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Synthesis and Characterization of the Inhibitory Activity of 4- (Dimethyl amino) benzaldehyde Schiff Bases

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ABSTRACT: Schiff bases were prepared by reacting 4- (dimethyl amino) benzaldehyde with different amino derivatives. The formation of these compounds was confirmed through measurements FT-IR, ^{1}H-NMR, and ^{13}C-NMR. Biological activity of all of the synthesis compounds were studied at three different concentrations against two types of positive and negative bacteria and compared with the drug azithromycin.

Keywords: Antibacterial; Schiff base, 4-(Dimethyl amino) benzaldehyde, $NaBH_4$

1. INTRODUCTION

Schiff bases, a part of organic chemistry, are of vital important.[1] Hugo Schiff, a chemist from Germany, originally described it.(*1*864) [2]. The azomethine group, which has the generic formula RHC=N-R1, is what unites these compounds structurally. R and R1 can be any of several different substituted alkyl, aryl, cycloalkyl, or heterocyclic groups. These substances are also known as azomethines, imines, and anils, several studies [3] They are often produced by condensing primary amines with active carbonyl groups [4]. Reduction of the azomethine group is a method for the preparation of primary and secondary amines [5] The iso methine group can be reduced to an amine by a number of reducing agents [6] NaBH4 (Sodium borohydride) effective reducing agent [7]. The -N=CH- (imine) group, which is characteristic of Schiff bases, is important in understanding the mechanism of the transamination and rasemination reactions in biological systems. [3]. Multiple Schiff bases are the most well-known chemical compound that has been shown to have a variety of biological activity.[1] antibacterial, antifungal [8], anticancer [9] antimicrobial [10] They are significant compound due to their wide range of industrial application. They act as a backbone as well for the synthesis of several heterocyclic compounds [11]. The synthesized compounds were described by used FT-IR, ^{1}H NMR, and ^{13}C NMR. The compounds displayed to effective antibacterial properties against Staph. aureus and E .coli. [12].

2. EXPERIMENTAL

2.1 Materials and Instrumentations:

4-(Dimethyl amino) benzaldehyde, NaBH4 and 1,2-phenyl diamine was purchased from Fluke. All organic solvents were purchased from Merck., FT-IR spectra was recorded using PERKIN ELMER SPEACTUM-65, JASCO, Infrared Spectro photometer within the range [4000-400] using KBr Disc, Baghdad University, College of Science ^{l}H and **^{13}C** NMR spectra were determined in DMSO (internal standard TMS) on Bruker spectrometer. Tehran **University.**

2.2. Synthesis 4-((4- (dimethyl amino) benzylidene) amino) phenol(A)

This compound has been prepared by dissolving (1g,0.006mol) 4-(dimethyl amino) Benz aldehyde in (50ml) ethanol, added dropwise with stirring to (0.73 g,0.006mol) of p-aminophenol (30 ml), and heated for 6 hours using reflux at70^0 C. To get a solid product, the solvent was evaporated under vacuum following an acetone wash, the product was dried.to from ,73%yield Scheme(I)

2.3 Synthesis 4-((4-(dimethyl amino) benzyl) amino) phenol(A1)

0.5 g of compound A is gradually dissolved in 100 ml of ethanol, then 5 g of $NaBH_4$ is added to the solution and left stirring for 12 hours at laboratory temperature. The mixture is left in the air to evaporate the solvent and obtain a dry precipitate. Then 400 ml of distilled water is added to the precipitate, and 1 N of HCl is added gradually until the precipitate is completely dissolved. After that, the pH of the solution is increased by adding 2 N of sodium hydroxide until the pH reaches 10... Scheme (II) . The result (73 %) of (A1) compound [13]

2.4 Synthesis 4-(((4-aminophenyl) amino) methyl)-N, N-dimethylaniline (B)

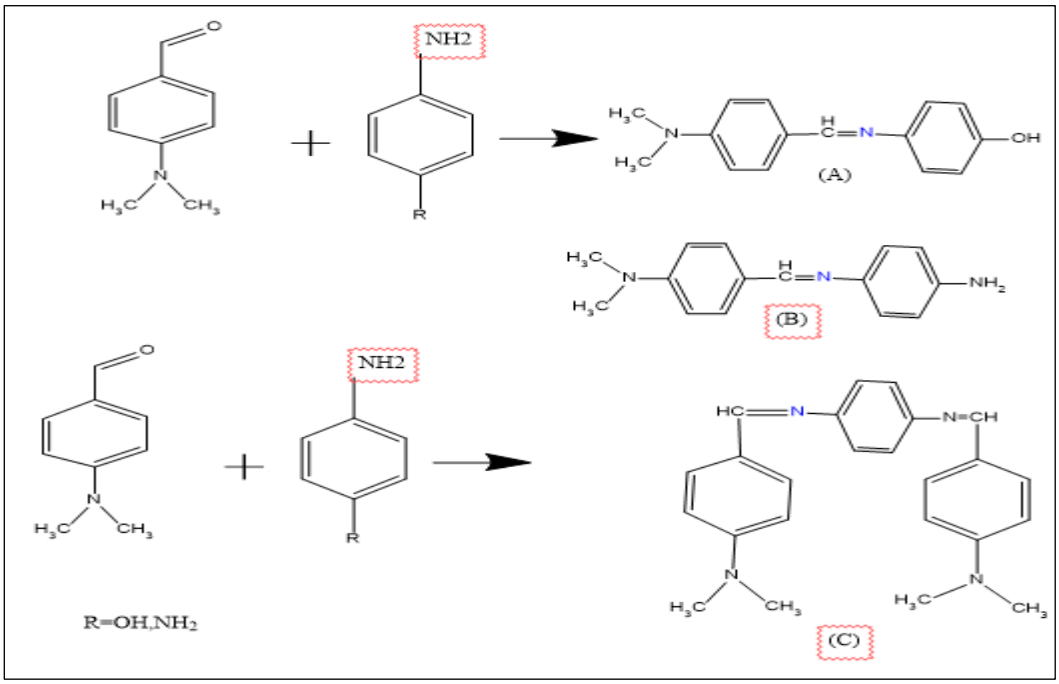
This compound has been prepared by dissolving 4-(dimethyl amino) benzaldehyde (1g,0.006mol) in ethanol, added dropwise while stirring to (0. 73 g,0.006mol) of 1,2 phenyl diamine (30 ml), and heated for three hours using refluxed at70 ^{0}C To get a solid product, the solvent was evaporated under vacuum. Following an acetone wash, the product was dried.to 65%yield. Scheme(I)

2.5 Synthesis 4,4'-((1,4-phenylenebis (azaneylylidene)) bis (methanelyldene)) bis (N, N-dimethylaniline) (C)

This compound has been prepared by (1g,0.006 mol(of 4-(dimethyl amino) benzaldehyde dissolving in ethanol, added dropwise while stirring to (0. 37 g0.003mol) of 1,2phenyldiamine (30 ml), and heated for three hours refluxat70^{0}C .The solvent was evaporated under vacuum to result solid product. The product was washed with acetone and dried under vacuum-dried to remove the residue. to from the result in (75 %). Scheme (I).

