Synthesis and Characterization of Some Imidazolidien and tetrazole derivatives

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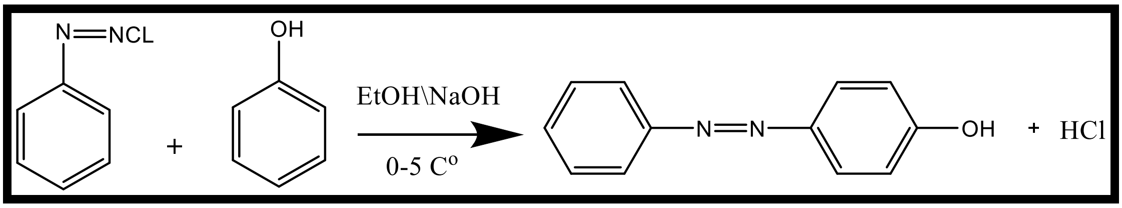
Abstract:

The present work included synthesis of novel (azo-shiff) via compounds in high yield, which react with (4-amino phenol , 3-nitro anilin and 4- methyl anilin) condensation reaction to produce various heterocycles (Five membered) ring like (Imidazolidine and tetrazole).The strcture of the newly synthesized compounds were monitored by (TLC) and identified by many techniques (FTIR , ^{1}HNMR and C^{13}NMR) and melting points.

Key words : Azo compounds , Schiff bases , Imidazolidien , tetrazole.

Introduction

Azo compounds are Organo-nitrogen derivative with the characteristic **–N=N-**[1] functionaliy and general formula **R'-N=N-R**[2]. where **R',R** group alphatic or aromatic, azo group is considerd biological active group , the most important method for preparing azo compounds is the coupling reaction between diazonium salts and phenols ,The diazonium salts attack as an electrophile reaction with the benzene ring of the coupling agent[3] .



Shiff bases or anils group are prepared of condensation reaction aromatic alhdehydes or ketone with primary amines The first report of the synthesis was obtained by Hugo Schiff 1864 [4] .Azo-Shiff bases are prepared by the reaction of azoketone with primary amine [5] .Various azo-shiff bases derivatives were prepared and some of them showed biological activity such as antivial [6] , antifungal [7], anticancer[8] , antibacterial and anticonvulsant[9] . Imidazolidine consist of adding (4) hydrogen atoms to the imidazole ring[10] , and the importance of the imidazolidien ring is due to its important roles as building blocks for the formation of biological active compounds [11] . The imidazolidien derivatives have interesting biotic activities such as antidepressants [12] , antifungal [13],antiviral [14] , antibiotic and digestive antibotiocs [15]. Extensive clinical practice[16]. Tetrazole ring was classified as (2+3) cycloddition [17] ,in which two atoms of the first component (anils) react with three atoms of the second component (azide group) [18].Tetrazole derivatives showed up fungicidal and antiviral activities [19].

Preparation Methods

(1) Synthesis 1-(3-((2-hydroxynaphthalen-1-yl)diazenyl)acetophenone (A)

3-aminoacetophenone (0.03 mol , 4.05 gm) was dissolved in (3ml)of concentrated hydrochloric acid and (20 ml) of distilled water . The solution was cold at (0 c^o) in ice-water bath. The sodium nitrite (0.03 mol ,2.07 gm)was dissolved in (10 ml) of distilled water and added drop wise to the solution with stirring .2- naphthol (0.03 mol ,4.32 gm) was dissolved in (20 ml) of ethanol and (10 ml) of sodium hydroxide 10% and cooled to (0C^o), added to the diazonium solution in drope wise and stirring at (0C^o)for (2h) for obtaining the coupling agent .The result of the orange gold compound was prcipited , filtered and washed with water **.**

(2)Synthesis of azo Schiff bases derivatives :

1-((3-(1-((4-hydroxyphenyl)imino)ethyl)phenyl)diazenyl)naphthalen-2-ol (S_1) **and** 1-((3-(1-((3-nitrophenyl)imino)ethyl)phenyl)diazenyl)naphthalen-2-ol (S_2) **and** 1-((3-(1-(p-tolylimino)ethyl)phenyl)diazenyl)naphthalen-2-ol (S_3)

Ethanolic mixture (30 ml) containing 1 drop of concentrated hydrochloric acid to azo acetophenone derivative (A) of (0.003 mol , 1.0 gm)then adding (0.37gm,0.47gm ,0.36 gm) of a primary aromatic amines (4-amino phenol ,3-nitro aniline and 4- methyl aniline) .The reaction mixture was refluxed with stirring for (10-35) hours at (78) C^o , the reaction was complete and monitored by using TLC (Methanol : dry benzene 1:4)recrystallized from ethanol.

(3)Synthesis of 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-(4

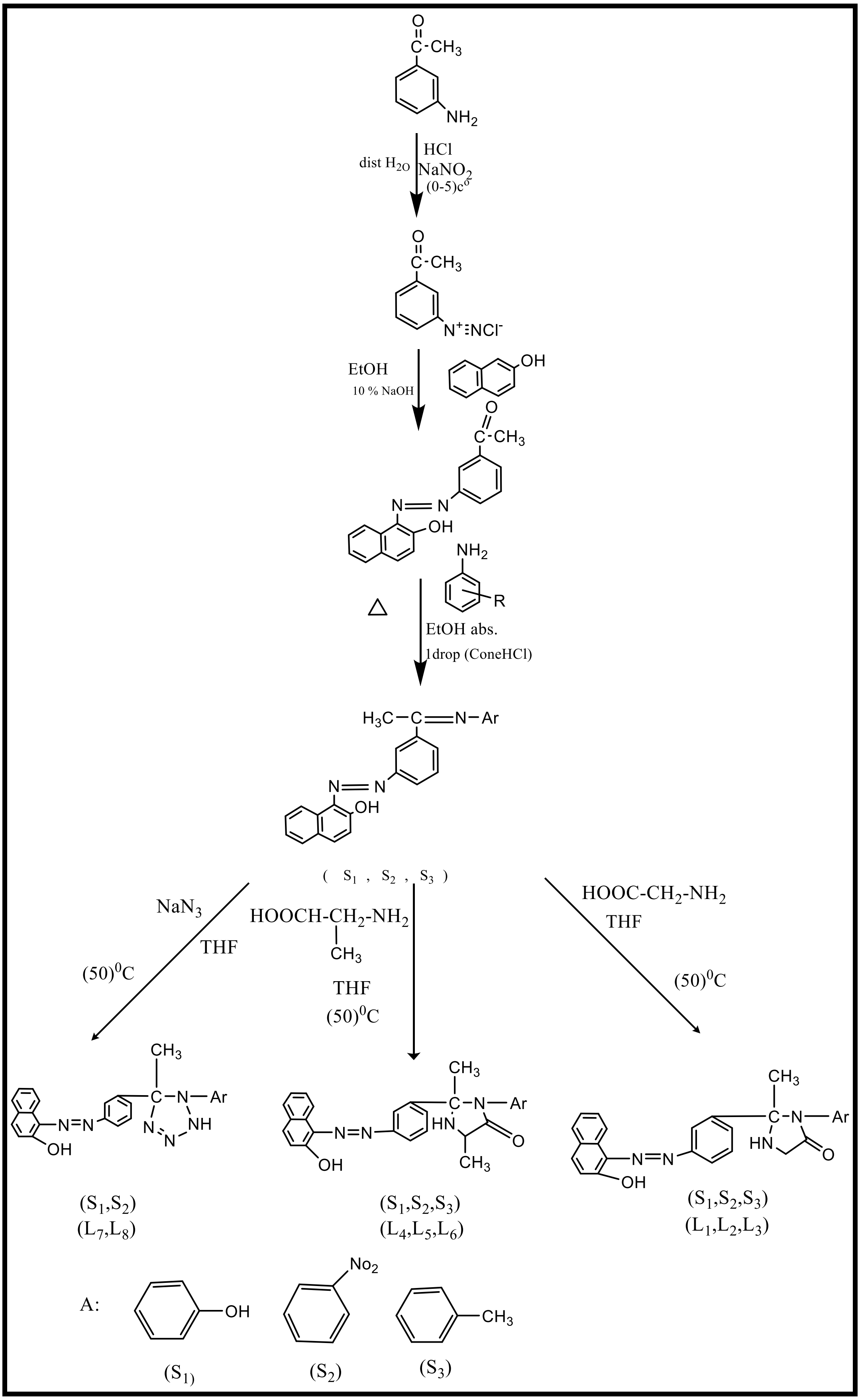
hydroxyphenyl)-2-methylimidazolidin-4-one (L_1) **and** 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-2-methyl-3-(3-nitrophenyl)imidazolidin-4-one (L_2) **and** 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-2-methyl-3-(p-tolyl)imidazolidin-4-one (L_3) A mixture of azo-schiff bases derivatives (S_1-S_3) (0.3 gm ,0.2 gm ,0.2 gm) with (0.1 gm , 0.036 gm , 0.05 gm) amino acid glycine respectively in (30 ml) of Tetrahydrofuran (THF) was refluxed for (23 , 10 ,13) hours for compounds (L_1-L_3) .

(4)Synthesisof2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-3-(4-hydroxyphenyl)-2,5-dimethylimidazolidin-4-one (L_4) **and** 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-2,5-dimethyl-3-(3-nitrophenyl)imidazolidin-4-one (L_5) **and** 2-(3-((2-hydroxynaphthalen-1-yl)diazenyl)phenyl)-2,5-dimethyl-3-(p-tolyl)imidazolidin-4-one (L_6): A mixture of azo-schiff bases derivatives (S_1-S_3) (0.3 gm ,0.2 gm ,0.2 gm) with (0.1 gm , 0.043 gm , 0.05 gm) amino acid alanine respectively in (30 ml) of Tetrahydrofuran (THF) was refluxed for (23 , 8 ,13) hours for compounds (L_4-L_6) .

(5) Synthesis of 1-((3-(1-(4-hydroxyphenyl)-5-methyl-2,5-dihydro-1H-tetrazol-5-yl)phenyl)diazenyl)naphthalen-2-ol (L_7) **and**1-((3-(5-methyl-1-(3-nitrophenyl)-2,5-dihydro-1H-tetrazol-5-yl)phenyl)diazenyl)naphthalen-2-ol (L_8) : A mixture of azo-schiff bases derivatives (S_1-S_2) (0.3 gm ,0.1 gm) with (0.07 gm , 0.015 gm) sodium azied respectively in (30 ml) of Tetrahydrofuran (THF) was refluxed for (23 , 7) hours for compounds (L_7-L_8)

Table-1- The physical properties of the prepared compounds:

No.	M.F	M.wt	m.p ^{0}C	Color	R_f	Time	Solvent	Yield %
A	$C_{18}H_{14}N_2O_2$	290.32	156-158	Golden Orange	…	3 hrs	EtOH +H_2O	91
S_1	$C_{24}H_{19}N_3O_2$	381.44	162-164	Green	0.9	35hrs	EtOH abs.	87
S_2	$C_{24}H_{18}N_4O_3$	409.43	160-162	Dark red	0.9	20 hrs	EtOH abs.	81
S_3	$C_{25}H_{21}N_3O_1$	379.46	174-176	Light red	0.7	10hrs	EtOH abs.	87
L_1	$C_{26}H_{22}N_4O_3$	438.49	132-134	Light Yellow	0.9	23hrs	THF	87
L_2	$C_{26}H_{21}N_5O_4$	467.49	100-102	Light brown	0.9	10 hrs	THF	88
L_3	$C_{27}H_{24}N_4O_2$	436.52	126-128	Dark red	0.9	13 hrs	THF	85
L_4	$C_{27}H_{24}N_4O_3$	452.51	136-138	Dark Yellow	0.8	23hrs	THF	84
L_5	$C_{27}H_{23}N_5O_4$	481.51	122-124	Aredish orang	0.8	8hrs	THF	90
L_6	$C_{28}H_{26}N_4O_2$	450.54	125-127	Light red	0.9	13hrs	THF	86
L_7	$C_{24}H_{20}N_6O_2$	424.46	130-132	Brown	0.9	23hrs	THF	90
L_8	$C_{24}H_{19}N_7O_3$	453.46	144-142	Light Pink	0.9	7hrs	THF	91



Scheme (1): The structares of all synthesis compounds

Spectral Characterization

Our derivative was identified with variety spectral methods like (FTIR , H.NMR , C^{13}.NMR) spetra:

(A) **FT-IR:** 1498 (N=N), 3421.72(OH) , 3062.96-3014.74(C-H , aromatic) , 1618.28 (C=C) , 1224.16-1203.58 (C-O) , 1147.65 (C-N) .**^{1}HNMR :** Singlet 2.101 ppm(CH_3),singlet 2.5 ppm (DMSO), multipleting singal at 6.996-7.377 ppm (phenol ring), singlet 11.01ppm(OH).**C^{13}NMR:** A\Singlet 26.36 ppm(CH_3),197.52ppm(C=O), multipleting singal at 111.1-149.148 ppm (phenol ring), singlet 155. 1ppm(OH).

