Synthesis, Characterization and Study Biological activity of some New 1,3-Oxazepine and 1,3-Diazepine derivatives

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Abstract :

New 1,3-oxazepine and 1,3-diazepine derivatives containing azo group have been prepared. The first step,(*O*-tolidine) was converted to [3,3`-dimethyl-(1,1`-biphenyl) -4,4`-diyl) bis (diazene-1,2-diyl))bis(naphthalene-2- amine)] Azo *O*-tolidine[A].by Azotization reaction with naphthyl amine. The second step, amine group of the azo derivative [A] was condensed with different aromatic aldehydes[*p*-dimethyleaminobenzaldehyde, 4-chlrobenzaldehyde,4-nitrobenzaldehyde,4-bromo benzal dehyde , 4-hydroxy-3-methoxybenzaldehyde] in the presence of absolute ethanol to give new azo Schiff bases derivatives [B-F] respectively. Then, the resulting imines derivatives [B-F] were reacted with maleic anhydride and phathalic anhydride in dry benzene to give new 1,3-oxazepine-4,7-dione ring derivatives [Ba-Fa] , [Bb-Fb] , all these compound reaction with sulphadiazene to producte 1,3-diazepine-4,7-dione ring derivatives [Ba_1-Fb_2]. Also study the Biological activity to this derivatives ; All prepared compounds were characterized by melting points and FT.IR spectroscopy, some of them are characterized by ^{1}H-NMR spectroscopy and C.H.N analysis.

تحضير وتشخيص ودراسة الفعالية البايلوجية لبعض المشتقات الجديدة3,1-الاوكسازبين و3,1-الدايازبين

رؤى وسام أدم عزت حسين زمام

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جامعة الكوفة

المفتاح :. اورثوتولد ين ,مركبات أزو , قواعد شف , 3,1-الأوكسازبين ,3,1-الدايازبين ,فعالية بايلوجية .

الخلاصه:
حضرت مشتقات 3،1-اوكسازبين و3,1- دايازبين جديدة تحتوي في تركيبها على مجموعة الأزو. الخطوة الأولى تتضمن تحول (الاورثوتولدين) إلى 3,`3 - بس (نفثيل-2-امين) ازو اورثوتولدين [A].عن طريق تفاعل الازدواج مع (نفثيل-2-أمين) الخطوة الثانية تتضمن إدخال مجموعة امين مشتق الأزو المحضرفي تفاعل تكاثف مع الديهايدات اروماتية مختلفة(بارا- داي مثيل امينو بنزلدهايد ,4- كلورو بنزلدهايد , 4- نايترو بنزلدهايد, , 4-برومو بنزلدهايد , 4-هايدروكسي- 3- ميثوكسي بنزلدهايد) بوجود الأيثانول المطلق فتم الحصول على مشتقات ازو قواعد شف الجديدة [B-F] على التوالي .بعد ذلك تم مفاعلة مشتقات إلايمين الناتجة [B-F]مع كل من إنهدريد المالك وإنهدريد الفثاليك في البنزين الجاف فتم الحصول على مشتقات حلقية جديدة 3,1- اوكسازيبين-7,4-دايون [Ba-Fa] و [Bb-Fb] على التوالي, وبعد ذلك تم مفاعلة كل المركبات المحضره مع السلفادايازبين في البنزين الجاف للحصول على مشتقات 3,1- دايازبين-7,4- دايون [Ba_1- Fb_2]. وتم دراسة الفعالية البايلوجية لكل المركبات المحضره .إن جميع المركبات المحضرة شخصت بوساطة درجات الأنصهار ومطيافية الأشعة تحت الحمراء والبعض منها شخصت بوساطة مطيافية الرنين النووي المغناطيسي للبروتون وتحليل العناصر الدقيق (كاربون, هيدروجين, نيتروجين).

Introdection

Azo compounds are molecules with one or more azo (-N=N-) bridges, linking substituted aromatic structures, and constitute the largest and mostdiverse group of dyes and pigments used in commercial applications[1,2] . Synthesis of most azo dyes involves diazotization of a primary aromatic amine, followed by coupling with one or more nucleophiles. Amino and hydroxyl groups are commonly used coupling components[3] . *o*-Tolidine is a commercially important aromatic amines used mainly for dye production[4] .

Schiff bases are one of the most prevalent and important of the mixed donor systems in the field of coordination chemistry. The first preparation of imines was reported in the 19th century by Schiff (1984), which are prepared by condensing primary amines with an aldehyde or a ketone under specific conditions[5] , Because of the relative easiness of preparation, synthetic flexibility and special property of C=N group, Schiff bases are considered as an excellent chelating agents. Schiff bases and its metal complexes have been found to exhibit biological activities including antifungal, antibacterial, antimalarial, antipyretic, larvicidal, antiviral and antitubucular activites[6-11] . .Oxazepine-diones is a seven-membered ring containing nitrogen, oxygen and two carbonyl group[12].Oxazepine and their derivatives have some important biological pharmacological activities[13].psychoactive drugs [14].such as enzyme inhibitors[15] .Analgesic [16].and antidepressant [17]. Diazepines is a class of seven-membered ring heterocyclic compounds consisting of two nitrogen atoms in the position -1, 2 , -1,3 and -1,4 in the cycloheptane ring. Benzodiazepine refers to the structure composed of benzene ring fused to the seven-membered diazepine ring[18] .

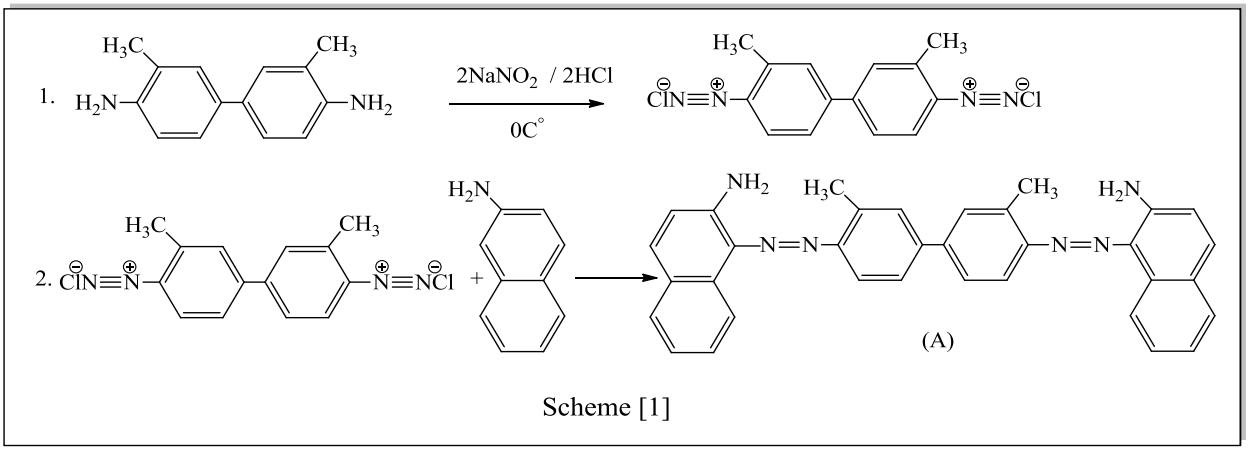
Experimental

All chemicals were used supplied from Merck , BDH and Fluke chemicals company . The melting points were recorded using thermometer melting point apparatus, UK. The elemental analyses were recorded using E.A.G.E.R.-100, Carlo Erba, Italy. FT.IR spectra were recorded using Fourier transform infrared SHIMADZU FT.IR-8400S infrared spectrophotometer by KBr disc .^{1}H-NMR were recorded on Fourier transform Bruker spectrometer, operating at 400 MH_Z.

Synthesis Methods

Synthesis of[19]: 1,1`-((3,3`-dimethyl-[1,1`-biphenyl] -4,4` -diyl) bis (diazene-1,2-diyl)) bis(naphthalene-2- amine)Azo*ortho*-tolidine[A].

