Supplementary information

Reaction of Unsymmetrical α-Bromo-1,3-diketones with *N*-Substituted Thioureas: Regioselective Access to 2-(*N*-arylamino)-5-acyl-4-methylthiazoles and/or Rearranged 2-(*N*-acylimino)-3-*N*-aryl-4-methylthiazoles

Ranjana Aggarwal,[a,b*] Shilpa Sharma,[a] Naman Jain,[a] Dionisia Sanz,[c] Rosa M. Claramunt,[c] Patricia Delgado,[d] M. Carmen Torralba,[e]

[a]*Department of Chemistry, Kurukshetra University, Kurukshetra, Haryana, India*

[b]*CSIR- National Institute of Science Communication and Policy Research, New Delhi, India*

[c]*Departamento de Química Orgánica y Bio-orgánica, Facultad de Ciencias, UNED, Avenida Esparta s/n, E-28232 Las Rozas, Madrid, Spain*

[d]*Unidad de Difracción de Rayos X - CAI de Técnicas Químicas, Facultad de Ciencias Químicas, UCM, E-28040 Madrid, Spain*

[e]*Departamento de Química Inorgánica, Facultad de Ciencias Químicas, UCM, E-28040 Madrid, Spain*

[*]Correspponding author:

Prof. Ranjana Aggarwal, CSIR- National Institute of Science Communication and Policy Research, New Delhi, India Tel. (+91) 9896740740

E-mails: *ranjana67in@yahoo.com*, *ranjanaaggarwal67@gmail.com*

TABLE OF CONTENTS

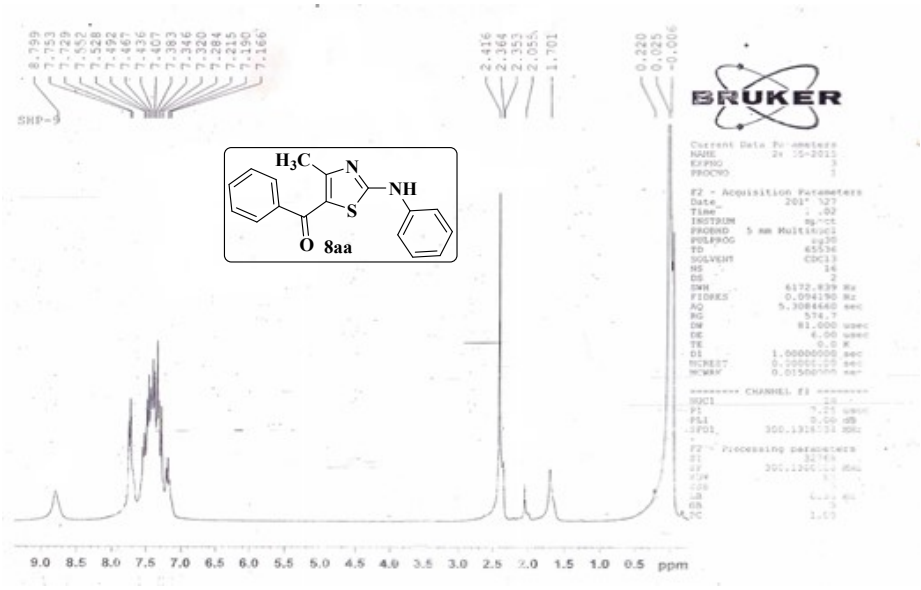
General method for the synthesis:

1,3-Diketone **1a-e** (1.0 mmol) was ground with *N*-bromo succinimide **2** (0.177 g, 1.0 mmol) in dry pestle mortar until a thick paste was formed and the reaction mass was added subsequently with *N*-substituted thiourea derivative **7a-f** (1.0 mmol) and sodium carbonate (0.108 g, 1.0 mmol). The reaction mixture was homogenized properly at room temperature for 5 min, transferred to a conical flask and heated at temperature 80 °C. The reaction progress was monitored with TLC. On completion of reaction, the reaction mixture was added with water and filtered to get the coarse product which was recrystallized from boiling ethanol.

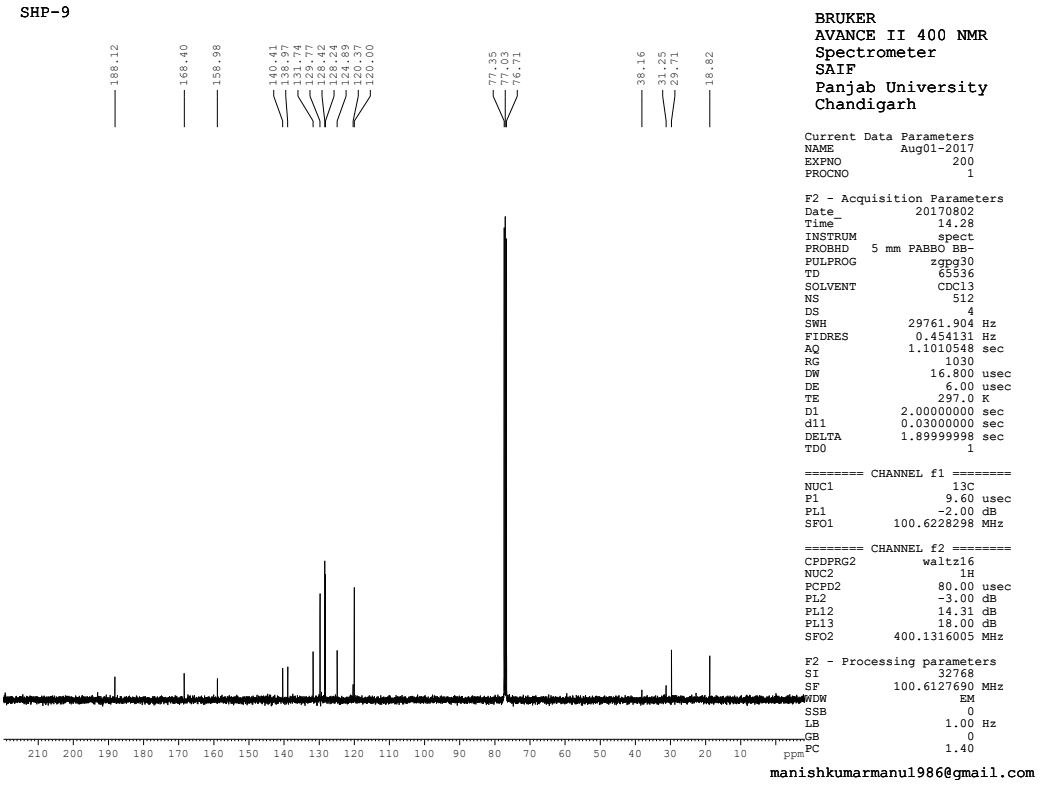
Characterization of final compounds

^{1}H NMR, ^{13}C NMR, HMBC and HMQC of final compounds

1. 2-(*N*-phenylamino)-4-methyl-5-benzoylthiazole (8aa)

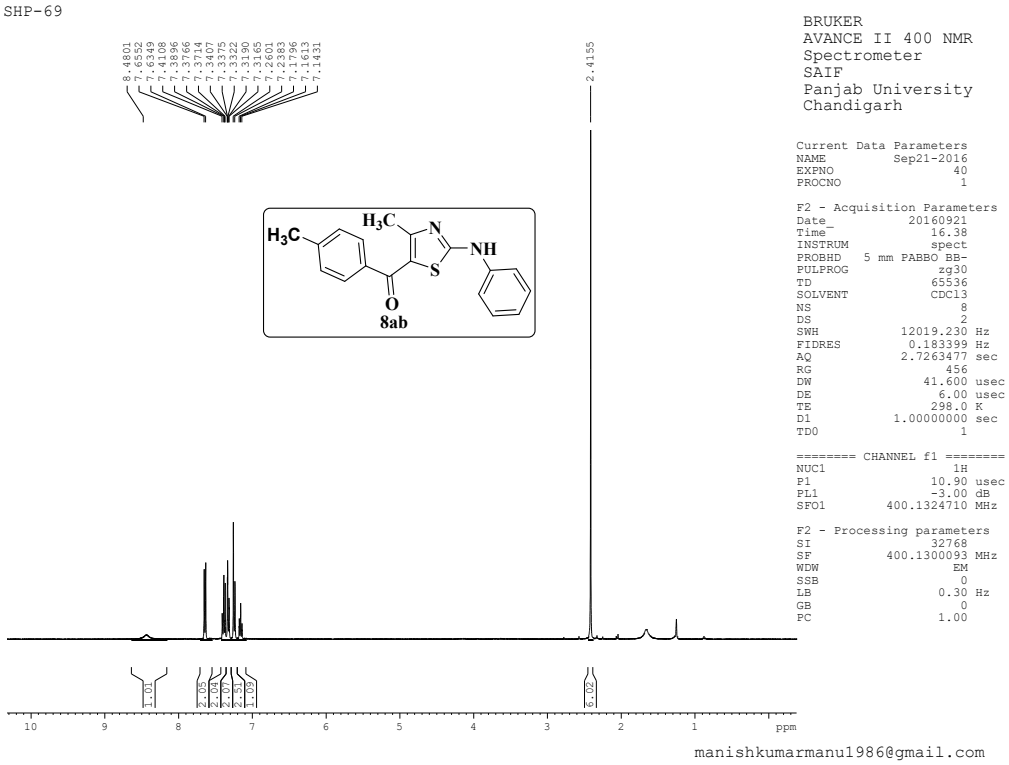


S1a: ^{1}H-NMR spectrum of compound **8aa**

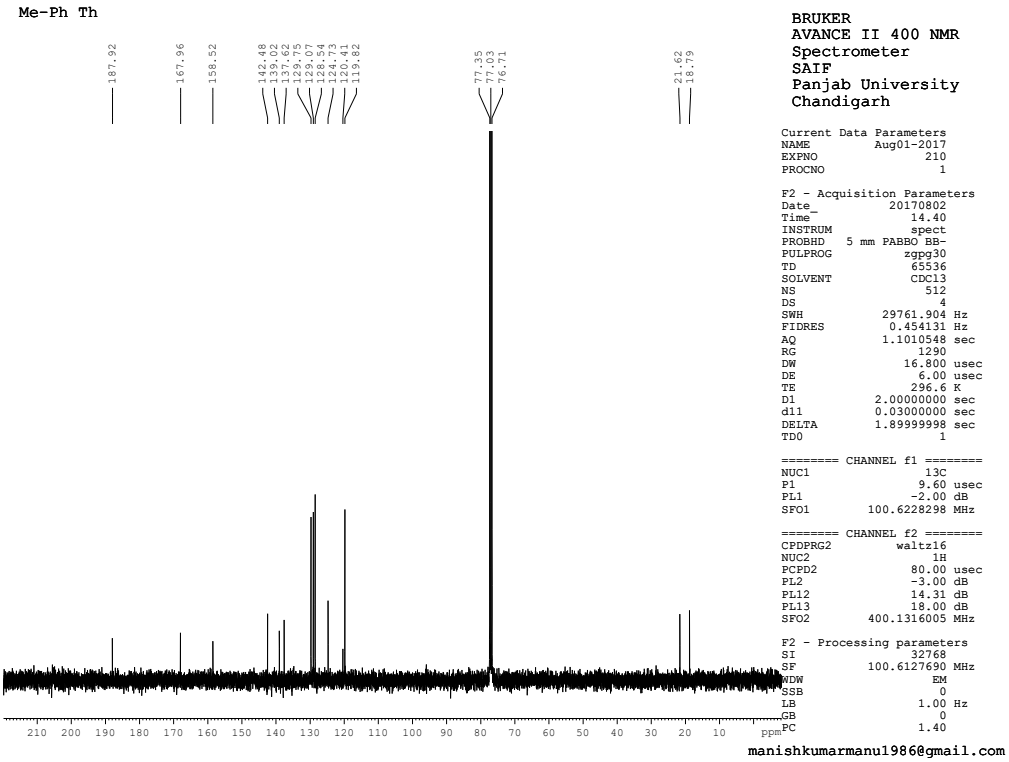


S1b: ^{13}C-NMR spectrum of compound **8aa**

2. 2-(*N*-phenylamino)-4-methyl-5-(*p*-methylbenzoyl)thiazole (**8ab**)

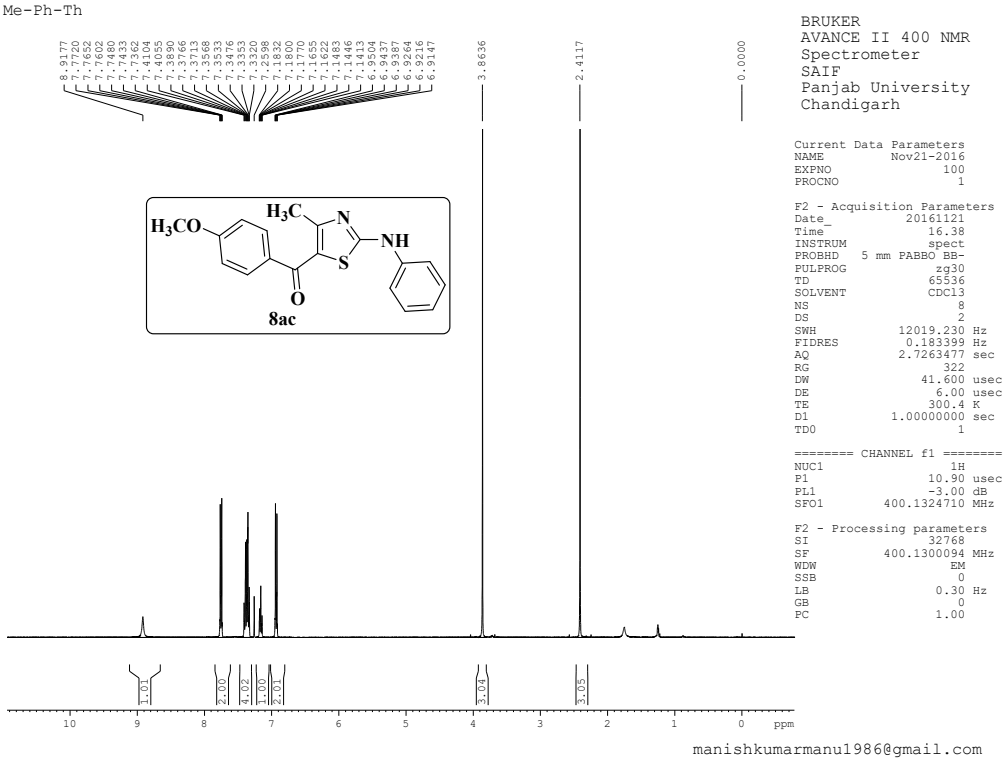


S2a: ^{1}H-spectrum of compound **8ab**

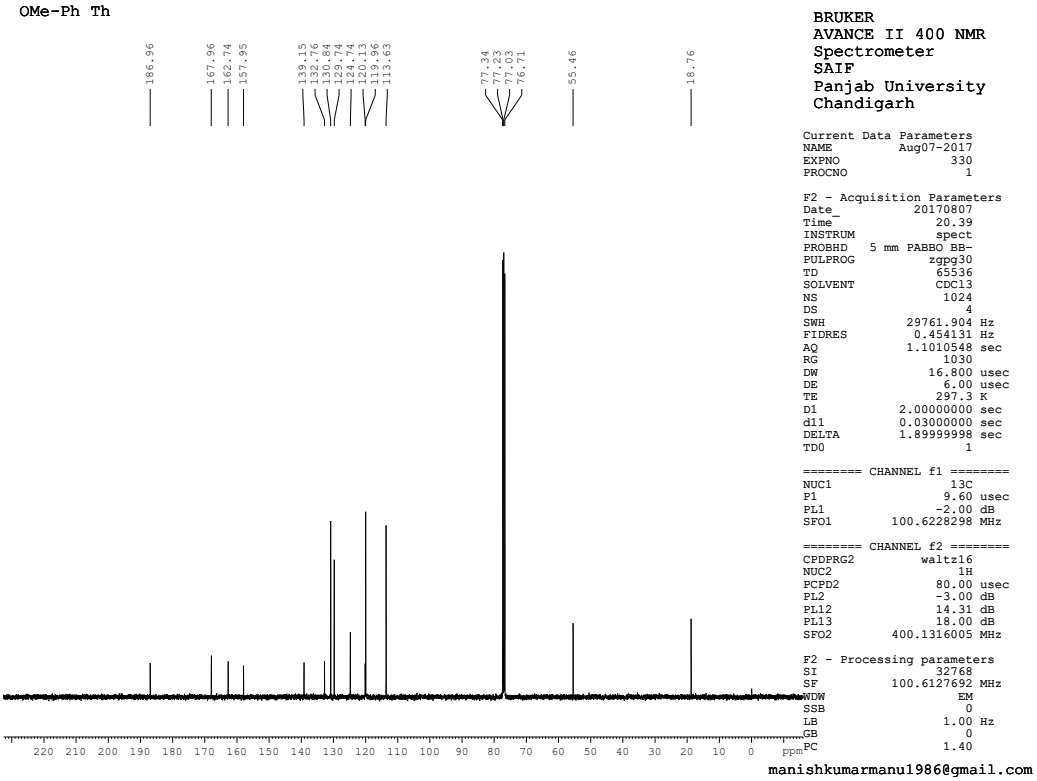


S2b: ^{13}C-spectrum of compound **8ab**

3. 2-(*N*-phenylamino)-4-methyl-5-(*p*-methoxybenzoyl)thiazole (8ac)