(S_1) **FT-IR:** 1683.86 (C=N) , 1502.55 (N=N) , 3061.03 -3030.17 (-CH,aromatic), 3414.00-3406.29(OH) , 1618.28 (C=C) , 1355.96(CH_3) .**^{1}HNMR :** Singlet 2.077ppm(CH_3), 2.512 ppm(DMSO) , multipleting singal at 6.998-7.643 ppm (phenal ring), 10.743-11-381 ppm (OH). **C^{13}NMR:** Singlet273ppm(CH_3), 159PPM (C=N) ,153-154 ppm (OH).

(S_2) **FT-IR:** 1683.86 (C=N) , 1500.62 (N=N) , 3066.82 -32972.31 (-CH,aromatic) , 3458.37-3437.15 (OH) , 1620.21 (C=C) , 1357.89 (CH_3) .**^{1}HNMR :** Singlet 2.064ppm(CH_3) , singlet 2.51ppm (DMSO) ,multipleting singal at 7.038-7.980 ppm (phenal ring) ,11.814 ppm (OH) . **C^{13}NMR:** Singlet 26.411(CH_3) , 159.054PPM(C=N) ,154 ppm (OH) .

(S_3) **FT-IR:** 1689.64 (C=N) , 1581.63 (N=N) , 3099.61 -3062.96 (-CH,aromatic) , 3439.08-3360.00(OH) , 1641.42 (C=C) , 1355.96 (CH_3) . **^{1}HNMR :** Singlet 1.718-2.088ppm (CH_3) , singlet 2.518ppm (DMSO) , multipleting singal at 7.401-8.498 ppm (phenal ring) , single 11.518ppm (OH) . **C^{13}NMR :** Singlet 21.605-25605 (CH_3) , 159.432PPMsi , ngle153.442PPM (OH) .

(L_1)FT-IR:1678.07 (N-C=O),1616.35(C=C)aromatic,1504.48(N=N),1359.82 (CH_3),3080.32 (NH),3394.72 (OH).HNMR: Single(2.510)ppm(CH_3),Single (2.521)ppm(DMSO-d^6), single (6.996)ppm(CH_2),multipeting single (7.377-7.027)ppm(phenal ring),Single (9.3520)ppm(NH),single (10.352)ppm (OH Phenol),(11.251)ppm(OH naphthol).C^{13}NMR: Signal (176.358)ppm (C=O), signal (161.253) ppm (C-N),), signal (155.684)ppm (OH naphthol) , signal (154.253) ppm (OH phenol), multipeting signl(105.199-142.462) ppm (C aromatic),Signal (55.798)ppm(C-CH_3) , Signle (39.116-40.779)ppm(DMSO-d^6 , signle (23.253) ppm (CH_3).

(L_2)FT-IR:1672.93 (N-C=O),1618.28(C=C)aromatic,1500.62(N=N),1355.96 (CH_3),3064.89 (NH),3448.72 (OH). **^{1}HNMR**: Single(1.685)ppm(CH_3),Single (2.528)ppm(DMSO-d^6), single (6.787)ppm(CH_2),multipeting single (6.976-8.155)ppm(phenal ring),Single (9.585)ppm(NH),(11.529) ppm(OH naphthol) .C^{13}NMR: Signal (176.971)ppm (C=O), signal (161.453) ppm (C-N),), signal (155.701)ppm (OH naphthol), multipeting signl(121.145-131.253) ppm (C aromatic),Signal (64.666)ppm(C- CH_3) , Signle (39.480-40.866)ppm(DMSO-d^6 , signle (25.408) ppm (CH_3).

(L_3)FT-IR:1681.93 (N-C=O),1618.28(C=C)aromatic,1498.69(N=N),1357.89 (CH_3),061.03(NH),3446.79 (OH). **^{1}HNMR**: Single(1.374)ppm(CH_3), Signal (1.874)ppm (CH_3),Single (2.606)ppm(DMSO-d^6), single (6.402) ppm (CH_2), multipeting single (7.419-8.144)ppm(phenal ring),Single (9.3520) ppm(NH) ,(11.251)ppm(OH naphthol).C^{13}NMR: Signal (175.349)ppm (C=O), signal (162.284) ppm (C-N),), signal (155.684) ppm (OH naphthol), multipeting signl(112.561-130.038) ppm (C aromatic),Signal (58.225)ppm(C-CH_3) , Signle (39.116-40.779)ppm(DMSO-d^6 , signle (24.253) ppm (CH_3). (L_4)**FT-IR**:1680.00 (N-C=O),1612.49(C=C)aromatic,1504.48(N=N),1357.89 (CH_3),3061.03

(NH),3169.04 (OH).^{1}**HNMR** : Single(1.721)ppm(CH_3),Single (2.516)ppm(DMSO-d^6),double Signal (3.474-3.452)ppm (C-CH_3), single (6.589) ppm(C-N),multipeting single (7.628-7.973) ppm(phenal ring) ,Single (9.818) ppm (NH) ,single (10.718) ppm (OH Phenol),(11.797) ppm (OH naphthol) .C^{13}NMR: Signal (177.411)ppm (C=O), signal (162.411) ppm (C-N),), signal (155.967) ppm (OH naphthol),Signal (154.967)ppm (OH phenol0 , multipeting signl(116.632-131.524) ppm (C aromatic),Signal (61.632)ppm(C-CH_3) , Signle (39.203-40.866) ppm (DMSO-d^6) , signle (18.411) ppm (CH_3).

(L_5)FT-IR:1678.07 (N-C=O) ,1622.13 (C=C) aromatic ,150419.91 (N=N) , 1348.24 (CH_3), 3332.99 (NH) ,3431.36 (OH) .^{1}HNMR : Single(1.719) ppm (CH_3),Single (2.522) ppm(DMSO-d^6), double single (3.393-3.385) ppm (C-CH_3) , Signal (6.526)ppm (CH_2) , multipeting single (7.458-8.292) ppm (phenal ring), Single (9.672) ppm(NH), (11.555) ppm (OHnaphthol) .C^{13}NMR: Signal (175.422)ppm (C=O), signal (162.745) ppm (C-N),), signal (155.701) ppm (OH naphthol), multipeting signl(117.632-131.426) ppm (C aromatic),Signal (59.431)ppm(C-CH_3) , Signle (39.203-40.866) ppm (DMSO-d^6) , signle (24.408) ppm (CH_3).

(L_6)FT-IR:1680.00 (N-C=O),1616. 35 (C=C) aromatic ,1500.62 (N=N) , 1357.89 (CH_3),3059.10 (NH),3428.72 (OH).^{1}HNMR : Single(1.587) ppm (CH_3),Signal (1.814)ppm (CH_3),Single (2.523) ppm(DMSO-d^6),dopel single (3.398-3.385)ppm(C-CH_3)),Signal (6.746)ppm (CH_2),multipeting single (7.494-7.811)ppm(phenal ring),Single (9.427)ppm (NH),single (11.627)ppm(OH naphthol).C^{13}NMR: Signal (178.465)ppm (C=O), signal (162.411) ppm (C-N),), signal (155.967) ppm (OH naphthol), multipeting signl(116.632-131.426) ppm (C aromatic),Signal (64.632)ppm(C-CH_3) , Signle (39.203-40.866) ppm (DMSO-d^6) , signle (18.589) ppm (CH_3) aromatic ring , signal (22.312)ppm (CH_3)cyclic ring , signal (24.408)ppm (CH_3)ketone.

(L_7)FT-IR:16780.00 (N-C) ,1610.56 (C=C) aromatic ,1504.48 (N=N) , 1357.89 (CH_3),3261.63 (NH),3396.64 (OH). ^{1}HNMR: Single (2.051) ppm (CH_3) ,Single (2.510)ppm(DMSO-d^6), multipeting single (7.042-7.947) ppm (phenal ring),Single (9.612)ppm(NH),single (10.685)ppm (OH Phenol),(11.627)ppm(OH naphthol).C^{13}NMR: Sign (160.922) ppm (C-N),), signal (155.673)ppm (OH naphthol) , signal (153.248) ppm (OH phenol), multipeting signl(116.644-132.007) ppm (C aromatic), Signle (39.207-40.871)ppm(DMSO-d^6 , signle (27.410) ppm (CH_3).

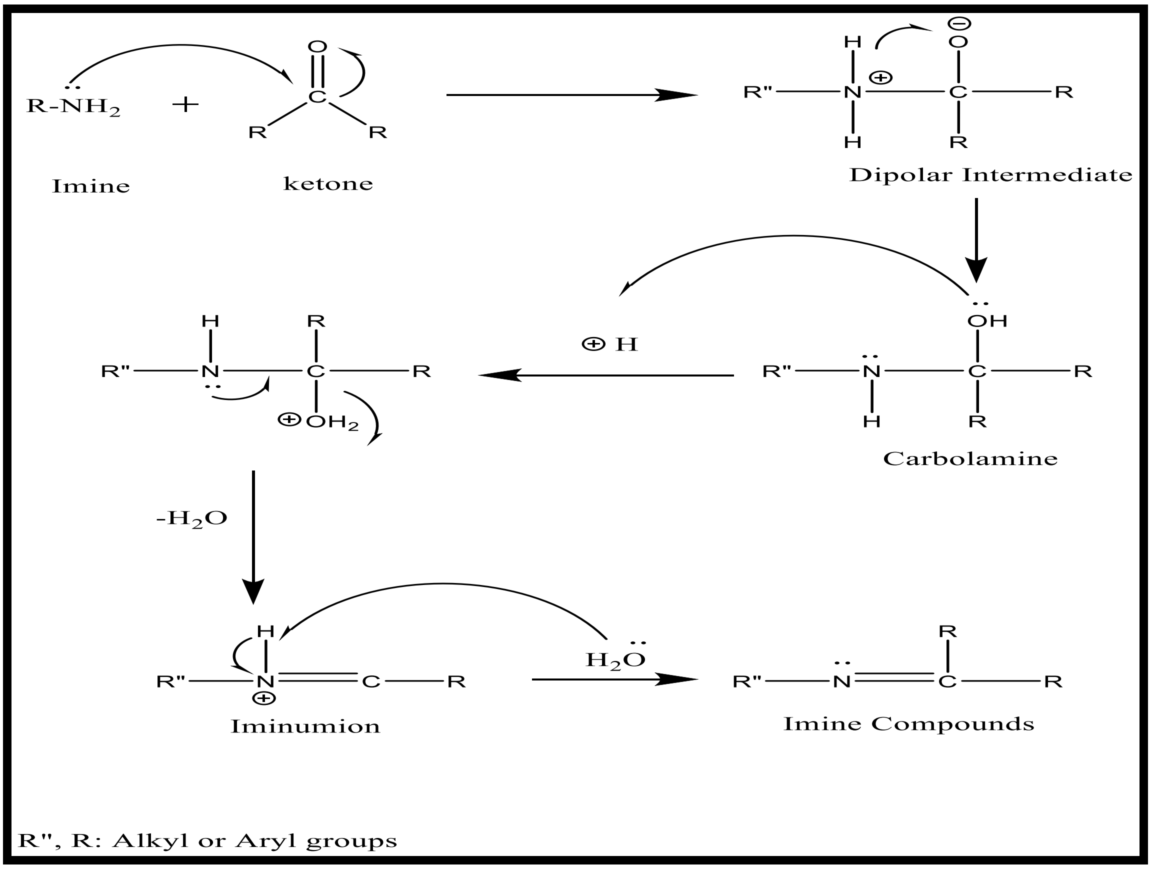
(L_8)FT-IR:1666.86 (N-C),1618.28(C=C)aromatic,1500.62(N=N),1398.39 (CH_3),3390.03 (NH),3458.37 (OH).HNMR: Single(1.969)ppm(CH_3),Single (2.528)ppm(DMSO-d^6), multipeting single (7.187-8.153)ppm (phenal ring) ,Single (9.685)ppm(NH), (11.069)ppm(OH naphthol).C^{13}NMR: signal (161.973) ppm (C-N),), signal (155.673)ppm (OH naphthol) , multipeting signl(116.644-130.662) ppm (C aromatic), Signle (39.207-40.871)ppm(DMSO-d^6 , signle (26.485) ppm (CH_3).