O-tolidine (2.12gm, 0.01 mole) was dissolved in mixture from (3.5ml) of concentrated hydrochloric acid and (40 ml) of distilled water. The mixture was cooled at (0 ^{0}C) in ice-water bath. A solution of sodium nitrite (1.72gm, 0.02 mole) dissolved in (6 ml) of distilled water. There was added a dropwise to the mixture with stirring. In the other beaker naphthyl amine (5.72gm, 0.02 mole) dissolved in (3gm) of sodium hydroxide and (200 ml) of distilled water and place this beaker in ice-water bath at (0 ^{0}C). The cold diazonium chloride was added to the coupling agent in small portions and stirred after each addition, A completing the addition, the reaction mixture was stirred at (0 ^{0}C) for (15) minutes. The black product was precipitated and filtered recrystallized from ethanol, yield (2.16 gm, 86%), (m.p.= 246 ^{0}C) and R_f =(0.72) (ethanol:Benzen , 1 : 3) the resulte of C.H.N identical. scheme(1).

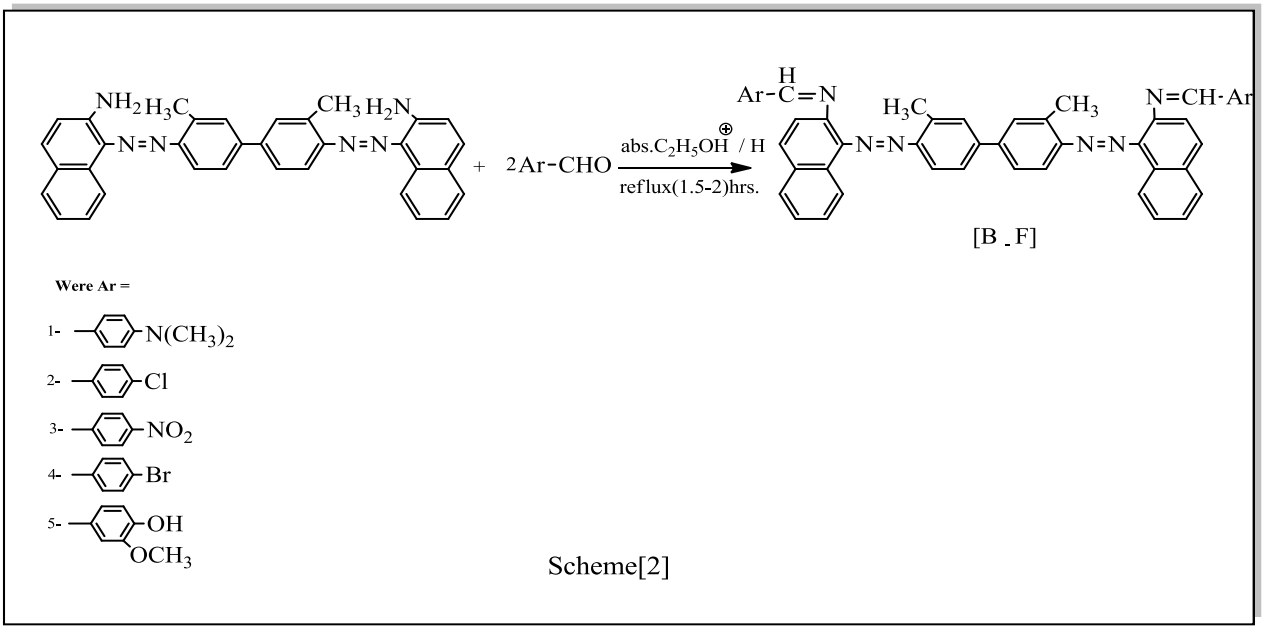


Scheme [1]

General procedure[20] : for Synthesis of Schiff bases derivaitives [B-F].

The Azo compound [A] (0.01mole) was added to a solution of the different benzaldehydes derivaitives (0.02mole) in 40ml of absolute ethanol and two drops of glacial acetic acid were, also,added to the above mixture. The mixture was refluxed for (1.5-2) hrs. The precipitates were

formed collected by filtration , dried and recrystallized from the appropriate and recrystallized from ethanol solvent.Then, TLC showed that the reaction was completed by using (ethyl acetate : toluene , 1 : 4). Scheme [2] . Table (1) represent some physical properties of compounds [B –F].



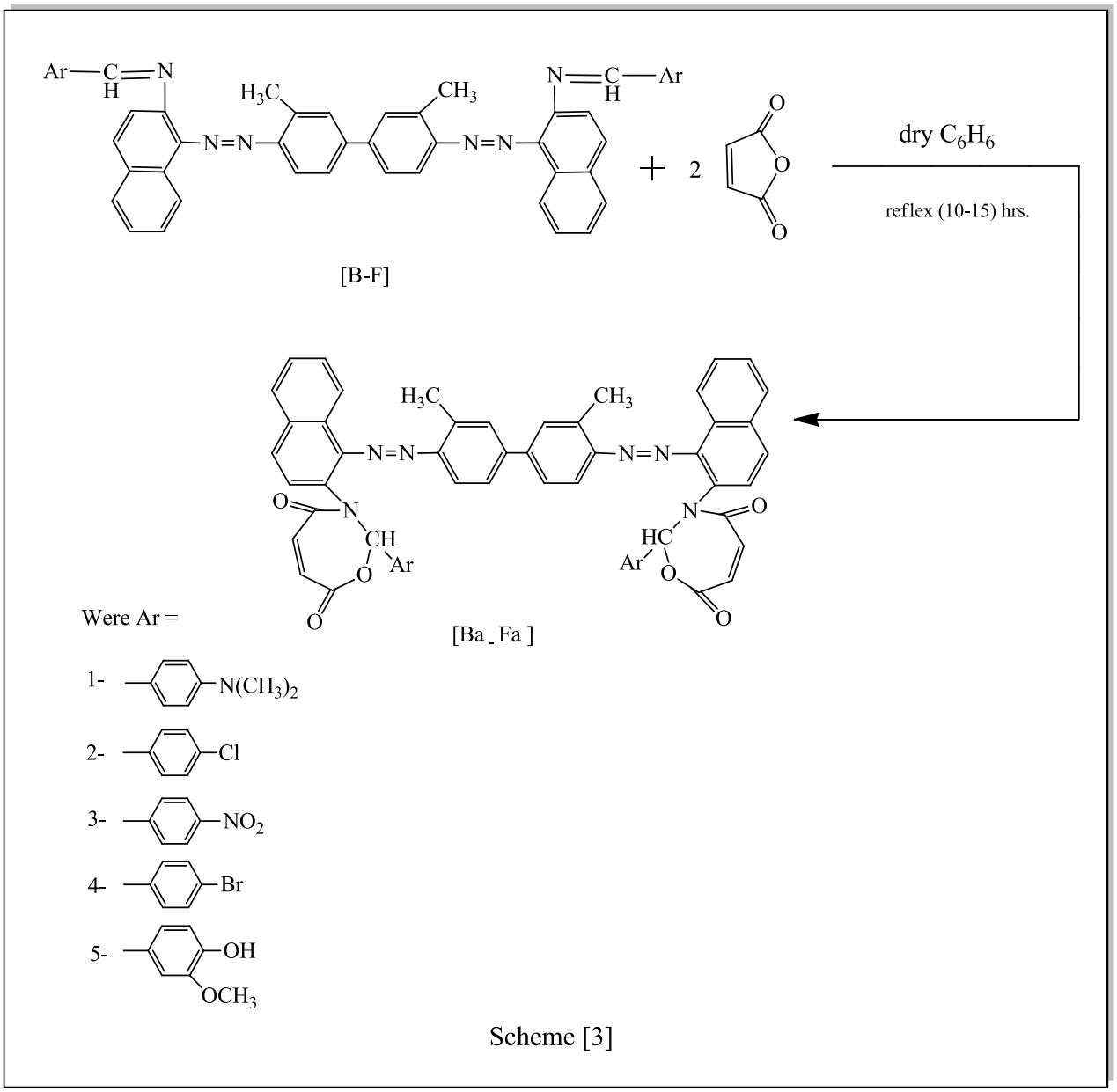
Scheme[2]

Table(1): some physical properties of compounds [B -F]

Comp. No	Molecular Formula	M.P ^{0}C	Yied %	R_f	Color	C.H.N		
B	$C_{54}H_{52}N_8$	126	83	0.65	Brown			
C	$C_{50}H_{40}Cl_2N_6$	115	86	0.56	Dark purple	C %	H %	N %
						75.46 (75.35)	5.07 (4.90)	10.56 (10.49)
D	$C_{50}H_{40}N_8O_4$	105	88	0.62	Black	C %	H %	N %
						73.51 (73.48)	4.94 (4.81)	13.72 (13.50)
E	$C_{50}H_{40}Br_2N_6$	118	85	0.58	Black Dark			
F	$C_{52}H_{46}N_6O_4$	110	87	0.68	Black glossy			

General procedure[21] :for Synthesis of 3,3`-(((3,3`-dimethyl-[1,1`-biphenyl]-4,4`diyl) bis (diazene-1,2-diyl)) bis(naphthalene-1,2-diyl))bis(2-aryl)-2,3-dihydro-1,3-oxazepine-4,7-dione]Azo *o*-tolidine [Ba-Fa] .

