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Synthesis and Characterization some Imidazolidine Derivatives and Study the Biological Activity

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ABSTRACT

This paper includes synthesis imidazolidine derivatives (five membered ring) derived from 4-aminoacetophenone and 2-naphthol by multistep reaction, the first step synthesis of azo derivative by the reaction between 4-aminoacetophenone and 2-napthol,after that synthesis shiff bases derivatives (S_1,S_2,S_3), by the reaction between azo derivative (A) with amine derivative (4-bromo,, 4-nitro and 4-chloro aniline), shiff bases derivatives used to prepare some new heterocyclic compounds (five membered ring) by the reaction between the shiff base derivatives (S_1,S_2,S_3) with amino acid (Glycine and Alanine) to prepare imidazolidine derivatives (M_1-M_6). The prepared compounds were characterized by FT-IR, some compound characterized by H^1NMR, ^{13}CNMR.All the prepared compounds were studied for antibacterial activity.

KEYWORD

P-aminoacetophenone, 2-naphthol, Biological Activity, Azo Compound Shiff bases Imidazolidine Derivative.

Introduction

Azo dyes are the most important, largest and versatile class of synthetic organic compounds with an enormous variety of applications in science and technology owing to their versatility in various fields[(1-4)]. Azo chromophores dye based on heterocyclic system has witnessed large invention in recent years[(5-8)], the presence of azo dyes in marine environments may pose significant ecological risk since they are highly recalcitrant and toxic[(9-14)].Shiff's bases are the compounds containing azomethine group (-HC=N-)[(4)] which were first reported by Hugo shiff in (1864)[(15-18)] and formed by condensation of primary amine with an active carbonyl compound and generally take place under acid base catalysis or with heat[(19-22)], Schiff bases have been widely used as ligands because of high stability of their coordination compounds and their good solubility in common solvents[(23-28)], Azomethine (C=N) has been reported to possess remarkable antibacterial, biological activities[(29-31)], Imidazolidine is generally a five-ring heterogeneous ring possessing formula($C_3H_8N_2$)[(32)]. Imidazolidines have attracted attention due to their important roles[(33-38)] as building blocks in the synthesis of active compounds [(39-43)],The hetero cyclic compounds containing (imidazolidine are the well class of compounds for its biological applications[(44-53)]

Materials and Methods

The chemicals compounds have high purity as supplied by sigma and GCC company, Melting point of the compounds recorded by electro thermal 9300, melting point engineering LTD, All measurments synthesis compounds were recorded by: FTIR spectra, fourier transform infrared shimadzu(8400), H^1NMR and C^1NMR –spectra in (ppm) in DMSO solvent by Bruker–

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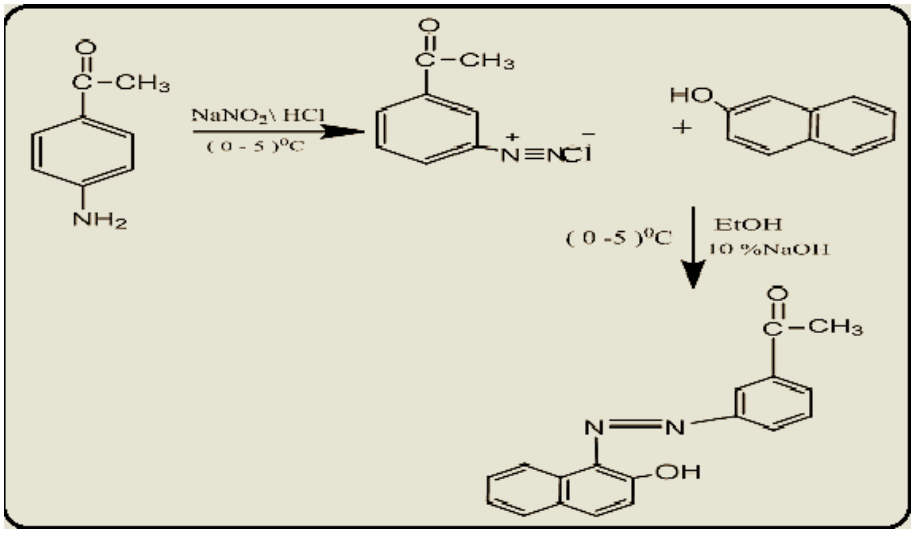
AVANCE AQS-300MH$_{Z,}$Iran, Thin layer chromatography used silica gel in (Benzene: methanol) solvent.

Experimental

Synthesis of Azo Compound, 1-(4-((2-hydroxynaphthalen-1-yl)diazenyl) acetophenone(A):

Prepare the compound (A) by dissolving 4.05gm, 0.03mol) (from 4-amino-acetofenone in a mixture consisting of (3ml) of concentrated (HCl) acid and (20 ml) of distilled water, cool the mixture in an ice bath at a temperature of (0-5) C, Then a solution consisting of 2.07gm, 0.03mol)) was added to sodium nitrite (NaNO2) dissolved in (10ml) of cold distilled water, drop by drop with constant stirring and making sure the temperature did not rise above 5 ° C), leaving the formed solution Duration of min (20) to settle to complete the aliasing process, then add the solution of diazonium formed drop by continuous stirring to a solution consisting of (0.03mol, gm. 32 4) of 2- dissolved naphthol in a mixture of ((40ml ethanol and (10 ml)) Of a hydroxide solution Sodium ((10% NaOH), the coloration of the solution was observed in orange color at pH = (7), the solution was left for three hours[15, 52], then filtered and washed, after the sedimentation process was completed with distilled water, I returned several times, then dried and recrystallized using absolute ethanol. Scheme(1).



Scheme 1. Synthesis of Azo compound (A)

Synthesis of Shiff bases derivatives (S_1-S_3)[25, 52]

Dissolve 1.0gm, 3mmol) of the prepared azo (A in (30ml) of absolute ethanol with a drop of concentrated hydrochloric acid (HCl) as a catalyst, with continuous stirring on the magnetic stirring device for a period of (20min) at the laboratory temperature Then (3mmol, 0.37gm (from4-bromo and 4-nitro and 4-chloro aniline) respectively are slowly added to the first step solution with continuous stirring[25, 52]. Then the mixing process was carried out at Co ((78 for a period of (20h.). The reaction was followed by (TLC) using (1.5: 3.5), Scheme (2).

