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Synthesis and Characterization of some New synthesis of N-(pyrimidin-2-yl)benzenesulfonamide derivatives combined with oxaimidizolidine

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Abstract

This work involved prepared of some new series of chemical compounds of 1,3-oxazepine and 1,3-Diazepine derivatives in scheme [I]. First step reaction of sulfadiazine with 4-amino acetophenone product of Schiff base (A)4-((1-(4-aminophenyl)ethylidene)amino)-*N*-(pyrimidin-2-yl)benzene sulfonamide. Then, Schiff base [A] enter reactions one of with glycine to product five-membrane ring (B) 4-(2-(4-aminophenyl)-2-methyl-5-oxoimidazolidin-1-yl)-*N*-(pyrimidin-2-yl)benzenesulfonamide. compounds (B) were condensed with different aromatic aldehydes such as (p-hydroxybenzeldehyde, 4-methoxybenzeldehyde and salicyaldehyde] in ethanol absolute absolute to Produce new benzanils derivatives [B_1-B_3] respectively, Then the Produce of benzanils derivatives [B_1-B_3] were enter reaction with phathalic anhydride in toluene to Produce new N-(pyrimidin-2-yl)benzenesulfonamide derivatives [B_1a-B_3a] ,reaction compound [B_2a] with Naphthyl amine to give 2-hydroxyphenyl)-4-(naphthalen-2-yl)-1,5-dioxo-3,4,5,5a-tetrahydro-1H-benzo[e][1,3]diazepin-2(9aH)-yl)phenyl)-2-methyl-5-oxoimidazolidin-1-yl)-*N*-(pyrimidin-2-yl) benzenesulfonamide [C].All compounds were characterized by FT-IR spectroscopy and M.P, some of them were characterized by ^{1}H-NMR and spectroscopy analysis.

Keyword :- Sulfadiazine, 4-aminoacetophenone, oxaimidizolidine, 1,3-Oxazepine , 1,3-Diazepine

INTRODUCTION:-

Sulfadiazine is *N*'-substituted derivative of the parent compound, sulfanilamide . antibacterial drug used typical sulfonamide structure [(1)], and Antihypertensive drugs agents can be design by conjunction sulfadiazine and Antihypertensive drugs in one compound [(2)]. In 1864 the German chemist Hugo Schiff described the formation of N-substituted imines so they are called (Schiff base) . the synthesis via density of primary amines with effective carbonyls Hydrazides derivatives have growing importance because of the wide spectrum of their biological applications like antibacterial, antitumoral, anti-inflammatory, antifungal and antitubercular agents[(3)] . Oxazepine is Heterogeneous seven member ring that contains two heteroatom (Oxygen and Nitrogen). Diazepine is an analogue to oxazepine and thiazepine but the difference is nitrogen, oxygen, Sulpher atom,Diazepam (valium) is a substituted benzodiazepine introduced in 1964 which was used for the organization of tension and anxiety states, the extenuation of muscle convulsion [(4)] . in medical Heterocyclic compounds has important, agrarian and manufacturing from these heterocyclic that contains nitrogen atom in it's structure , which specialized in good properties as a drugs and repeller , polymers and dyes. There for some important pharmaceuticals which contains oxazepine used as a convulsant drug with bleakness and schezofrenic diseases and anti convulsive, antithrob[(5-6)] .This research involved preparation some new heterocyclic derivative like oxazole,oxazepine,diazapine.

SYNTHESIS METHODS

Procedure: Preparation of *N*-(pyrimidin-2-yl)benzene sulfonamide (A,B_1,B_2&B_3) [(7)].

1-Dissolve of (2.5 mg)from sulfadiazine with (1.35mg) of 4-amino acetophenone in 40mL of ethanol absolute .

2-Add to the previous solution two drops from glacial acetic acid .

3- The mixture refluxed for (20) hour at a temperature 78C^0.

4- collect the product by filtration .

5- the reaction showed by TLC that completed by using (ethyl acetate:toluene,1 :4).

1- 1- 4-((1-(4-aminophenyl)ethylidene) amino)-*N*-(pyrimidin-2-yl)benzenesulfonamide[A].

2- 4-(2-(4-((4-hydroxybenzylidene)amino)phenyl)-2-methyl-5-oxo imidazolidin-1-yl)-*N*-(pyrimidin-2-yl)benzenesulfonamide[B_1].

3-4-(2-(4-((2-hydroxybenzylidene)amino)phenyl)-2-methyl-5-oxoimidazolidin-1-yl)-*N*-(pyrimidin-2-yl)benzenesulfonamide[B_2].

4-4-(2-(4-((4-methoxybenzylidene)amino)phenyl)-2-methyl-5-oxo imidazolidin-1-yl)-*N*-(pyrimidin-2-yl)benzenesulfonamide[B_3].

Procedure;- of 4-(2-(4-aminophenyl)-2-methyl-5-oxoimidazolidin-1-yl)-*N*-(pyrimidin-2-yl)benzene sulfonamide[B] [(8)].

To the mixture of Schiff bases [A](0.01 mol) in THF (20 mL),was added glycine (0.01 mol, 1.48 mg) . mixture was stirred for (6 hour) when temperature (50 ^{0}C). The separated solid was dried and re-crystallized by mixture of (75% THF + 25% EtOH).

