Supporting Information

Novel Hybrid-Pyrrole Derivatives: Their Synthesis, Antitubercular Evaluation and Docking Studies

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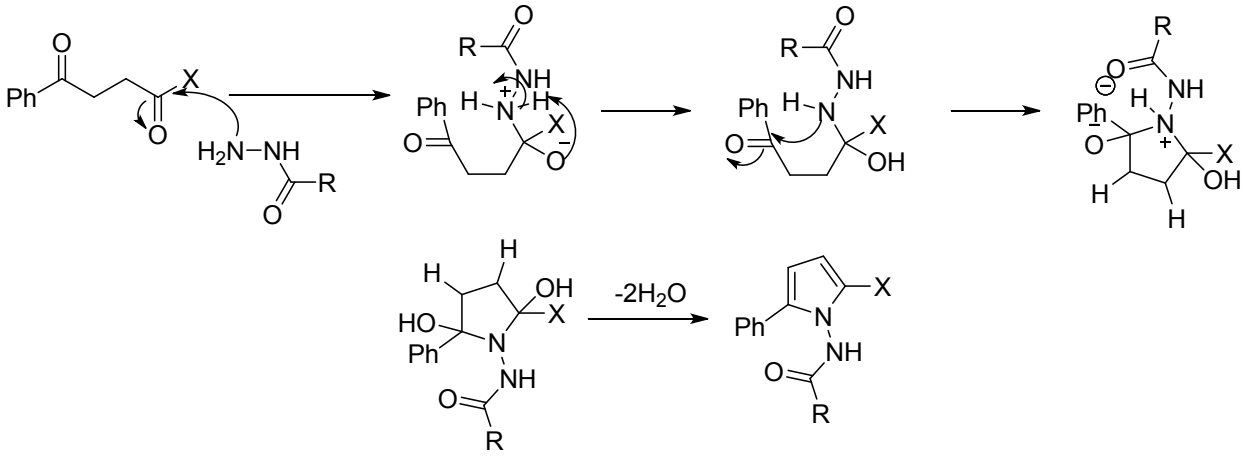
Contents

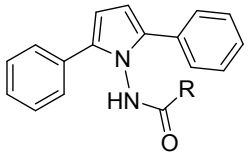
7-Hydroxy-4-methyl-2*H*-chromen-2-one

7-Hydroxy-4-methyl-2*H*-chromen-2-one was synthesized using the Pechmann reaction, as described in literature. Recorcinol (1.0 g) and ethyl acetoacetate (1.15 mL) were dissolved in sulfuric acid (6 mL) in a round bottom flask at cooling condition. The solution was stirred for 24 h. The mixture was quenched by addition of ice-cold water (30 mL). After 1 hour at 0°C, a precipitate was formed that was filtered off and washed with water, and dried, gave white solid as product.

Scheme 2. Possible mechanism for the formation of **7a-p** & **8a-p**



Supporting Table 1 Physical and analytical data of hybrid-pyrroles (**7a-p** & **8a-p**)



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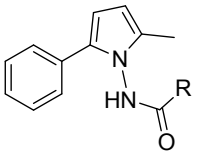
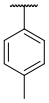
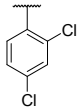
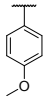
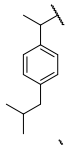
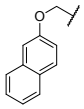
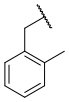
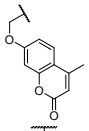
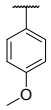
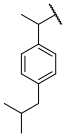
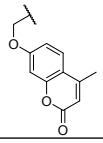


8

ID	R	Color	R_f[a]	MP(°C)	Conventional method	Microwave method
					Yield/Time(h)	Yield/Time(min)
7a		White solid	0.41	245-246	20(12)	76(10)
7b		White solid	0.42	210-212	10(24)	79(10)
7c		White solid	0.47	214-215	70(18)	68(10)
7d		Greyish solid	0.42	206-207	20(16)	75(10)
7e		White solid	0.74	277-274	10(24)	47(7)
7f		White solid	0.45	242-244	20(24)	47(10)
7g		White solid	0.54	275-277	10(15)	52(10)
7h		Brown solid	0.55	176-177	24(18)	44(10)
7i		White solid	0.47	172-174	18(10)	76(10)
7j		White solid	0.54	270-271	15(10)	67(7)
7k		Greyish solid	0.42	125-126	10(18)	55(10)
7l		White solid	0.48	172-174	0(18)	79(15)
7m		White solid	0.50	274-275	0(18)	55(10)
7n		White solid	0.48	210-211	0(18)	50(10)
7o		White solid	0.45	200-202	21(18)	60(8)

7p		White solid	0.34	164-165	0(16)	50(15)
8a		White solid	0.5	210-212	16(18)	76(7)
8b		White solid	0.5	114-116	12(24)	54(10)
8c		White solid	0.5	168-170	45(18)	81(10)
8d		Greyish solid	0.4	152-154	20(24)	48(10)
8e		White solid	0.5*	188-190	27(24)	49(10)
8f		Off-white solid	0.5	174-176	10(24)	62(12)
8g		White solid	0.25	188-190	10(15)	78(12)
8h		Light Brown solid	0.5	120-122	32(18)	72(15)
8i		Greyish solid	0.33	128-170	18(24)	68(10)
8j		White solid	0.25	188-190	18(24)	81(10)
8k		White solid	0.28	128-170	10(18)	51(10)
8l		Brown solid	0.5	90-92	16(18)	60(10)
8m		White solid	0.33	116-118	0(18)	56(10)
8n		White solid	0.35	199-200	12(18)	83(10)
8o		White solid	0.35	118-120	25(18)	52(12)
8p		Off-white solid	0.44*	178-140	10(16)	45(15)

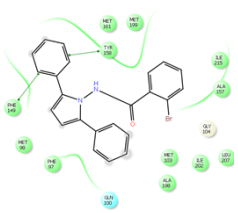
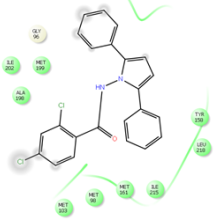
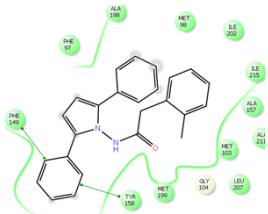
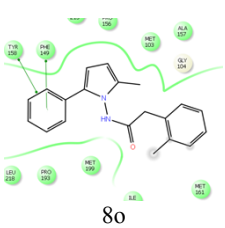
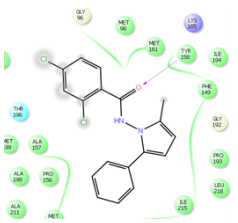
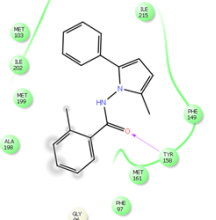
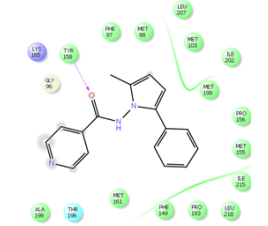
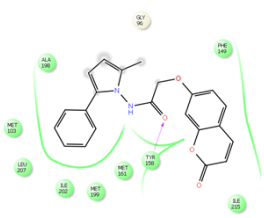
a: TLC solvent system Hexane : Ethyl acetate 7: 3; *: TLC solvent system Hexane : Ethyl acetate 5: 5; Yield expressed in percentage

Supporting Table 2 Calculation of properties of the compounds (**7a-p** & **8a-p**) computed by Molinspiron property calculator program

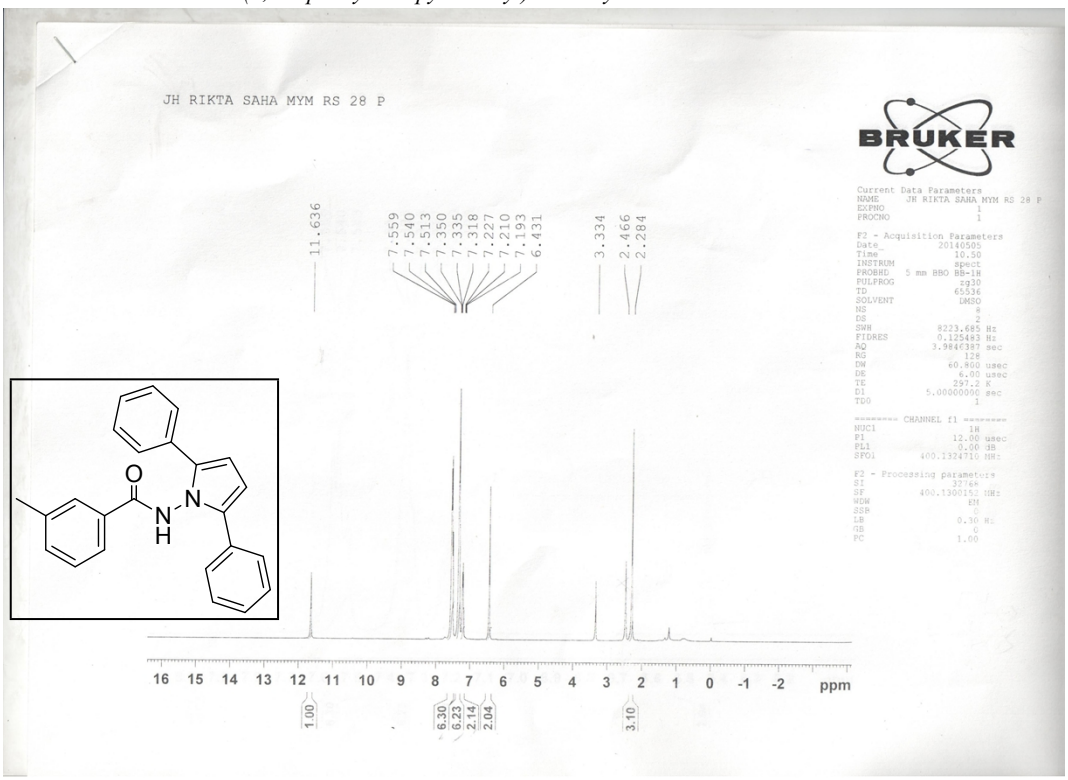
Entry	TPSA Å²	no. of rotatable bond	MW	MV	no. of OH, NH donor	no. of ON acceptor	mi LogP[a]
Acceptable range	☺	☺	<500☺	-	<5☺	<10☺	<5
7a	34	4	338	315	1	3	5.05
7b	34	4	352	331	1	3	5.45
7c	34	4	352	331	1	3	5.48
7d	34	4	352	331	1	3	5.50
7e	46	4	339	310	1	4	3.77☺
7f	34	4	417	332	1	3	5.82
7g	34	4	372	328	1	3	5.68
7h	34	4	407	342	1	3	6.34
7i	43	6	368	340	1	4	5.02
7j	43	5	368	340	1	4	5.11
7k	34	5	352	331	1	3	5.15
7l	34	7	422	415	1	3	7.25
7m	34	5	402	375	1	3	6.31
7n	43	6	418	384	1	4	6.21
7o	34	5	366	348	1	3	5.51
7p	73	6	450	401	1	6	5.45
8a	34	3	276	260	1	3	3.60☺
8b	34	3	290	276	1	3	4.00☺
8c	34	3	290	276	1	3	4.03☺
8d	34	3	290	276	1	3	4.05☺
8e	46	3	277	256	1	4	2.31☺
8f	34	3	355	278	1	3	4.37☺
8g	34	3	310	273	1	3	4.23☺
8h	34	3	345	287	1	3	4.89☺
8i	43	5	306	285	1	4	3.57☺
8j	43	4	306	285	1	4	3.66☺
8k	34	4	290	276	1	3	3.69☺
8l	34	6	360	360	1	3	5.79
8m	34	4	340	320	1	3	4.86☺
8n	43	5	356	329	1	3	4.76☺
8o	34	4	304	293	1	3	4.10☺
8p	73	5	388	347	1	6	4.00☺

a nViol, no. of violations; miLog P, molinspiration predicted Log P; MW, molecular weight; nON, no. of hydrogen bond acceptors; nOHNH, no. of hydrogen bond donors; and nrotb, no. of rotatable bond. ☺ Smiley symbols indicate the drug-like properties are acceptable

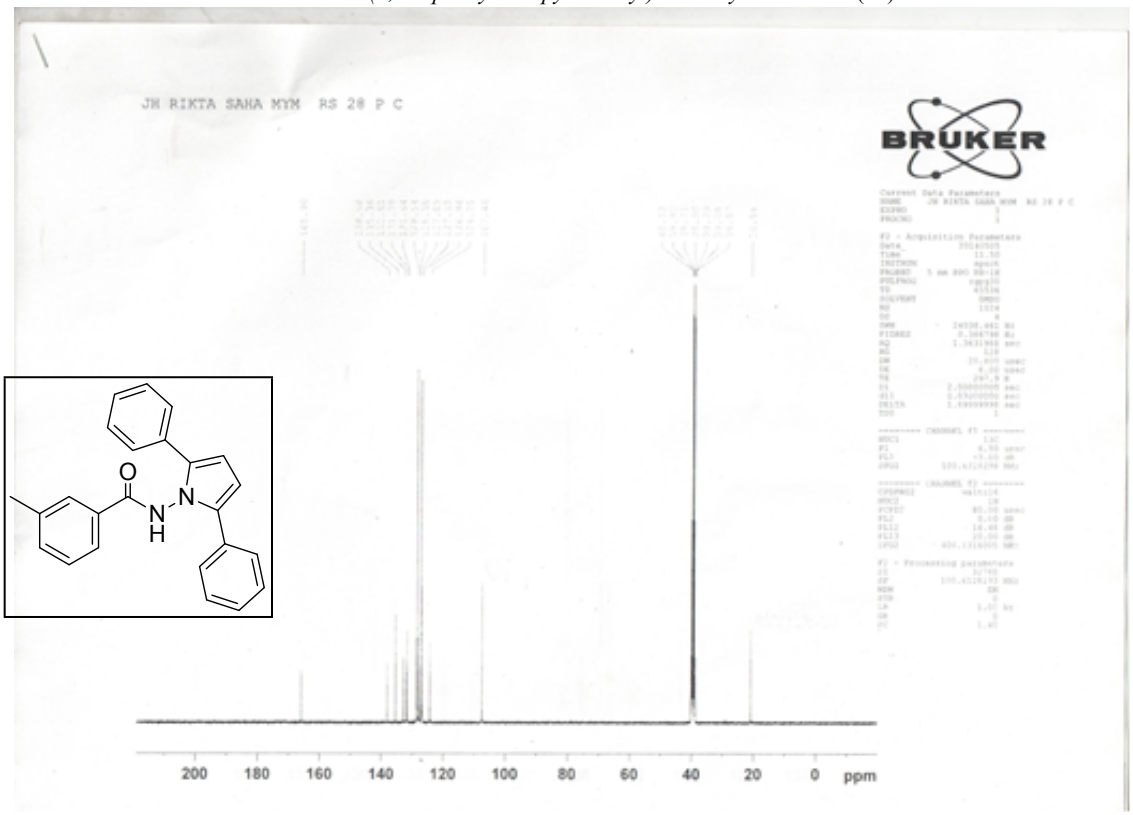
Ligplots of active and inactive compounds showing different interactions