2.6 Synthesis N1, N4-bis (4-(dimethyl amino) benzyl) benzene-1,4-diamine(C1)

0.5 g of compound C is gradually dissolved in 100 ml of ethanol, then 5 g of $NaBH_4$ is added to the solution and left stirring for 12 hours at laboratory temperature. The mixture is left in the air to evaporate the solvent and obtain a dry precipitate. Then 400 ml of distilled water is added to the precipitate, and 1 N of HCl is added gradually until the precipitate is completely dissolved. After that, the pH of the solution is increased by adding 2 N of sodium hydroxide until the pH reaches 10. Scheme (II). The result (68 %) of (C1) compound [13].



Scheme (I) - Synthesis of Compounds (A, B and C).

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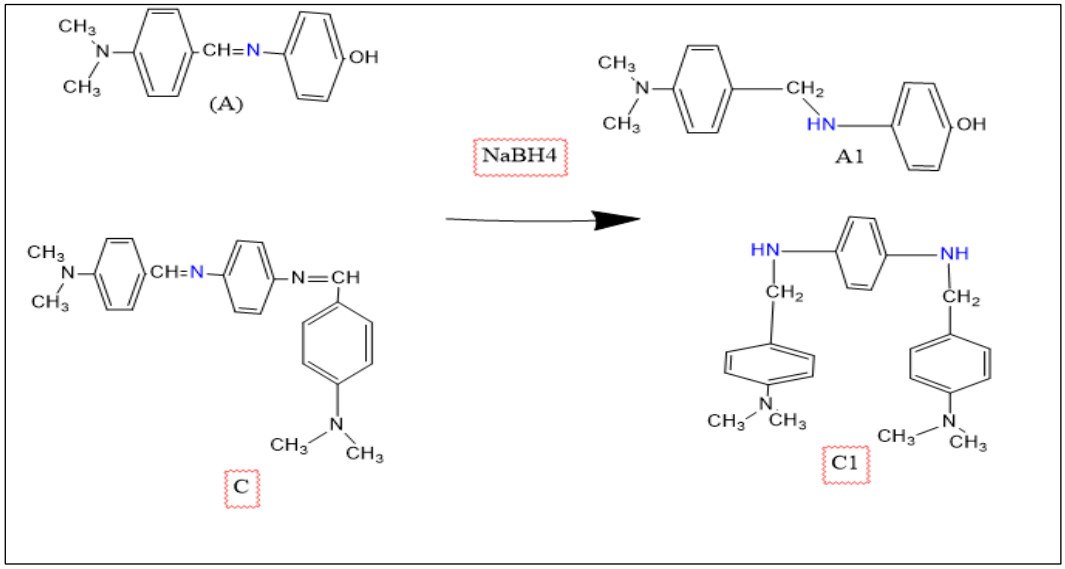

Scheme (II) synthesis of compounds (A1 and C1).

3. CHARACTERIZATION

Compounds are studied with various analysis techniques**.**

3. *I.* Analytical data

Table (1) FT-IR spectra for the prepared Schiff base compounds

Compound	Chemical Formula	Molecular weight	IR		
A	$C_{15}H_{16}N_2O$	240.31	0H υ cm^{-1}	C=N υ cm^{-1}	NH υ cm^{-1}
A1	$C_{15}H_{18}N_2O$	242.32	3422	1589	--------
B	$C_{15}H_{17}N_3$	239.14	3449	------	3359
C	$C_{24}H_{26}N_4$	370.50	------	1550	----------
C1	$C_{24}H_{30}N_4$	374.25	------	1552	----------

Table (2) ^{13}C -NMR spectral data(ppm)of compound (A, B and C)

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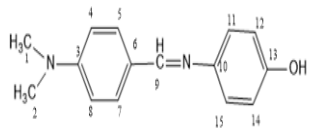
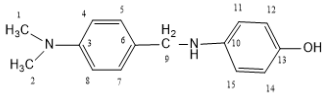
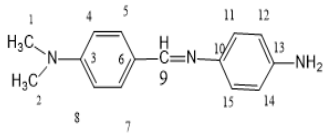
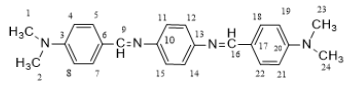
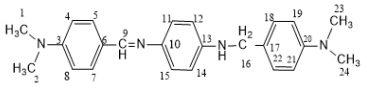
Compound	13C -NMR spectral data(ppm)
A	157.96-151.84(C3,C9,C10C16,C17,C20) 129.9-122.48(C5,C7,C11andC15) 117.7-112.01(C4,C8,C12andC14) 40.01(C1andC2)
B	157.96-151.11(C3,C9andC13) 129.3-121.5(C5,C7,C11,C12,C14C15,C19and21) 117.64-113.12(C4,C8,C12andC14) 40.22(C1andC2)
C	159.96-152.80(C3,C9andC13) 129.7-125.48(C5,C7,C11andC15) 115.33-111.01(C4,C8,C18andC22) 39.8-39.59(C1andC2

Table (3) ^{1}H-NMR spectral data(ppm) of compound (A, A1, B, C and C1)

Compound		^{1}H-NMR spectral data(ppm)
A		2.89(DMSO)3.48(s,6H, N-CH3)3.53(s,6H, N-CH3); 6.77-7.74(m,8H, AR-H); 8.41(s,1H.N=CH);936.(s,1H,OH)
A1		2.89(DMSO)3.43(s,6H, N-CH3)3.48(s,6H, N-CH3); 6.33-7.36 (m,8H, AR-H); 7.74(t,1H.NH-CH);9.30.(s,1H,OH); 4.03(d,4H.NH-CH2);
B		2.7(DMSO)3.47(s,6H, N-CH3)3.43(s,6H, N-CH3);5.52(s,2h,-NH2)6.61-7.79(m,8H,Ar-H); 8.50(s,1H.N=CH);
C		3.44-3.43(s,12H, N-CH3);6.78-7.79(m,12H, AR-H);8.42(s,1H. N=CH); 8.5(s,1H. N=CH);
C1		3.34(s,12H, N-CH3);6.41-7.9(m,12H, AR-H);6.66(t,2H.NH-CH2); 4.02(d,4H.NH-CH2);

4. RESULT AND DISCUSSION

All synthesis compounds are colored. The synthesized product was characterized by1- Infrared Spectra (IR): The IR absorption bands were determined in KBr disk. The compounds were identified by their infrared spectrum and comparing them with the infrared spectrum of the starting materials (4-(Dimethylamine) benzaldehyde, P-phenylene diamine). The most important feature of the spectrum of the starting materials 4-(Dimethyl amino) benzaldehyde the carbonyl group's (C=O) absorption band appearing at the wave number (1662) cm-1[14]. As for the spectrum of the starting material (P-

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phenylene diamine) it has Its infrared spectrum showed a double-headed band at wavenumbers 3201-3306, belonging to the stretching of the symmetrical and asymmetric N-H bond, respectively [14]. Comparing the spectrum of the two primary substances with the spectrum of compounds showed the appearance of new bands and the disappearance of other bands, as the double-headed band disappeared at The wave number (3306-3201) due to the stretching of the N-H bond is evidence of the loss of proton, the disappearance of the stretch band (C=O) at 1625 cm-1, and the appearance of a new band at the wave number(1589 cm-1)A,(1552 cm-1) B,(1550 cm-1) C due to the stretching of the C=N bond[15]as well as the appearance of a band at(3419,3422,3446) dating back to the stretching of the OH bond.[16]. The FT. IR spectrum of (A1andC1) compound shows bands changing in comparison with (A and C) compound spectrum table (1). figure (1,3and4). The most important to note is the band disappearing at 1582 cm-1, and 1560 cm-which are due to the imine group of (A1andC1) compound and the appearance of a new band at (3359, 3321) cm-1 which is due to the secondary amine group formation (-NH-) These noticeable changes indicate the Schiff base reduction and the formation of the secondary amine compound. Table (1) figure(2and5)

