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Research Article

SYNTHESIS AND BIOLOGICAL STUDY OF NITROGEN CYCLIC COMPOUNDS

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Abstract

In this work , di carbonyl compounds has been used to the reaction with P -formal benzaldehyde forming the corresponding bis(Dimethyl malonate) which ciclyze with di amine compounds to produce bis { (5,6,7) –memberedof di aze cycles } , & some of them reacts with different amino compounds to produce corresponding bis substituted .The structures of the synthesized compounds [1-10] have been confirmed by (FT.IR -spectra , H.NMR -spectra , C.H.N - analysis) & melting points .

Keywords: carbonyl compounds , diazolidine , formal.

Introduction

Di alkyl malonate is important class of compounds is several field of organic chemistry such as alkylation of carbonyl[(1,2)] compounds , incorporation with heterocyclic compounds to produce pharmaceutical compounds which have a wide range of pharmacologcal properties[(3-5)] in pharmaceutical chemistry field , because of the number & the significance of these applications , many methods[(6,7)] have been reported for the preparation of these compounds in the last years (diazolidine , diazine , diazepan)[(8-11)] .

Di nitrogen (di az)-containing heterocyclic compounds[(12,13)] have received considerable attention due to their biological activity which represented as anti tumer , anti viral , anti fungal , anti cancer , analagesic , anti -Hiv , anti microbial ...etc .

In recent years , chemistry of di az compounds developed very fast due to the discovery of the diverse biologically active (diazolidine , diazine , diazepan) derivatives[(14)] .

Experimental

All chemical used from BDH & sigma -company , FT.IR -spectra were recorded on shimadzu 8300 , Kbr -disk ., H.NMR -spectra & (C.H.N) -analysis were recorded in Malaysia , the melting points were determined by digital - electrothermal 9300 LTD , UK .

Synthesis of compounds [1,2] :

A mixture of P -formal benzaldehyde (0.1 mole) reacted with di methyl malonate (0.2 mole) in basic medium of sodium hydroxide (10%) with mechanical stirr at room temperature for (4hrs) , the precipitate was filtered & recrystallized to yield 88% of compounds [1] , which (0.1 mole) reacts according to procedures[(2,9)] with (0.1 mole) of methylene di amine under reflux for (3hrs) in presence of absolute ethanol , the precipitate was filtered & recrystallized to give 89% of compounds [2] .

Synthesis of compounds [3-6] :

The synthesis of these compounds was carried out according literature[(2,9)] , a mixture of compound [2] (0.01 mole) with one of (0.01 mole) from (hydrazine , methylene di amine , quanidine , ethelyne di amine) respectively were heated under reflux for (5hrs) in presence of absolute ethanol , the precipitate was filtered & recrystallized to yield (87 , 85 , 87 , 89) % of compounds [3-6] respectively .

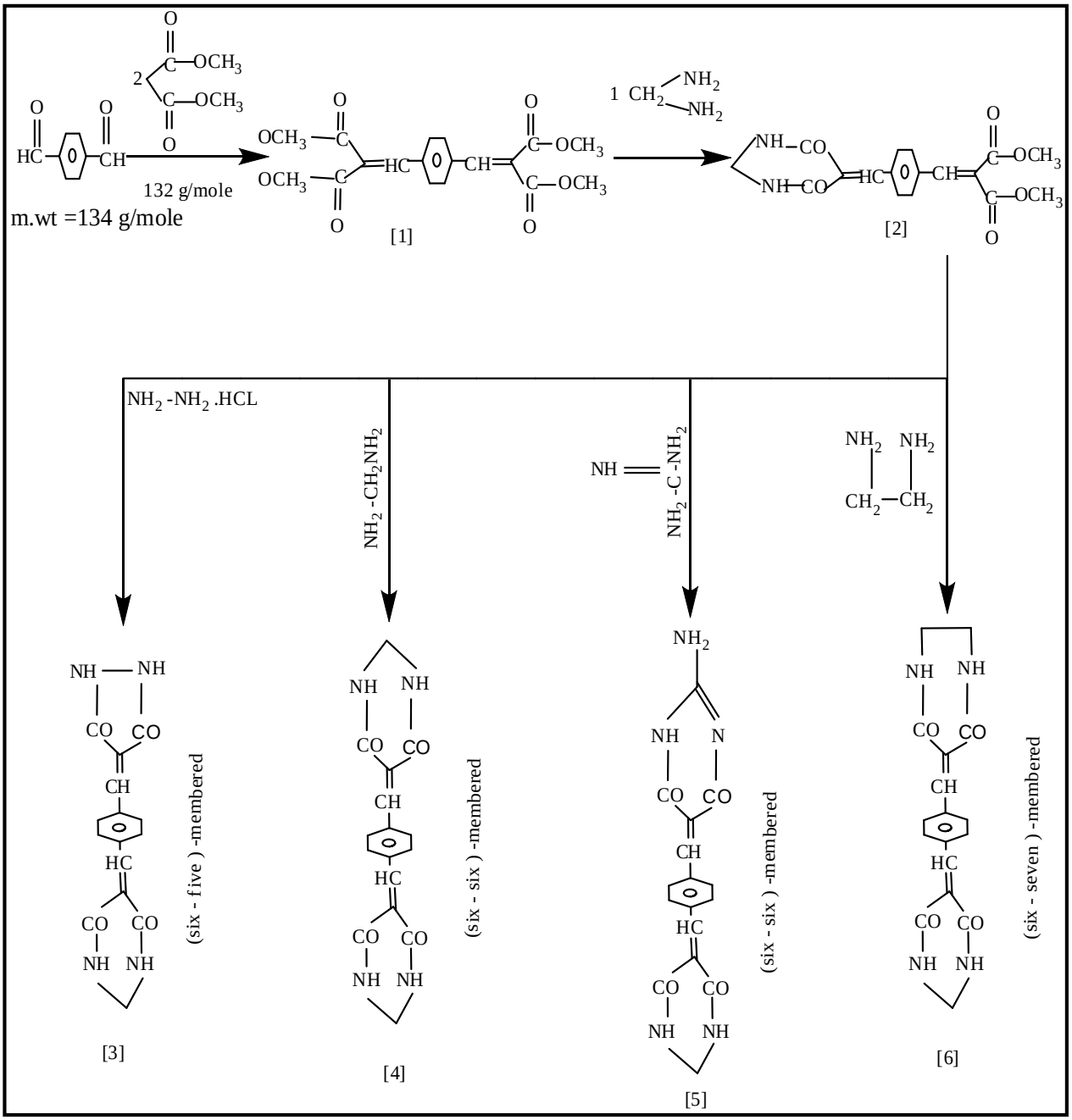
Synthesis of compounds [7-9]