2D plot of inactive molecules	 7f	 7h	 7o	 8o
2D plot of active molecules	 8h	 8b	 8e	 8n

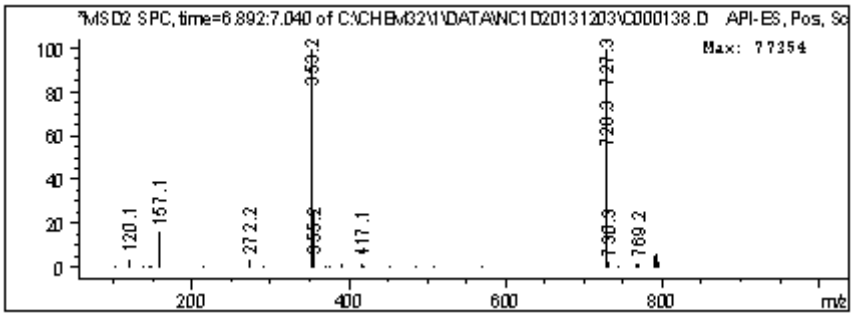
Compound 7c *[1]H NMR N-(2,5-diphenyl-1H-pyrrol-1-yl)-3-methylbenzamide*

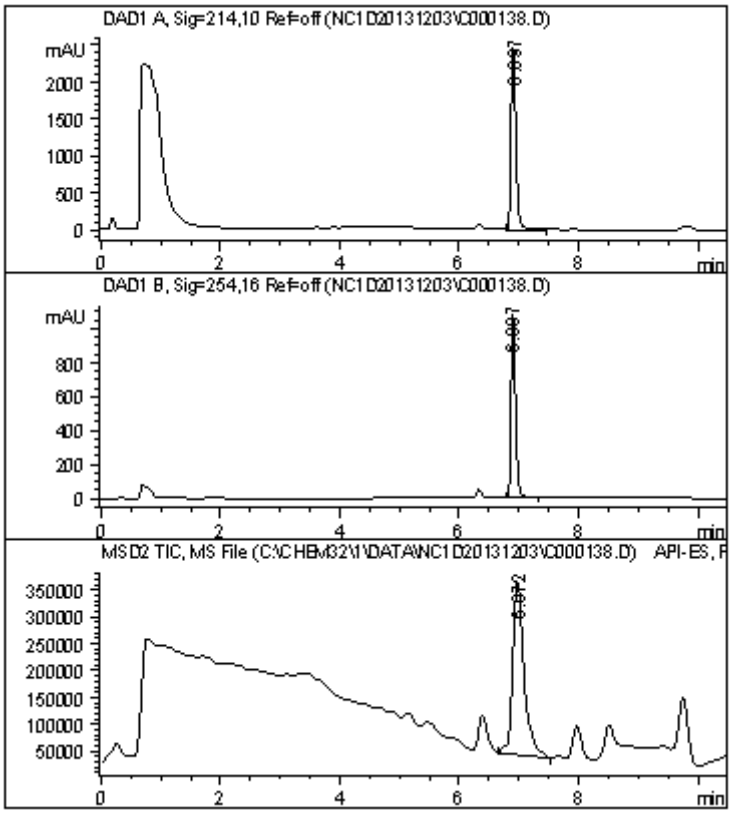


[13]C NMR N-(2,5-diphenyl-1H-pyrrol-1-yl)-3-methylbenzamide (7c)

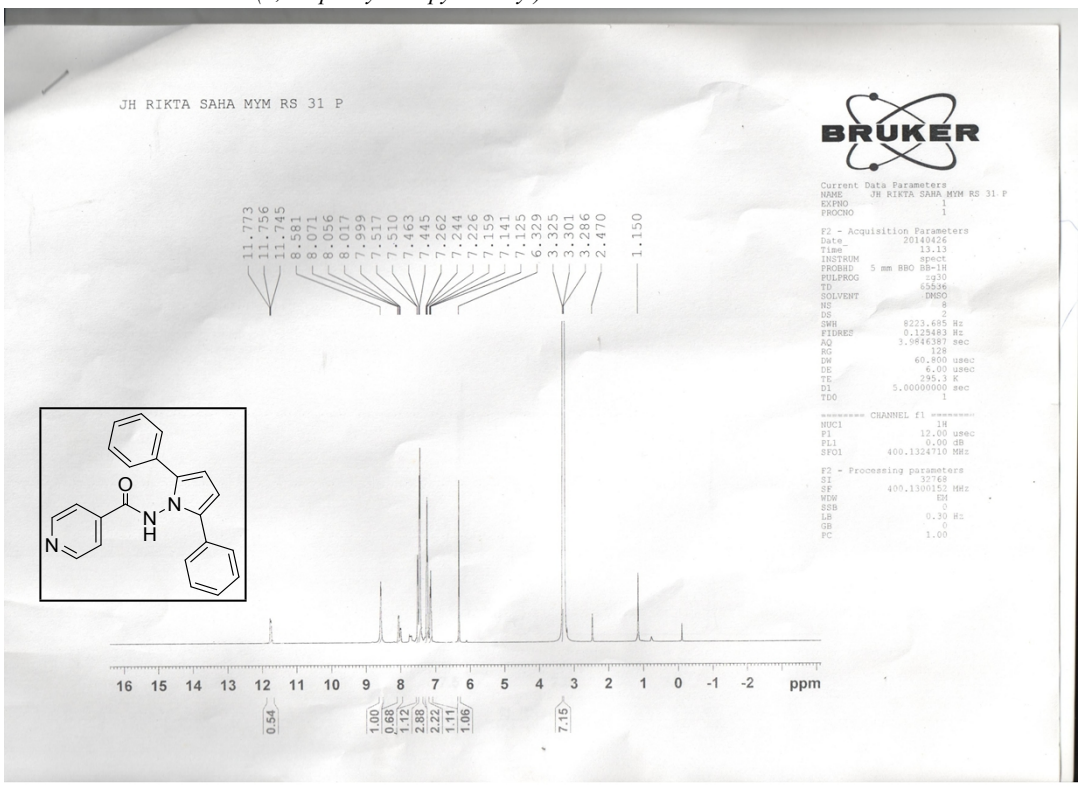


HPLC and Mass data of N-(2,5-diphenyl-1H-pyrrol-1-yl)-3-methylbenzamide (7c)

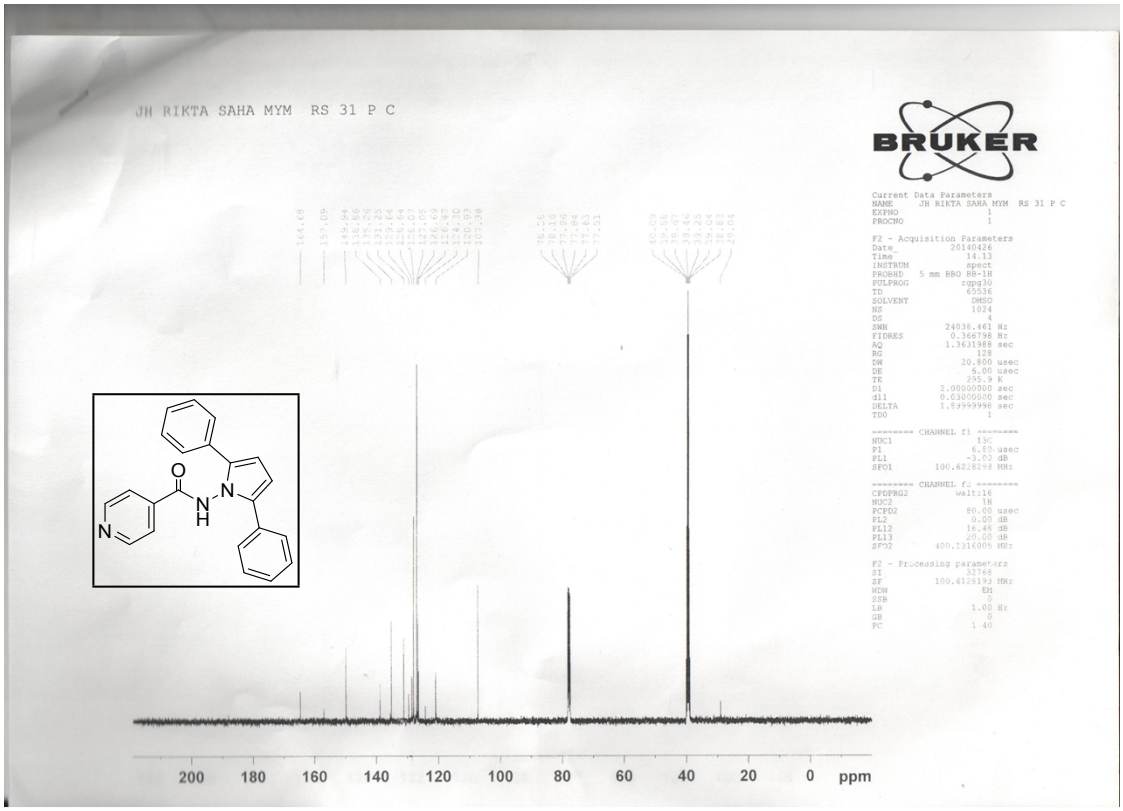




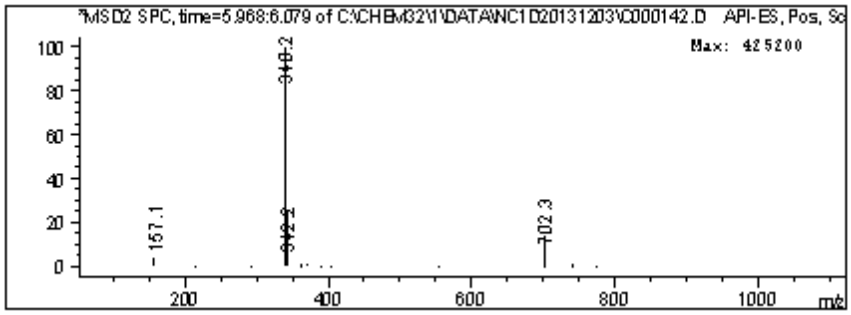
Compound 7e *[1]H NMR N-(2,5-diphenyl-1H-pyrrol-1-yl)isonicotinamide*

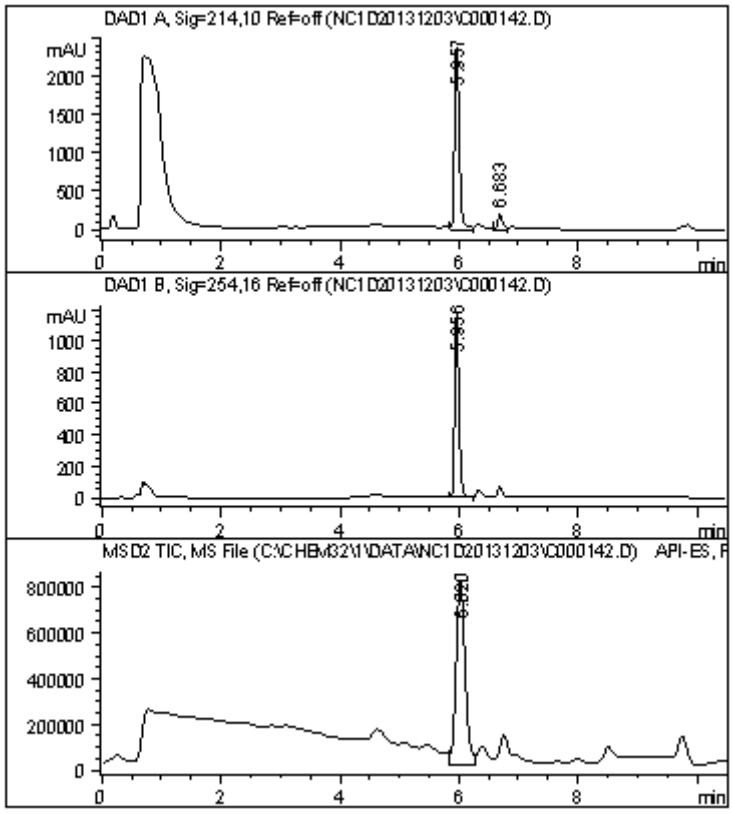


[13]C NMR *N-(2,5-diphenyl-1H-pyrrol-1-yl)isonicotinamide* (7e)

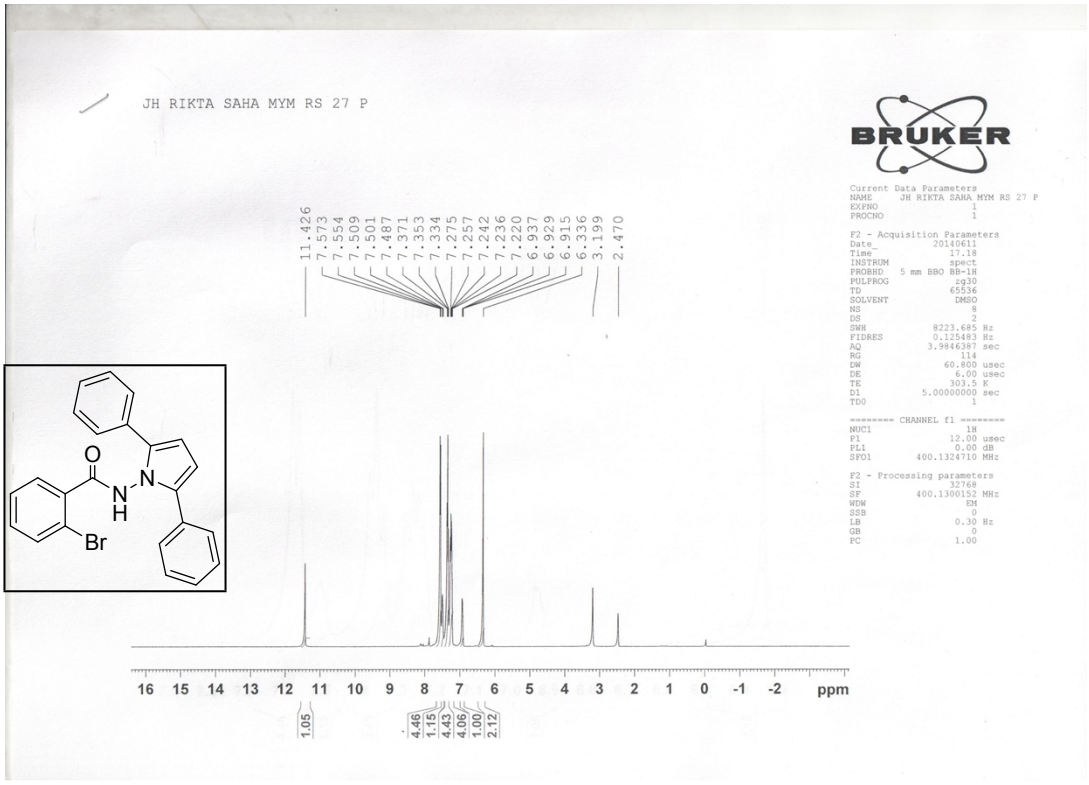


HPLC and Mass data of *N-(2,5-diphenyl-1H-pyrrol-1-yl)isonicotinamide* (7e)

