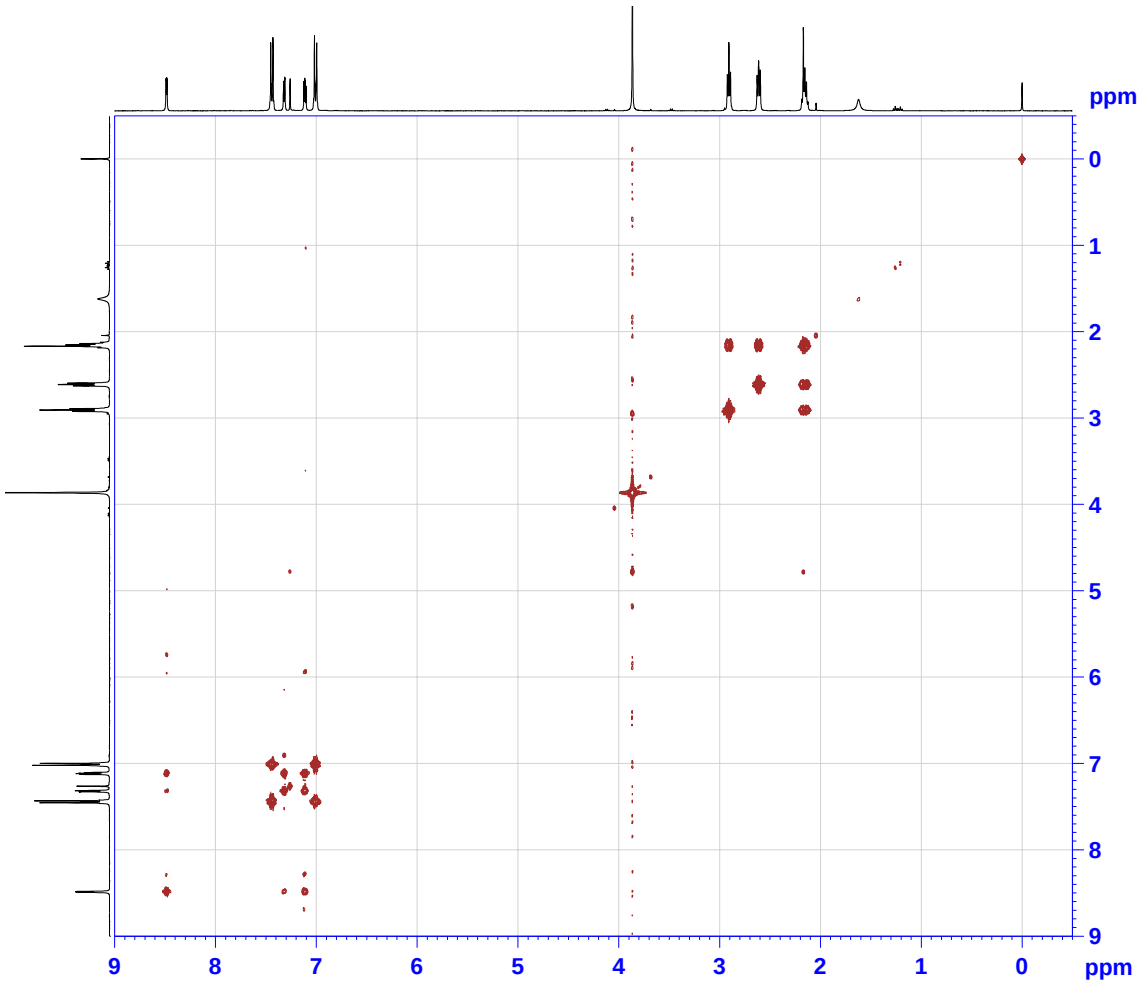
HSQC **(7c)**



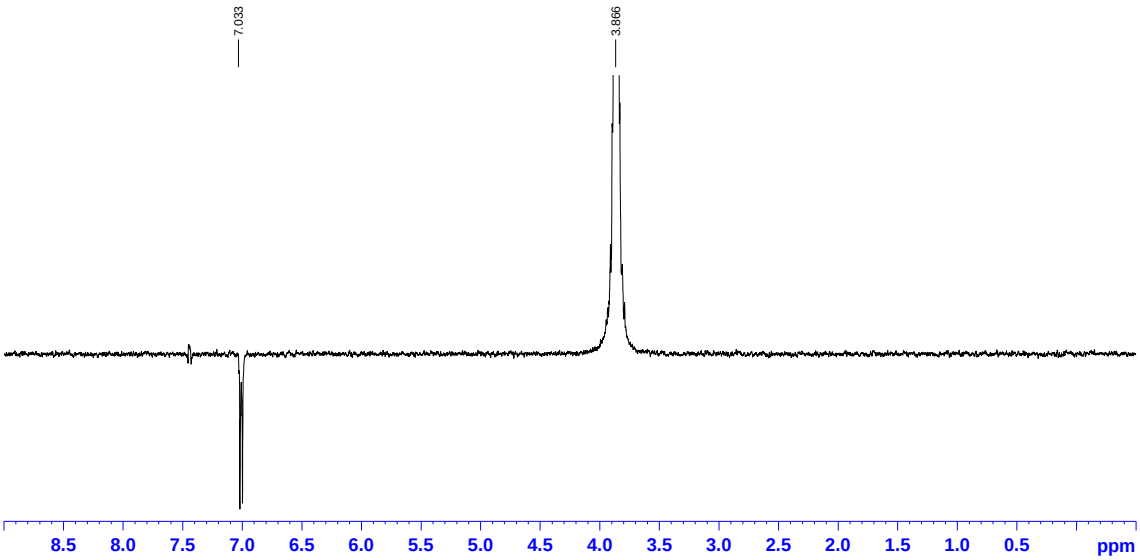
HMBC **(7c)**

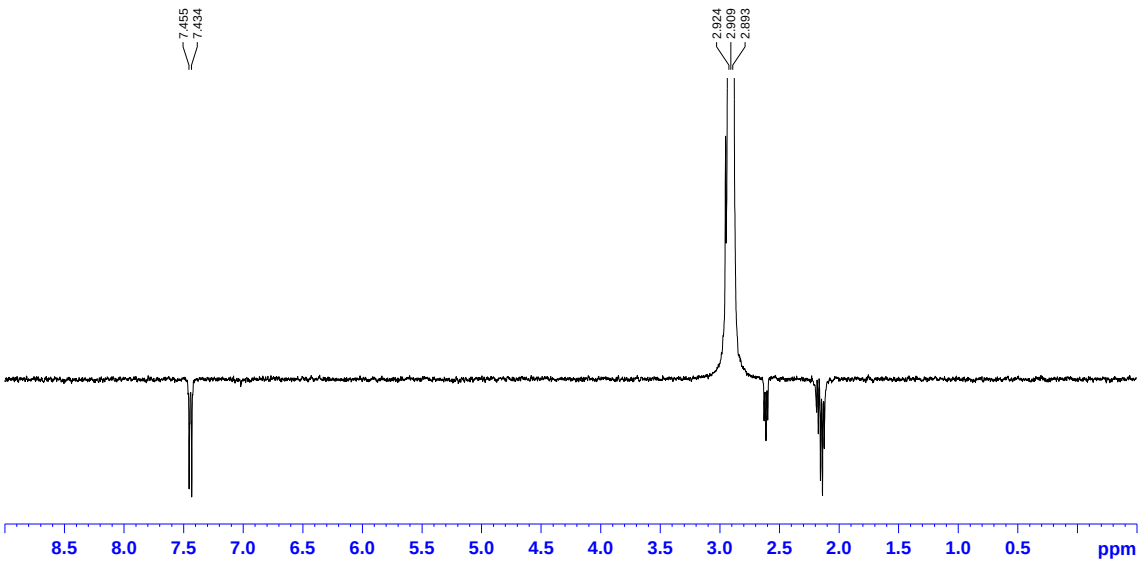


COSY **(7c)**



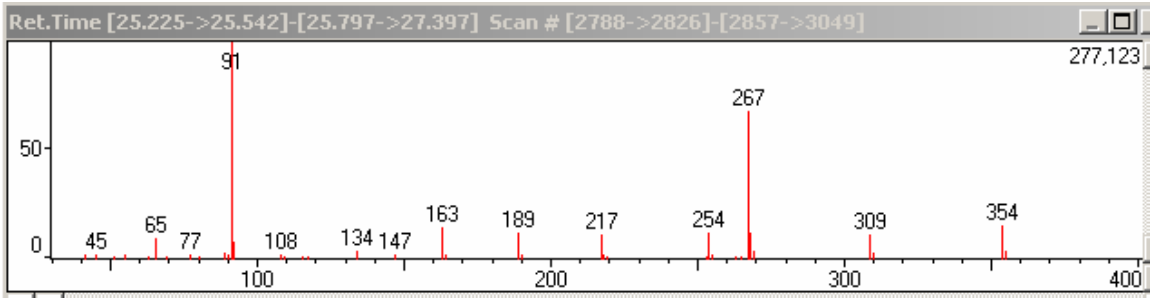
ROESY **(7c)**



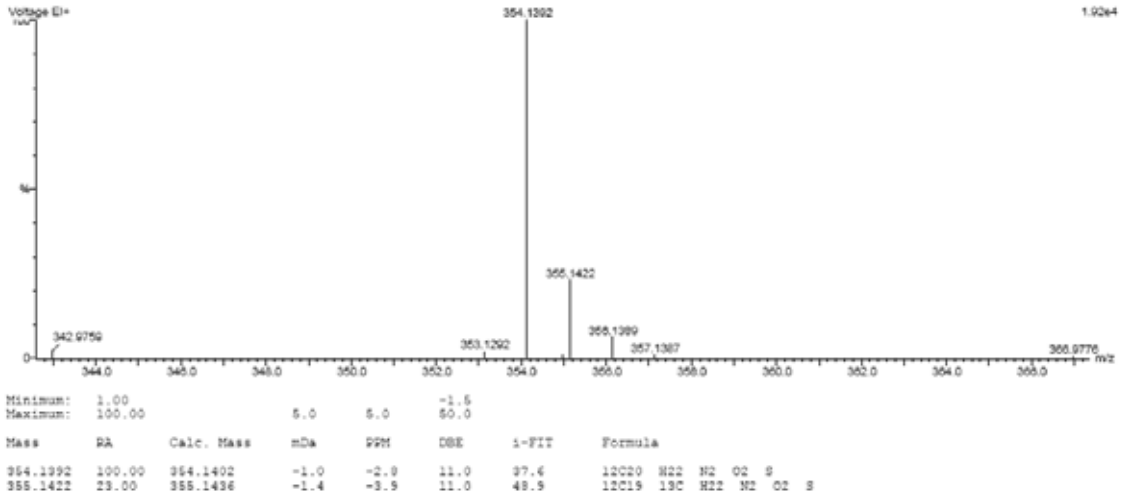

7.455
7.434
2.924
2.909
2.893
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

2-[(benzylhydrazono)(2-thienyl)methyl]-3-ethoxycyclohex-2-en-1-one (8d): Brown solid. Yield 24.3% (0.0432 g). MS: *m/z* (%) = 354 $[M]^+$ (15), 309 (11), 268 (12), 267 (67), 254 (12), 217 (12), 189 (12), 163 (15), 91 (100), 65 (9).

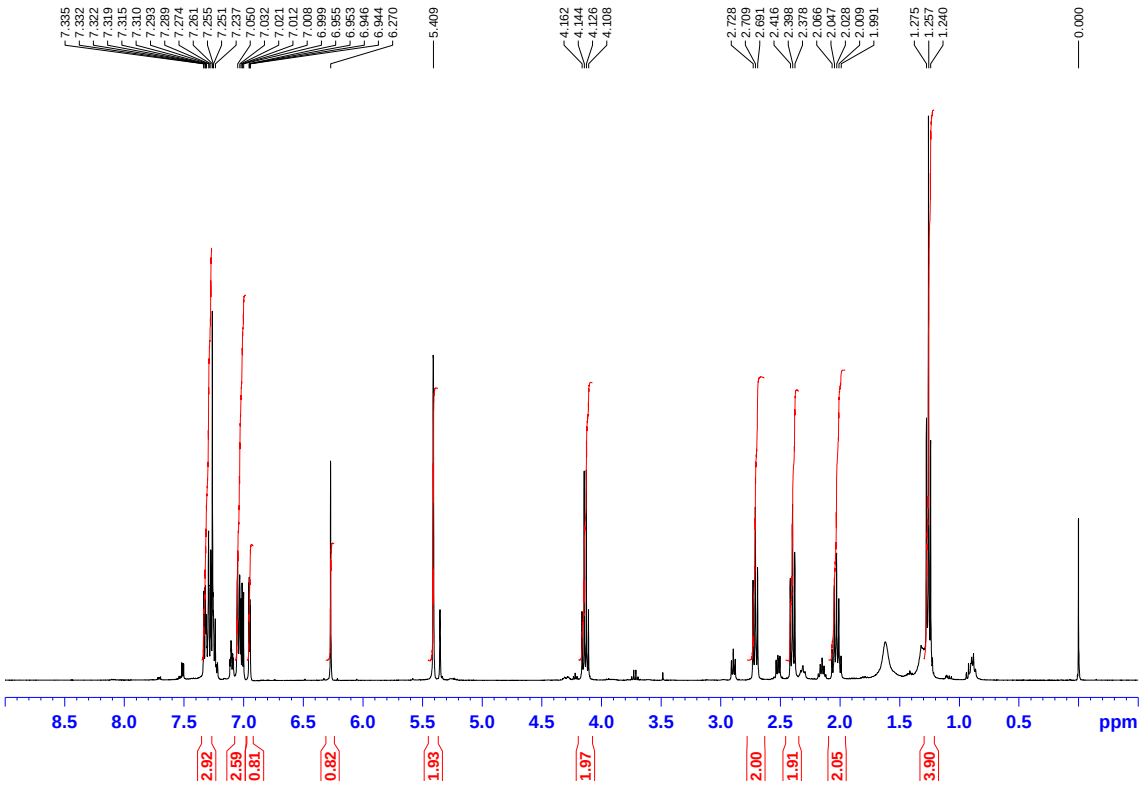
MS **(8d)**

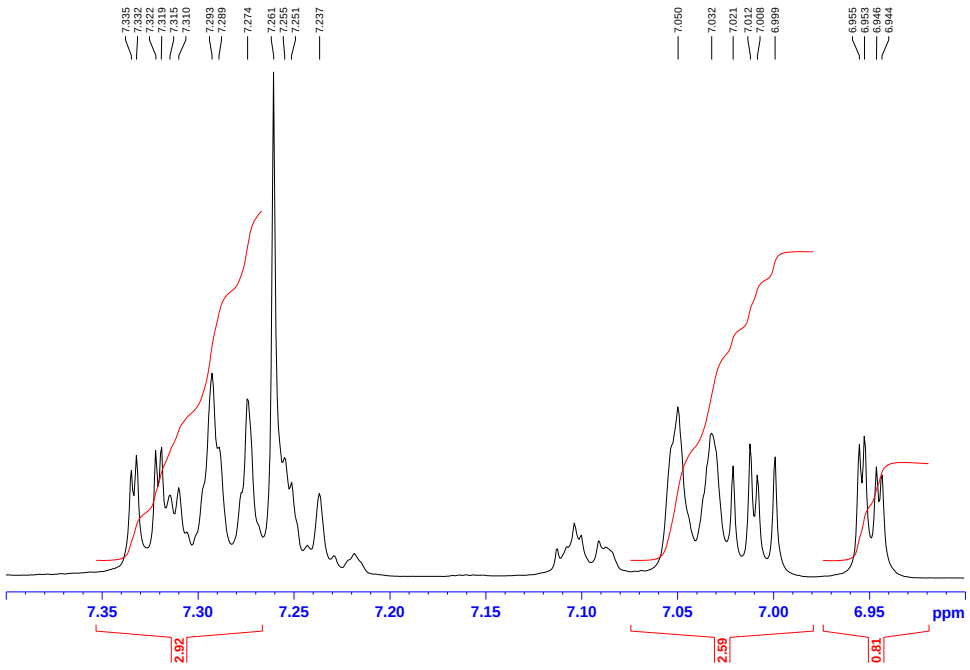


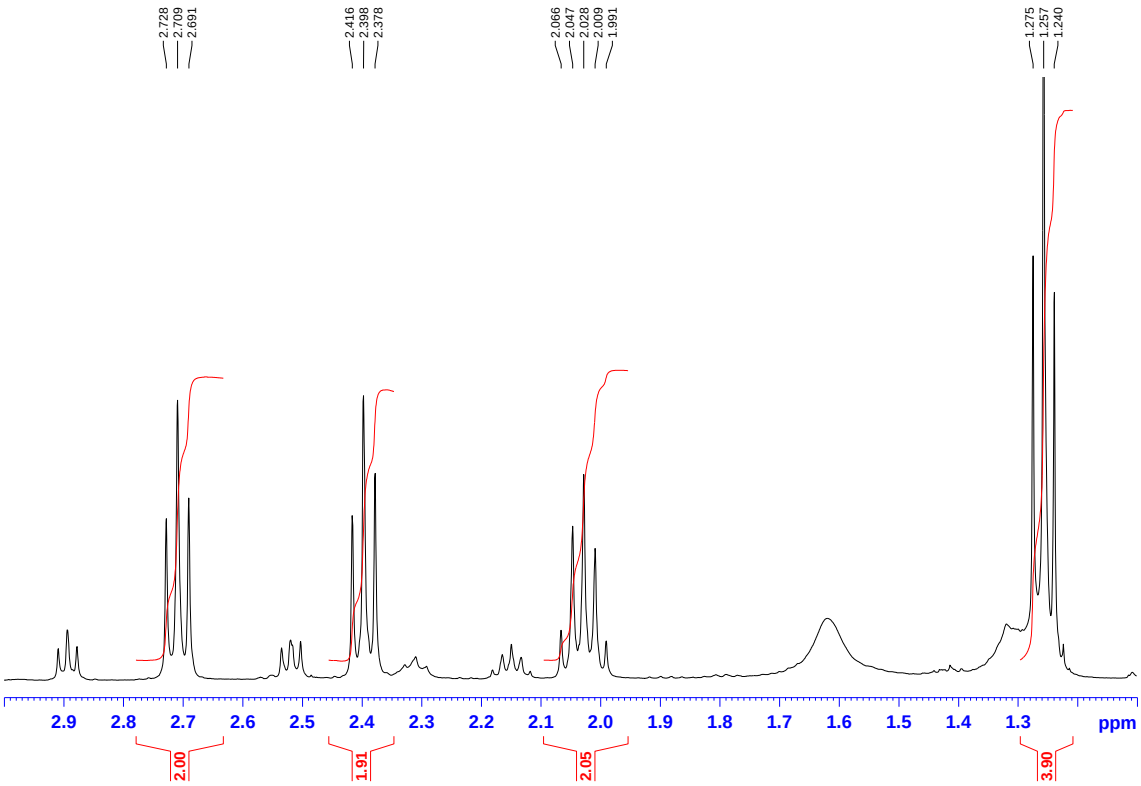
HRMS **(8d)**



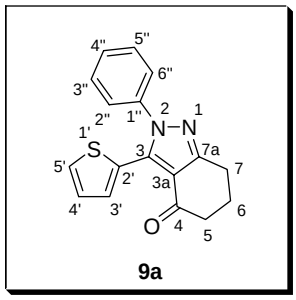
^{1}H (8d)


7.335
7.332
7.322
7.319
7.315
7.310
7.293
7.289
7.274
7.261
7.255
7.251
7.237
7.050
7.032
7.021
7.012
7.008
6.999
6.955
6.953
6.946
6.944
6.270
5.409
4.162
4.144
4.126
4.108
2.728
2.709
2.691
2.416
2.398
2.378
2.066
2.047
2.028
2.009
1.991
1.275
1.257
1.240
0.000
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
ppm
2.92
2.59
0.81
0.82
1.93
1.97
2.00
1.91
2.05
3.90


7.335
7.332
7.322
7.319
7.315
7.310
7.293
7.289
7.274
7.261
7.255
7.251
7.237
7.050
7.032
7.021
7.012
7.008
6.999
6.955
6.953
6.946
6.944
7.35
7.30
7.25
7.20
7.15
7.10
7.05
7.00
6.95
ppm
2.92
2.59
0.81


2.728
2.709
2.691
2.416
2.398
2.378
2.066
2.047
2.028
2.009
1.991
1.275
1.257
1.240
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
ppm
2.00
1.91
2.05
3.90

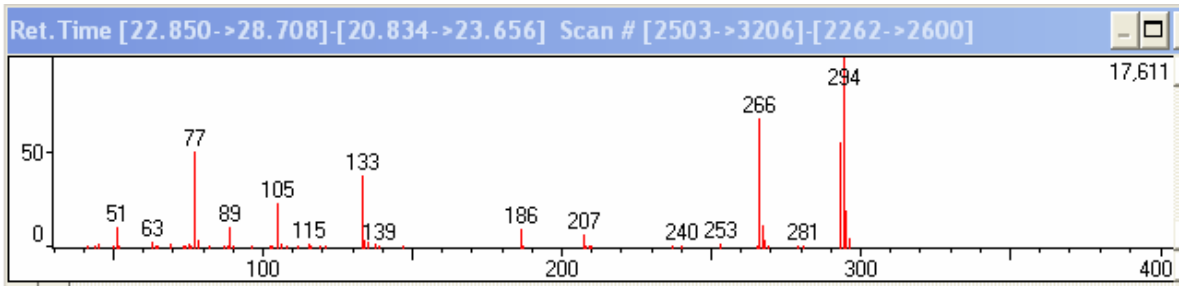
2-phenyl-3-(2-thienyl)-2,5,6,7-tetrahydro-4*H*-indazol-4-one (9a): Yellow solid. Yield < 5 % (0.007 g) ^{1}H NMR ($CDCl_3$): δ = 2.20 (quintuplet, J = 6.3 Hz, 2 H, H-6), 2.59 (t, J = 6.3 Hz, 2 H, H-5), 2.96 (t, J = 6.3 Hz, 2 H, H-7), 6.99 (dd, J = 5.0 and 3.7 Hz, 1 H, H-4´), 7.32 (m, 2 H, H-2´´,6´´), 7.38 (dd, J = 5.0 and 1.2 Hz, 1 H, H-5´), 7.40 (m, 2 H, H-3´´,5´´), 7.40 (m, 1 H, H-4´´), 7.49 (dd, J = 3.7 and 1.2 Hz, 1 H, H-3´) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.44 (C-6), 23.66 (C-7), 40.07 (C-5), 116.77 (C-3a), 126.55 (C-2´´,6´´), 126.93 (C-4´), 128.34 (C-2´), 129.05 (C-5´), 129.05 (C-1´´), 129.31 (C-3´´,5´´), 132.02 (C-3´), 137.76 (C-3), 139.44 (C-4´´), 157.42 (C-7a), 193.93 (C-4) ppm. MS: *m/z* (%) = 295 (20), 294 [M]$^{+}$ (100), 293 (67), 267 (10), 266 (65), 186 (11), 133 (36), 105 (23), 77 (50), 51 (11).