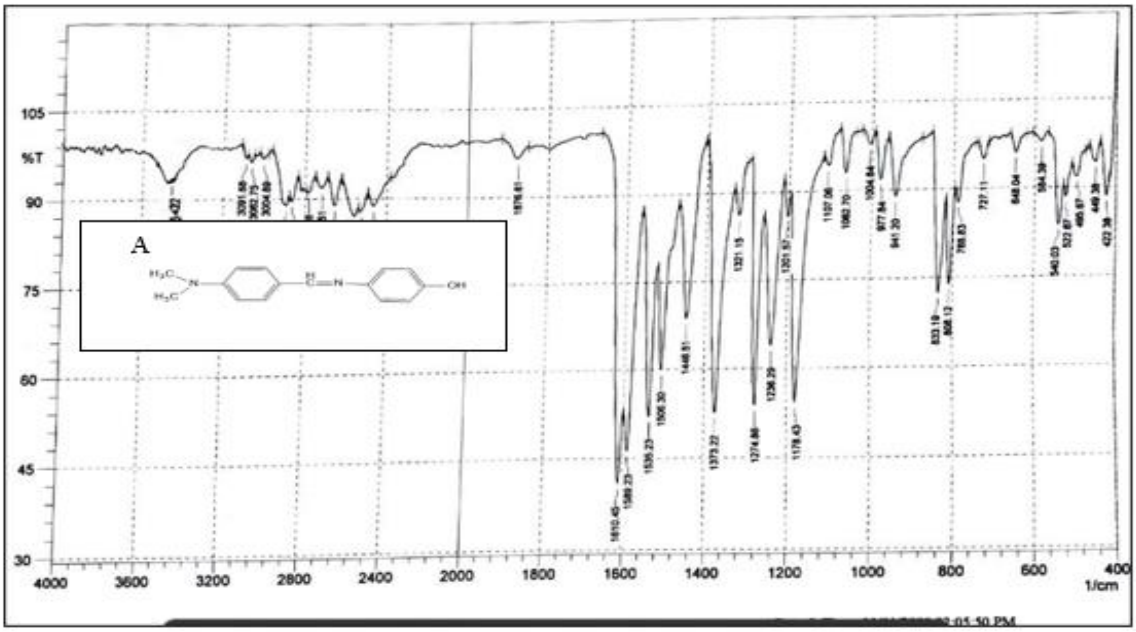

FIGURE 1. - FT-IR spectrum of compound [A]

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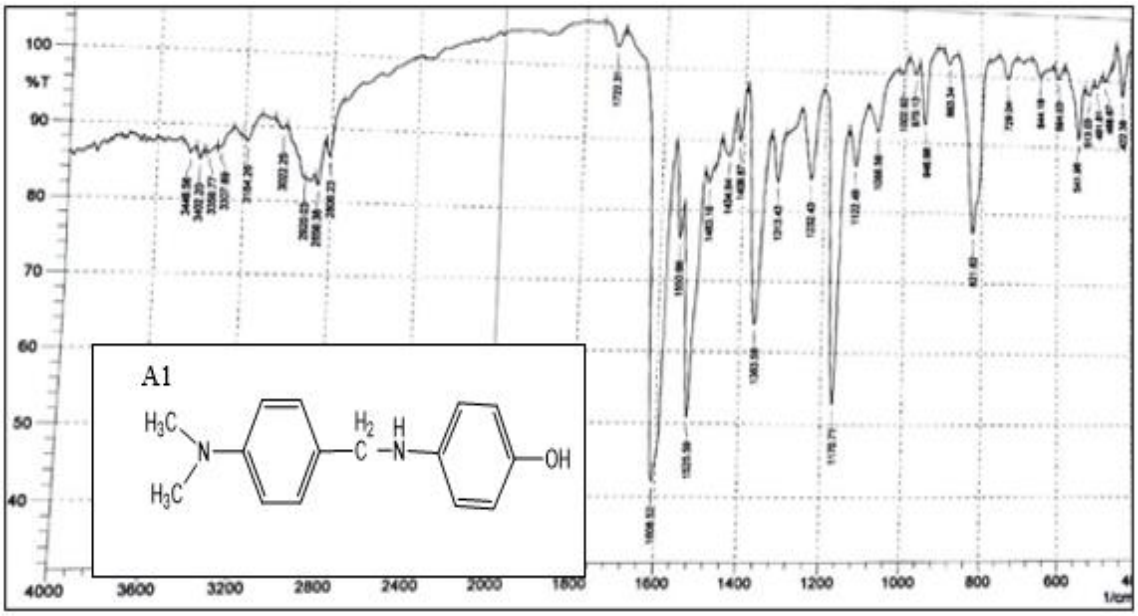

FIGURE (2) FT-IR spectrum of compound [A1]

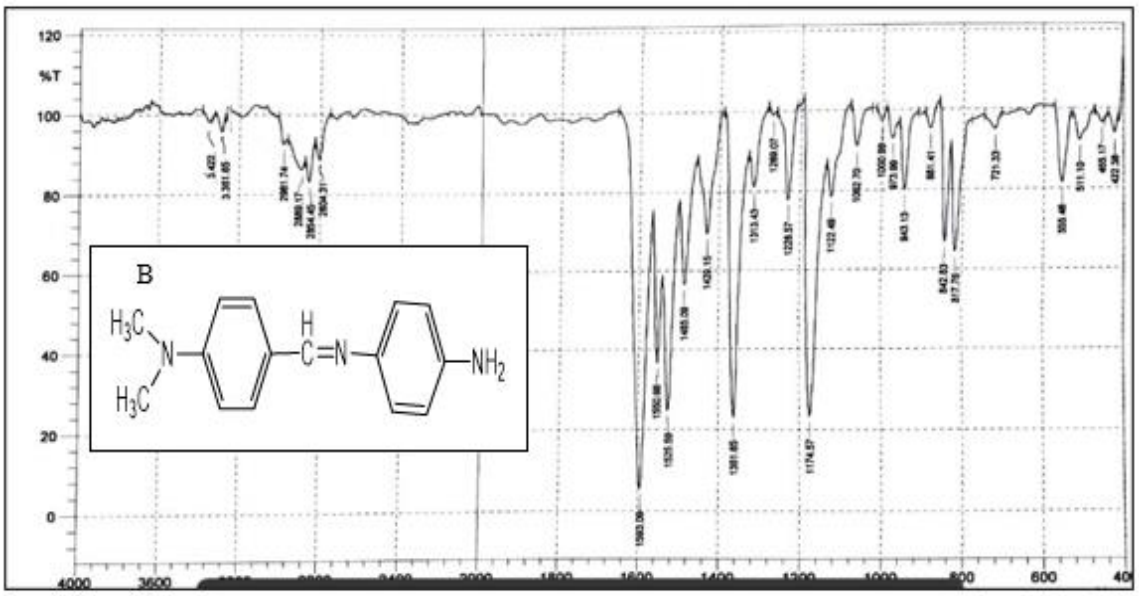

FIGURE (3). FT-IR spectrum of compound [B]