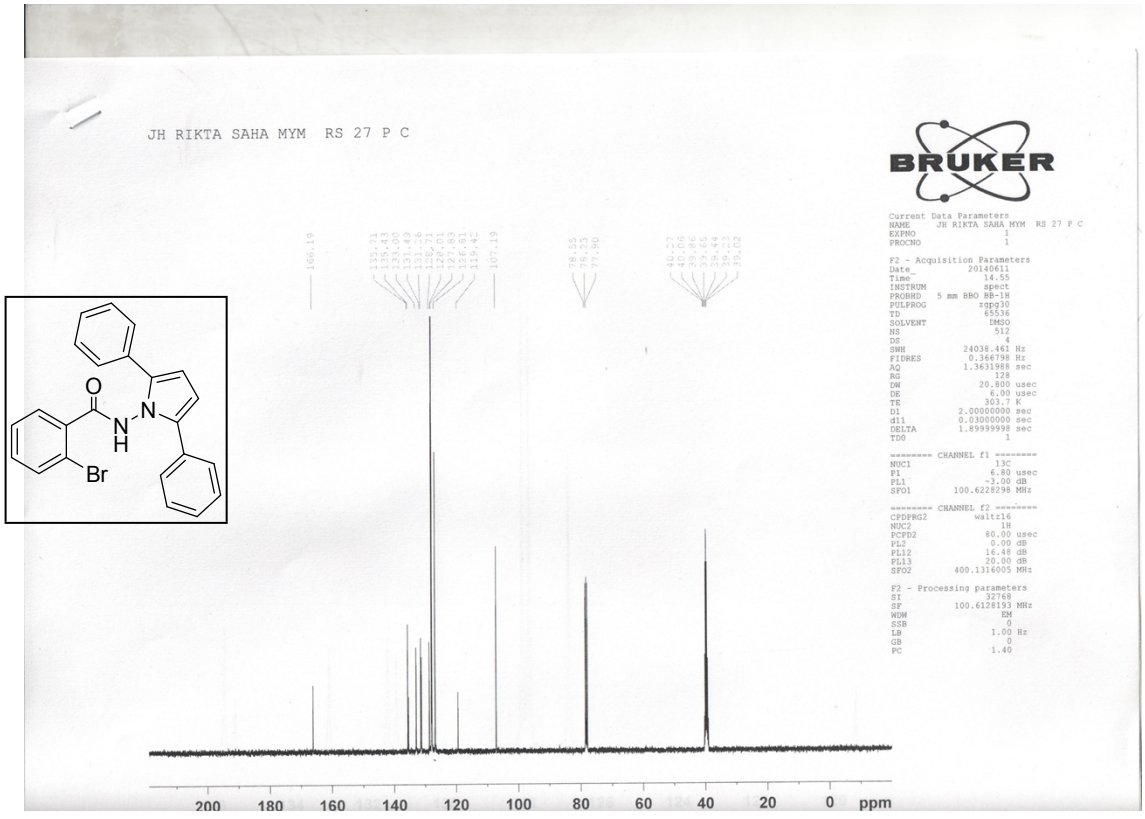




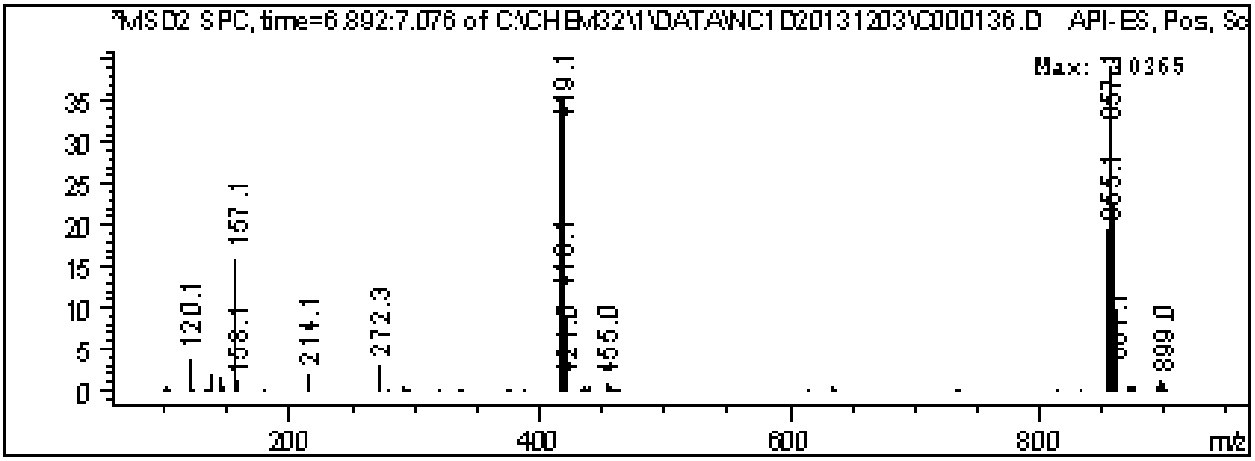
Compound 7f *[1]H NMR 2-bromo-N-(2,5-diphenyl-1H-pyrrol-1-yl)benzamide*



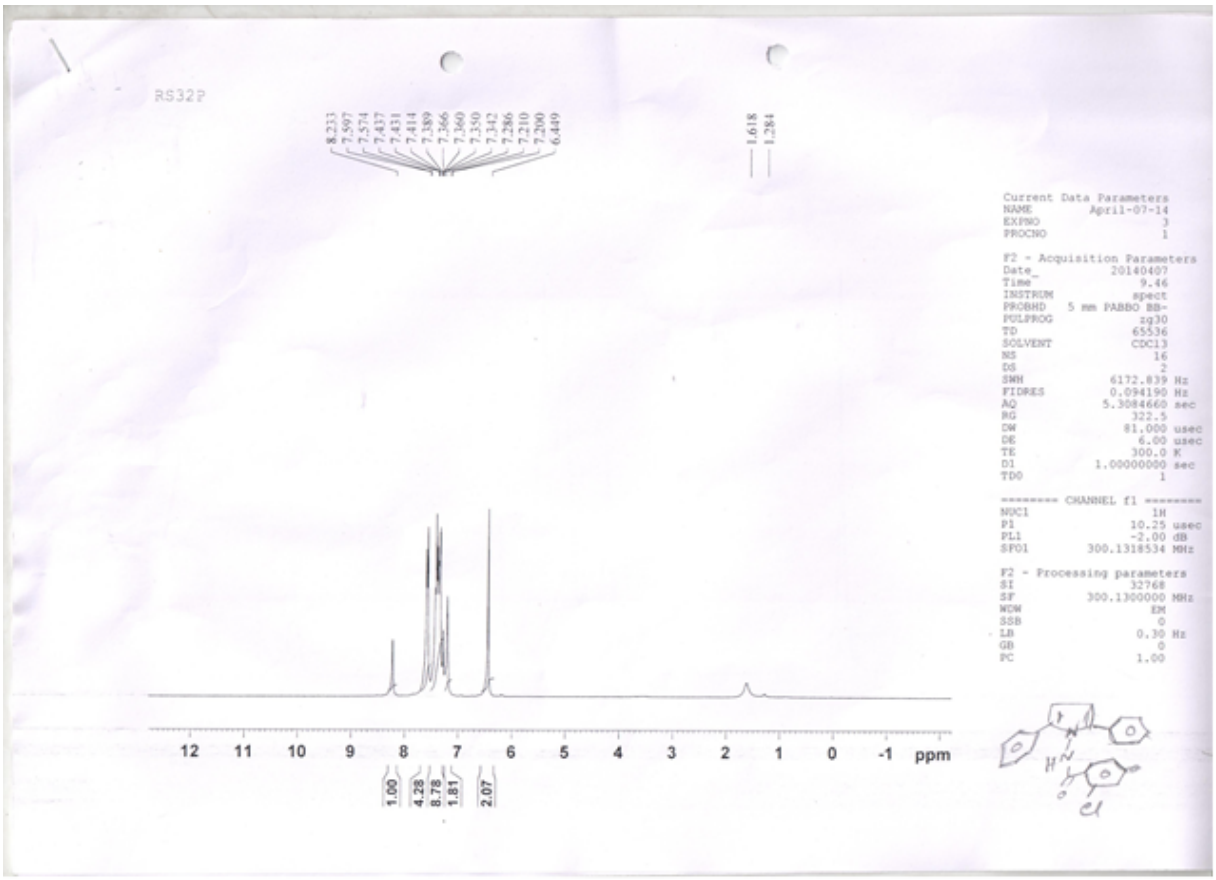
Compound 7f *[13]C NMR 2-bromo-N-(2,5-diphenyl-1H-pyrrol-1-yl)benzamide*



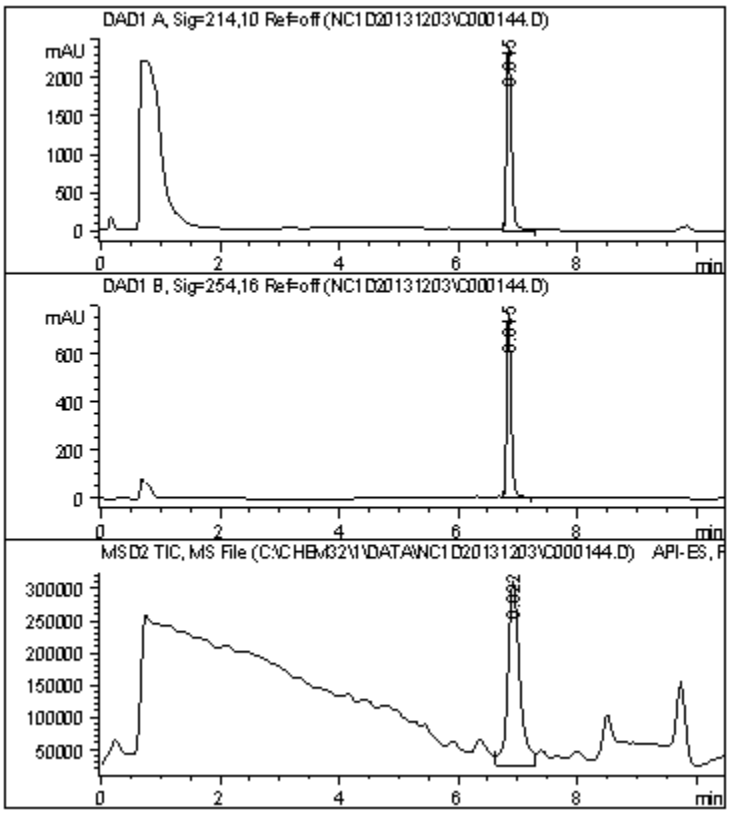
Mass data of **7f**



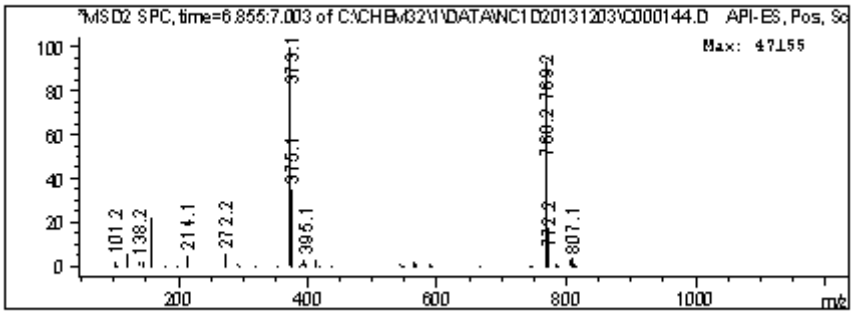
Compound 7g *[1]H NMR 2-chloro-N-(2,5-diphenyl-1H-pyrrol-1-yl)benzamide*



Compound 7g ***HPLC and Mass data of*** *2-chloro-N-(2,5-diphenyl-1H-pyrrol-1-yl)benzamide*