Procedure:-for perparation of 1,3-oxazepine-4,7-dione derivatives [B_1a- B_3a] [(9-10)].

A mixture of equal mole from compound [B_1- B_3] and appropries phthalic anhydride in (250 mL) of toluene, The solution was stirred for (15 hour) . Heating at Boiling point of the solvent, The residue were collected by filtration and the product colored crystalline solid was Crystal restoration from dry 1,4-dioxan . the reaction showed by TLC that completed by using (ethyl acetate : toluene ,1: 4).

1-synthesis of 4-(2-(4-(3-(4-hydroxy-2-methylphenyl)-1,5-dioxo-1,5,5a,9a-tetrahydrobenzo[e][1,3]oxazepin-4(3H)-yl)phenyl)-2-methyl-5-oxo imidazolidin-1-yl)-*N*-(pyrimidin-2-yl)benzenesulfonamide[B_1a].

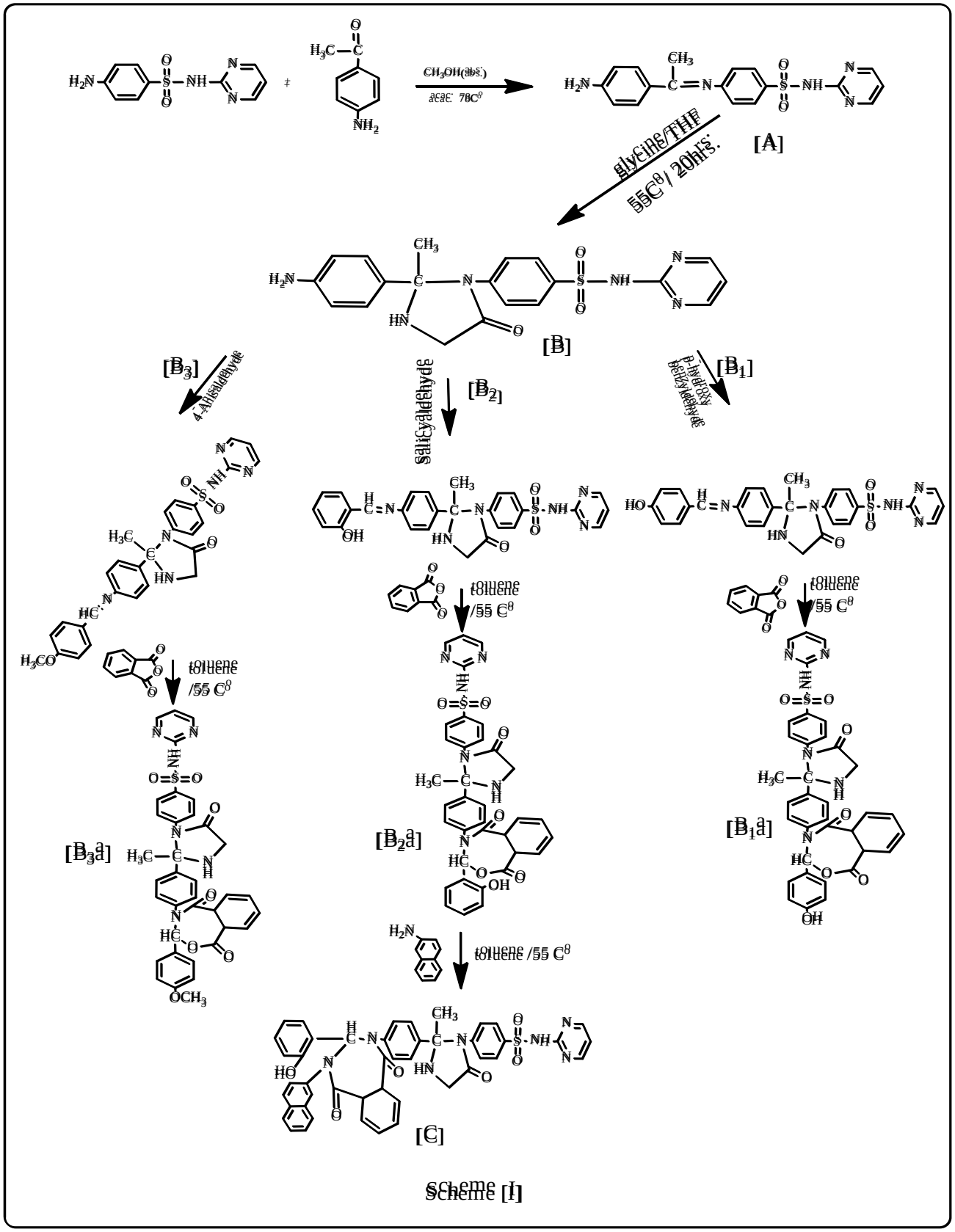
2-synthesis.of.4-(2-(4-(3-(2-hydroxyphenyl)-1,5-dioxo-1,5,5a,9a-tetrahydrobenzo[e][1,3]oxazepin-4(3H)-yl)phenyl)-2-methyl-5-oxoimidazolidin-1-yl)-*N*-(pyrimidin-2-yl)benzenesulfonamide [B_2a].

3-Synthesis.of.4-(2-(4-(3-(4-methoxyphenyl)-1,5-dioxo-1,5,5a,9a-tetrahydrobenzo[e][1,3]oxazepin-4(3H)-yl)phenyl)-2-methyl-5-oxoimidazolidin-1-yl)-*N*-(pyrimidin-2-yl)benzenesulfonamide[B_3a].