To the mixture of Azo Schiff bases [B-F](0.01mol) and maleic anhydride (0.02mol,1.96gm) in dry benzene (250 ml), The reaction mixture was stirred for (10-15 hrs.) at(55 ^{0}C),and at the end of the reaction.The precipitates were collected by filtration and the resulting colored crystalline solid was recrystallized from dry 1,4-dioxan. the TLC showed that the reaction was complete by using (ethyl acetate : toluene , 1 : 4) scheme[3]. Table(2) represent some physical properties of compounds [Ba-Fa] .



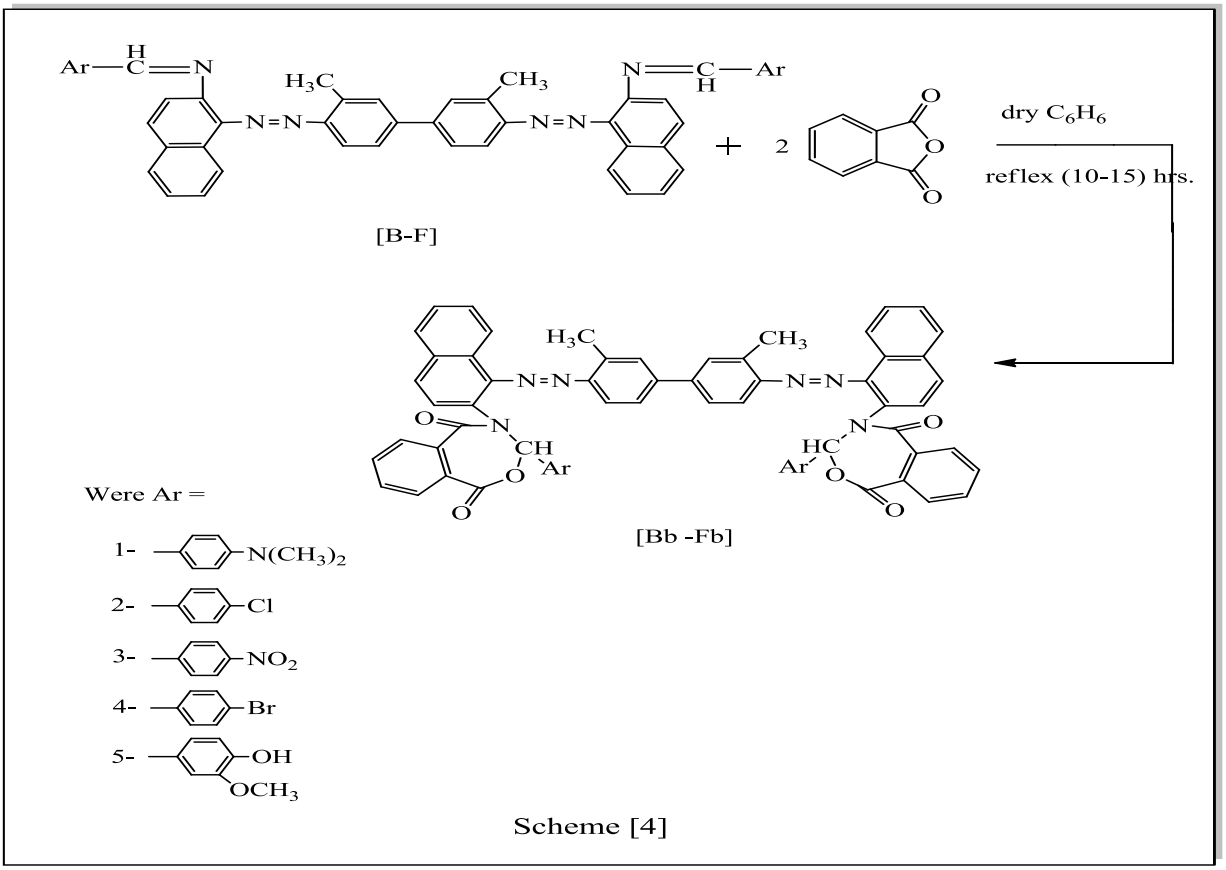
Scheme [3]

Table(2): Some physical properties of compounds [Ba-Fa]

Comp. No.	Molecular Formula	M.P ^{0}C	Yield %	R_f	Color	C.H.N		
						C %	H %	N %
Ba	$C_{60}H_{50}N_8O_6$	135	70.29	0.72	Black	73.60 (73.44)	5.15 (5.10)	11.14 (11.07)
Ca	$C_{56}H_{38}Cl_2N_6O_6$	138	77.9	0.66	Black			
Da	$C_{56}H_{38}N_8O_{10}$	148	73.5	0.78	Black			
Ea	$C_{56}H_{38}Br_2N_6O_6$	144	77.4	0.63	Black			
Fa	$C_{58}H_{44}N_6O_{10}$	141	80	0.68	Black			

General procedure[22] : for Syenthesis of 4,4'(((3,3`-dimethyl -[1,1`-biphenyl]-4,4`-diyl)bis(diazene-1,2-diyl))bis (naphthalene1,2-diyl))bis(3-(aryl-3,4-dihydrobenzol[e][1,3] oxazepine -1,5-dione] Azo *o*-tolidine [Bb-Fb].

To the mixture of Azo Schiff bases [B-F](0.01mol) and phthalic anhydride (0.02mol, 2.96gm) in benzene(250 ml), The reaction mixture was stirred for (10-15 hrs.) at(55 ^{0}C) .and at the end of the reaction. The precipitates were collected by filtration and the resulting colored crystalline solid was recrystallized from dry 1,4-dioxan. the TLC showed that the reaction was complete by using (ethyl acetate : toluene , 1 : 4) scheme(4) . Table(3) represent some physical properties of compounds [Bb-Fb].