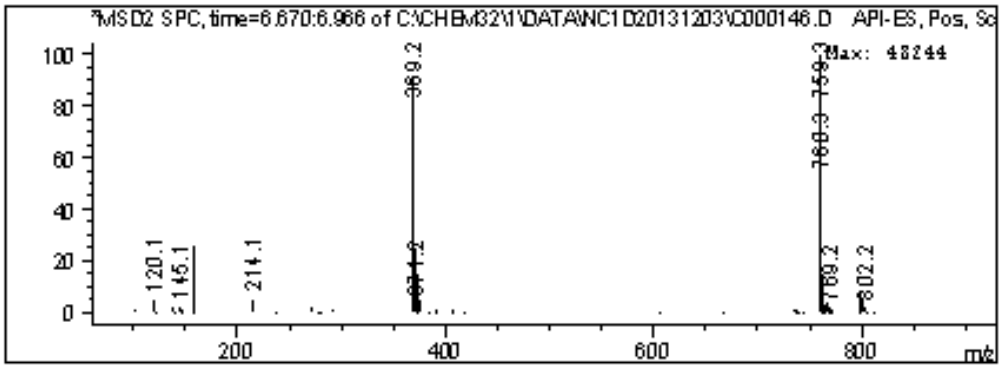


6.922 3978356 373.10 I

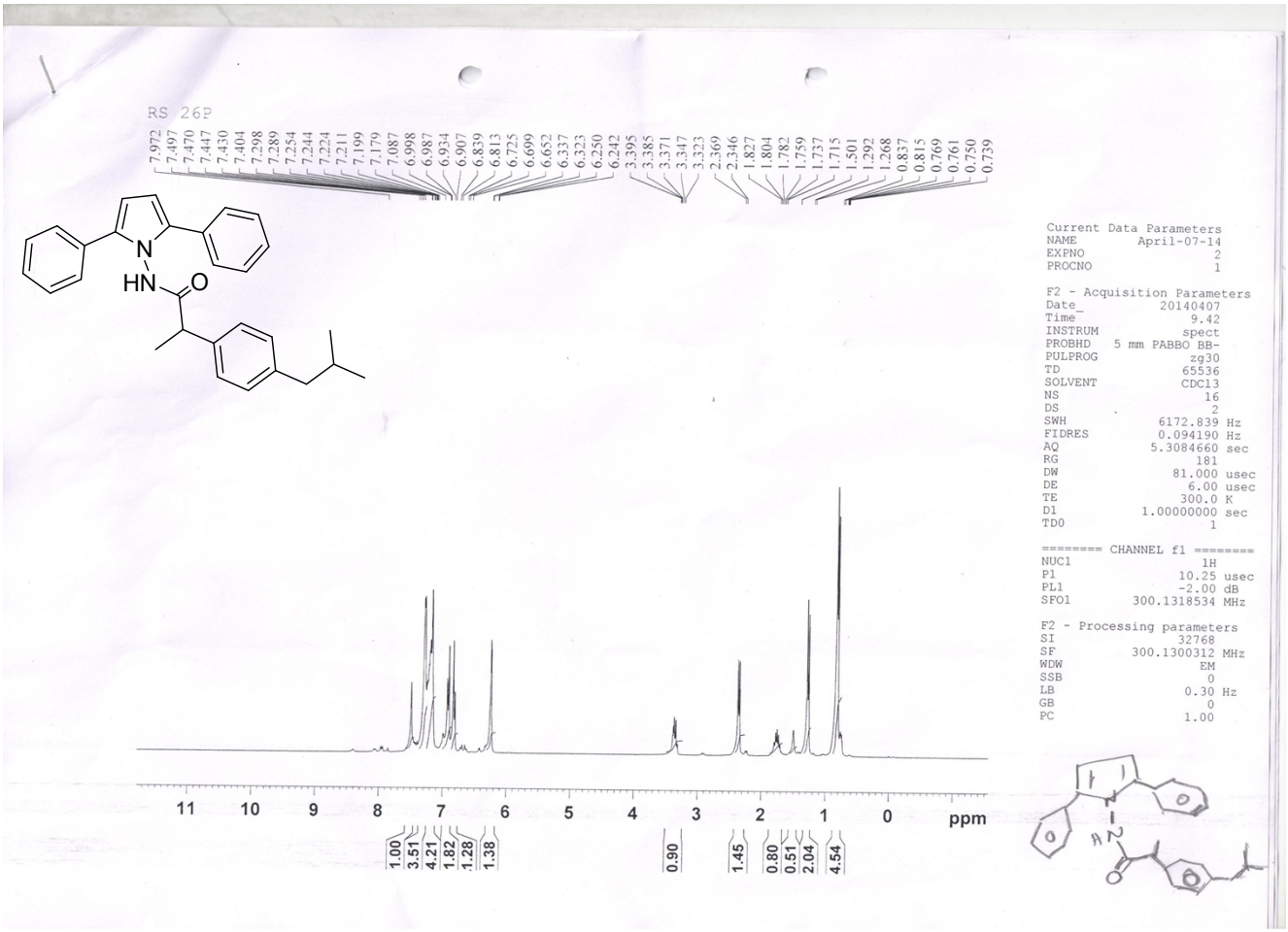


*** End of Report ***

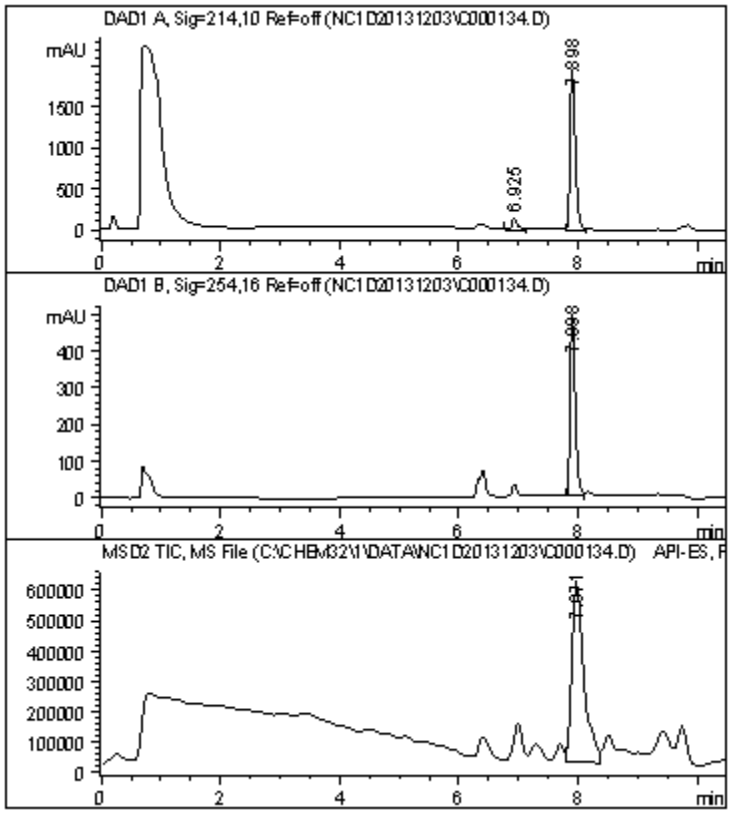
Compound 7j ***Mass data of*** *N-(2,5-diphenyl-1H-pyrrol-1-yl)-4-methoxybenzamide*

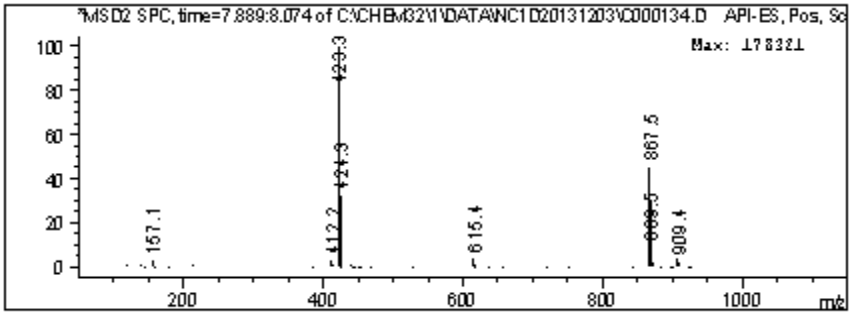


Compound 7l *[1]H NMR N-(2,5-diphenyl-1H-pyrrol-1-yl)-2-(4-isobutylphenyl)propanamide*

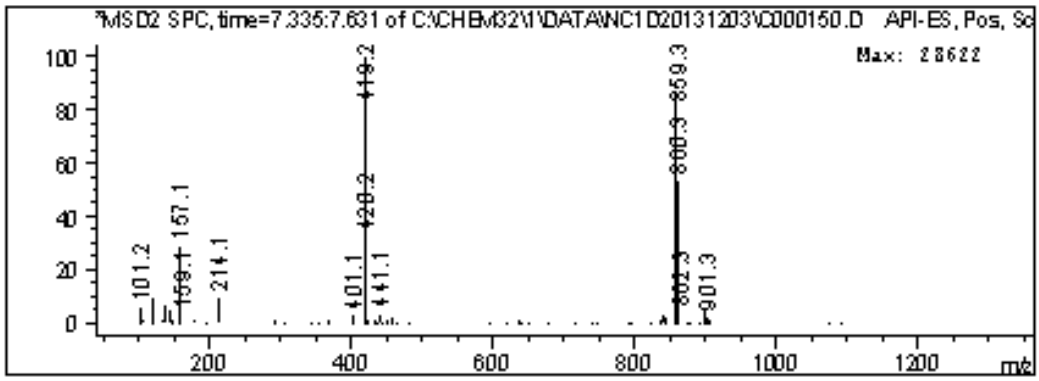


HPLC and Mass data of *N-(2,5-diphenyl-1H-pyrrol-1-yl)-2-(4-isobutylphenyl)propanamide(7l)*

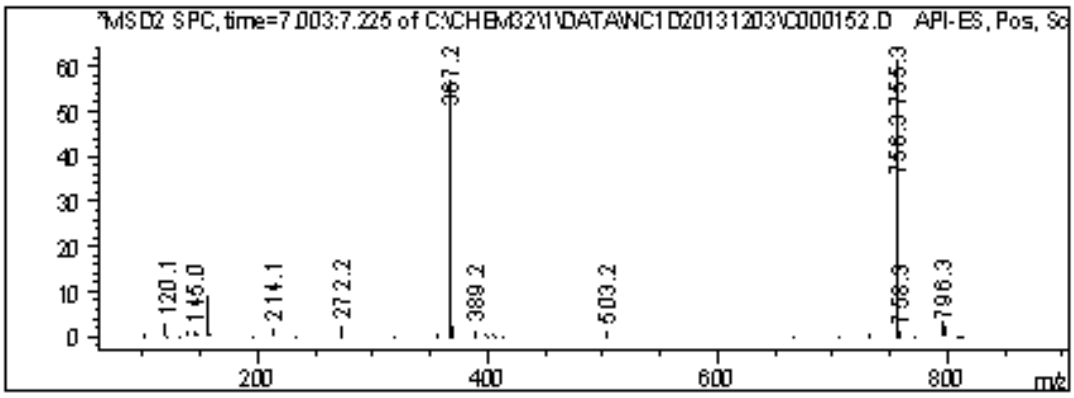




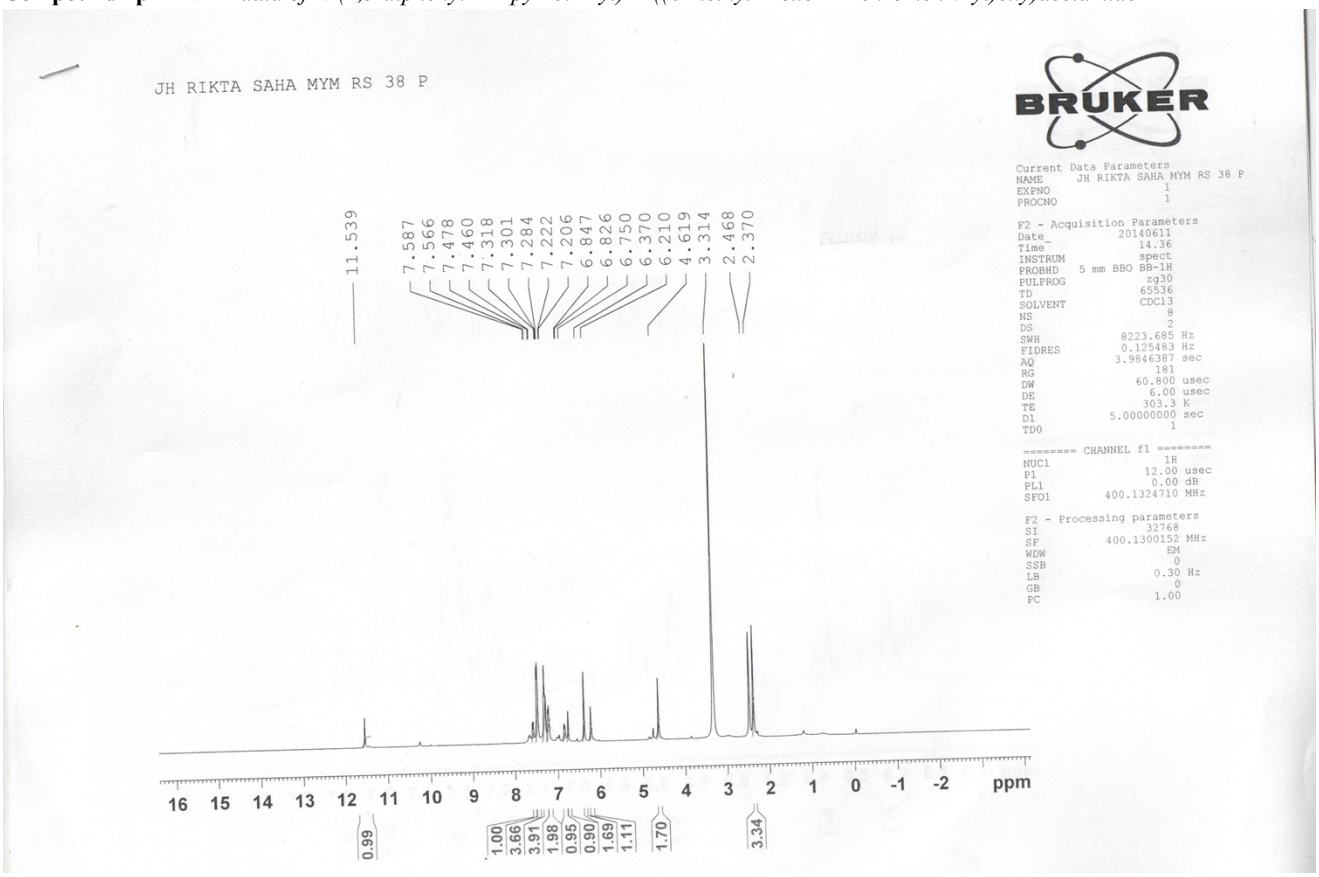
Compound 7n *Mass data of N-(2,5-diphenyl-1H-pyrrol-1-yl)-2-(naphthalen-2-yloxy)acetamide*



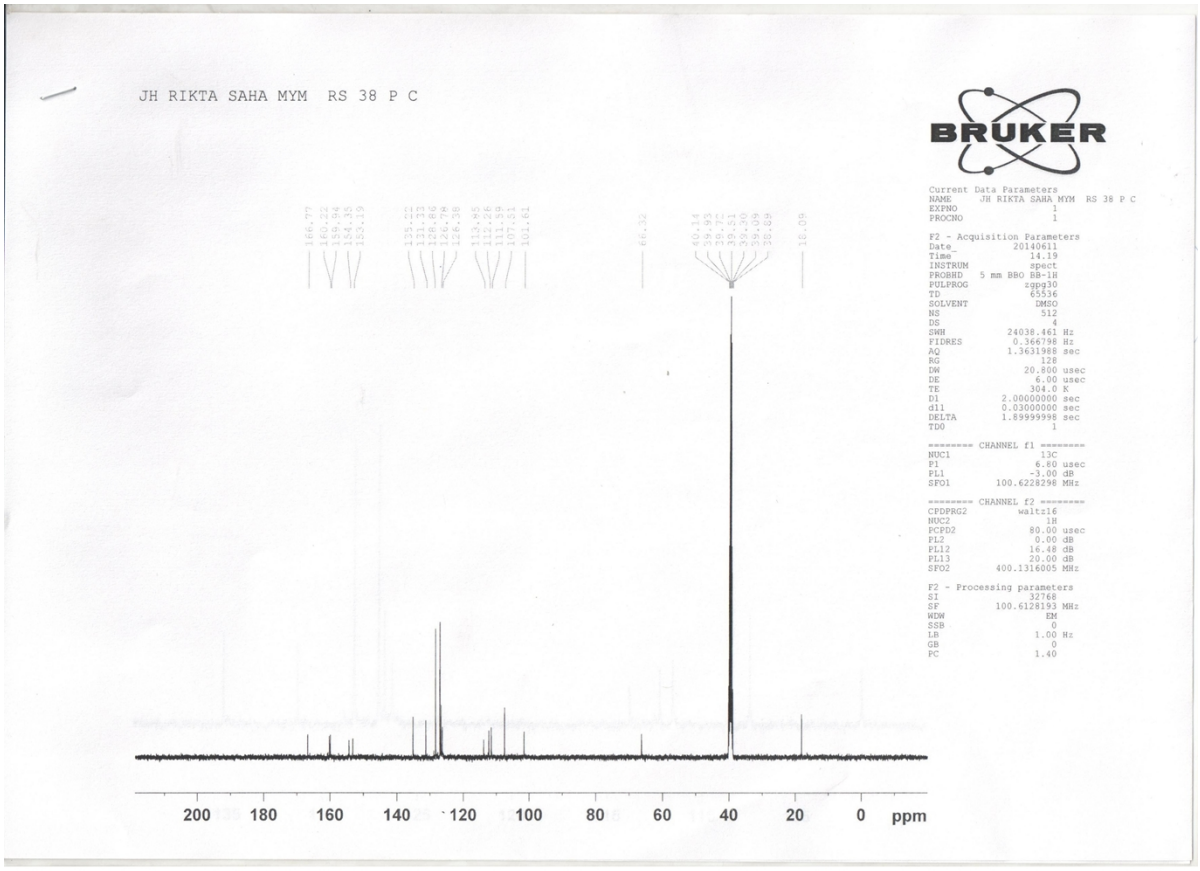
Compound 7o *Mass data of N-(2,5-diphenyl-1H-pyrrol-1-yl)-2-(o-tolyl)acetamide*