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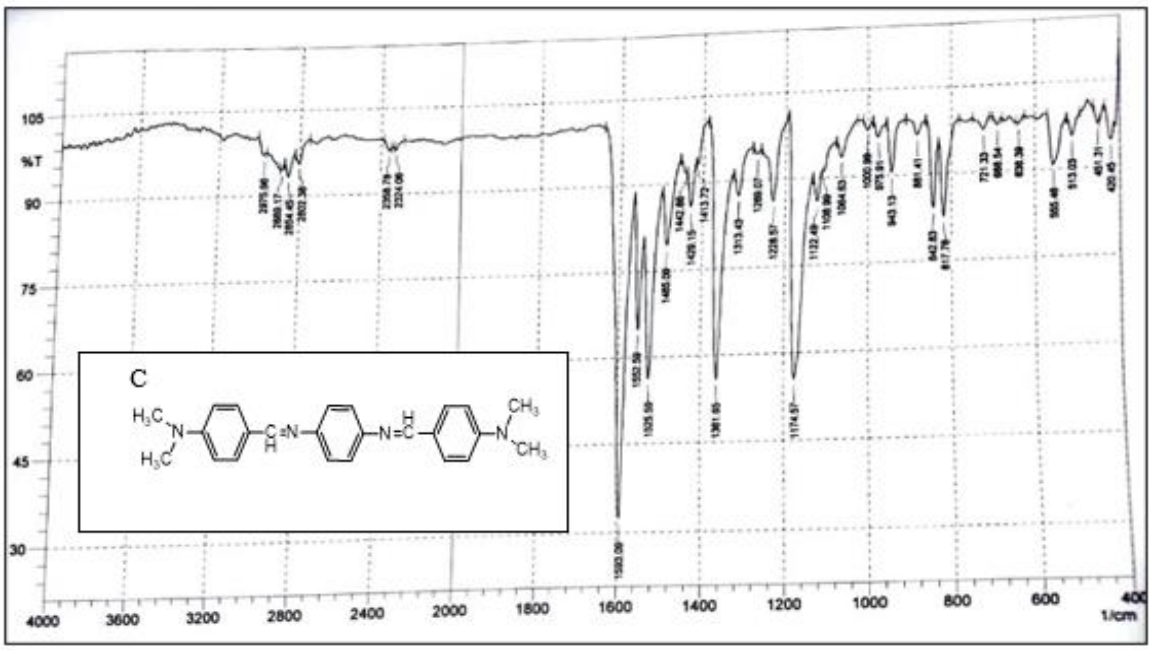

FIGURE (4) FT-IR spectrum of compound [C]

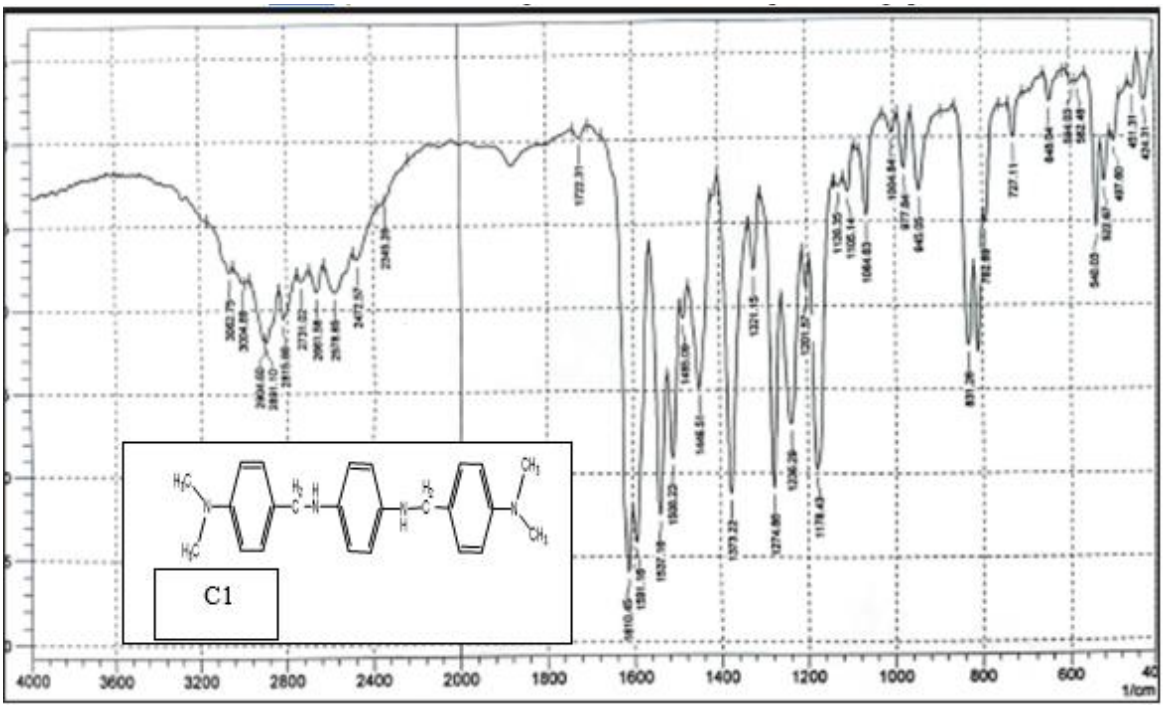

FIGURE (5). FT-IR spectrum of compound [C1]

4.1-NMR

Show [1]HNMR spectrum of the prepared compound (A1),(C1) resulting from the reduction of compound(A), (C). Shows disappearance of the imine peak and appearance of methylene and secondary amine functional group, as follows: 8.41(s,1H. N=CH),4.03(d,4H. NH-CH2),);7.74(t,1H. NH-CH);4.02ppm (4H, CH2),6.66ppm (2H, NH)8.42-8.5(s,2H. N=CH); (figure (6,8, and10) table (3)) [17]

[13]C NMR spectrum for compound shows disappearance of the aldehyde group peak at 192 ppm and appearance of the imine peak at157.96(A),157 .96(B),15 9.96(C) Figure(12,13and14).table(2)