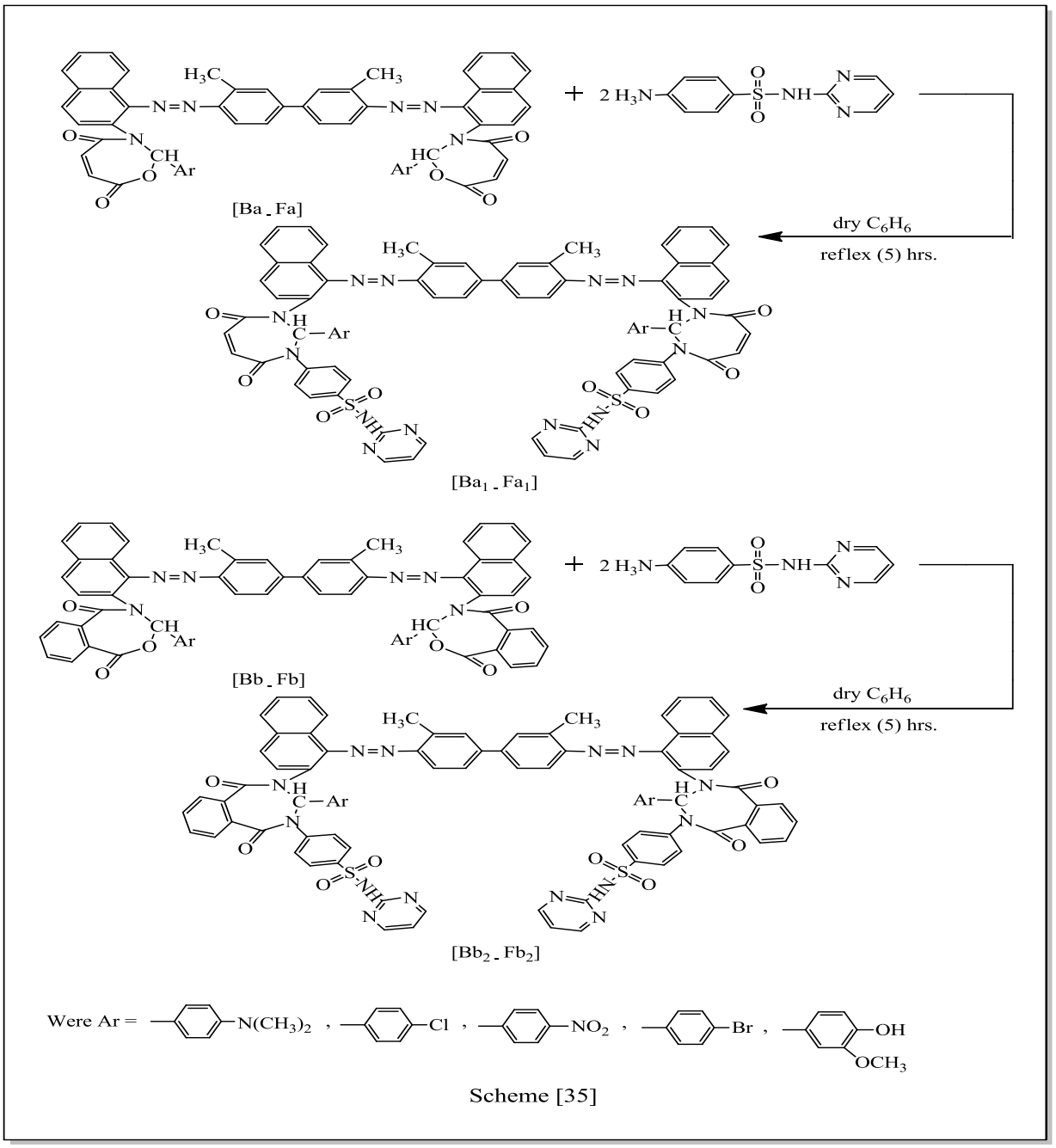
Scheme [4]

Table(3): Some physical properties of compounds [Bb-Fb].

Comp. No.	Molecular Formula	M.P ^{0}C	Yield %	R_f	Color	C.H.N		
Bb	$C_{68}H_{54}N_8O_6$	155	81.7	0.75	Dark orange			
C b	$C_{64}H_{42}Cl_2N_6O_6$	163	75.4	0.58	Dark orange			
Db	$C_{64}H_{42}N_8O_{10}$	158	80	0.76	Dark orange			
Eb	$C_{64}H_{42}Br_2N_6O_6$	168	72.43	0.72	Dark orange	C %	H %	N %
						66.79 (66.69)	3.68 (3.50)	7.30 (7.19)
Fb	$C_{66}H_{48}N_6O_{10}$	152	77.75	0.66	Dark orange			

General procedure[23] : Reaction of N-(pyrimidin-2-yl)benzene sulfonamide compound with3,3`-(((3,3`-dimethyl-[1,1`-biphenyl]-4,4`-diyl) bis (diazene-1,2-diyl))bis (naphthalene-1,2-diyl))bis(2-aryl)-1-methyl-2,3-dihydro-1*H*-1,3-diazepine-4,7-dione) (2:1)]Azo *o*-tolidine [Ba_1-Fb_2].

A mixture (0.0001mol) of oxazepin compounds and (0.0001mol) of sulfadiazene in (30ml) of dry benzen was placed. The reaction mixture was refluxed in water bath at 78 ^{0}C for(3- 5hrs) then allowed to cool to room tempreture and separated crystalline was filterd and re-crystallized from Ethanol . the TLC showed that the reaction was complete by using (ethyl acetate : toluene , 1 : 4).scheme[5]. Table(4) represent some physical properties of compounds [Ba_1-Fb_2] .



Scheme [35]

Table(4): Some physical properties of compounds [Ba_1-Fb_2].

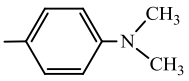
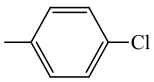
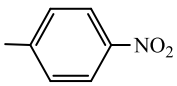
Comp. No.	Molecular Formula	M.P ^0C	Yield %	R_f	Color	C.H.N			
Ba_1	$C_{82}H_{74}N_{16}O_8S_2$	200	75.29	0.62	Yellowish orange				
Ca_1	$C_{78}H_{62}Cl_2N_{14}O_8S_2$	221	72.9	0.72	Brown				
Da_1	$C_{78}H_{62}N_{16}O_{12}S_2$	248	74.5	0.81	Yellow	C %	H%	N %	S%
						63.32 (46.52)	4.22 (4.48)	15.15 (20.10)	4.33 (11.70)
Ea_1	$C_{78}H_{62}Br_2N_{14}O_8S_2$	240	79.4	0.58	Yellowish brown				
Fa_1	$C_{80}H_{68}N_{14}O_{12}S_2$	227	77.54	0.53	Brown				
Bb_2	$C_{90}H_{78}N_{16}O_8S_2$	266	70.29	0.6	Yellowish orange				
Cb_2	$C_{86}H_{66}Cl_2N_{14}O_8S_2$	276	70.29	0.6	Yellowish brown				
Db_2	$C_{86}H_{66}N_{16}O_{12}S_2$	262	78.5	0.75	Light Brown				
Eb_2	$C_{86}H_{66}Br_2N_{14}O_8S_2$	272	75.4	0.7	Pale yellow				
Fb_2	$C_{88}H_{72}N_{14}O_{12}S_2$	268	79.54	0.83	Yellow	C %	H %	N %	S%
						66.82 (66.70)	4.59 (4.47)	12.40 (12.33)	4.05 (3.90)

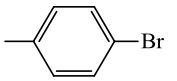
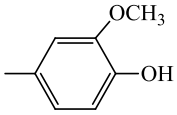
Results and discussion

The key intermediate compound [A]was made first by converted *o*- tolidine to the *o*-tolidine diazonium chloride by reaction with concentrated hydrochloric acid and sodium nitrite at $0C^0$. Diazonium salt was directly introduced in a coupling reaction naphthalene-2-amine to produce 4,4'-bis (3-amino phenol) Azo *o*- tolidine. The synthesis azo compound [A] was identified with FT.IR, showed disappearance of the two absorption bands at (3338cm^{-1}) and (3371 cm^1) were due to the stretching vibrations of (-NH_2) group of *o*-tolidine Figure [1] appearance of the azo compound showed of two absorption bands at (3441) cm^{-1} and (3367) cm^{-1} of the assymmetric and symmetric streching vibration of the two (-NH_2)groups. FT.IR spectrum also showed the appearance of absorption band at (1481cm^{-1}) for (N=N) group.stretching vibration of the (C-H) aromatic appear at (2929) cm^{-1}, The absorption bands at (827 cm^{-1}) were due to the bending vibration of (C-H) aromatic out of plane.

Azo *o*-tolidine derivative reaction with different carbonyl derivatives so as to form new schiff bases compounds [B -F] these compounds were characterized by FT.IR which showed disappearance of two absorption bands at (3441) $cm^{-1}$and (3367) cm^{-1} of the assymmetric and symmetric streching vibration of the two (-NH_2) groups . and appearance band at (1591-1598) cm^{-1} of streaching vibraition of two (C=N) imine group .Other data of functional groups were showed in table [5].

Table(5): FT .IR data of compounds[B-F].

Comp. No.	Ar	υ (C=C) Str. Aromatic cm^{-1}	υ (C=N) Str. Imine cm^{-1}	υ (N=N) cm^{-1}	δ(C-H) Bending cm^{-1}	Others cm^{-1}
B		1352 1377	1595	1541	885	υ(C-N) Str. :1178
C		1386 1413	1598	1510	997	υ (C-Cl) Str. : 777 750
D		1404	1593	1521	844 819	υ (C-NO_2) Str. : 1346 asy.