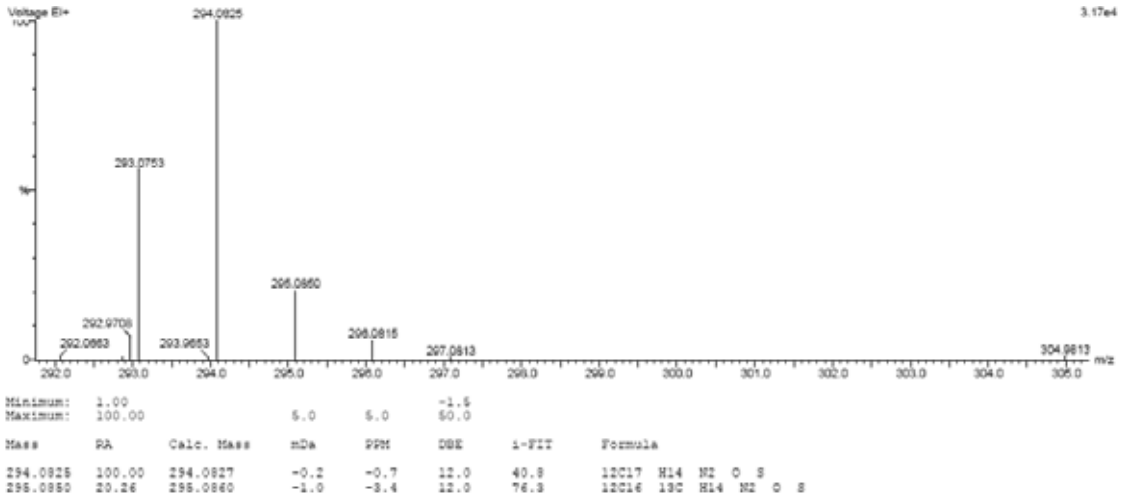
9a

Carbon Number	δH (ppm) (*J* in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.38, dd (5.0, 1.2), 1 H	129.05	3', 4'	2', 3', 4'	
4'	6.99, dd (5.0, 3.7), 1 H	126.93	3', 5'	2', 3', 5	
3'	7.49, dd (3.7, 1.2), 1 H	132.02	4', 5'	2', 4', 5', 3	
2'		128.34			
3		137.76			
3a		116.77			
4		193.93			
5	2.59, t (6.3), 2 H	40.07	6, 7	3a, 4, 6, 7	
6	2.20, quintuplet (6.3), 2 H	23.44	5, 7	4, 5, 7, 7a	
7	2.96, t (6.3), 2 H	23.66	5, 6	3a, 5, 6, 7a	
7a		157.42			
1''		129.05			
2''/6''	7.31-7.33, m, 2 H	126.55	3'', 5''	3'', 5''	
3''/5''	7.37-7.41, m, 2 H	129.31	2'', 6''	2'', 4'', 6''	
4''	7. 37-7.41, m, 2 H	139.44	3'', 5''	3'', 5''	

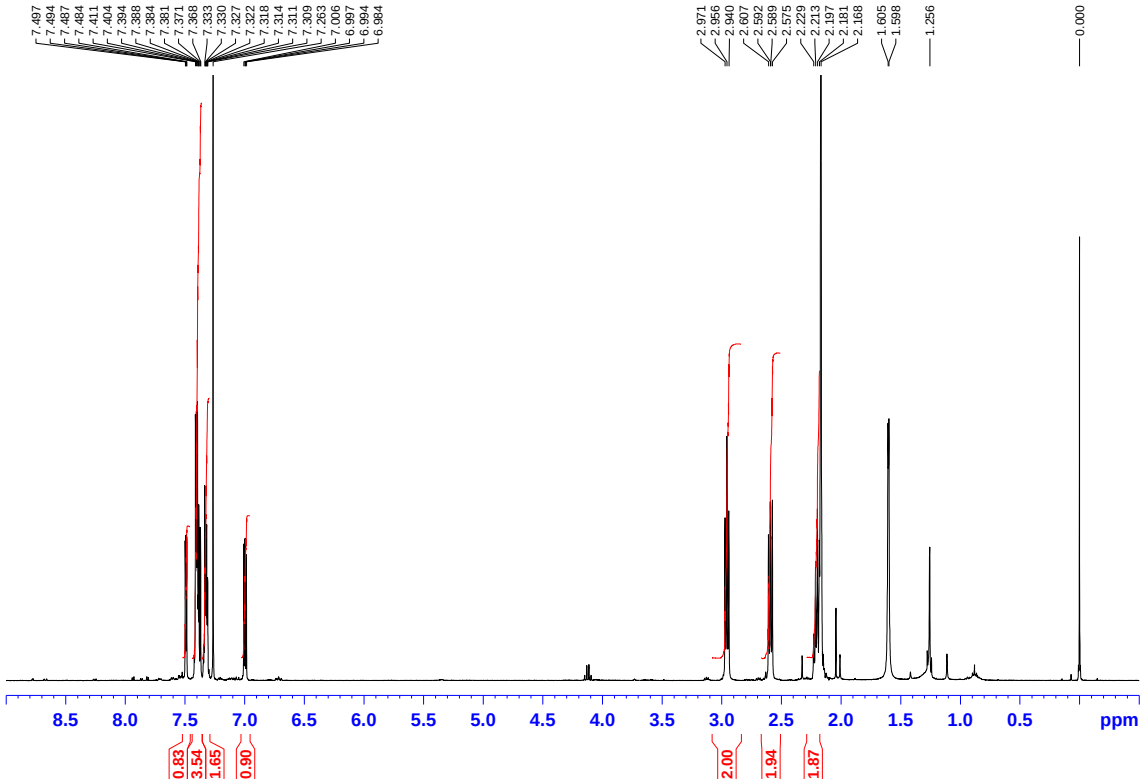
MS **(9a)**

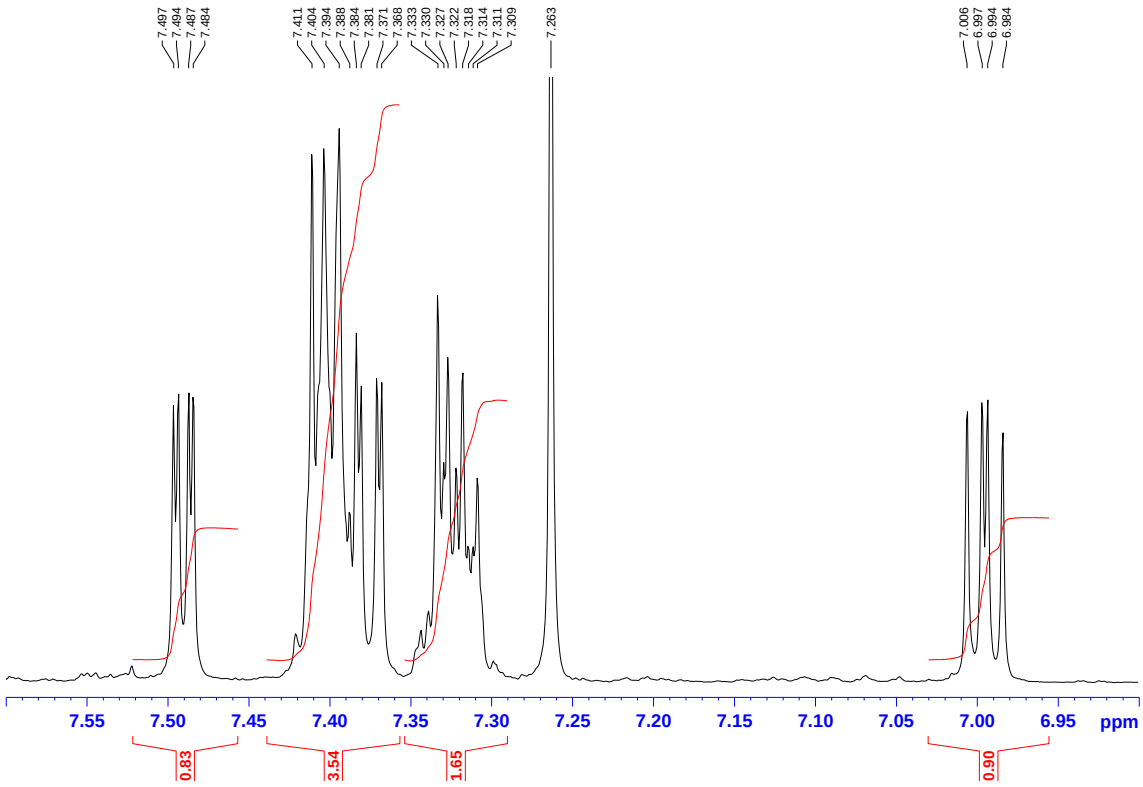

Ret.Time [22.850->28.708]-[20.834->23.656] Scan # [2503->3206]-[2262->2600]
17,611
294
266
77
133
105
51
63
89
115
139
186
207
240
253
281
50
0
100
200
300
400

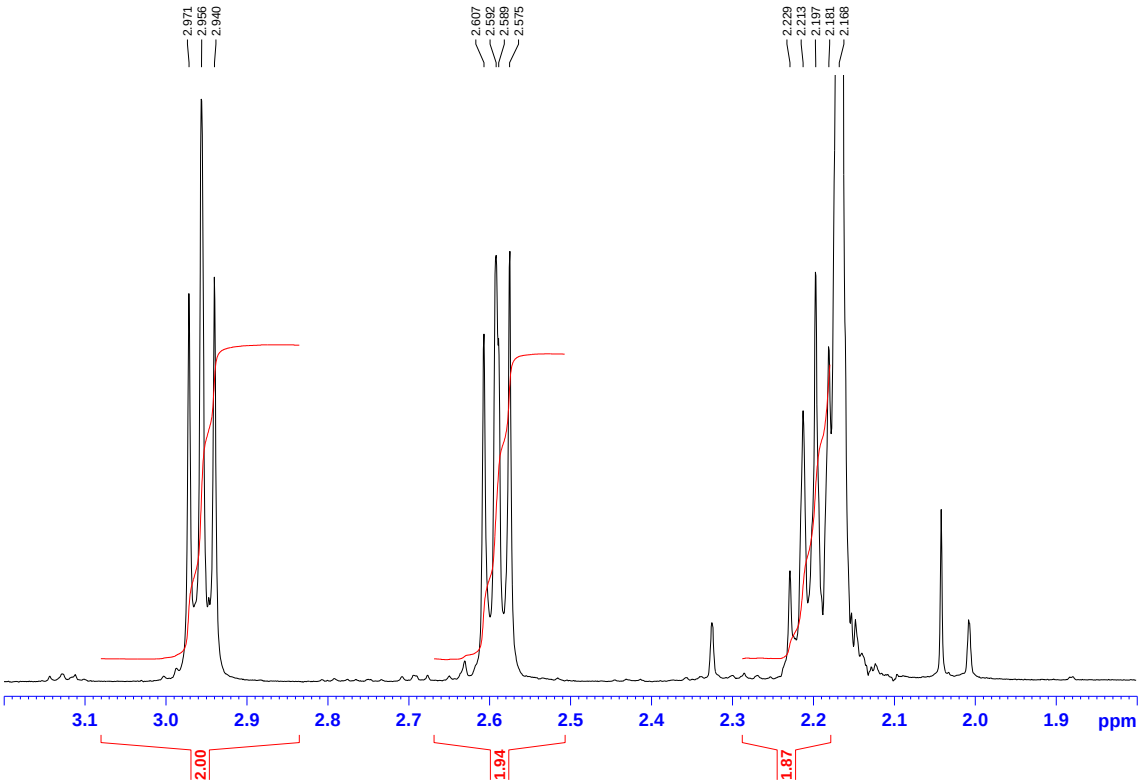
HRMS **(9a)**


Voltage El+
294.0825
3.17e4
293.0753
296.0860
292.9708
296.0815
292.0663
293.9653
297.0813
304.9813
m/z
Minimum: 1.00 -1.5
Maximum: 100.00 5.0 5.0 50.0
Mass RA Calc. Mass mDa PPM DBE i-FIT Formula
294.0825 100.00 294.0827 -0.2 -0.7 12.0 40.9 12C17 H14 N2 O S
296.0860 20.26 296.0860 -1.0 -3.4 12.0 76.9 12C16 13C H14 N2 O S

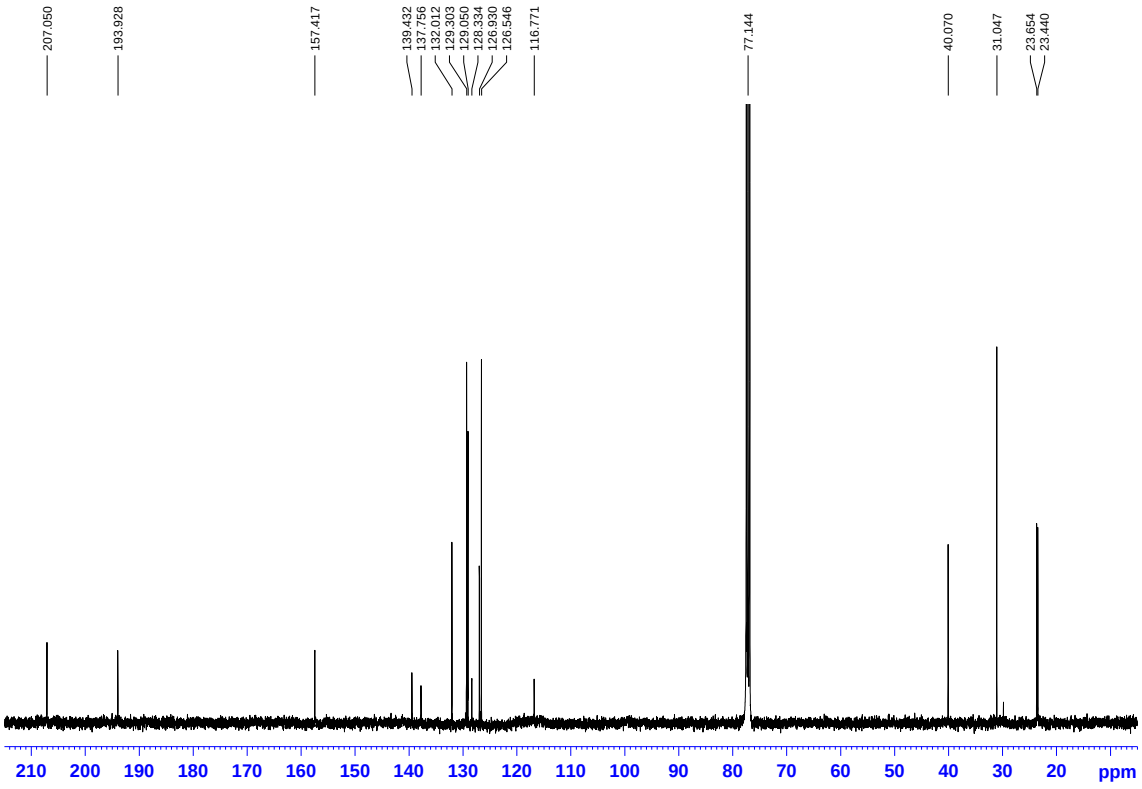
^{1}H **(9a)**

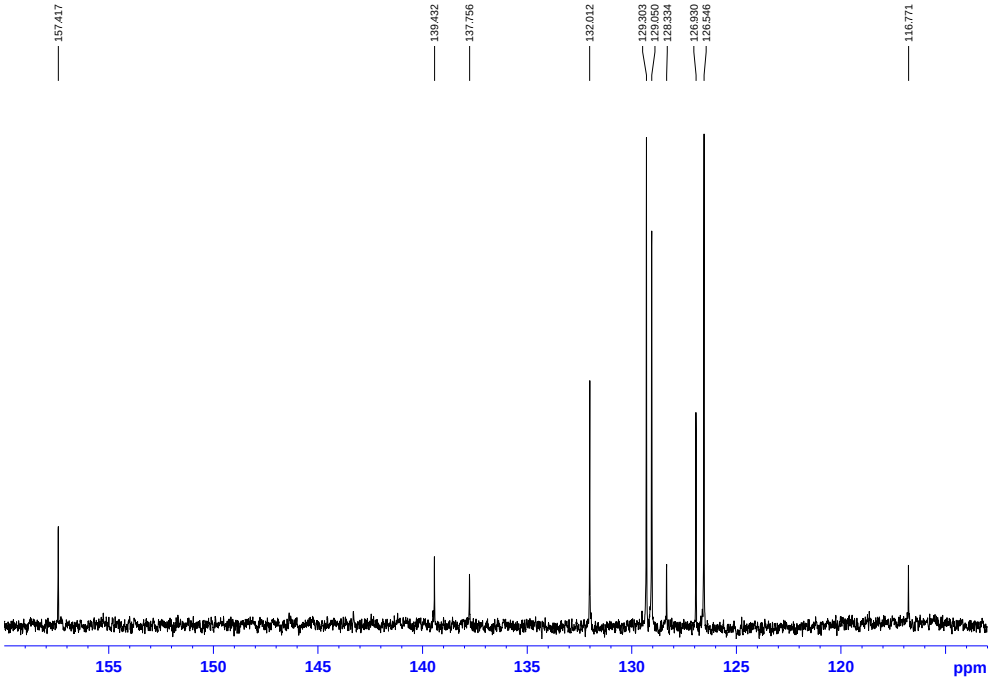

7.497
7.494
7.487
7.484
7.411
7.404
7.394
7.388
7.384
7.381
7.371
7.368
7.333
7.330
7.327
7.322
7.318
7.314
7.311
7.309
7.263
7.006
6.997
6.994
6.984
2.971
2.956
2.940
2.607
2.592
2.589
2.575
2.229
2.213
2.197
2.181
2.168
1.605
1.598
1.256
0.000
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.83
3.54
1.65
0.90
2.00
1.94
1.87


7.497
7.494
7.487
7.484
7.411
7.404
7.394
7.388
7.384
7.381
7.371
7.368
7.333
7.330
7.327
7.322
7.318
7.314
7.311
7.309
7.263
7.006
6.997
6.994
6.984
7.55
7.50
7.45
7.40
7.35
7.30
7.25
7.20
7.15
7.10
7.05
7.00
6.95
ppm
0.83
3.54
1.65
0.90

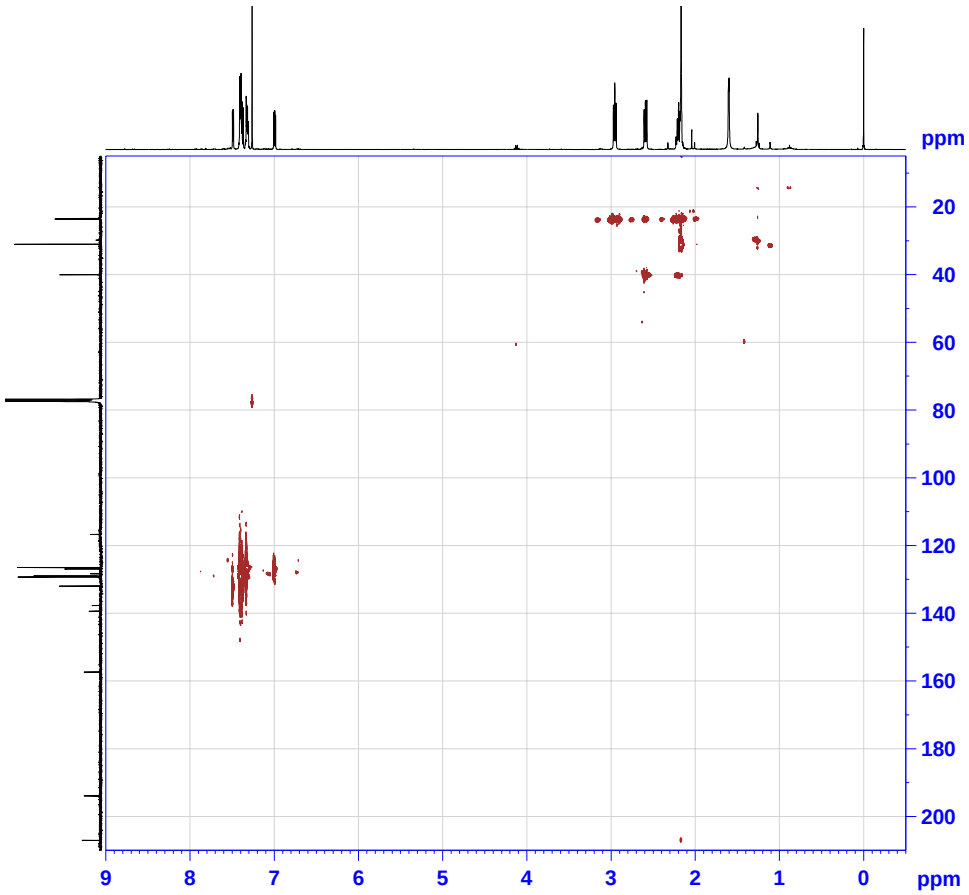

2.971
2.956
2.940
2.607
2.592
2.589
2.575
2.229
2.213
2.197
2.181
2.168
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
ppm
2.00
1.94
1.87

^{13}C **(9a)**

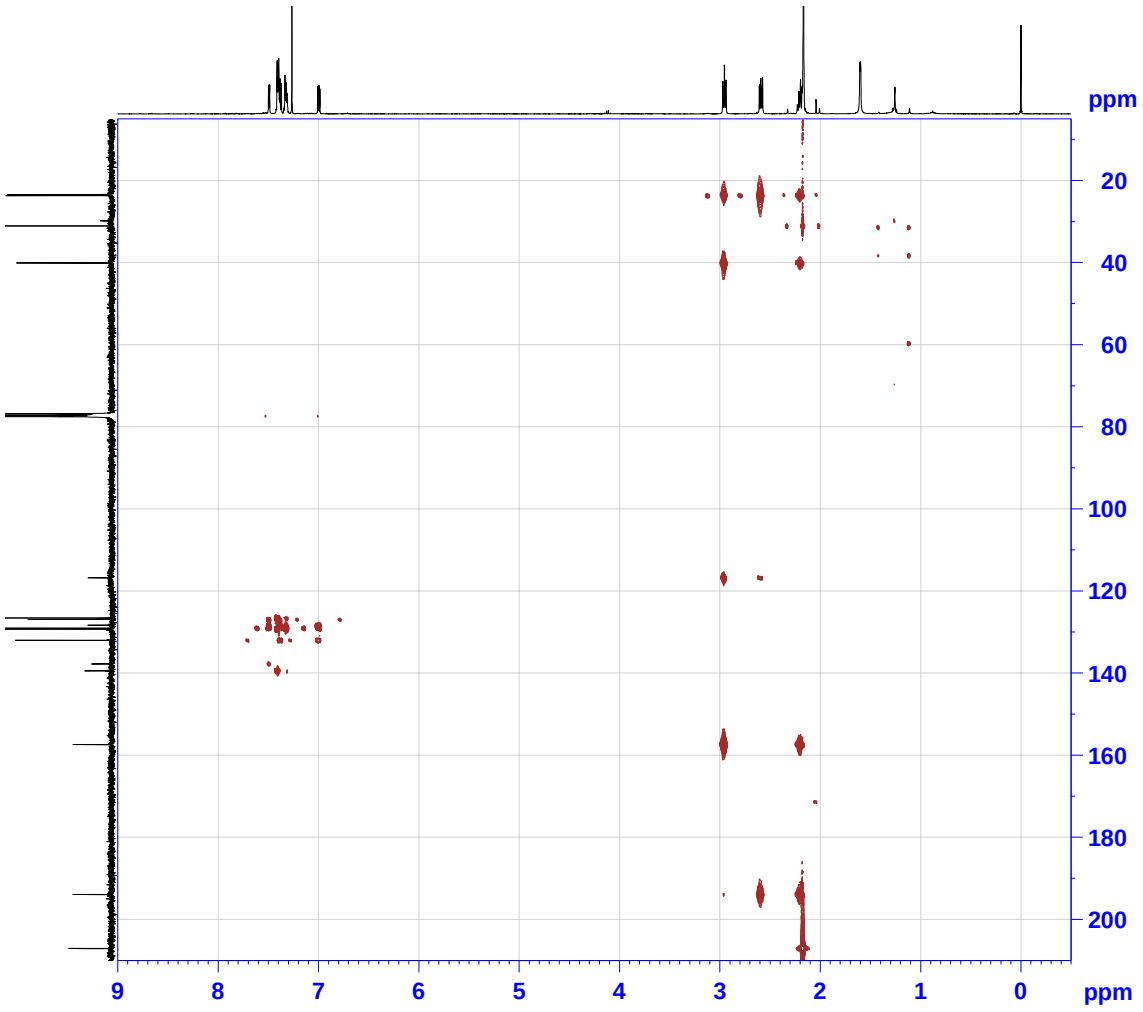

207.050
193.928
157.417
139.432
137.756
132.012
129.303
129.050
128.334
126.930
126.546
116.771
77.144
40.070
31.047
23.654
23.440
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


157.417
139.432
137.756
132.012
129.303
129.050
128.334
126.930
126.546
116.771
155
150
145
140
135
130
125
120
ppm