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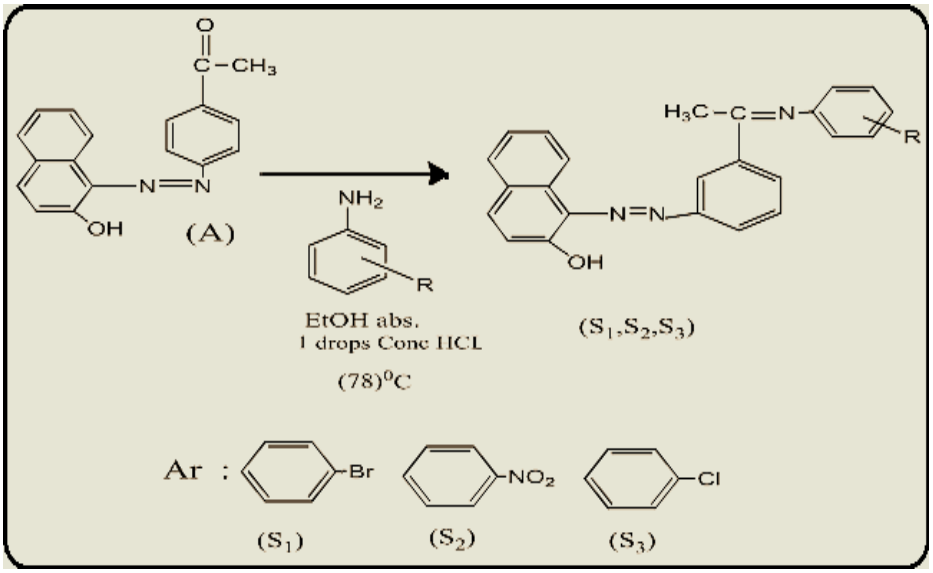

Scheme 2. Synthesis derivative shiff basses(S_1-S_3)

Synthesis the compounds (M_1-M_3)[16, 37]

Dissolve (0.5mmol, 0.4mmol, 0.7mmol) compounds ((S1 and S2)) and (S3) which equals (0.3gm), (0.2gm) and (0.2gm) in (30ml) of THF with continuous stirring on the magnetic stirring machine until thawed. Then add (0.7mmol, 0.1gm), (4mmol 0., 0.036gm) and (0.5mmol, 0.05 gm) of the amino acid claisin, respectively, while continuing the stirring process. At (CO) 50 degree, the escalation process was carried out for (23h), (10h) and (13h), respectively Scheme (3).

Synthesis the compounds (M_4-M_6)[30, 52]

Dissolve (0.5 mmol, 0.4mmol, 0.7mmol) from the prepared lip bases ((S1 and S2)) and (S3) which equals (0.3gm), (0.2gm) and (0.2gm) in (30ml) of (THF) with continuous stirring by means of the magnetic stirring device until dissolution, then 0.7mmol (0.1gm, 0.043gm, 0.4mmol) and 5mmol 0.05gm were added from the amino acid as the stirring process continued. (50) Co escalation was performed for (23h), (8h) and (13h), respectively The reaction was followed up by TLC technique using (1.5: 3.5) (Methanol: dry benzene) and (1: 4) (Methanol: dry benzene). After the reaction was completed, the precipitate was filtered and recrystallized by absolute ethanol. Scheme (3).

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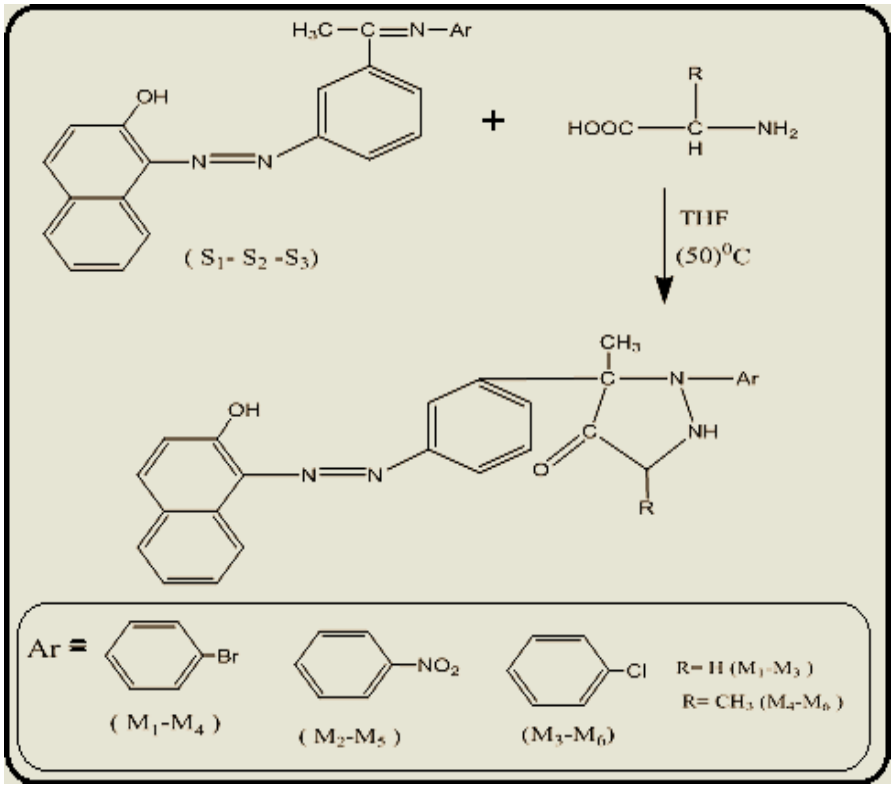

Scheme 3. Synthesis of imidazolidine derivatives (M_1-M_6)

Results and Discussion

All compounds in this papers prepared according to procedures[25, 26, 37] by azotation, coupling, condensation reactions, then the prepared compounds identified with many spectral techniques and bio-assay:

FT.IR –Spectra

Compound [A] gave band at (3300) Cm^{-1} for (OH) of phenol, other band at (1708) for carbonyl of ketone (C=O), bands at (1417, 1510) for azo group (-N=N-). But in compound[S1],other bands appeared such as (OH) of phenol gave at (3290),bands at (1434, 1510) for azo group (-N=N), band at (1625) for schiff base (C=N-), band at (770) for (C-Br).,While compound[S2] appeared band at (OH) of phenol gave at (3320),bands at (1440, 1530) for azo group (-N=N), band at (1620) for schiff base (C=N-), bands at (1320, 1500) for ($C-NO_2$).Compound[S3] gave bands at (OH) of phenol gave at (3330),bands at (1430, 1520) for azo group (-N=N), band at (1630) for schiff base (C=N-), band at (700) for (C-Cl). The remaining bands for compound [M1] at (3310) for (OH) of phenol,(-N=N-)azo group at (1400, 1530),(C=O) carbonyl group of ketone at (1715),(NH) amine in imidazole cycle: (3250),(C-Br) at (690)., on the other hand the compound [M2]: gave bands at (3300) for (OH) of phenol,(-N=N-)azo group at (1420, 1500),(C=O) carbonyl group of ketone at (1717),(NH) amine in imidazole cycle: (3200),(C-NO2) at (1310, 1520)., But the compound [M3]: gave bands at (3350) for (OH) of phenol,(-N=N-)azo group at (1436, 1515),(C=O) carbonyl group of ketone at (1712),(NH) amine in imidazole cycle: (3190),(C-Cl) at (730).,Compound [M4]: gave bands at (3330) for (OH) of phenol,(-N=N-)azo group at (1432, 1520),(C=O) carbonyl group of ketone at (1710),(NH) amine in imidazole cycle: (3200),(C-Br) at (700).,Compound [M5]: gave bands at (3322) for (OH) of phenol,(-N=N-)azo group at (1442, 1513),(C=O) carbonyl group of ketone at (1718),(NH) amine in imidazole cycle: (3185),(C-NO2) at (1325,

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1500).,Compound [M6]: gave bands at (3320) for (OH) of phenol,(-N=N-)azo group at (1430, 1534),(C=O) carbonyl group of ketone at (1710),(NH) amine in imidazole cycle: (3200),(C-Cl) at (740).,Other bands in figures(1-10):