According to procedure[9] , a mixture of compounds [2] (0.01 mole) with one of {(0.02 mole) from (2 -amino thiophene, 2 -aminothiazole) (0.01 of aniline)} respectively were refluxed for (5-6 hrs) in presence of absolute ethanol , the precipitate filtered recrystallized to yield (85 , 87 , 88) % of compounds [7-9] respectively .

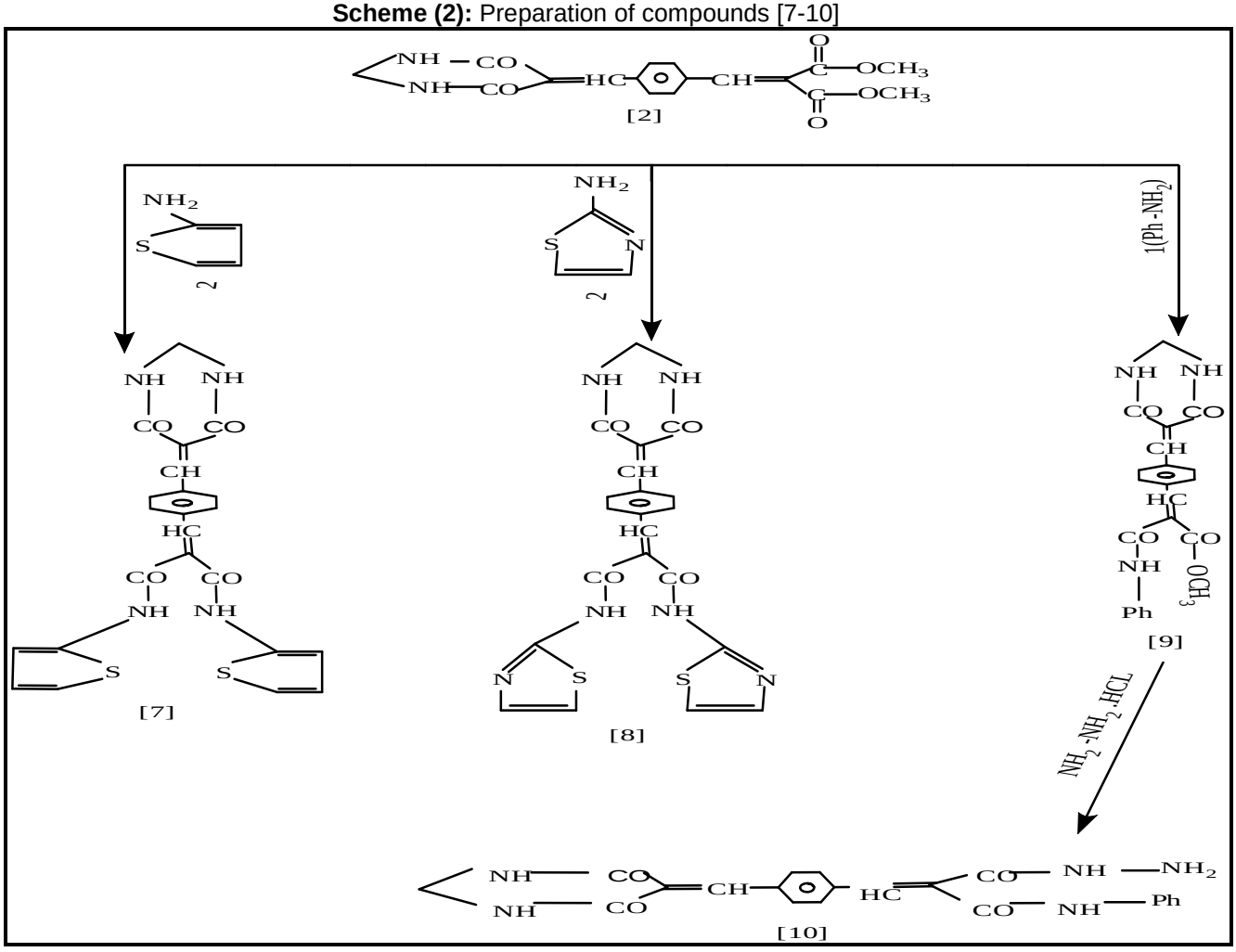
Synthesis of compound [10]