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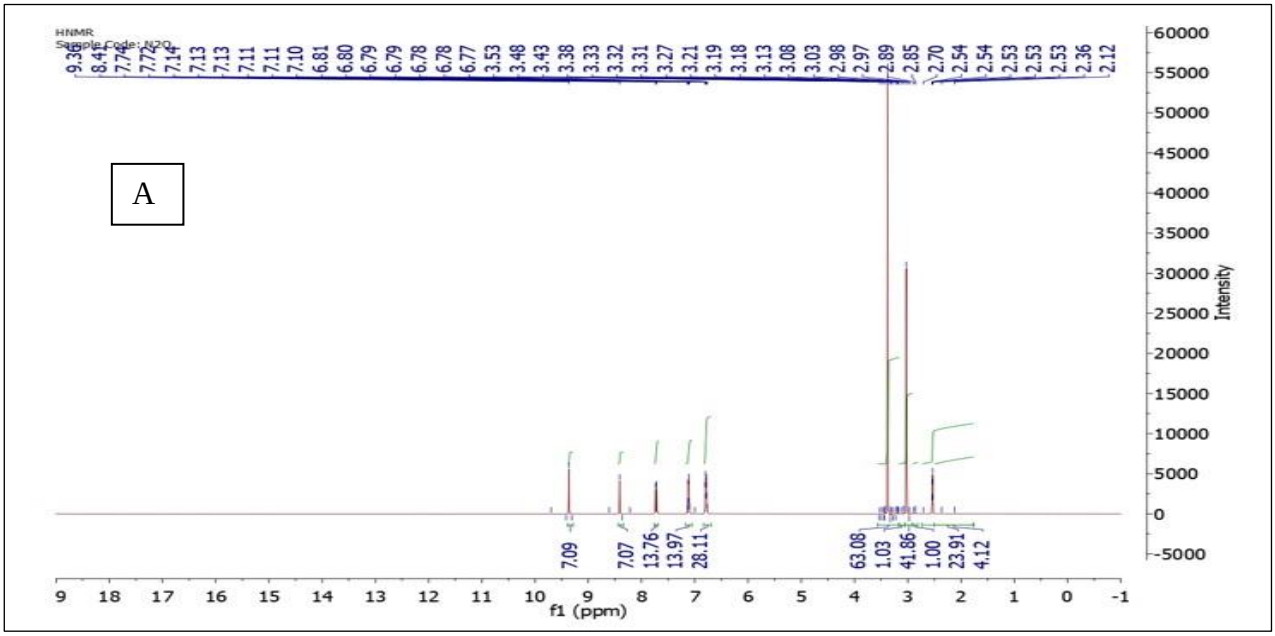

FIGURE (6) ^{1}H -NMR spectrum of compound[A]

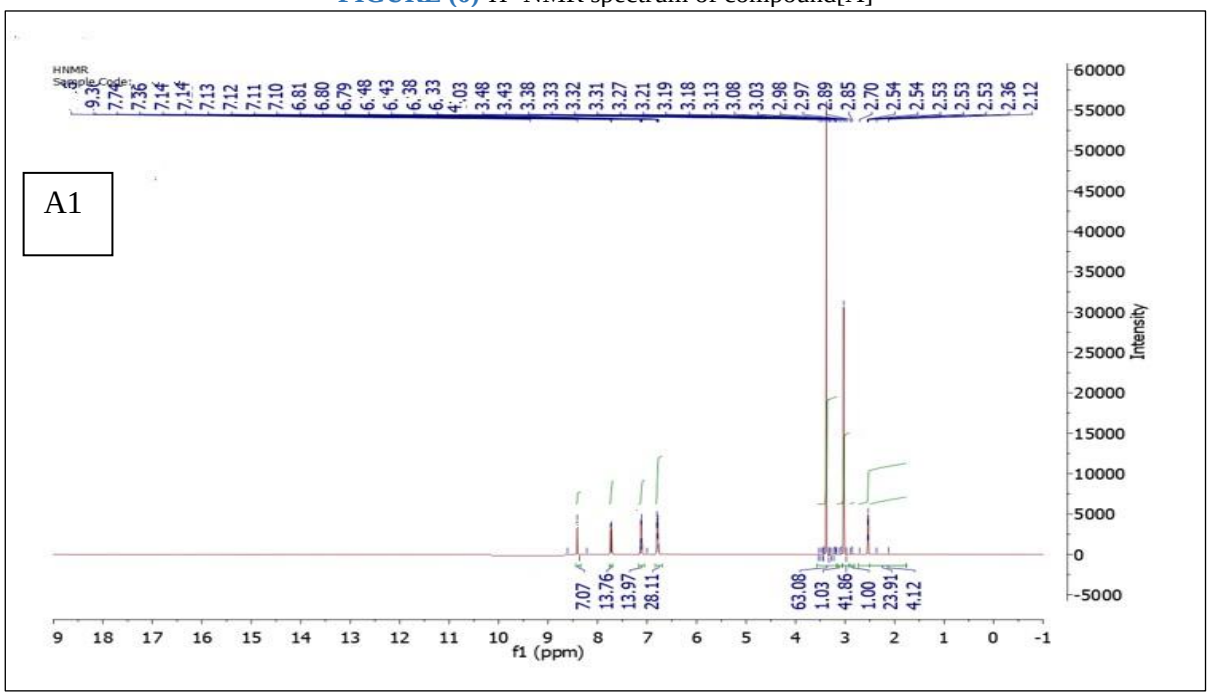

FIGURE (7) ^{1}H -NMR spectrum of compound[A1]

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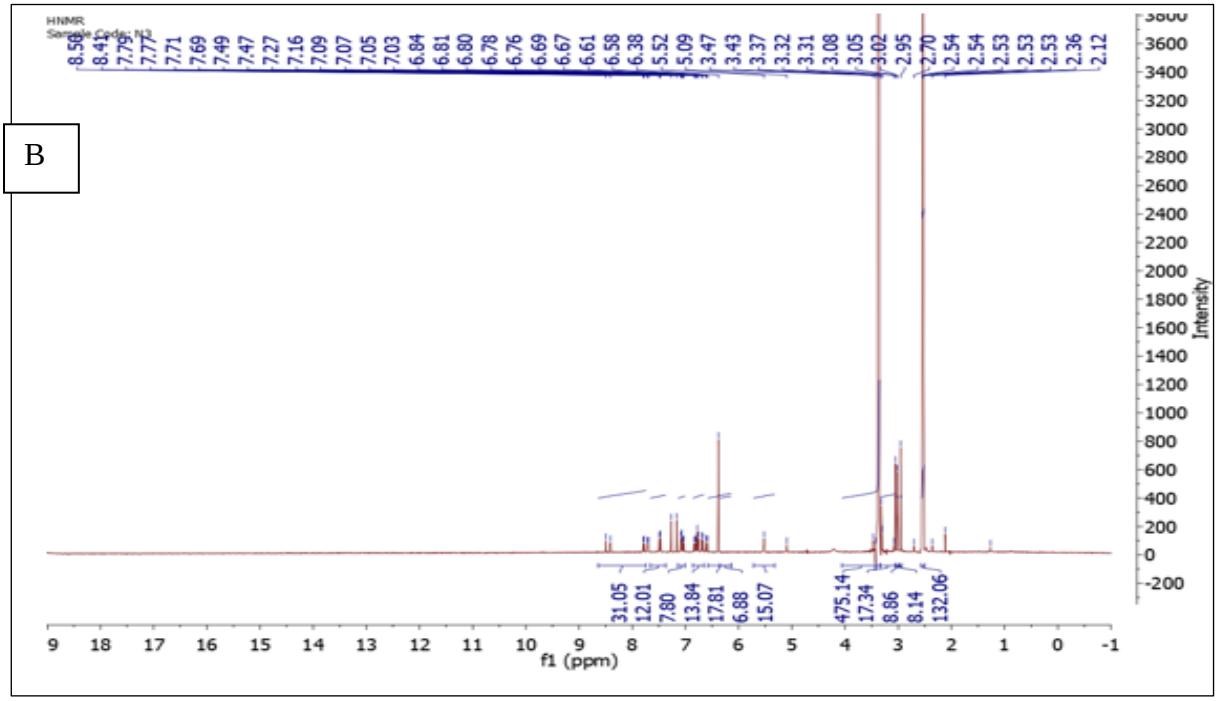

FIGURE (8) ^{1}H -NMR spectrum of compound[B]