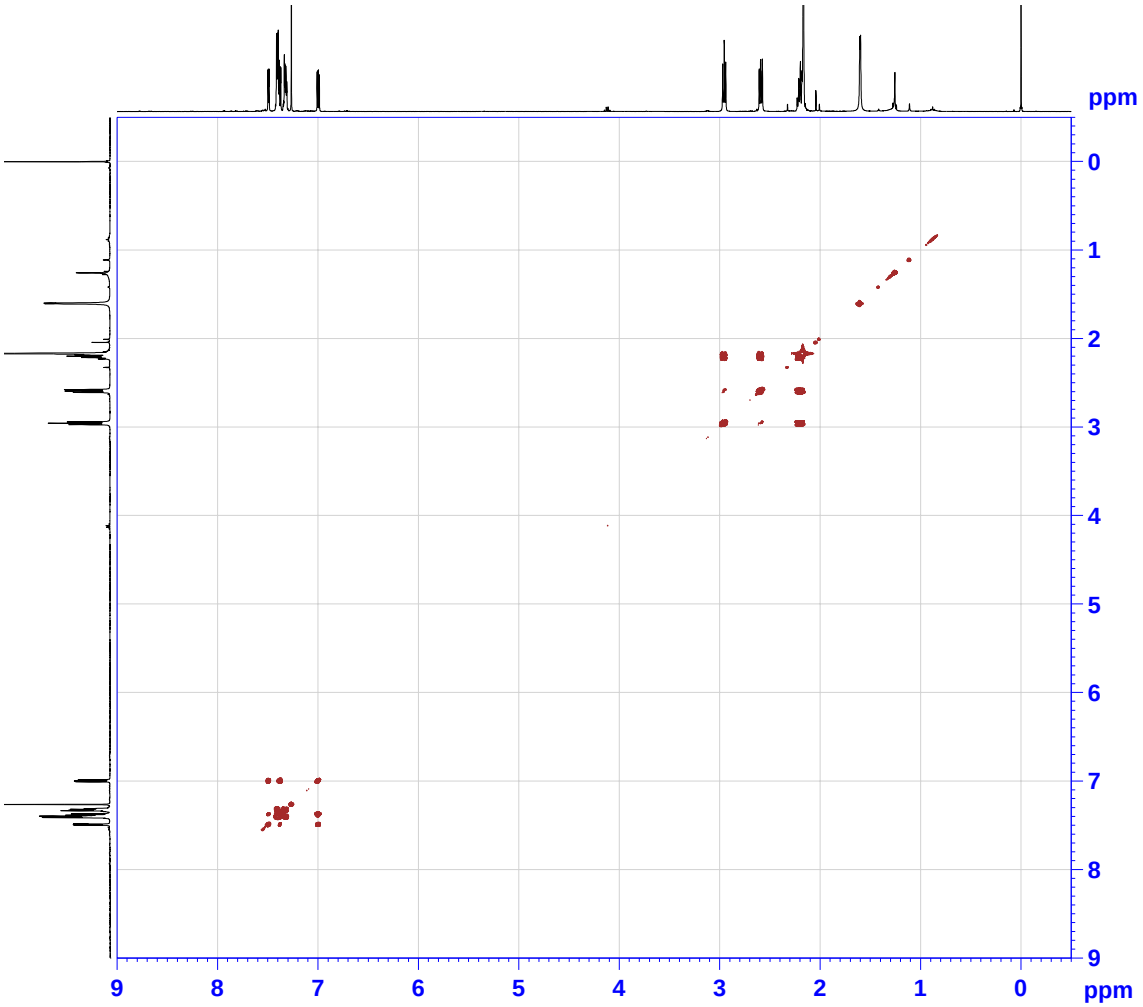
HSQC **(9a)**


ppm
20
40
60
80
100
120
140
160
180
200
9
8
7
6
5
4
3
2
1
0
ppm

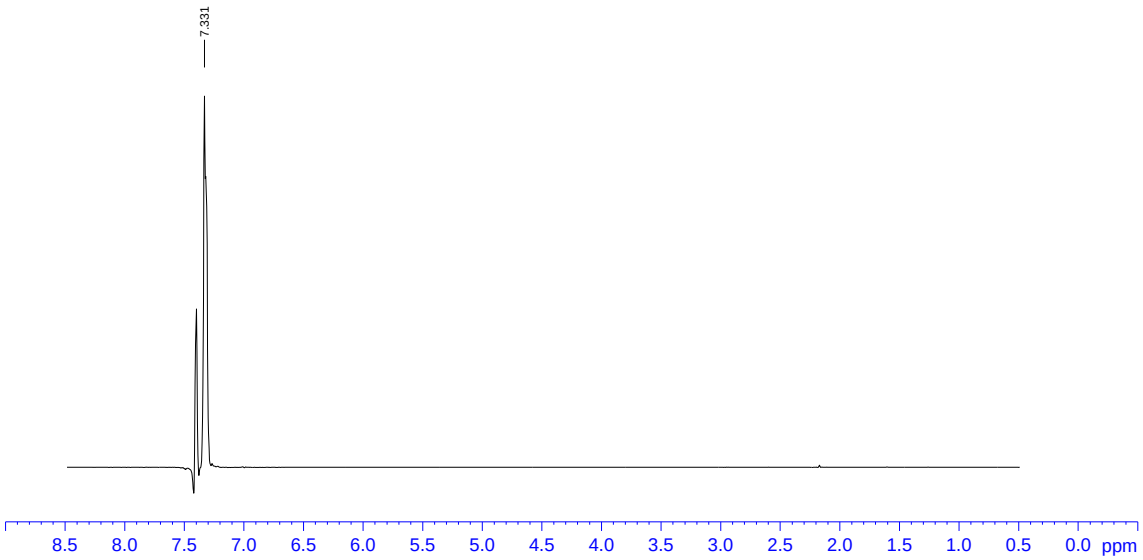
HMBC **(9a)**

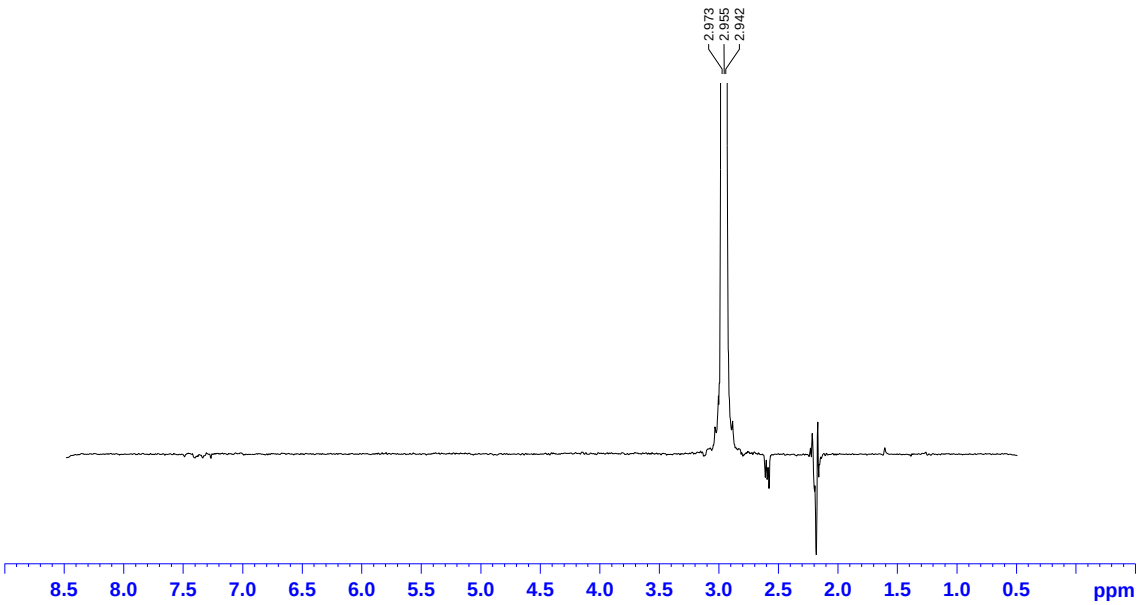


COSY **(9a)**

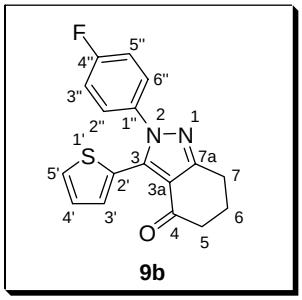


ROESY **(9a)**




2.973
2.955
2.942
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
ppm

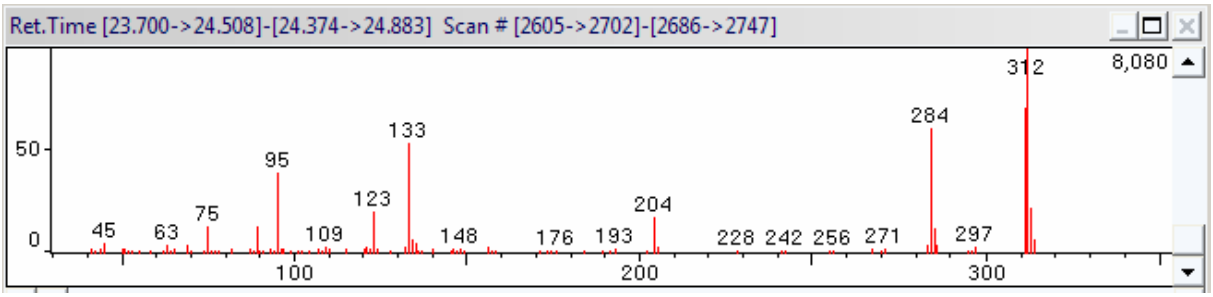
2-(4-fluorophenyl)-3-(2-thienyl)-2,5,6,7-tetrahydro-4*H*-indazol-4-one (9b): Pale yellow solid. Yield 12.8 % (0.018 g) ^{1}H NMR ($CDCl_3$): δ = 2.19 (quintuplet, J = 6.3 Hz, 2 H, H-6), 2.59 (t, J = 6.3 Hz, 2 H, H-5), 2.94 (t, J = 6.3 Hz, 2 H, H-7), 7.01 (dd, J = 5.0 and 3.7 Hz, 1 H, H-4´), 7.09 (collapsed dd, J = 9.2 and 5.0 Hz, 2 H, H-3´´,5´´), 7.31 (dd, J = 9.2 and 5.0 Hz, 2 H, H-2´´,6´´), 7.39 (dd, J = 5.0 and 1.1 Hz, 1 H, H-5´), 7.52 (dd, J = 3.7 and 1.1 Hz, 1 H, H-3´) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.36 (C-6), 23.58 (C-7), 40.02 (C-5), 116.32 (J_{CF} = 22.9 Hz, C-3´´,5´´), 116.74 (C-3a), 127.03 (C-4´), 128.04 (C-2´), 128.42 (J_{CF} = 9.2 Hz, C-2´´,6´´), 129.17 (C-5´), 132.12 (C-3´), 135.44 (J_{CF} = 3.0 Hz, C-1´´), 137.90 (C-3), 157.45 (C-7a), 162.63 (J_{CF} = 250.0 Hz, C-4´´), 193.86 (C-4) ppm. ^{19}F NMR ($CDCl_3$): δ = -111.43 ppm (ddd, J = 12.3, 8.0 and 4.3 Hz, F-4´´) MS: *m/z* (%) = 313 (20), 312 $[M]^+$ (100), 311 (66), 285 (11), 284 (63), 204 (16), 133 (54), 123 (18), 95 (40), 89 (13), 75 (13).



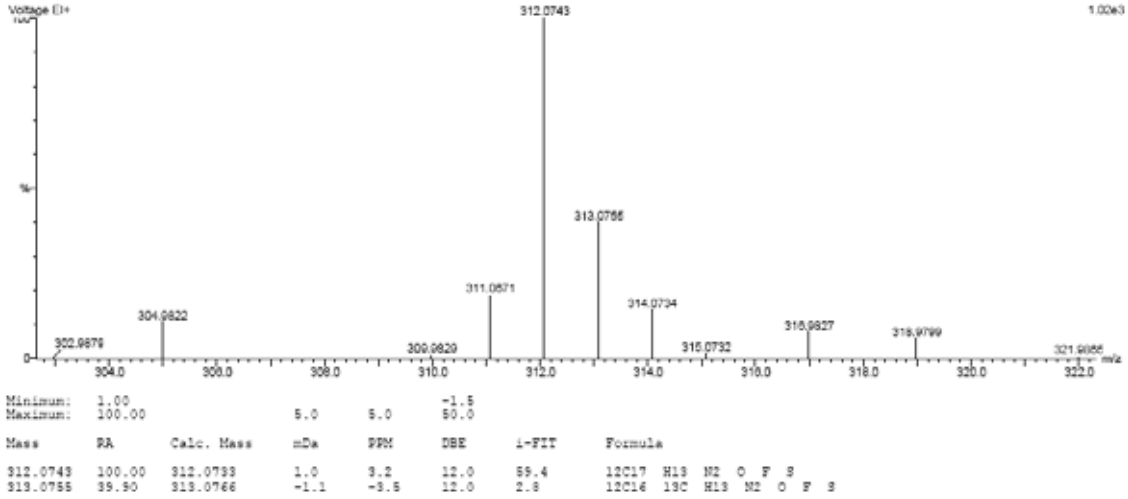
9b

Carbon Number	δH (ppm) (*J* in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.39, dd (5.0, 1.1), 1 H	129.17	3', 4'	2', 3', 4', 3	
4'	7.01, dd (5.0, 3.7), 1 H	127.03	3', 5'	2', 3', 5'	
3'	7.52, dd (3.7, 1.1), 1 H	132.12	4', 5'	2', 4', 5', 3	
2'		128.04			
3		137.90			
3a		116.74			
4		193.86			
5	2.59, t (6.3), 2 H	40.02	6, 7	3a, 4, 6, 7	
6	2.19, quintuplet (6.3), 2 H	23.36	5, 7	4, 5, 7, 7a	
7	2.94, t (6.3), 2 H	23.58	5, 6	3, 3a, 4, 5, 6, 7a	
7a		157.45			
1''		135.44 J_{C-F}=3.0 Hz		2'', 3'', 5'', 6''	
2''/6''	7.31, dd (9.2,5.0), 2 H	128.42 J_{C-F}=9.2 Hz	3'', 5''	1'', 2'', 3'', 4'', 5'', 6''	
3''/5''	7.09, collapsed dd (9.2,5.0), 2 H	116.32 J_{C-F}=22.9 Hz	2'', 6''	1'', 2'', 3'', 4'', 5'', 6''	
4''		162.63 J_{C-F}=250.0 Hz		2'', 3'', 5'', 6''	
^{19}F	-111.43	J_{C-F}= (12.3, 8.0, 4.3) Hz			

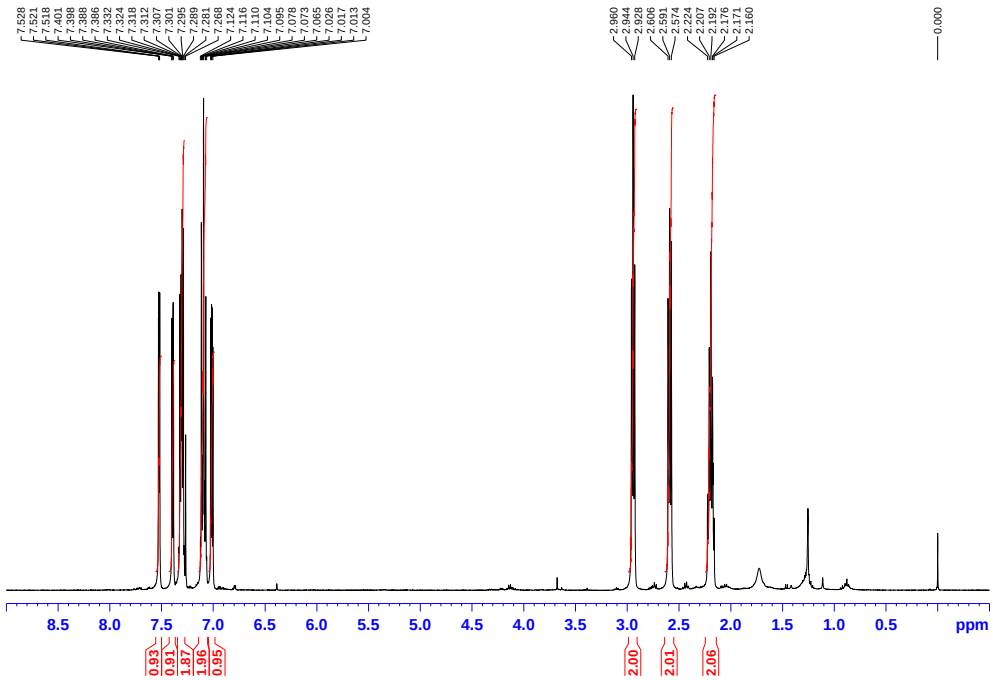
MS **(9b)**

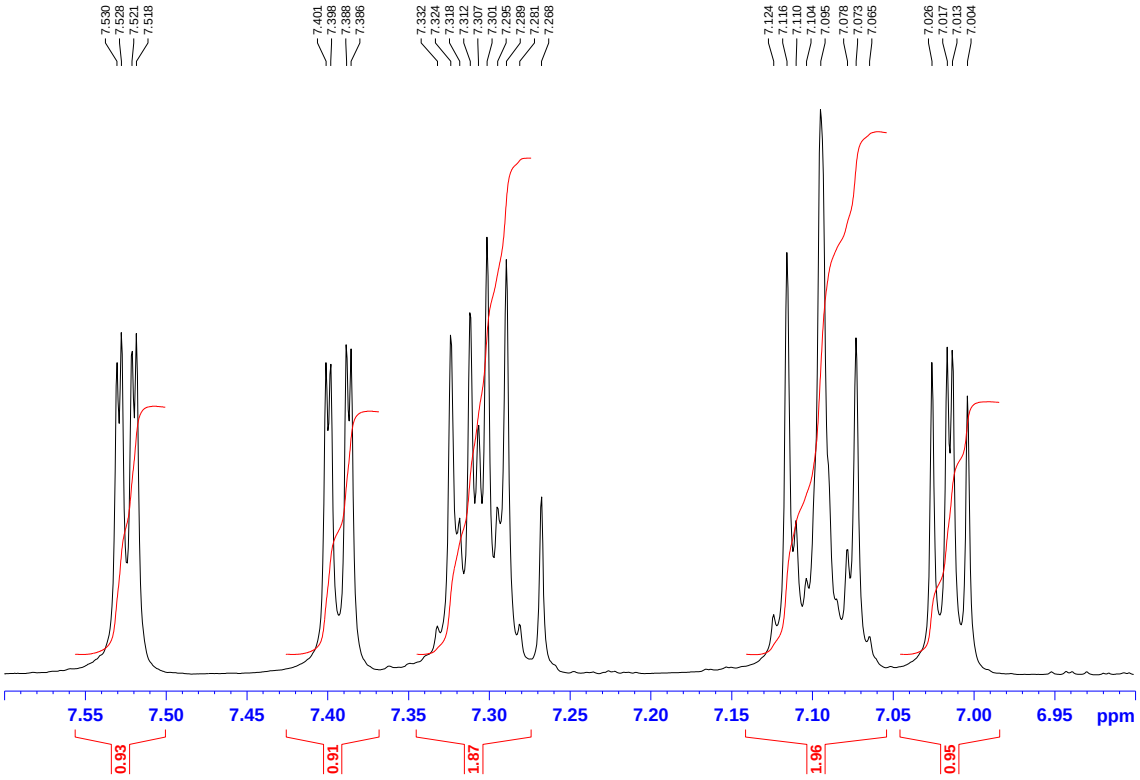


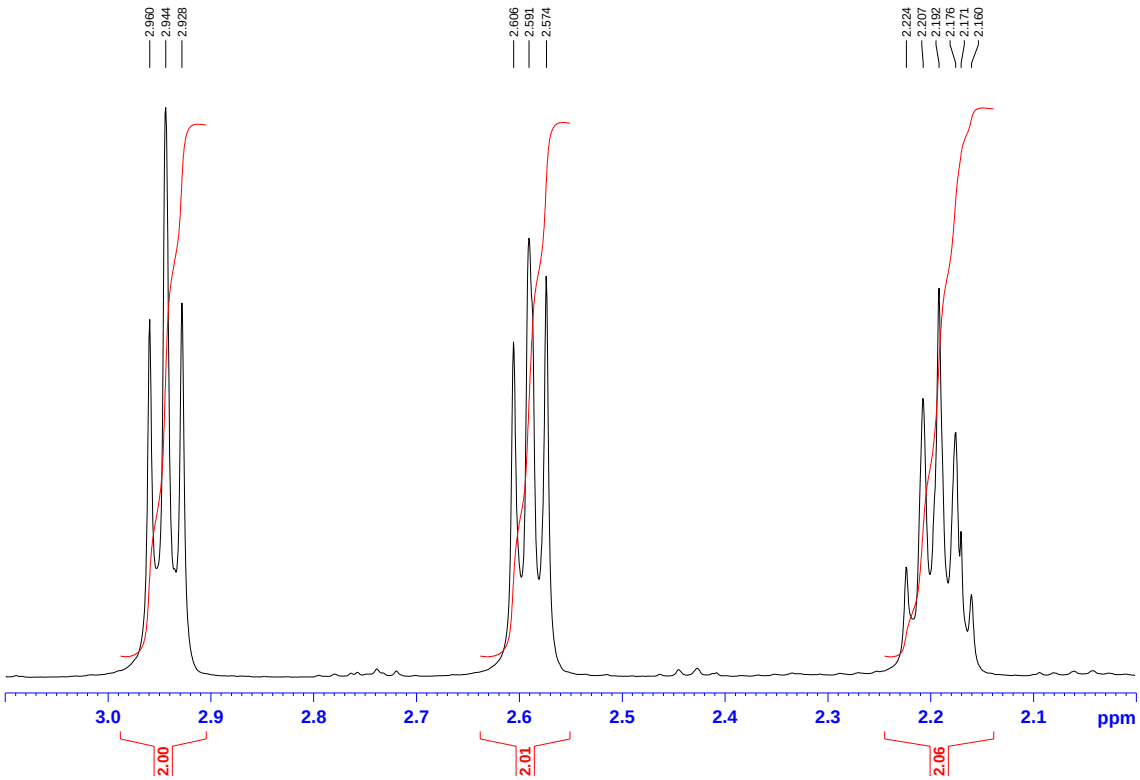
HRMS **(9b)**



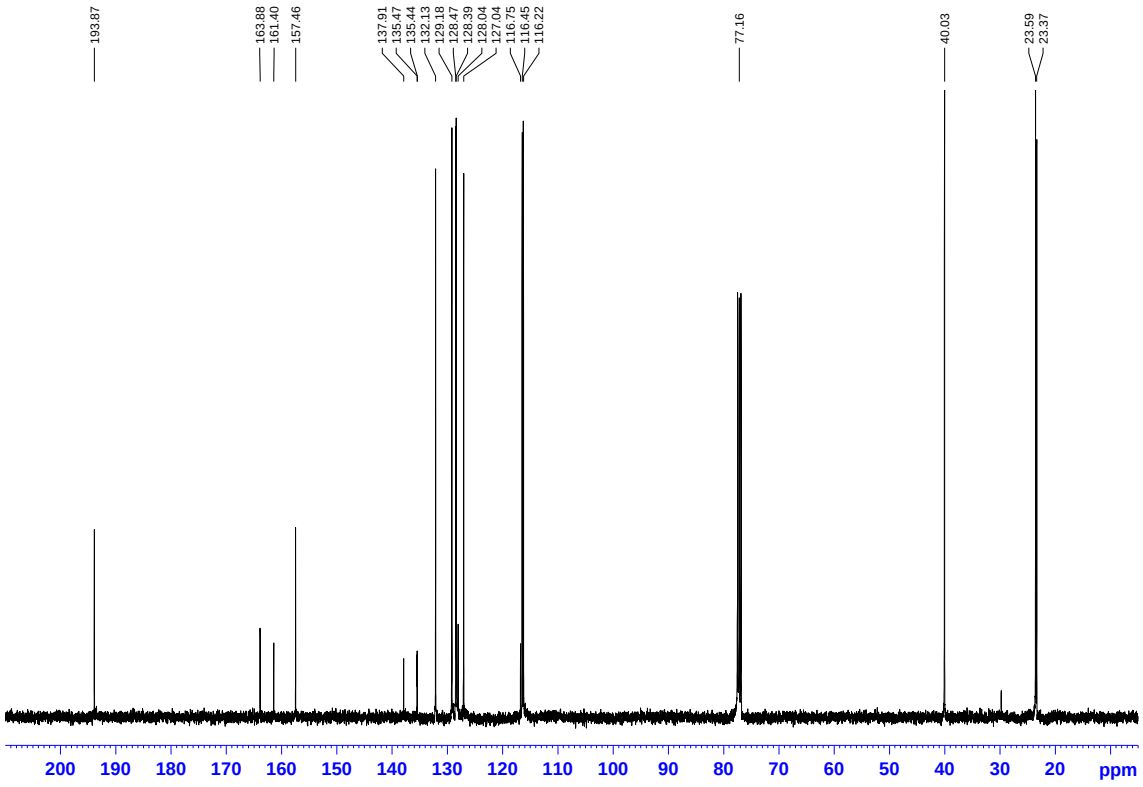
^{1}H **(9b)**



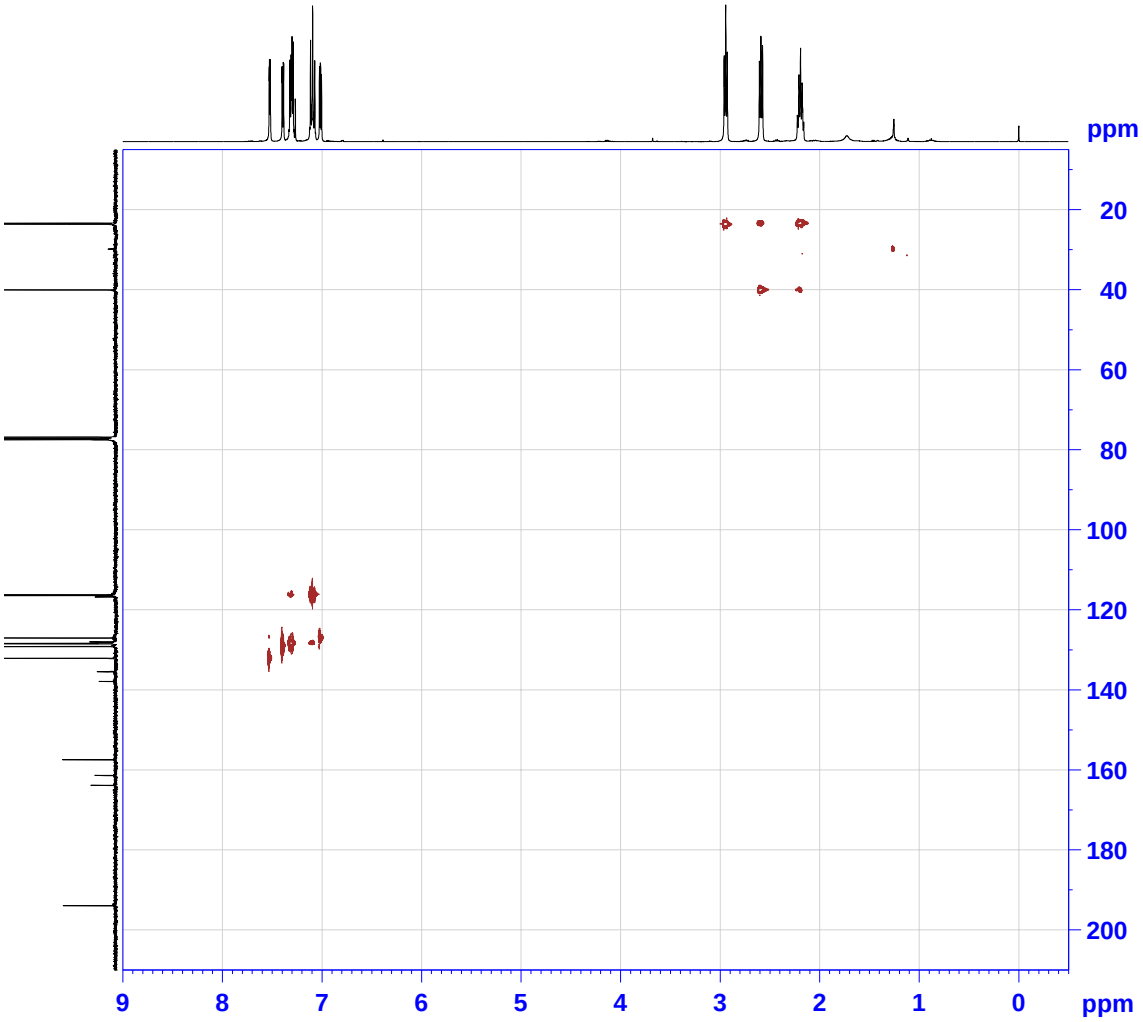

7.530
7.528
7.521
7.518
7.401
7.398
7.388
7.386
7.332
7.324
7.319
7.312
7.307
7.301
7.295
7.289
7.281
7.268
7.124
7.116
7.110
7.104
7.095
7.078
7.073
7.065
7.026
7.017
7.013
7.004
7.55
7.50
7.45
7.40
7.35
7.30
7.25
7.20
7.15
7.10
7.05
7.00
6.95
ppm
0.93
0.91
1.87
1.96
0.95