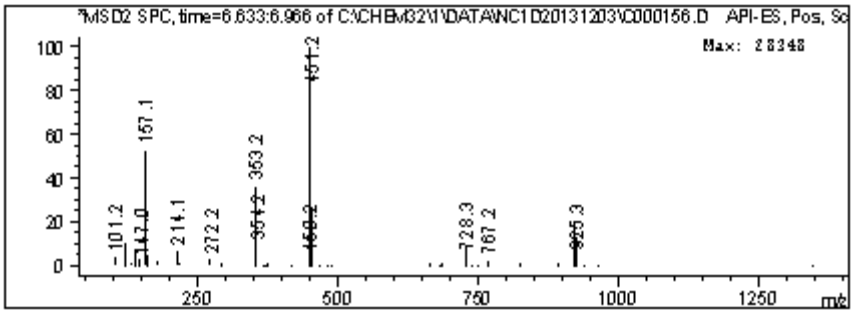
Compound 7p [1]HNMR *data of N-(2,5-diphenyl-1H-pyrrol-1-yl)-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetamide*



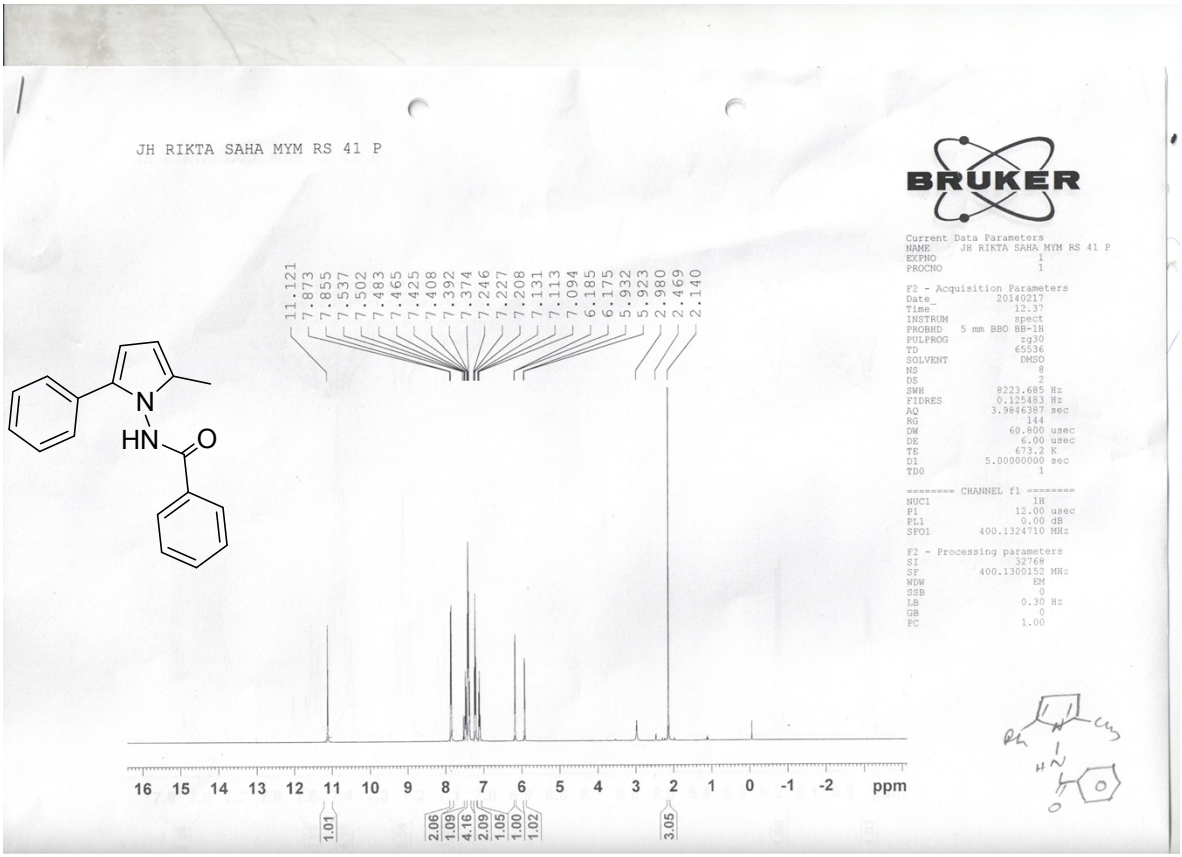
Compound 7p ^{13}CNMR *data of N-(2,5-diphenyl-1H-pyrrol-1-yl)-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetamide*



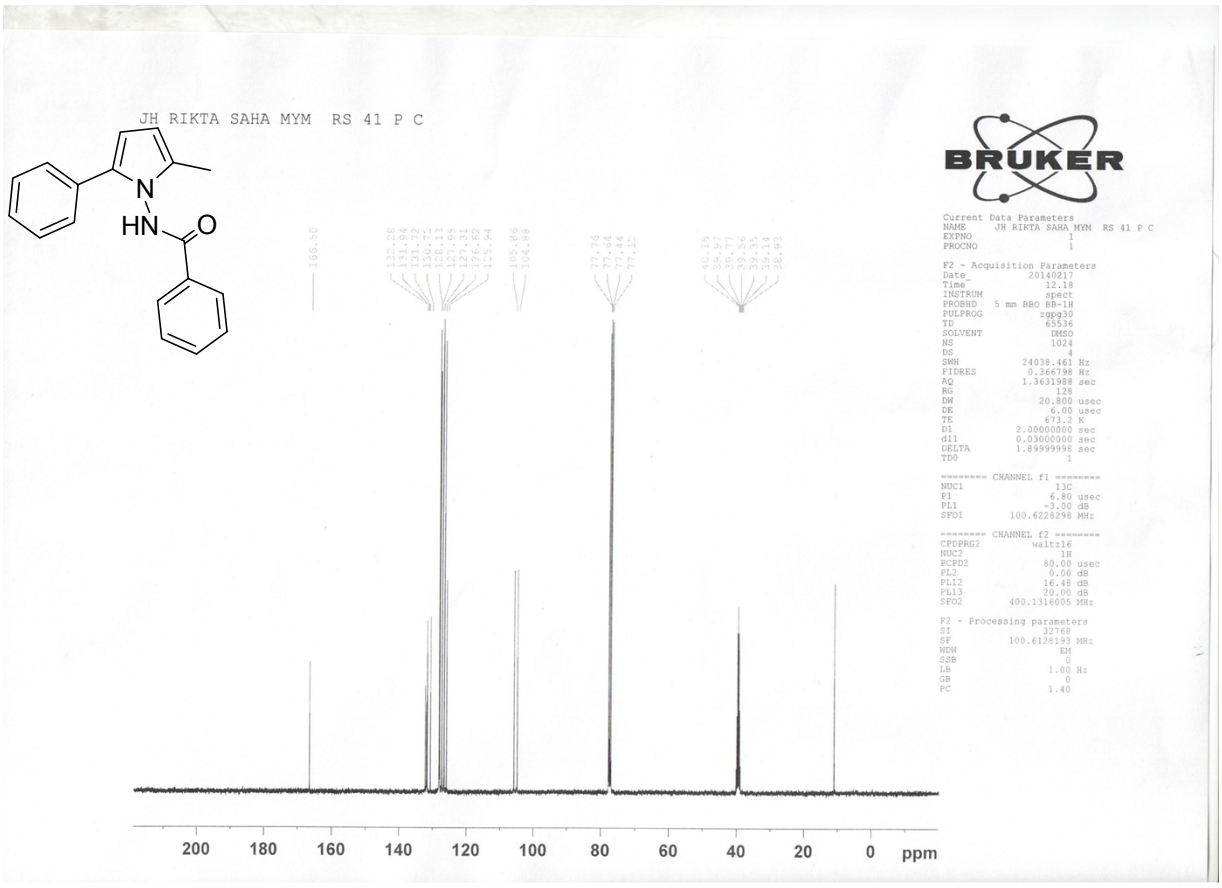
Compound 7p *Mass data of N-(2,5-diphenyl-1H-pyrrol-1-yl)-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetamide*



Compound 8a **[1]HNMR** data of *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*

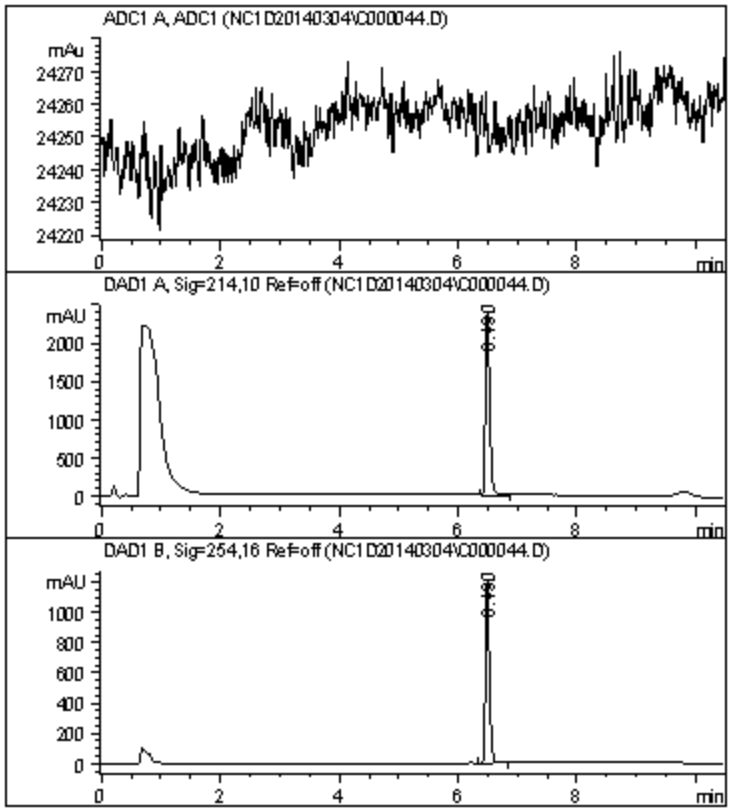


Compound 8a **[13]CNMR** data of *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*

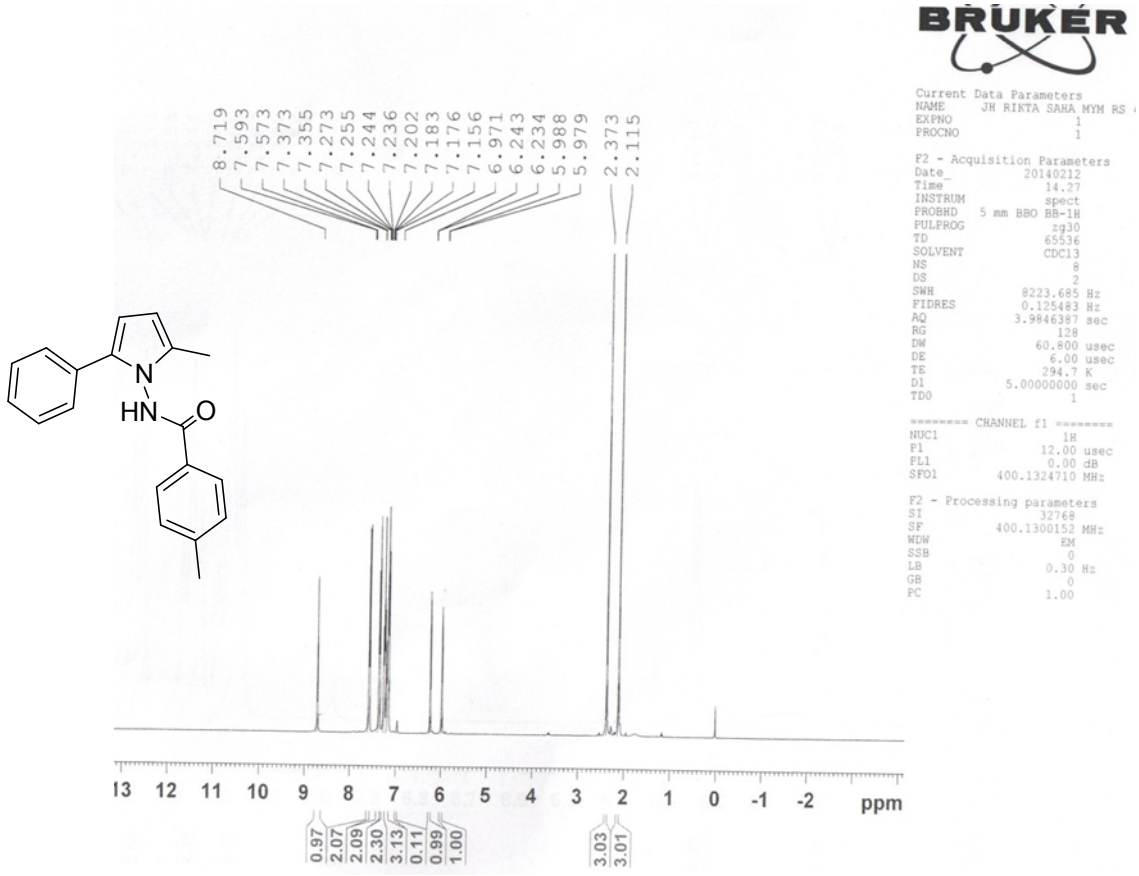


Data File C:\CHEM32\1\DATA\NC1D20140304\C000044.D
Sample Name: NCI-0000678

Acq. Operator	: James A	Seq. Line	: 44
Acq. Instrument	: Instrument 1	Location	: Vial 22
Injection Date	: 3/4/2014 11:41:10 PM	Inj	: 1
		Inj Volume	: Inj prog
Acq. Method	: C:\CHEM32\1\METHODS\0 NIH ES ONLY YO.M		
Last changed	: 10/28/2013 4:11:24 PM by Mai Ann Bailey Thayer		
Analysis Method	: C:\CHEM32\1\METHODS\0 NIH ES ONLY_YO.M		
Last changed	: 3/5/2014 8:50:12 AM by Susantha (modified after loading)		
Method Info	: Electrosparay ionization, Positive		



Compound 8d *4-Methyl-N-(2-methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*