Procedure:-for perparad of 1,3-diazepine-4,7-dione)[C] [(11)].

A mixing up equal mole from compounds oxazepine and naphthyl amine in toluene(30mL) in round bottom flask. The solution was stirred for (5 hour) . Heating at Boiling point of the solvent then allowed to cool to room temperature and separated precipitate was filtered and Crystal restoration from ethanol. the reaction showed by TLC that completed by using (ethyl acetate : toluene , 1 : 4).

1- 4-(2-(4-(3-(2-hydroxyphenyl)-4-(naphthalen-2-yl)-1,5-dioxo-3,4,5,5a-tetrahydro-1H-benzo[e][1,3]diazepin-2(9aH)-yl)phenyl)-2-methyl-5-oxoimidazolidin-1-yl)-*N*-(pyrimidin-2-yl)benzenesulfonamide[C].


[A]
[B]
[B3]
[B2]
[B1]
4-Anisaldehyde
Salicylaldehyde
toluene /55 C°
[B3a]
[B2a]
[B1a]
[C]

Scheme [I]

Table (1) some physical properties of compounds [A-C].

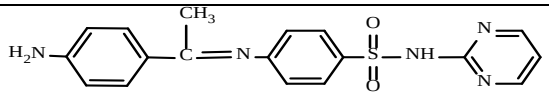
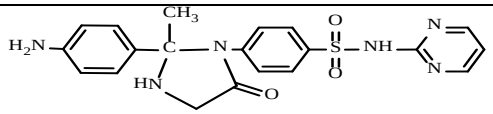
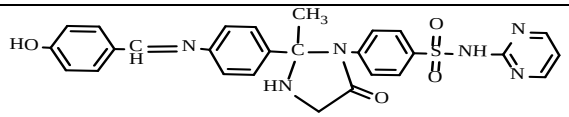
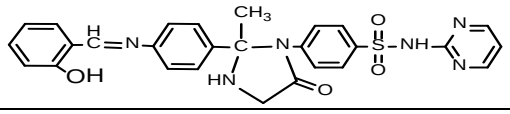
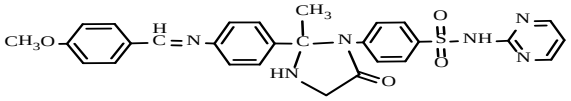
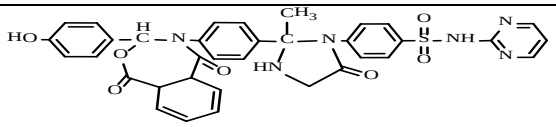
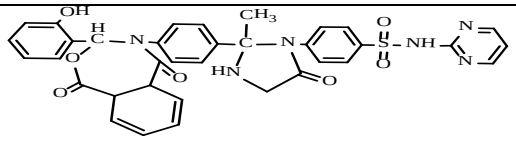
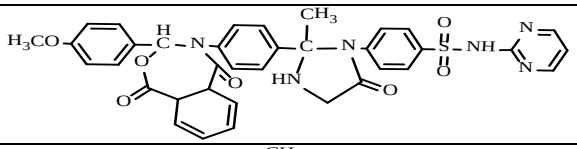
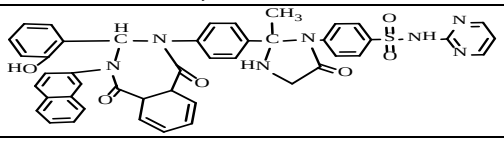
Comp. No.	Structural formula	Molecular Formula	M.P ^{0}C	Yield %	R_f
A		$C_{18}H_{17}N_5O_2S$	276-278	90	0.65
B		$C_{20}H_{20}N_6O_3S$	259-261	85	0.56
B_1		$C_{27}H_{24}N_6O_4S$	276-277	86	0.58
B_2		$C_{27}H_{24}N_6O_4S$	269-271	80	0.72
B_3		$C_{28}H_{26}N_6O_4S$	265-266	82	0.68
B_1a		$C_{36}H_{34}N_6O_7S$	280-281	80	0.63
B_2a		$C_{35}H_{30}N_6O_7S$	300-301	84	0.75
B_3a		$C_{36}H_{32}N_6O_7S$	264-265	87	0.68
C		$C_{45}H_{37}N_7O_6S$	250-251	81	0.72

Table [2] FT-IR data of Schiff bases compounds [A-B_3].

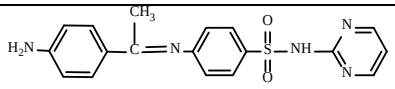
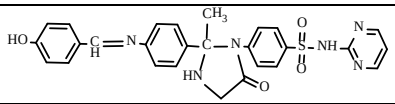
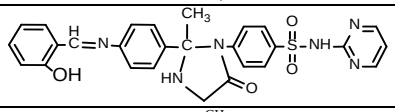
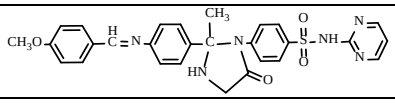
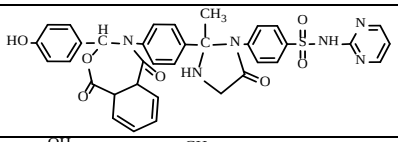
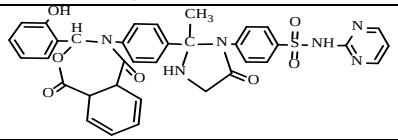
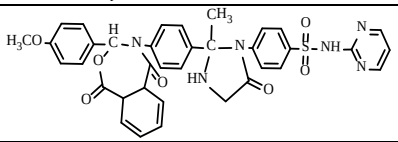
Comp.No.	Ar	υ (C=N) Imine cm^{-1}
A		1576
B_1		1575
B_2		1578
B_3		1577

Table [3] FT-IR data of compound [B_1a- B_3a] .