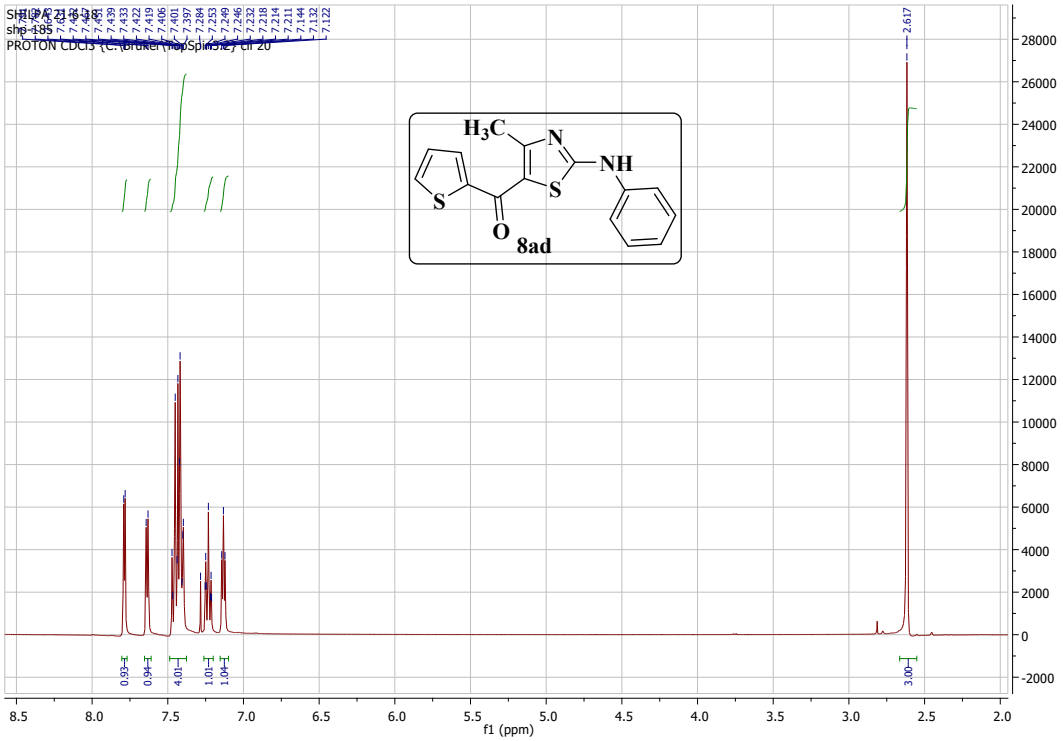


S3a: ^{1}H-spectrum of compound **10ac**

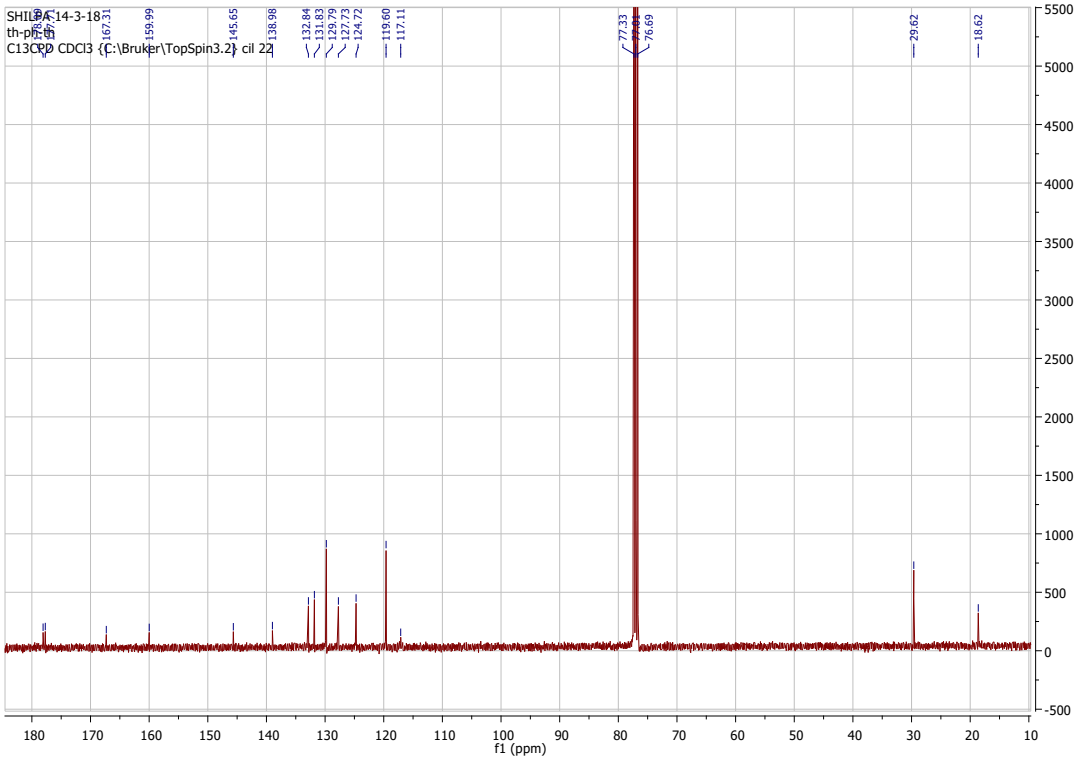


S3b: ^{13}C-spectrum of compound **8ac**

4. 2-(*N*-phenylamino)-4-methyl-5-(2-thienoyl) thiazole (8ad)

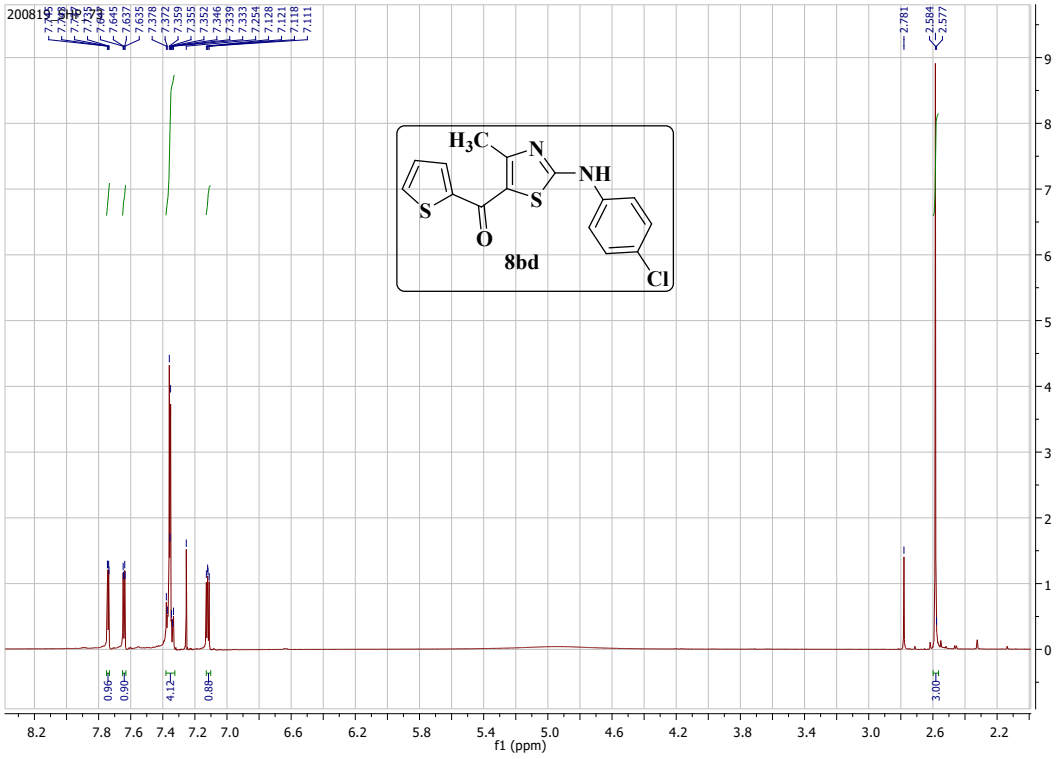


S4a: ^{1}H-spectrum of compound **8ad**

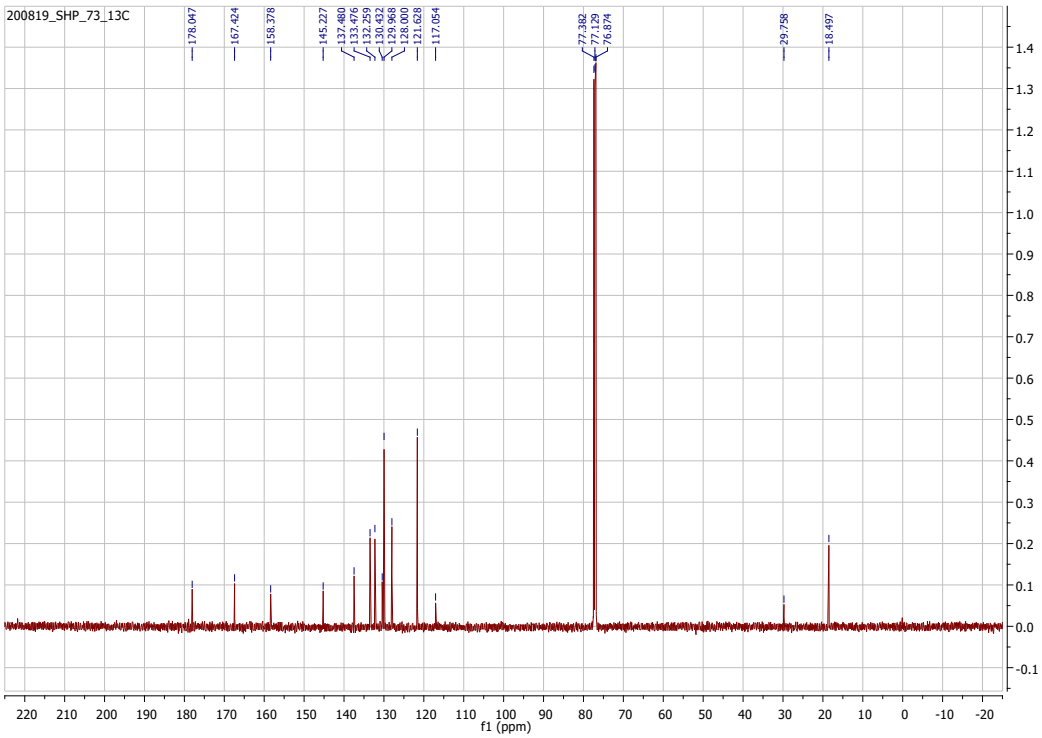


S4b: ^{13}C-spectrum of compound **8ad**

5. 2-(*N*-(*p*-chlorophenyl)amino)-4-methyl-5-(2-thienoyl)thiazole (8bd)

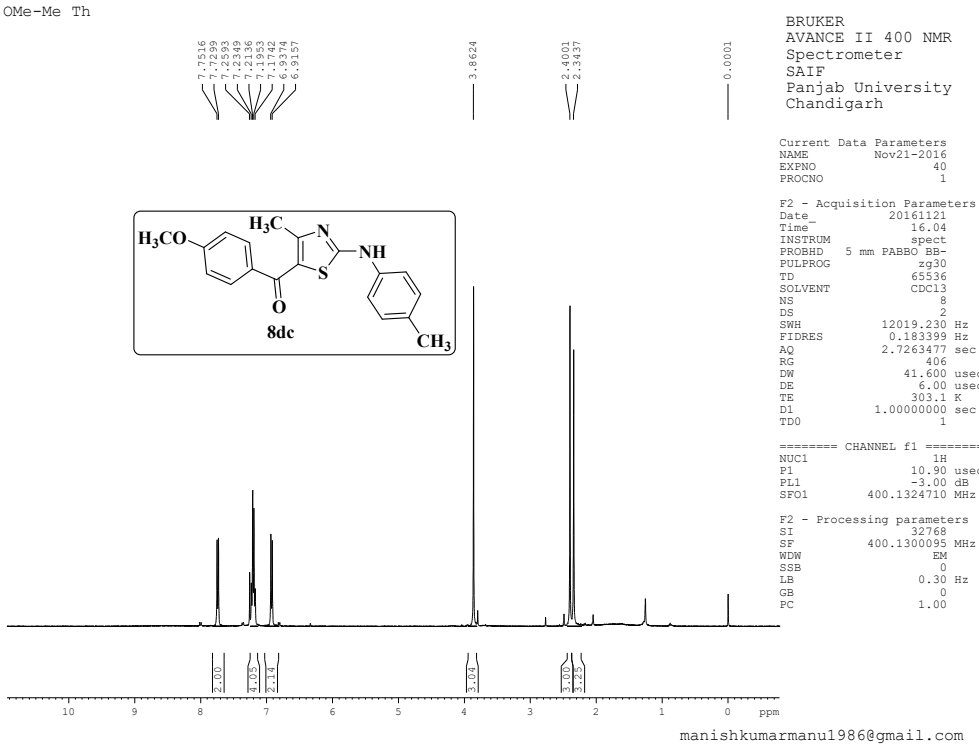


S5a: ^{1}H-NMR spectrum of compound **8bd**

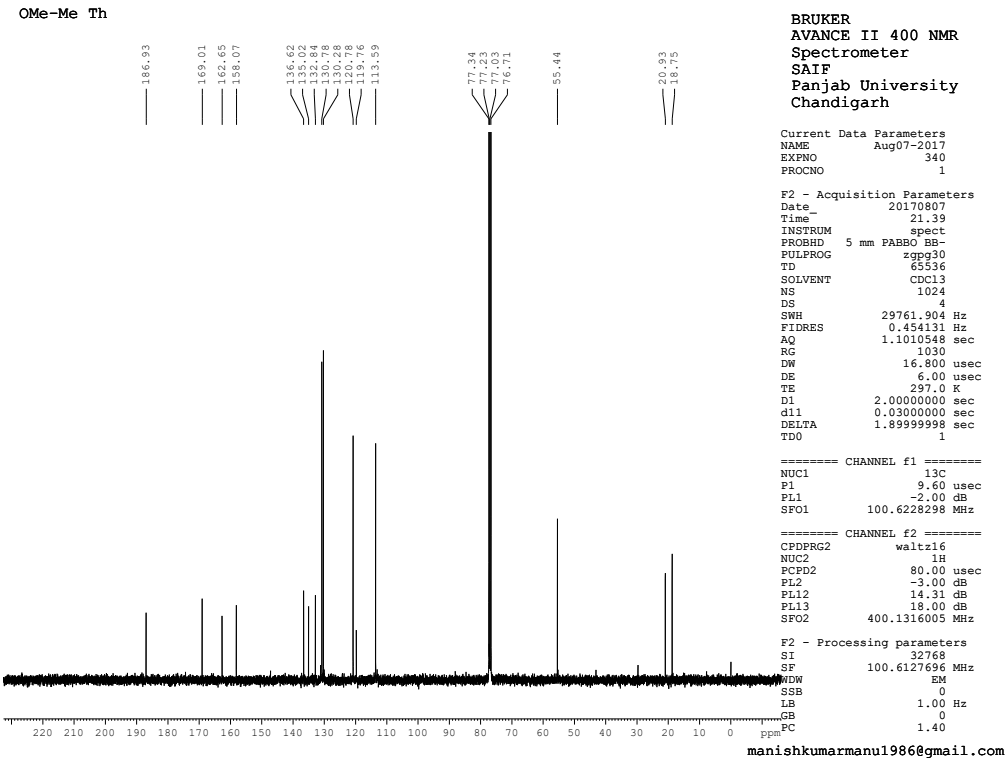


S5b: ^{13}C-NMR spectrum of compound **8bd**

6. 2-(*N*-(*p*-methylphenyl)amino)-4-methyl-5-(*p*-methoxybenzoyl)thiazole (8dc)