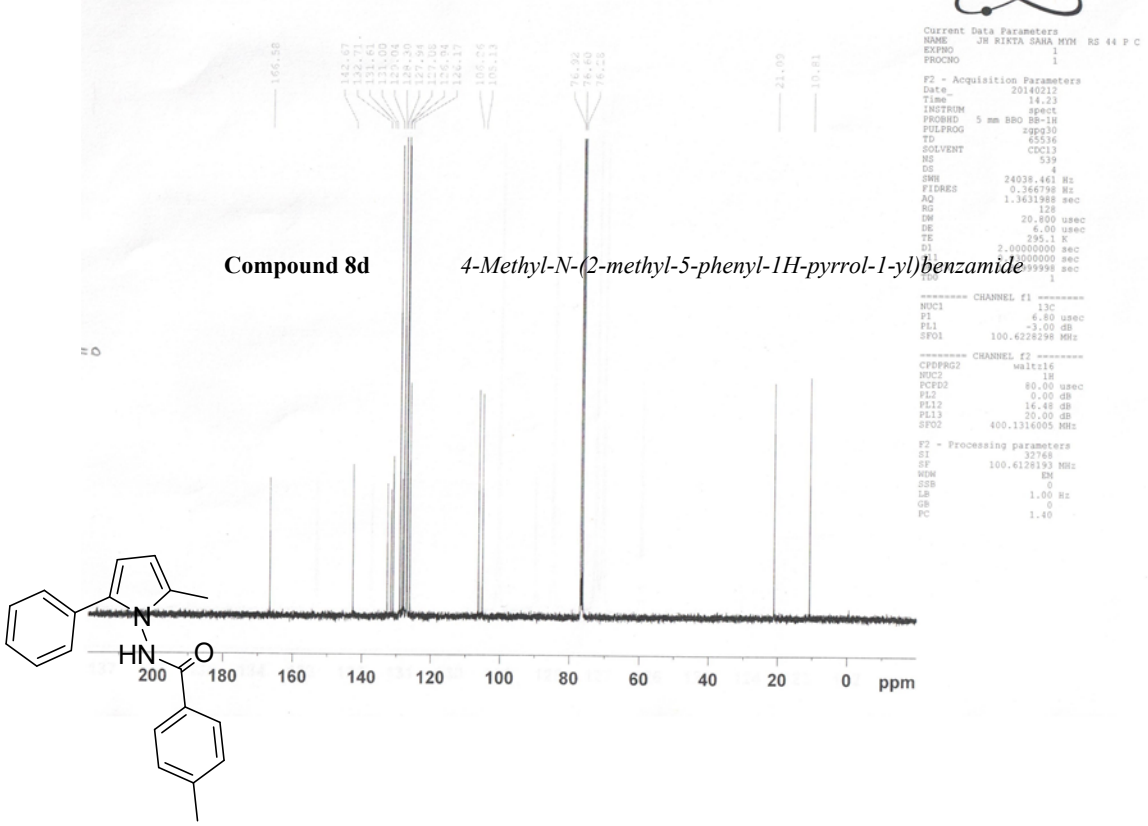
BRUKER

Current Data Parameters
NAME JH RIKTA SAHA MYM RS
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140212
Time 14.27
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 128
DW 60.800 usec
DE 6.00 usec
TE 294.7 K
D1 5.00000000 sec
TD0 1

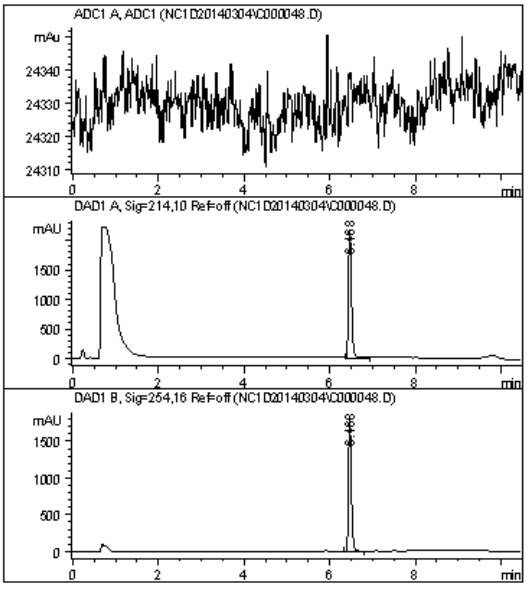
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 0.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300152 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

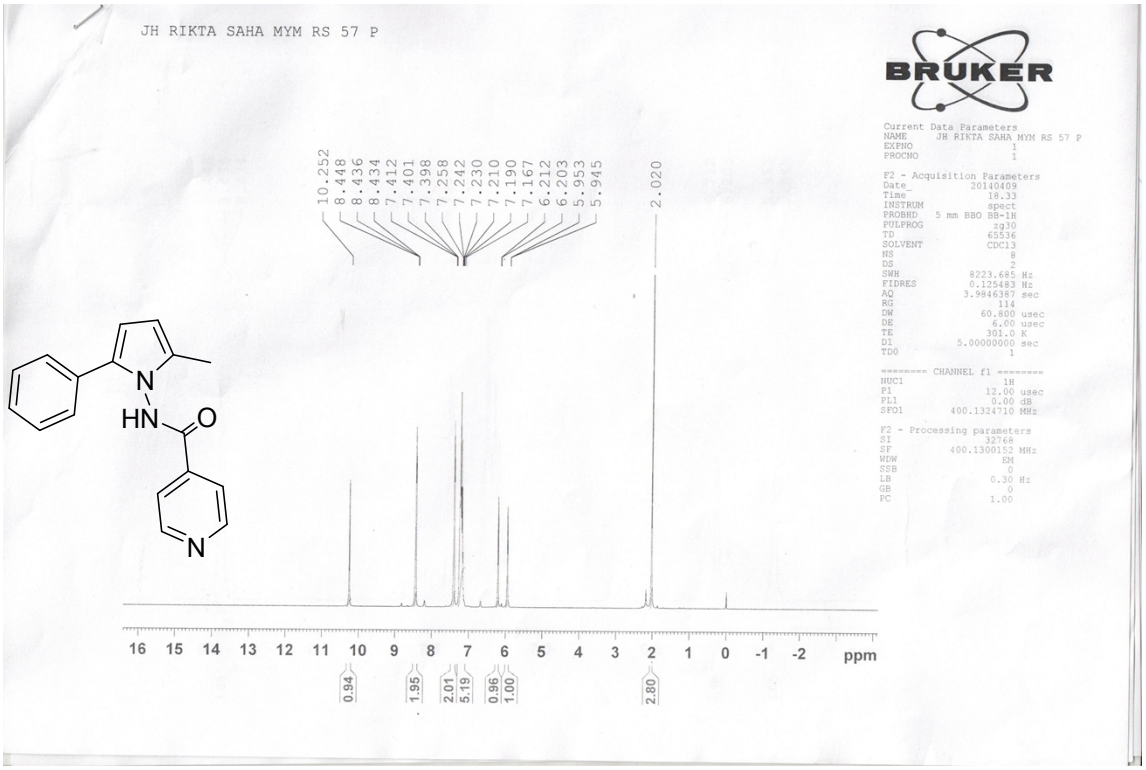


Compound 8d *4-Methyl-N-(2-methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*

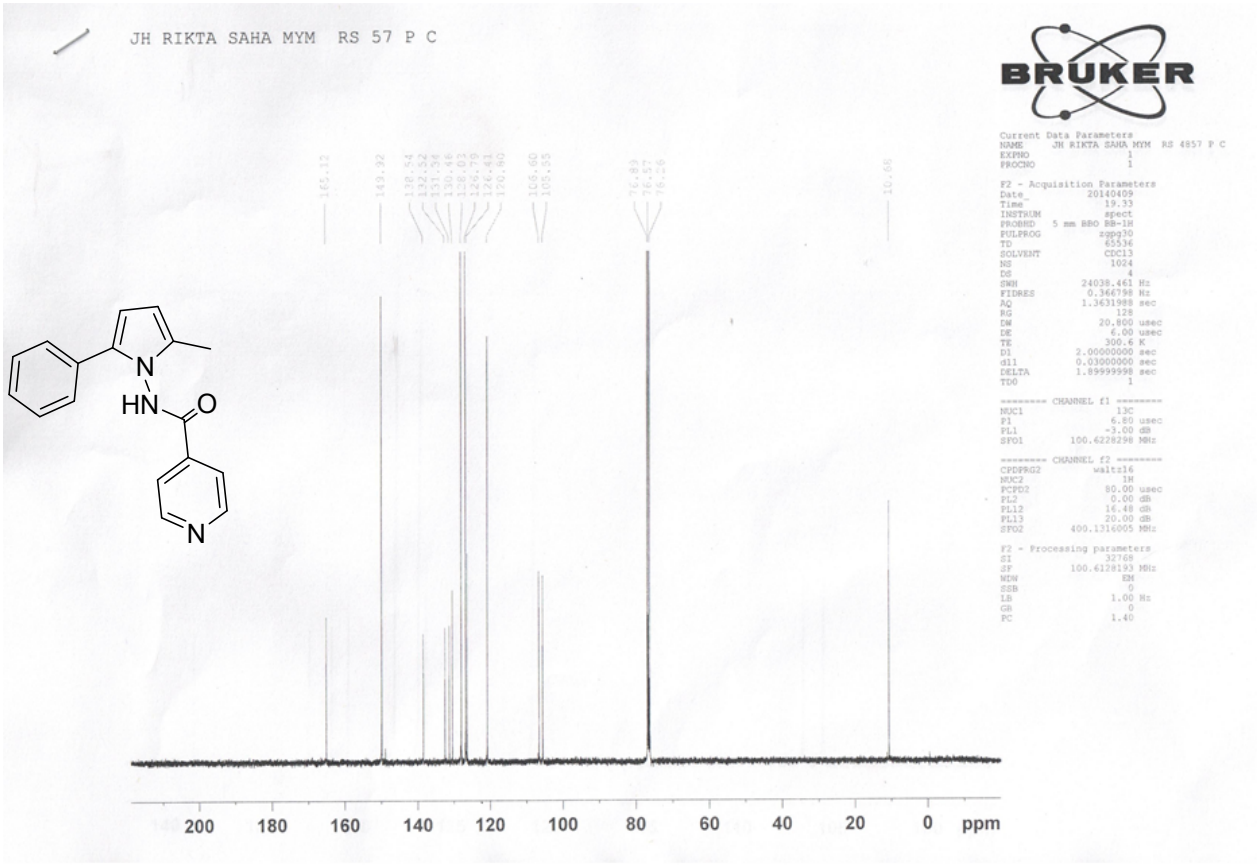
HPLC data



Compound 8e **1HNMR of** *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)isonicotinamide*



Compound 8e *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)isonicotinamide*



Compound 8e *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)isonicotinamide* **HPLC data**

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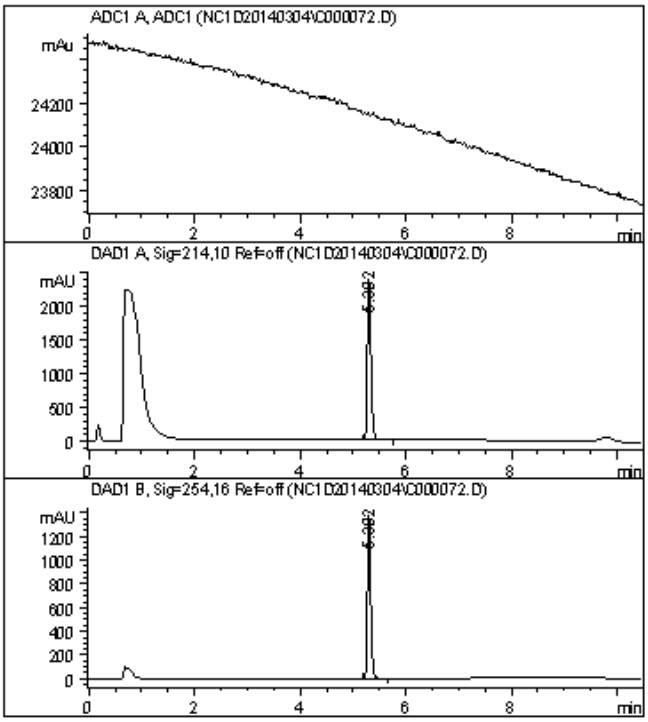
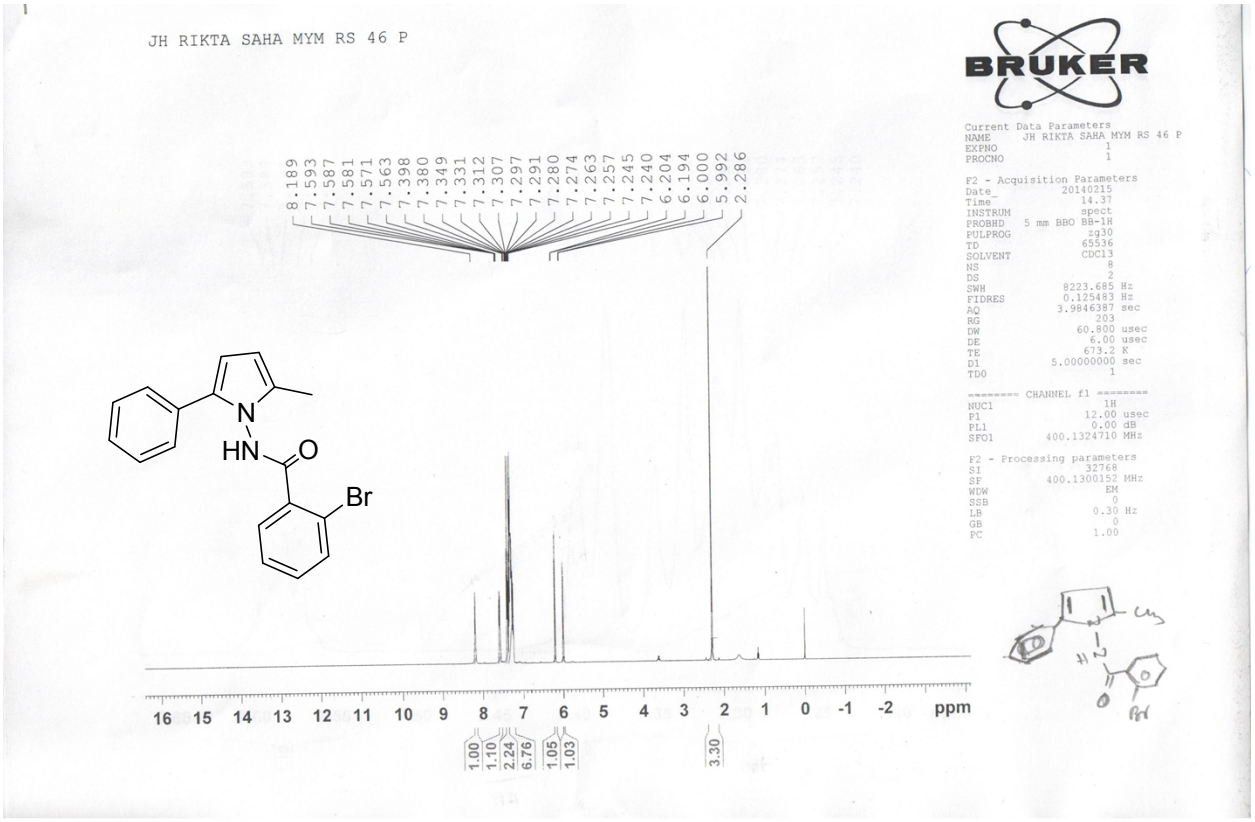
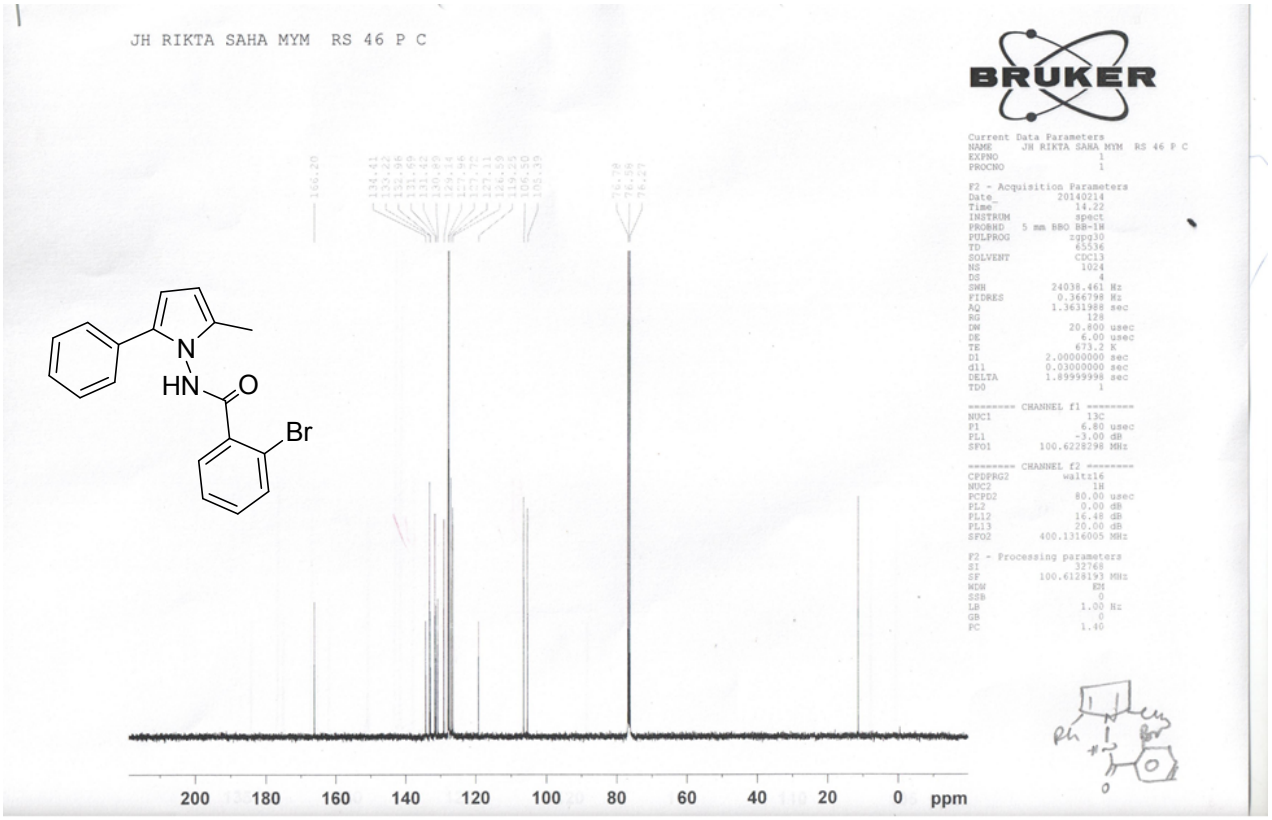