Comp No.	Ar	υ (C=C) Aromatic cm^{-1}	υ (C-H) Oxazepine ring cm^{-1}	υ (C=O)str. Lactone Lactam cm^{-1}	υ (C-N) cm^{-1}	υ(C-O) Lactone cm^{-1}
B_1a		1410 1442	3109	1653 1704	1160	1282
B_2a		1405 1449	3036	1762 1791	1168 1257	1281
B_3a		1404 1440	3024	1761 1790	1167	1257

DISCUSSION:-

3.1- **Synthesis and Identification of Schiff bases Derivatives [A-B_1,B_2,B_3]:**

Schiff bases were synthesized by the condensation reactions of different.aromaticaldehydes such as p-hydroxybenzeldehyde, 3-methoxy benzaldehyde, salicyaldehyde with amine derivatives in the existence of glacial acetic acid as catalyst in absolute ethanol .The preparation compounds [**A-$B_1$$B_2$$B_3$**] were characterized by FT-IR which showed band at (1575-1588) cm^{-1} of stretching vibration of imine group (C=N) [12,13].Other information of functional groups.

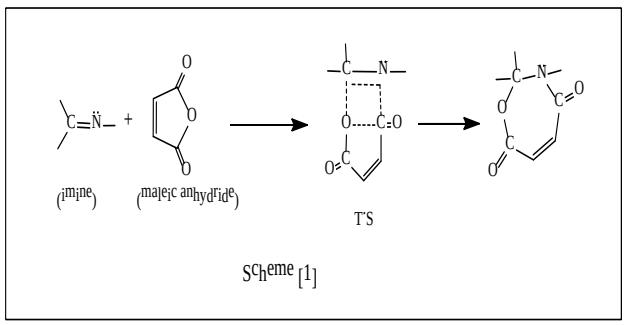
Synthesis and characterization of 4-(2-(4-aminophenyl)-2-methyl-5-oxoimidazolidin-1-yl)-*N*-(pyrimidin-2-yl)benzene sulfonamide[B].

The compound [B] was synthesis by the reaction of Schiff base [A] with the amino acid glycin in THF .

The FT.IR spectra of the compounds [B] showed disappearance of showed disappearance of absorption bands at (1576) cm^{-1} was return the (C=N) of imine group and appearance of absorption band at (1647 lactam – 1707 lactone)[14] cm^{-1} was return the stretching vibration from the group(C=O). in compound (imidazolidin), & the emergence from two packages in signatories (2924 – 3039) cm^{-1} which dated back to the stretching frequency (C-H) aromatic and aliphatic respectively.

synthesis and Identification of 1,3-oxazepine-4,7-dione derivatives [B_1a- B_3a].

Pericyclic reactions, between imine groups of schiff bases [B_1-B_3] and cyclic acid anhydride [maleic anhydride] in toluene, were carried out to the synthesis of 1,3-oxazepine derivatives [B_1a-B_3a]. Mechanism[15] of the pericyclic reaction for the preparation seven membrane shown in scheme[1].



Scheme [1]

The synthesized compounds [B_1a-C_5b] were characterized by FT-IR spectra, some of them were describe by ^{1}H-NMR spectra .

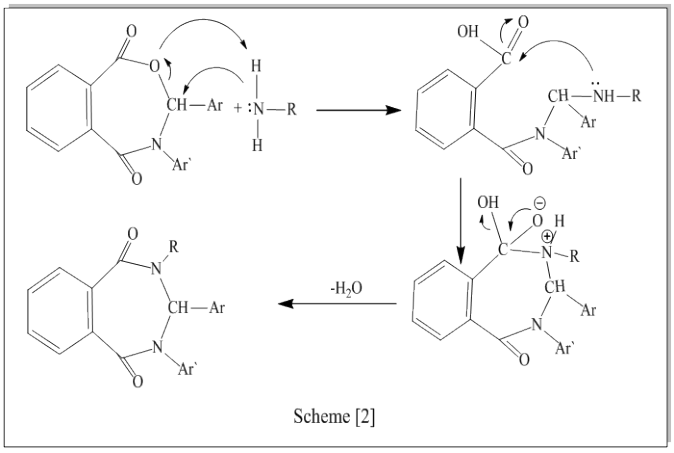
The FT-IR spectra of the compounds [B_1a-C_5b] showed appearance of the powerful absorption band at (1701-1790) cm^{-1} was due to (C=O) lactone group the stretching vibration [16], the appearance of the stretching vibration of the (C=O) lactam group at (1653-1762) cm^{-1} [17]. Other information of functional groups were shown at following table [2].

Syenthesis and Identification of for Synthesis of 1,3-diazepine-4,7-dione) [C].