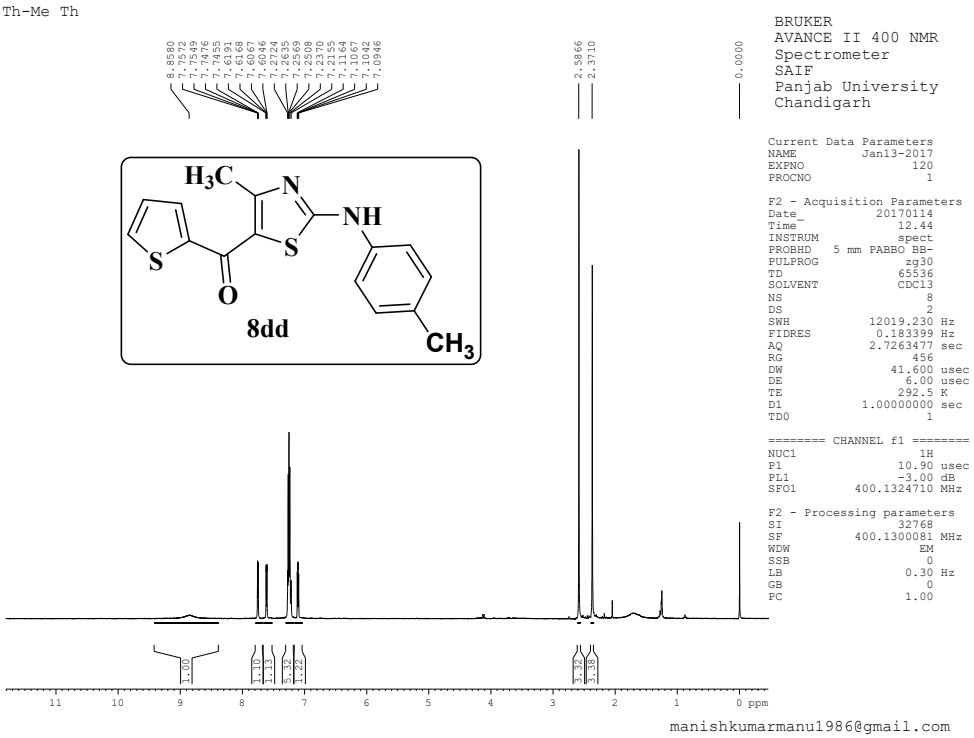


S6a: ^{1}H-spectrum of compound **8dc**

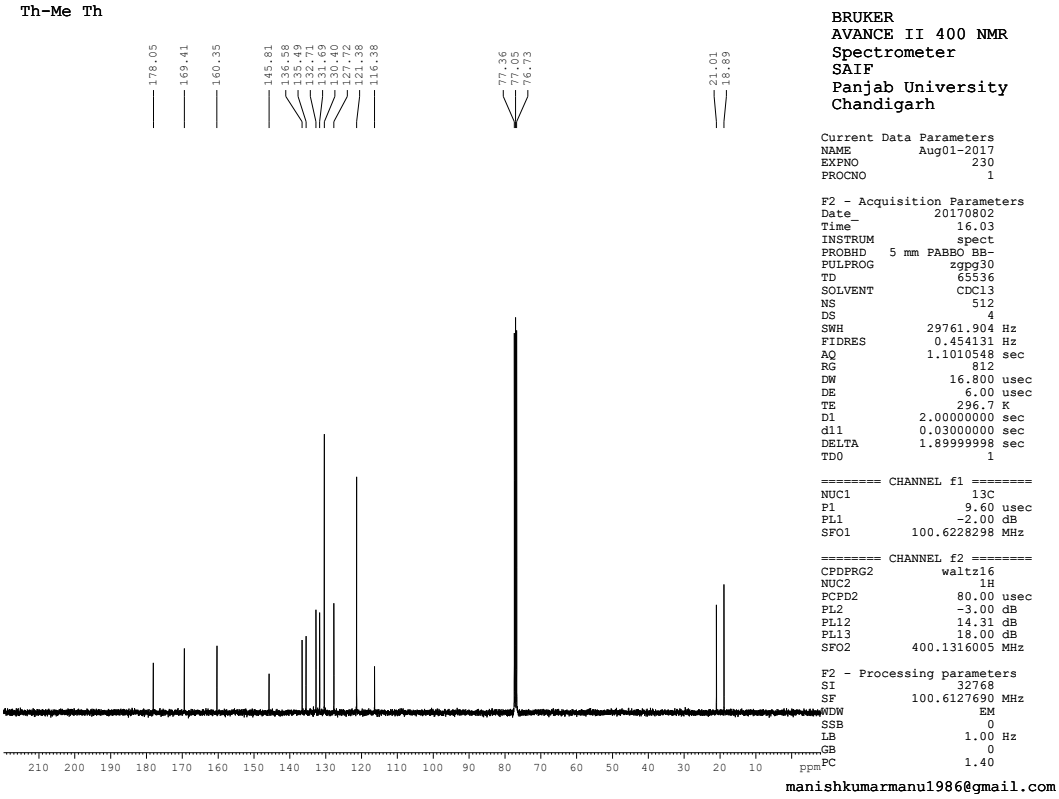


S6b: ^{13}C-spectrum of compound **8dc**

7. 2-(*N*-(*p*-methylphenyl)amino)-4-methyl-5-(2-thienoyl)thiazole (8dd)

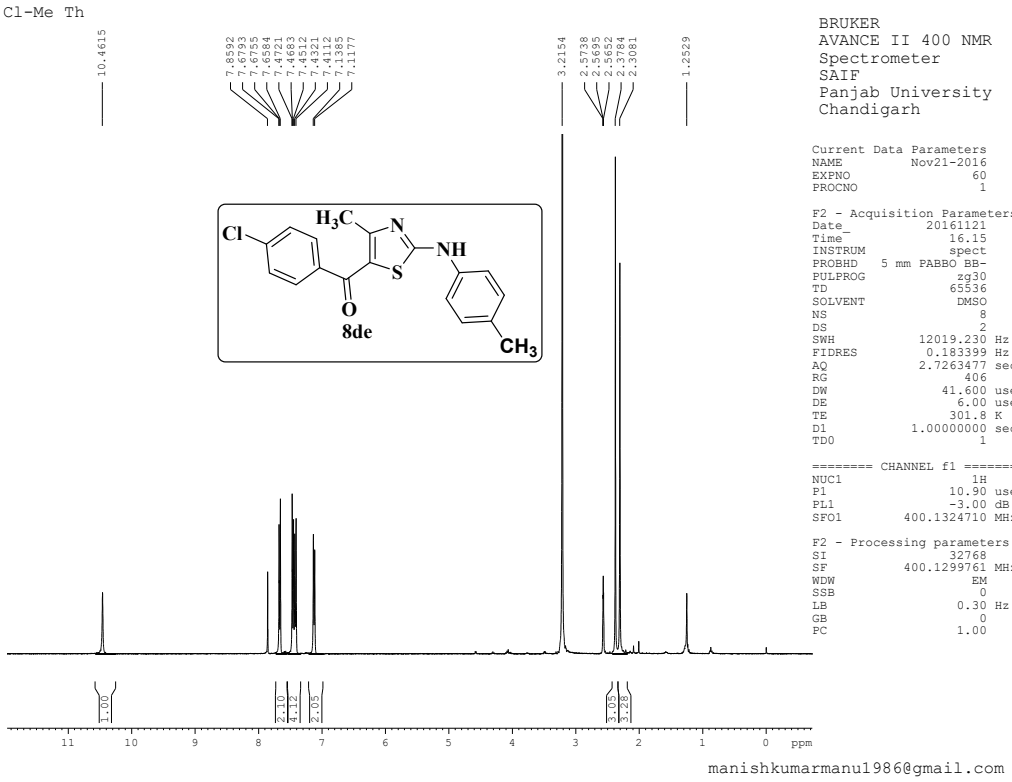


S7a: ^{1}H-spectrum of compound **8dd**

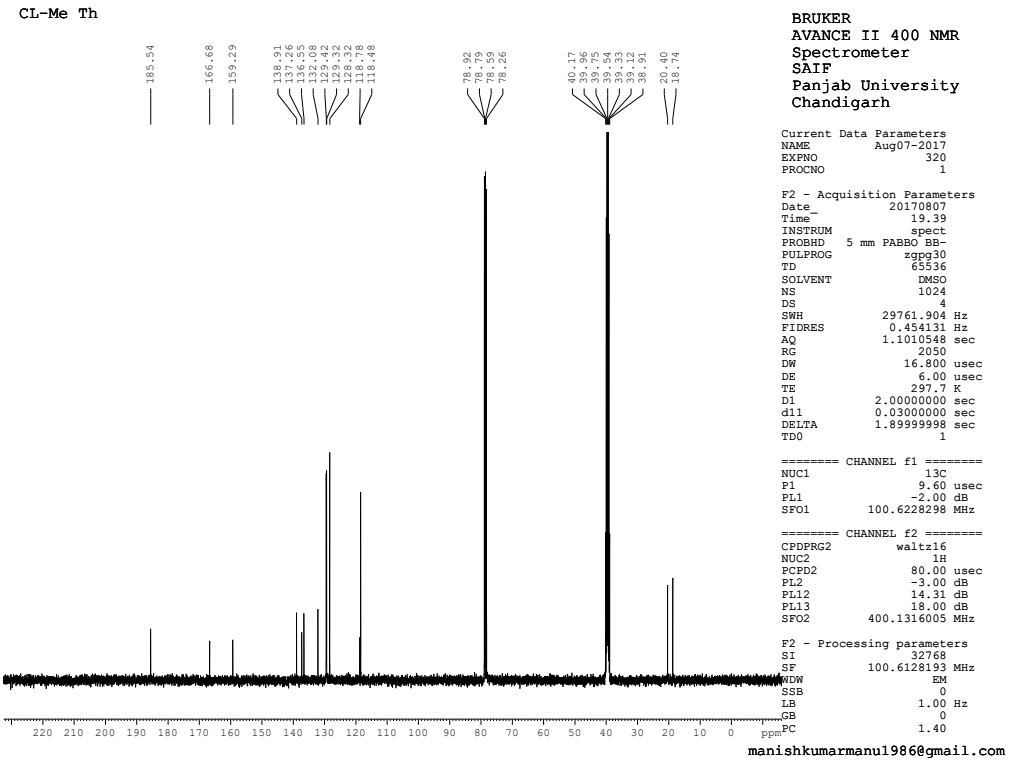


S7b: ^{13}C-spectrum of compound **8dd**

8. 2-(*N*-(*p*-methylbenzyl)amino)-4-methyl-5-(*p*-chlorobenzoyl)thiazole (8de)

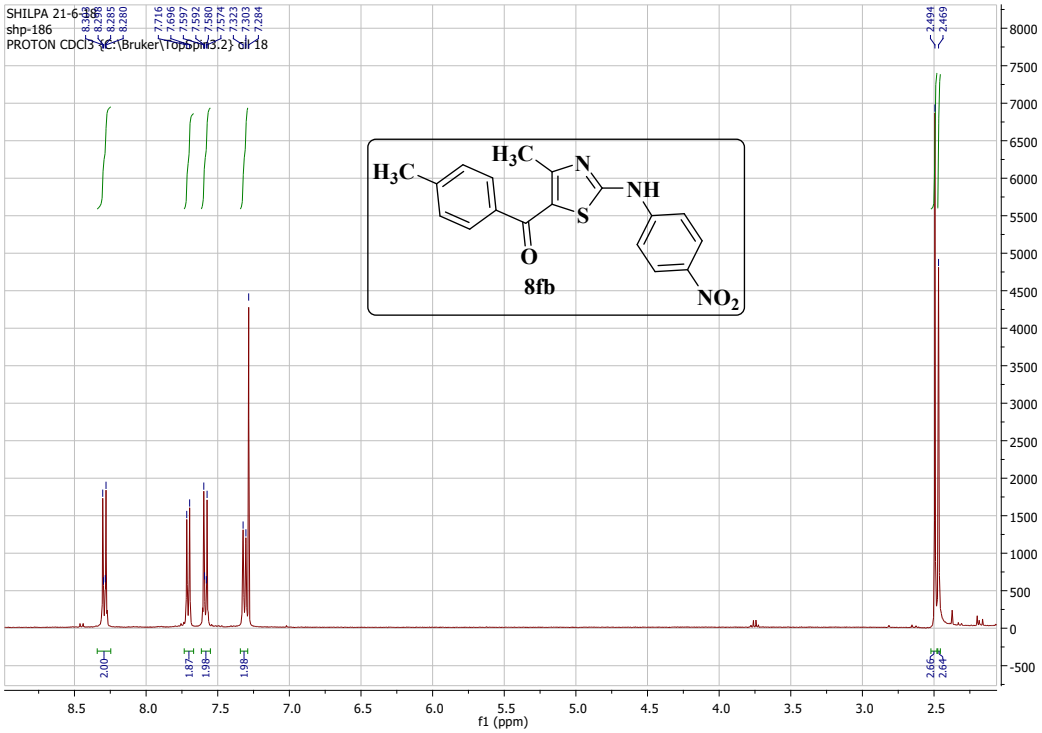


S8a: ^{1}H-spectrum of compound **8de**

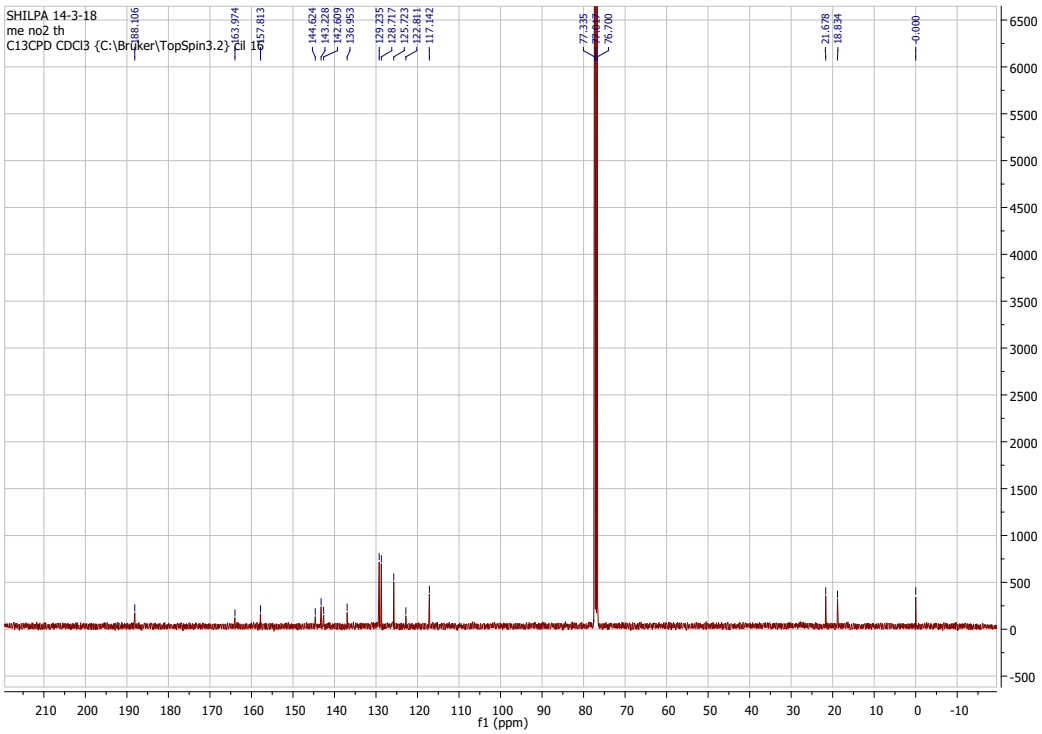


S8b: ^{13}C-spectrum of compound **8de**

9. 2-(*N*-(*p*-nitrophenyl)amino)-4-methyl-5-(*p*-methylbenzoyl)thiazole (8fb)

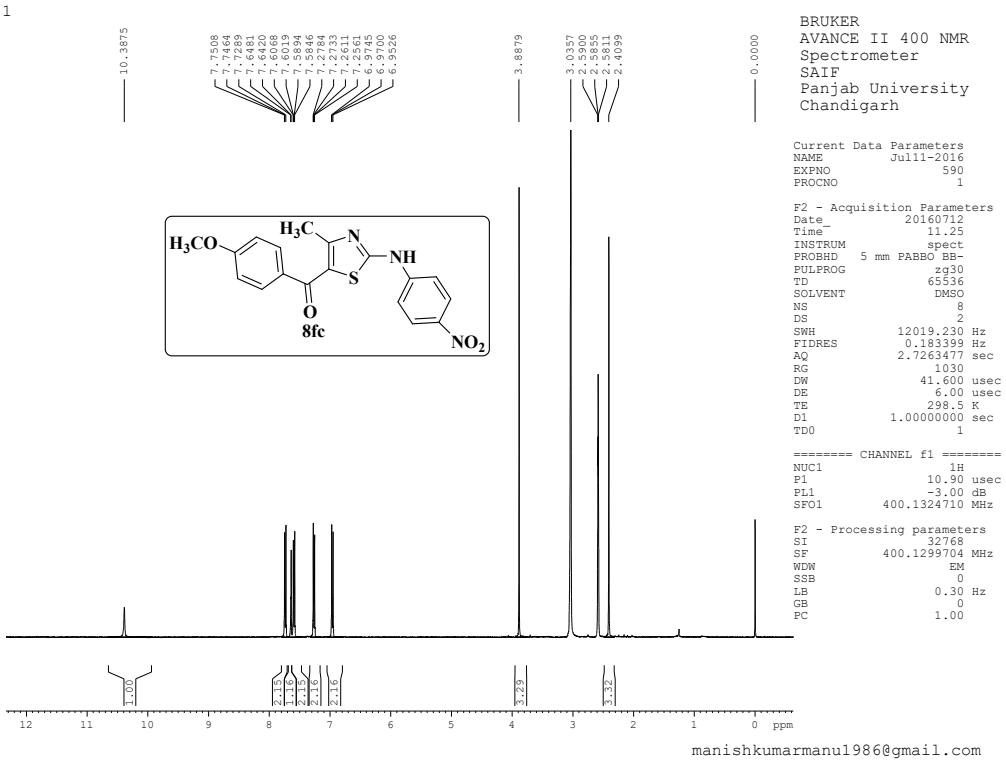


S9a: ^{1}H-NMR spectrum of compound **8fb**

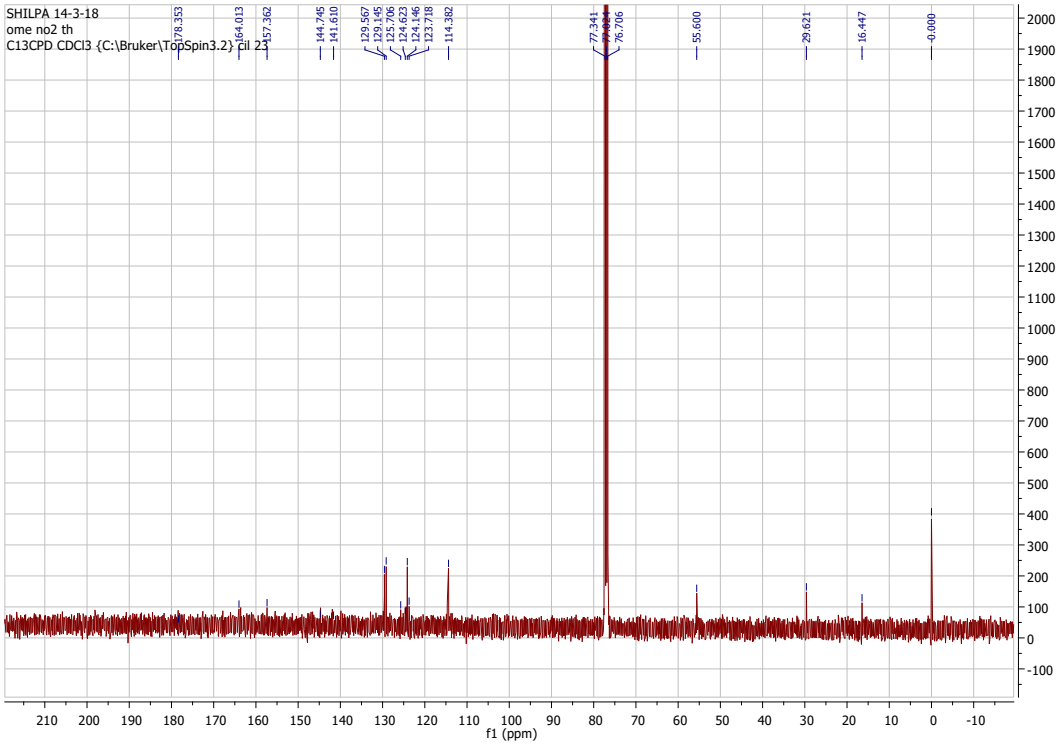


S9b: ^{13}C-NMR spectrum of compound **8fb**

10. 2-(*N*-(*p*-nitrophenyl)amino)-4-methyl-5-(*p*-methoxybenzoyl)thiazole (8fc)