Result and Discussion:

Imine was prepared by thermal condensation reaction of 1-(3-((2-hydroxynaphthalen-1-yl)diazenyl)acetophenone with 4-aminophenol , 3-nitro aniline , 4- Methal aniline . In absolute ethanol under reflux condition and used as starting materials for the synthesis Imidazolidine , tetrazole derivatives .Characterization by confirming their structure by some physical properties and

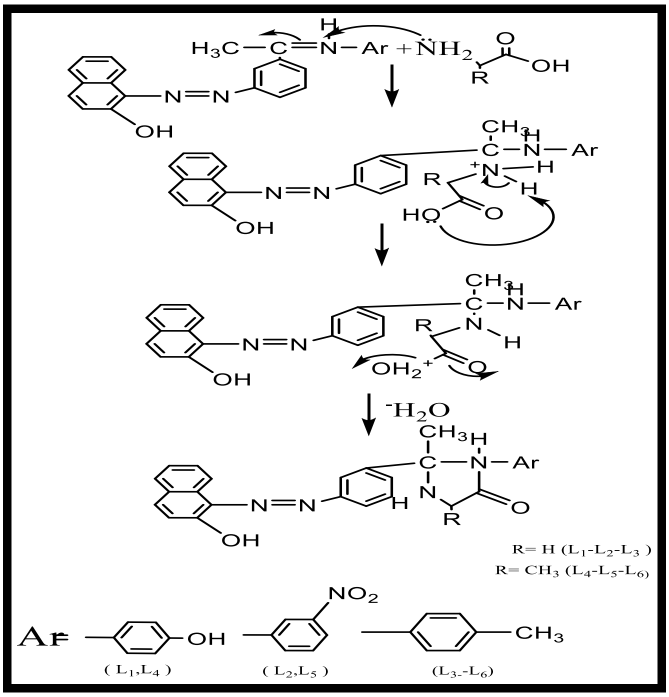
FTIR spectra .The FTIR spectra of compounds (S_1,S_2,S_3) showed that the disappearance of the stretching frequency absorption bands of ($-NH_2$) and (C=O) group for amine and ketone respectively and the appearance of characteristic absorption bands at (3421.72) Cm^{-1} due to **OH** , due to (1683.86,1683.86 ,1689.64) Cm^{-1} respectively **C=N** imine group , due to (1618.28.1620.21,1600.92) Cm^{-1} respectively **C=C** aromatic , due to (1502.55,1500.62,1581.63) Cm^{-1} **N=N** .

The formation of Imine compounds is general mechanism is suggested to take place by nuclophilic addition of the amine group to the carbonyl group associated ,following by extract of water to give the product as shown in scheme(2).



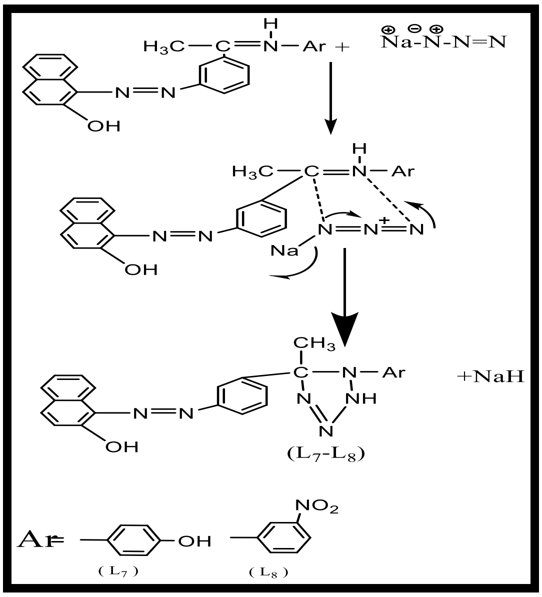
Scheme 2: proposed mechanisam for the formation of Imine compounds

The amino acid (glycine , alanine) are then added to Imine group C=N to take place by nuclophilic attack from the electron double of the nitrogen atom and extract of water to give the product as shown in scheme (3).



Scheme 3: proposed mechanisam for the formation of five- membered ring (Imidazolidien)

Then synthesis tetrazole compounds by reaction of Imine group with Sodium azied in THF is suggested of mechanism for the reaction (1,3-dipolar cyclo addition) one of the types of cyclic addition the product as shown in scheme (4).



Scheme 4: proposed mechanisam for the formation of five- membered ring (tetrazole.)

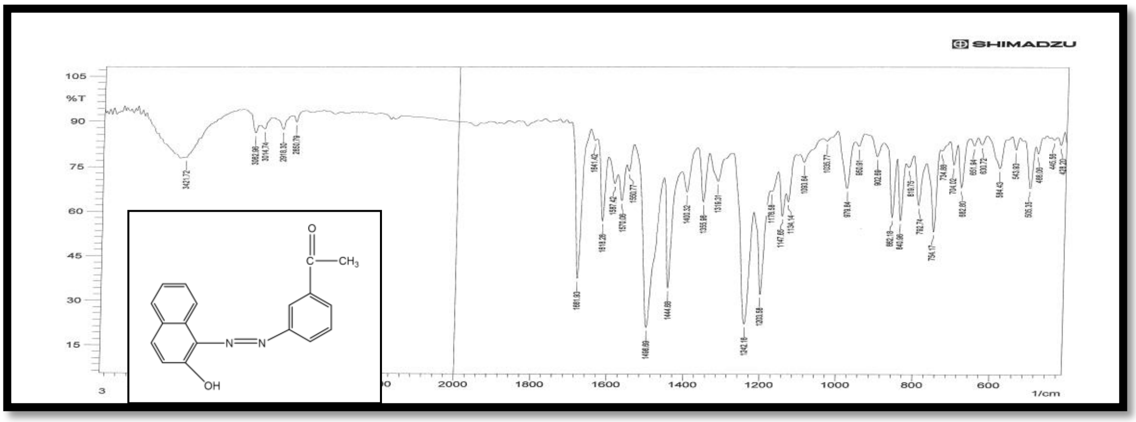
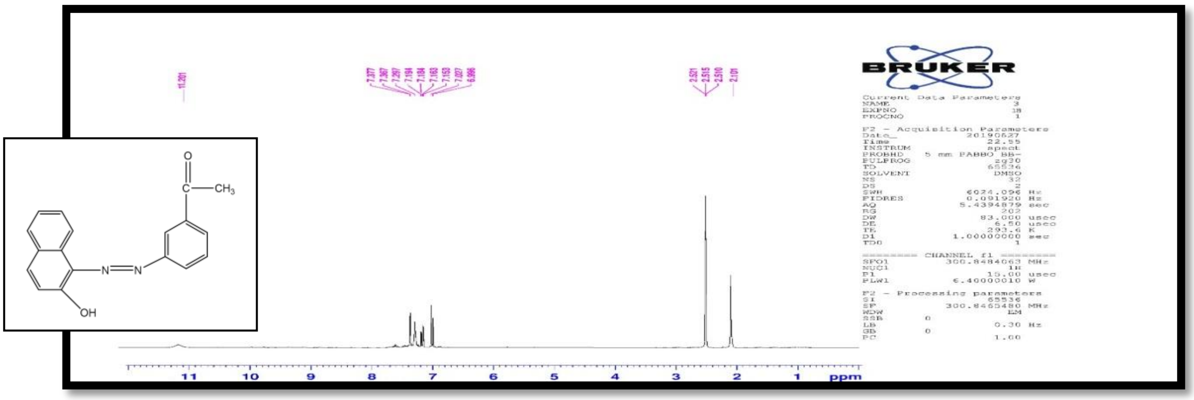


Figure1: FTIR Spectra of Azo compound(A)



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TD                  65536
SOLVENT              DMSO
NS                     32
DS                      2
SWH              6024.096 Hz
FIDRES           0.091920 Hz
AQ              5.4394879 sec
RG                    202
DW                 83.000 usec
DE                   6.50 usec
TE                  293.6 K
D1             1.00000000 sec
TD0                     1

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NUC1                   1H
P1                  15.00 usec
PLW1           6.40000010 W

F2 - Processing parameters
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SF            300.8465480 MHz
WDW                    EM
SSB      0
LB                   0.30 Hz
GB       0
PC                   1.00
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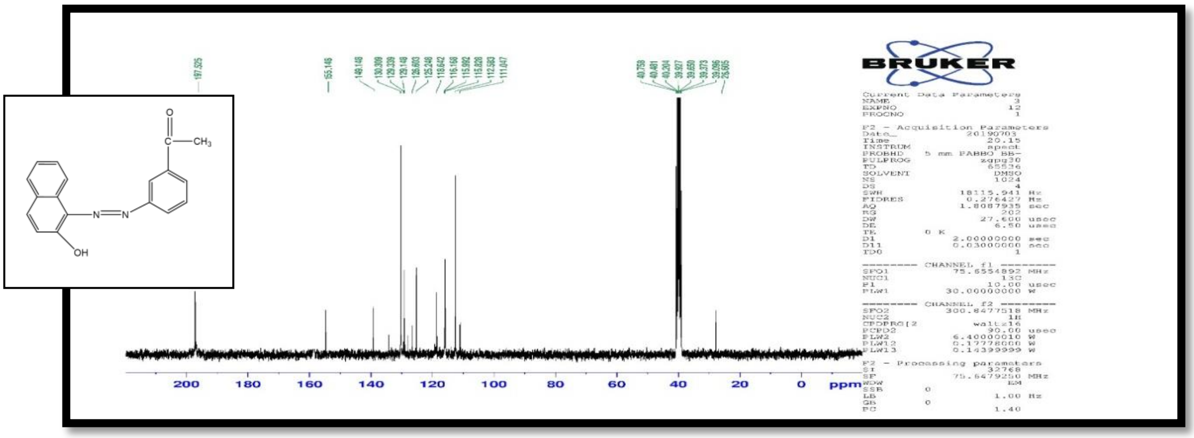
Figure2: ^{1}HNMR Spectra of Azo compound (A)



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DS                      4
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FIDRES           0.276427 Hz
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RG                    202
DW                 27.600 usec
DE                   6.50 usec
TE            0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

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NUC1                  13C
P1                  10.00 usec
PLW1          30.00000000 W

======== CHANNEL f2 ========
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NUC2                   1H
CPDPRG[2          waltz16
PCPD2               90.00 usec
PLW2           6.40000010 W
PLW12          0.17778000 W
PLW13          0.14399999 W

F2 - Processing parameters
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WDW                    EM
SSB      0
LB                   1.00 Hz
GB       0
PC                   1.40
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Figure3: ^{13}CNMR Spectra of Azo compound(A)