A mixture of equimolar (0.01 mole) of compound [9] with hydrazine were reacted under reflux for (4hrs) &stirr , precipitate was filtered & dried ,recrystallized to yield 86 % of compound [10] .

Scheme (1): Preparation of compounds [1-6]



Scheme (2): Preparation of compounds [7-10]



Results and discussion

The formation of compound [1] as starting compound proceed via reaction between dimethyl malonate with di aldehyde compound such as P -formal benzaldehyde , then compound [1] reacts with diamine compounds such as (methylene diamine , hydrazine , guanidine , ethylene diamine to yield cyclic compounds [2-6] , & compound [2] reacts with primary amine compounds in one side or two side from compound [2] to yield compounds [7-10] .

All these compounds characterized by I.R -spectra , (C.H.N) -analysis , melting points &some of them by H.NMR -spectra :

The I.R -spectra , showed an absorption band at (3026-3095) cm^{-1} due to (CH=C) of alkene in all compounds [1-10] for formation of double bond of alkene , absorption band at (1728) cm^{-1} due to carbonyl of ester group[(2)] (CO-O-) in compounds [1,2] which disappeared one of them & appeared other bands such as {(1660 - 1696) , (3278 - 3478) } due to {(carbonyl of amide CO-NH) , (amine of amide NH - CO) }[(2)] respectively in compounds [3-10] , & other bands are summarized in table (1) & figures (1-10) .

The H.NMR -spectra showed important peaks at ȝ(6.40-6.60) due to proton of (CH=C) alkene in all compounds , peaks at ȝ(10.03-10.28) due to (NH-CO) proton of amide[(2)] in compounds [2,3,8,9] , peaks at ȝ (3.85 ,4.30) due to protons of methyl group in ester (-$COOCH_3$) in compounds [2,9] respectively , peaks at ȝ(3.35-3.62) due to protons of methylen[(15)] in cycle (NH-CH_2-NH) in compounds [2,3,8,9] , & other signals of functional groups show in the following , table (2).

The (C.H.N)-analysis & melting points , the experimental data were good results with calculated data , all these data & physical properties in table (3)

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Table (1) : (FT.IR) -data (cm^{-1}) of compounds [1-10]

Comp. No.	(Only important frequency)			
	(CO) carbonyl of amide	(NH) of amide	(CH=C)	Other groups
[1]	----	----	3048	(CO-O-)carbonylof ester :1728
[2]	1660	3482	3046	(CO-O)carbonyl of ester: 1714
[3]	1695	3299	3091	-------
[4]	1696	3290	3070	------
[5]	1688	3312	3080	(C=N) :endocycle : 1537 , (NH_2) :3478 .
[6]	1691	3492	3091	------
[7]	1696	3317	3091	(C-S) in thiophene ring :676 ,1271
[8]	1686	3278	3081	(C-S) in thiophene ring :675 , 1211 , (C-N) in thiophene ring :1168
[9]	1682	3478	3026	(CO-O-) carbonyl of ester :1728
[10]	1688	3278	3095	(NH_2) : 3300 .

Table (2) : H.NMR (ƍ ppm) of some Compounds .

Comp. No.	$H.NMR_{((DMSO))}$ ((Only important peaks))			
	(NH) of amide	(CH=C)	methylene of ($NH-CH_2-NH$)	Other peaks
[2]	10.04	6.60	3.62	4.30($COOCH_3$)methyl of ester .
[3]	10.10 , 10.28	6.40 , 6.66	3.50	----
[8]	10.08 , 10.22	6.45	3.55	7.35 (proton of thiazol ring)
[9]	10.24 , 10.03	6.50	3.35	3.85 ($COOCH_3$)methyl of ester

Table (3) : Physical properties & (C.H.N) -analysis of Compounds [1-10] .