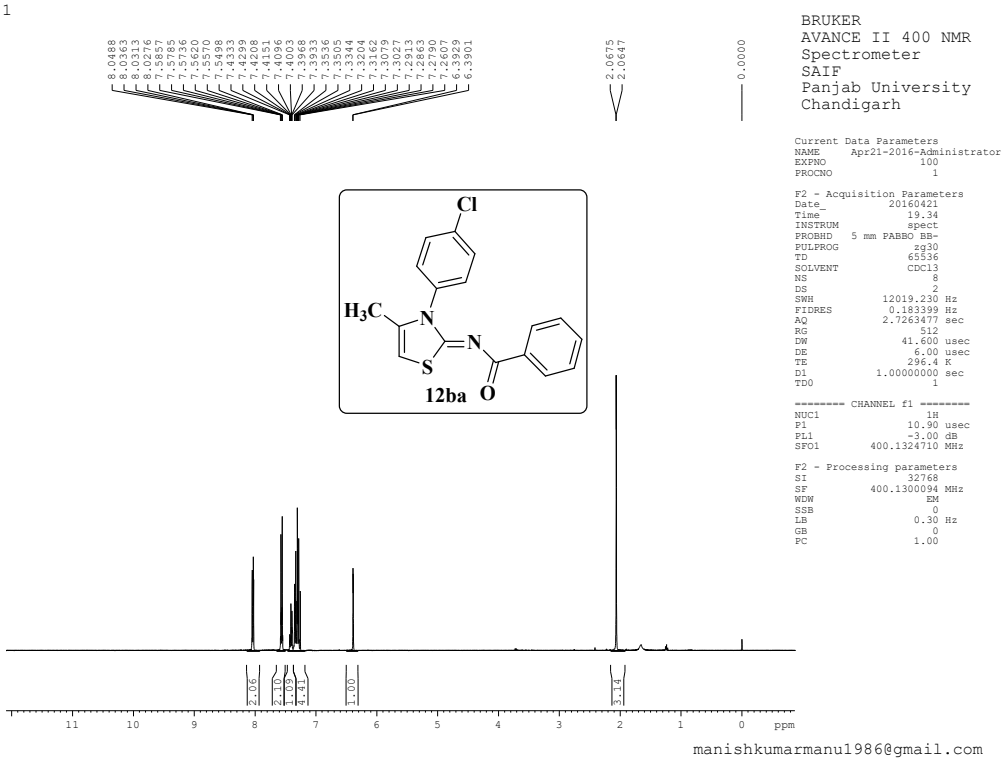


S10a: ^{1}H-NMR spectrum of compound **8fc**

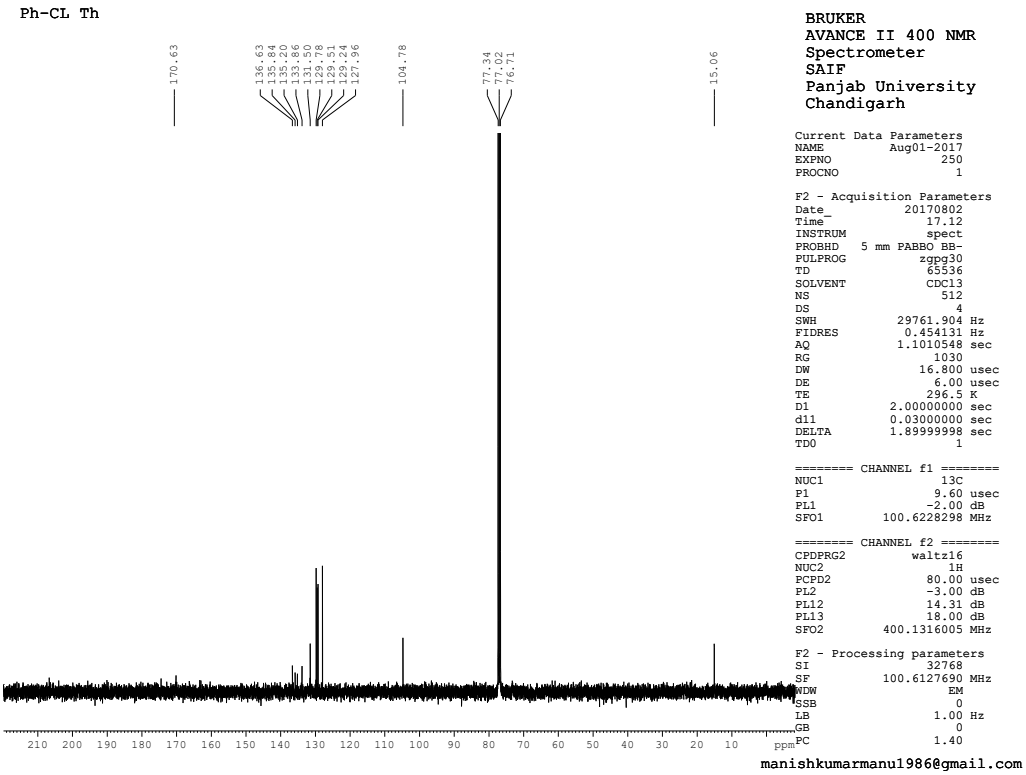


S10b: ^{13}C-NMR spectrum of compound **8fc**

11. 2-(*N*-benzoylimino)-3-*N*-(*p*-chlorophenyl)-4-methylthiazole (12ba)

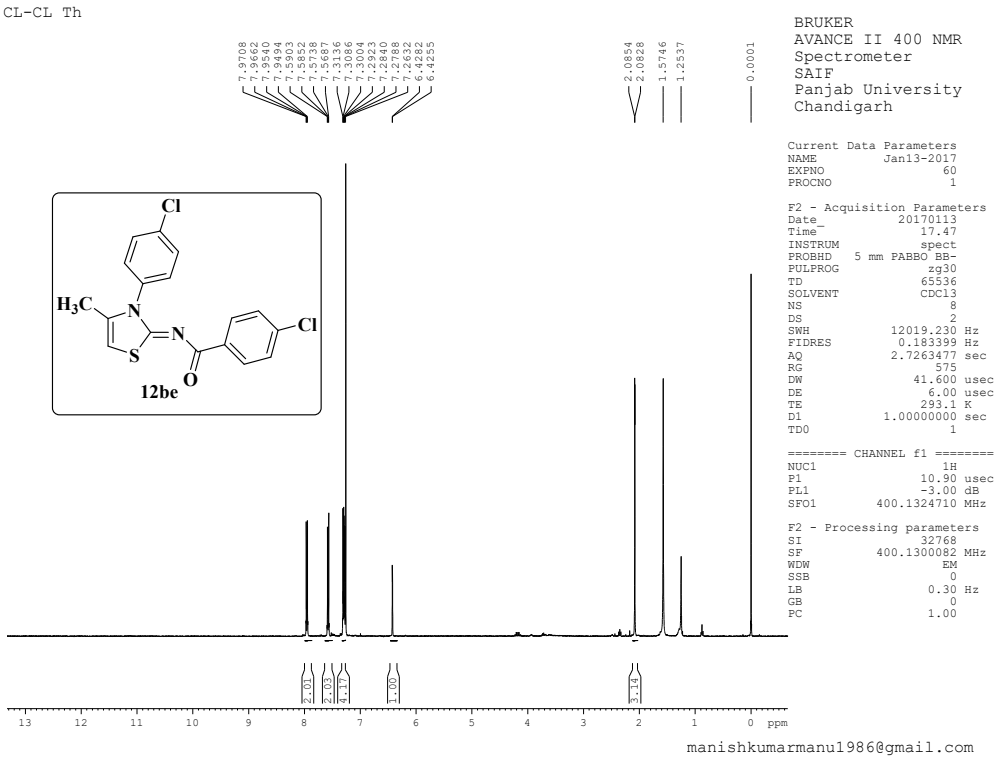


S11a: ^{1}H-NMR spectrum of compound **12ba**

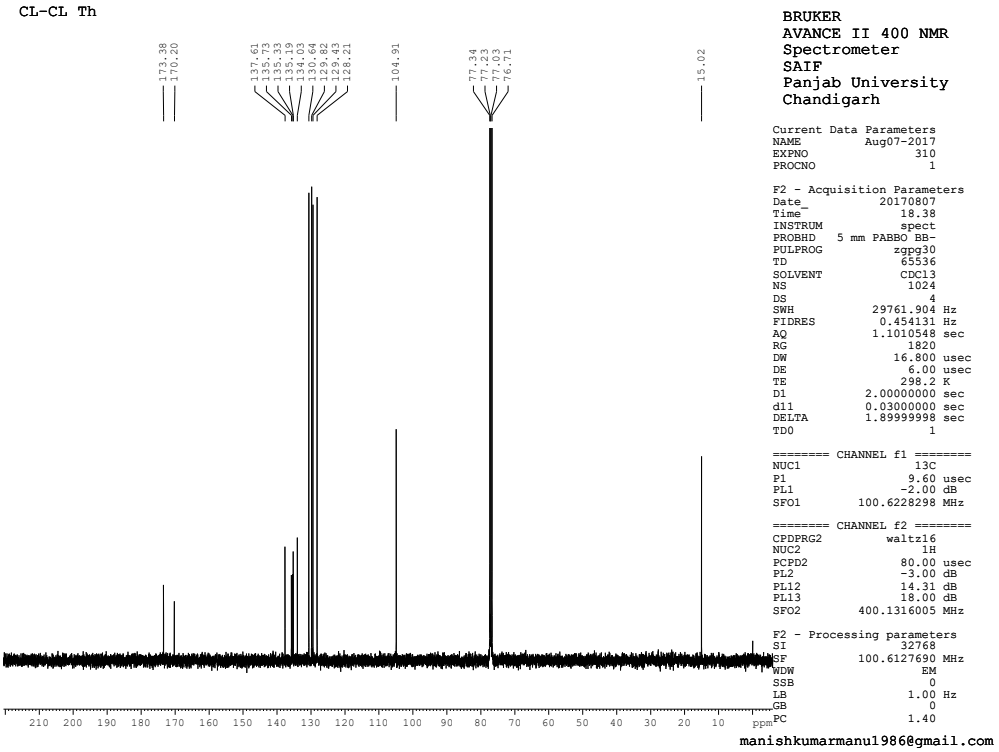


S11b: ^{13}C-NMR spectrum of compound **12ba**

12. 2-(*N*-(*p*-chlorobenzoyl)imino)-3-*N*-(*p*-chlorophenyl)-4-methylthiazole (12be)

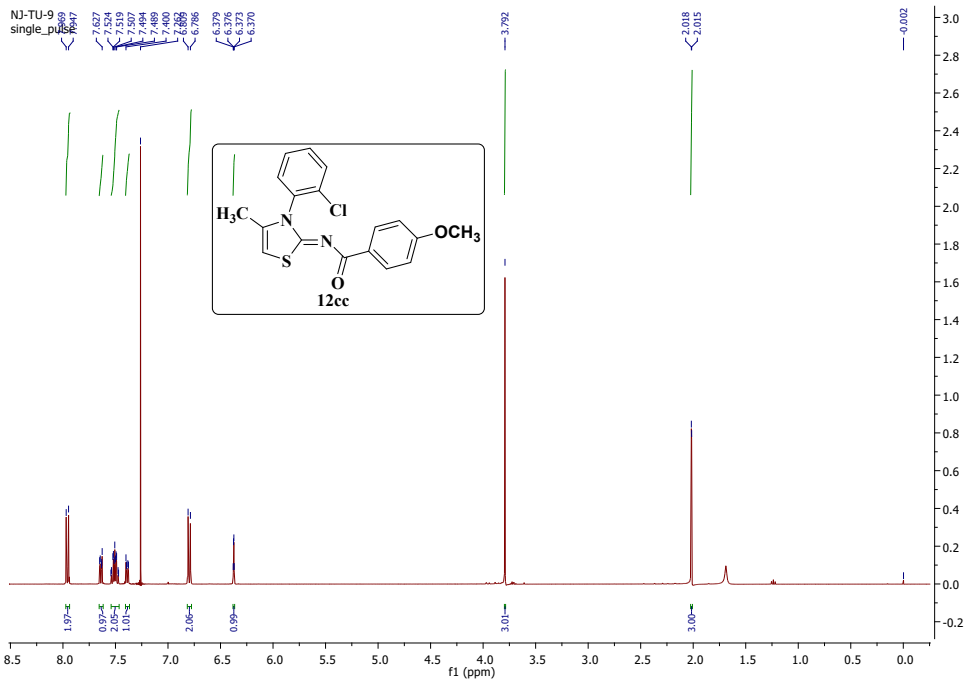


S12a: ^{1}H-spectrum of compound **12be**

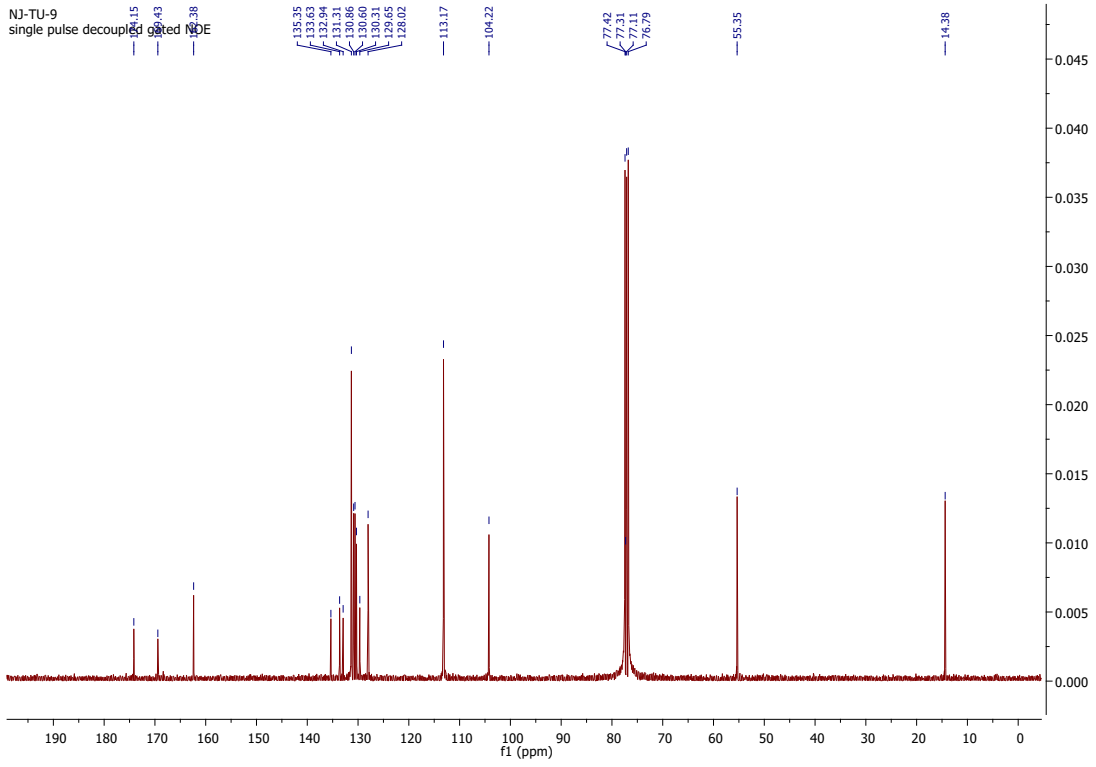


S12b: ^{13}C-spectrum of compound **12be**

13. 2-(*N*-*p*-methoxybenzoylimino)-3-*N*-(*o*-chlorophenyl)-4-methylthiazole (12cc)