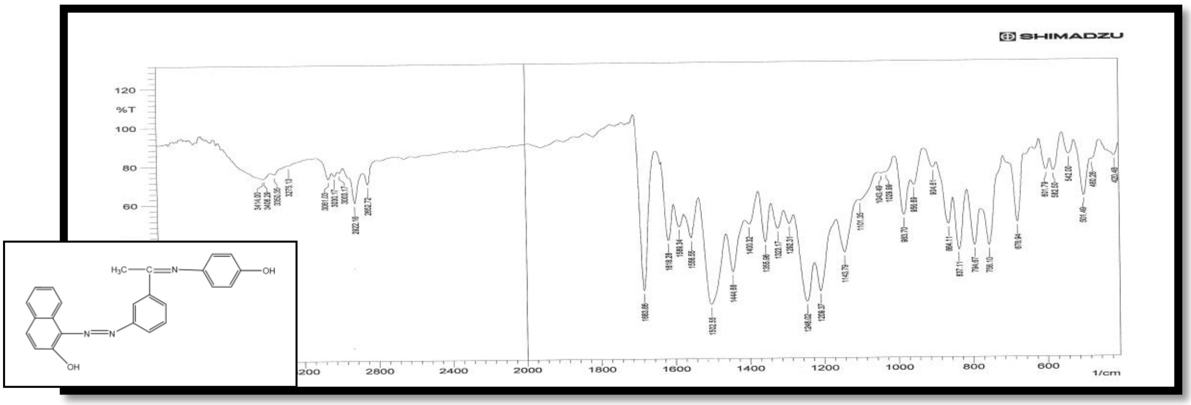


Figure4: FTIR Spectra of compound (S_1)

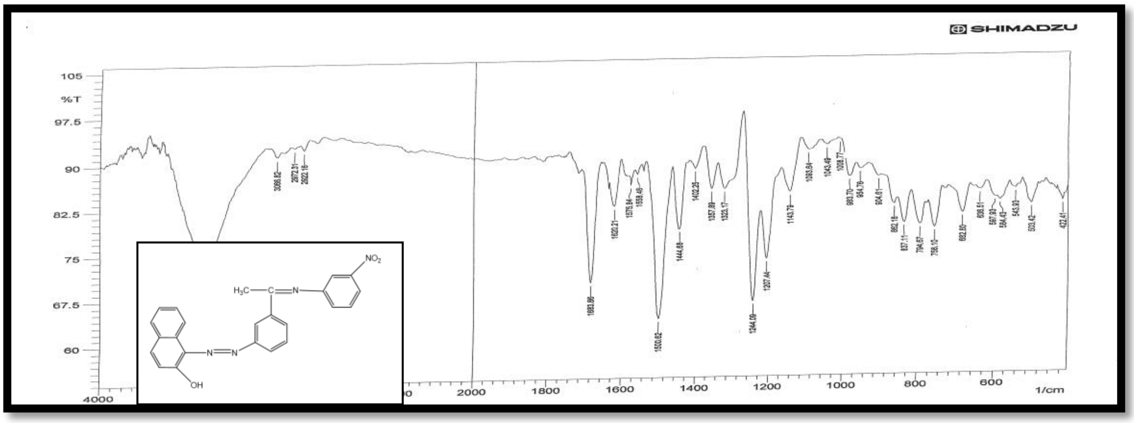


Figure5: FTIR Spectra of compound (S_2)

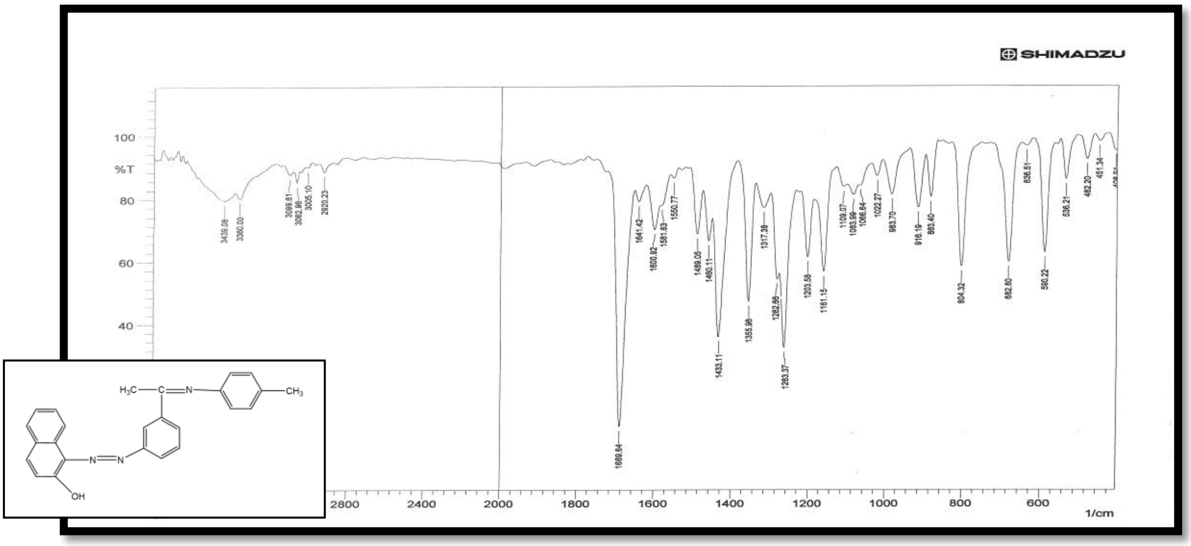


Figure6: FTIR Spectra of compound (S_3)

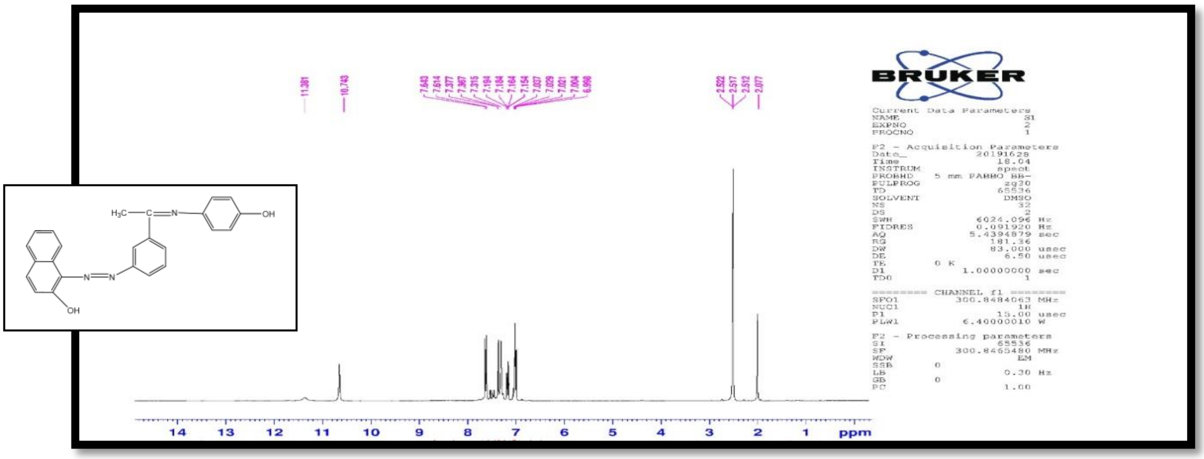


Figure7: ^{1}HNMR Spectra of compound (S_1)

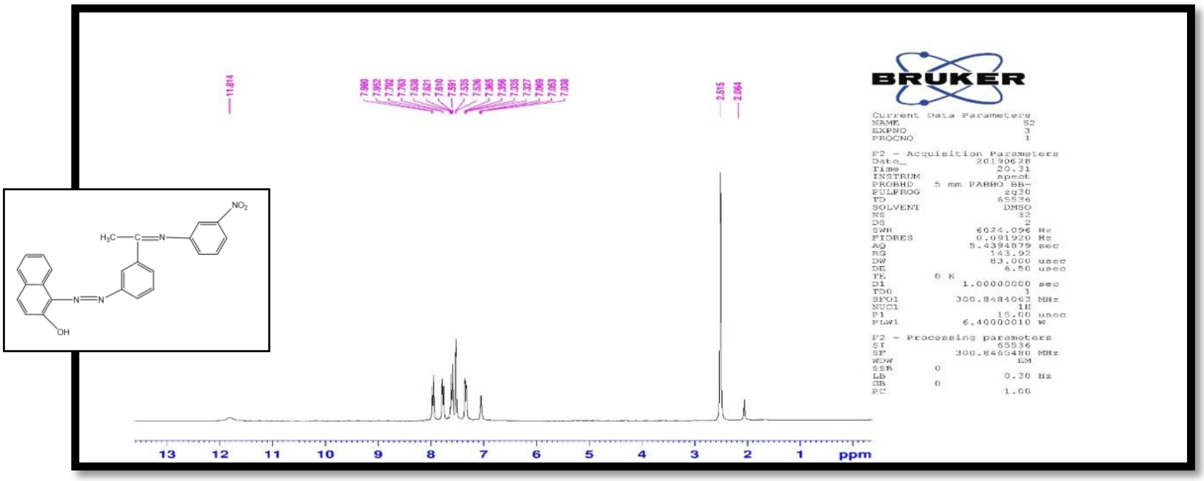


Figure8: ^{1}HNMR Spectra of compound (S_2)

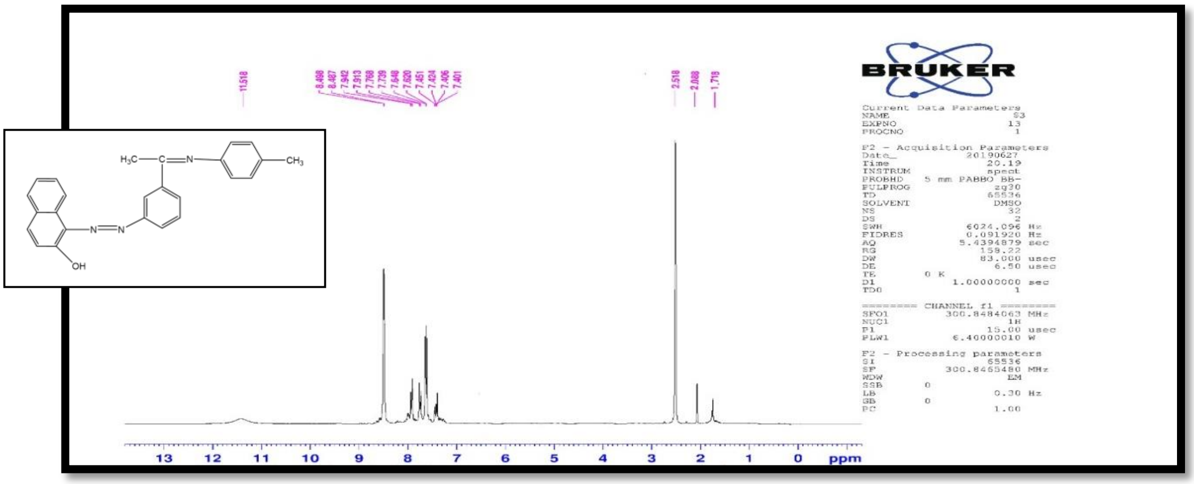


Figure9: ^{1}HNMR Spectra of compound (S_3)

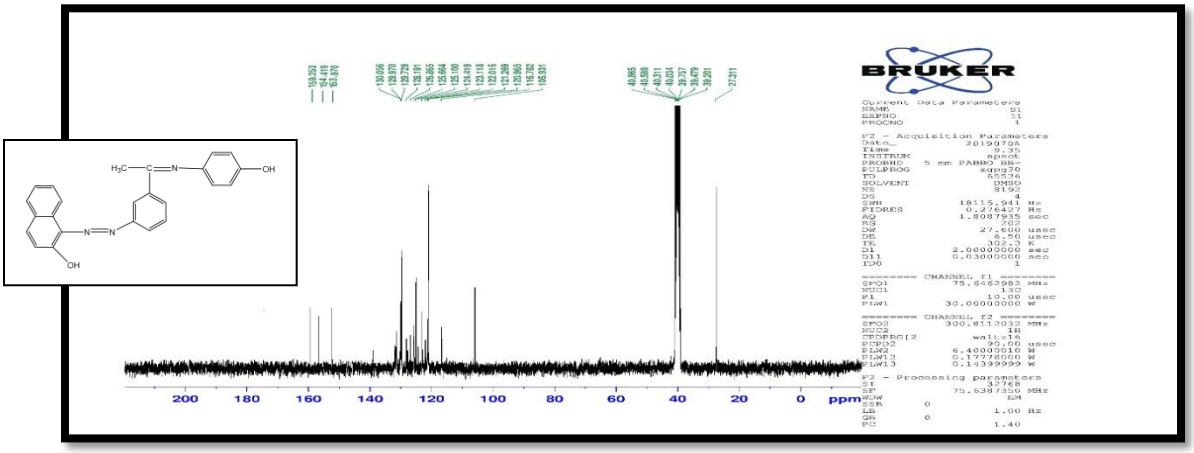


Figure10: ^{13}CNMR Spectra of compound (S_1)