Comp. No.	M.F	M.p (+2)C	Name of compounds	Calc. /Found.		
				%C	&H	%N
[1]	$C_{18}H_{18}O_8$	162	1-{(1ˉ,4ˉ-phenyl)-tetra methyl -bis (2 -ene - propanoate)} .	59.668 59.421	4.972 4.763	--- ---
[2]	$C_{17}H_{16}O_6N_2$	189	1-{2-(diazane-4,6-dione)styrene}-3-dimethyl-2-ene-propanoate	59.302 59.188	4.651 4.44	8.139 8.09
[3]	$C_{15}H_{12}O_4N_4$	194	2-(diazane-4,6-dione)-2-(diazolidine-3,5-dione)-4- ethene-1-styrene .	57.692 57.38	3.846 3.67	17.948 17.71
[4]	$C_{16}H_{14}O_4N_4$	198	2,2-bis(diazane-4,6-dione)-4-ethene -styrene .	58.895 58.625	4.294 4.13	17.177 17.05
[5]	$C_{16}H_{13}O_4N_5$	220	2-(diazine-4,6-dione-2-amino)-2-(diazane-4,6-dione)-4-ethenestyrene .	56.637 56.37	3.384 3.601	20.64 20.41
[6]	$C_{17}H_{16}O_4N_4$	208	2-(diazepane-5,7-dione)-2-(diazane-4,6-dione)-4-ethene-styrene .	60.00 59.93	4.705 4.44	16.470 16.25
[7]	$C_{23}H_{18}O_4N_4S_2$	241	(1,4-phenyl)-2-(diazane -4,6-	57.740	3.765	11.715

			dione)-ethene-2-bis (thiophene amide) ethene .	57.51	3.56	11.54
[8]	$C_{21}H_{16}O_4N_6S_2$	284	(1,4-phenyl)-2-(diazane -4,6-dione)-ethene-bis (thiazole amide) ethene .	52.5 52.31	3.33 3.20	17.50 17.27
[9]	$C_{22}H_{19}O_5N_3$	273	(1,4-phenyl)-2-(diazane -4,6-dione)-ethene-2-(phenyl amide)-3-methyl-1-ene -propanoate .	65.18 65.04	4.69 4.43	10.37 10.27
[10]	$C_{21}H_{19}O_4N_5$	259	(1,4-phenyl)-2-(diazane-4,6-dione)-ethene-2-(phenyl amide)-3-hydrazo-3-one -1-propane .	62.22 62.10	4.69 4.29	17.28 17.15

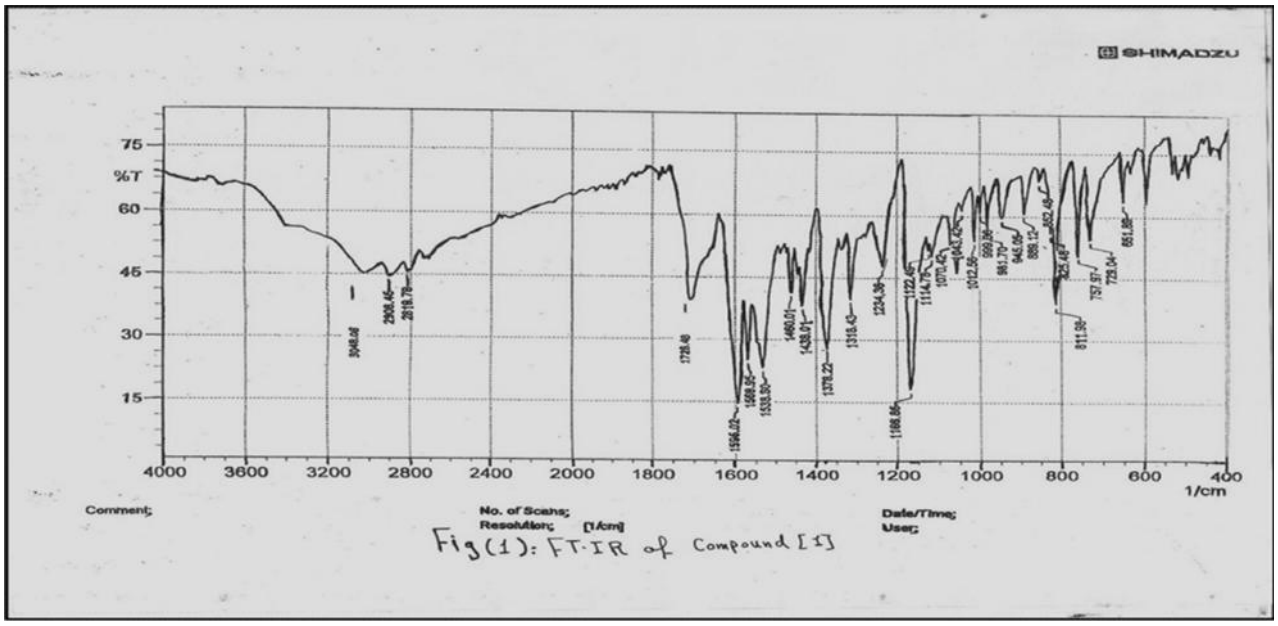


Fig (1) : FT.IR of compound [1]