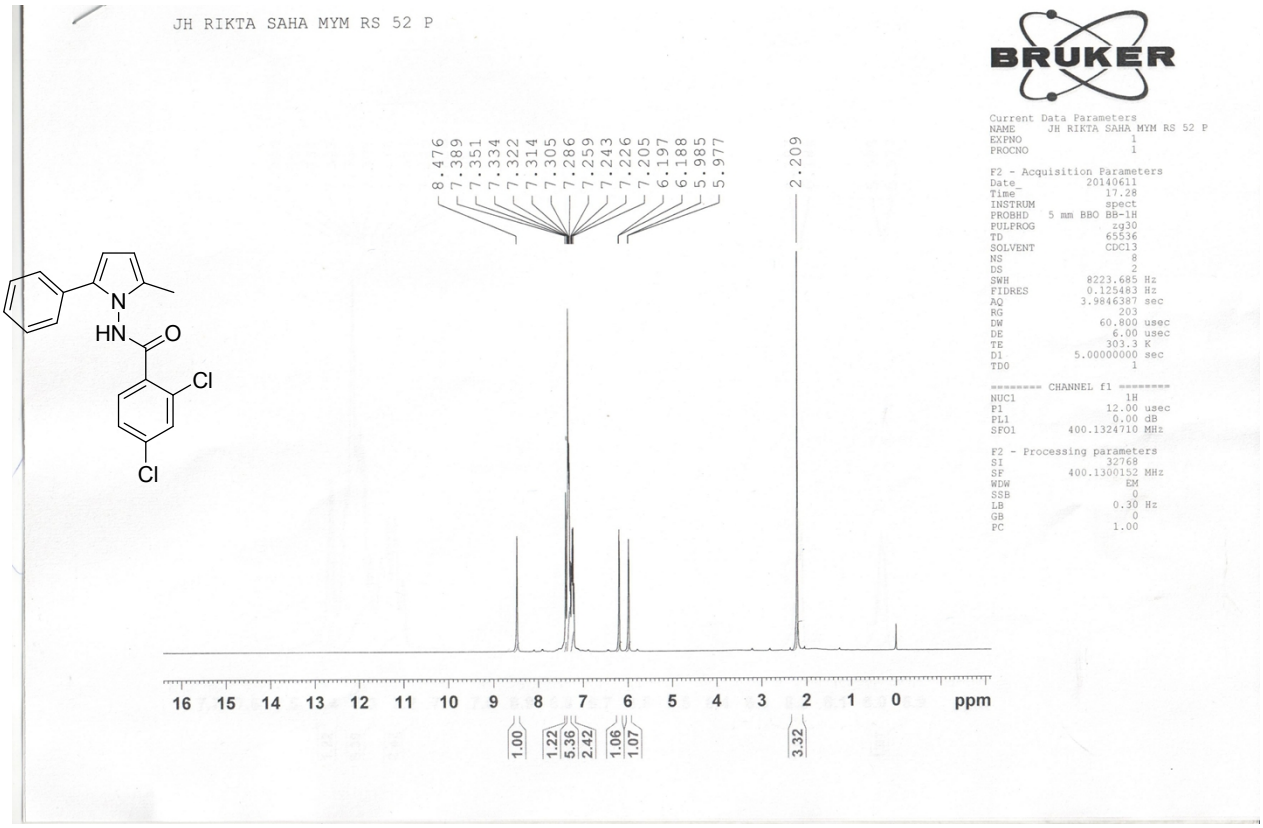
Compound 8f *2-Bromo-N-(2-methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*



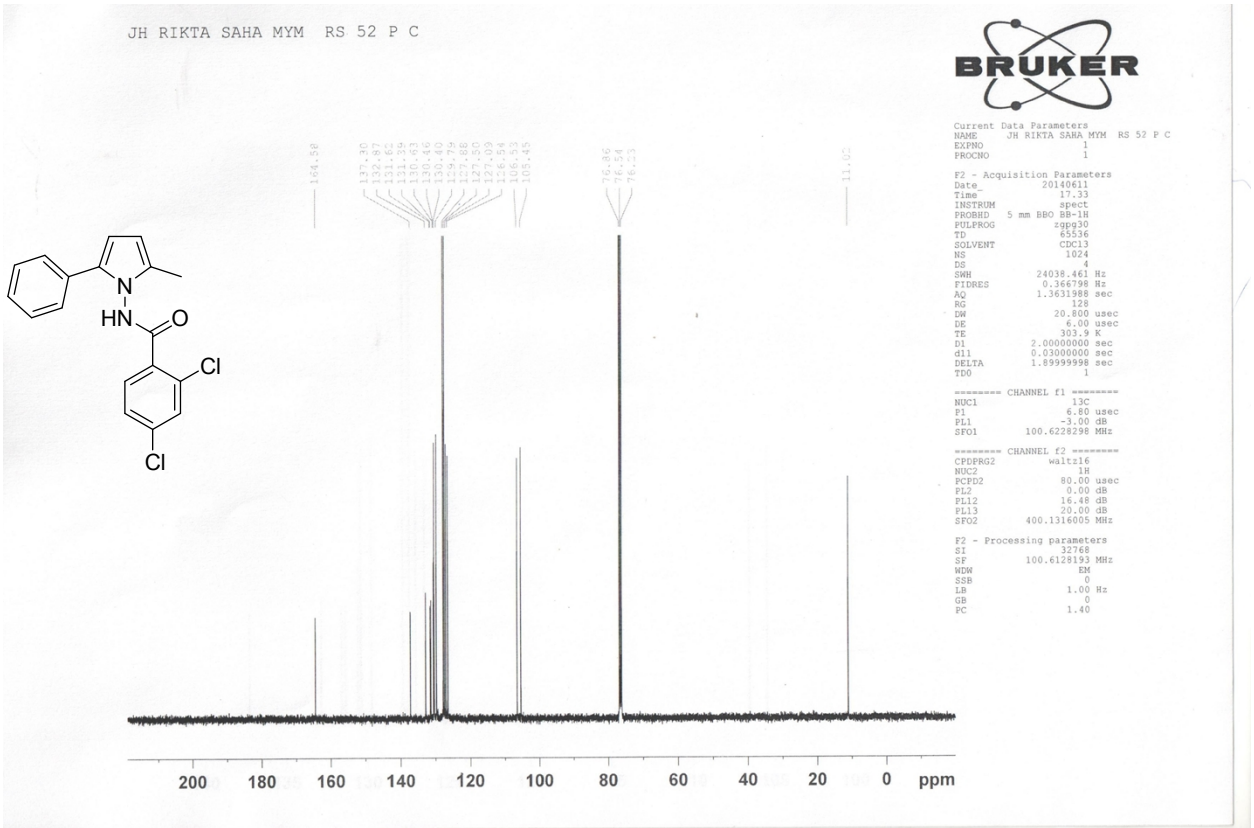
Compound 8f *2-Bromo-N-(2-methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*



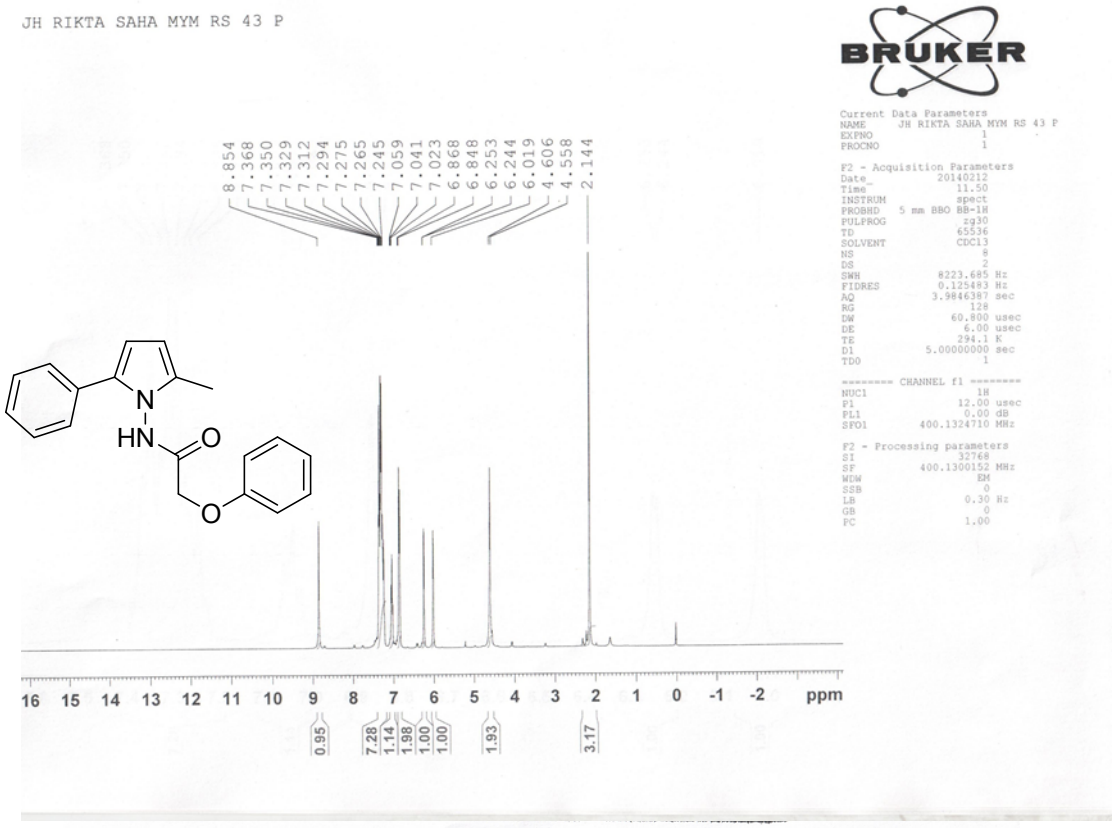
Compound 8h *2,4-Dichloro-N-(2-methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*



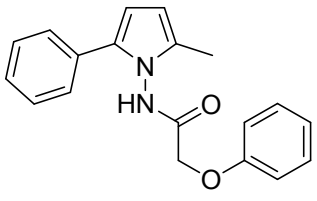
Compound 8h *2,4-Dichloro-N-(2-methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*



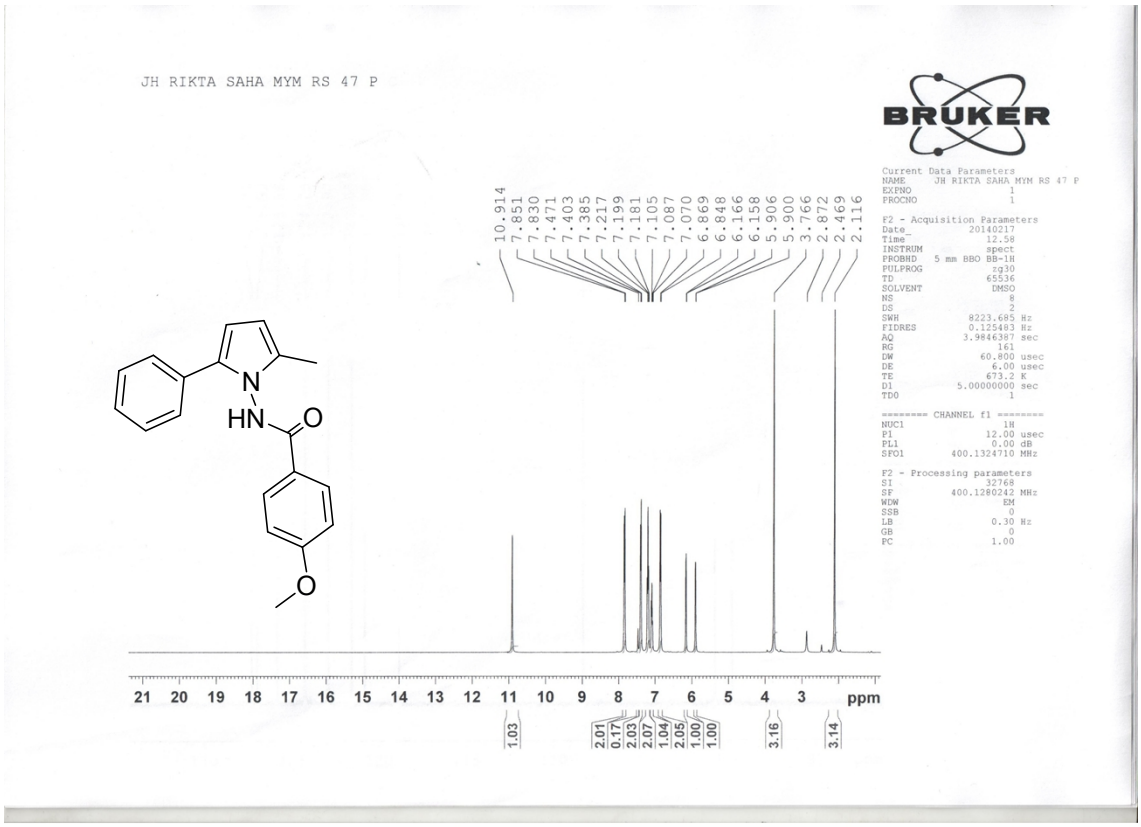
Compound 8i *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)-2-phenoxyacetamide*