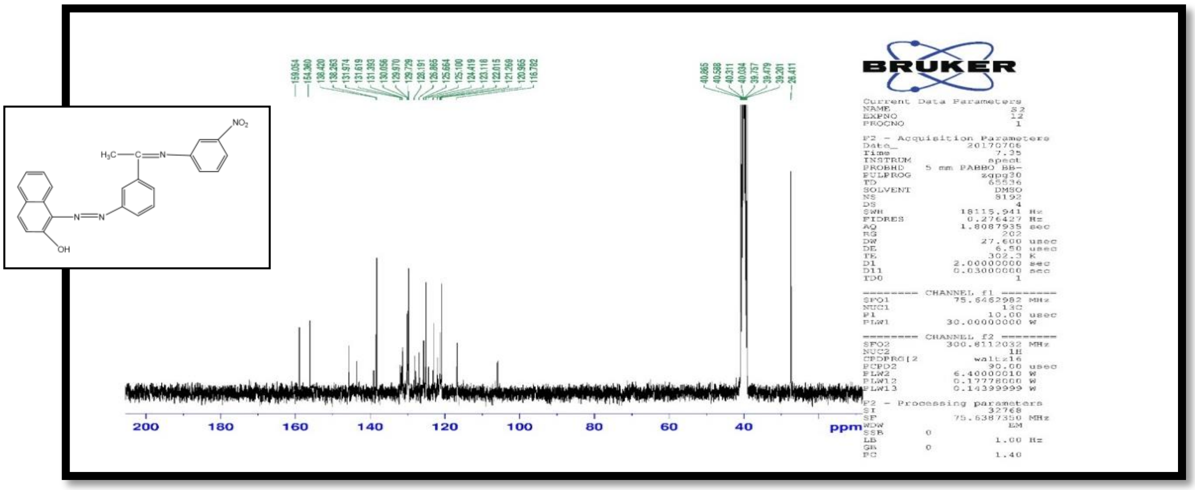


Figure11: ^{13}CNMR Spectra of compound (S_2)

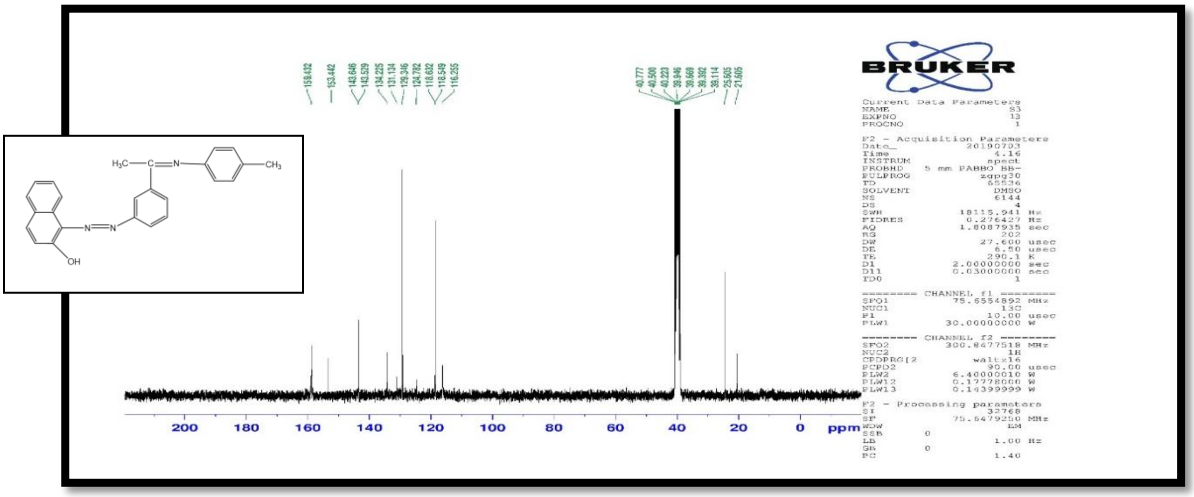


Figure12: ^{13}CNMR Spectra of compound (S_3)

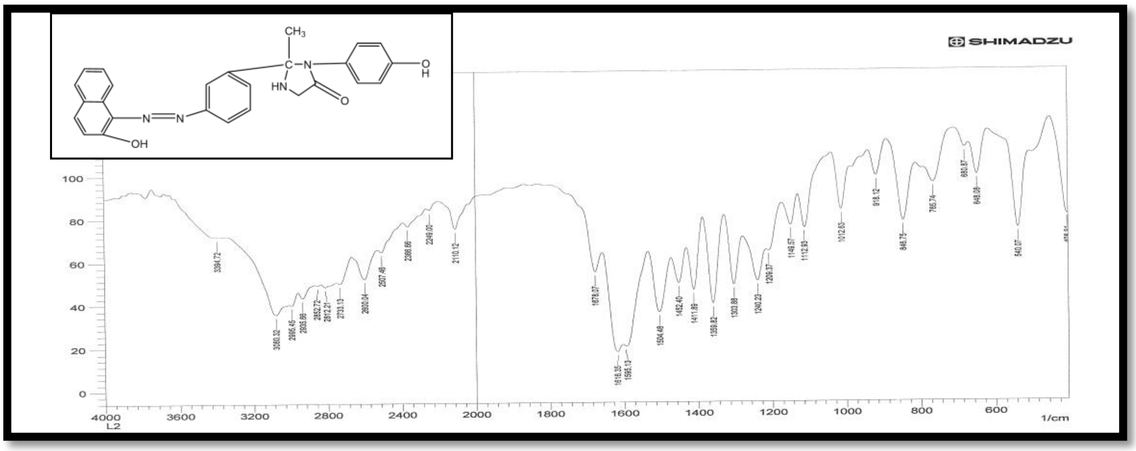


Figure13: FTIR Spectra of compound (L_1)

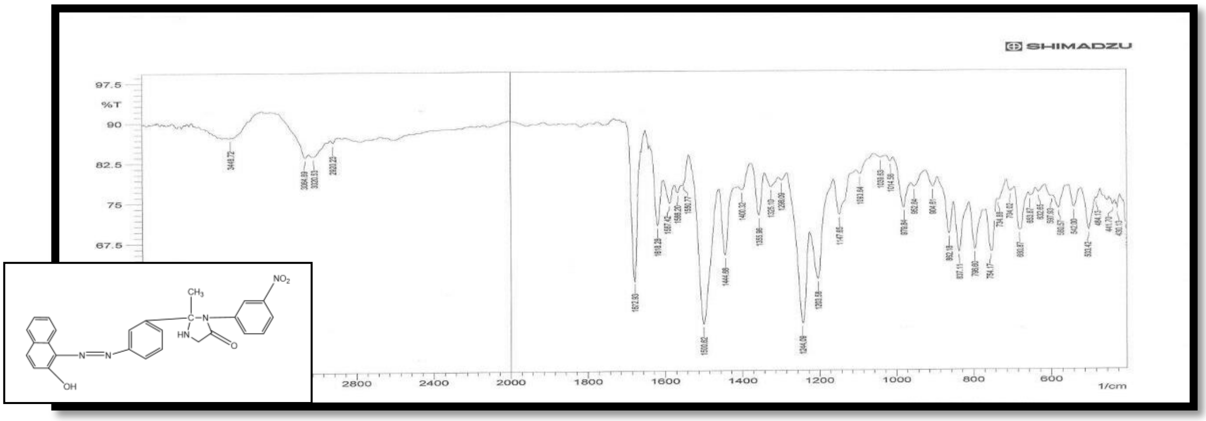


Figure14: FTIR Spectra of compound (L_2)

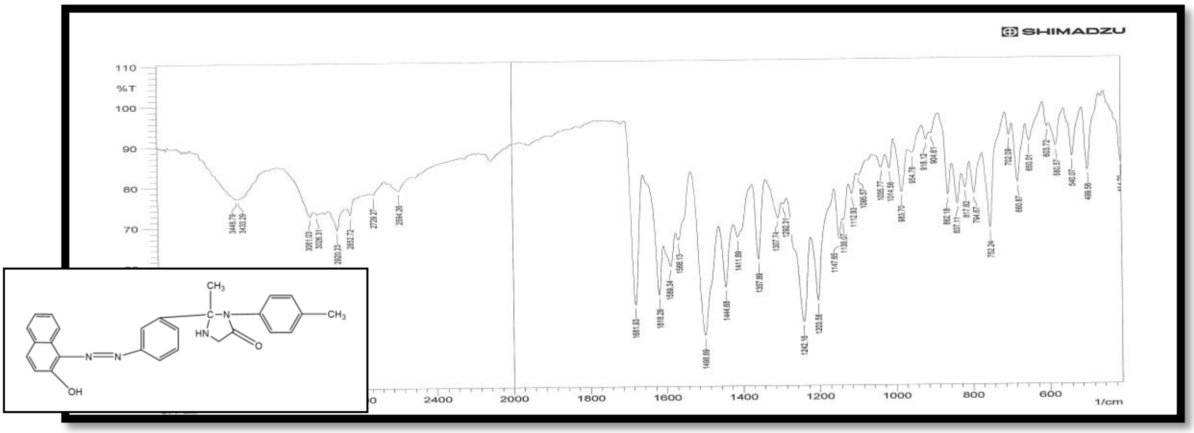


Figure15: FTIR Spectra of compound (L_3)

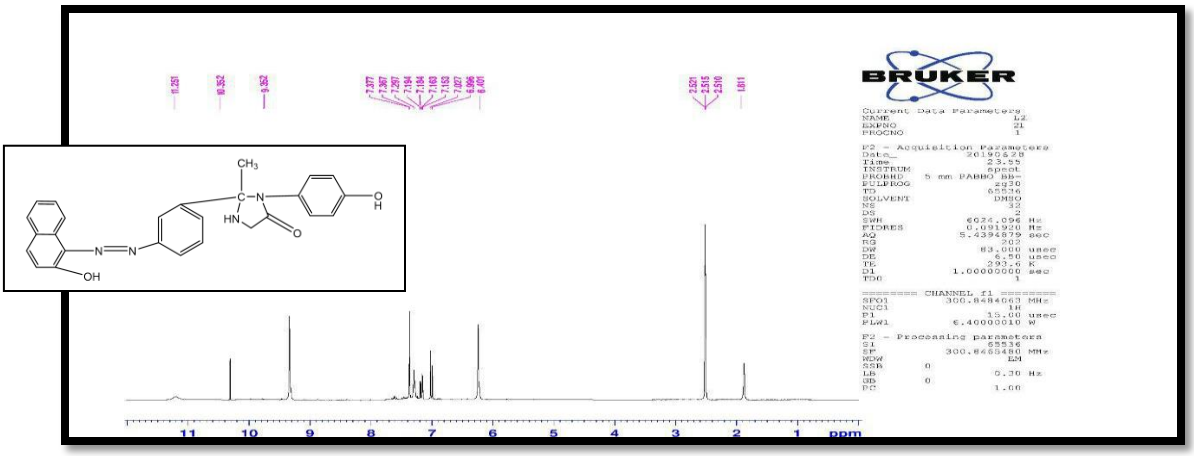


Figure16: ^{1}HNMR Spectra of compound (L_1)