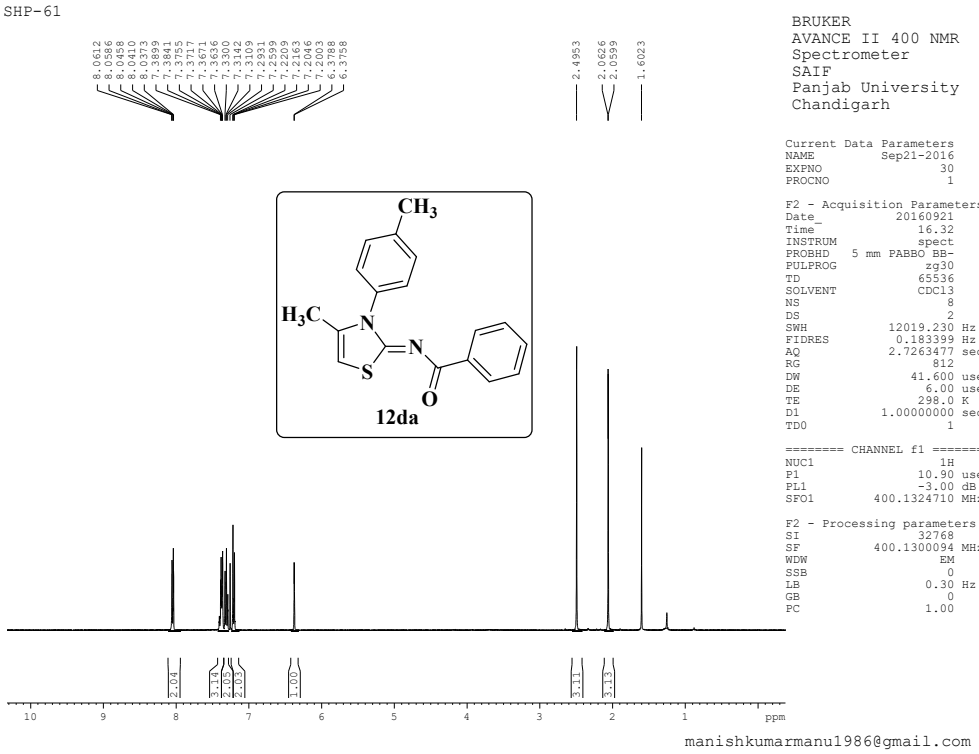


S13a: ^{1}H-NMR spectrum of compound **12cc**

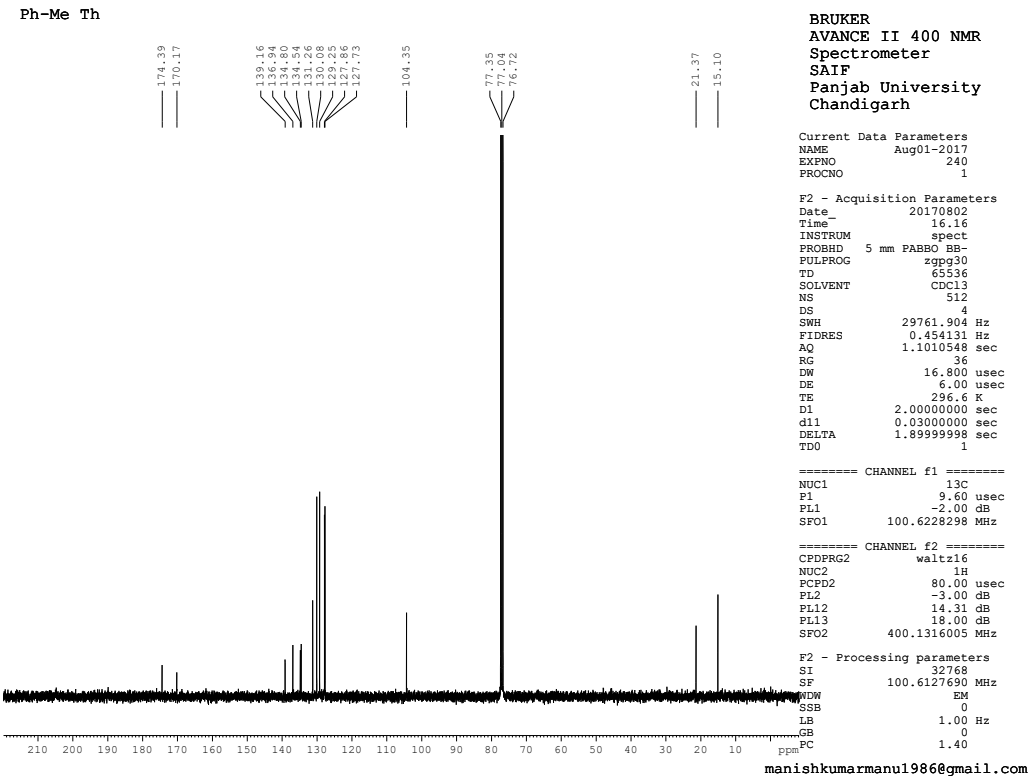


S13b: ^{13}C-NMR spectrum of compound **12cc**

14. 2-(*N*-benzoylimino)-3-*N*-(*p*-methylphenyl)-4-methylthiazole (12da)

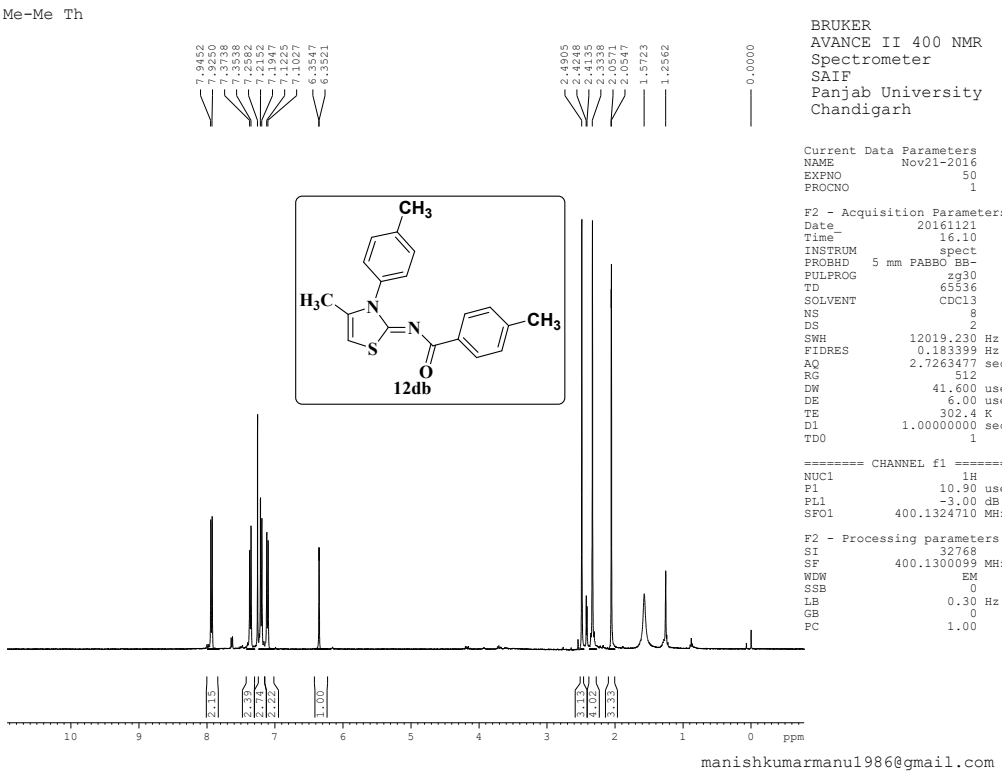


S14a: ^{1}H-NMR spectrum of compound **12da**

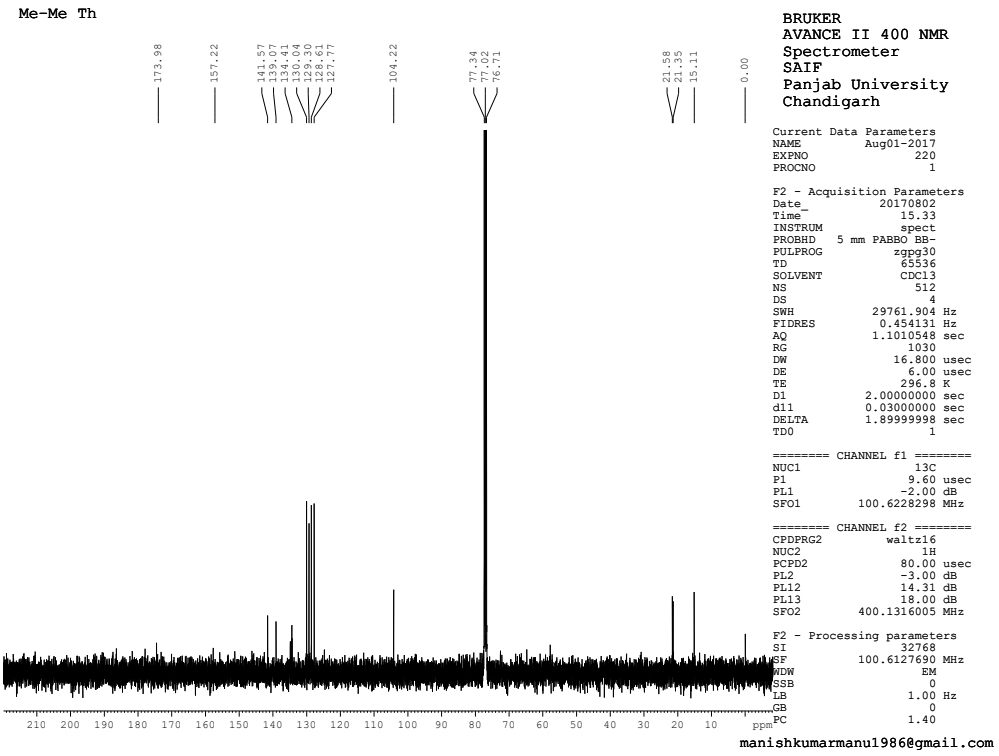


S14b: ^{13}C-NMR spectrum of compound **12da**

15. 2-(*N*-(*p*-methylbenzoyl)imino)-3-*N*-(*p*-methylphenyl)-4-methylthiazole (12db)

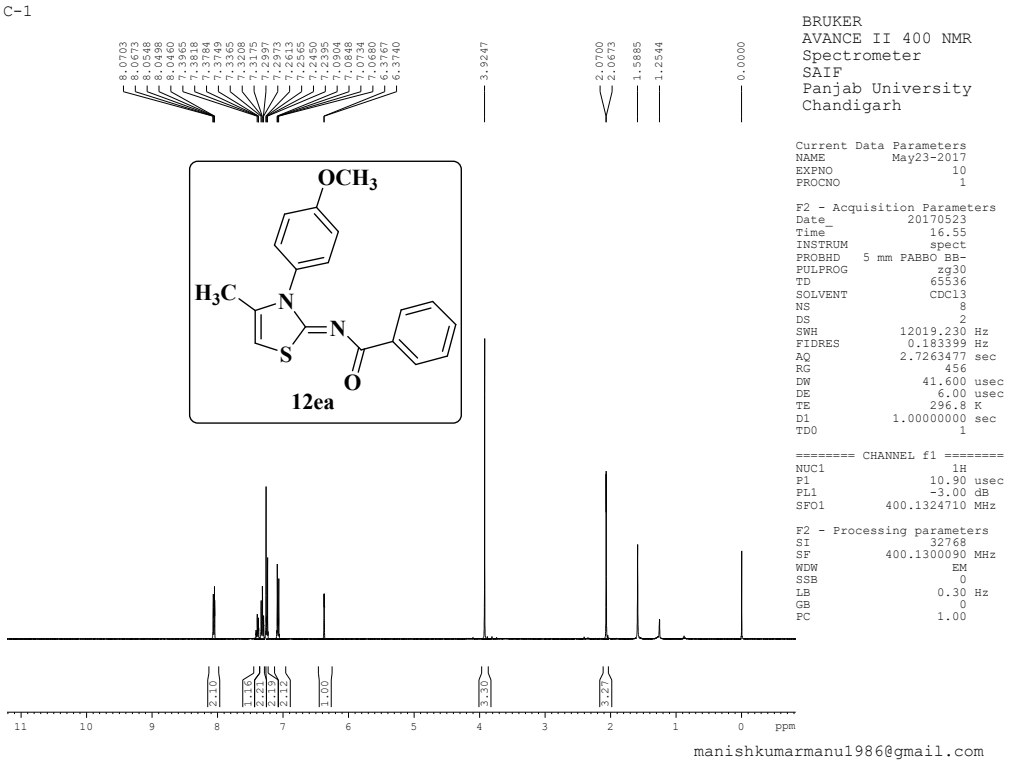


S15a: ^{1}H-NMR spectrum of compound **12db**

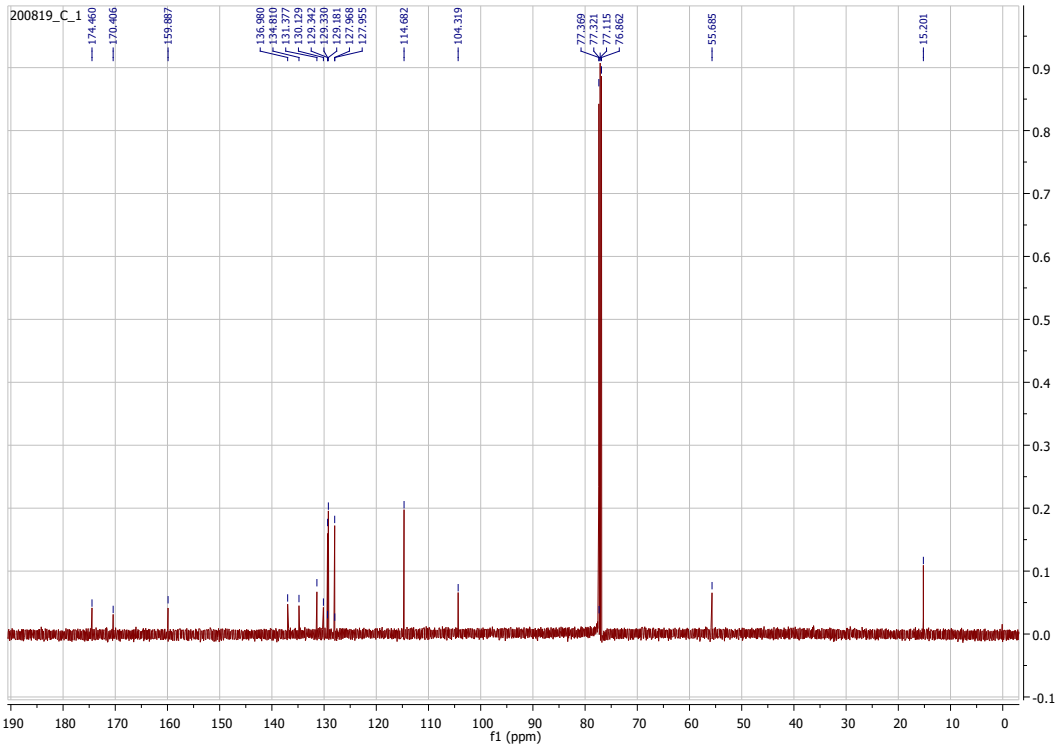


S15b: ^{13}C-NMR spectrum of compound **12db**

16. 2-(*N*-benzoylimino)-3-*N*-(*p*-methoxyphenyl)-4-methylthiazole (12ea)

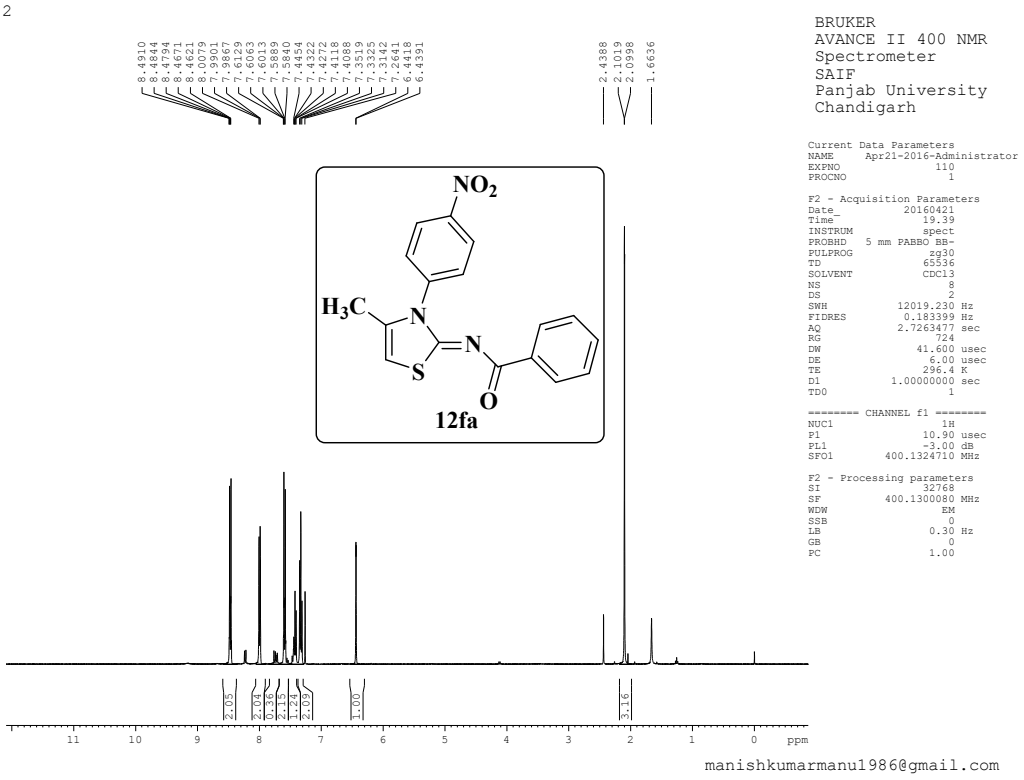


S16a: ^{1}H-NMR spectrum of compound **12ea**

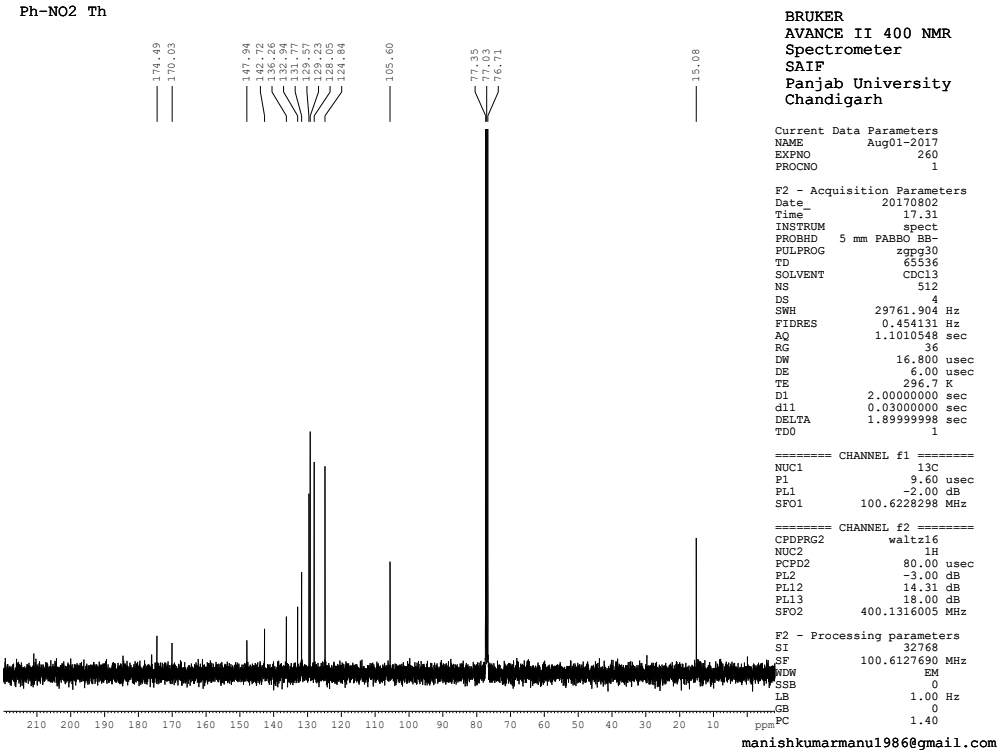


S16b: ^{13}C-NMR spectrum of compound **12ea**

17. 2-(*N*-benzoylimino)-3-*N*-(*p*-nitrophenyl)-4-methylthiazole (12fa)