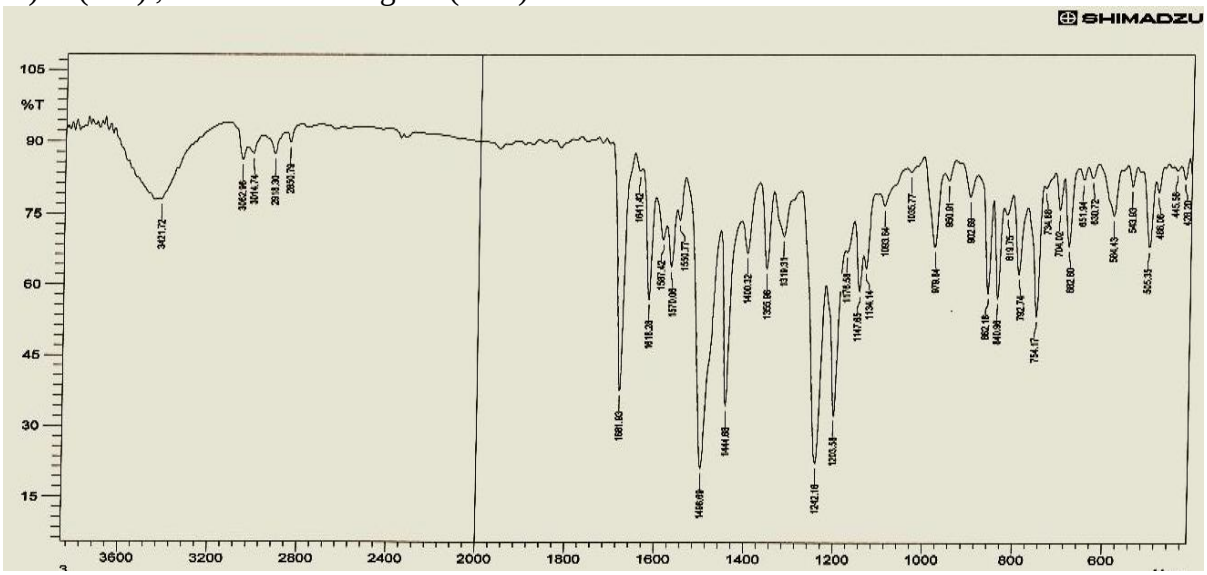

Fig. 1. FT.IR of Compound[A]

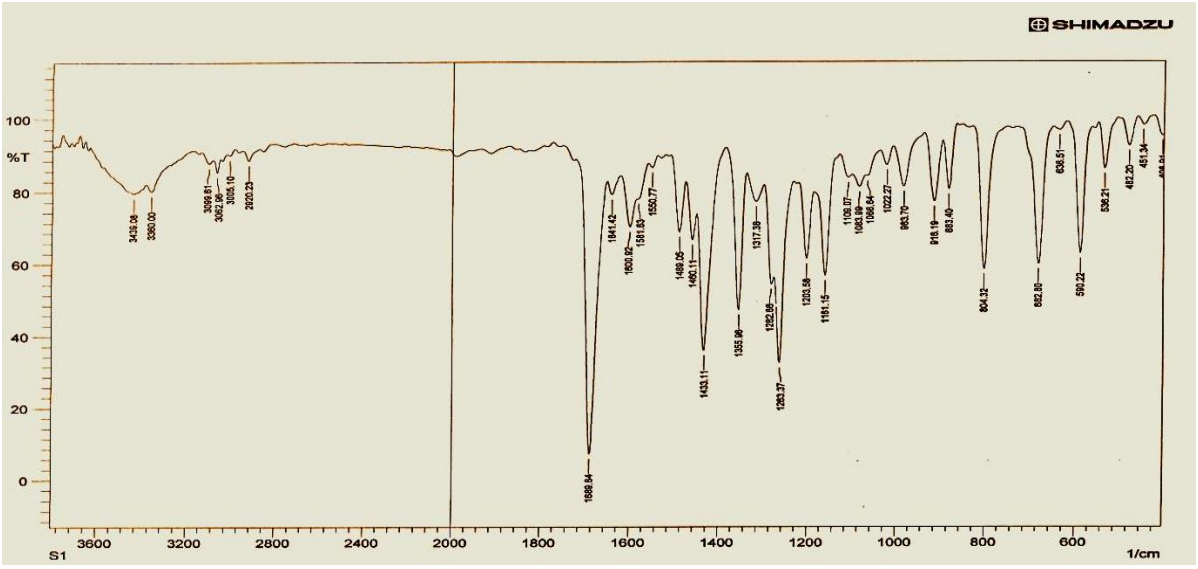

Fig. 2. FT.IR of Compound[S1]

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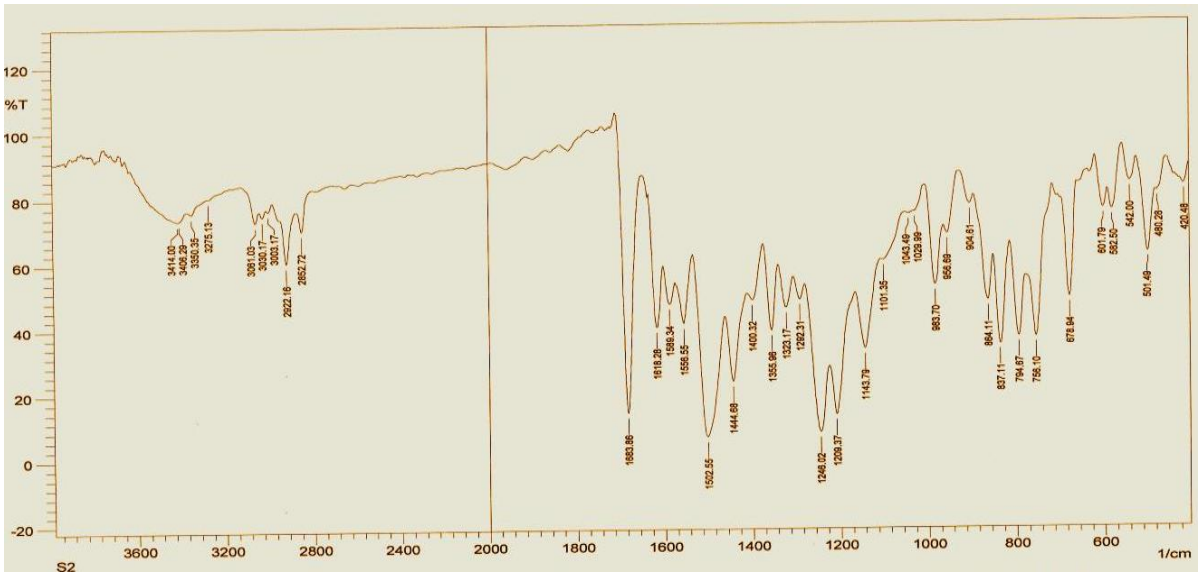

Fig. 3. FT.IR of Compound[S2]