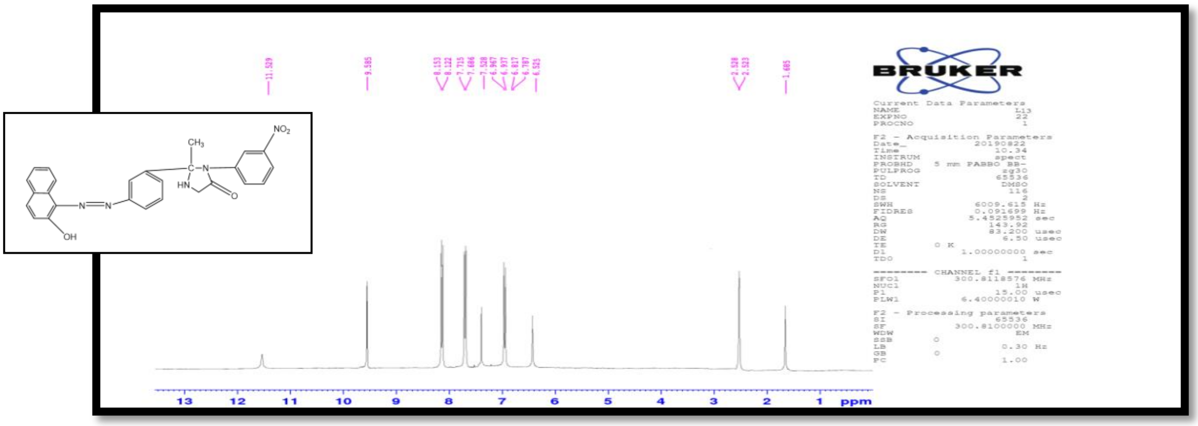


Figure17: ^{1}HNMR Spectra of compound (L_2)

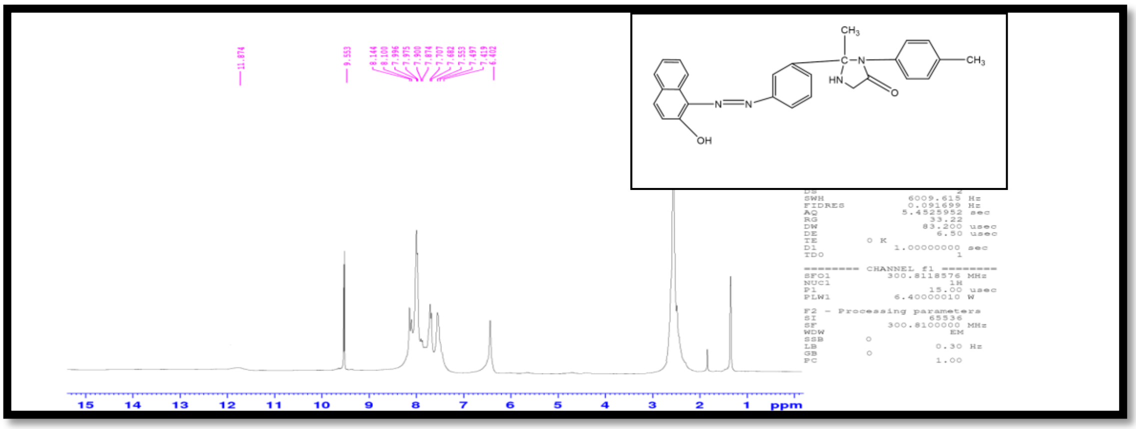


Figure18: ^{1}HNMR Spectra of compound (L_3)

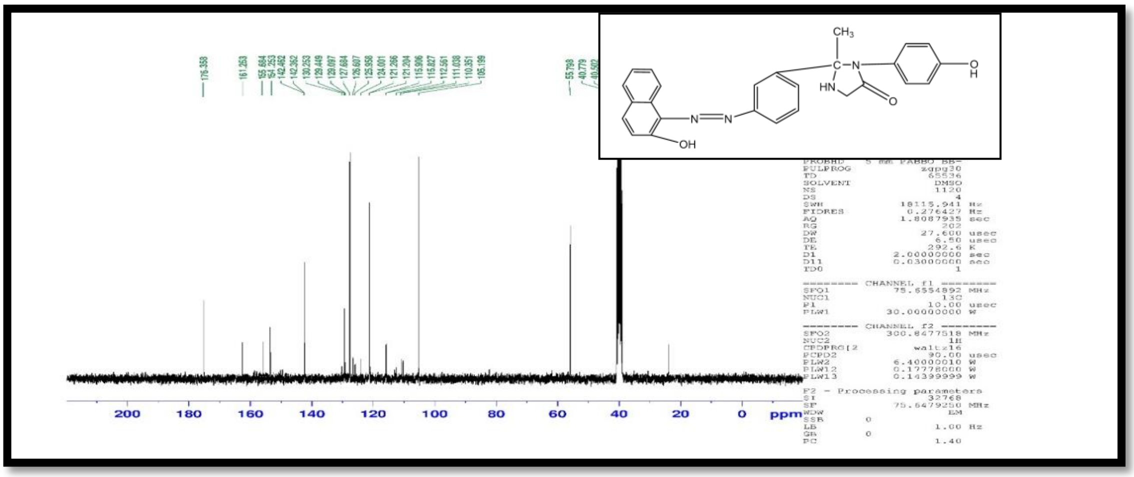


Figure19: ^{13}CNMR Spectra of compound (L_3)

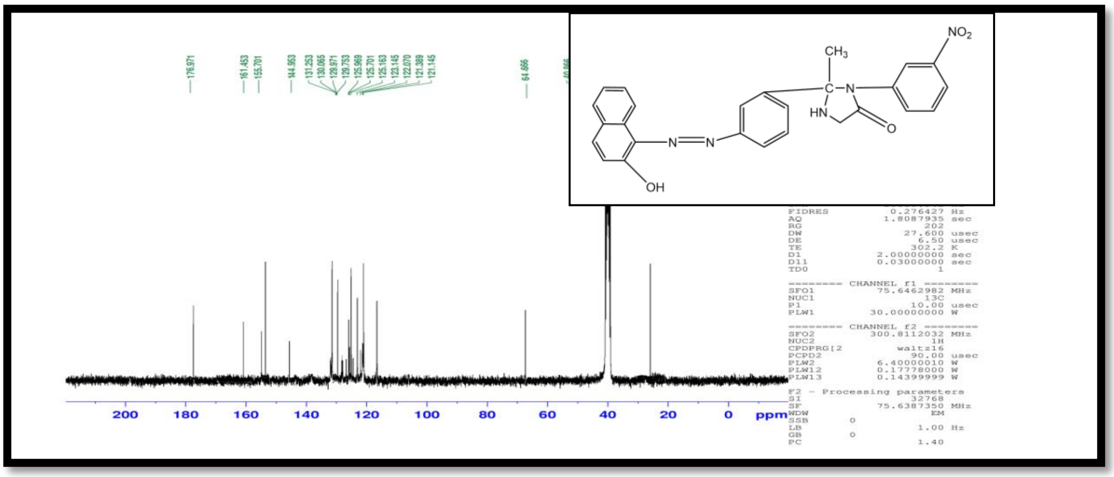


Figure20: ^{13}CNMR Spectra of compound (L_3)

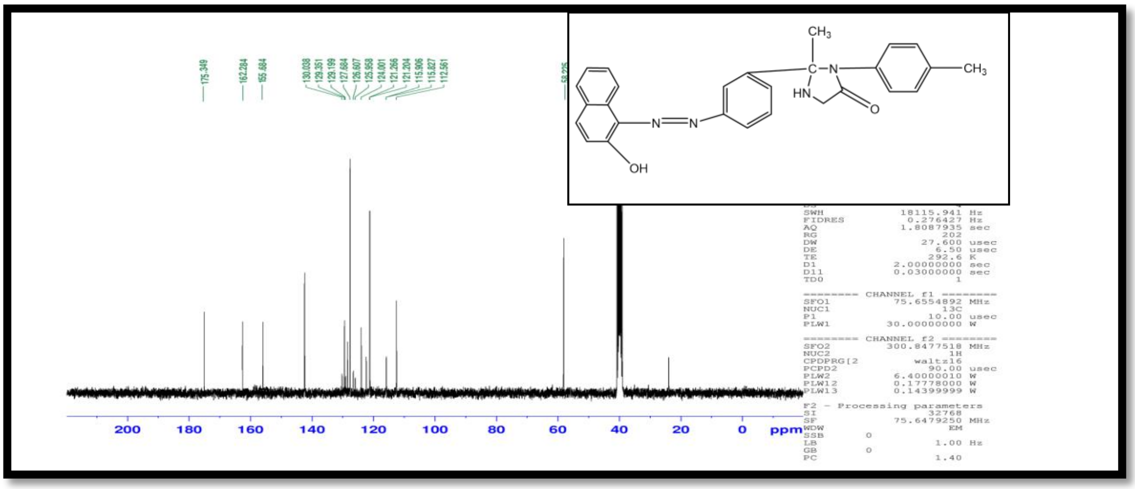


Figure21: ^{13}CNMR Spectra of compound (L_3)

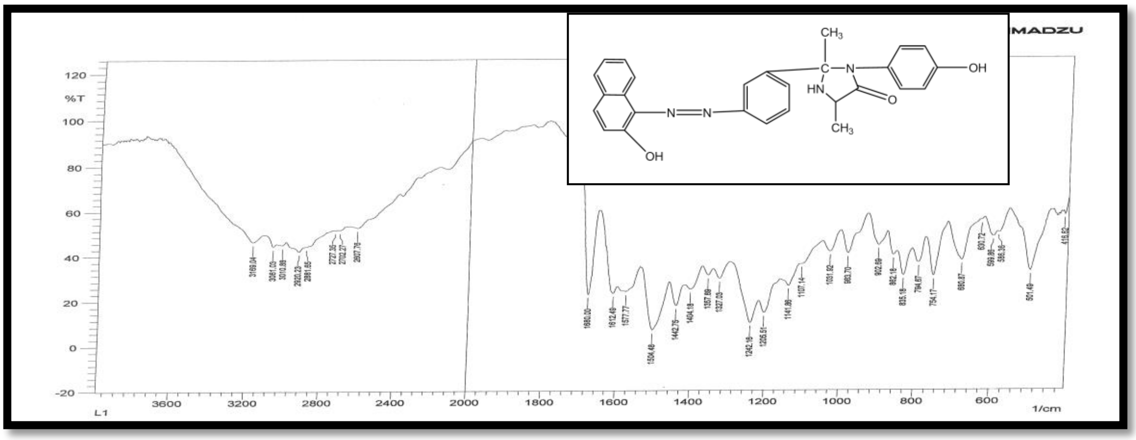


Figure22: FTIR Spectra of compound (L_4)

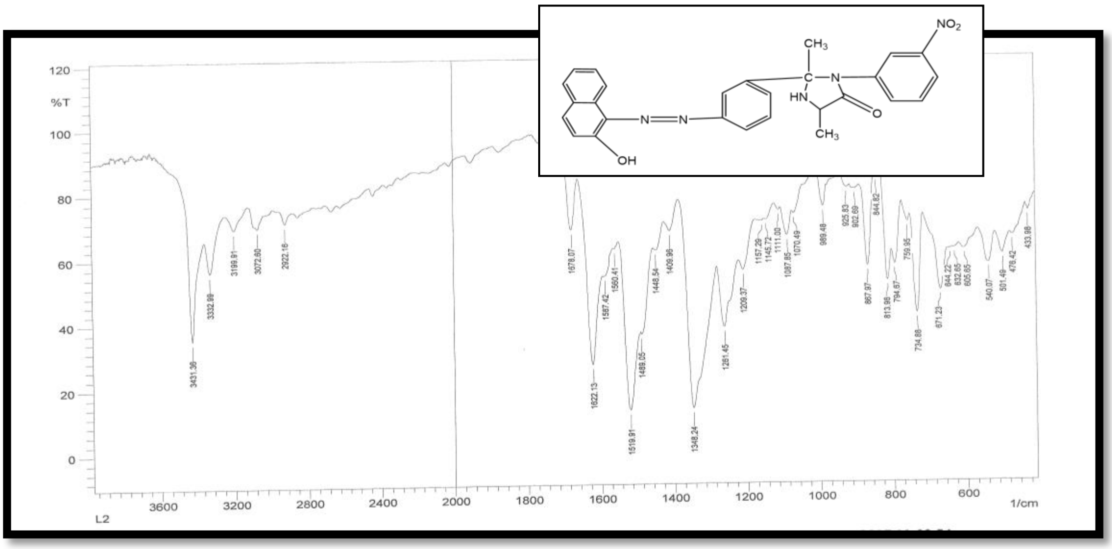


Figure23: FTIR Spectra of compound (L_5)