1,3-Dizepine derivatives were prepared from reaction between 1,3-oxazepine with sulphadiazine in dry benzene and the following compounds are prepared [C]. Mechanism[18] of the synthesis 1,3-diazepine ring is shown in scheme [4].

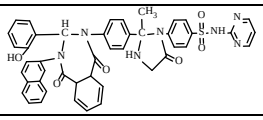
FT-IR spectra describe The synthesized compounds [C] the stretching vibration of the (C=O) lactone group showed disappearance at (1651-1652) cm^{-1} [19], the stretching vibration of the (C=O) lactam group the appearance of the strong absorption band at (1699-1710) cm^{-1} [20]. following table [3].

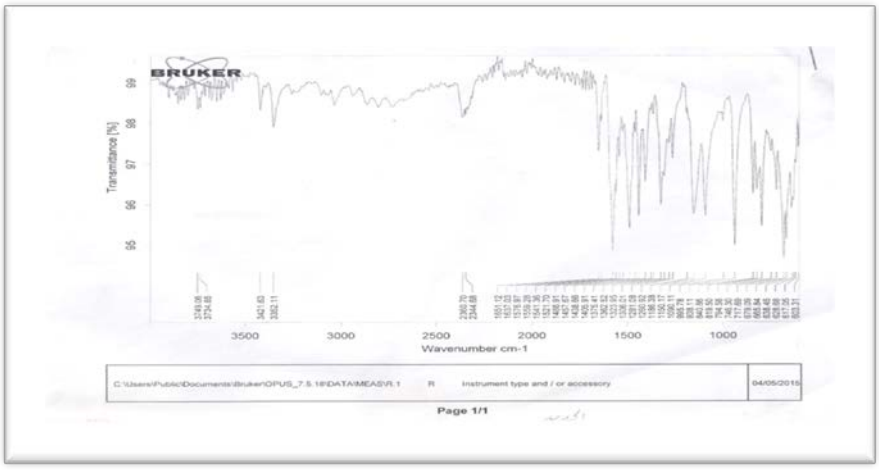
^{1}H-NMR spectrum of compounds [B_1 and C] showed the following characteristic signals (DMSO-d_6 as a solvent) the multiplet signal at δ(7.6-8.1 ppm) that could be attributed to the aromatic protons for ten phenyl rings and the doublet signal at δ(6.5-7.1)ppm that could be attributed to the two protons of seven membered ring of oxazepine(2H of double bond of oxazepine ring) group The ^{1}H-NMR spectrum also showed the singlet signal at δ(7.3-7.9 ppm) that could be attributed to the one proton of oxazepine(CH of oxazepine ring) group[21] and other data of groups containing protons were showed in table [4].



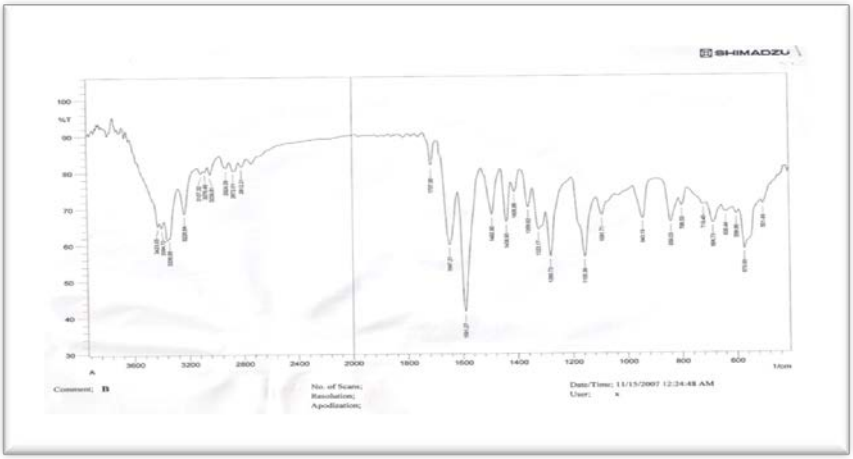
Scheme [2]

Table [4] FT-IR data of compound [C].

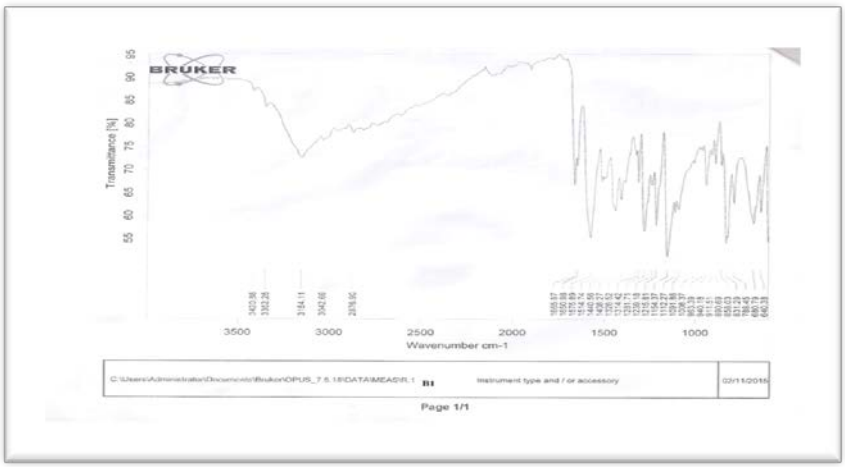
Comp. No.	Ar	υ (C-H) oxazepine ring cm^{-1}	υ(C=O)str. Lactone Lactam cm^{-1}	υ (C-N) Lactone cm^{-1}	υ (NH) bending cm^{-1}	Others cm^{-1}
C		3225	1652 1699	1288	1458 1485	υ(C-OH) :3340