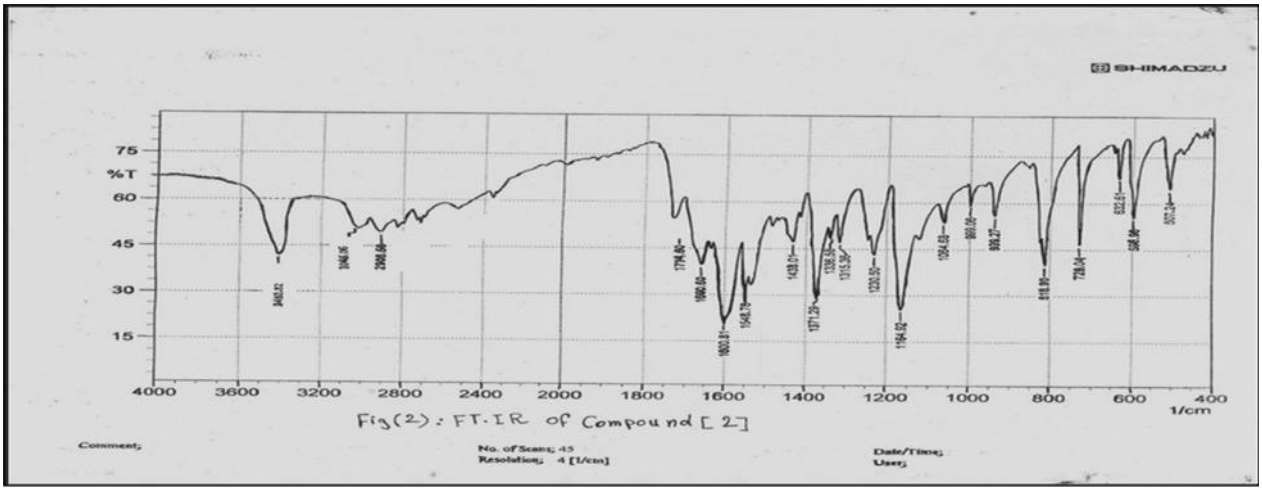
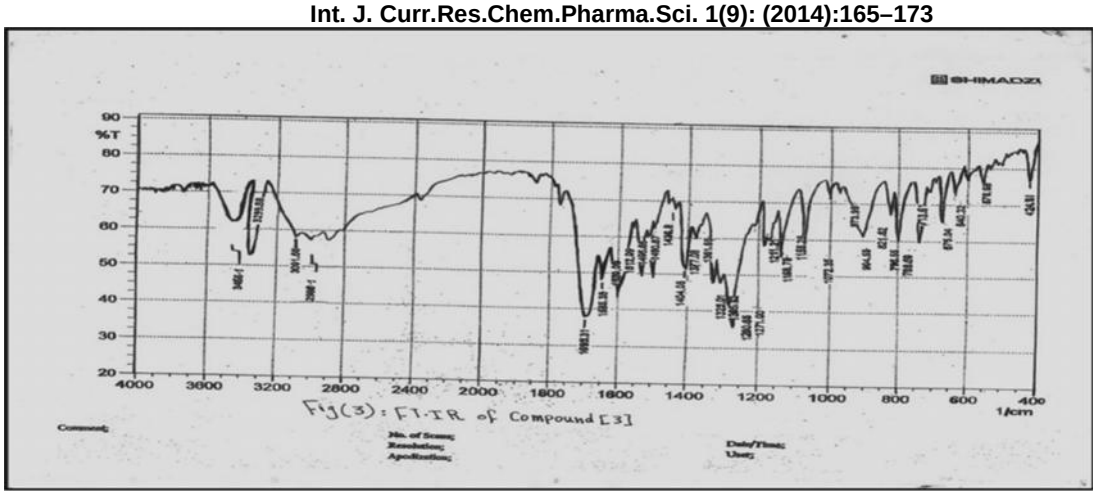


Fig (2) : FT.IR of compound [2]