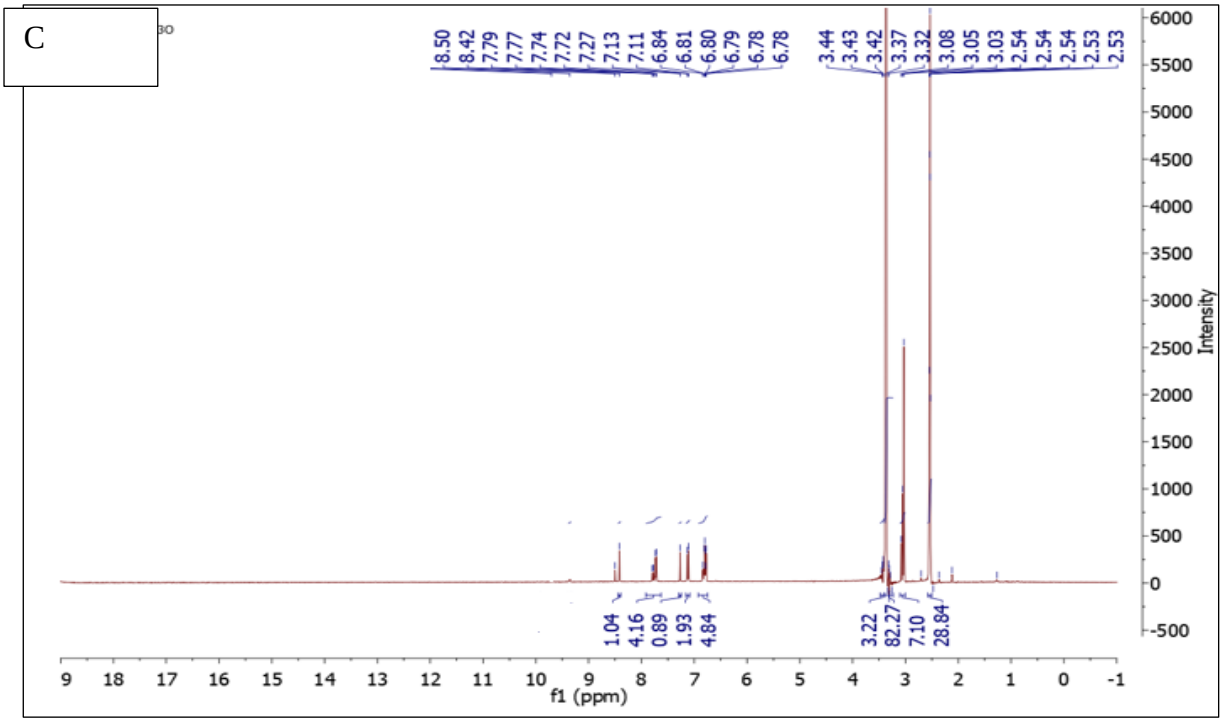

FIGURE (9) ^{1}H -NMR spectrum of compound[C]

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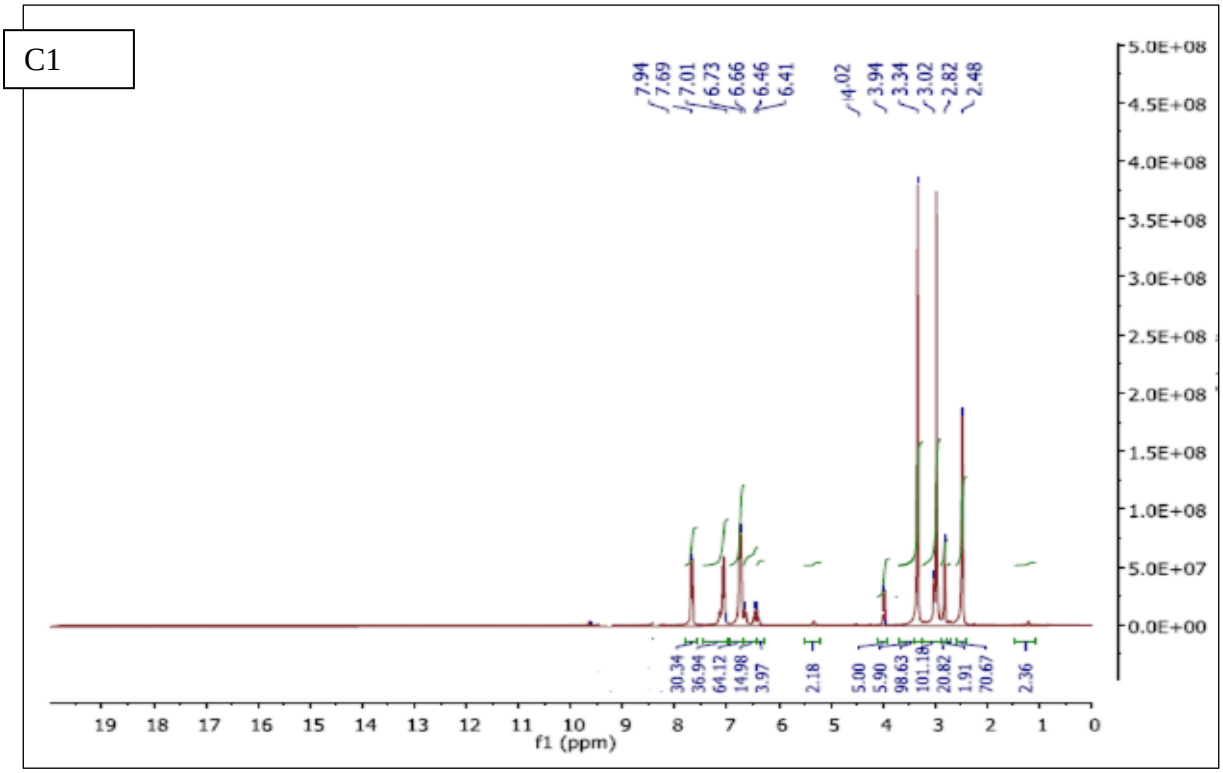

FIGURE (10) ^{1}H -NMR spectrum of compound[C1]