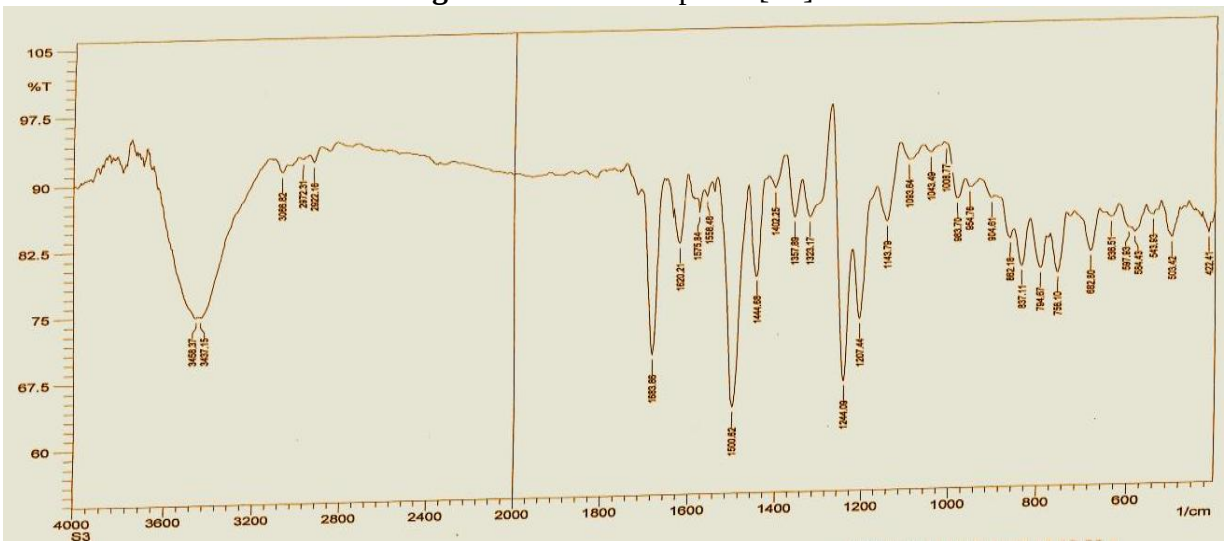

Fig. 4. FT.IR of Compound[S3]

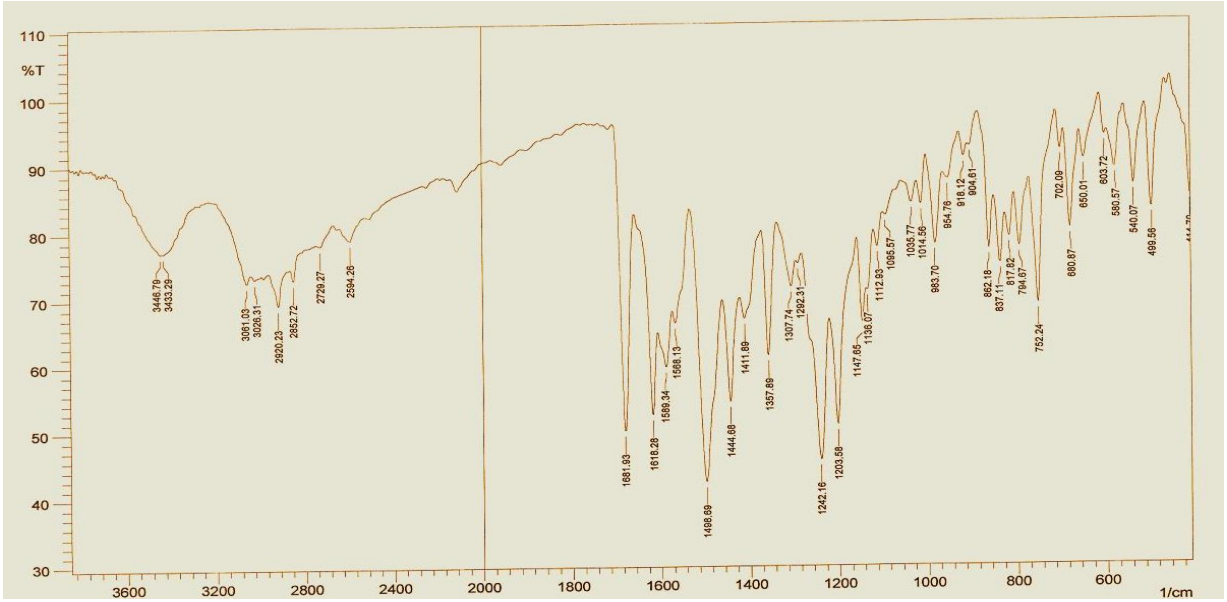

Fig. 5. FT.IR of Compound[M1]

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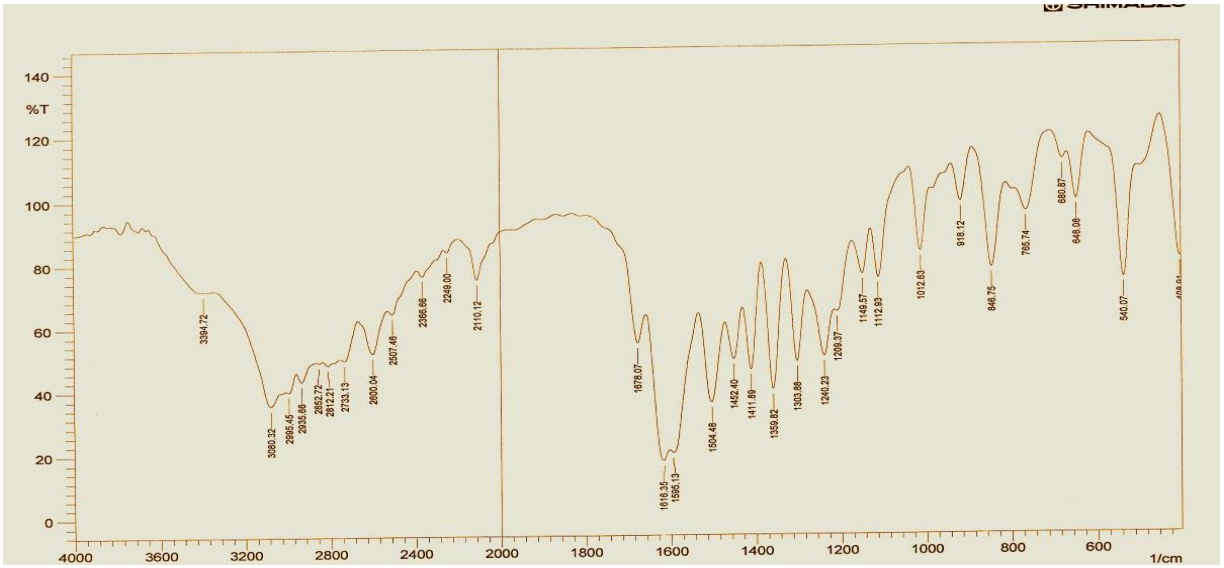

Fig. 6. FT.IR of Compound[M2]