E		1483	1591	1541	881	υ (Ar-Br)Str. : 813 763
F		1402	1593	1521	815	υ(Ar-OH) Str. : 3427

Then, the imines results derivatives [B -F] were reacted with maleic anhydride and phathalic anhydride in dry benzene to give new 1,3-oxazepine-4,7-dione ring derivatives [Ba-Fa] and [Bb-Fb] respectively. these compounds were characterized by FT.IR in Table 6,7 as flow:-

Table(6): FT .IR data of compounds[Ba-Fa].

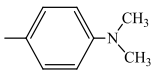
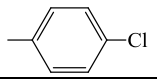
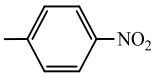
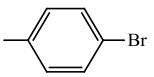
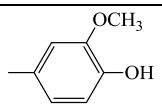
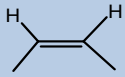
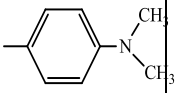
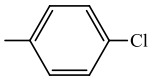
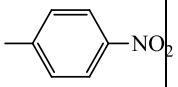
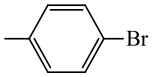
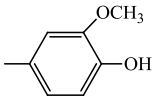
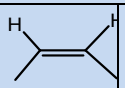
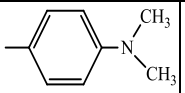
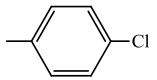
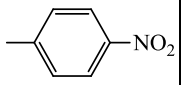
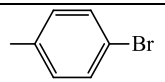
Comp. No.	**Ar**	**υ (C=C) Aromatic cm^{-1}**	**υ (C-H) Str. Benzylic cm^{-1}**	**υ (C=O)str Lactone Lactam cm^{-1}**	**υ (C-N) Str. cm^{-1}**	**υ (N=N) cm^{-1}**	**υ(C-O) Str. Lactone cm^{-1}**	**Others cm^{-1}**
Ba		1433 1462	3059	1710 1637	1219	1593	1263	υ(N-CH_3) Str: 2796asym. 2605sym.
Ca		1435 1460	3059	1708 1639	1166	1591	1263	υ (C-Cl) Str. 866
Da		1435 1462	3059	1708 1637	1219	1595	1265	υ(C-NO_2) Str:1341
Ea		1433 1462	3061	1710 1633	1217	1579	1263	υ(Ar-Br)Str. : 866
Fa		1435 1463	3059	1708 1635	1219	1568 1593	1265	υ(Ar-OH) Str. : 3433

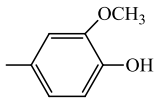
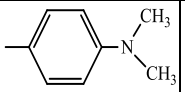
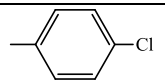
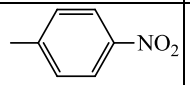
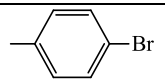
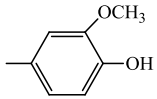
Table (7):FT .IR and ^{1}H-NMR data of compound [Bb-Fb].

FT.IR						^{1}H-NMR			
Comp No.	**Ar**	**υ (C-H) Str. Benzylic cm^{-1}**	**υ(C=O)str Lactone Lactam cm^{-1}**	**υ (C-N) Str. cm^{-1}**	**υ (C-O) Str. Lactone cm^{-1}**	**δ(C-H) Aromat. ppm**		**CH of oxazepine ring**	**3H of CH_3 *O*-tolidine**
Bb		3062	1766 1691	1163	1259				
Cb		3064 3095	1764 1633	1166	1257	8.1	6.9-7.1	7.9	2.5
Db		3095 3142	1764 1674	1165	1255				
Eb		3132	1764 1631	1165	1255	8.2	7.2-7.3	7.8	2.5
Fb		3061 3097	1762 1629	1166	1255	7.9	7.4-7.5	7.8	2.4

Then,1,3-Oxazepine derivatives [Ba-Fa] and [Bb-Fb] were reacted with sulphadiazine in dry benzene to give new 1,3-Dizepine -4,7-dione ring derivatives [Ba_1-Fb_2] . these compounds were characterized by FT.IR in Table(8).

Table (8):FT .IR and ^{1}H-NMR data of compound [Ba_1-Fb_2].

FT.IR								^{1}H-NMR						
Comp. No.	Ar	υ (N-H) Str. cm^{-1}	υ (CH=N) Pyrimidine cm^{-1}	υ(C=O)str. Lactone Lactam cm^{-1}	υ SO_2 Str. cm^{-1}	υ (N-H) Bending cm^{-1}	υ (C-N) Str. Lactone cm^{-1}	δ(C-H) Aromatic ppm		CH of Diazepine ring	NH Sulphadiazene	HC=N pyrimidne	δ(C-H) of CH_3 *O*-tolidine	Others ppm
Ba_1		3363 3425	3035 3105	1727 1641	1327asy. 1155sy.	1402 1446	1259	7.6	6.5-6.7	7.3	11.3	8.5	2.5	(s , 6H , N-CH_3): δ1.8
Ca_1		3356 3421	3076 3105	1710 1651	1325asy. 1155sy.	1406 1442	1261							
Da_1		3358 3423	3080 3105	1724 1627	1325asy. 1153sy.	1442	1261	7.9	6.6-6.8	7.3	11.2	8.5	2.5	-
Ea_1		3363 3423	3082 3105	1720 1643	1325asy. 1155sy.	1406 1442	1259							

Fa_1		3358 3423	3082 3105	1710 1647	1325asy. 1155sy.	1406 1442	1259	7.8	6.5-6.7	7	11.5	8.5	2.5	(s,3H ,O-CH_3) :δ3.80 (s , H ,OH): δ6.0
Bb_2		3358 3423	3037 3107	1717 1651	1325asy. 1153sy.	1406 1442	1263	7.6	6.5-6.8	7.1	11.2	8.5	2.5	(s , 6H , N-CH_3): δ1.5
Cb_2		3361 3423	3078 3103	1705 1645	1323asy. 1153sy.	1406 1440	1265							
Db_2		3356 3421	3076 3105	1716 1649	1323asy. 1153sy.	1406 1440	1265	7.7	6.5-6.7	7	11.3	8.5	2.5	-
Eb_2		3360 3425	3078 3101	1718 1639	1323asy. 1153sy.	1402 1442	1269							
Fb_2		3389 3423	3037 3107	1743 1662	1325asy. 1155sy.	1406 1444	1257							

Antibacterial activity:

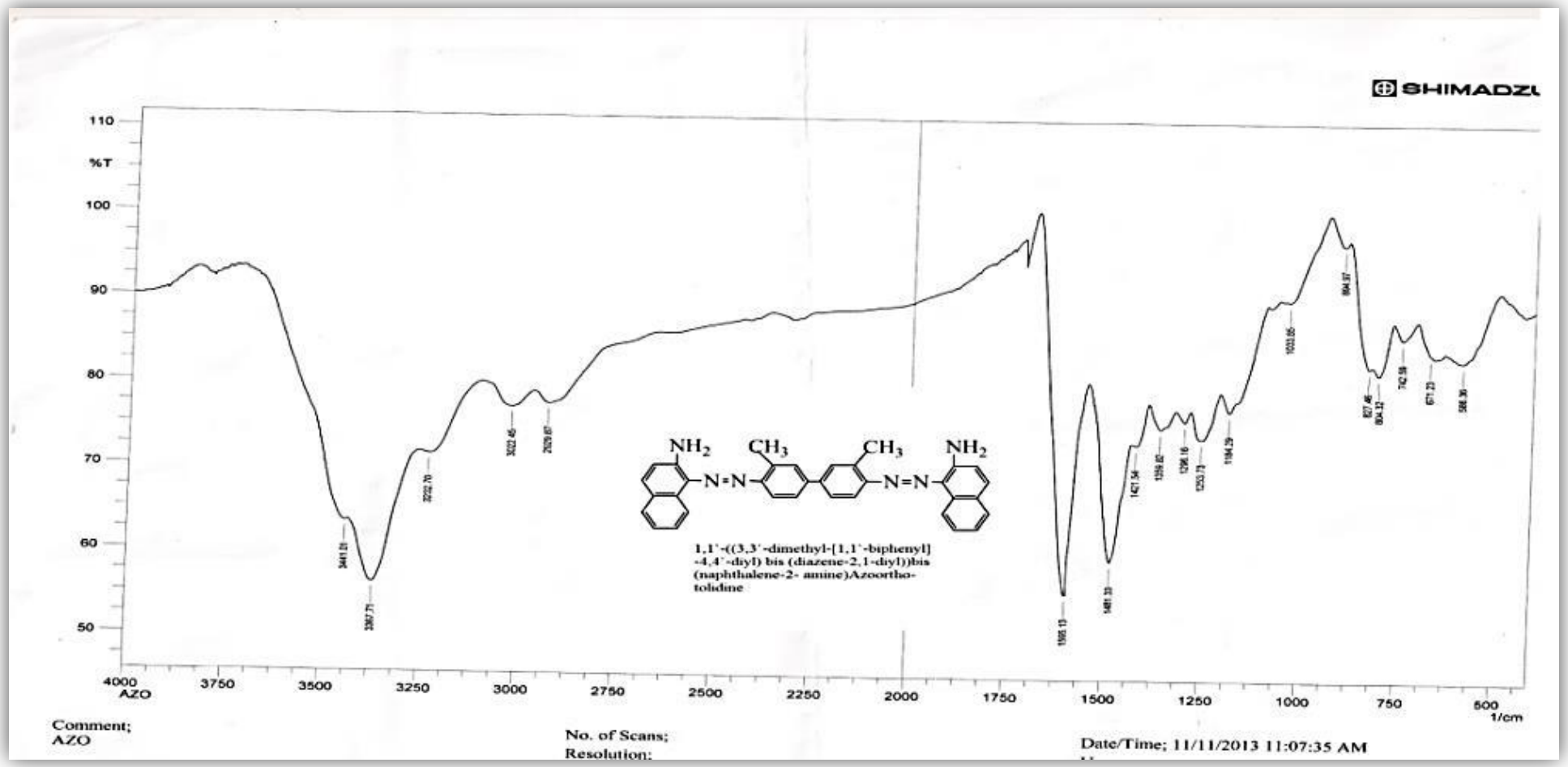
The prepared compounds**(Ea_1,Db, Fa_1,Ea,Da_1,Gb,Eb,Cb,Ba_1 and Bb_2)** were examined for antibacterial activity against *Staphylococcus aureous, Staphylococcus saprophyticus* (Gram-positive) and *Kelebsiella pneumonia, Escherichia. Coli* (Gram-negative) in Diluted solution Figure [3-38] and the concentration solution Figure [3-39] by Well diffusion method in Mueller-Hinton agar medium. After 24 hours were measured for zone of inhibition around each disc. The test results presented in Table [11] and [12].

Table [9] Antibacterial activity of compound(Ea_1,Db, Fa_1,Ea,Da_1 ,Fb, Eb, Cb, Ba_1,Bb_2) in Diluted solution.

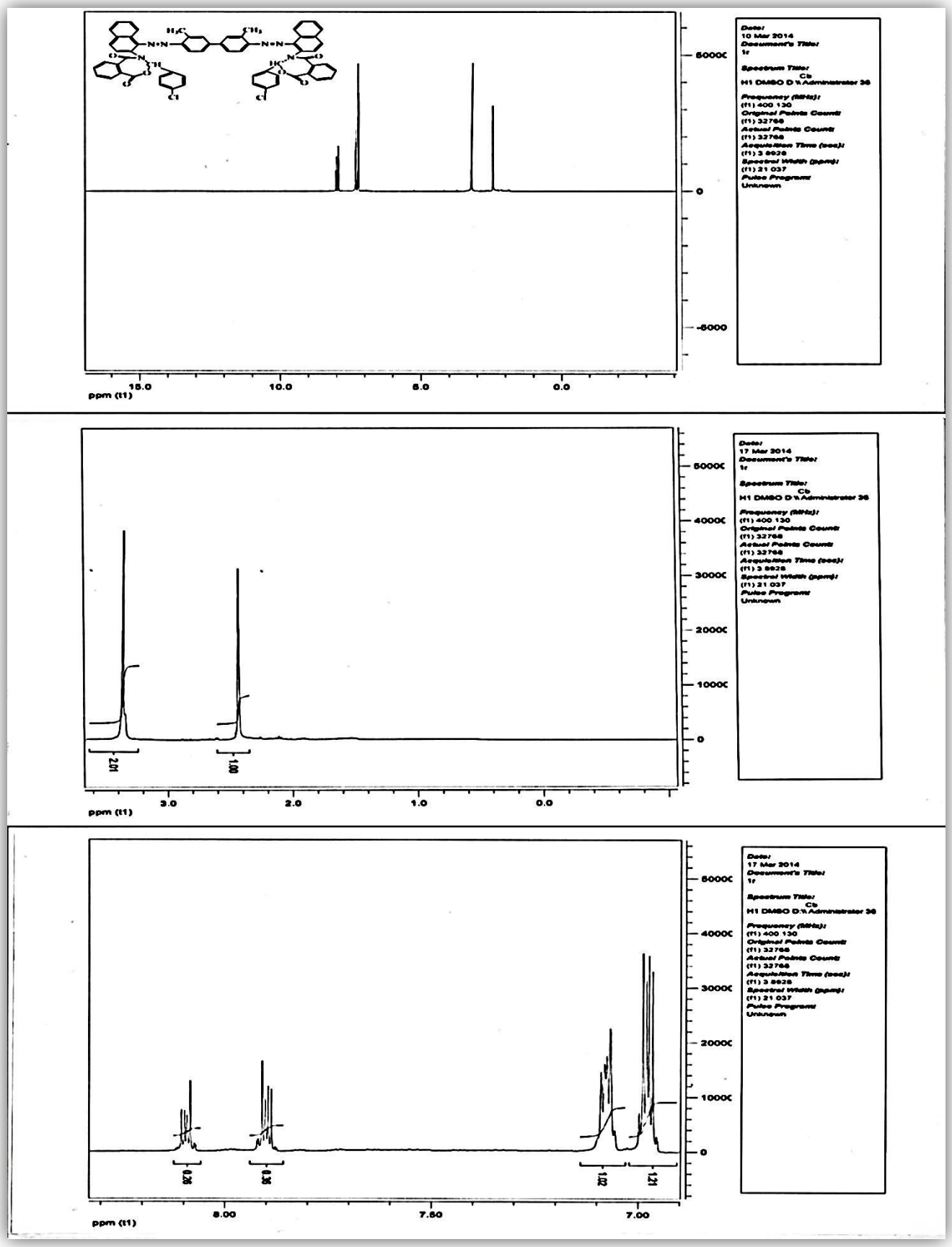
Bacteria	**(Gram-positive)**		**(Gram-negative)**	
Comp. No.	***Staphylococcus aureous***	***Staphylococcus saprophyticus***	***Escherichia Coli***	***Klebsiella Pneumonia***
1-Ea_1	-	-	-	1.7
2-Db	1.5	1.3	-	1
3-Fa_1	-	-	-	1.6
4-Ea	1	1.6	-	-
5-Da_1	-	-	-	1.8
6-Fb	1.9	1.6	1.5	1.5
7-Eb	1.4	1.5	1.4	1.4
8-Cb	1.3	1.9	1.3	1.3
9-Ba_1	-	-	-	-
10-Bb_2	-	-	-	-

Table [10] Antibacterial activity of compound(Ea_1,Db, Fa_1,Ea,Da_1, Fb ,Eb,Cb,Ba_1,Bb_2) in concentration solution.