2.960
2.944
2.928
2.606
2.591
2.574
2.224
2.207
2.192
2.176
2.171
2.160
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
ppm
2.00
2.01
2.06

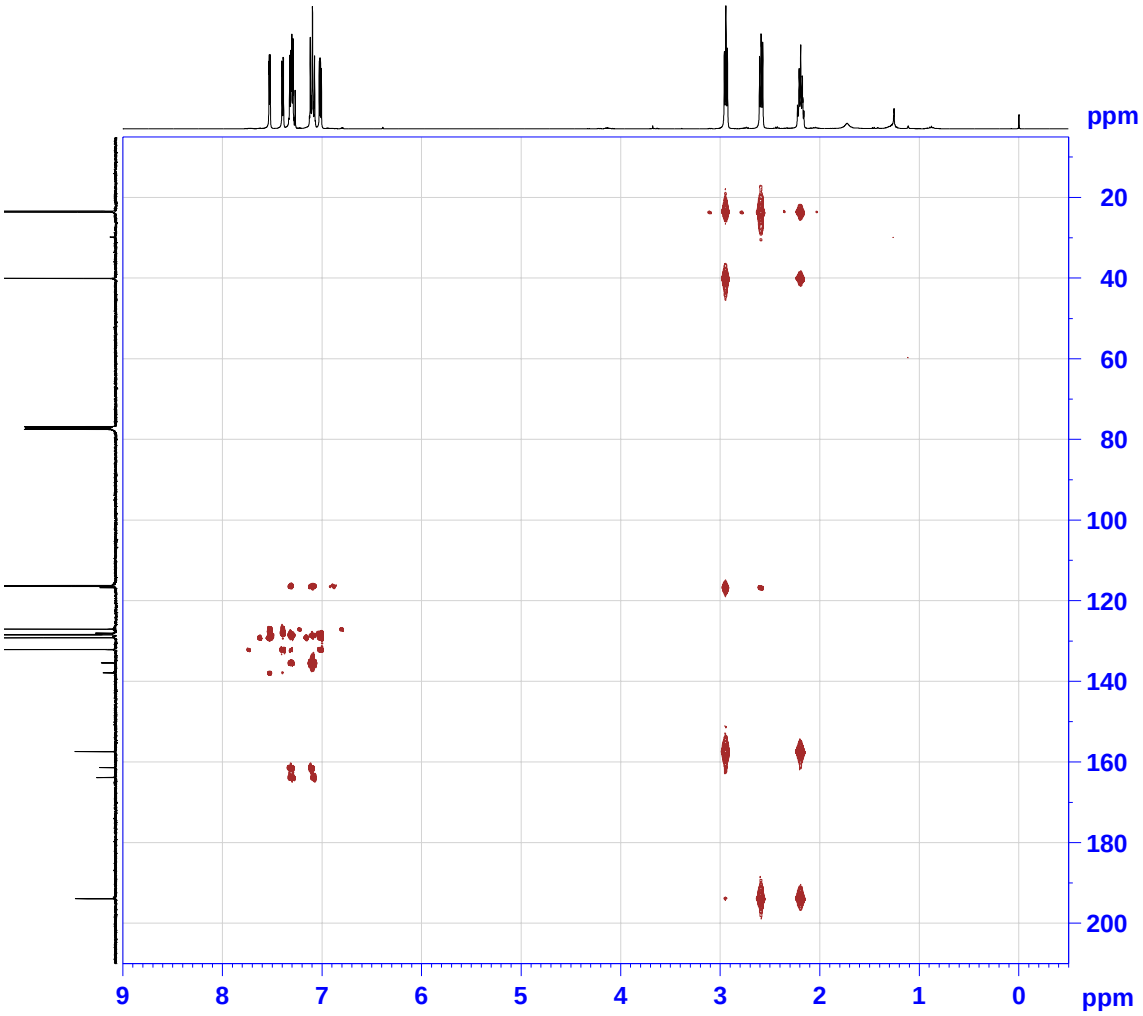
^{13}C **(9b)**


193.87
163.88
161.40
157.46
137.91
135.47
135.44
132.13
129.18
128.47
128.39
128.04
127.04
116.75
116.45
116.22
77.16
40.03
23.59
23.37
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

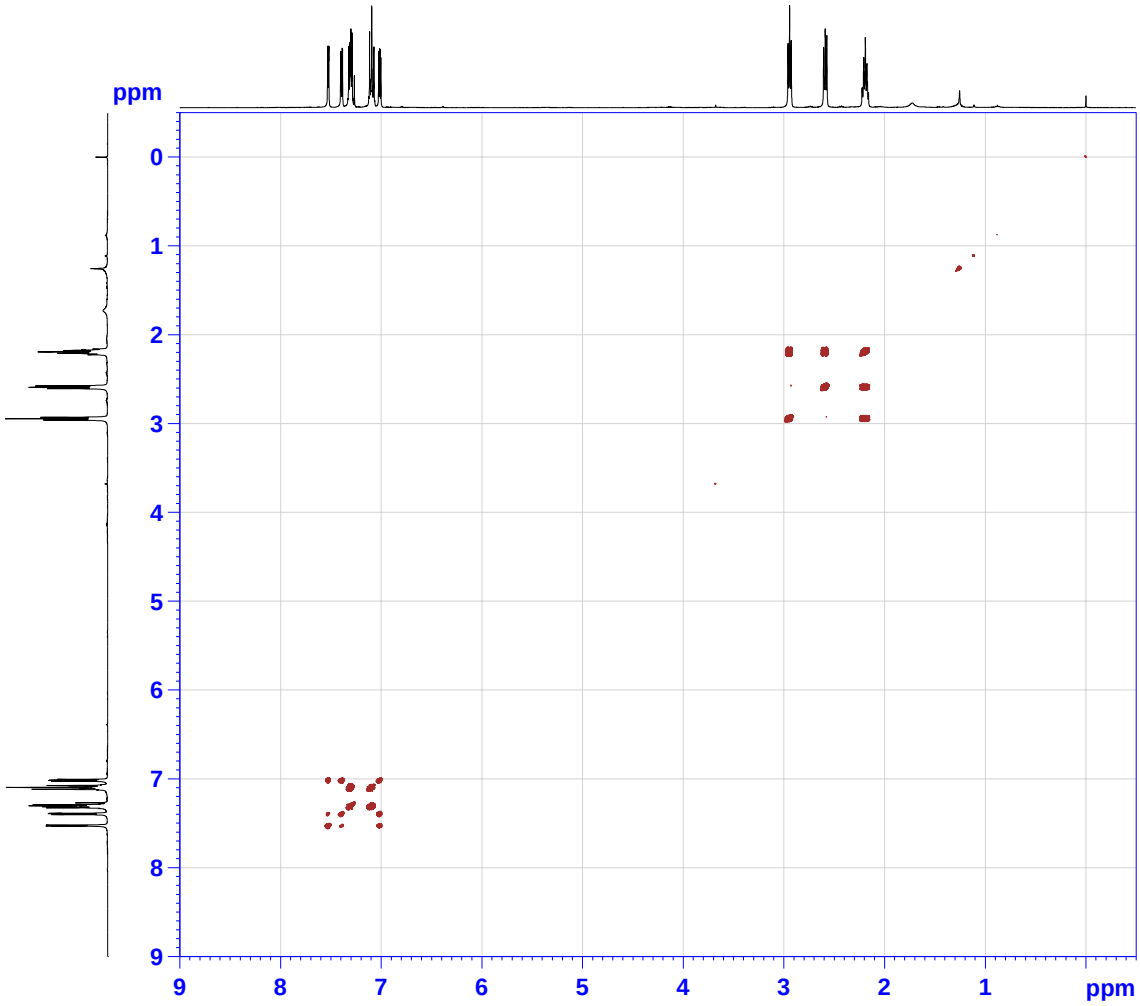
HSQC **(9b)**



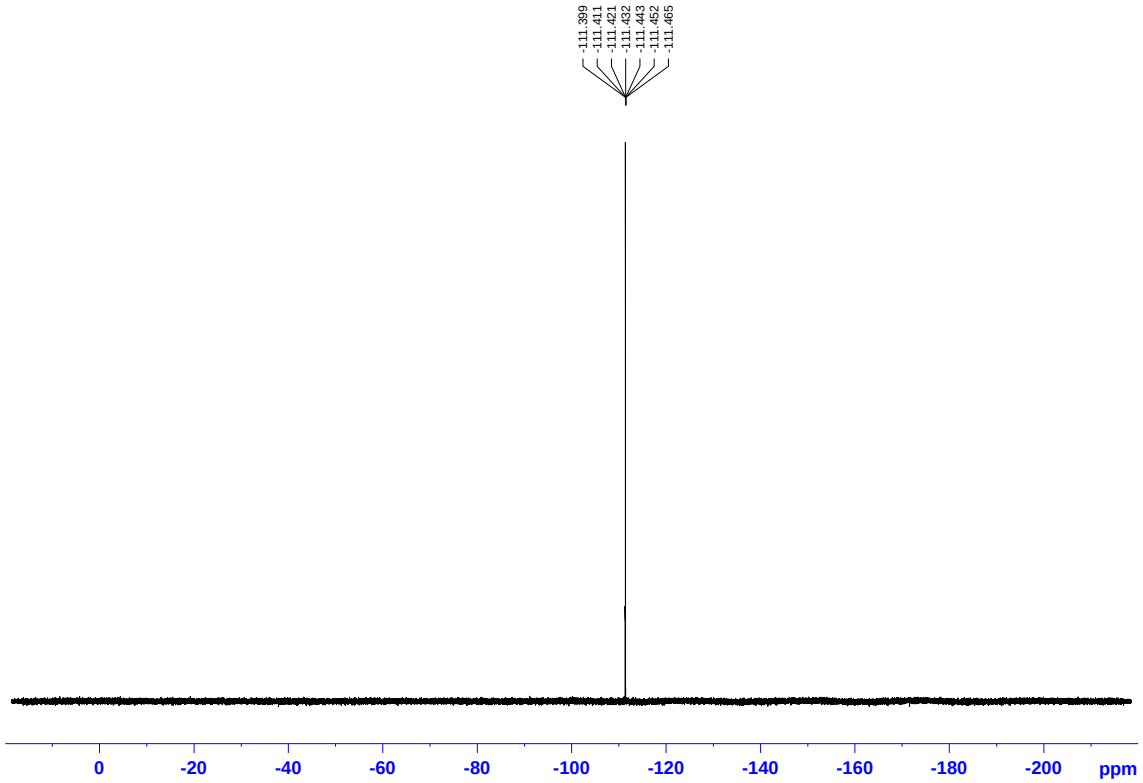
HMBC **(9b)**



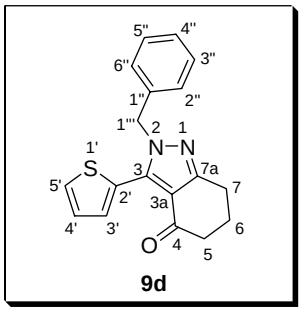
COSY **(9b)**



^{19}F **(9b)**


-111.399
-111.411
-111.421
-111.432
-111.443
-111.452
-111.465
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

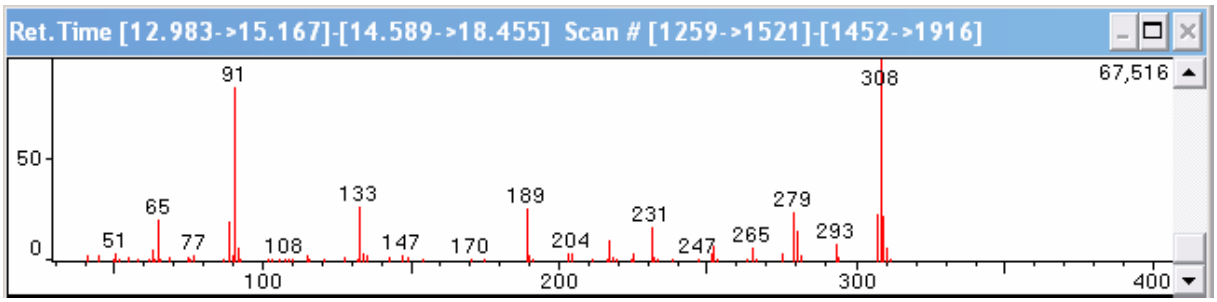
2-benzyl-3-(2-thienyl)-2,5,6,7-tetrahydro-4*H*-indazol-4-one (9d): Pale yellow solid, m.p. 166.3-168.2 ºC. (Dec.) Yield 29.9 % (0.0430 g). ^{1}H NMR ($CDCl_3$): δ = 2.15 (quintuplet, J = 6.2 Hz, 2 H, H-6), 2.52 (t, J = 6.2 Hz, 2 H, H-5), 2.89 (t, J = 6.2 Hz, 2 H, H-7), 5.35 (s, 2 H, H-1´´´), 7.10 (m, 2 H, H-2´´,6´´), 7.10 (dd, J = 5.0 and 3.7 Hz, 1 H, H-4´), 7.25 (dd, J = 3.7 and 1.0 Hz, 1 H, H-5´), 7.29 (m, 2 H, H-3´´,5´´), 7.29 (m, 1 H, H-4´´), 7.51 (dd, J = 5.0 and 1.0 Hz, 1 H, H-3´) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.46 (C-6), 23.46 (C-7), 39.67 (C-5), 53.34 (C-1´´´), 116.86 (C-3a), 126.96 (C-2´´,6´´), 127.17 (C-4´), 127.79 (C-2´), 127.88 (C-5´), 128.78 (C-3´´,5´´), 128.85 (C-4´´), 130.61 (C-3´), 136.38 (C-1´´), 137.42 (C-3), 156.89 (C-7a), 193.66 (C-4) ppm. MS: *m/z* (%) = 309 (22), 308 $[M]^+$ (100), 307 (27), 280 (16), 279 (25), 231 (17), 217 (12), 189 (28), 133 (27), 91 (77), 89 (19), 65 (19).



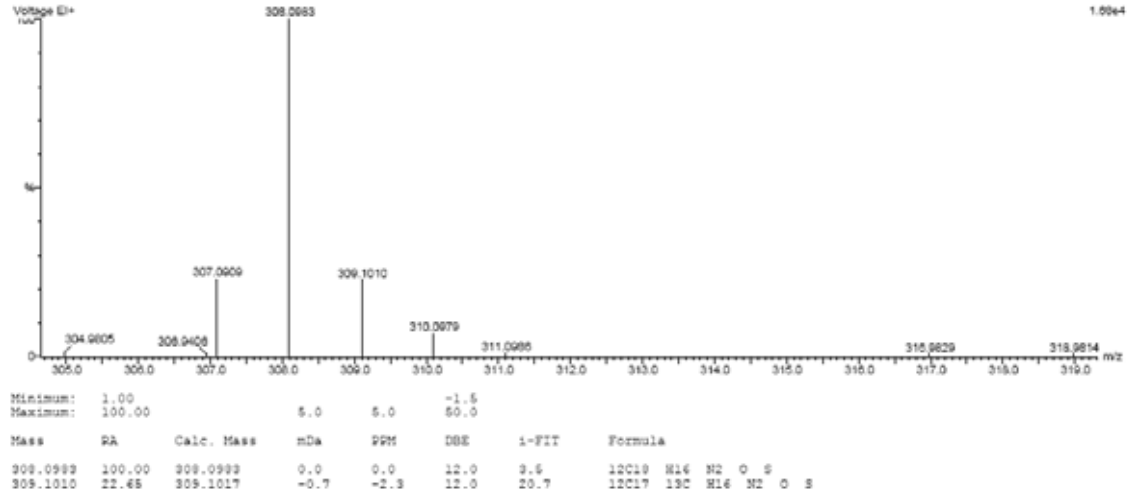
9d

Carbon Number	δH (ppm) (*J* in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.25, dd (5.0, 1.0), 1 H	127.88	3', 4'	2', 3', 4'	
4'	7.10, dd (5.0, 3.7), 1 H	127.17	3', 5'	3', 5'	
3'	7.51, dd (5.0, 1.0), 1 H	130.61	4', 5'	2', 4', 5'	
2'		127.79			
3		137.42			
3a		116.86			
4		193.66			
5	2.52, t (6.2), 2 H	39.67	6, 7	3a, 4, 6, 7	
6	2.15, quintuplet (6.2), 2 H	23.46	5, 7	4, 5, 7, 7a	
7	2.89, t (6.2), 2 H	23.46	5, 6	3a, 5, 6, 7a	
7a		156.89			
1'''	5.35, s, 2 H	53.34	2'', 6''	1'', 2'', 6''	
1''		136.38			
2''/6''	7.09-7.11, m, 2 H	126.96	3'', 4'', 5''	3'', 4'', 5''	
3''/5''	7.25-7.33, m, 2 H	128.78	2'', 4'', 6''	2'', 4'', 6''	
4''	7.25-7.33, m, 1 H	128.85	2'', 3'', 5'', 6''	3'', 5''	