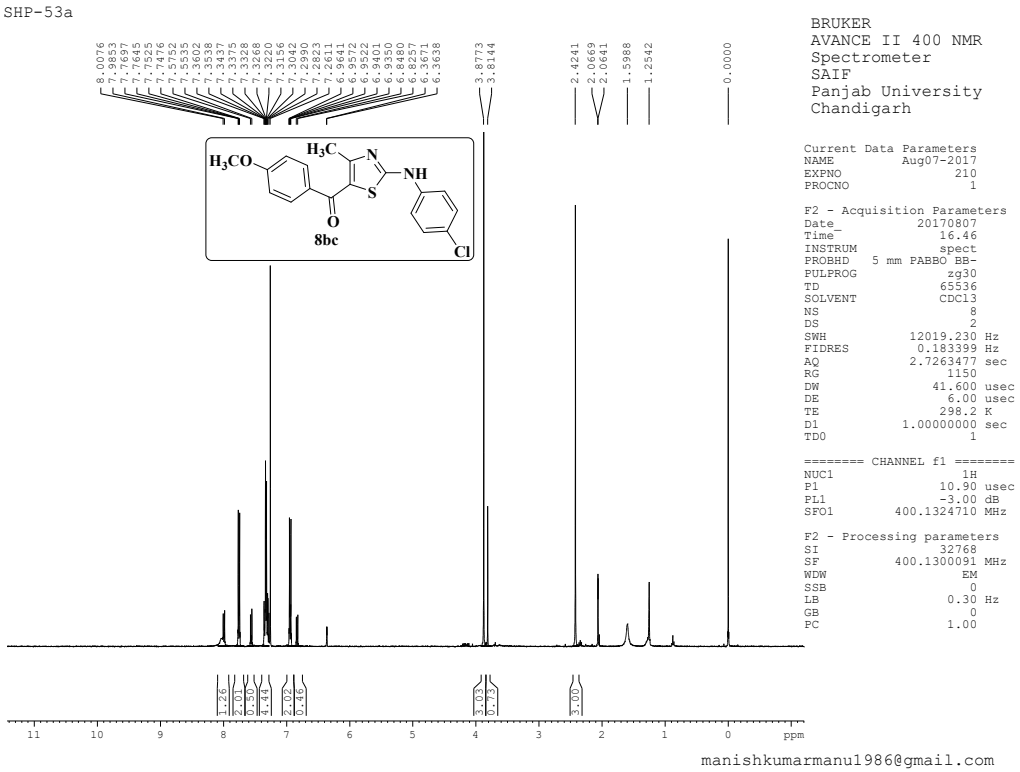


S17a: ^{1}H-NMR spectrum of compound **12fa**

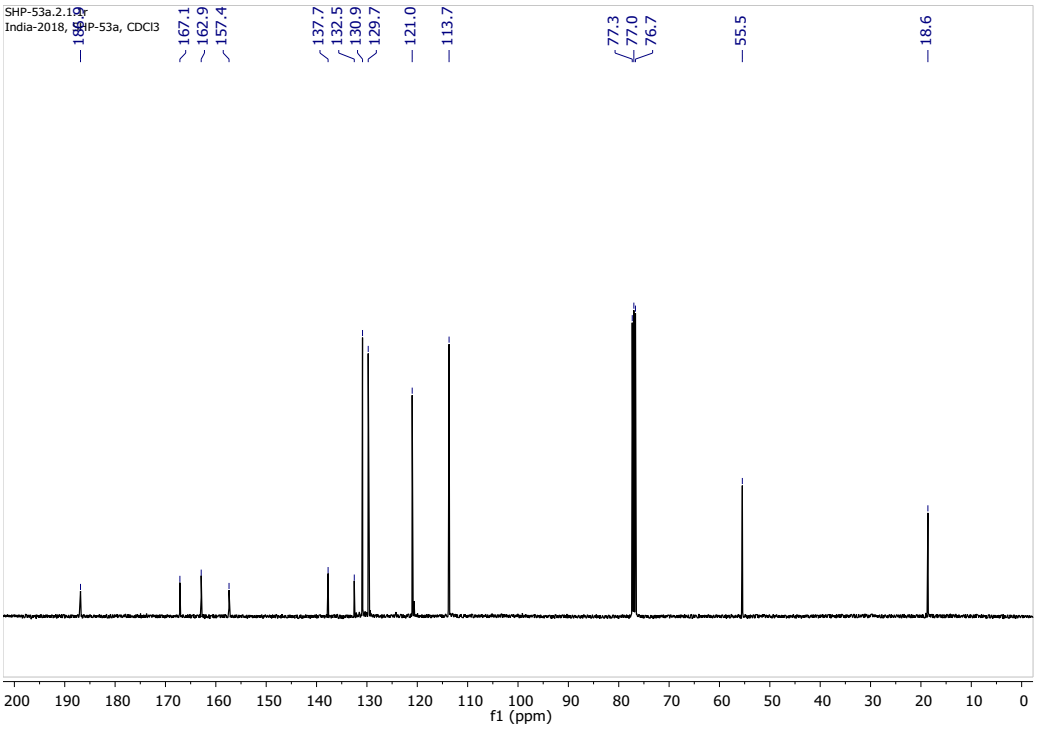


S17b: ^{13}C-NMR spectrum of compound **12fa**

18. 2-(*N*-(*p*-chlorophenyl)amino)-4-methyl-5-(*p*-methoxybenzoyl)thiazole (8bc)

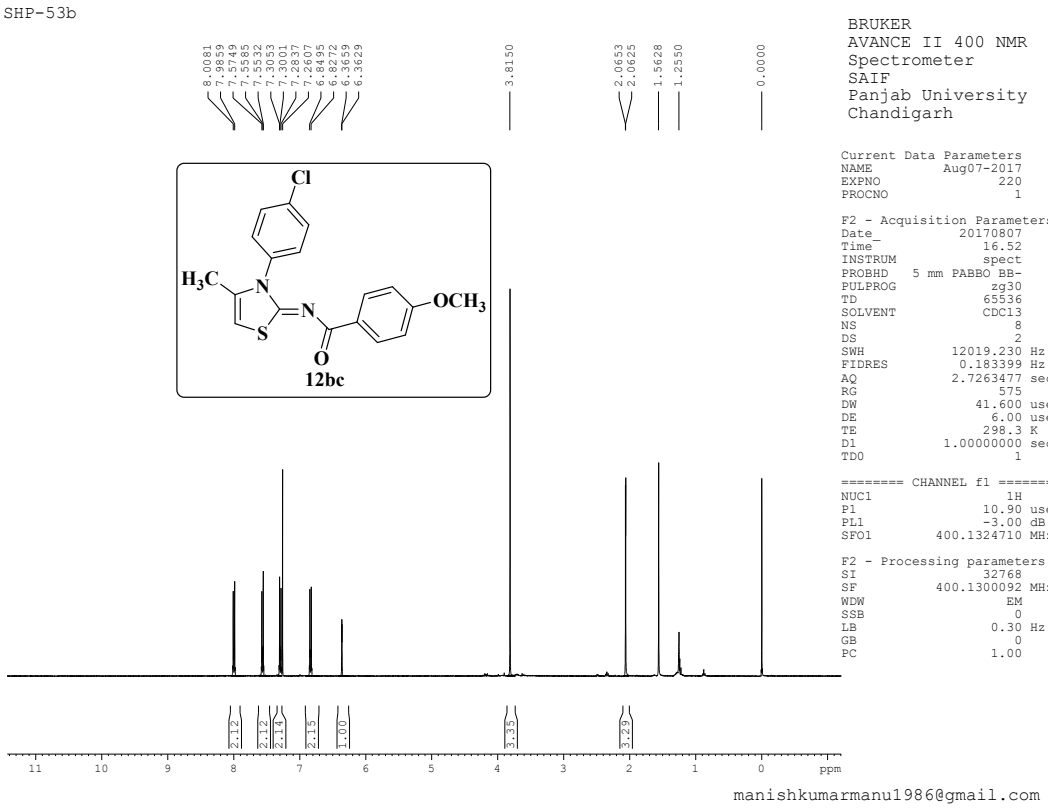


S18a: ^{1}H-spectrum of compound **8bc**

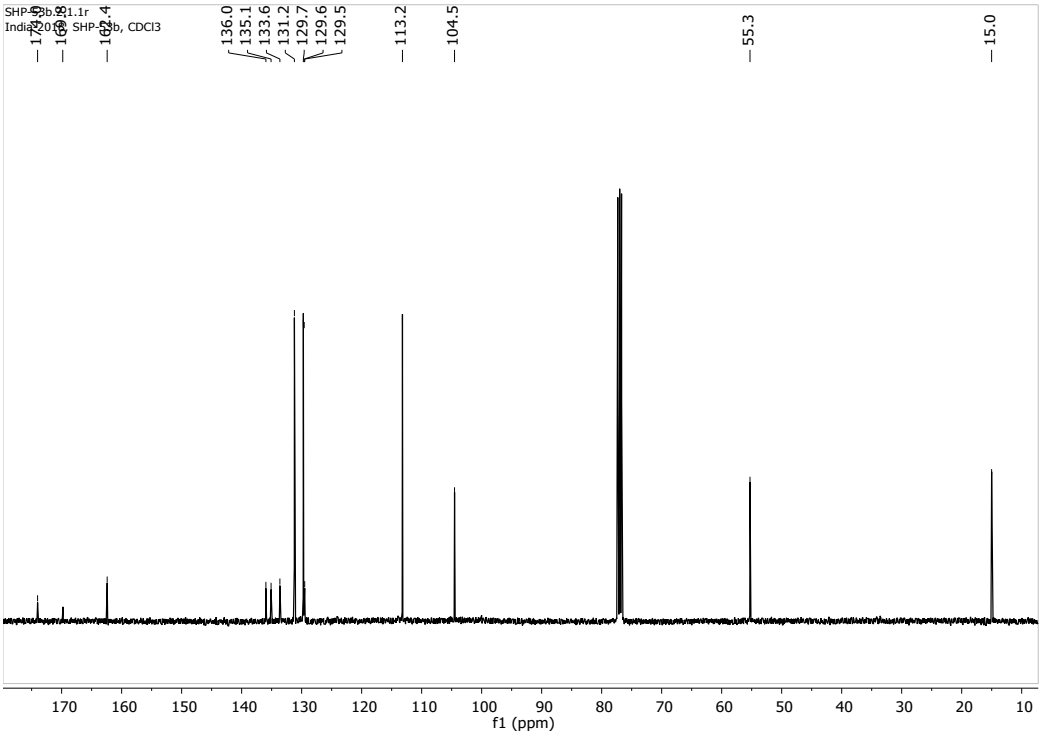


S18b: ^{13}C-spectrum of compound **8bc**

19. 2-(*N*-(*p*-methoxybenzoyl)imino)-3-*N*-(*p*-chlorophenyl)-4-methylthiazole (12bc)

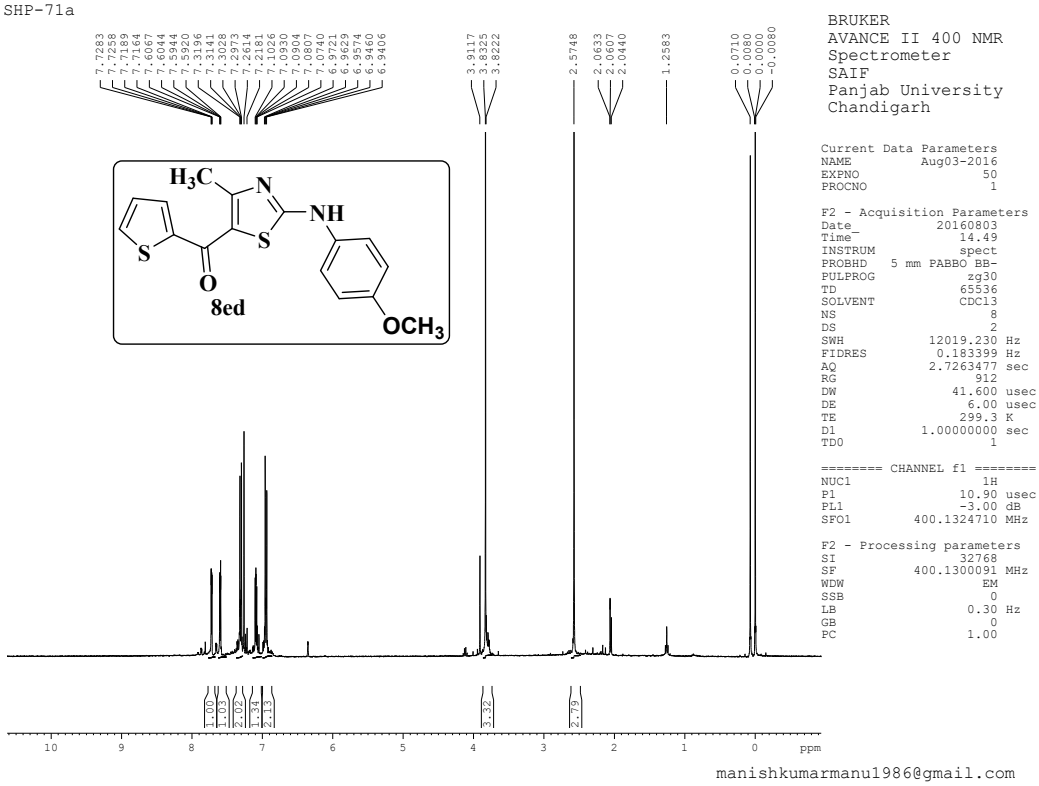


S19a: ^{1}H-spectrum of compound **12bc**

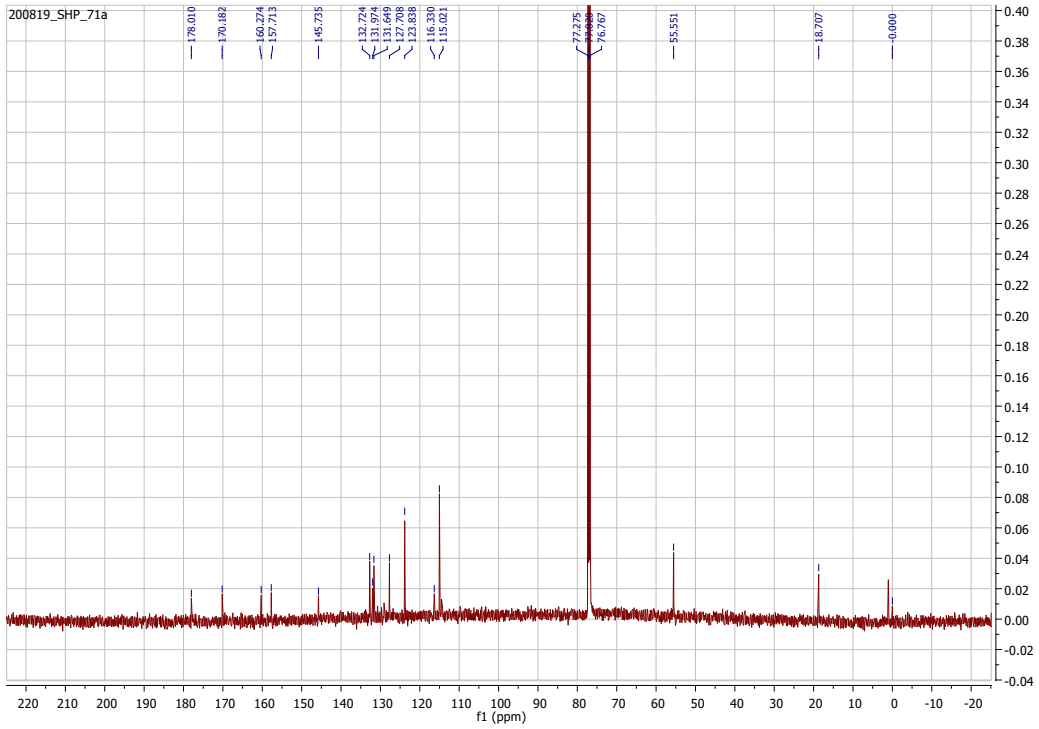


S19b: ^{13}C-spectrum of compound **12bc**

20. 2-(*N*-(*p*-methoxyphenyl)amino)-4-methyl-5-(2-thienoyl)thiazole (8ed)