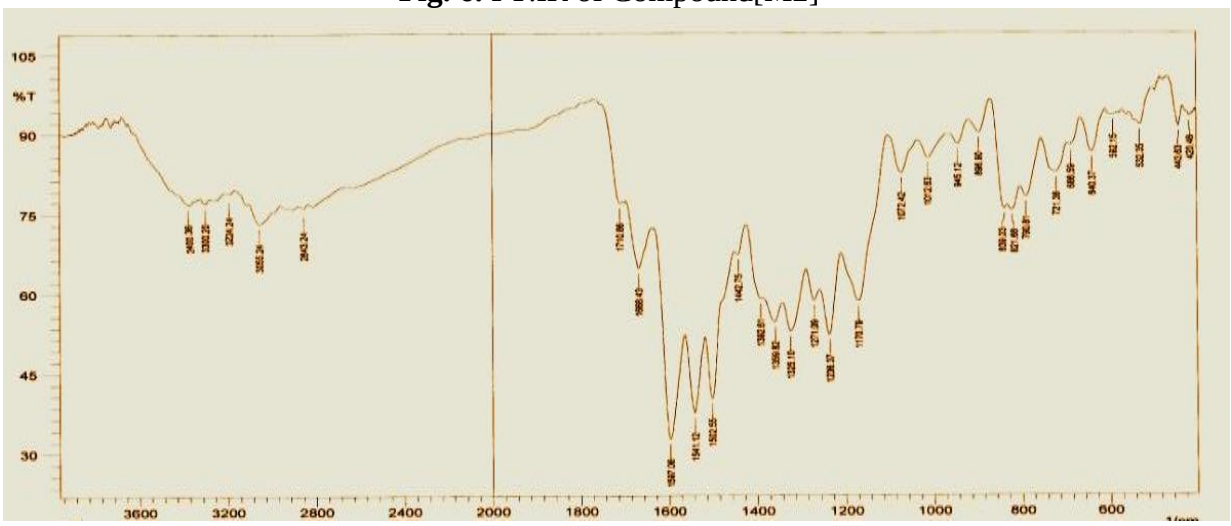

Fig. 7. FT.IR of Compound[M3]

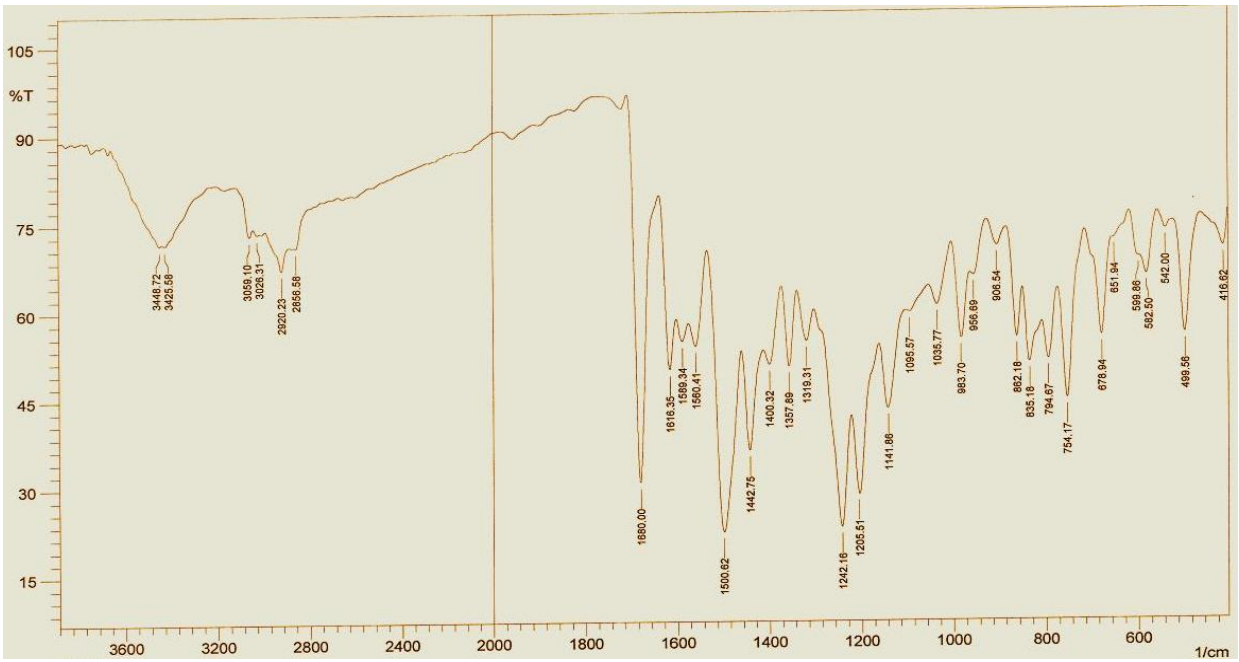

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Fig. 8. FT.IR of Compound[M4]

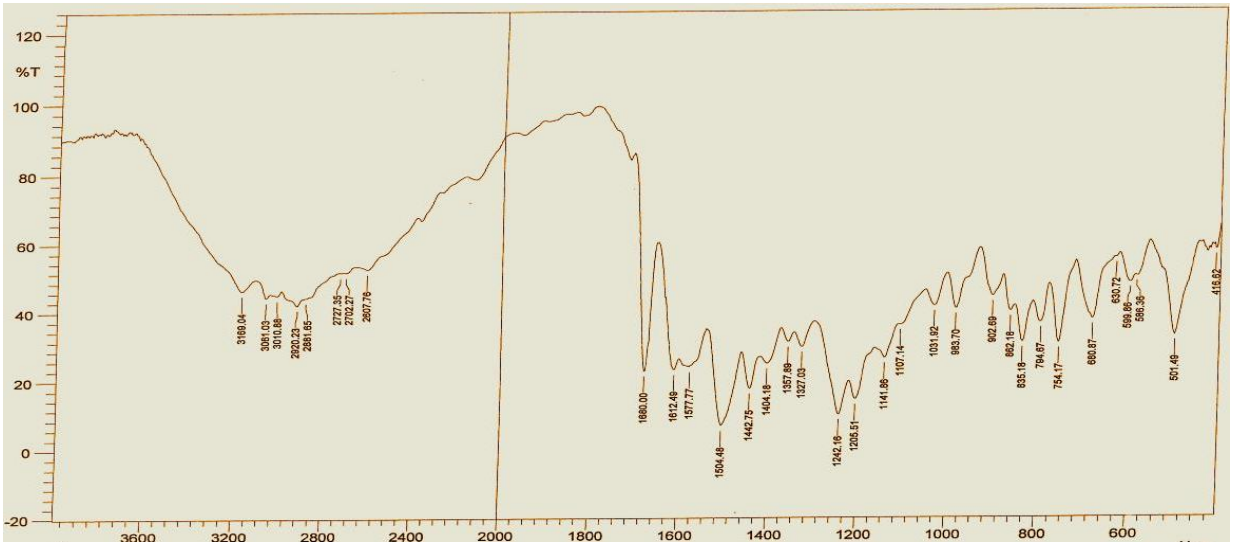

Fig. 9. FT.IR of Compound[M5]