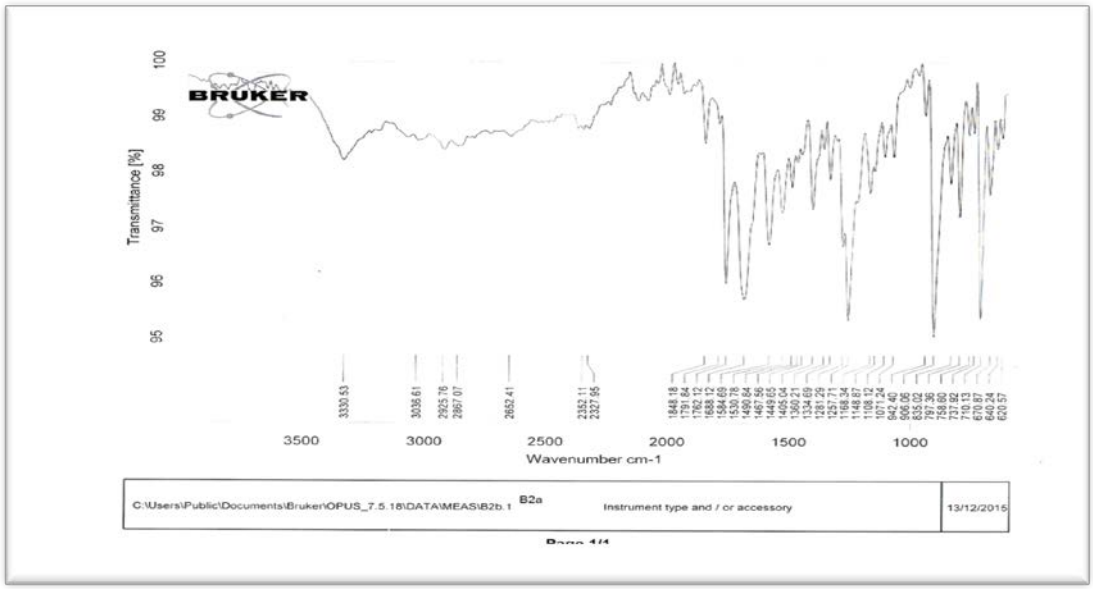
FT-IR spectrum of compound [A]



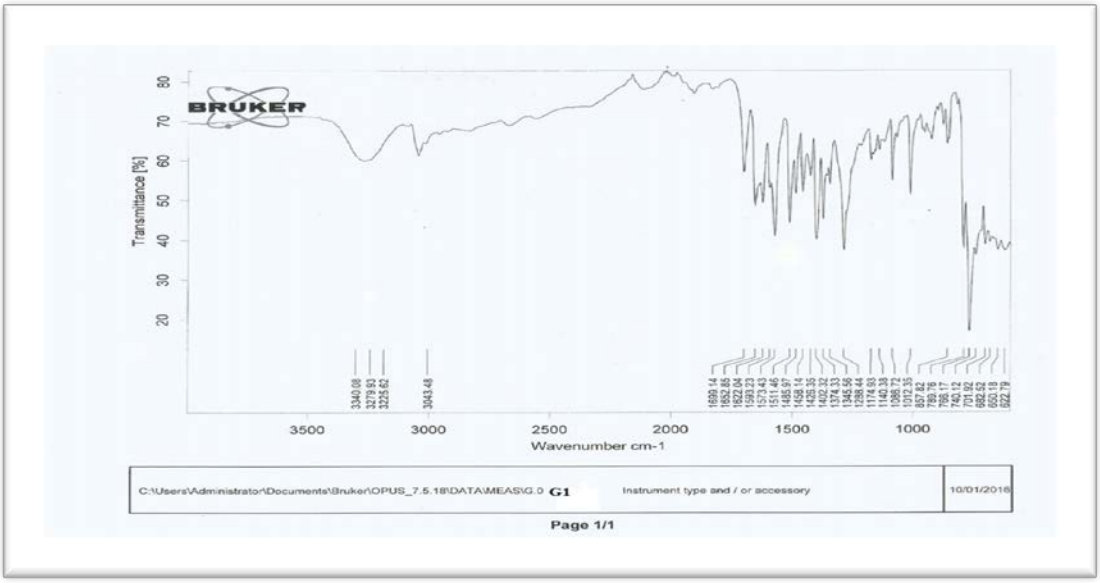
FT-IR spectrum of compound [B]



FT-IR spectrum of compound [B_1]

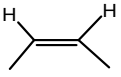
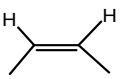