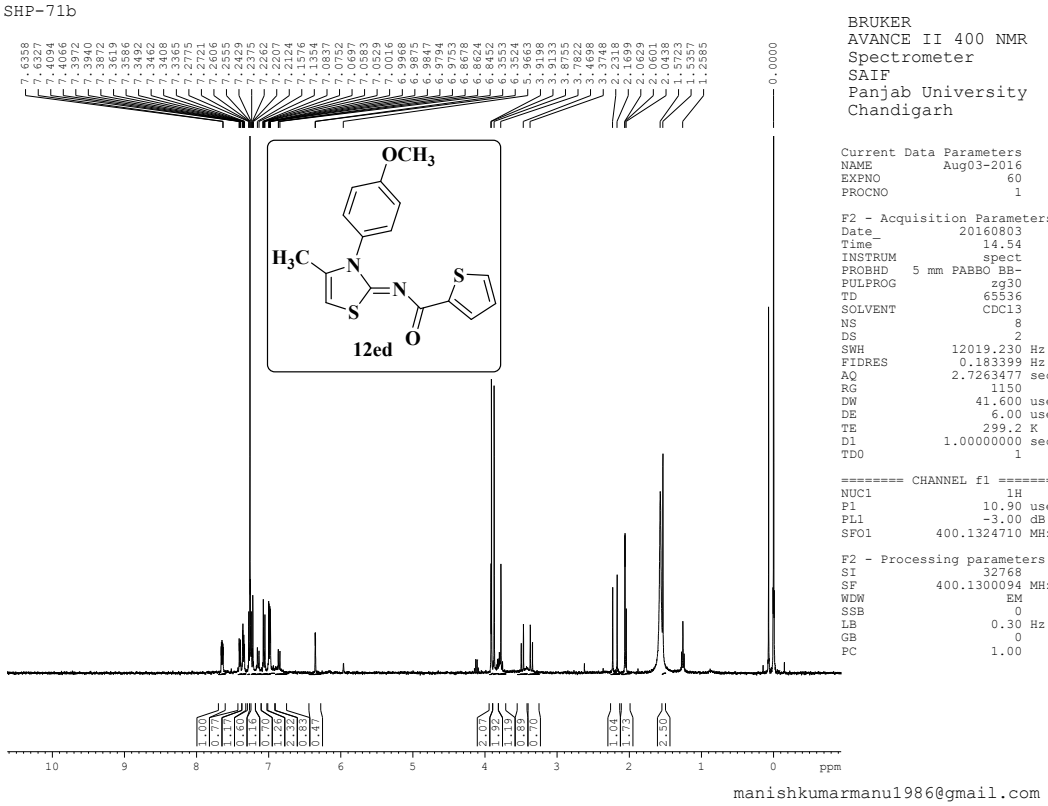


S20a: ^{1}H-spectrum of compound **8ed**



S20b: ^{13}C-spectrum of compound **8ed**

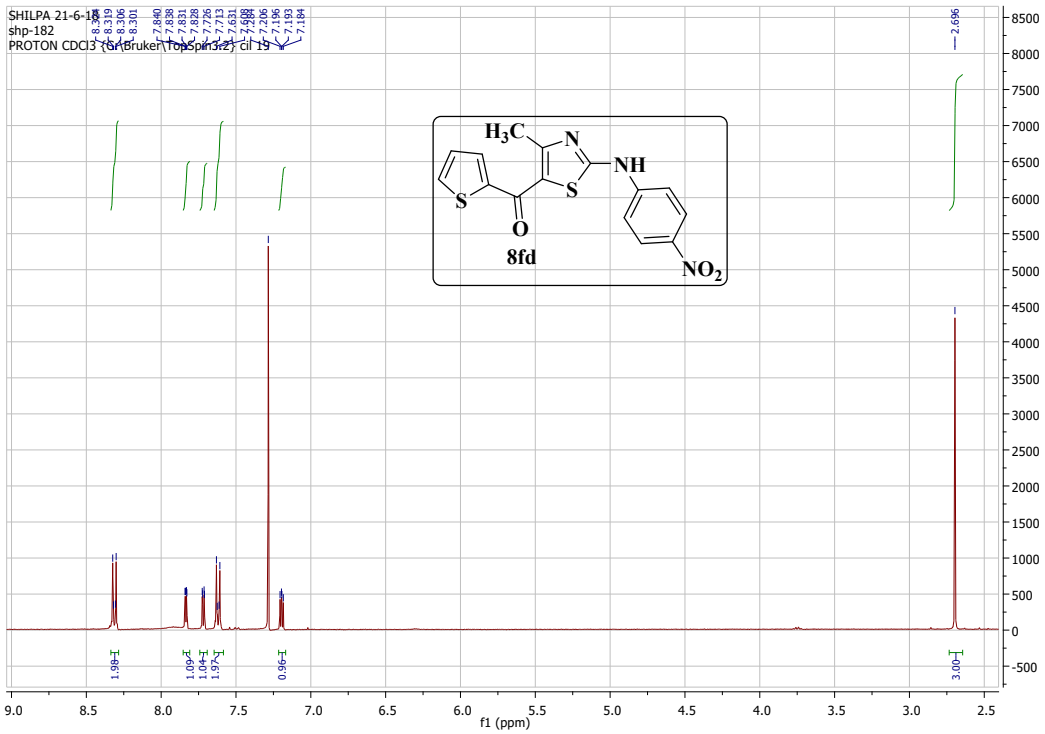
21. 2-(*N*-(2-thienoyl)imino)-3-*N*-(*p*-methoxyphenyl)-4-methylthiazole (12ed)



manishkumarmanu1986@gmail.com

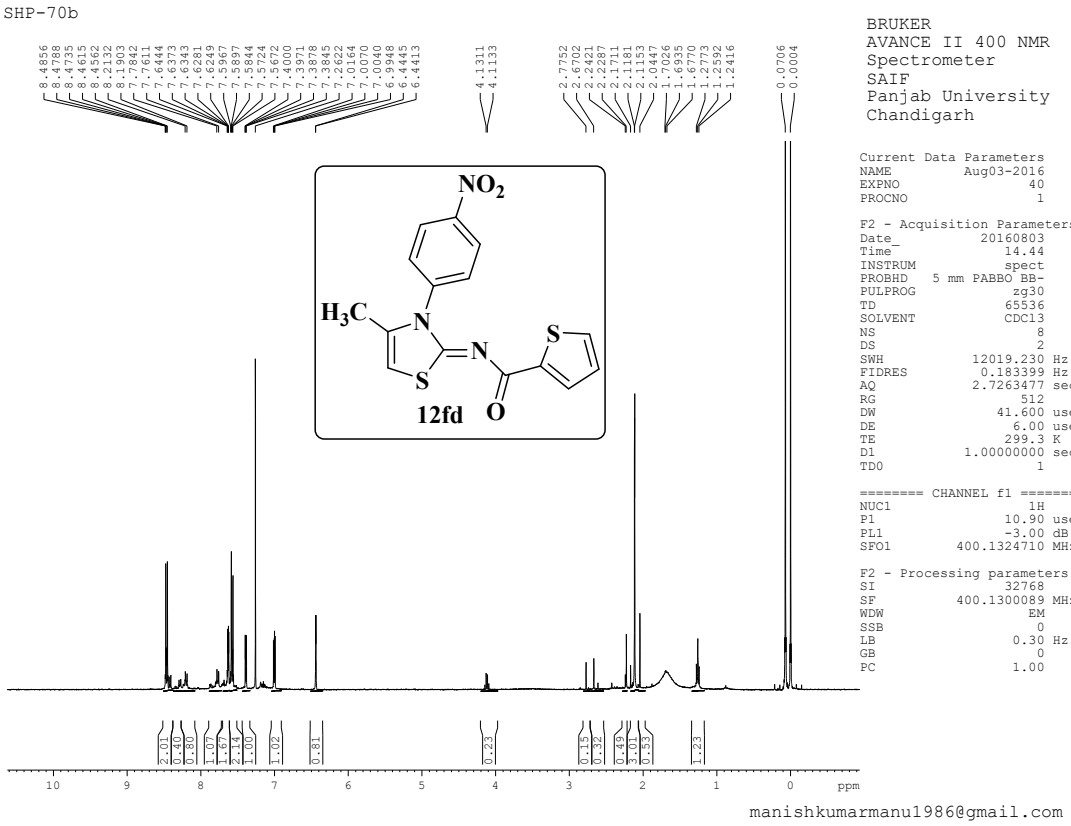
S21: ^{1}H-spectrum of compound **12ed**

22. 2-(*N*-(*p*-nitrophenyl)amino)-4-methyl-5-(2-thienoyl)thiazole (8fd)



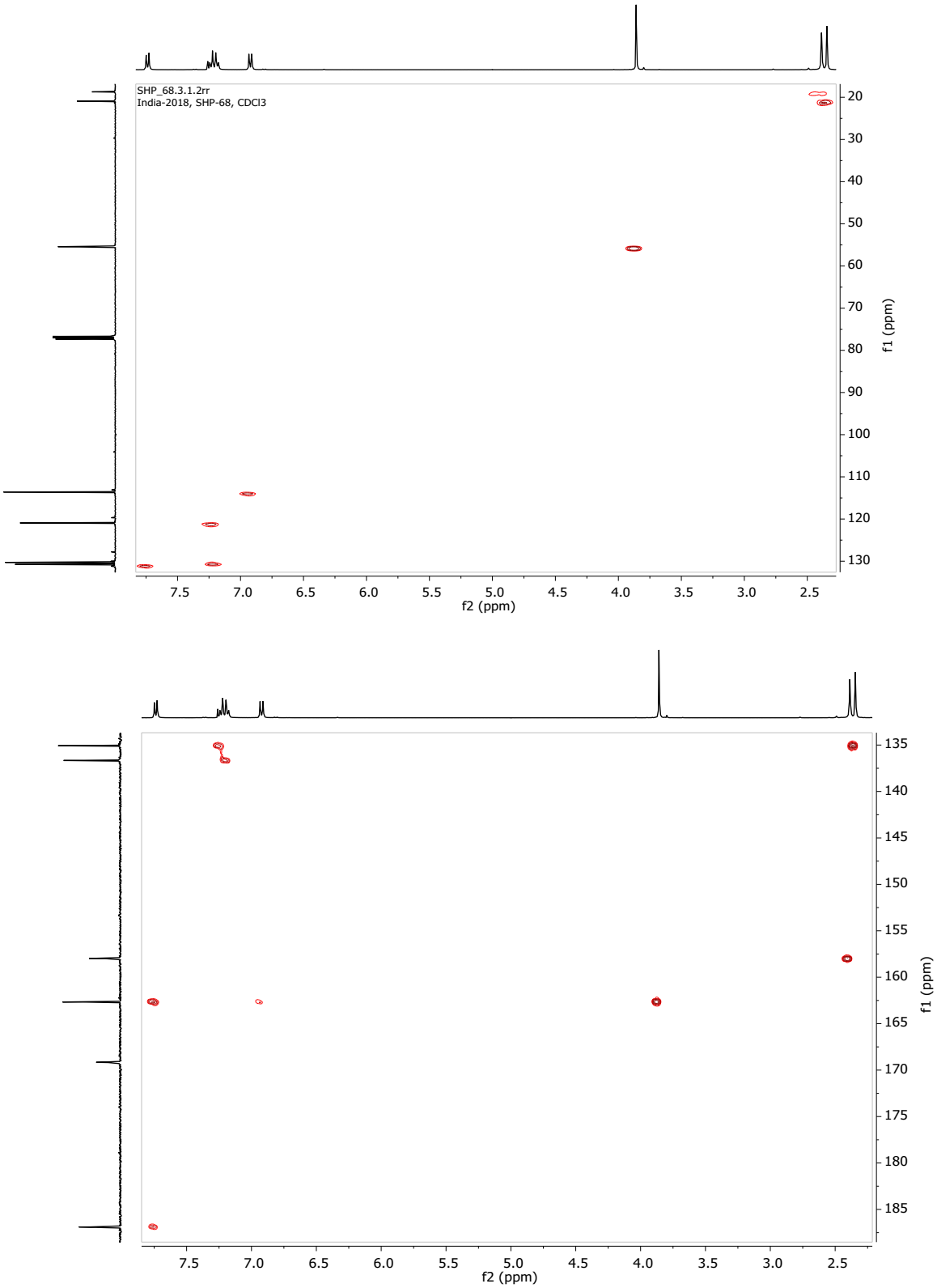
S22: ^{1}H-NMR spectrum of compound **8fd**

23. 2-(*N*-(2-thienoyl)imino)-3-*N*-(*p*-nitrophenyl)-4-methylthiazole (12fd)



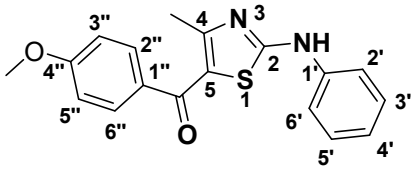
S23: ^{1}H-NMR spectrum of compound **12fd**

2D NMR (HMBC and HMQC)

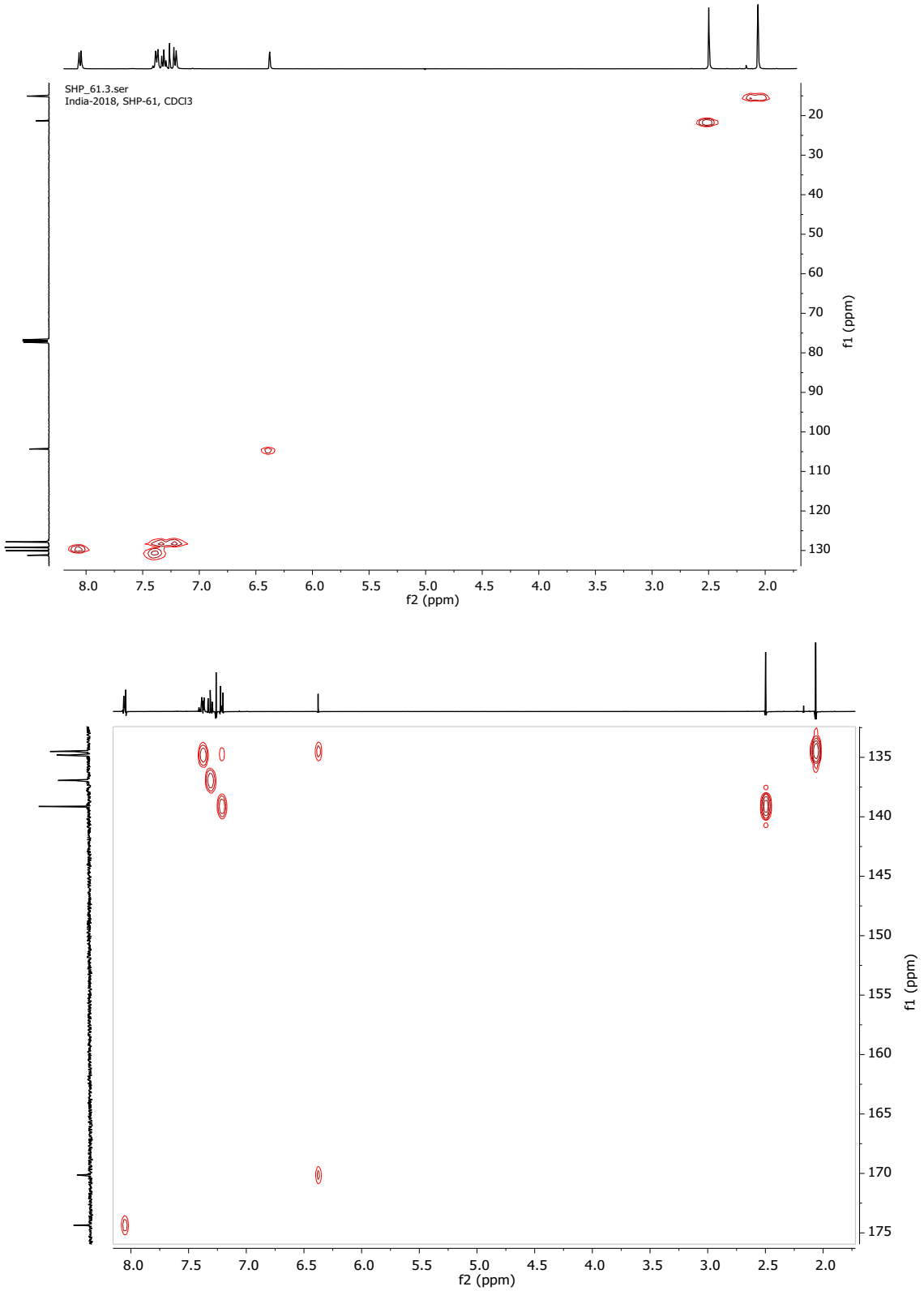


S7: 2D-spectrum of 2-(*N*-phenylamino)-4-methyl-5-(*p*-methoxybenzoyl)thiazole (**8ac**)

Table-S1: NMR data in $CDCl_3$, chemical shifts (δ, ppm) and coupling constants (*J*, Hz) for compound **8ac**

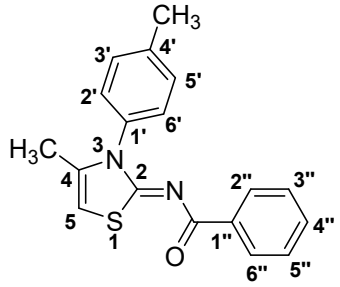


Chemical shifts (δ in ppm)	gs-HMQC correlation	gs-HMBC correlation	Assignments
186.9	---	7.74 (2",6"-H)	CO
169.2	---	-----	C-2
162.7	---	7.74 (2",6"-H)	C-4"
		6.92(3",5"-H)	
		3.86 (4"-OCH_3)	
158.0	---	2.39 (4-CH_3)	C-4
136.6	---	7.19 (3',5'-H)	C1'
135.1	---	7.23 (2',6'-H)	C-4'
		2.34 (4'-CH_3)	
132.9	---	6.92 (3",5"-H)	C-1"
130.7	7.74 (2",6"-H)	7.74 (2",6"-H)	C-2",6"
130.3	7.19 (3',5'-H)	7.19 (3',5'-H)	C-3',C5'
		2.34 (4'-CH_3)	
120.9	7.23 (2',6'-H)	7.23 (2',6'-H)	C-2',6'
		2.39 (4-CH_3)	
119.7	-	2.39 (4-CH_3)	C-5
113.6	6.92 (3",5"-H)	6.92 (3",5"-H)	C-3",5"
55.4 (^1J=144.1)	3.86 (4"-OCH_3)	-	4"-OCH_3
20.9 (^1J=126.5)	2.34 (4'-CH_3)	7.19 (3',5'-H)	4'-CH_3
18.7 (^1J=126.7)	2.39 (4-CH_3)	-	4-CH_3