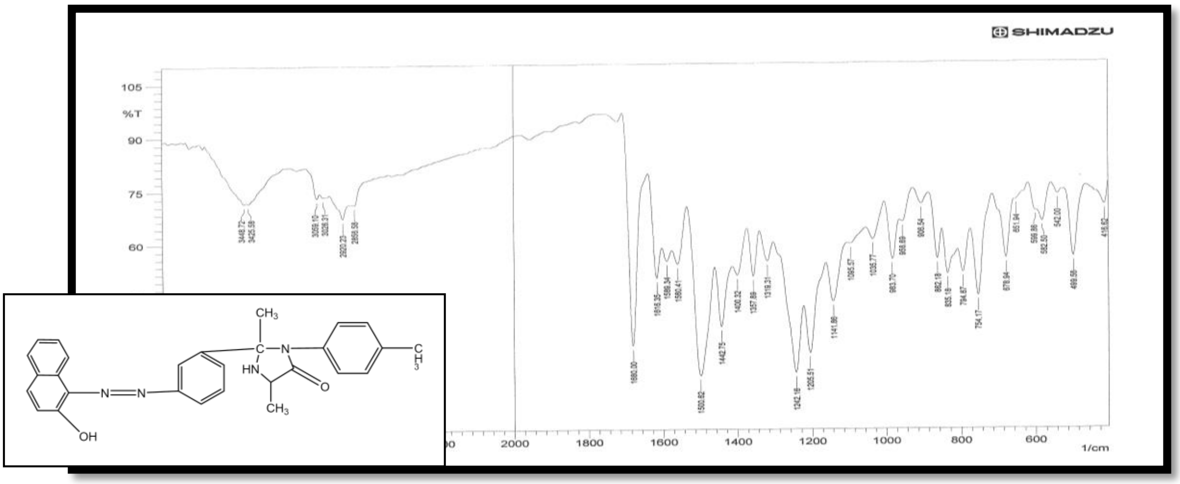


Figure24: FTIR Spectra of compound (L_6)

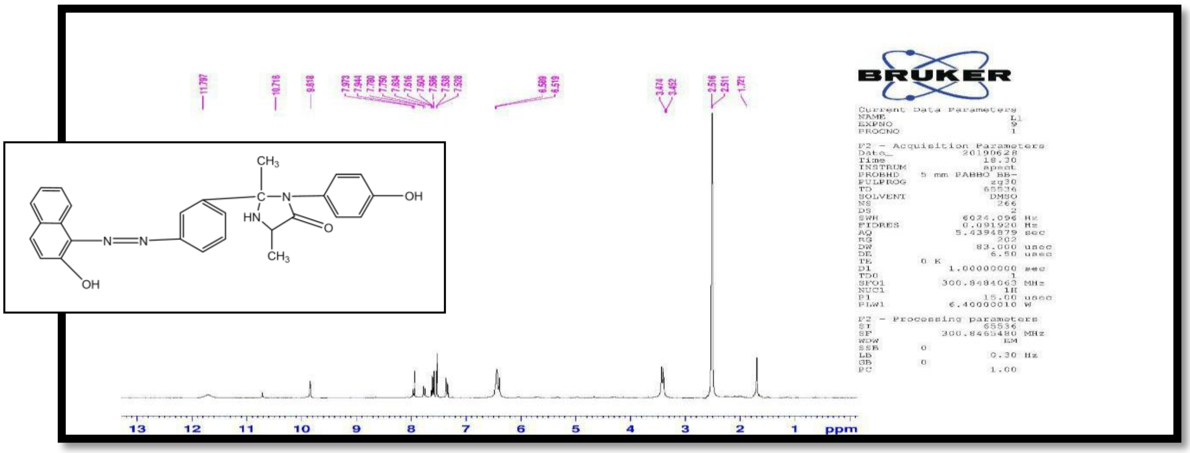


Figure25: ^{1}HNMR Spectra of compound (L_4)

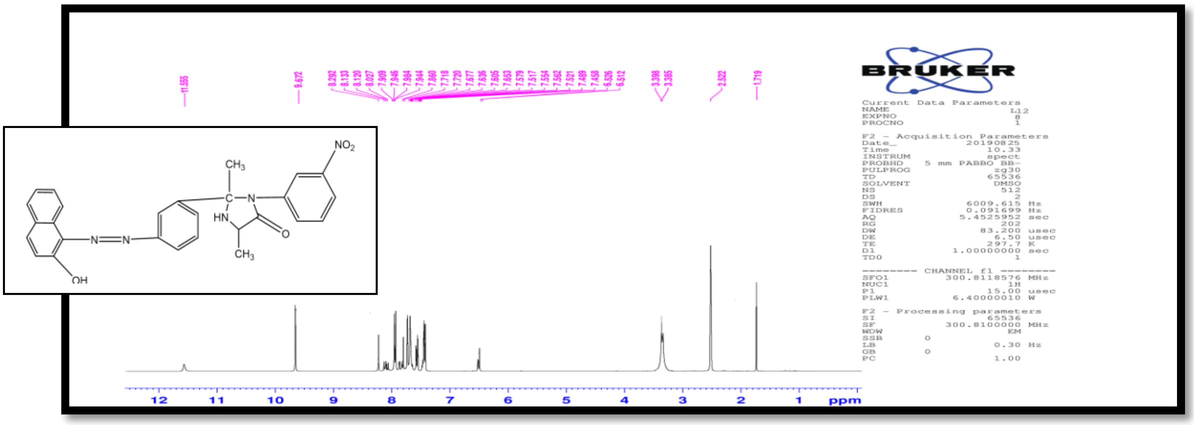


Figure26: ^{1}HNMR Spectra of compound (L_5)

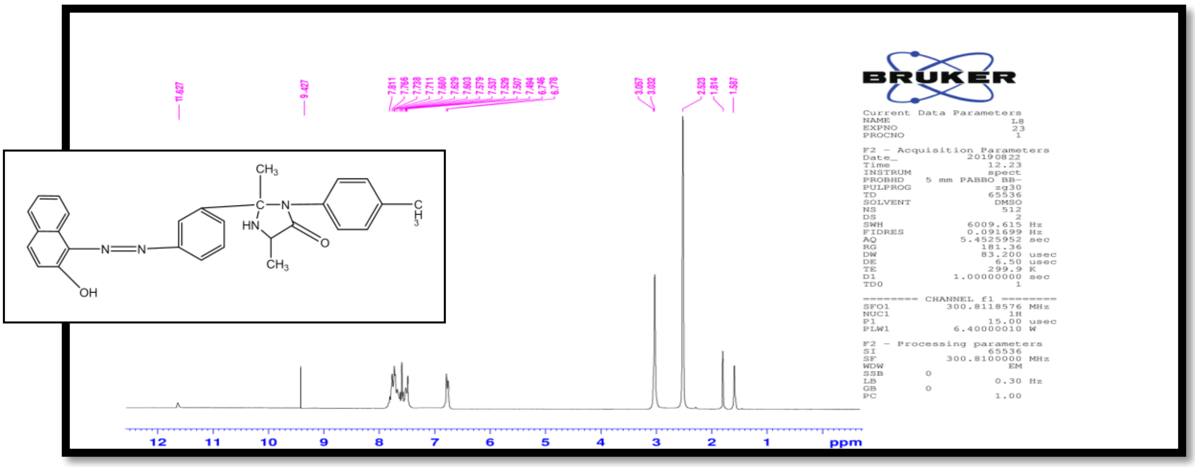


Figure27: ^{1}HNMR Spectra of compound (L_6)

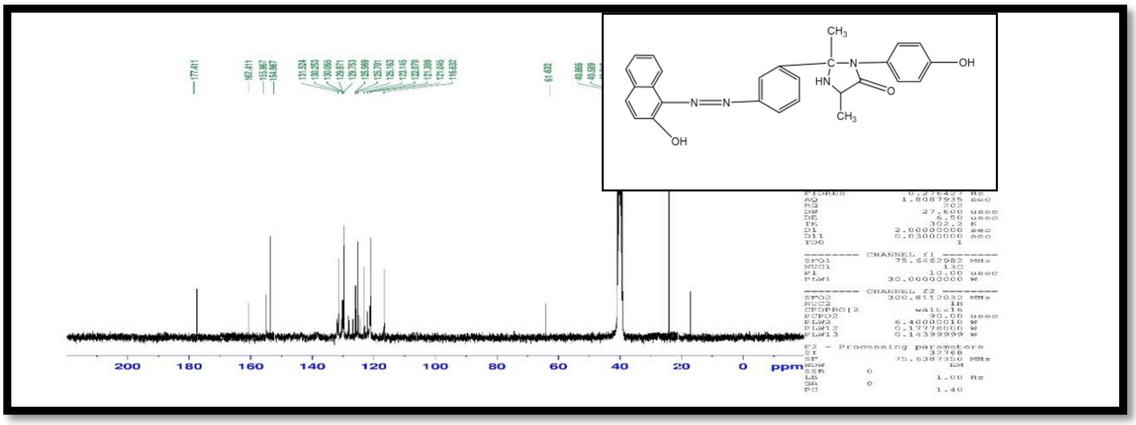


Figure28: ^{13}CNMR Spectra of compound (L_4)

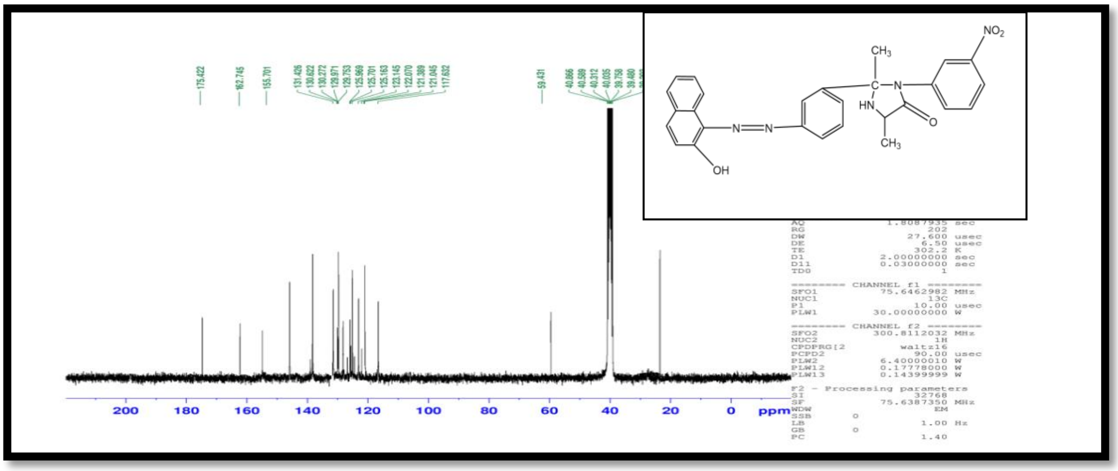


Figure29: ^{13}CNMR Spectra of compound (L_5)

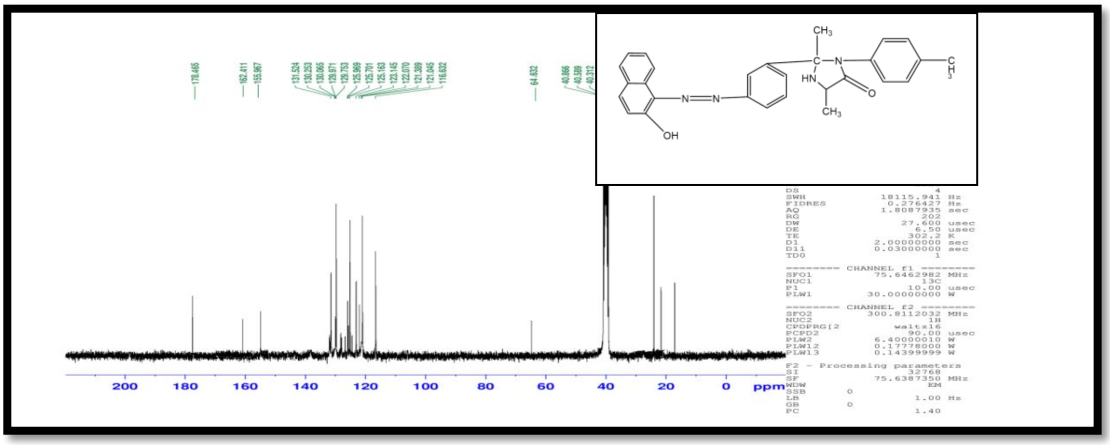


Figure30: ^{13}CNMR Spectra of compound (L_6)