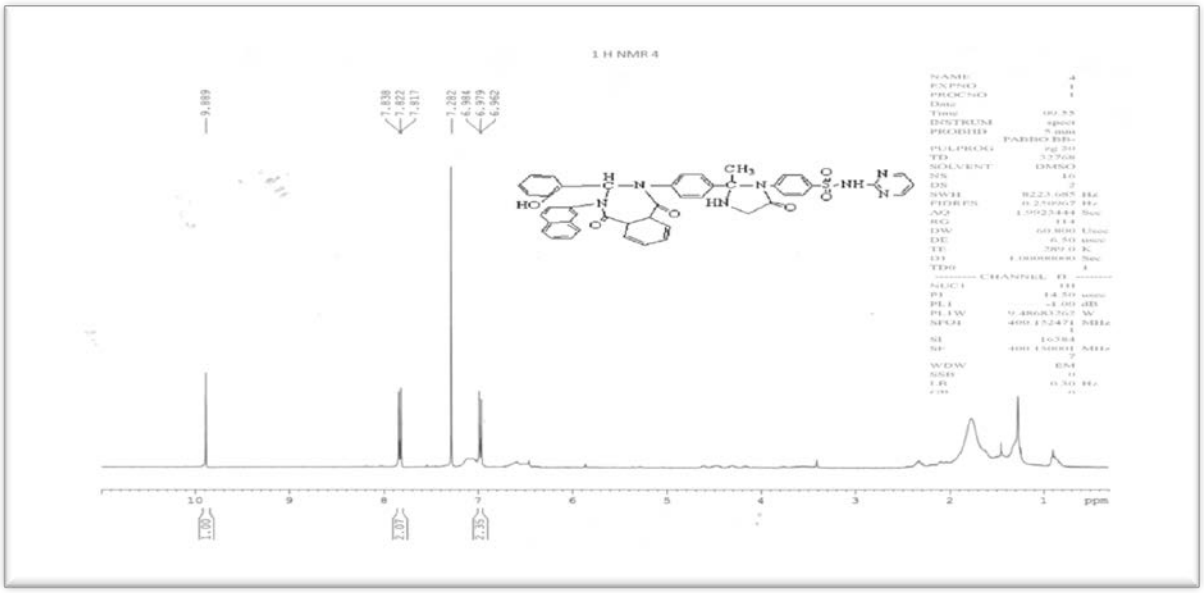
FT-IR spectrum of compound [B_2a]



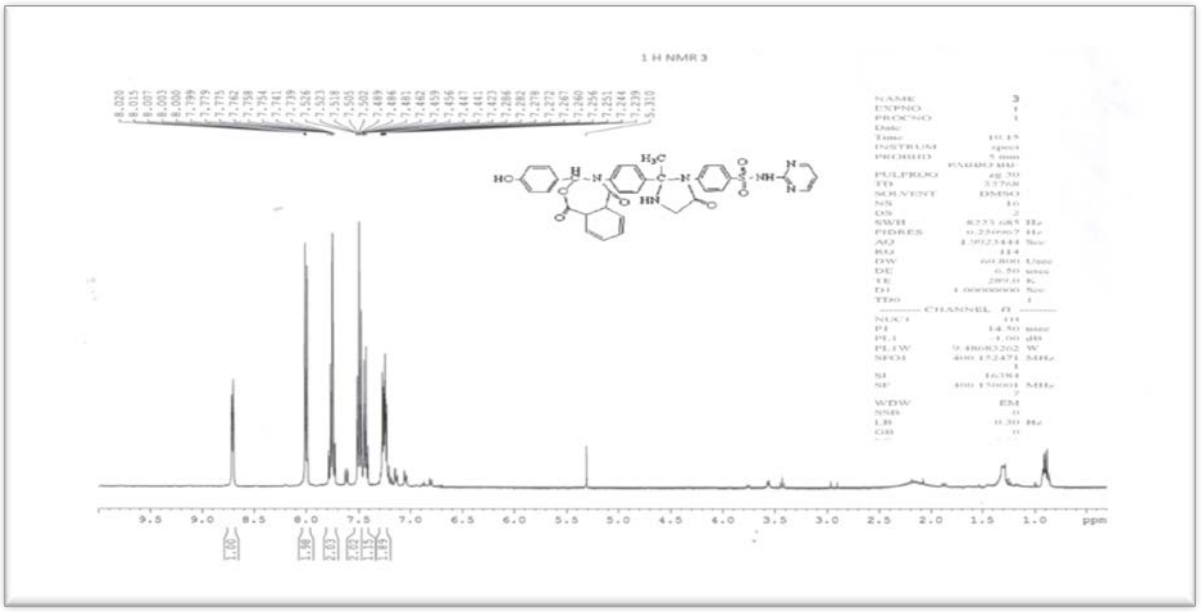
FT-IR spectrum of compound [C]

Table [4] H-NMR data of compound [B_1a-C].

Comp. No.	**δ(C-H) Aromatic ppm**		**CH of oxazepine ring**	**NH Sulphadiazene**	**HC=N Pyrimidine**	**δ(C-H) of CH_3 *o*-tolidine**	**Others Ppm**
B_1a	7.6	6.5-6.7	7.3	11.3	8.5	2.5	(s , 6H , N-CH_3): δ1.8
Comp. No.	**δ(C-H) Aromatic**		**CH of Diazepine ring**	**3H of CH_3 *o*-tolidine**	**Others Ppm**		
C	8.1	6.9-7.1	7.9	2.5	_		



H-NMR spectrum of compound [C]



H- NMR spectrum of compound [B_1a]

CONCLUSIONS:

The study arrived at the following Conclusions:

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 relation to stability.

3-Pericyclic reactions, between imine groups and maleic anhydride, phthalic anhydride were carried out to the synthesis of 1,3-oxazepine derivatives.