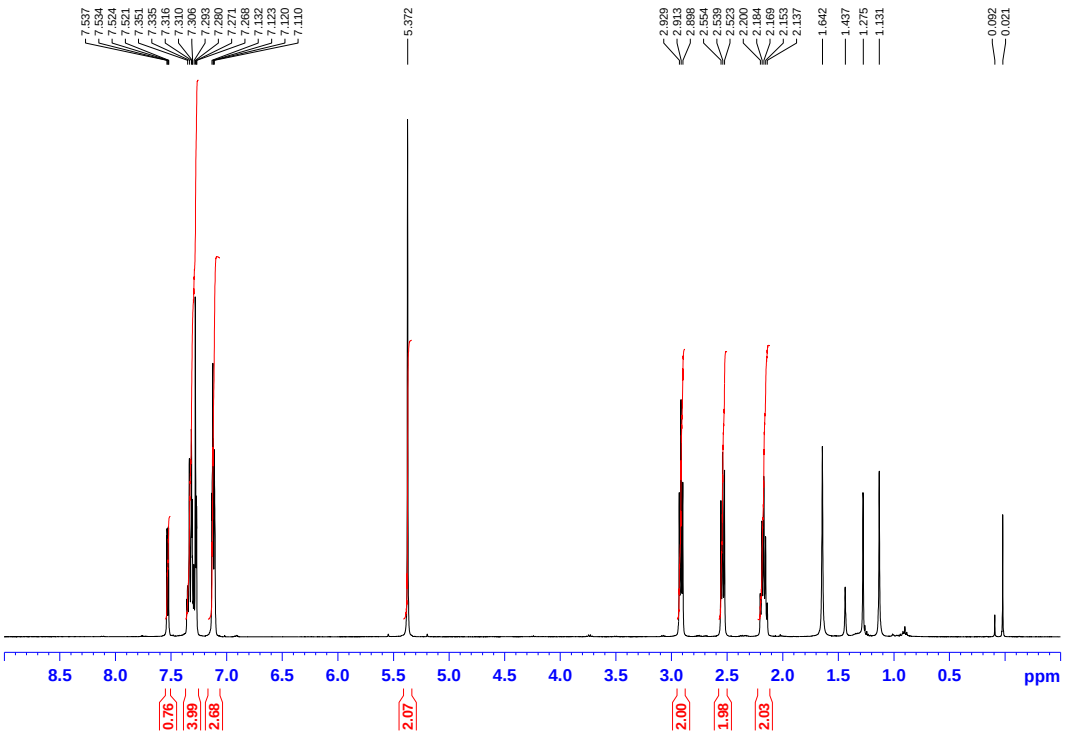
MS **(9d)**

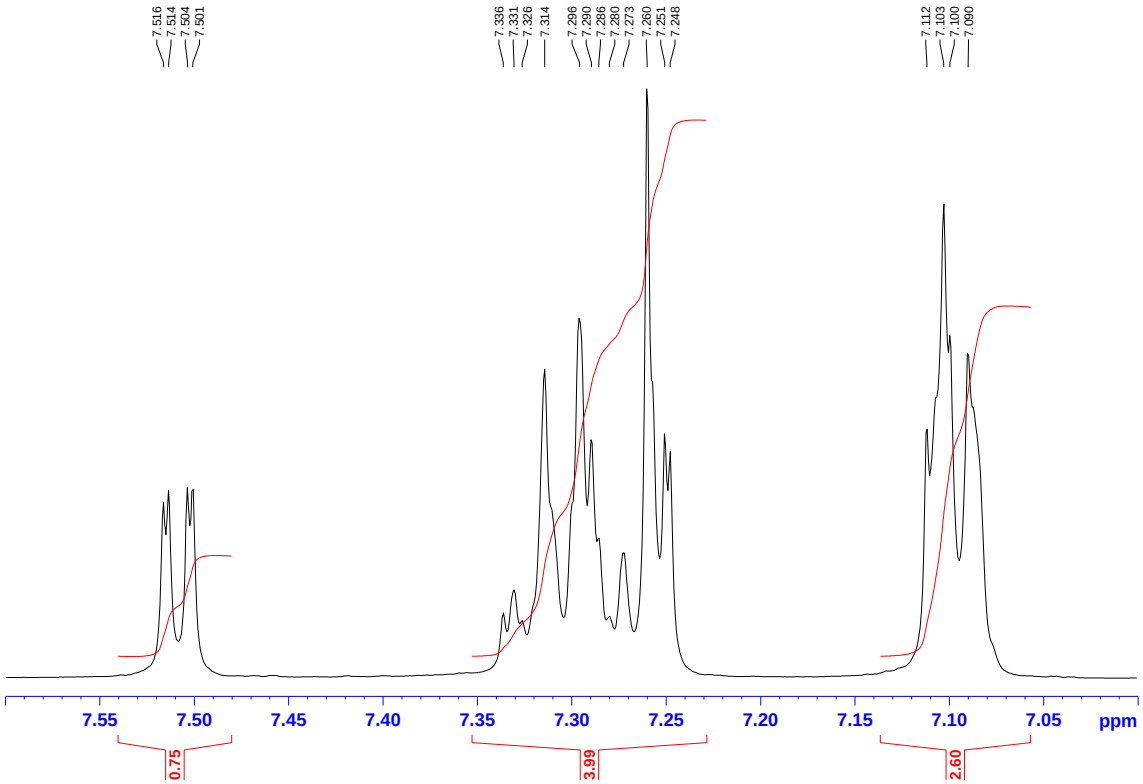


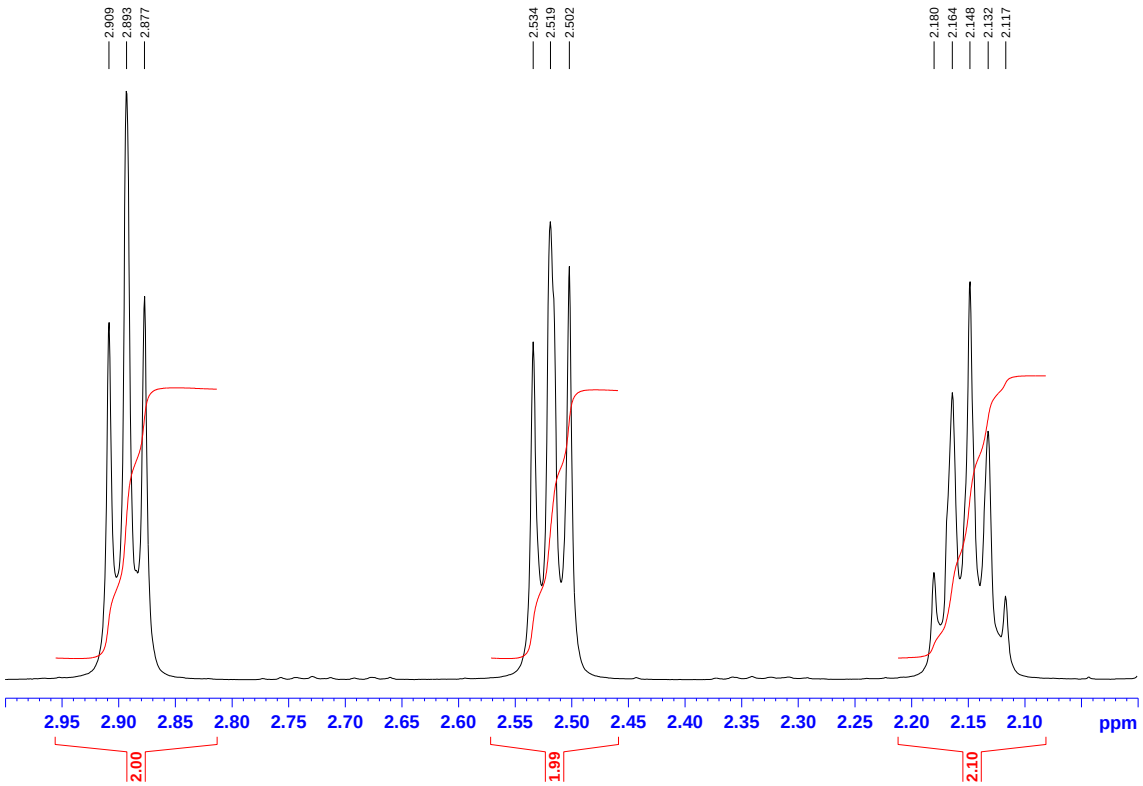
HRMS **(9d)**



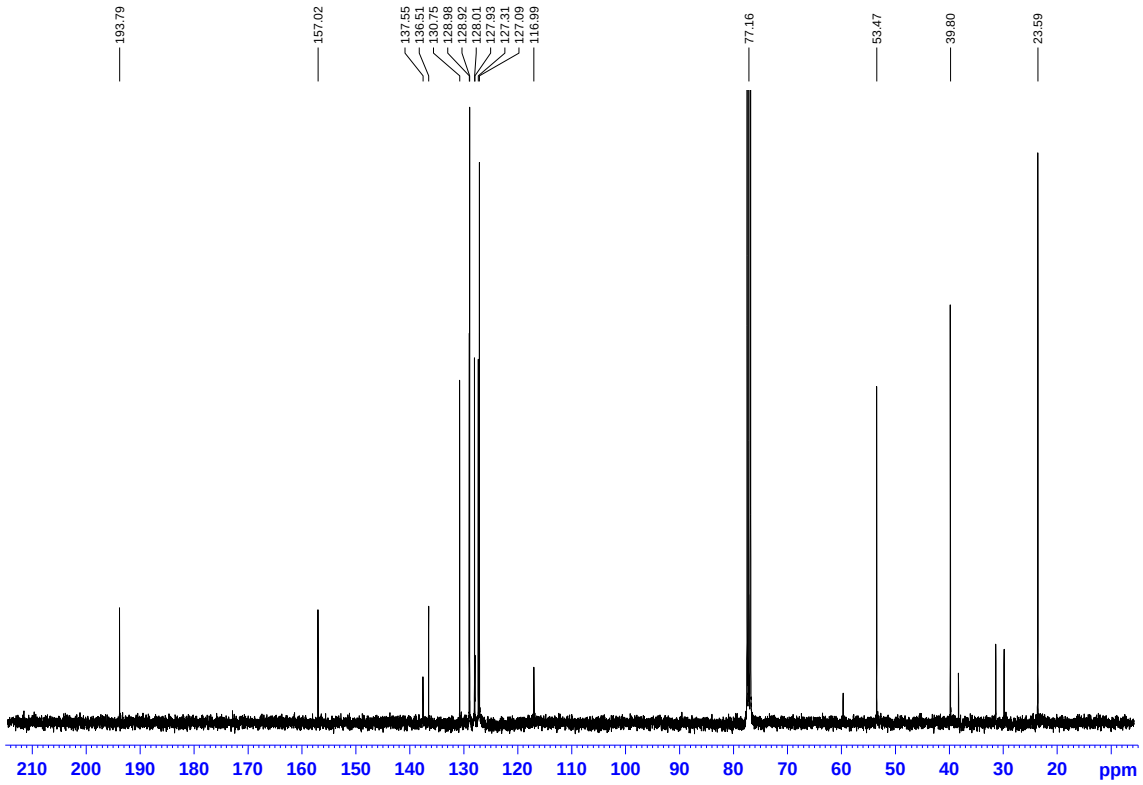
^{1}H **(9d)**



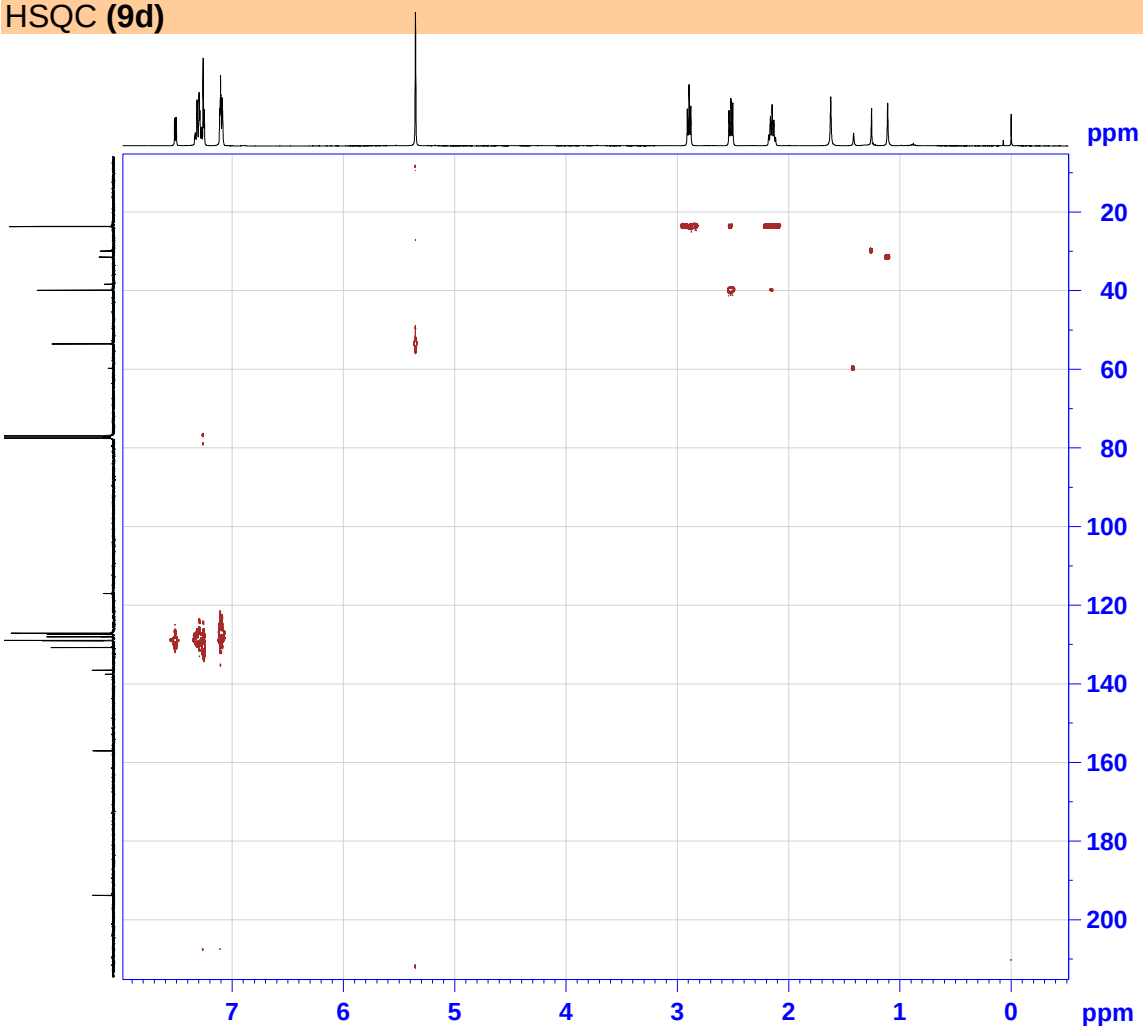

7.516
7.514
7.504
7.501
7.336
7.331
7.326
7.314
7.296
7.290
7.286
7.280
7.273
7.260
7.251
7.248
7.112
7.103
7.100
7.090
7.55
7.50
7.45
7.40
7.35
7.30
7.25
7.20
7.15
7.10
7.05
ppm
0.75
3.99
2.60


2.909
2.893
2.877
2.534
2.519
2.502
2.180
2.164
2.148
2.132
2.117
2.95
2.90
2.85
2.80
2.75
2.70
2.65
2.60
2.55
2.50
2.45
2.40
2.35
2.30
2.25
2.20
2.15
2.10
ppm
2.00
1.99
2.10

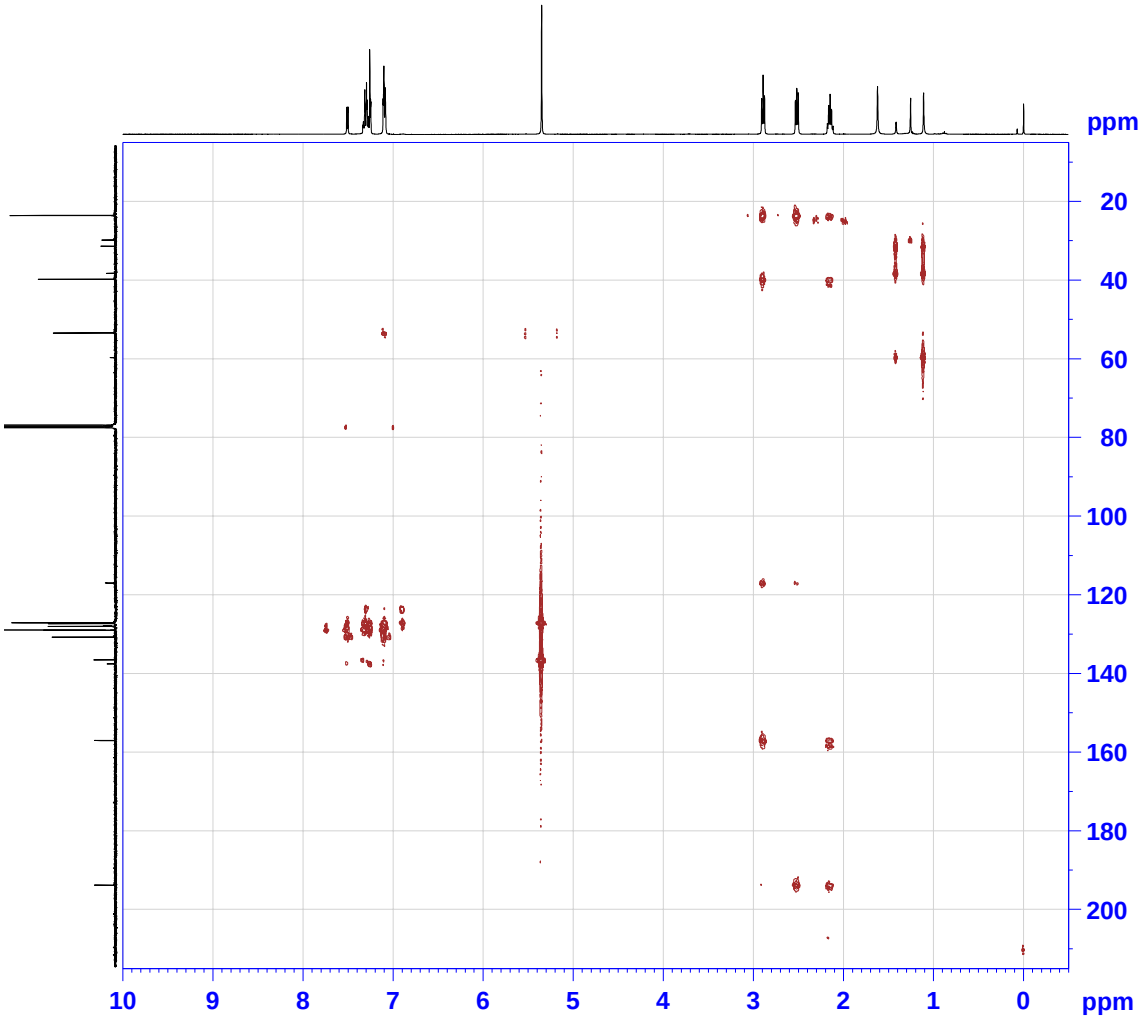
^{13}C **(9d)**



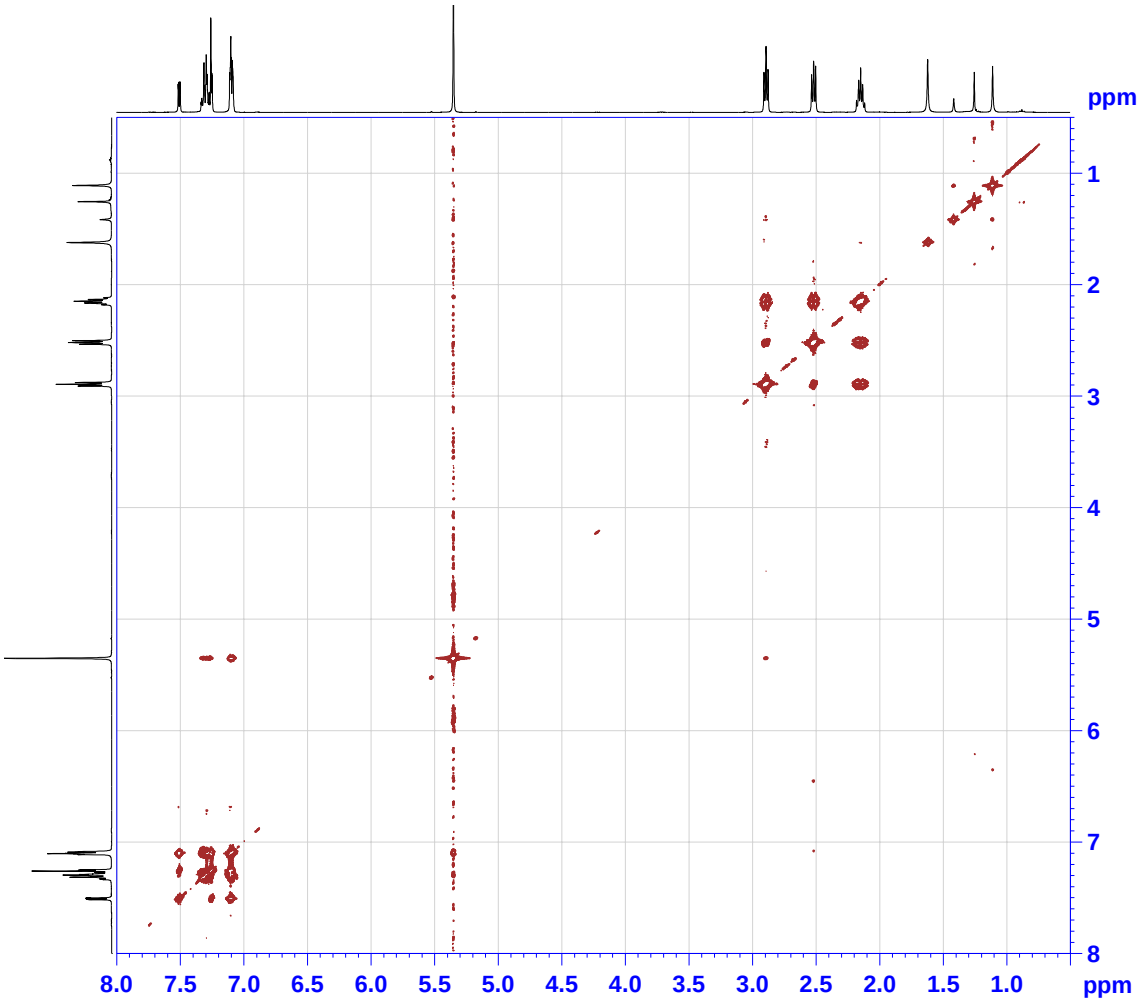
HSQC **(9d)**



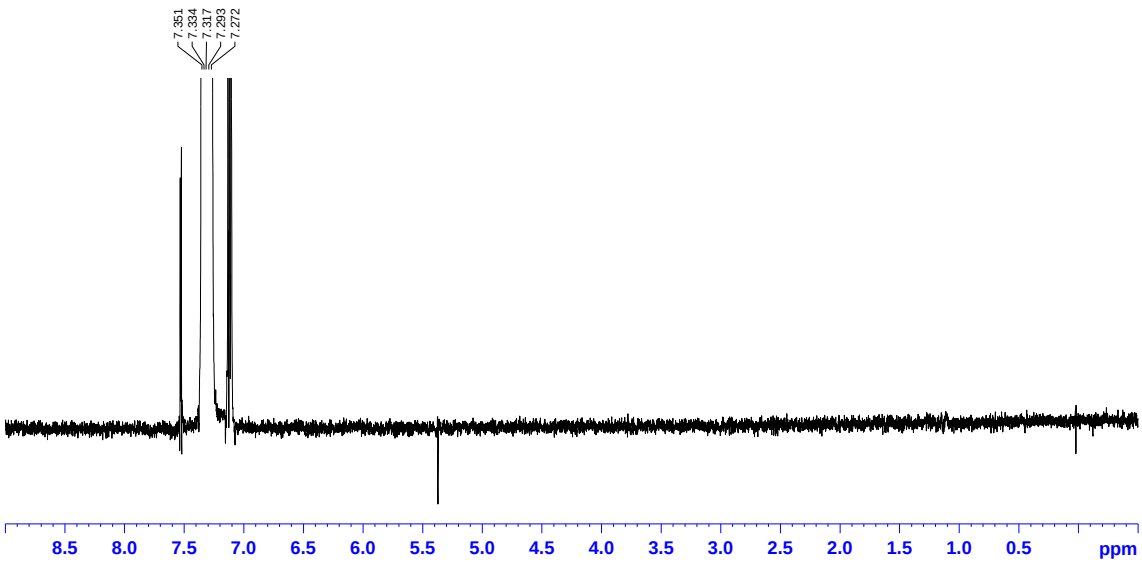
HMBC **(9d)**



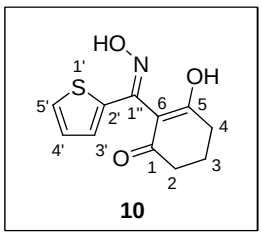
COSY **(9d)**



ROESY **(9d)**



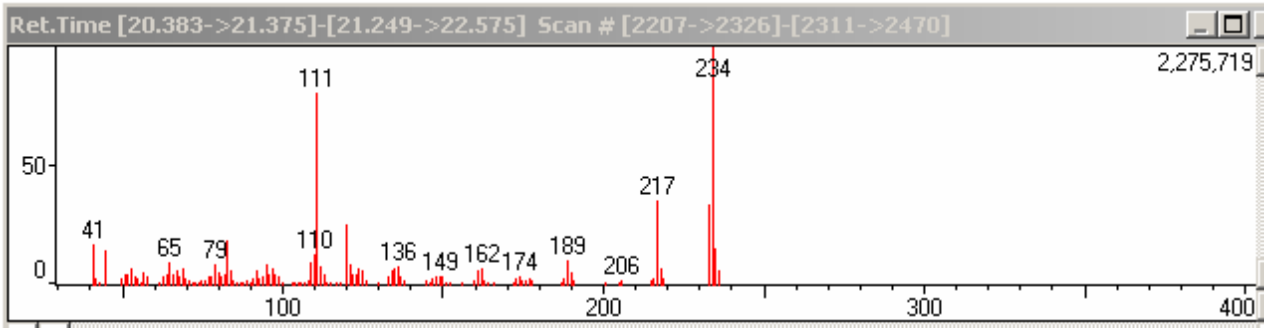
3-hydroxy-2-[(hydroxyimino)(2-thienyl)methyl]cyclohex-2-en-1-one (10): Pale yellow solid, m.p. 189 ºC (dec.). Yield 26.9 % (0.0287 g). ^{1}H NMR (CD_3CN): δ = 1.90 (quintuplet, J = 6.2 Hz, 2 H, H-3), 2.75 (t, J = 6.2 Hz, 2 H, H-4), 2.78 (t, J = 6.2 Hz, 2 H, H-2), 7.21 (dd, J = 5.0 and 3.8 Hz, 1 H, H-4´), 7.67 (dd, J = 5.0 and 1.1 Hz, 1 H, H-5´), 8.44 (dd, J = 3.8 and 1.1 Hz, 1 H, H-3´), 9.10 (s; 1 H, OH-5) ppm. ^{13}C NMR (CD_3CN): δ = 21.56 (C-3), 22.20 (C-4), 23.58 (C-2), 108.00 (C-6), 128.80 (C-4´), 130.41 (C-2´), 131.08 (C-5´), 131.78 (C-3´), 150.51 (C-5), 160.33 (C-1´´), 163.85 (C-1) ppm. IR (KBr): ν = 3085, 3063, 2916, 2873, 1716, 1628, 1591, 1404, 941, 892, 710 cm^{-1}. MS: *m/z* (%) = 237 (1) [M]$^{+}$, 235 (15), 234 (100), 233 (33), 217 (27), 120 (25), 111 (76), 110 (12), 83 (17), 45 (14), 41 (16).



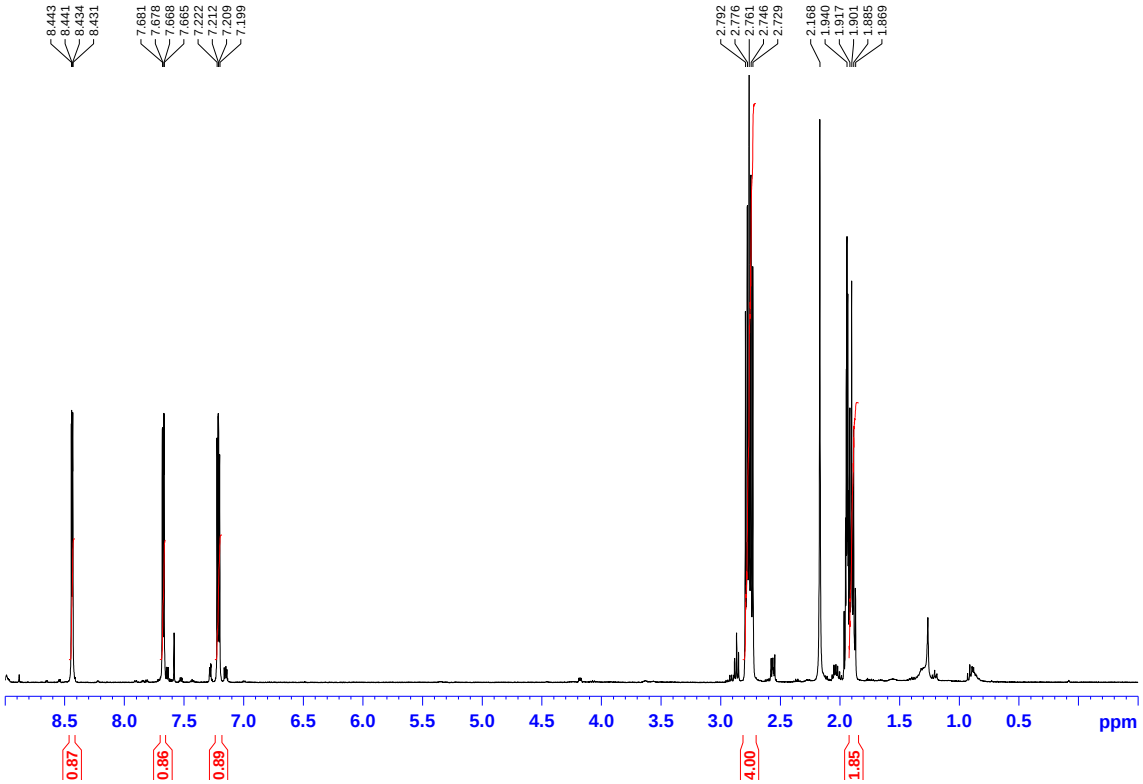
10

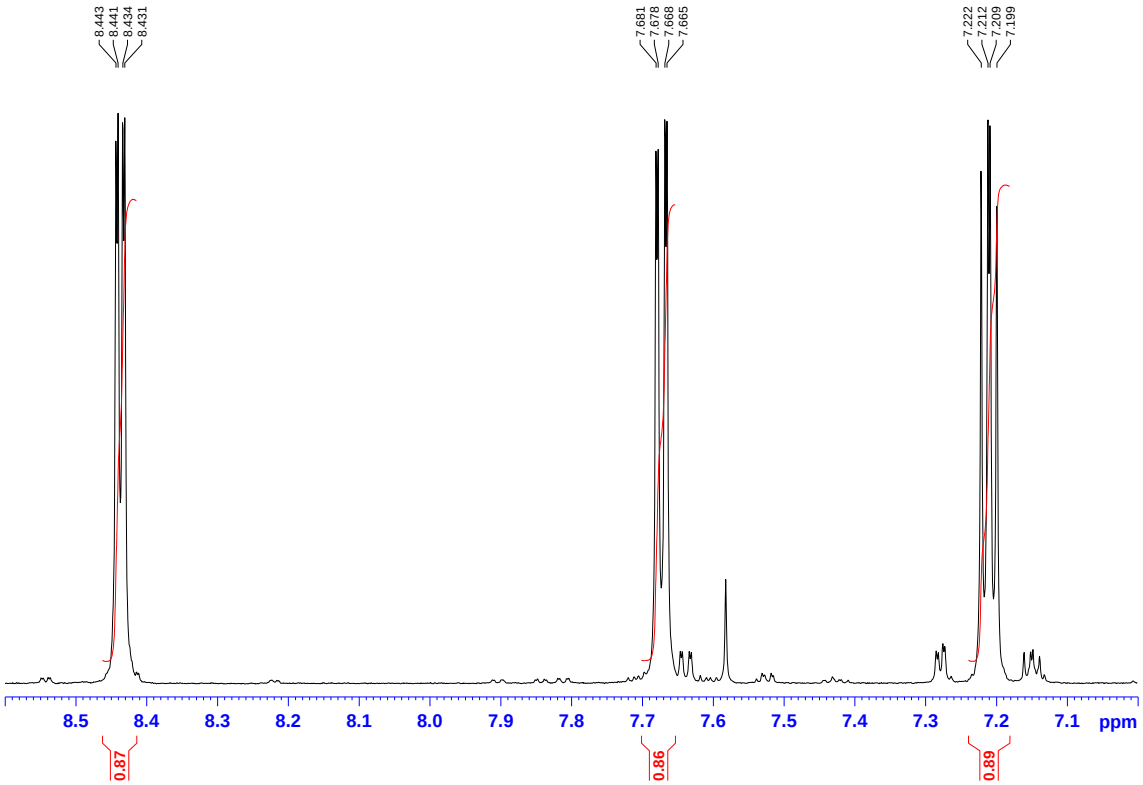
Carbon Number	δH (ppm) (J in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.67, dd (5.0, 1.1), 1 H	131.08	3', 4'	2', 3', 4'	
4'	7.21, dd (5.0, 3.8), 1 H	128.80	3', 5'	3', 5'	
3'	8.44, dd (3.8, 1.1), 1 H	131.78	4', 5'	2', 4', 5', 1''	
2'		130.41			
1''		160.33			
6		108.00			
1		163.85			
2	2.78, t (6.2), 2 H	23.58	3, 4	1, 3, 4, 6	
3	1.90, quintuplet (6.2), 2 H	21.56	2, 4	1, 2, 4, 5	
4	2.75, t (6.2), 2 H	22.20	2, 3	2, 3, 5, 6	
5 (OH)	9.10, s, 1 H (OH)	150.51			