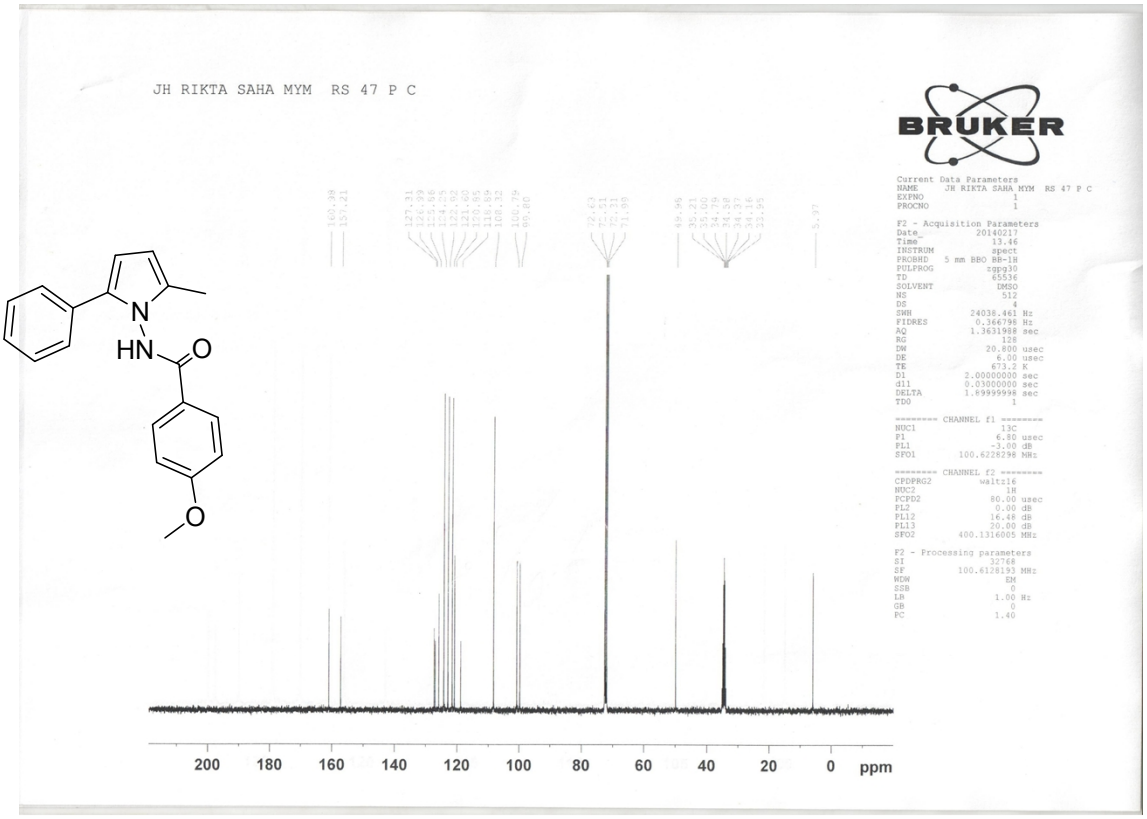
Compound 8i **^{13}CNMR** *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)-2-phenoxyacetamide*



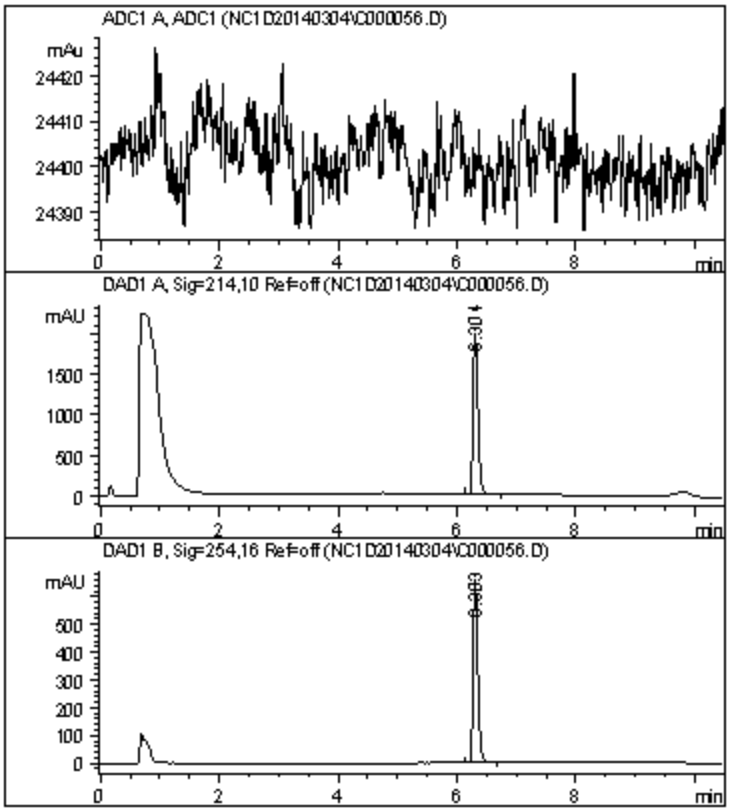
Compound 8j **[1]HNMR** *4-Methoxy-N-(2-methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*



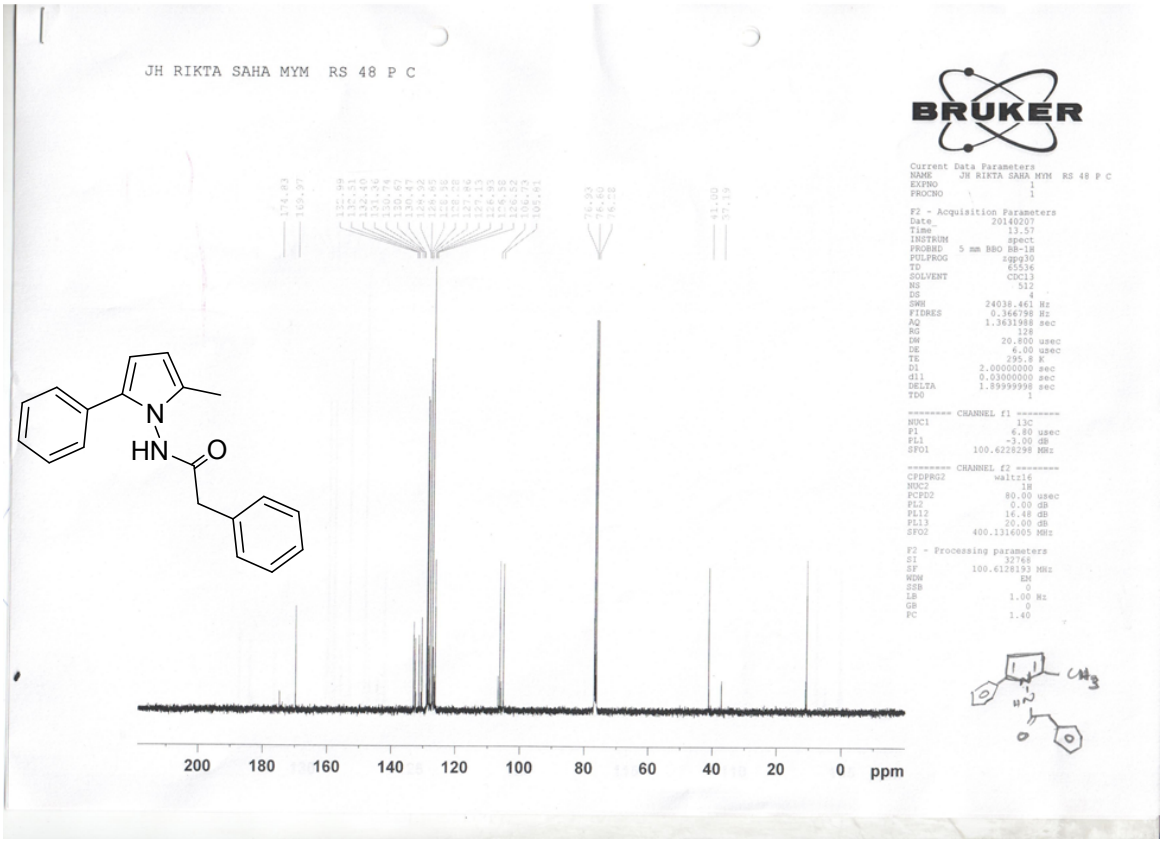
Compound 8j **[13]CNMR** *4-Methoxy-N-(2-methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*



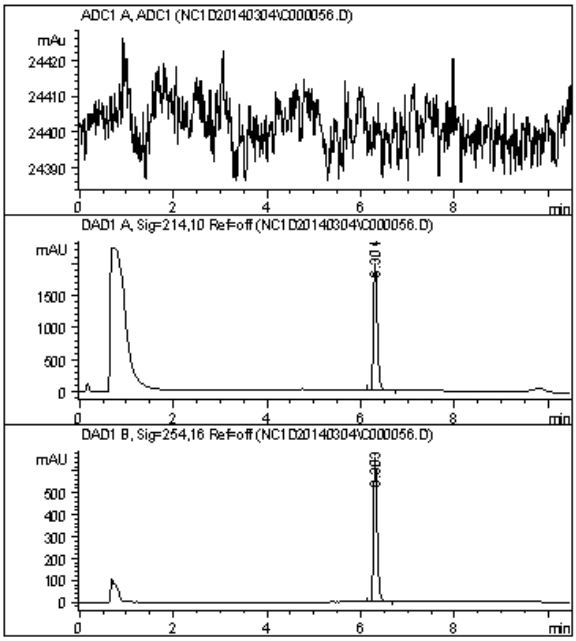
Compound 8j HPLC data of *4-Methoxy-N-(2-methyl-5-phenyl-1H-pyrrol-1-yl)benzamide*



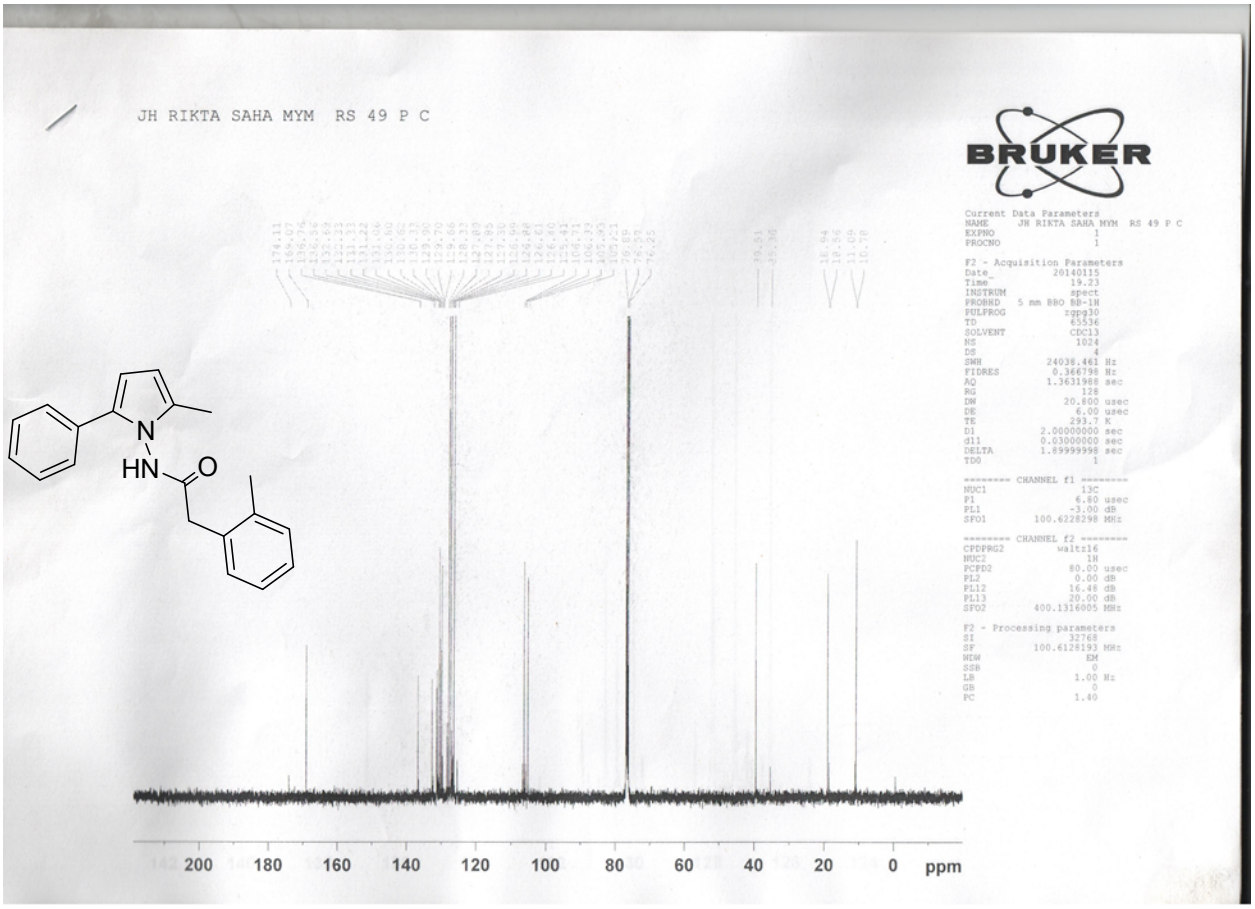
Compound 8k **^{13}CNMR** *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)-2-phenylacetamide*



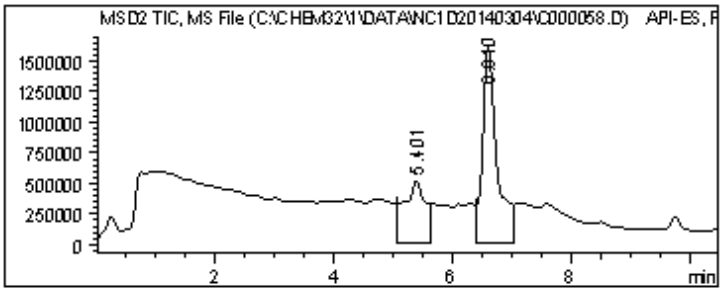
Compound 8k **HPLC data of** *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)-2-phenylacetamide*



Compound 8o **^{13}CNMR of** *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)-2-(o-tolyl)acetamide*



Compound 8o HPLC data of *N-(2-Methyl-5-phenyl-1H-pyrrol-1-yl)-2-(o-tolyl)acetamide*



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Area Percent Report
==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: ADC1 A, ADC1

Signal 2: DAD1 A, Sig=214,10 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.341	VV	0.0970	745.07306	107.28176	5.4920
2	6.545	VV	0.0970	1.28215e4	2049.74414	94.5080
Totals :				1.35666e4	2157.02590	

Signal 3: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.545	BB	0.0869	3419.17187	615.09943	100.0000
Totals :				3419.17187	615.09943	