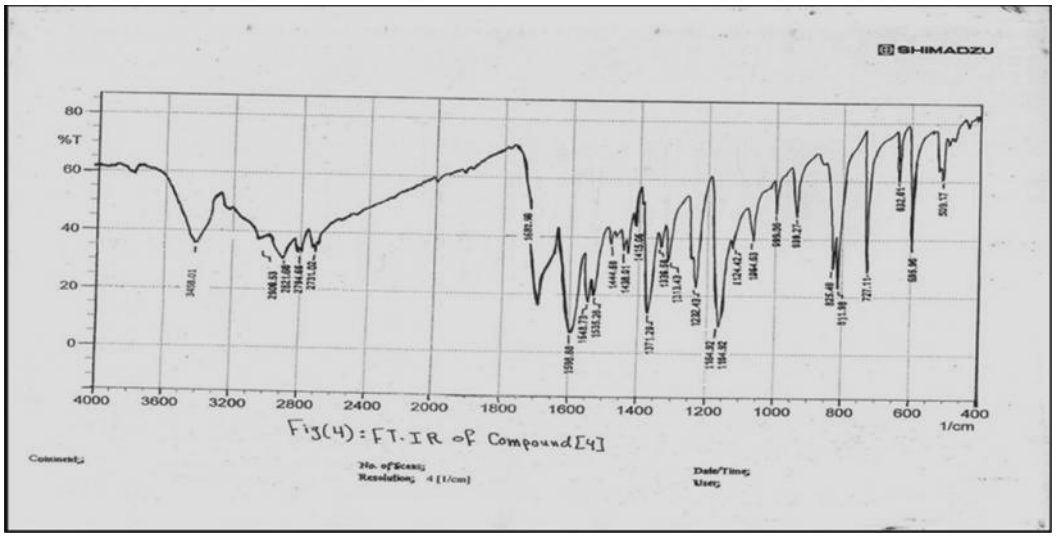


Fig (3 , 4) : FT.IR of compound [3 , 4]

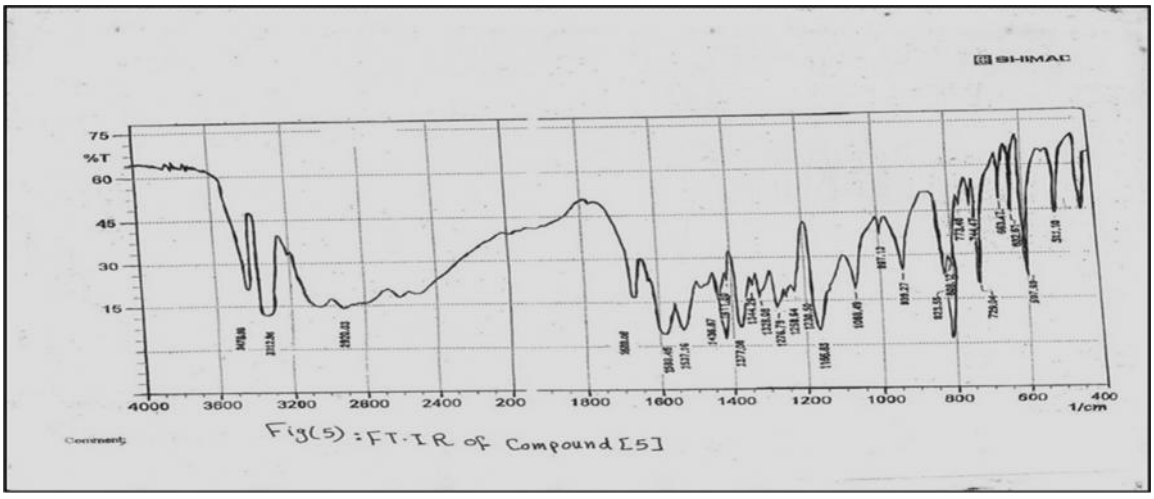


Fig (5) : FT.IR of compound [5]

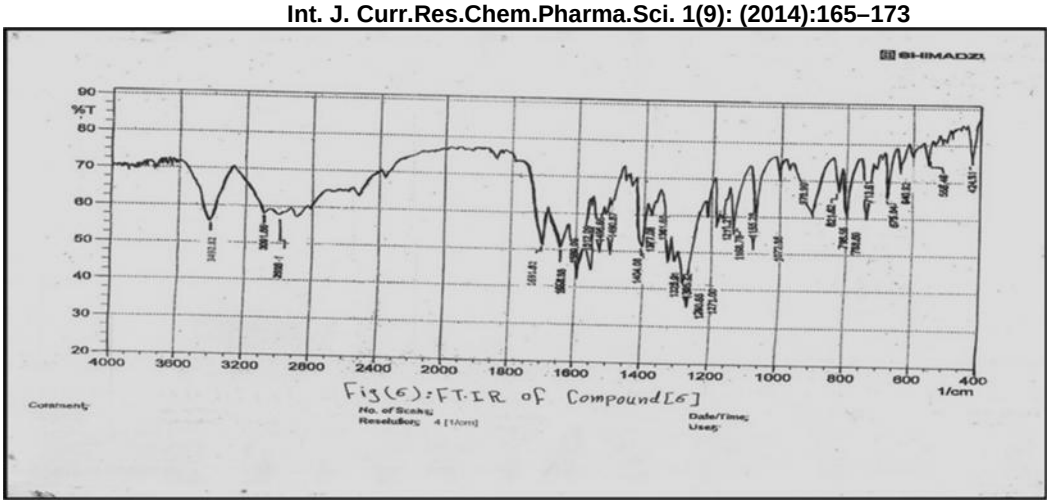
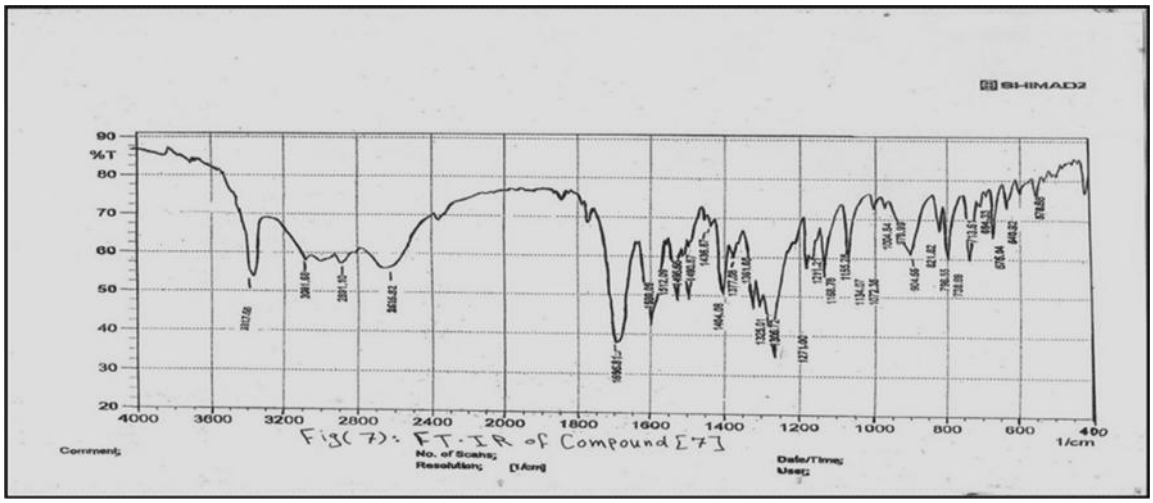