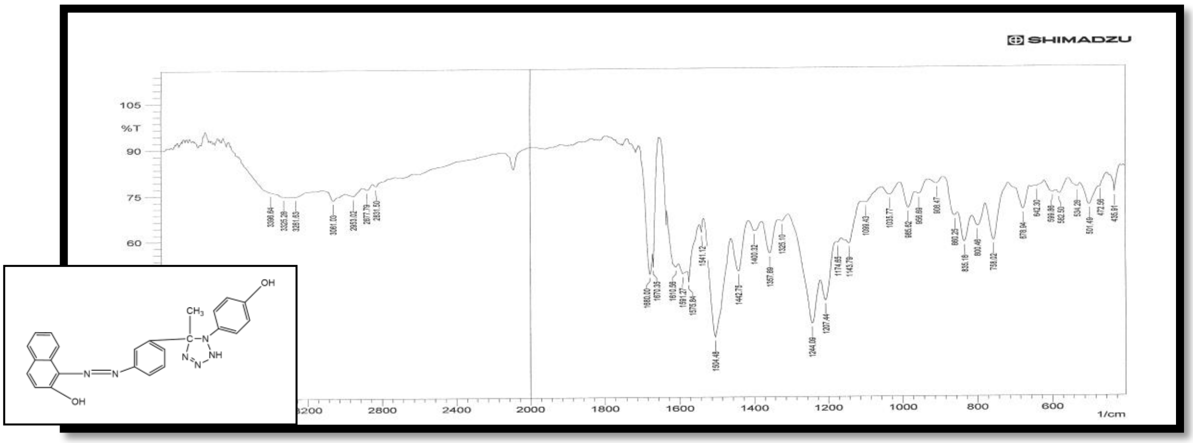


Figure31: FTIR Spectra of compound (L_7)

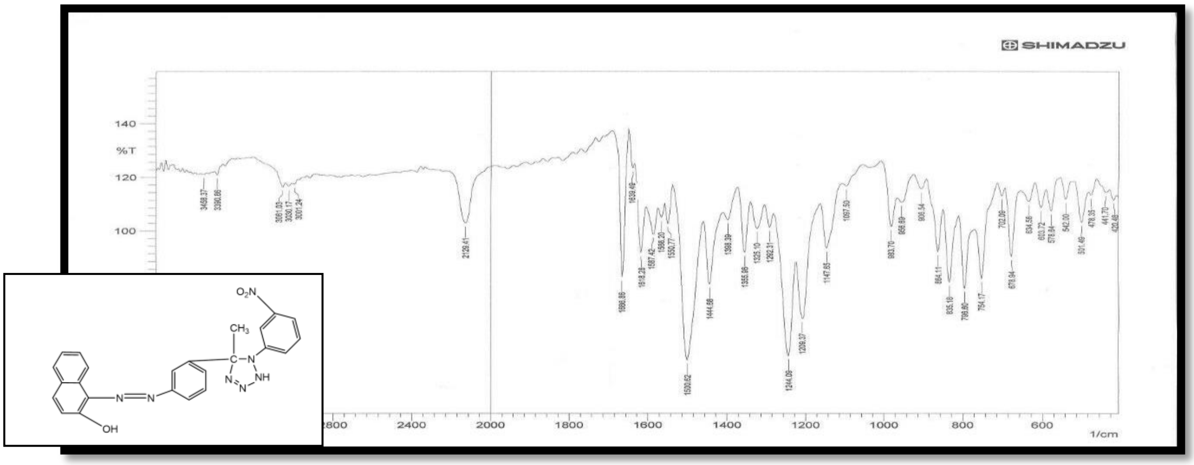
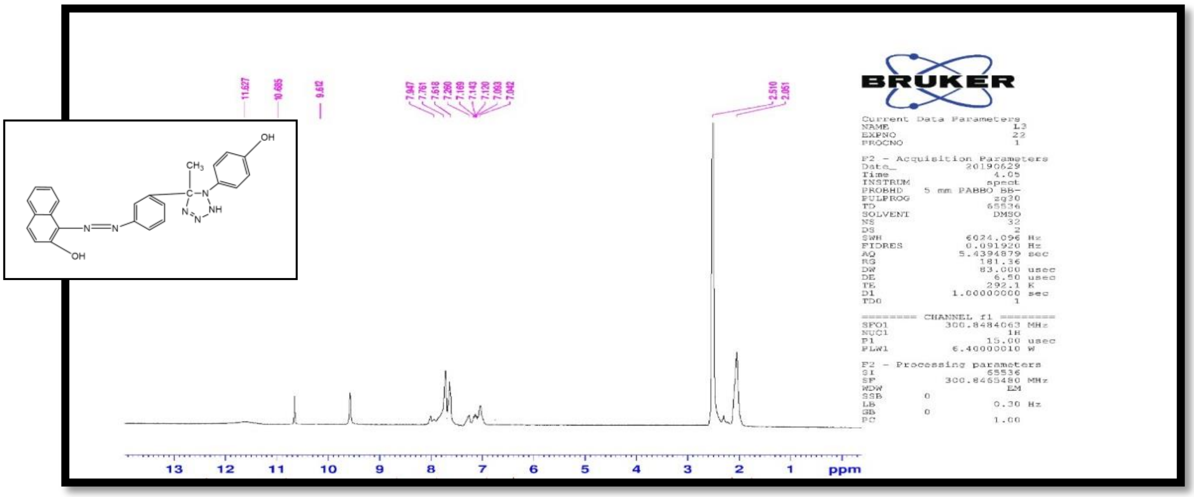


Figure32: FTIR Spectra of compound (L_8)



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Current Data Parameters
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EXPNO                  22
PROCNO                  1

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Time                 4.05
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PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     32
DS                      2
SWH              6024.096 Hz
FIDRES           0.091920 Hz
AQ              5.4394879 sec
RG                 181.36
DW                 83.000 usec
DE                   6.50 usec
TE                  292.1 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1          300.8484063 MHz
NUC1                   1H
P1                  15.00 usec
PLW1           6.40000010 W

F2 - Processing parameters
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SF            300.8465480 MHz
WDW                    EM
SSB          0
LB                   0.30 Hz
GB           0
PC                   1.00
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Figure33: ^{1}HNMR Spectra of compound (L_8)

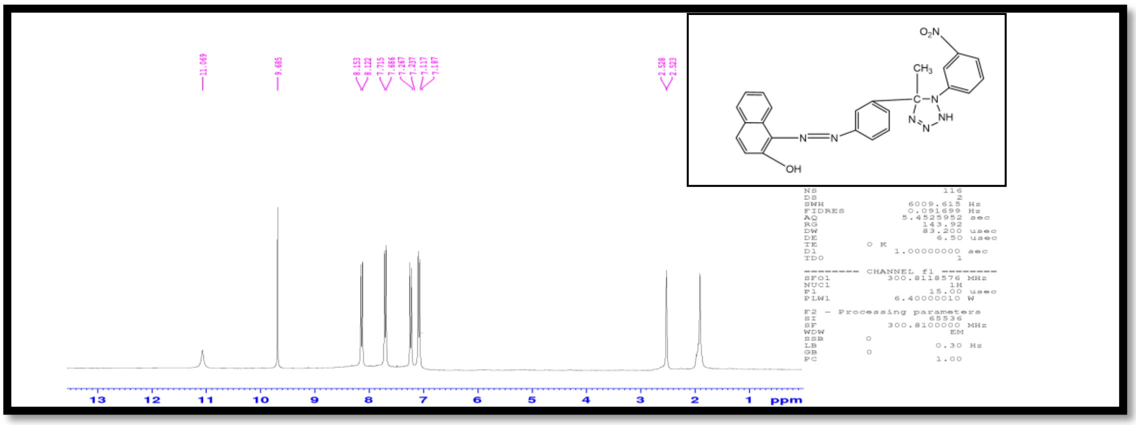

Figure34: ^{1}HNMR Spectra of compound (L_8)

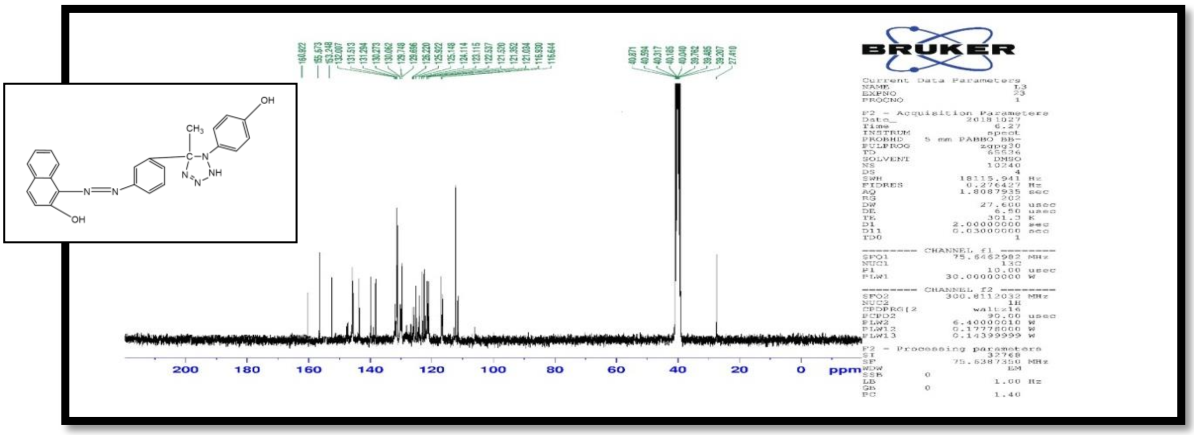

Figure35: ^{13}CNMR Spectra of compound (L_7)

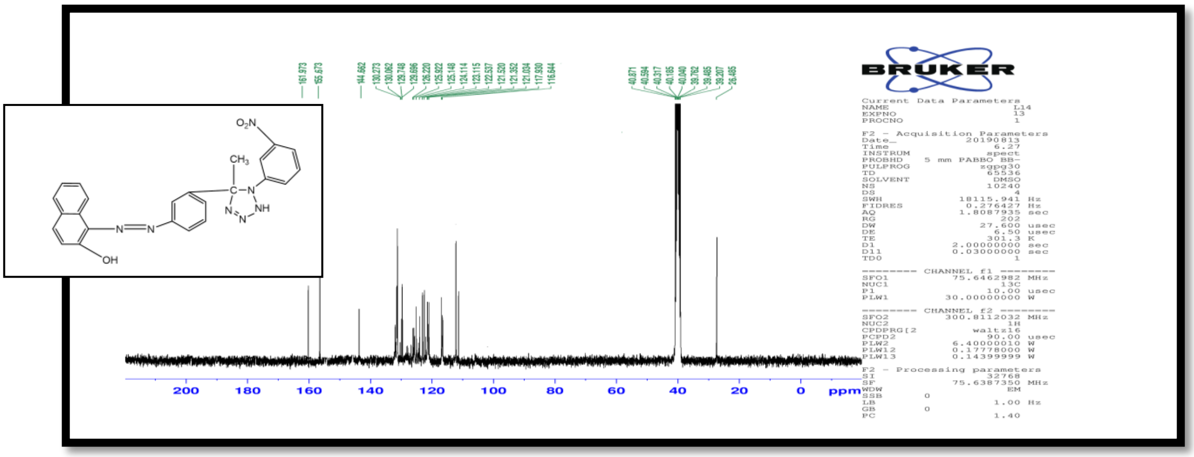

Figure36: ^{13}CNMR Spectra of compound (L_8)

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