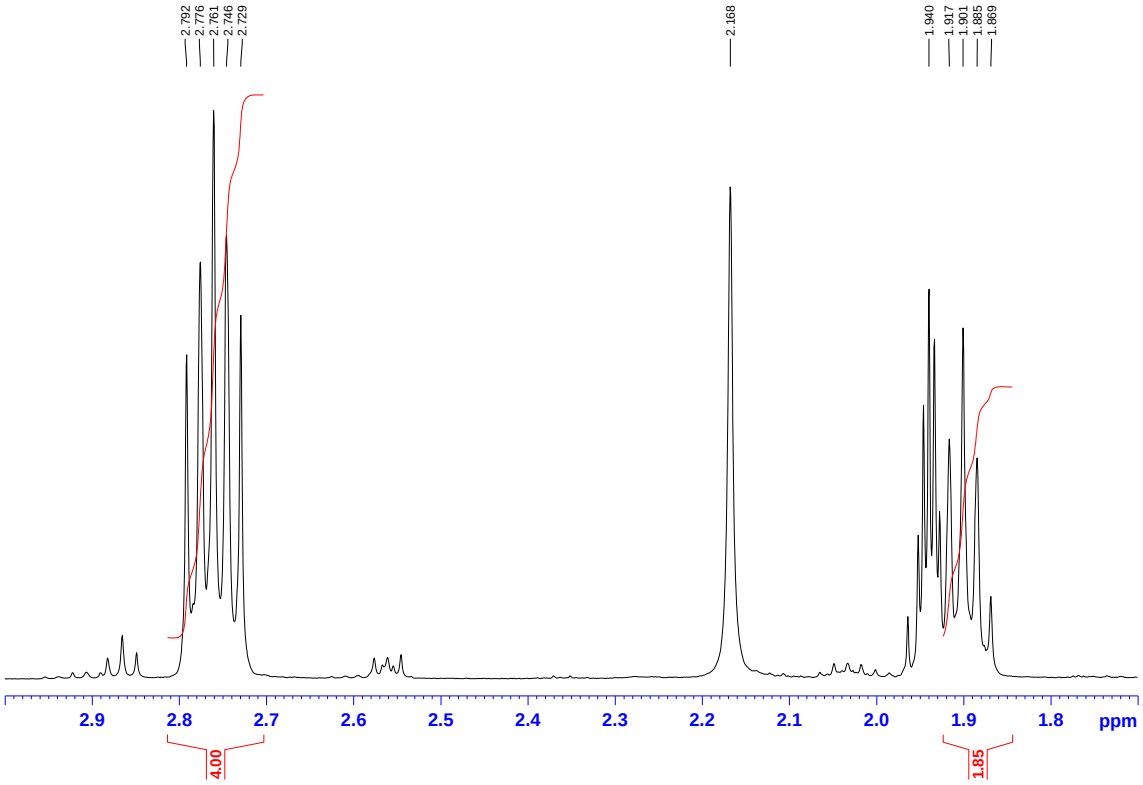
MS **(10)**



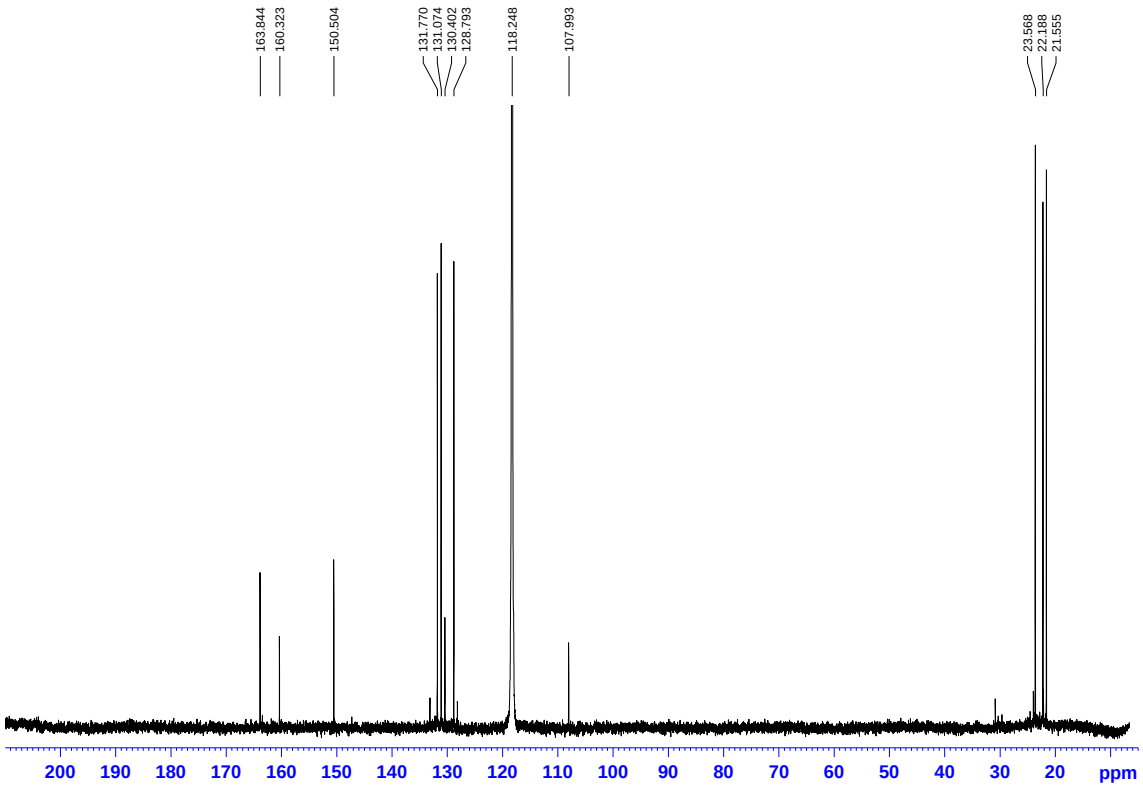
^{1}H **(10)**


8.443
8.441
8.434
8.431
7.681
7.678
7.668
7.665
7.222
7.212
7.209
7.199
2.792
2.776
2.761
2.746
2.729
2.168
1.940
1.917
1.901
1.885
1.869
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 ppm
0.87
0.86
0.89
4.00
1.85

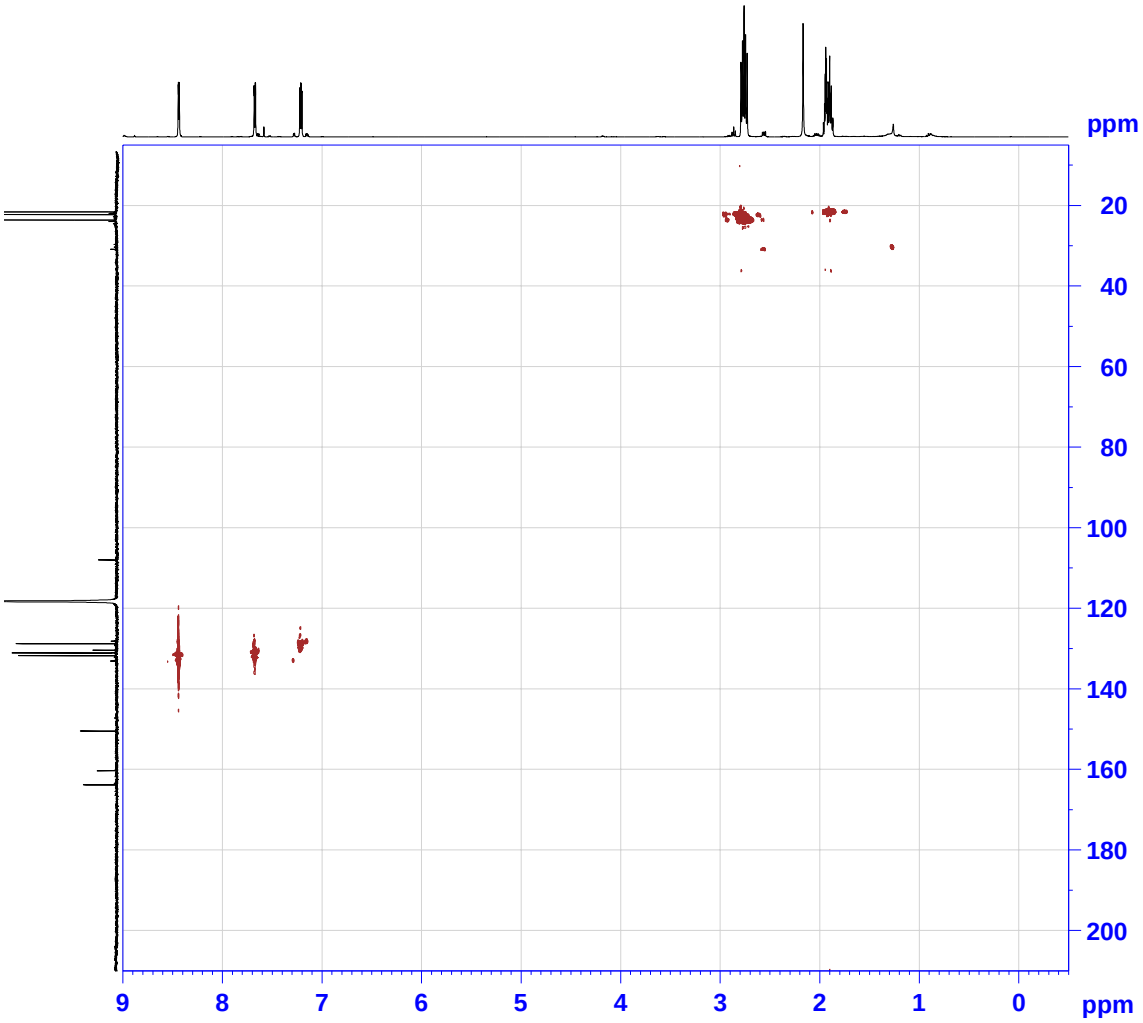

8.443
8.441
8.434
8.431
7.681
7.678
7.668
7.665
7.222
7.212
7.209
7.199
8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 ppm
0.87
0.86
0.89


2.792
2.776
2.761
2.746
2.729
2.168
1.940
1.917
1.901
1.885
1.869
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
ppm
4.00
1.85

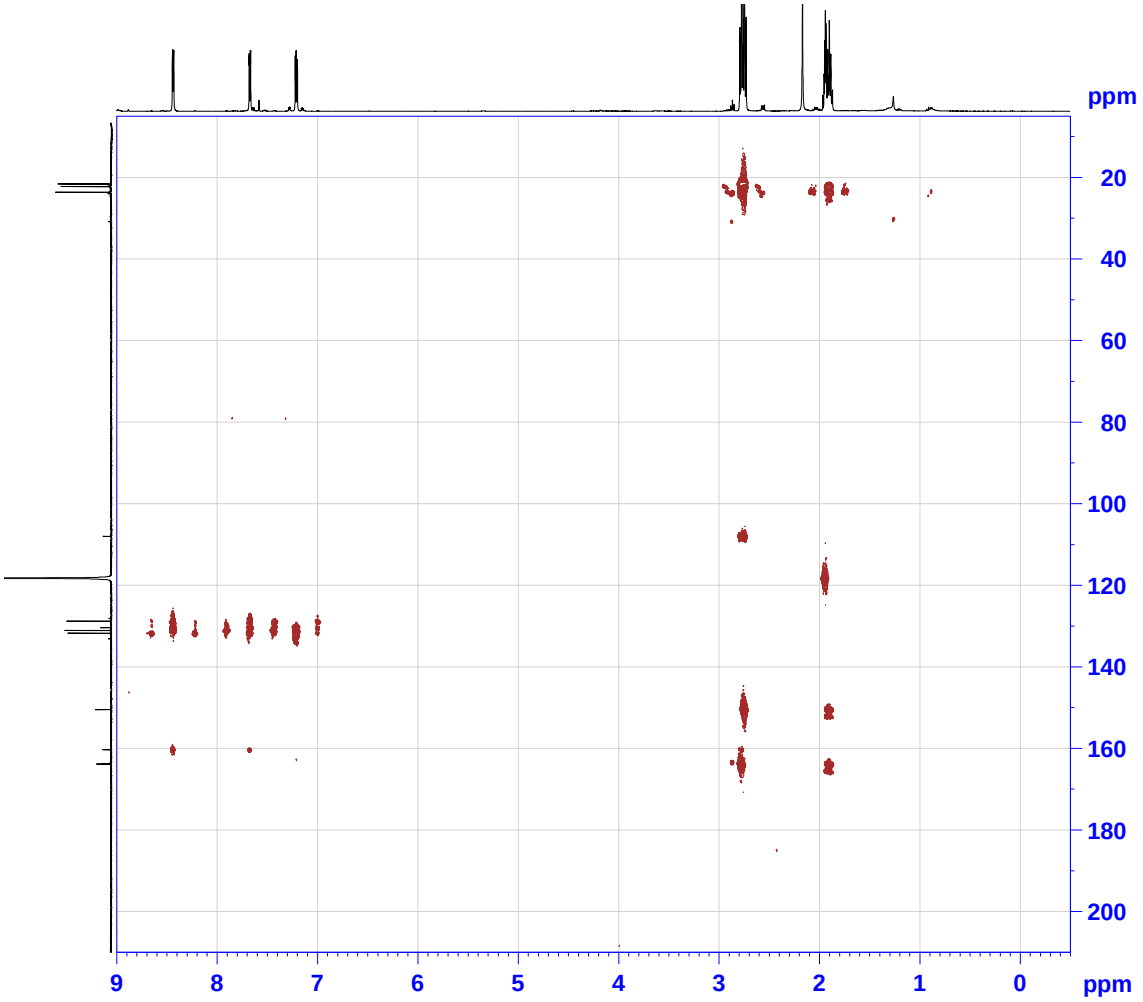
^{13}C **(10)**


163.844
160.323
150.504
131.770
131.074
130.402
128.793
118.248
107.993
23.568
22.188
21.555
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

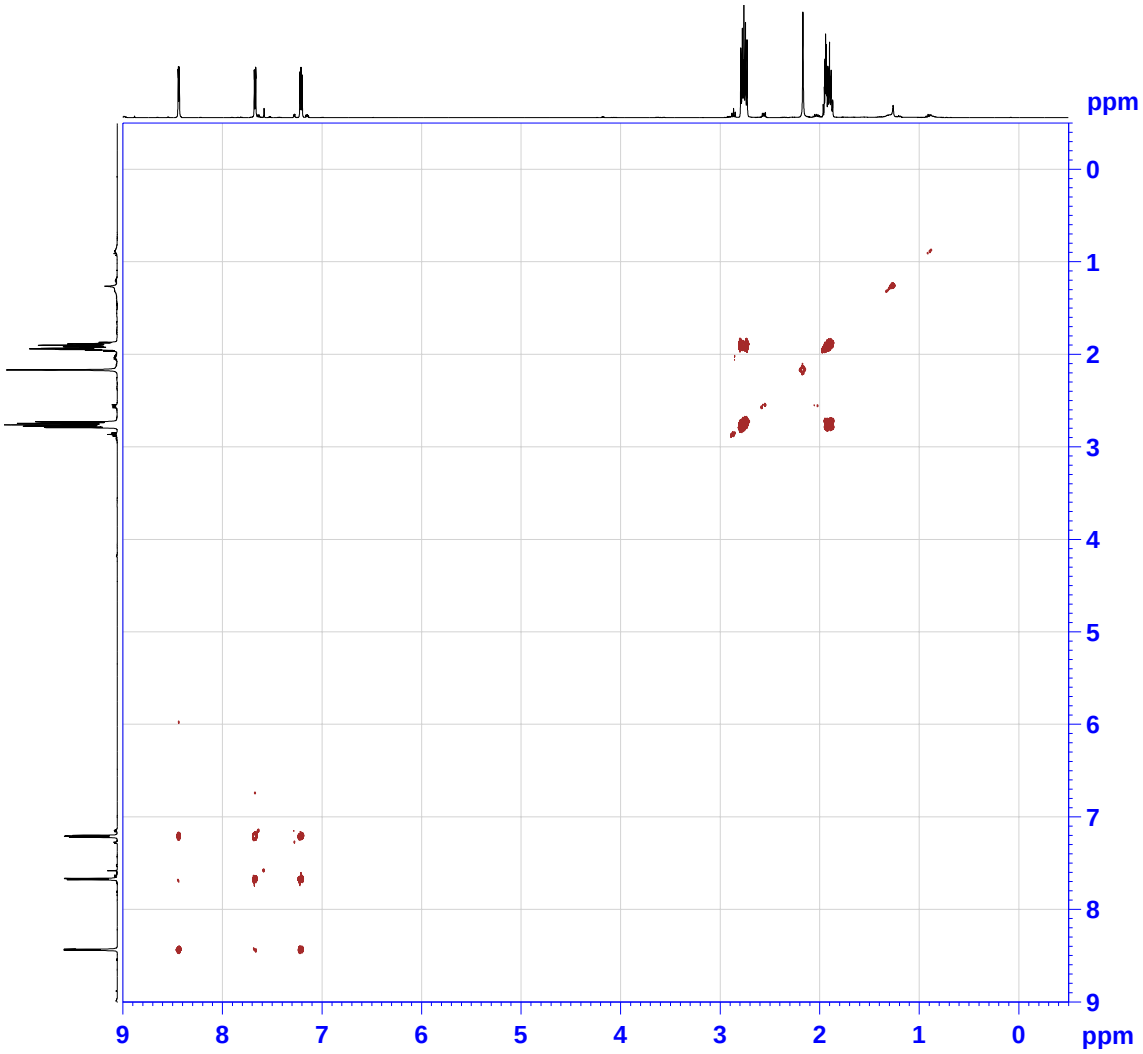
HSQC **(10)**



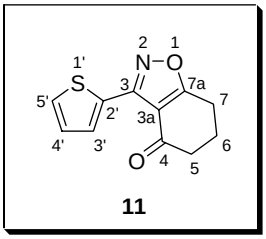
HMBC **(10)**



COSY **(10)**



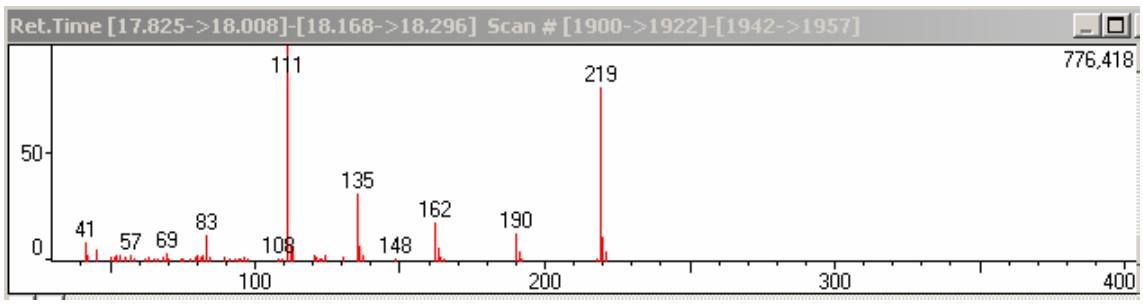
3-(2-thienyl)-6,7-dihydro-1,2-benzisoxazol-4(5*H*)-one (11): White solid, m.p. 137–139.5 ºC. Yield 42.4 % (0.0418 g). ^{1}H NMR (CD_3CN): δ = 2.13 (quintuplet, J = 6.2 Hz, 2 H, H-6), 2.56 (t, J = 6.2 Hz, 2 H, H-5), 2.91 (t, J = 6.2 Hz, 2 H, H-7), 7.28 (t, J = 5.0 Hz, 1 H, H-4´), 7.81 (d, J = 5.0 Hz, 1 H, H-5´), 8.54 (d, J = 3.7 Hz, 1 H, H-3´) ppm. ^{13}C NMR (CD_3CN): δ = 21.94 (C-7), 22.89 (C-6), 39.95 (C-5), 111.86 (C-3a), 128.83 (C-2´), 129.41 (C-4´), 133.53 (C-3´), 133.62 (C-5´), 165.46 (C-3), 166.03 (C-7a), 193.68 (C-4) ppm. IR (KBr): ν = 3111, 3090, 2948, 2912, 2847, 1729, 1676, 1575, 1480, 1427, 1296, 745 cm^{-1}. MS: *m/z* (%) = 220 (16), 219 $[M]^+$ (99), 190 (22), 163 (10), 162 (28), 136 (12), 135 (55), 112 (11), 111 (100), 83 (21), 41 (15).



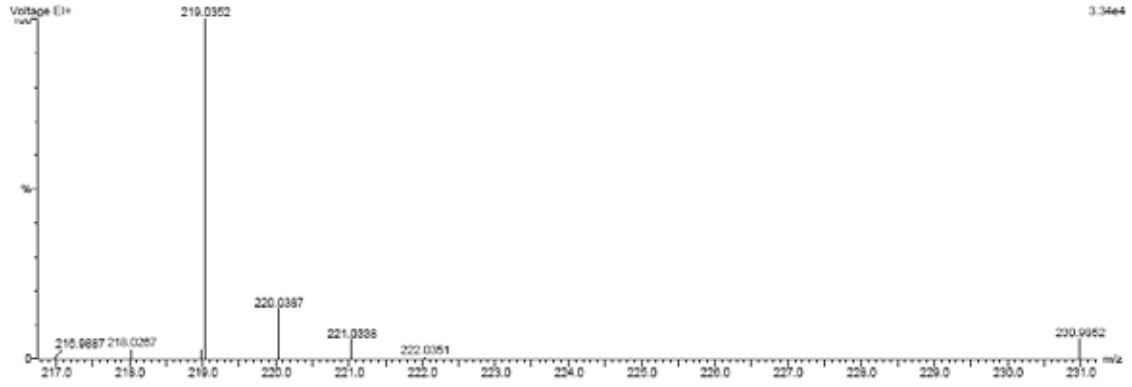
11

Carbon Number	δH (ppm) (*J* in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.81, d (5.0), 1 H	133.62	3', 4'	2', 3', 4'	
4'	7.28, t (5.0), 1 H	129.41	3', 5'	2', 3', 5'	
3'	8.54, d (3.7), 1 H	133.53	4', 5'	2', 4', 5', 3	
2'		128.83			
3		165.46			
3a		111.86			
4		193.68			
5	2.56, t (6.2), 2 H	39.95	6, 7	3a, 4, 6, 7	
6	2.13, quintuplet (6.2), 2 H	22.89	5, 7	4, 5, 7, 7a	
7	2.91, t (6.2), 2 H	21.94	5, 6	3a, 5, 6, 7a	
7a		166.03			