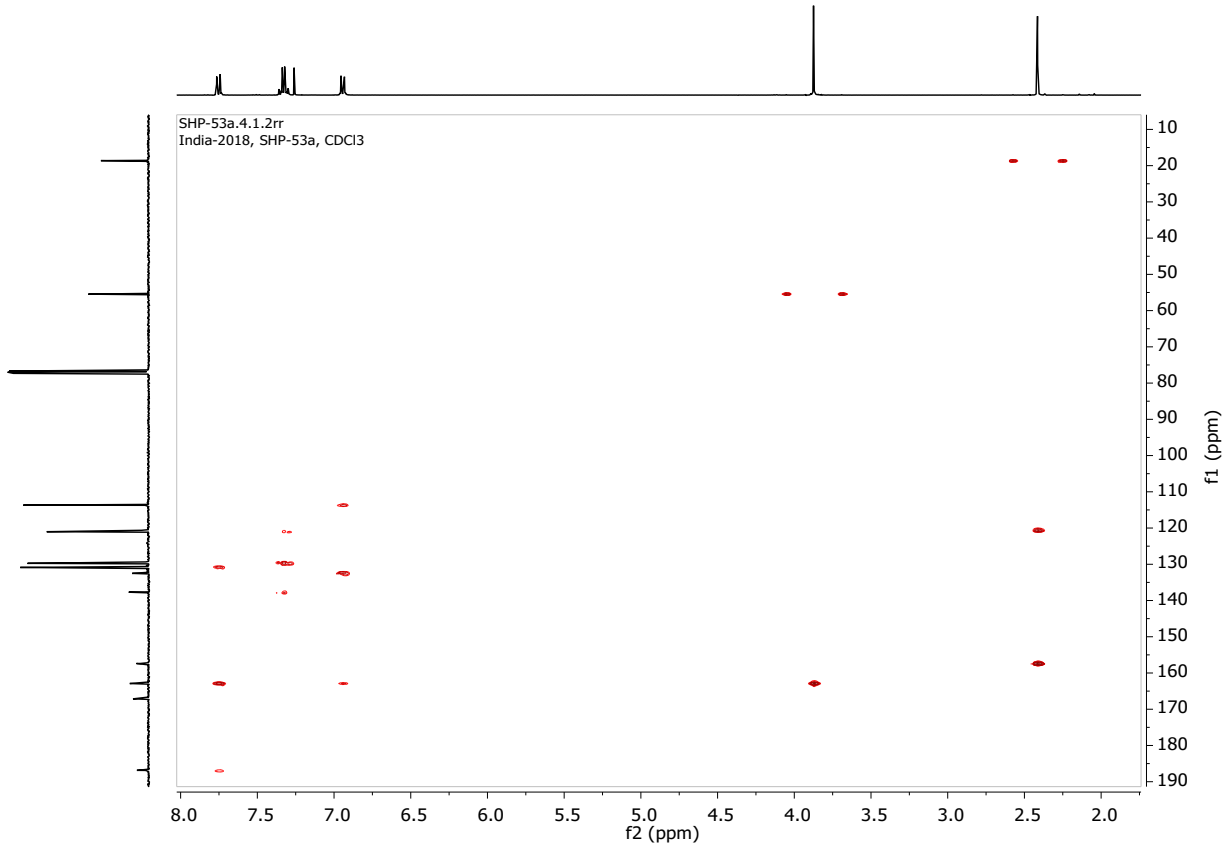
S30: 2D-NMR spectrum of 2-(*N*-benzoylimino)-3-*N*-(*p*-methylphenyl)-4-methylthiazole (**12da**)

Table S2: NMR data in $CDCl_3$, chemical shifts (δ, ppm) and coupling constants (*J*, Hz) for compound **8da**



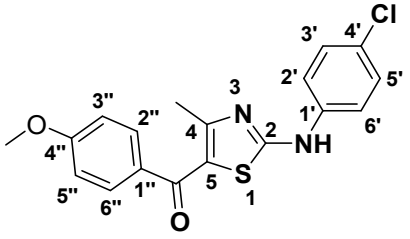
Chemical shifts (δ in ppm)	gs-HMQC correlation	gs-HMBC correlation	Assignments
174.3	-	8.05 (2",6"-H)	CO
170.1	-	6.38 (5-H)	C-2
139.1	-	2.50 (4'-CH_3) / 7.21 (2',6'-H)	C-4'
136.9	-	7.37-7.41 (3',5'-H)	C-1'
134.8	-	7.37-7.41 (4"-H)	C-1"
134.5	-	2.06 (4-CH_3) / 6.38 (5-H)	C-4
131.2	7.37-7.41 (4"-H)	8.05 (2",6"-H)	C-4"
130.1	7.37-7.41(3',5'-H)	2.50 (4'-CH_3)	C-3',5'
129.2	8.05 (2",6"-H)	7.37-7.41 (4"-H)	C-2",6"
127.8	7.31 (3",5"-H)	7.31 (3",5"-H)	C-3",5"
127.7	7.21 (2',6'-H)	-	C-2',6'
104.3	6.38 (5-H)	2.06 (4- CH_3)	C-5
21.3 (^1J=132.0)*	2.50 (4'-CH_3)	7.37-7.41 (3',5'-H)	4'-CH_3
15.1 (^1J=129.2)*	2.06 (4-CH_3)	6.38 (5-H)	4-CH_3
-206.1	-	2.06 (4-CH_3) / 6.38 (5-H)	N

*Measurements on HMBC

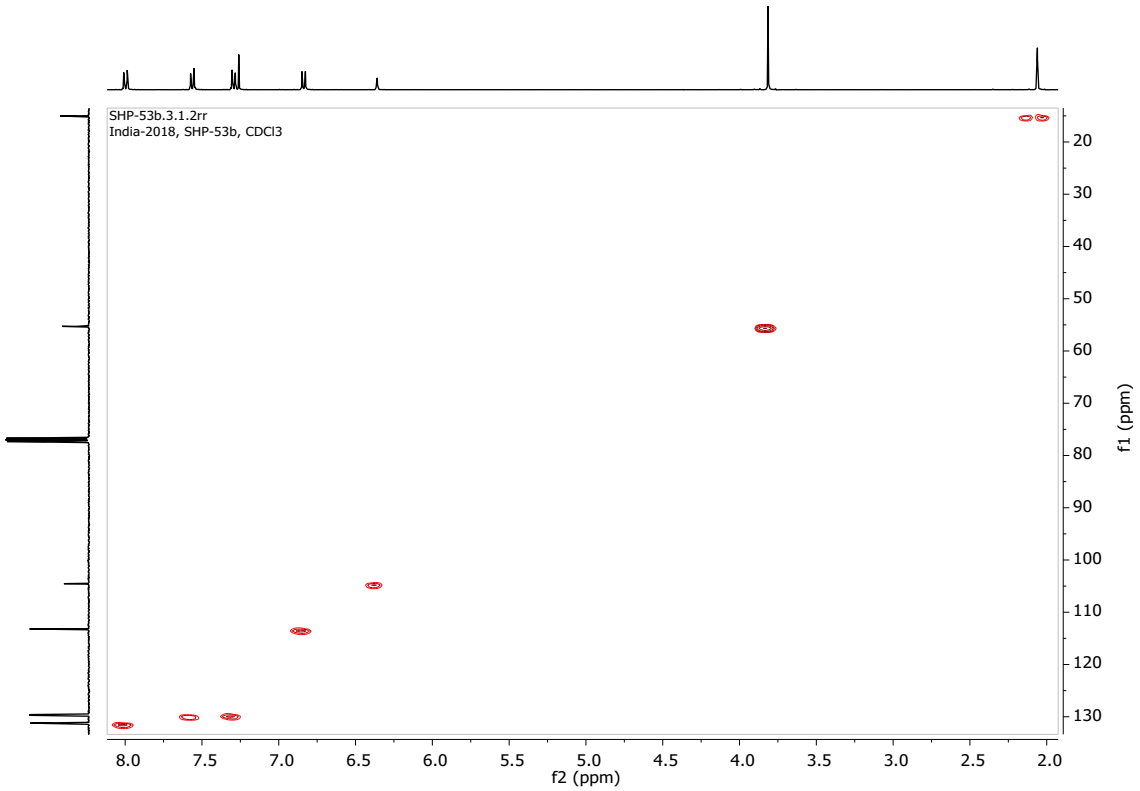


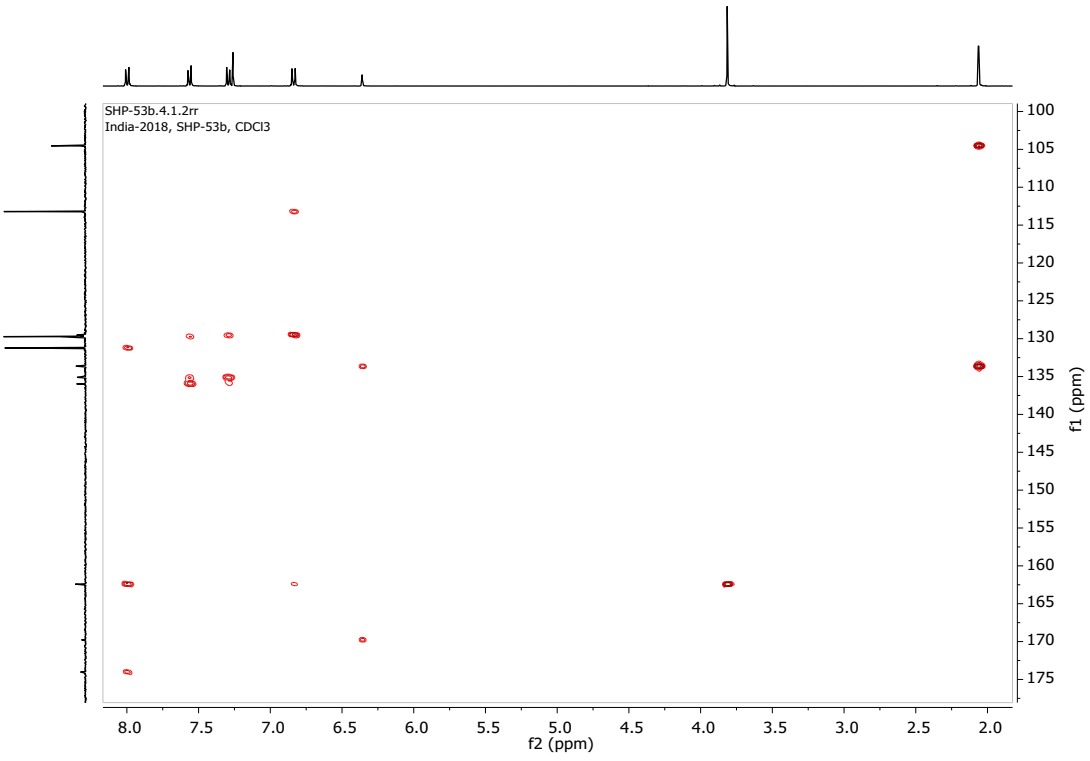
S39: 2D-spectrum of 2-(*N*-(*p*-chlorophenyl)amino)-4-methyl-5-(*p*-methoxybenzoyl)thiazole (**8bc**)

Table S3: NMR data in $CDCl_3$, chemical shifts (δ, ppm) and coupling constants (*J*, Hz) for compound **8bc**



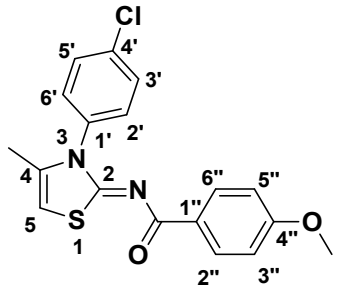
Chemical shifts (δ in ppm)	gs-HMQC correlation	gs-HMBC correlation	Assignments
186.9	-	7.75 (2",6"-H)	CO
167.1	-	-	C-2
162.9	-	3.87 (4"-OCH_3)	C-4"
		6.94 (3",5"-H)	
		7.75 (2",6"-H)	
157.4	-	2.41 (4-CH_3)	C-4
137.7	-	7.35 (3',5'-H)	C-4'
132.5	-	6.94 (3",5"-H)	C-1"
130.9	7.75 (2",6"-H)	7.75 (2",6"-H)	C-2",6"
129.7	7.35 (3',5'-H)	7.35 (3',5'-H)	C-3',5'
121.0	7.31 (2',6'-H)	7.31 (2',6'-H)	C-2',6'
120.6	-	2.41 (4-CH_3)	C-3
113.7	6.94 (3",5"-H)	6.94 (3",5"-H)	C-3",5"
55.5	3.87 (4"-OCH_3)	-	4"-OCH_3
18.6	2.41 (4-CH_3)	-	4-CH_3





S42: 2D-spectrum of 2-(*N*-(*p*-methoxybenzoyl)imino)-3-*N*-(*p*-chlorophenyl)-4-methylthiazole (**12bc**)

Table S4: NMR data in $CDCl_3$, chemical shifts (δ, ppm) and coupling constants (*J*, Hz) for compound **12bc**



Chemical shifts (δ in ppm)	gs-HMQC correlation	gs-HMBC correlation	Assignments
174.0	-	8.00 (2",6"-H)	CO
169.8	-	6.36 (5-H)	C-2
162.4	-	8.00 (2",6"-H)/ 6.84 (3",5"-H)/ 3.81 (4"-OCH_3)	C-4"
136.0	-	7.56 (2',6'-H)/ 7.29 (3',5'-H)	C-1'
135.1	-	7.56 (2',6'-H)/ 7.29 (3',5'-H)	C-4'
133.6	-	6.36 (5-H)/ 2.06 (4-CH_3)	C-5
131.2 (^1J=161.9)	8.00 (2",6"-H)	8.00 (2",6"-H)	C-2",6"
129.7 (^1J=161.8)	7.56 (2',6'-H)	7.56 (2',6'-H)	C-2',6'
129.6 (^1J=162.3)	7.29 (3',5'-H)	7.29 (3',5'-H)	C-3',5'
129.5	-	6.84 (3",5"-H)	C-1"
113.2 (^1J=158.7)	6.84 (3",5"-H)	6.84 (3",5"-H)	C-3",5"
104.5 (^1J=189.4)	6.36 (5-H),	2.06 (4-CH_3)	C-4
55.3 (^1J=144.5)	3.81 (4"-OCH_3)	-	4"-OCH_3

15.0 (^1J=130.1)	2.06 (4-CH_3)	6.36 (5-H),	4-CH_3

X-RAY ANALYTICAL DATA

Table S5: Summary of the fundamental crystal and refinement data for compounds **8aa**, **12bc** and **12da**.

	8aa	**12bc**	**12da**
Empirical formula	$C_{17}H_{14}N_2OS$	$C_{18}H_{15}N_2O_2SCl$	$C_{18}H_{16}N_2OS$
Formula weight	294.08	358.83	308.39
Crystal system	Monoclinic	Triclinic	Orthorhombic
Space group	*C*2/*c*	*P*-1	*Pnma*
a/Å	19.262(3)	9.463(1)	20.128(1)
b/Å	4.9631(9)	9.661(1)	6.9154(5)
c/Å	30.819(5)	11.003(1)	11.3450(9)
α/°	90	107.810(2)	90
β/°	98.509(3)	110.578(2)	90
γ/°	90	96.950(2)	90
Volume/Å^3	2913.8(9)	866.6(2)	1579.2(2)
Z	6	2	4
ρcalcg/cm^3	1.342	1.375	1.297
μ/mm^{-1}	0.222	0.353	0.208
F(000)	1232.0	372.0	648.0
Crystal size/mm^3	0.64 × 0.11 × 0.03	0.34 × 0.15 × 0.11	0.31 × 0.25 × 0.09
2Θ range for data collection/°	2.672 to 57.888	4.266 to 58.18	4.048 to 57.976
Index ranges	-24 ≤ h ≤ 24, -6 ≤ k ≤ 6, -40 ≤ l ≤ 39	-12 ≤ h ≤ 12, -12 ≤ k ≤ 12, -14 ≤ l ≤ 14	-25 ≤ h ≤ 26, -9 ≤ k ≤ 9, -15 ≤ l ≤ 15
Reflections collected	13672	9160	15926
Independent reflections	3533 [Rint = 0.0849, Rσ = 0.0951]	4135 [Rint = 0.0444, Rσ = 0.0561]	2163 [Rint = 0.0629, Rσ = 0.0424]

Data/restraints/parameters	3533/0/233	4135/0/219	2163/0/129
Goodness-of-fit on F^2	0.967	0.970	1.004
Final R indexes [I>=2σ (I)][a]	R1 = 0.0580 wR2 = 0.1336	R1 = 0.0485 wR2 = 0.1116	R1 = 0.0441 wR2 = 0.1198
Final R indexes [all data][b]	R1 = 0.1173 wR2 = 0.1535	R1 = 0.0995 wR2 = 0.1292	R1 = 0.0880 wR2 = 0.1378
Largest diff. peak/hole / e $Å^{-3}$	0.29/-0.36	0.25/-0.23	0.19/-0.23

[a] $R1=\Sigma||F_o|-|F_c||/\ \Sigma|F_o|$

[b] $wR2=\{\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]\}$