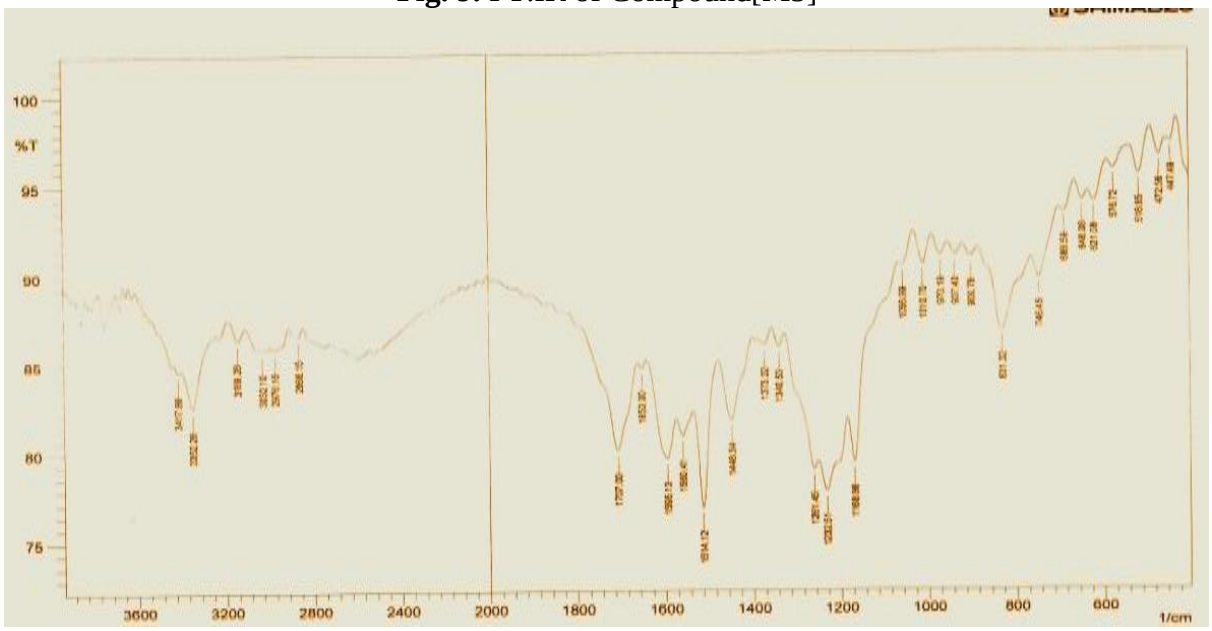

Fig. 10. FT.IR of Compound[M6]

H.NMR –Spectra: all spectra gave bands at (2. 50) for solvent (DMSO-d6)., all spectra appeared peaks at (9.50 to 11.0) due to (OH) of phenol, other peaks at (6.50 to 7.80) due to protons of aromatic Ring, other compounds like [M4,M5, M6] appeared signal at (4.5 to 5.50) due to amine group in Imidazoline cycle in these compounds and like that in other spectra in figures (11-13):

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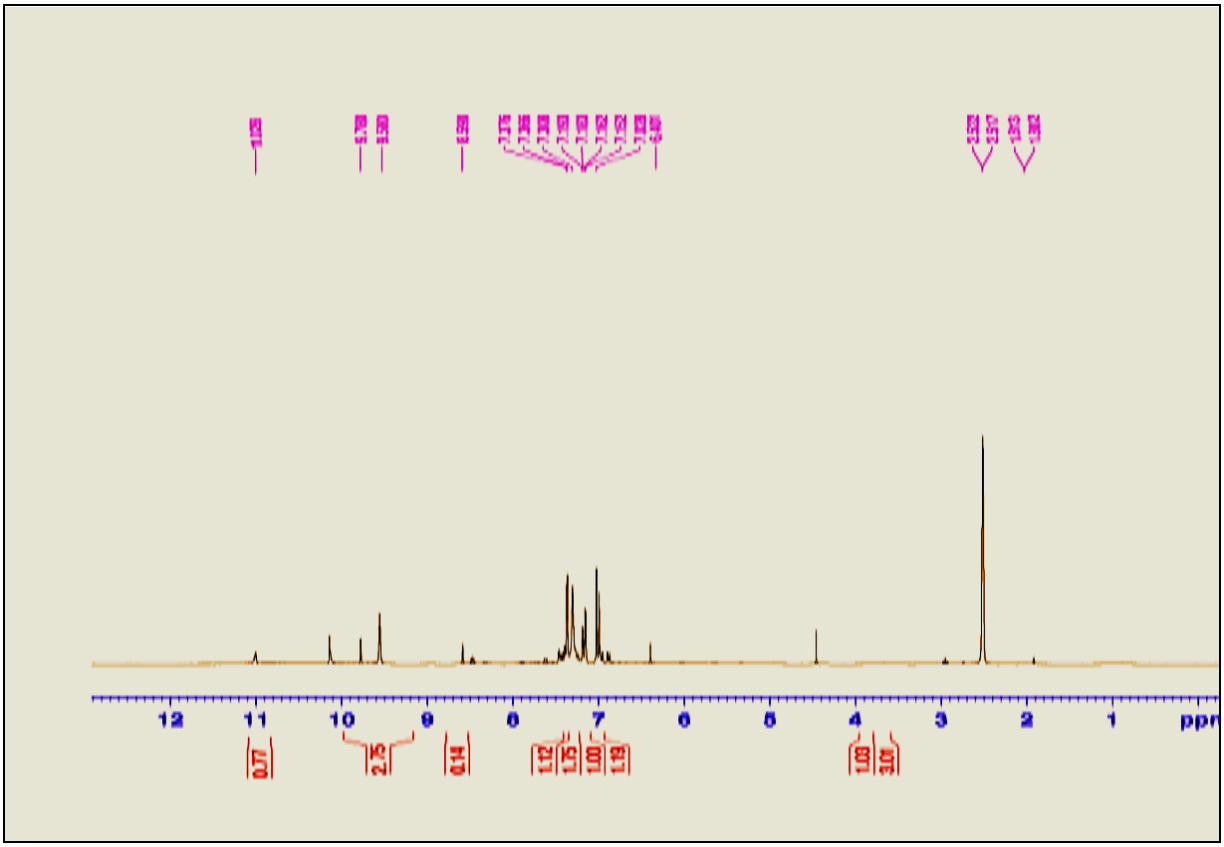

Fig. 11. H.NMR of Compound[A]