MS **(11)**



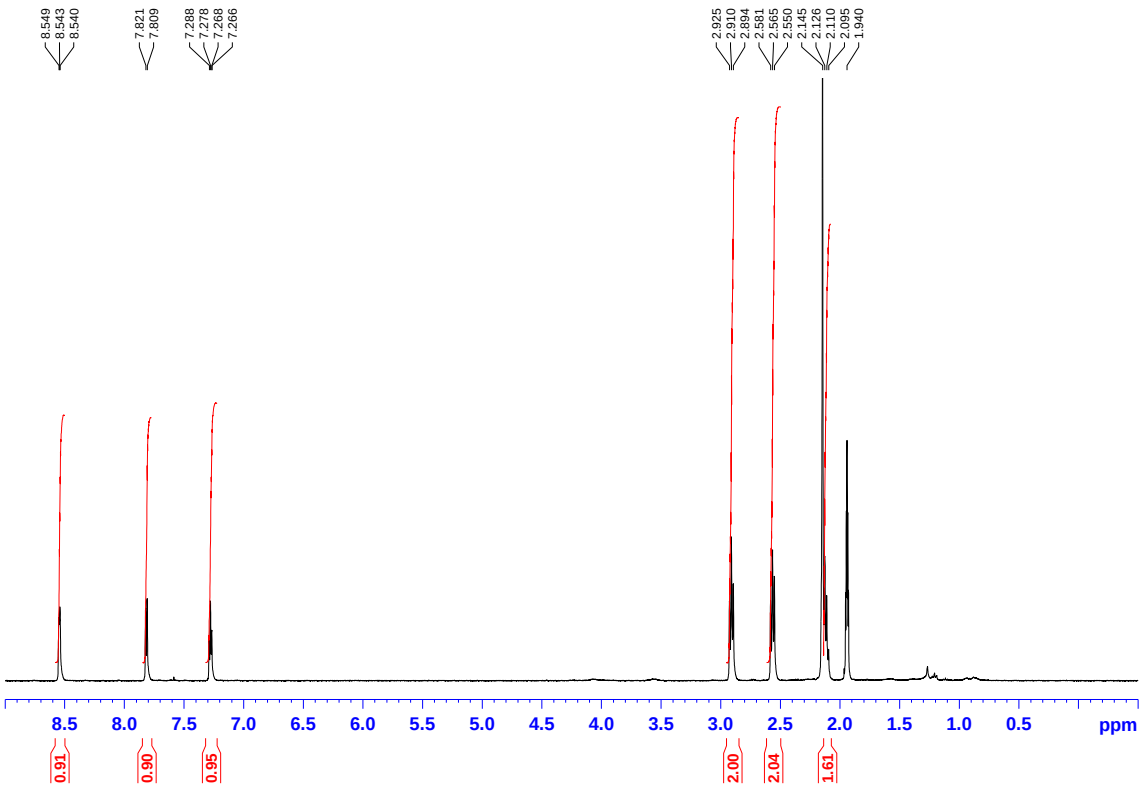
HRMS **(11)**

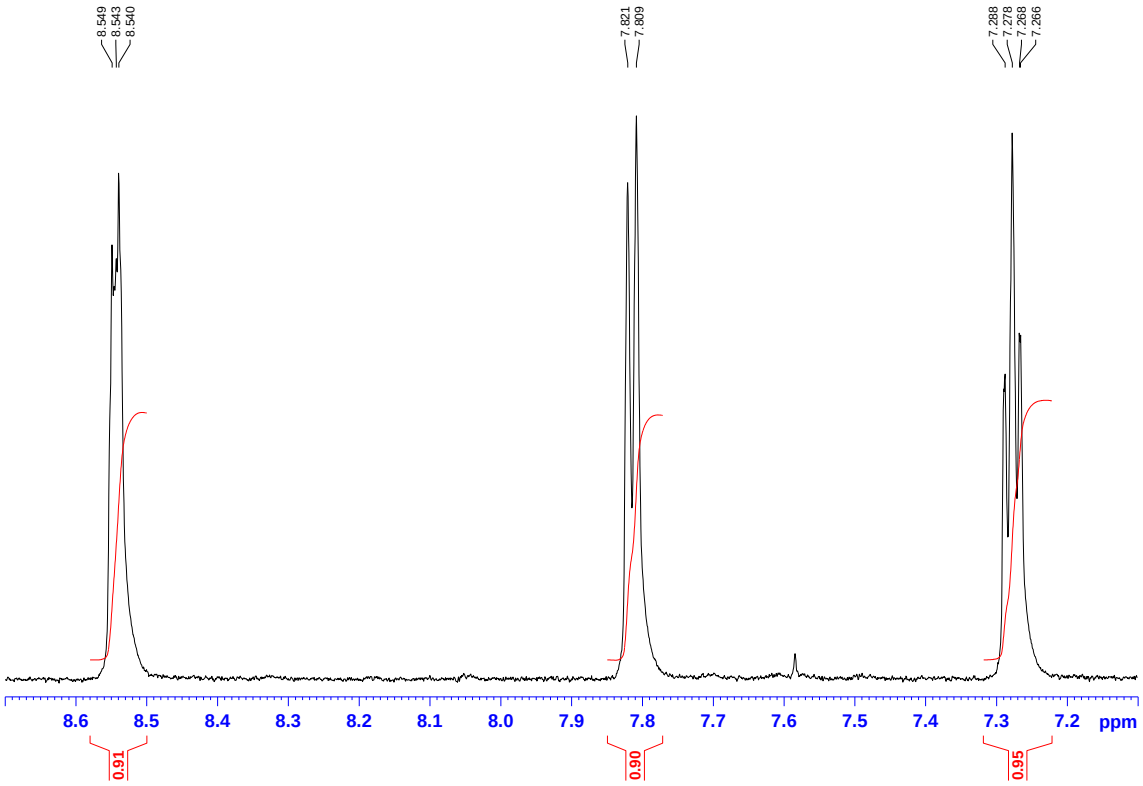


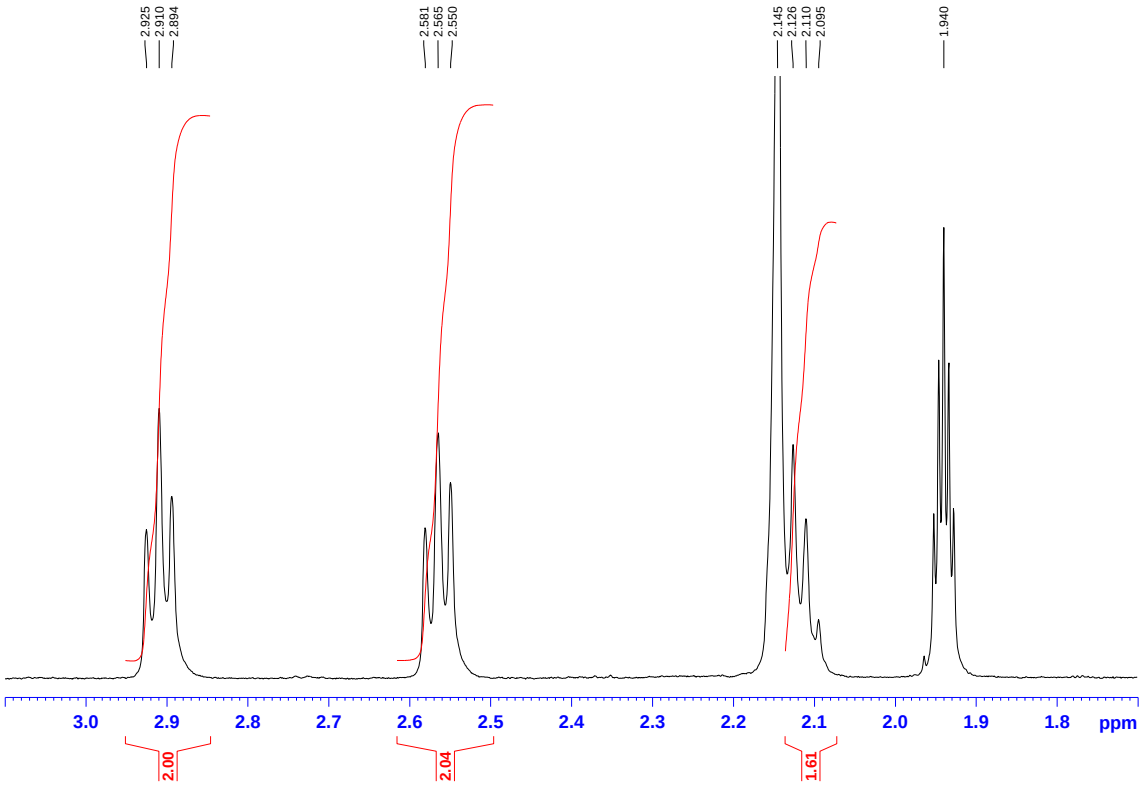
Minimum: 1.00
Maximum: 100.00 5.0 5.0 -1.5 50.0

Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
219.0352	100.00	219.0354	-0.2	-0.9	8.0	15.7	12C11 H9 N O2 S
220.0387	14.54	220.0388	-0.1	-0.5	8.0	69.4	12C10 13C H9 N O2 S

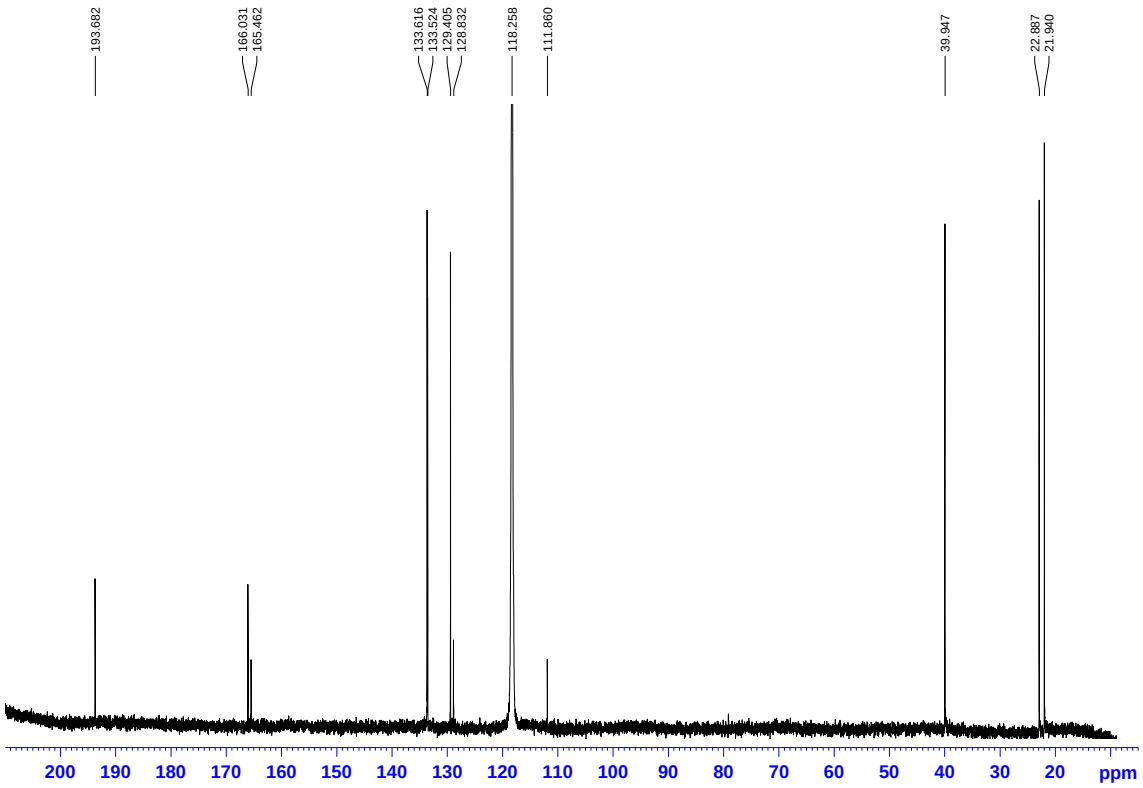
^{1}H **(11)**



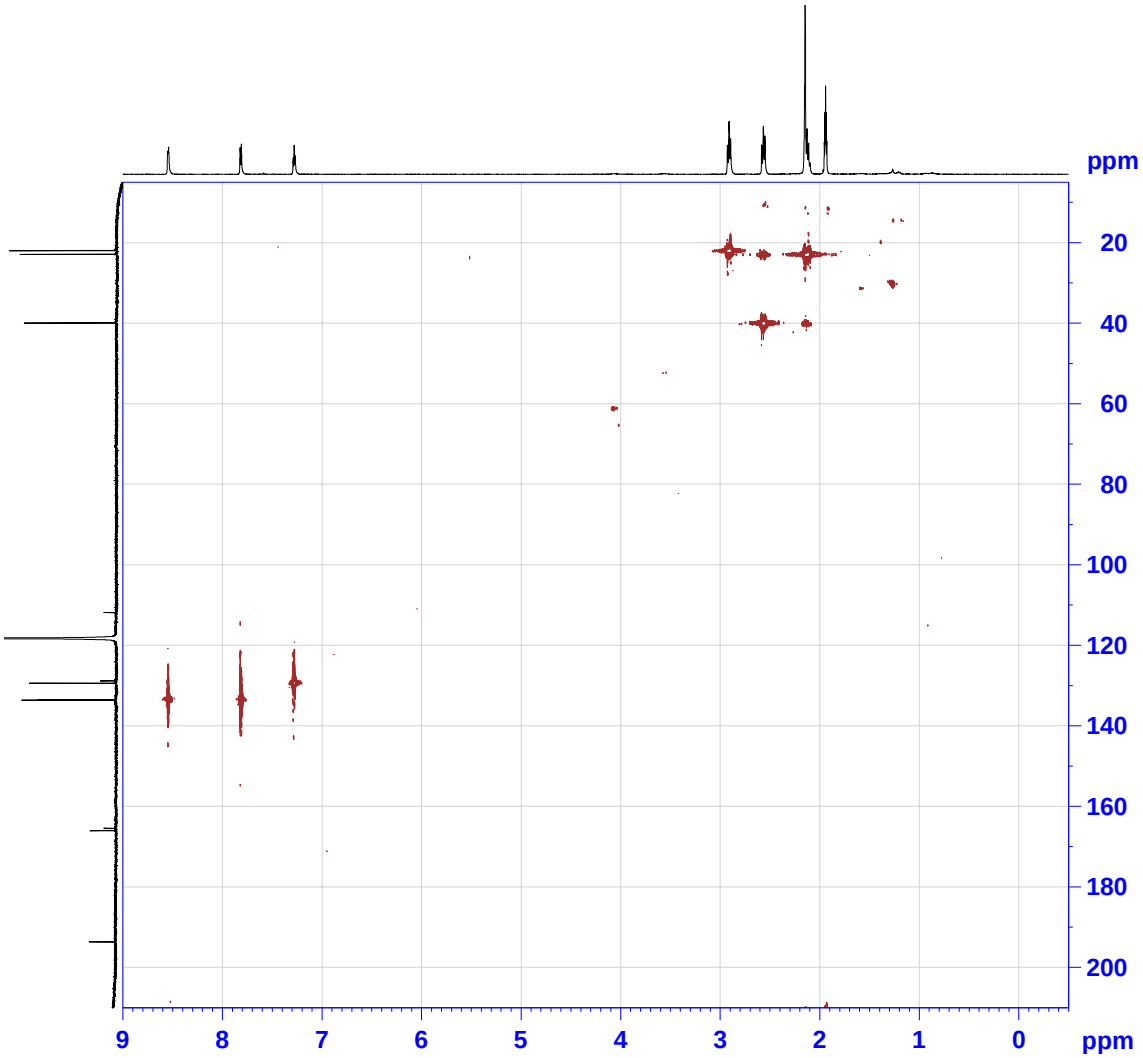

8.549
8.543
8.540
7.821
7.809
7.288
7.278
7.268
7.266
8.6
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
ppm
0.91
0.90
0.95


2.925
2.910
2.894
2.581
2.565
2.550
2.145
2.126
2.110
2.095
1.940
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
ppm
2.00
2.04
1.61

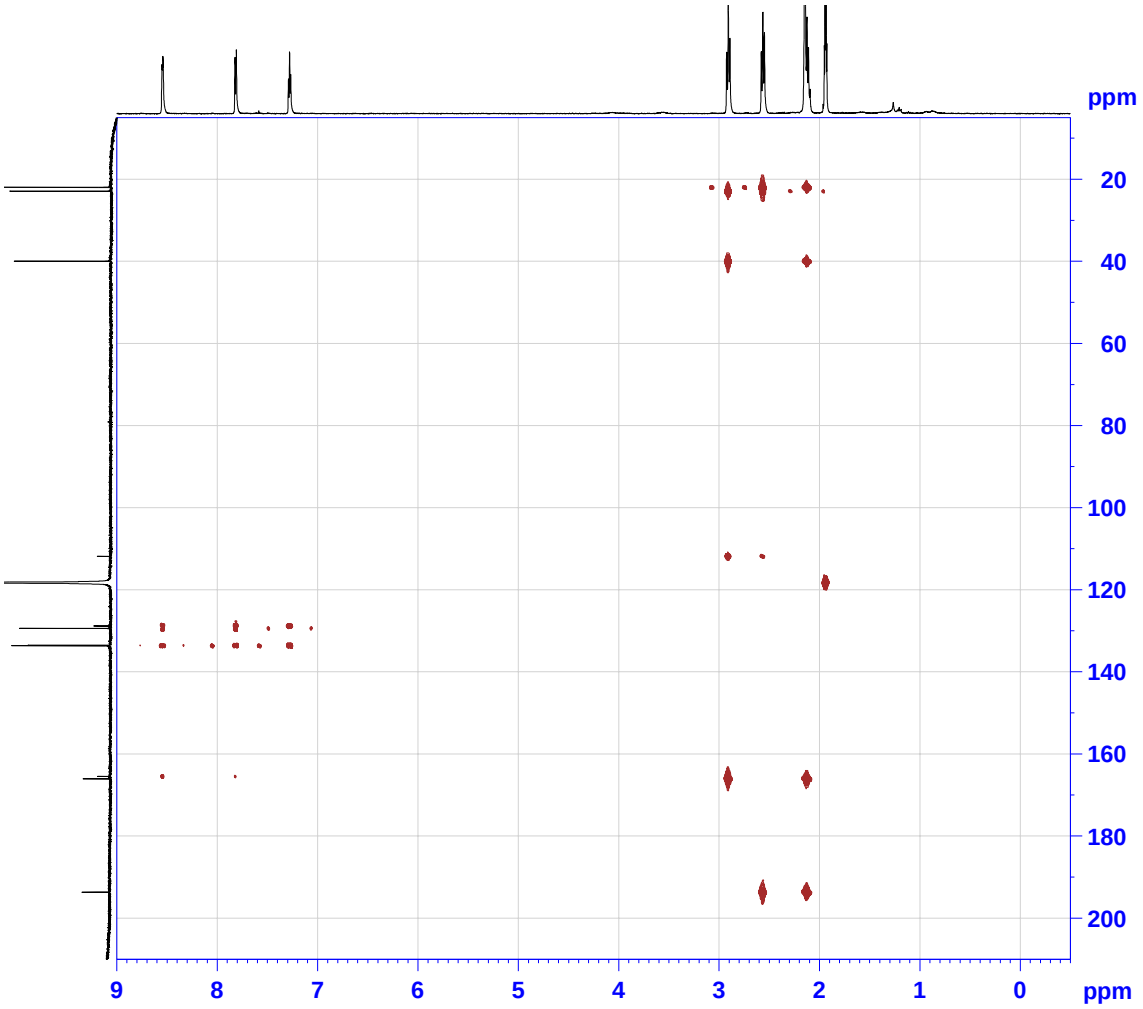
^{13}C **(11)**


193.682
166.031
165.462
133.616
133.524
129.405
128.832
118.258
111.860
39.947
22.887
21.940
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

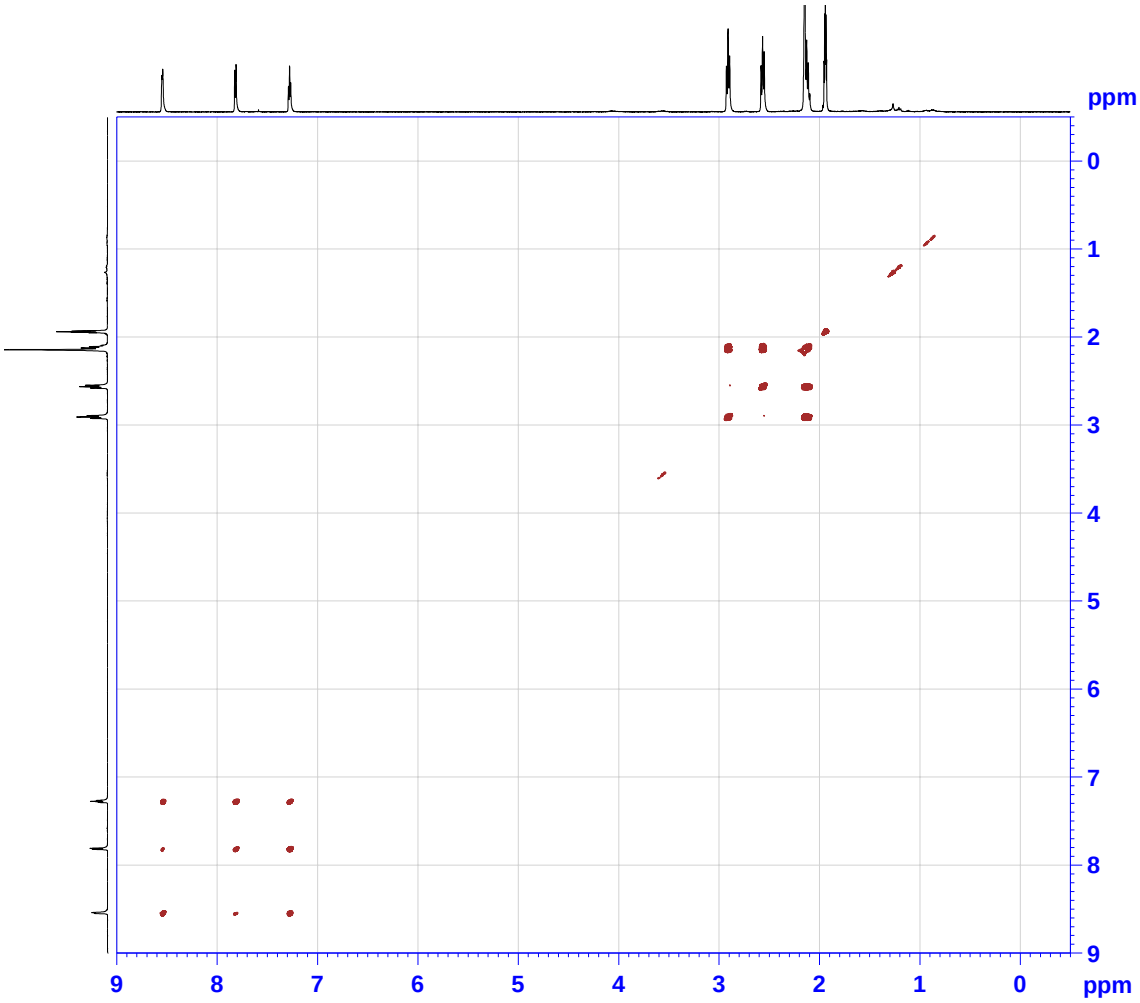
HSQC **(11)**



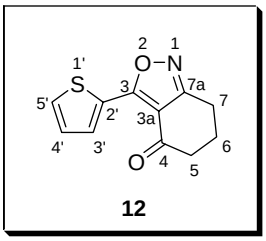
HMBC **(11)**



COSY **(11)**



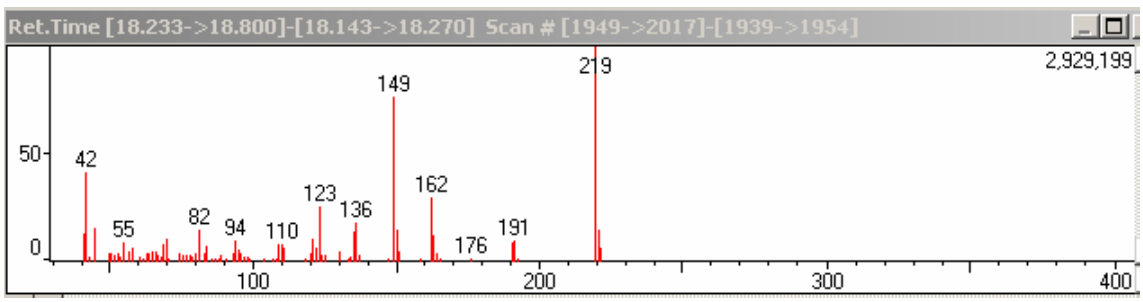
3-(2-thienyl)-6,7-dihydro-2,1-benzisoxazol-4(5*H*)-one (12): White solid. Yield 10.2 % (0.0108 g). ^{1}H NMR (CD_3CN): δ = 2.21 (quintuplet, J = 6.4 Hz, 2 H, H-6), 2.56 (t, J = 6.4 Hz, 2 H, H-5), 3.04 (t, J = 6.4 Hz, 2 H, H-7), 7.19 (dd, J = 5.1 and 3.7 Hz, 1 H, H-4´), 7.59 (dd, J = 5.1 and 1.1 Hz, 1 H, H-5´), 8.45 (dd, J = 3.7 Hz and 1.1, 1 H, H-3´) ppm. ^{13}C NMR (CD_3CN): δ = 21.45 (C-6), 22.82 (C-7), 38.16 (C-5), 113.25 (C-3a), 127.95 (C-4´), 128.51 (C-5´), 129.20 (C-2´), 132.70 (C-3´), 154.29 (C-3), 183.47 (C-7a), 192.59 (C-4) ppm. IR (KBr): $\tilde{\nu}$ = 3096, 3068, 2959, 2914, 2854, 1720, 1679, 1579, 1456, 1269, 1119, 1068 cm^{-1}. MS: *m/z* (%) = 220 (15), 219 $[M]^+$ (100), 163 (12), 162 (30), 150 (14), 149 (77), 136 (18), 135 (13), 123 (25), 82 (15), 45 (15), 42 (42), 41 (13).