Fig (6) : FT.IR of compound [6]



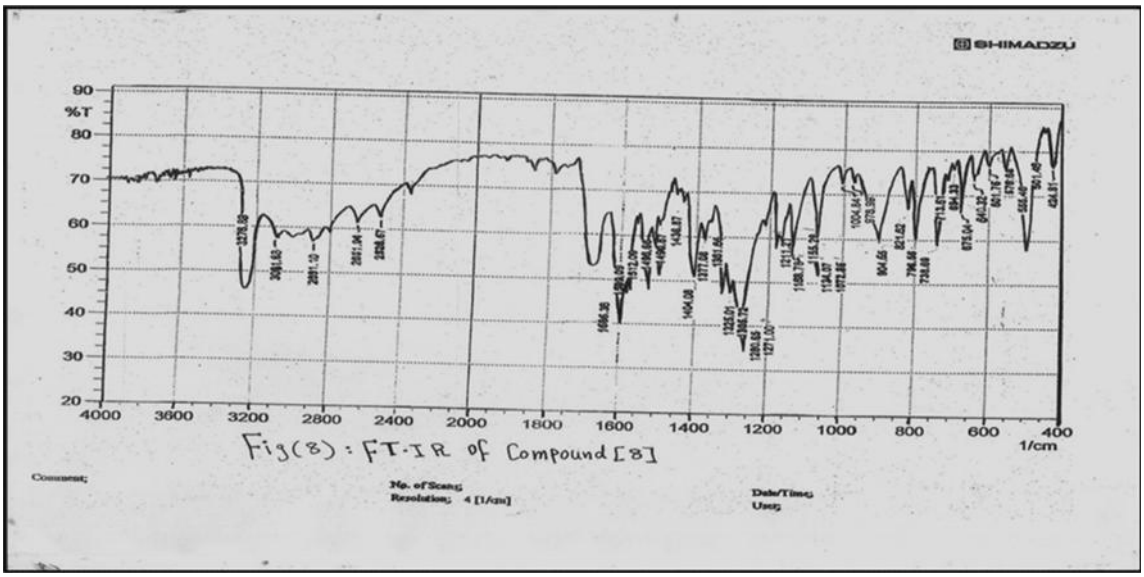


Fig (7 ,8) : FT.IR of compound [7 ,8]