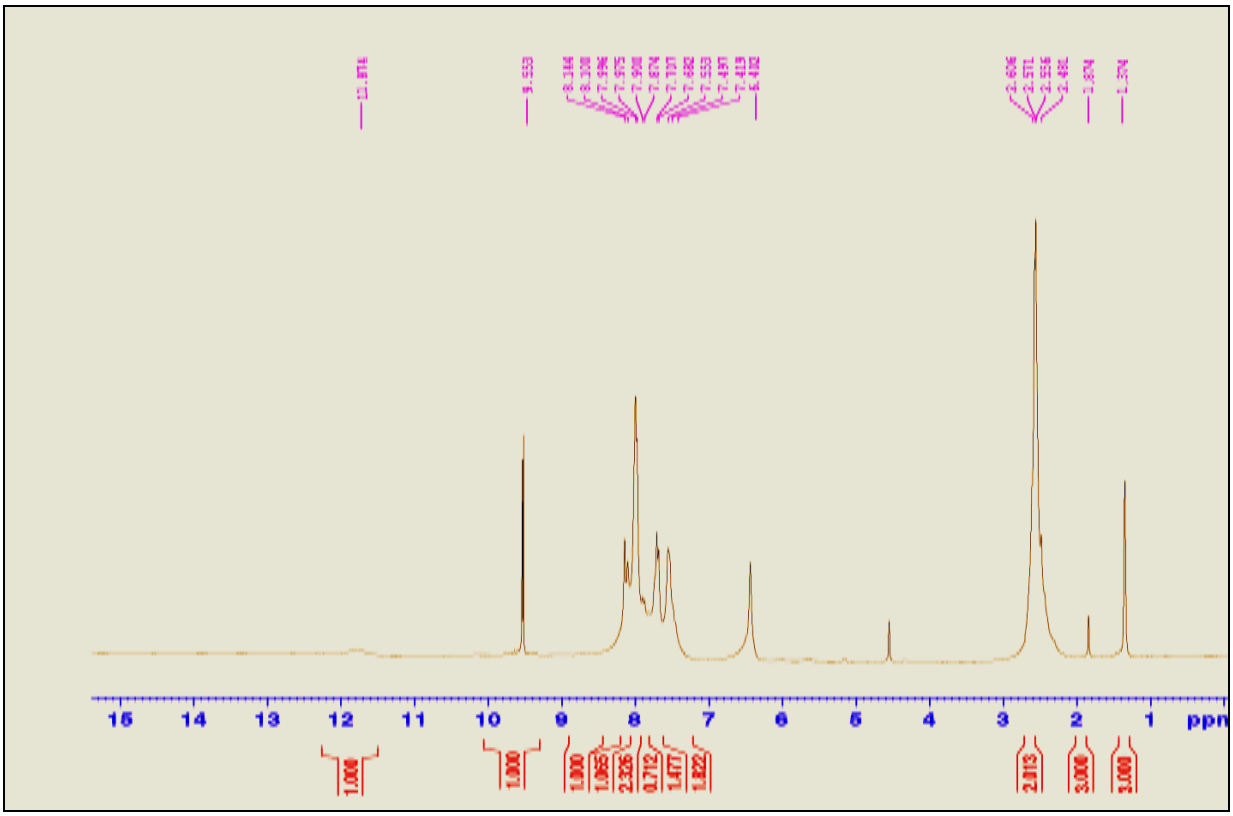

Fig. 12. H.NMR of Compound[S1]

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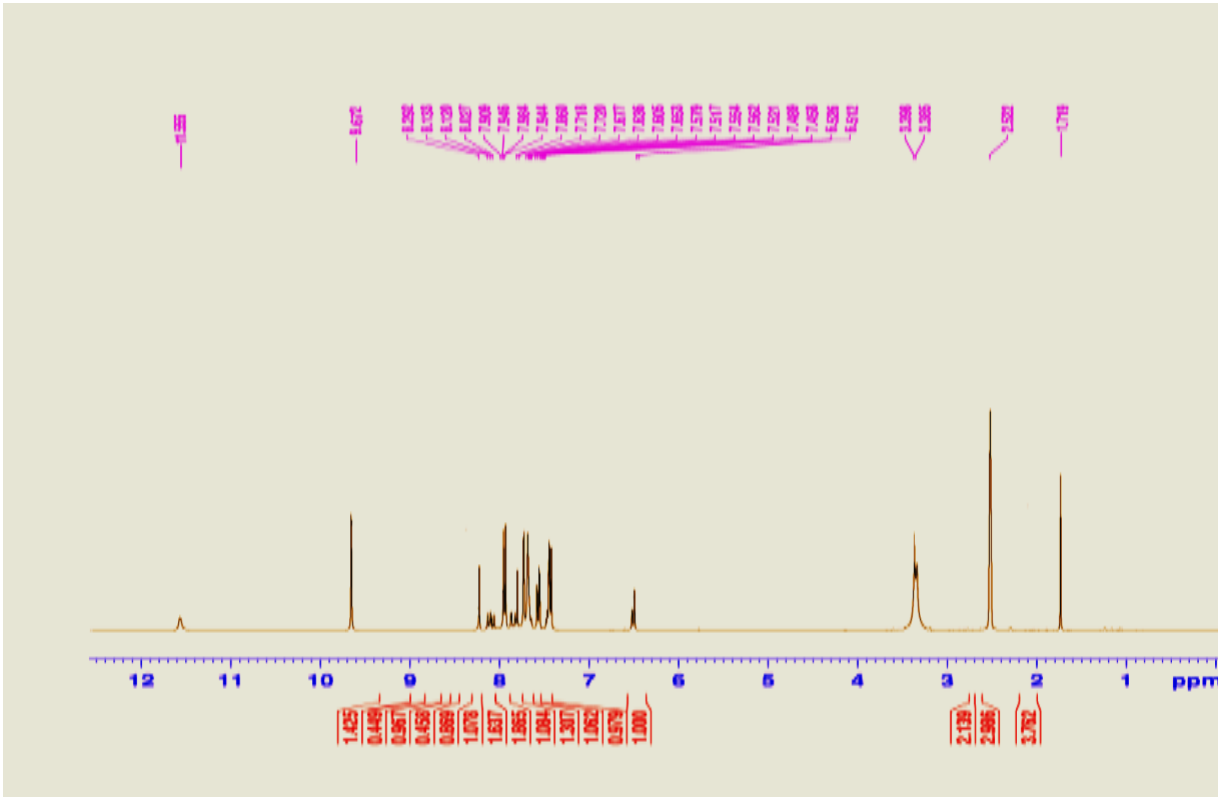

Fig. 13. H.NMR of Compound[M3]

C.NMR –Spectra:all spectra gave bands at (2. 50) for solvent (DMSO-d6)., some spectra appeared peaks at (157.0 to 159. 0) due to (C=N) of Schiff base, other peaks at (105.0 to 145.0) due to carbon atoms of aromatic Ring in all compounds, other compounds like [M4,M5, M6] appeared signal at (55.50 to 5.58) due to carbon atoms (C-NH-N-) in Imidazoline cycle in these compounds and like that in other spectra in figures (14-16):

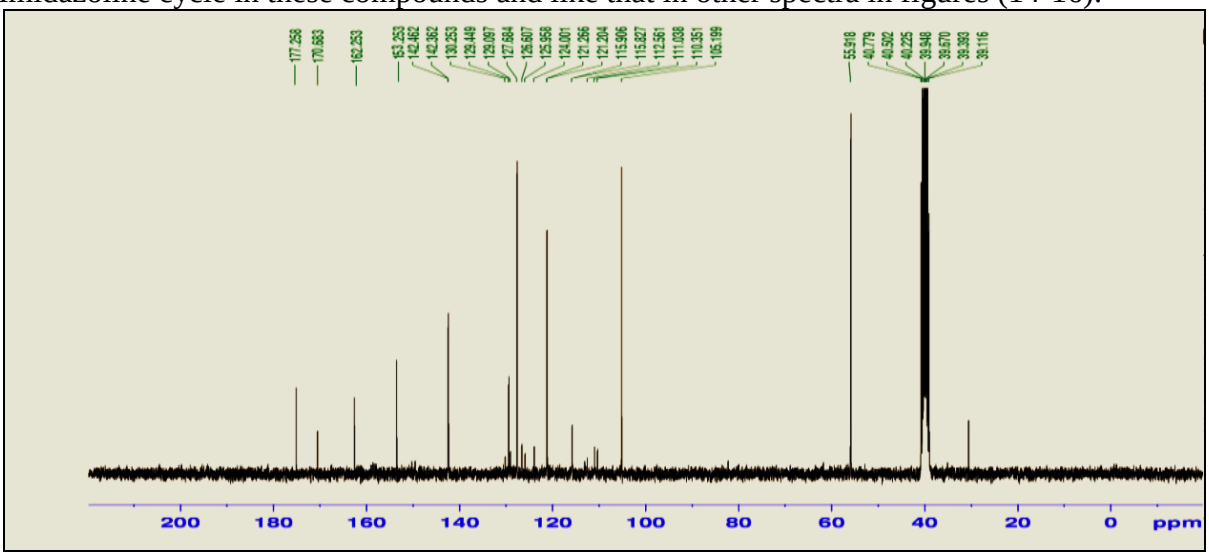

Fig. 14. C.NMR of Compound[M4]