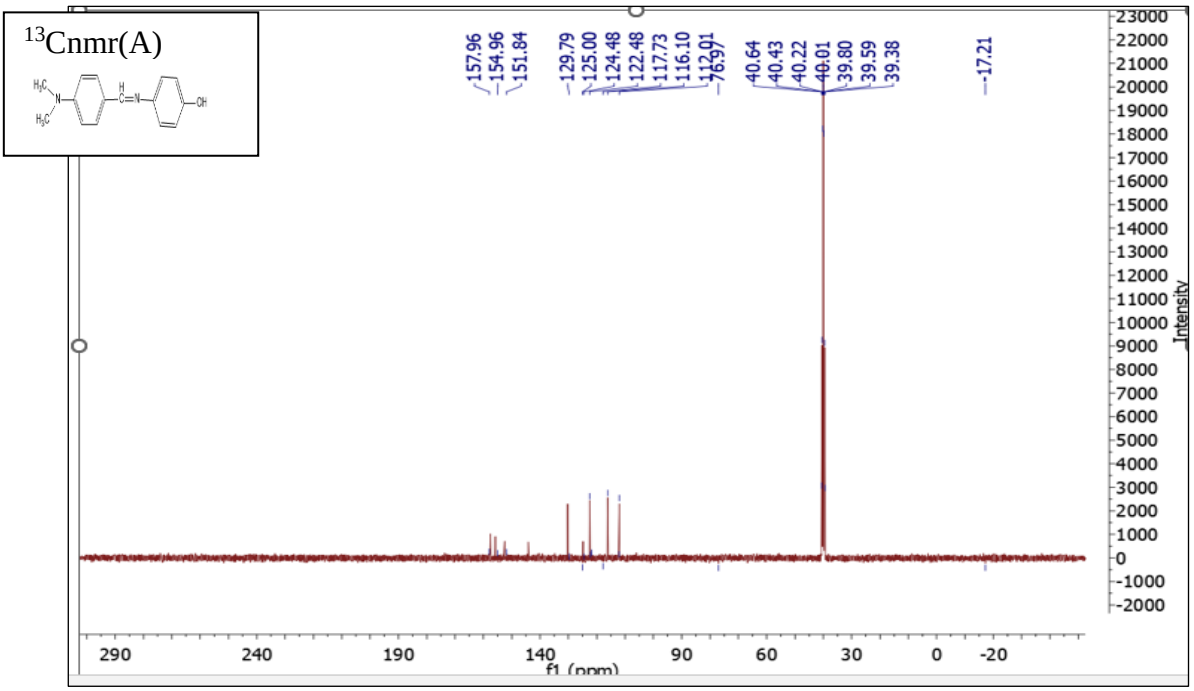

FIGURE (11) ^{13}C -NMR spectrum of compound[A]

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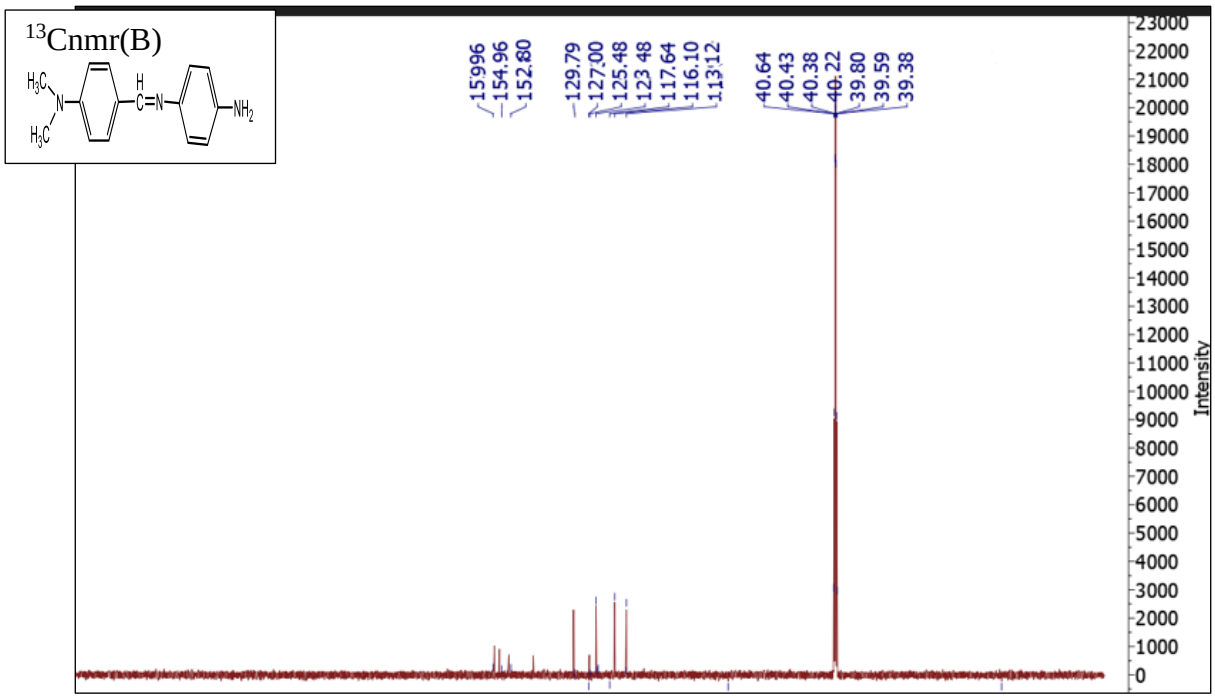

FIGURE (12) ^{13}C -NMR spectrum of compound[B]

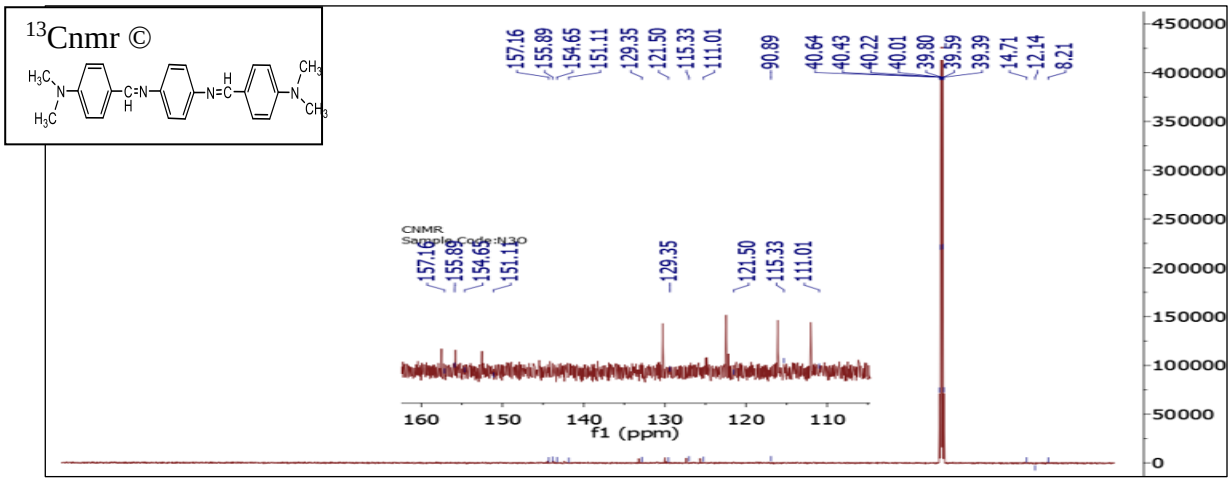

FIGURE (13) ^{13}C -NMR spectrum of compound[C]

5. STUDY OF ANTIMICROBIAL ACTIVITY

To prepare, Schiff bases were dissolved in dimethyl sulfoxide (DMSO) (75 % ,50 % ,25 %) Each compound's antibacterial properties were assessed using the agar disc-diffusion method. The solid agar medium was covered with tightly compressed discs and then injected with prepared Schiff bases. For twenty-four hours, the Petri plates were kept at 37°C. Using a zone reader, the zones of inhibition that developed on the medium at the end of time were measured in millimeters. The antibacterial activity of the synthesized compound was compared with marketed preparation of antibiotic (azithromycin) Concentration Compound (0. 01g/ml).