REFERENCES:-

1- N. Calvert, T. A. Connors, W.C. J. Ross, Arylhalogenoalkylamines of sulphanilamide designed for selective deposition in neoplastic tissue ,*Eur. J. Cancer*, 1986, 4(6): 627-633.

3- Z. Huang, G. Yang, Z. Lin & J. Huang , 2-[N^1-2-Pyrimidyl-aminobenzenesulfon amido] ethyl 4-bis(2-chloroethyl) aminophenyl butyrate: A potent antitumor agent, *Bioorganic and Medicinal Chemistry Letters*, 2001, Vol. 11, Issue 6:1099-1103.

4- M. S. Al-Rawi, J. H. Tomma & D. F. Hussen , The New C-2,C-3 Substituted Heterocyclic Derivatives of L-Ascorbic acid: Synthesis, Characterization, and Bacterial Activity, *Iraqi NaϴonaI Journal of Chemistry*, 2014,volume 55:264-274.

5- A. F. Kareem & H. T. Ghanim,Synthesis And Identification Some Of 1, 3-Oxazepine Derivatives Containing Azo Group, Journal of Applied, *Physical and Biochemistry Research (JAPBR*), Jun 2015, Vol. 5, Issue 1:45-56.

5- C.O. Wilson & O. Givold, *"Text book of Organic Medicinal and pharmaceutical Chemistry"*, Ptiman Medical Publishing Co.London coppy right .Cby. J.B. Lippin Cott Company, 5 th Edition, (1966).

6- B. A.Kherallah, Synthesis and Identification of some 1,3-oxazepine derivatives containing pmethoxy phenyl and studying their anti bacterial activity, *Kerbala Journal of Pharmaceutical Sciens* , 2014,Number7 :31.
7- Z. A. Sallal, H. T.Ghanem, Synthesis of New 1,3-Oxazepine Derivatives Containing Azo Group, *Journal of Kufa for Chemical Science* , 2011,No.(2) :12.
8- A. Thamer. Salem, *P.hD thesis* , *AL-Nahrain university*, (2008) .
9- R. W. Adam, E..H.Zimam, Synthesis, Characterization and Study Biological activity of some New 1,3- Oxazepine and 1,3-Diazepine derivatives, *Kerbala Journal of Pharmaceutical Sciens*, 2014, Number7 :199-200.
10- H. M. Sadiq,Synthesis And Characterization Of Novel 1,3-Oxazepine Derivatives From Aminopyrazine, *World Journal of Pharmacy and Pharmaceutical Sciences*, 2017, Vol 6, Issue 5 :186-198.
11-I. A. Yass, Synthesis of substitutead 1,3-Oxazepine and 1,3-Diazepine Via Schiff Bases for Selfamethoxazole drug, *Kerbala Journal Of Pharmaceutical Sciences*, 2010, Number1:50.
12- A. .I. Mustafa, Novel synthesis and antibacterial activities of new derivatives of 7,8-Dichlorodibenzo(b, d)thiophene-2-carboxcyilic acid of pharmaceutical interest ,*Diyala journal for pure sciences*, January 2015, Vol: 11 No: 1:81 .
13- E. H. Sahap, R. W. Adam, Z. L. Razzaq, Synthesis and Characterization of Some New 1,3-Oxazepine and 1,3-Diazepine Derivatives Combined with Azetidine-2-one, *Journal of Global Pharma Technology*, 2018,10(03) :289-297.
14 – H. M. Sheerali, H. T. Ghanim,Synthesis And Characterization Of Various Imides And New Heterocyclic Compounds Containing Azo Group, *Journal of Kufa for Chemical Science*, 2013, No. (7) June : 6.
15- K.F Ali., Ph.D. Thesis, Faculty of Education Ibn-Al-Haitham, University of Baghdad (2005).
16- A. Hameed, Microwave Synthesis of Some New 1,3-Oxazepine Compounds as Photostabilizing Additives for Pmma Films, *Journal of Al-Nahrain University*, 2012,Vol.15 (4), December :47-59.
17- M. Abdul,J. Mohammed ,A.H. H. Salman,Z. R. Abdul-Hussein, Synthesis, Characterization and Antibacterial Activity of Some New Oxazepine compounds, *J.Thi-Qar Sci*., 2014, Vol.5 (1) :34.
18- M. Liang, C. Saiz, C. Pizzo, & P. Wipf, Synthesis of pyrrolo[1,3]diazepines by a dipolar cycloaddition –*retro*-Mannich domino reaction , *Tetrahedron Lett.* , 2009, December 1; 50(49) : 6810–6813.
19- S. M. Ahmad, Synthesis and Characterization of 1,2-disubstituted -3-(pyrimidine-2-yl)-2,3-dihydro-1H-1,3-diazepine-4,7-dione, *Journal of Al-Nahrain University* , September 2011,Vol.14 (3): 24-34.
20- M. J. Kadhim , H. T Ghanim , Synthesis And Identification 1-3 Diazepine From Ibuprofen ,*International Journal Of Scientific & Technology Research*, October 2014, Volume 3, Issue 10:215.
21- A. W. Naser , A. F. Abdullah, Synthesis of some new N-saccharin derivatives of possible biological activity, *Journal of Chemical and Pharmaceutical Research*, 2014, 6(5):872-879.