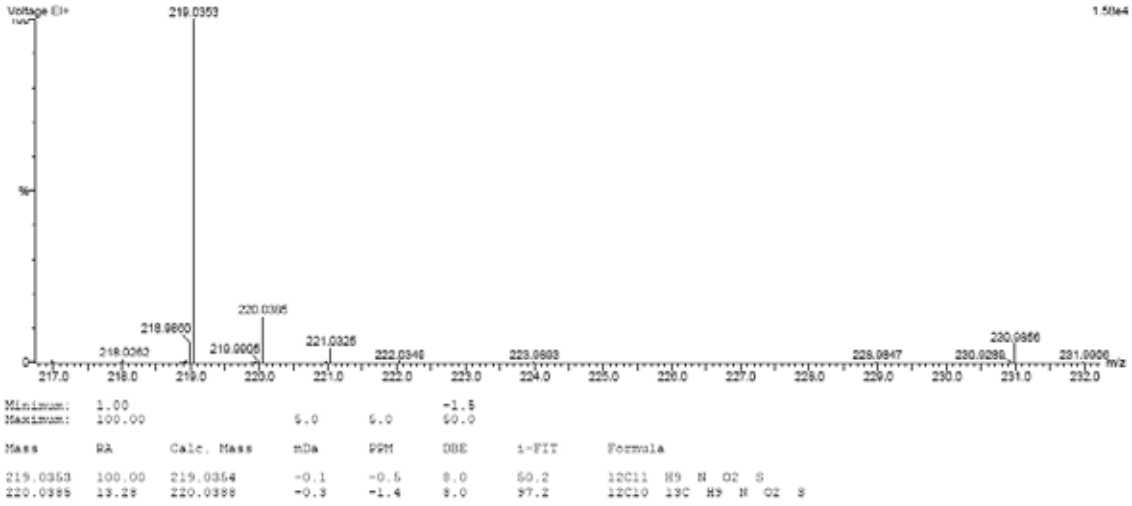
12

Carbon Number	δH (ppm) (*J* in Hz)	δC (ppm)	^{1}H-^{1}H COSY	HMBC	NOE
5'	7.59, dd (5.1, 1.1), 1 H	128.51	3', 4'	2', 3', 4'	
4'	7.19, dd (5.1, 3.7), 1 H	127.95	3', 5'	2', 3', 5'	
3'	8.45, dd (3.7, 1.1), 1 H	132.70	4', 5'	2', 4', 5', 3	
2'		129.20			
3		154.29			
3a		113.25			
4		192.59			
5	2.56, t (6.4), 2 H	38.16	6, 7	3a, 4, 6, 7	
6	2.21, quintuplet (6.4), 2 H	21.45	5, 7	4, 5, 7, 7a	
7	3.04, t (6.4), 2 H	22.82	5, 6	3a, 5, 6, 7a	
7a		183.47			

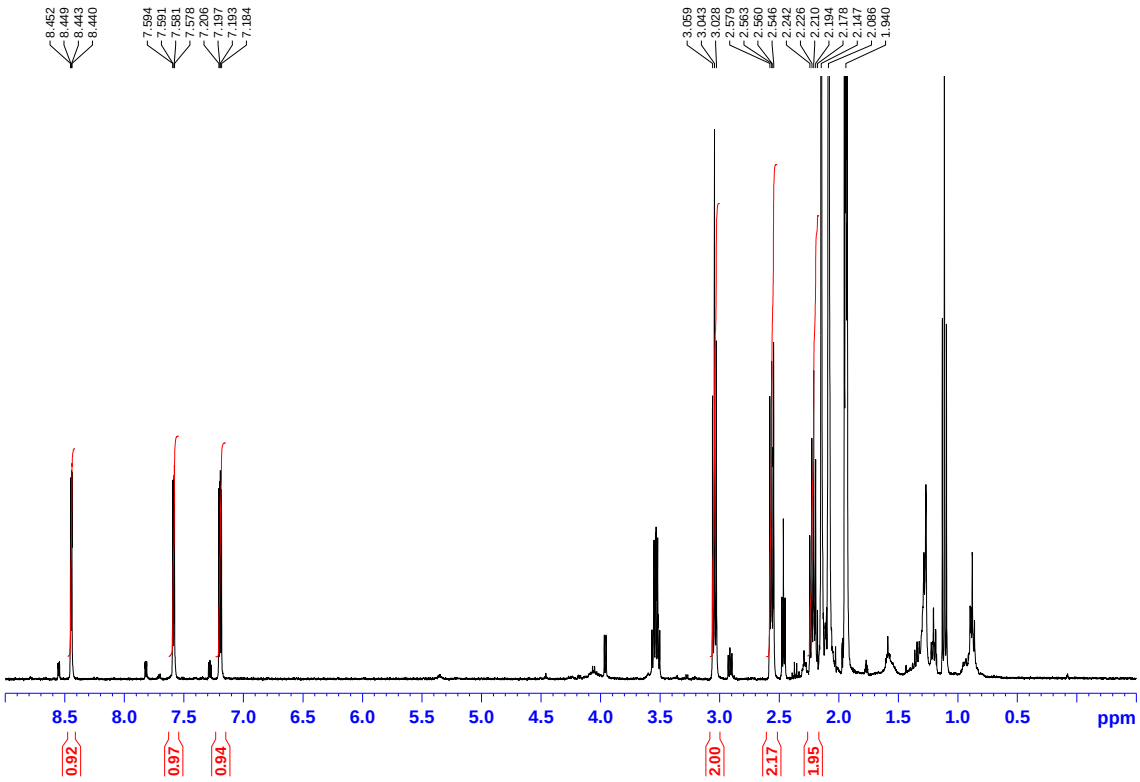
MS **(12)**

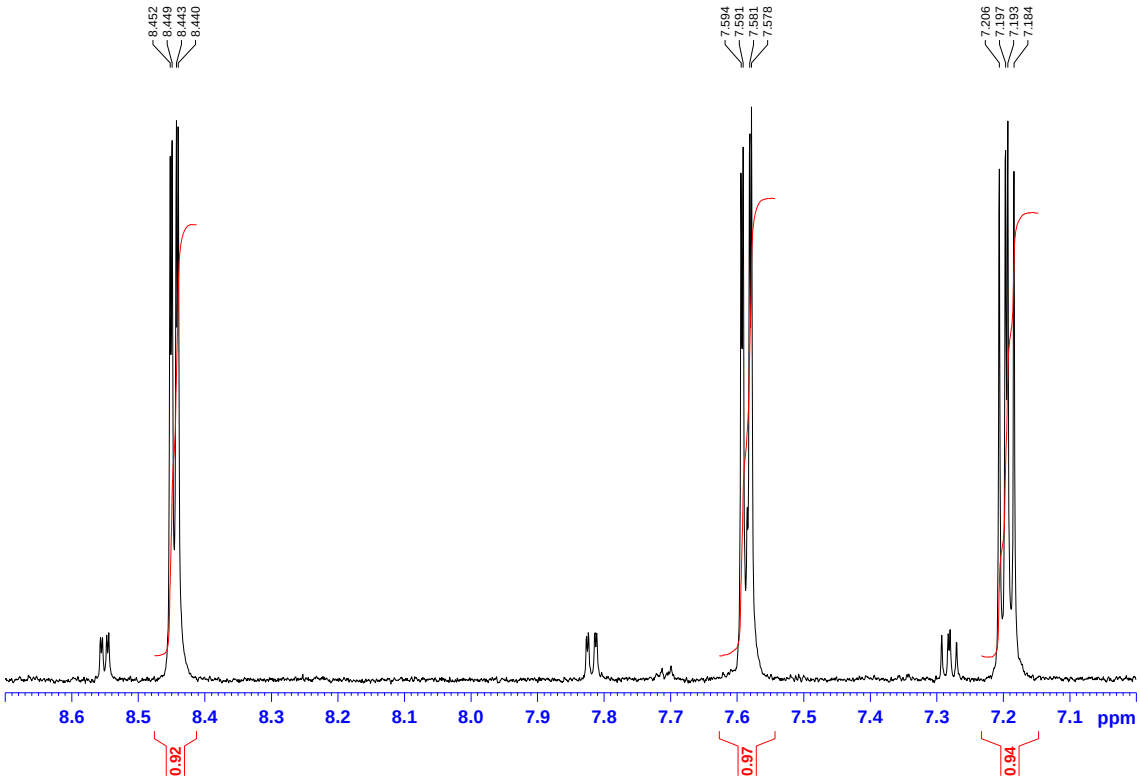


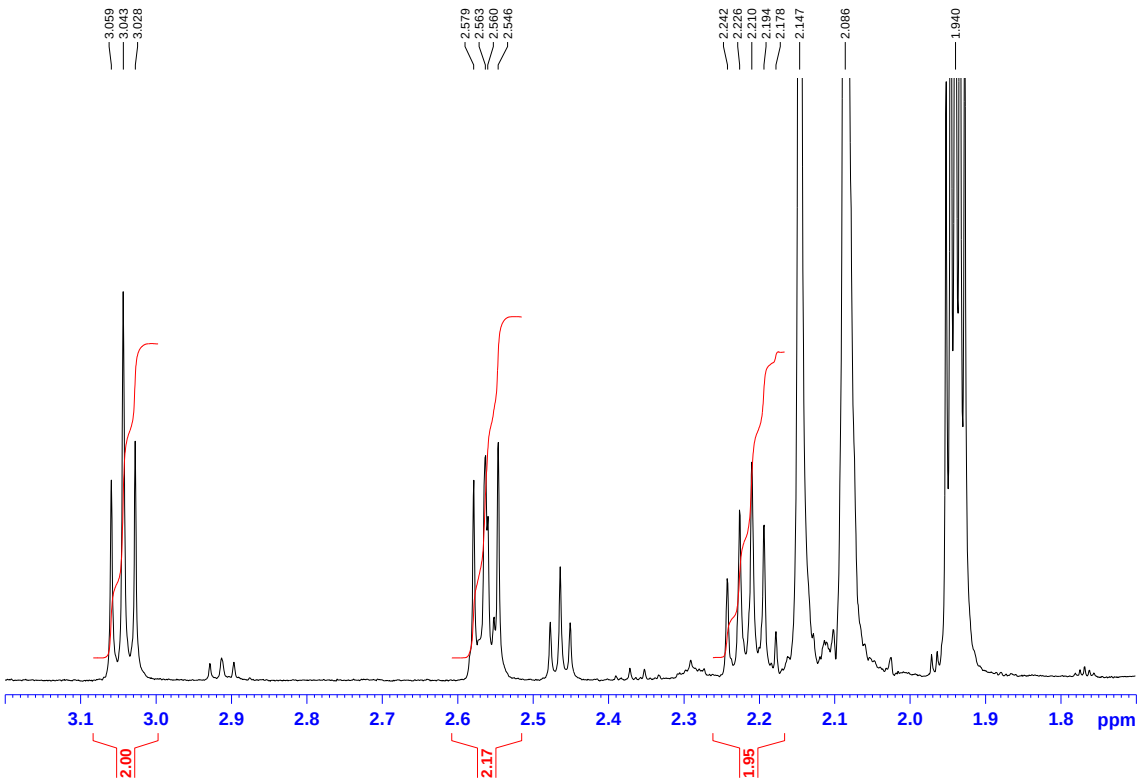
HRMS **(12)**


Voltage EI+
219.0353
1.50e4
%
218.9860
220.0395
218.0363
219.9905
221.0325
222.0346
223.0693
228.0847
230.0298
230.9856
231.0006
m/z
Minimum: 1.00 -1.5
Maximum: 100.00 5.0 5.0 50.0
Mass RA Calc. Mass mDa PPM DBE i-FIT Formula
219.0353 100.00 219.0354 -0.1 -0.5 8.0 50.2 12C11 H9 N O2 S
220.0999 13.28 220.0988 -0.9 -1.4 8.0 97.2 12C10 13C H9 N O2 S

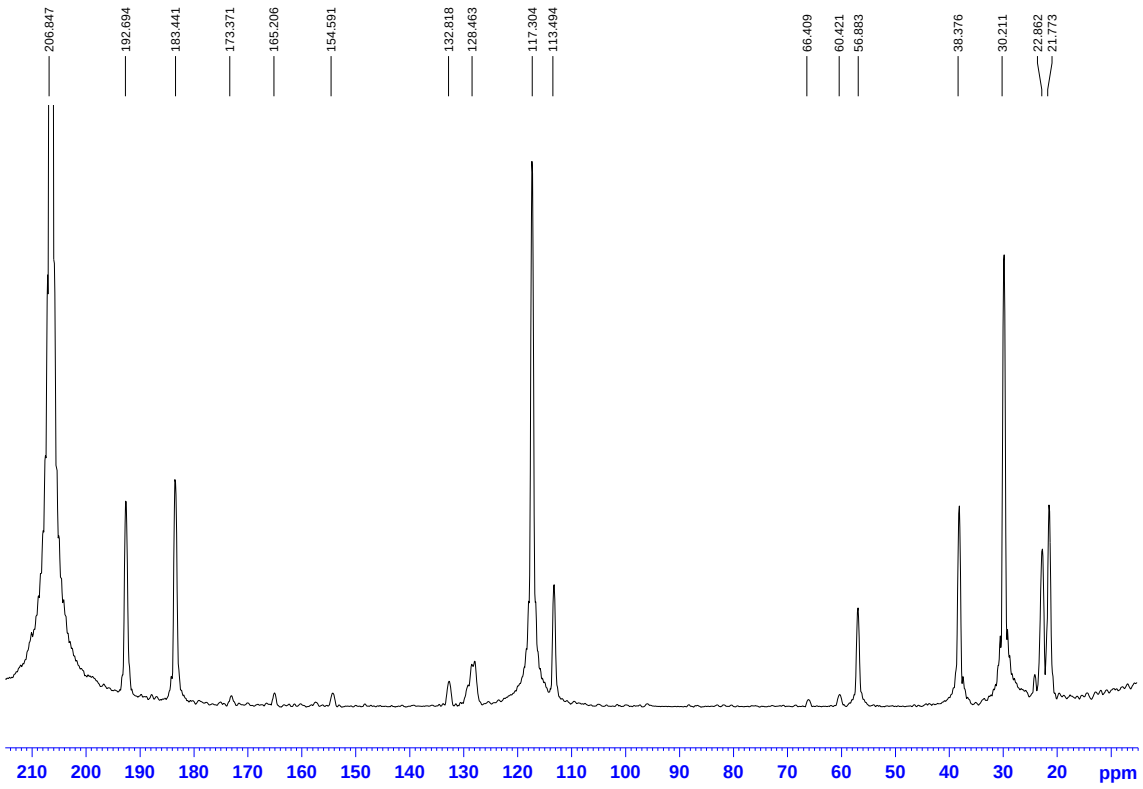
^{1}H **(12)**


8.452
8.449
8.443
8.440
7.594
7.591
7.581
7.578
7.206
7.197
7.193
7.184
3.059
3.043
3.028
2.579
2.563
2.560
2.546
2.242
2.226
2.210
2.194
2.178
2.147
2.086
1.940
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 ppm
0.92
0.97
0.94
2.00
2.17
1.95

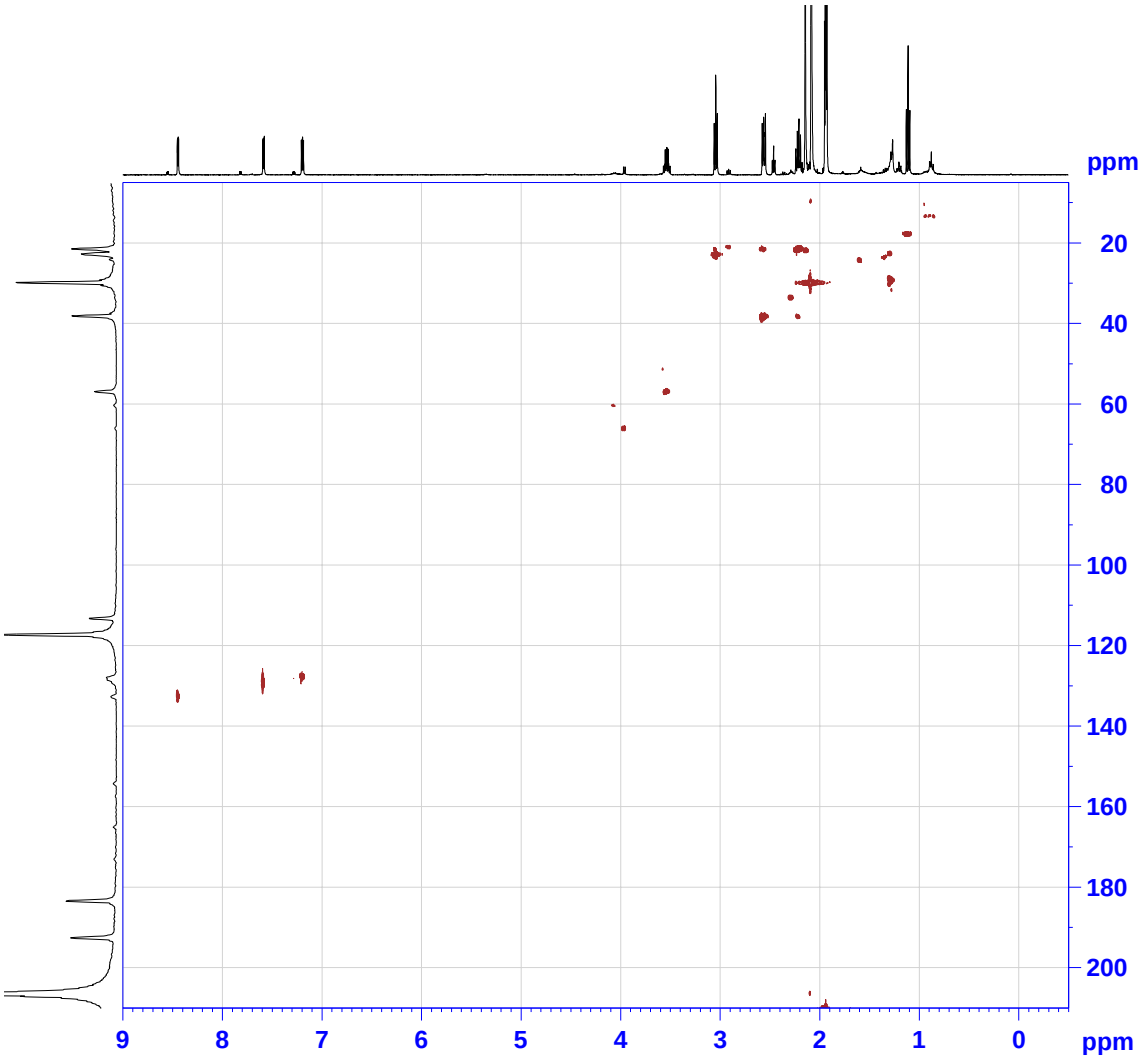

8.452
8.449
8.443
8.440
7.594
7.591
7.581
7.578
7.206
7.197
7.193
7.184
8.6
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
ppm
0.92
0.97
0.94


3.059
3.043
3.028
2.579
2.563
2.560
2.546
2.242
2.226
2.210
2.194
2.178
2.147
2.086
1.940
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
ppm
2.00
2.17
1.95

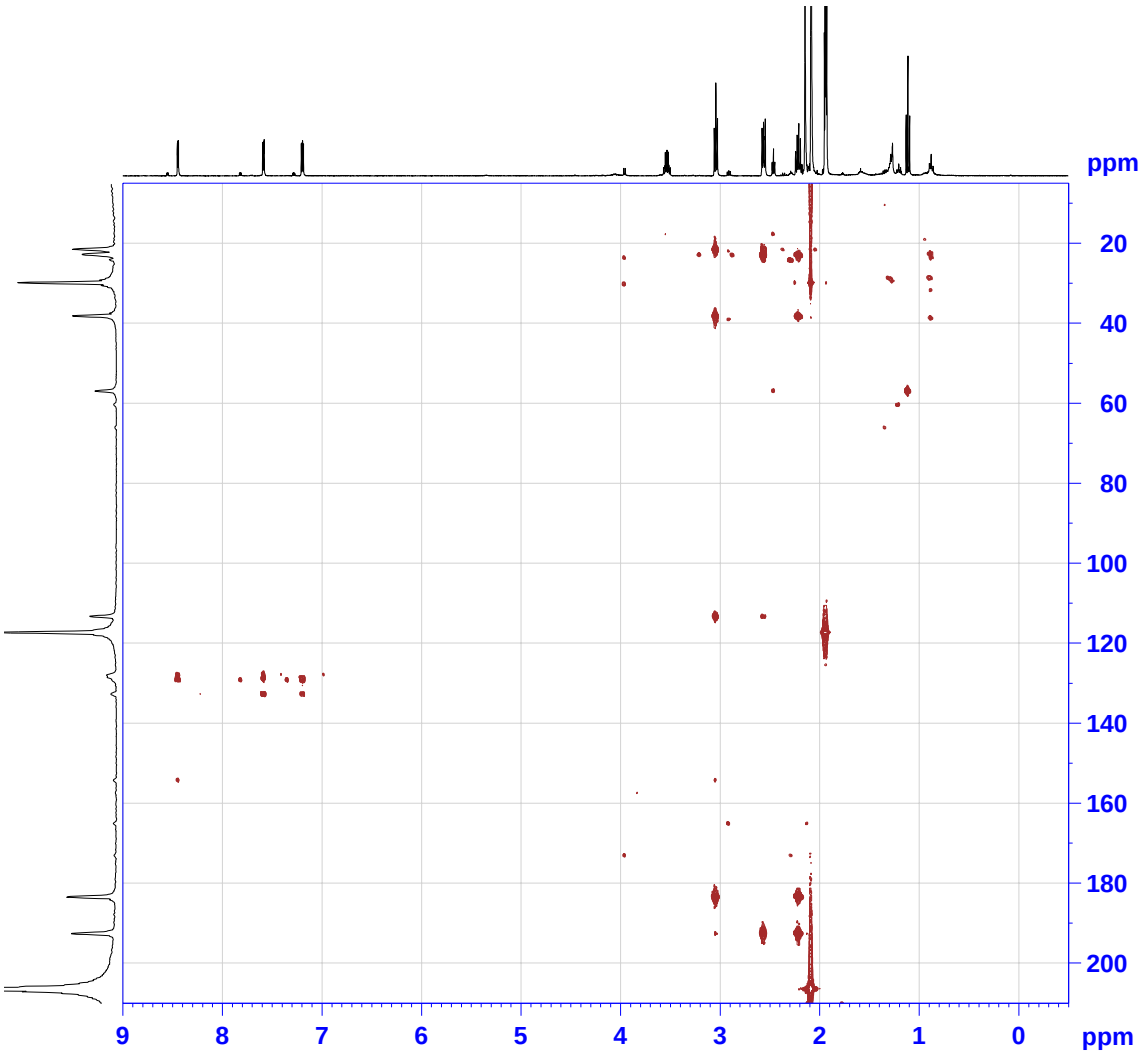
^{13}C **(12)**


206.847
192.694
183.441
173.371
165.206
154.591
132.818
128.463
117.304
113.494
66.409
60.421
56.883
38.376
30.211
22.862
21.773
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

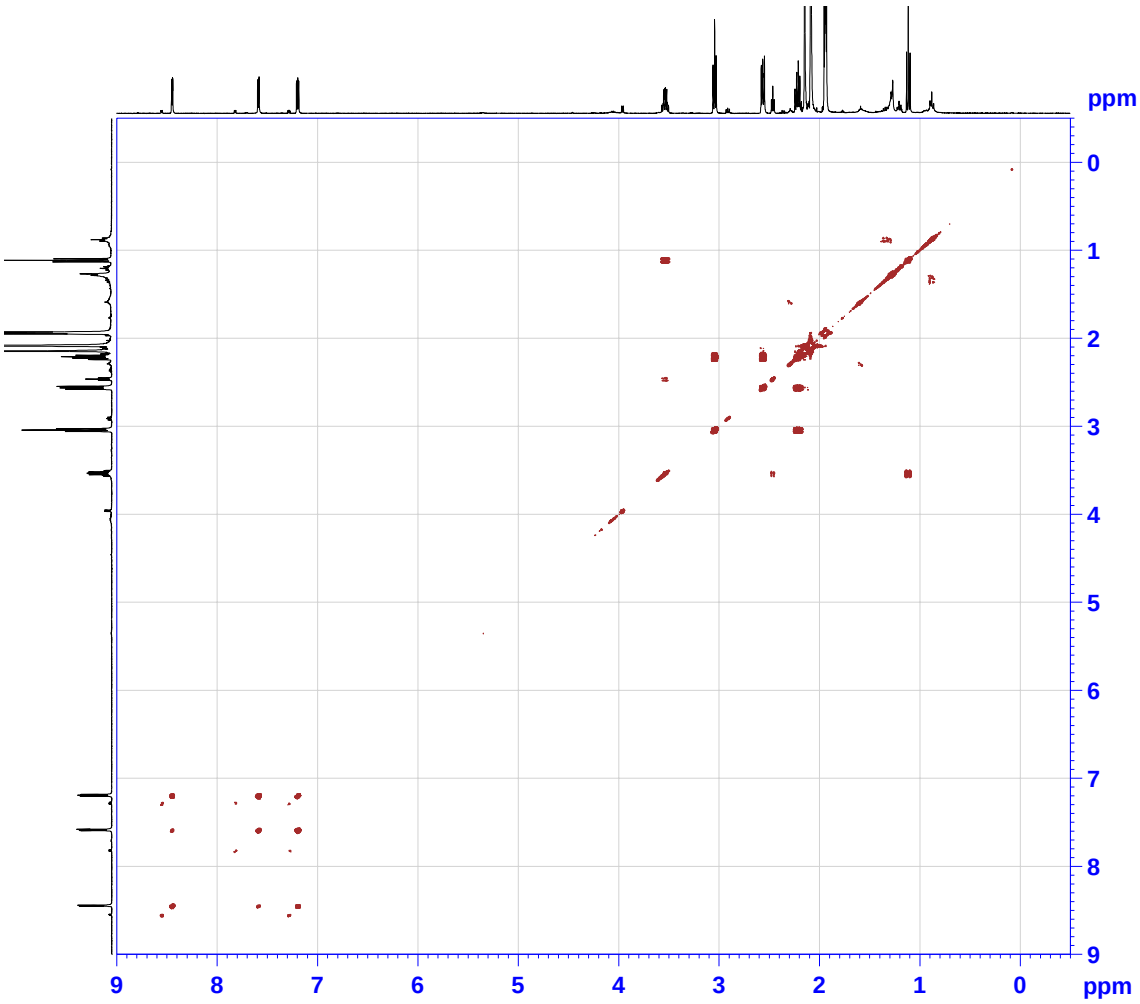
HSQC **(12)**



HMBC **(12)**

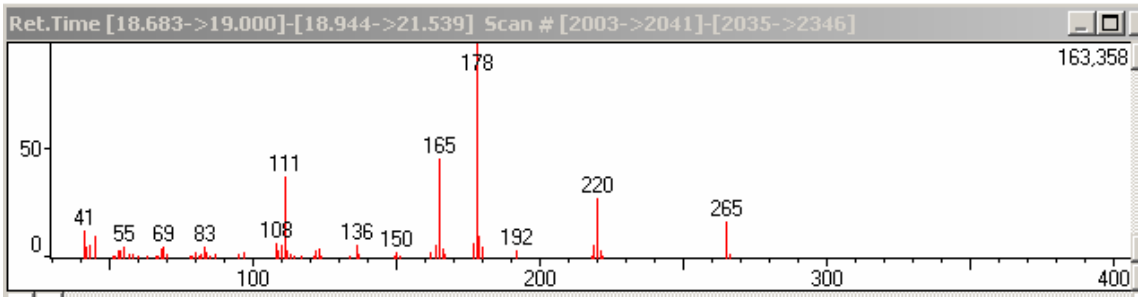


COSY **(12)**



3-ethoxy-2-[(hydroxyimino)(2-thienyl)methyl]cyclohex-2-en-1-one (13): Pale yellow solid. Yield 2.1 % (0.0025 g). ^{1}H NMR ($CDCl_3$): δ = 1.23 (t, J = 7.2 Hz, 3 H), 2.00 (quintuplet, J = 7.5 Hz, 2 H), 2.40 (t, J = 7.5 Hz, 2 H), 2.74 (t, J = 7.5 Hz, 2 H), 4.09 (q, J = 7.2 Hz, 2 H), 7.20 (dd, J = 5.1 and 3.7 Hz, 1 H), 7.60 (dd, J = 3.7 and 1.0 Hz, 1 H), 7.69 (dd, J = 5.1 and 1.0 Hz, 1 H), 10.51 (s, 1 H). IR (KBr): $\tilde{\nu}$ = 3070, 2952, 2926, 2854, 1724, 1457, 1283, 1118, 1062, 738 cm^{-1}. MS: m/z (%) = 265 $[M]^+$ (18), 220 (28), 179 (11), 178 (100), 177 (9), 165 (46), 111 (38), 45 (11), 41 (13).

MS **(13)**



HRMS **(13)**