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Table 4: Result of Antimicrobial activity E.coli

Concentration%	Zone of Inhibition (mm)					
	A(N2O)	A1(22)	B(N3)	C(N3O)	C1	
75	19	19	14	20	22	
50	17	16	13	18	17	
25	15	15	13	16	15	

Table 5: Result of Antimicrobial activity Staph. aureus

Concentration%	Zone of Inhibition (mm)				
	A(N2O)	A1(22)	B	C(N3O)	C1
75	27	16	16	17	29
50	19	11	13	15	20
25	12	0	11	0	11

Table 6: Activity drug azithromycin

	Staph. aureus	**E.coli**
azithromycin	23	15

6. DISCUSSION

The biological activity of the prepared compounds was tested against one strain of Gram+ve (Staph. aureus) bacteria and Gram –ve bacteria (Escherichia coli. It was found that (A and C1) compound prepared at a concentration of 75% higher biological activity compared to azithromycin antibiotic for Staphylococcus aureus, while it was found that (A, A1, C, C1) compound prepared at a concentration (25,50,75) % showed high biological activity compared to azithromycin antibiotic for E. coli. The resulted are presented in table (4,5and6), figure (14). Graph (I and II) show C1 75% more biological activity compared to azithromycin antibiotic for Staphylococcus aureus and E coli.

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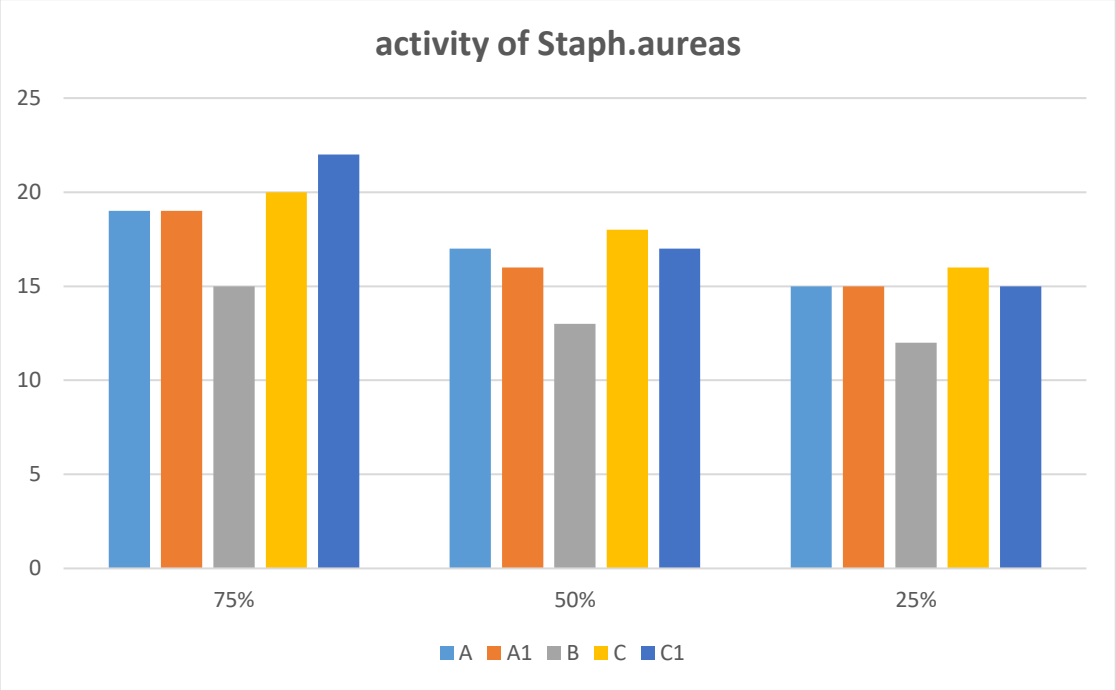
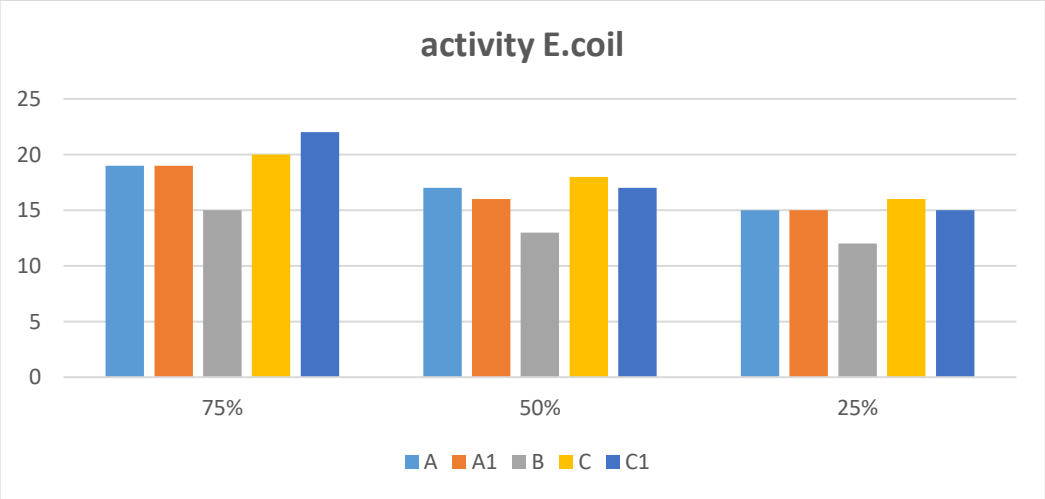


Graph (I)showing antimicrobial activity of Staph. aureus



Graph (II) showing Antimicrobial activity E.coil

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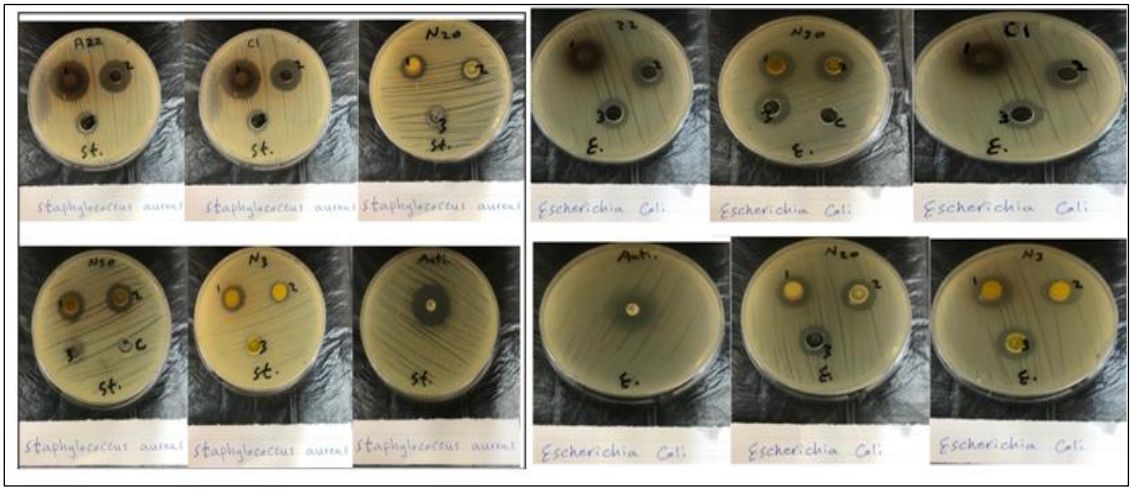

Figure (14) showing zone of inhabitation against subtilis, Staph. aureus and E. coli

7. CONCLUSION

The prepared compounds were proven by known analytical methods (IR, NMR13C,1H). most of the compounds were a higher biogenic effectiveness with increasing concentration compared to a drug azithromycin. Compound N1, N4-bis (4-(dimethyl amino) benzyl) benzene-1,4-diamine)) C1)75% concentration show more effective inhabitation against Staph. aureus and E. coli compared to other compounds.

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