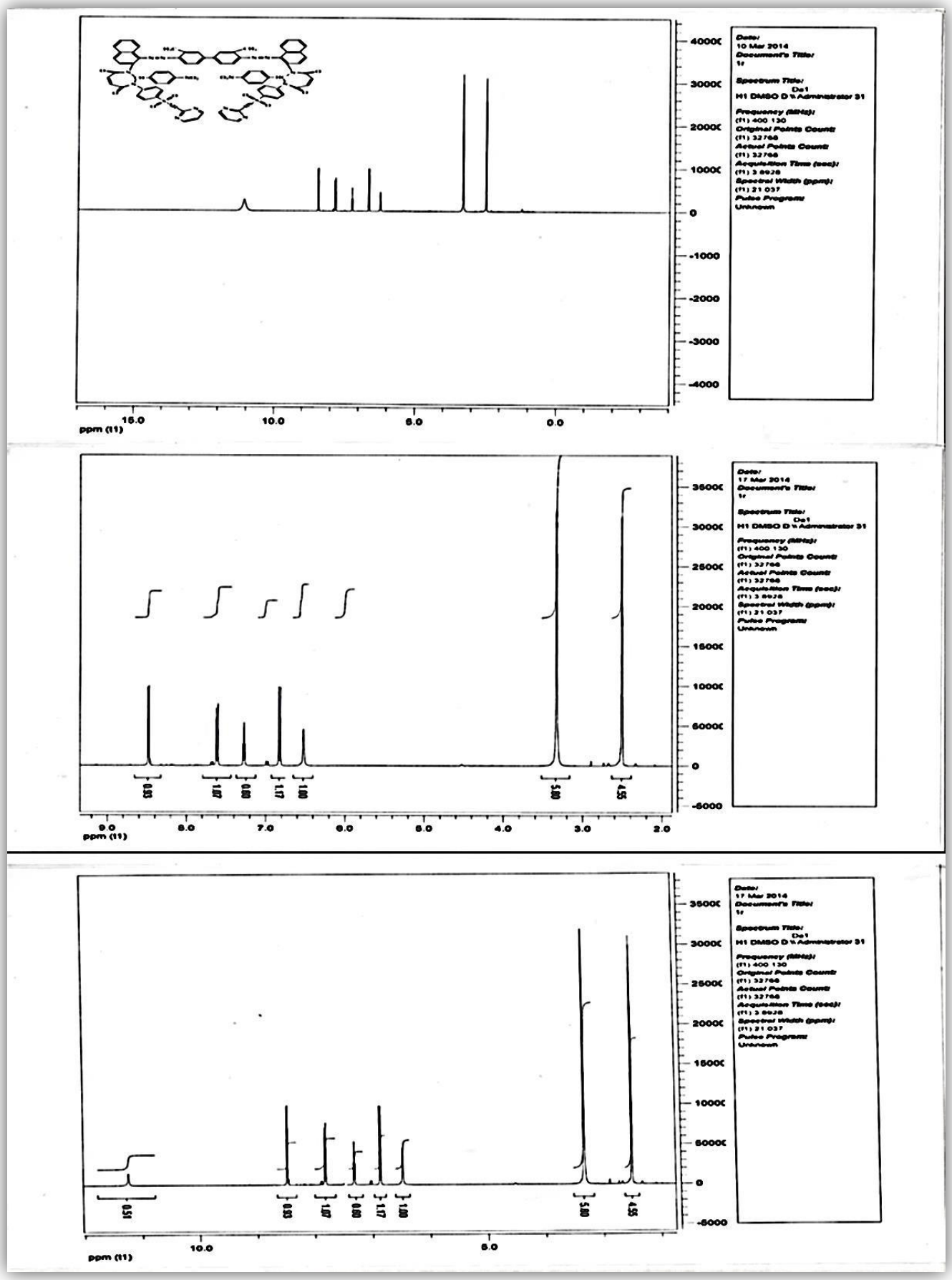
Bacteria / **Comp. No.**	**(Gram-positive)**		**(Gram-negative)**	
	Staphylococcus aureous	***Staphylococcus Saprophyticus***	***Escherichia Coli***	***Klebsiella Pneumonia***
1-Ea_1	-	-	-	-
2-Db	1	1.5	1.5	1.5
3-Fa_1	-	-	-	2.3
4-Ea	-	-	1.5	2
5-Da_1	-	-	-	1.5
6-Fb	1.9	1.4	2.5	2
7-Eb	1.5	1.5	2	1.5
8-Cb	1.4	1.3	2	1.5
9-Ba_1	-	-	-	2
10-Bb_2	-	-	-	1.5



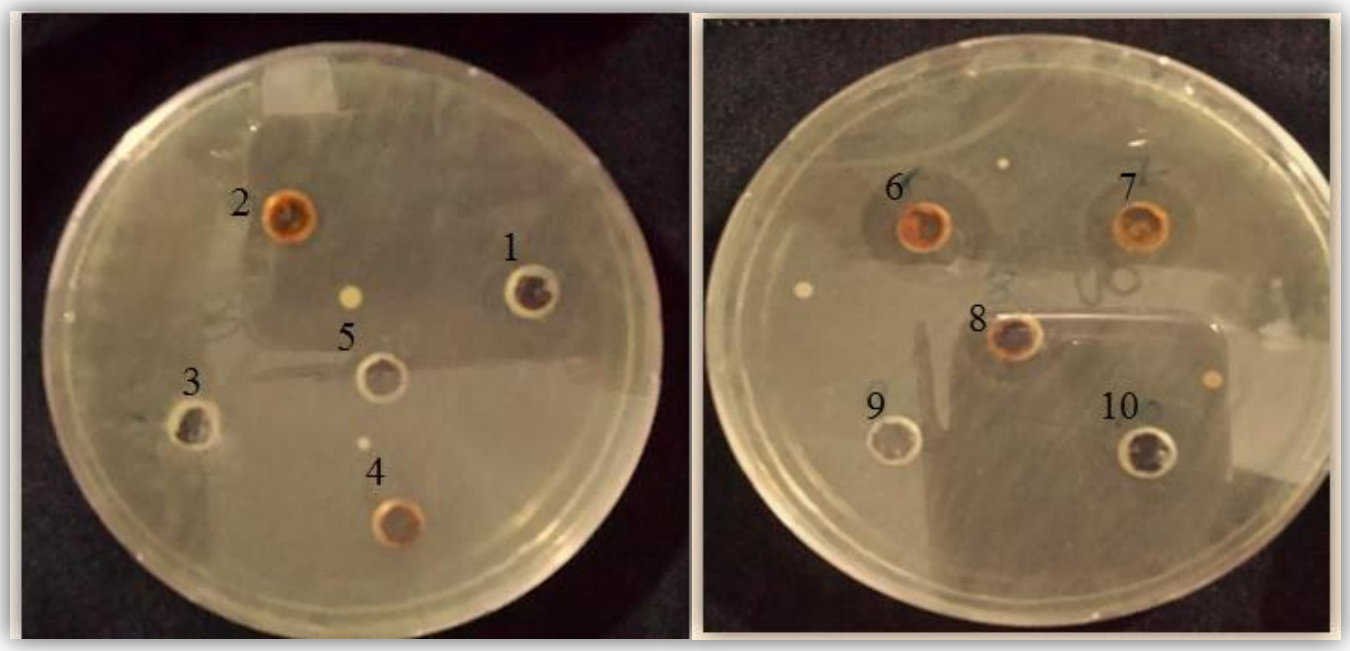
Figure(1)FT.IR spectrum of compound [A]



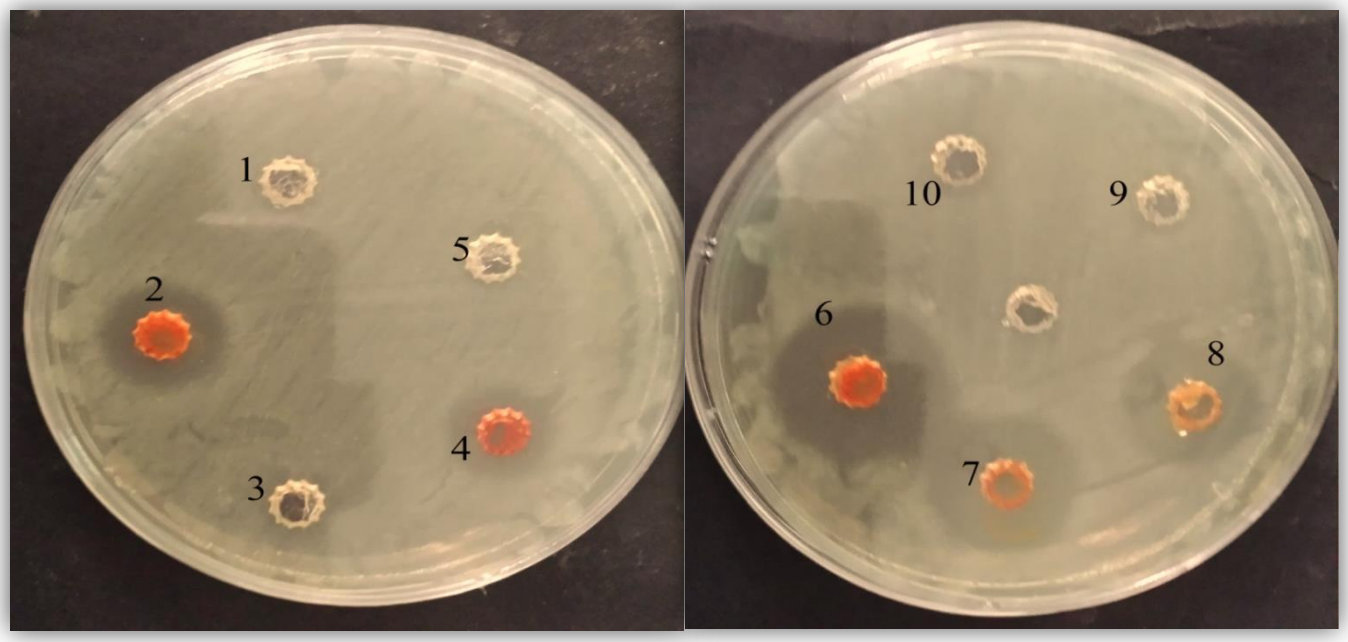
Figure[2] ^{1}H-NMR Spectrum of Compound [Cb].