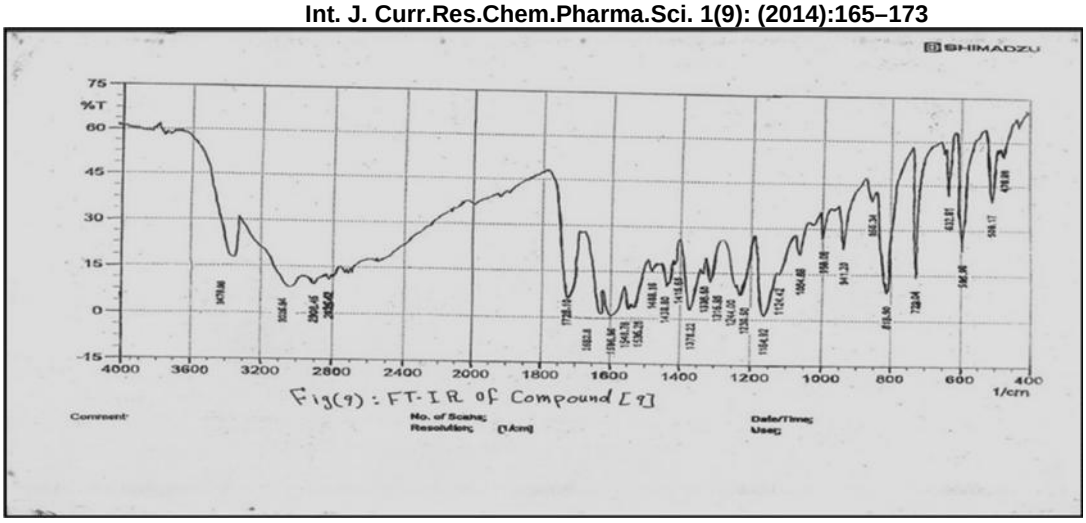


Fig (9) : FT.IR of compound [9]

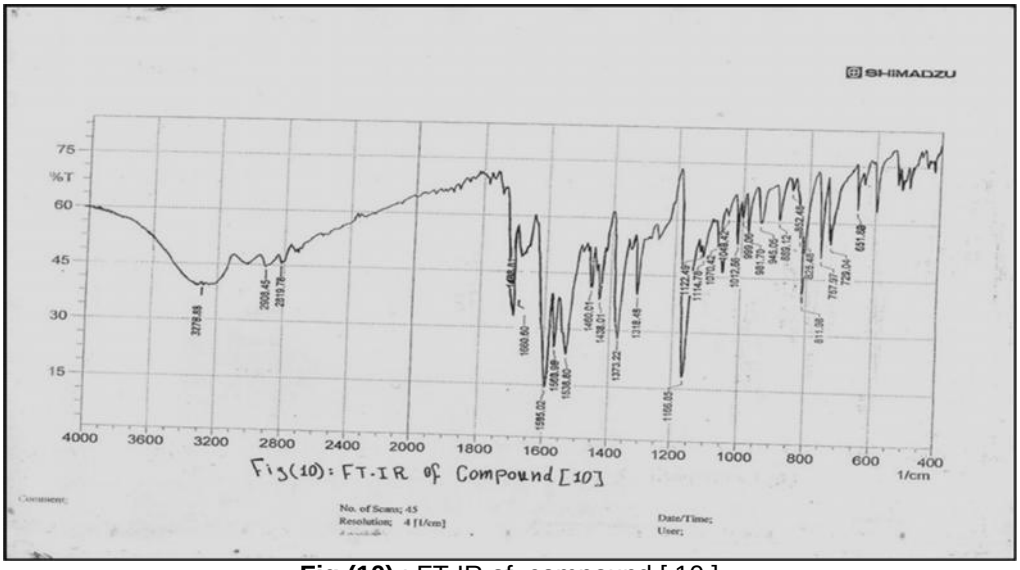


Fig (10) : FT.IR of compound [10]

Assay of antimicrobial activity [(15)]:

All materials and bacteria supplied from bio-lab in college education.Antimicrobial activity was tested by the filter paper disc diffusion method against gram positive bacteria *(Staphylococcus aureus)* and gram negative bacteria (*Pseudomonas aeruginosa*) , 0.1 ml of the bacterial suspensions was seeded on agar .To determine minimum inhibitory concentration(MIC) for each compounds[1-10] were ranged between (6-30)mg/ml by dissolved in (DMSO) and preparation 0.1mg/ml standard antibiotic amoxyline as positive standardand reference .

The positive results or sensitivity were established by the presence of clear zone of inhibition around active compounds which were measured with a meter rule and diameters were recorded based on (mm), the assays were performed with two replicates .Generally, The results showed that the compounds[1-10] have good inhibitory effect against tested bacteria as compared with synthetic antibiotic Amoxyline.

Table (4) showed the zone of inhibition of the compounds[1-10] in this study ranged (from 30 to 6) mm. From results, we noted that the compounds[7 , 8] have higher antibacterial activity against *S.aureus and P.aeruginosa*is due to the presence more than one of nitrogen atoms(N) and sulfur atom in their structures .,these compounds become more effective in precipitating proteins on bacteria cell walls.

Table(4): Antibacterial activity of the compounds[1-10].

Compounds[1-10]	diameter of zone(mm)	
	G+: Staphylococcus. aureus	*G-: Pseudomonas. aeruginosa*
compounds[1]	12	6
compounds[2]	16	10
compounds[3]	18	12
compounds[4]	20	14
compounds[5]	22	16
compounds[6]	22	16
compounds[7]	30	22
compounds[8]	28	24
compounds[9]	24	18
compounds[10]	24	18
Amoxyline**	36	28

*Minimum Inhibitory concentration (MIC)of compounds[1] (5mg/ml).
**Amoxyline (0.1mg/ml) .

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