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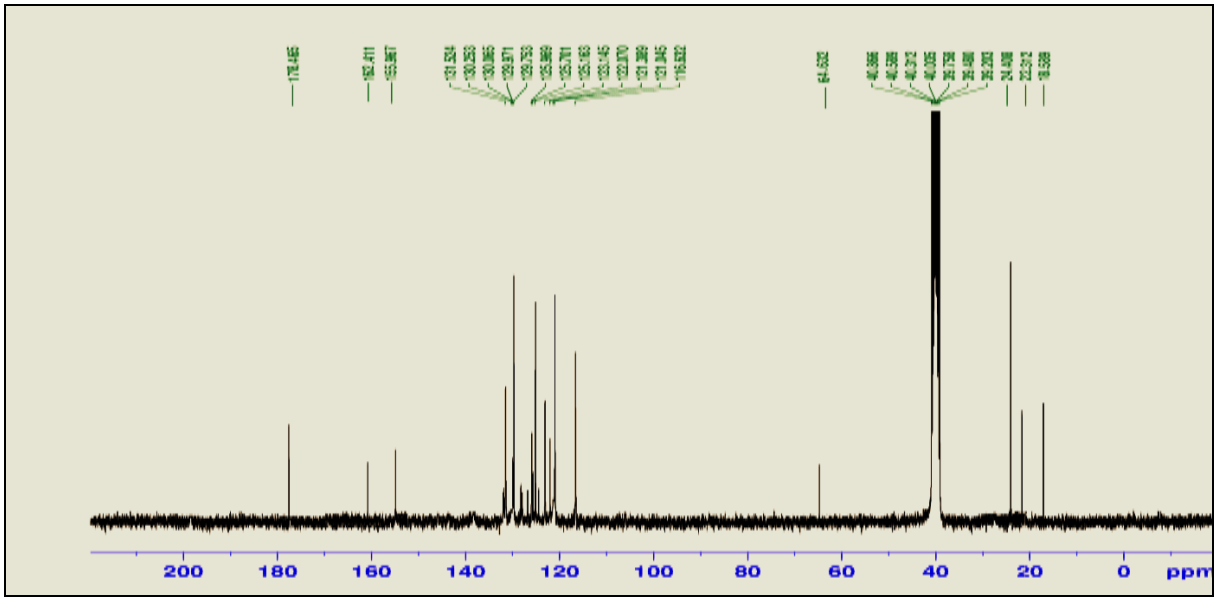

Fig. 15. C.NMR of Compound[M5]

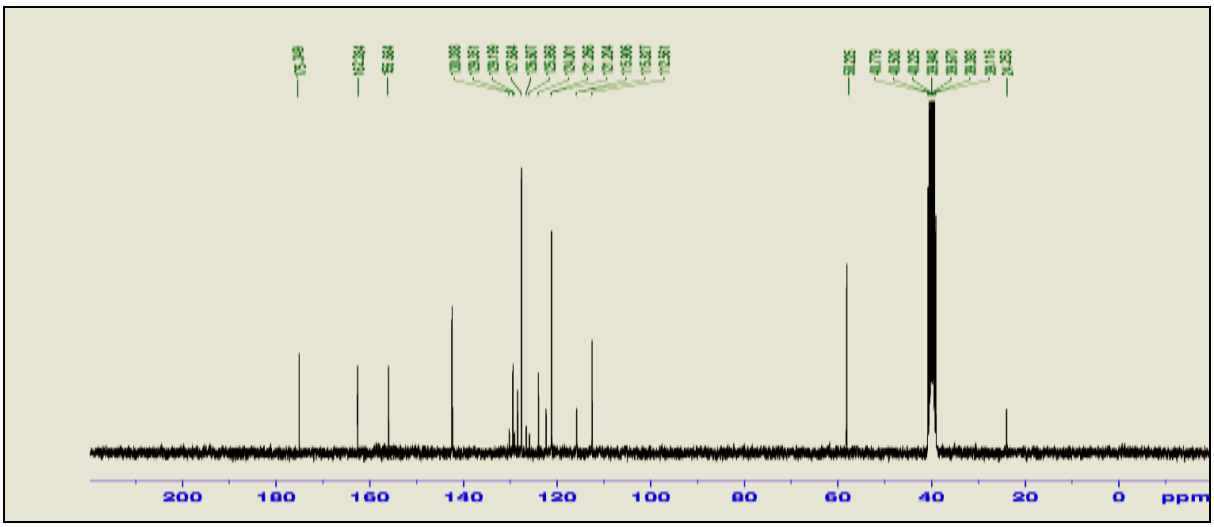

Fig. 16: C.NMR of Compound[M6]

Table 1. Physical properties of synthesis 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	157-159	Orange	-	3 hrs	EtOH +H_2O	91
S_1	$C_{24}H_{18}N_3OBr$	443.44	162-164	Green	0.9	35hrs	EtOH abs.	87
S_2	$C_{24}H_{18}N_4O_3$	409.43	160-162	red	0.9	20 hrs	EtOH abs.	81
S_3	$C_{24}H_{20}N_3OCl$	401.46	174-176	red	0.7	10hrs	EtOH abs.	87
M_1	$C_{26}H_{21}N_4O_2B_r$	500.49	132-134	Yellow	0.9	23hrs	THF	87
M_2	$C_{26}H_{21}N_5O_4$	467.49	100-102	brown	0.9	10 hrs	THF	88
M_3	$C_{26}H_{21}N_4O_2Cl$	456.52	126-128	red	0.9	13 hrs	THF	85
M4	C27H23N4O2Br	514.51	136-138	Yellow	0.8	23hrs	THF	84
M5	C27H23 N5O4	481.51	122-124	orang	0.8	8hrs	THF	90
M6	C27H23N4O2Cl	470.54	125-127	red	0.9	13hrs	THF	86

Study of The Biological Activity of the compound by paper technique disks[37].

Antibacterial activity was measured by using filtering paper type (Whitman NO.1) to prepared

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(120) pills after purification, after that,the pills put in the test tube average (5) pills for every tube and added (1 mml) from synthesized compounds solution were used weight of (5mg,10 mg,20mg) from the synthesized compounds, Table (2):

Table 2. Inhibition Zone of synthesis compounds against bacteria

Type of bacteria Comp.NO.	**Inhibition zone(mm) 5mg 10mg 20mg (mg\mol) - Bacteria**			
	klebsiella pneumonia	***Staphylococcus***	***Enterococcus faecalis***	***pseudomonas aeruginosa***
A	**-,5,8**	**-, -, 6**	**-,-,5**	**-,-,6**
S_1	**-,-,5**	**-, -, 5**	**-,-,5**	**-,-,8**
S_2	**-**	**-, -,4**	**-,-,8**	**-,-,8**
S_3	**-, -, 8**	**-, 5, 8**	**-,-,-**	**-,-,6**
M_1	**-,-,6**	**-,-,10**	**8,10,20**	**-, -, 10**
M_2	**-**	**-,-,10**	**-,8,10**	**-,-,7**
M_3	**-**	**-**	**-,8,10**	**12,18,20**
M_4	**-, -, 5**	**-, 5, 8**	**-,-,-**	**10,15,25**
M_5	**-,-,8**	**-,-,10**	**-,6,12**	**8,10,20**
M_6	**-,-,8**	**-,-,10**	**-,-,8**	**10,15,20**

The data of our results appeared good inhibition zone for all types of selected bacteria at these concentration for compounds [M1 to M6] due to imidazoline cycle in their structures that gave high effect to inhibit activity of bacteria, while compounds [M4] gave higher inhibition due to (Br) in its structure with imidazoline cycle in this compound.

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