Figure[3] ^{1}H-NMR Spectrum of Compound [Da_1]

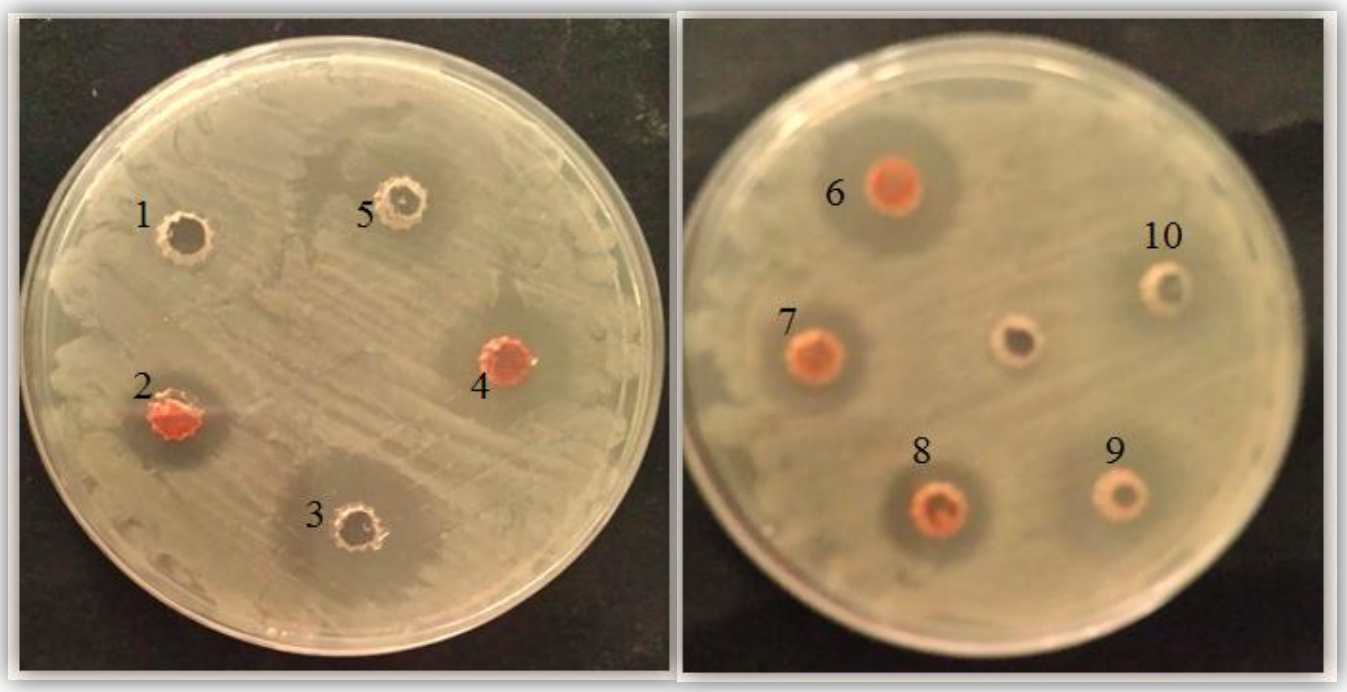


Staphylococcus aureus

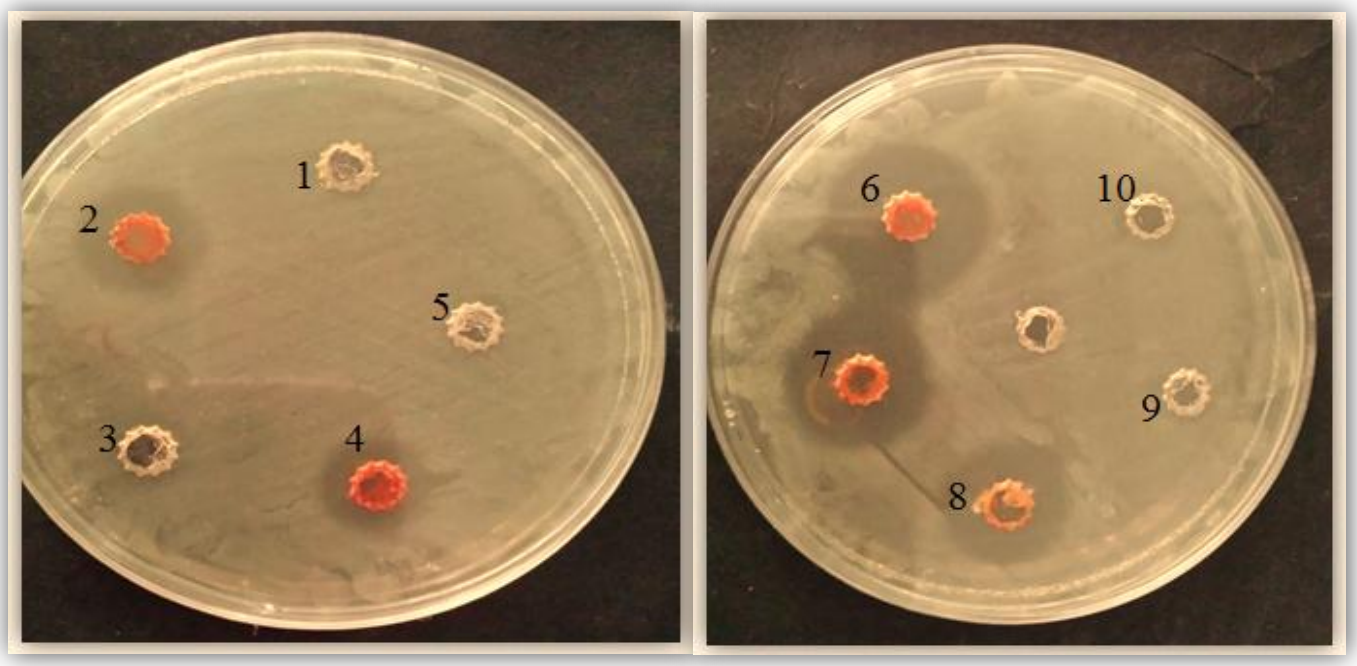


Staphylococcus Saprophyticus

Figure [4] antibacterial activity in Diluted solution



Klebsiella pneumoniae



Escherichia coli

Figure [5] antibacterial activity in concentration solution

Conclusions:

The study arrived at the following Conclus:

1-The electron-donating and the electron-withdrawing groups affect the determination of the time of the reaction. The electron-donating group increases the rate of the reaction, therefore the time of the reaction decreases.While the electron-withdrawing group decreases, the rate of the reaction, therefore, the time of the reaction was increases'.

2-All synthesized compounds were stable by resonance and having high melting points relatively; this is another evidence in relaition to stability.

3-Diazepine derivaitives is more stable than the other derivatives due to connected with sulphadiazine moleculer,which are increase stability due to highly moleculer weight and highly resonance.

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