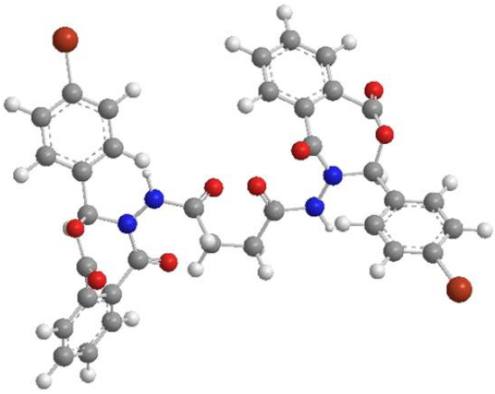
JOURNAL OF ZANKOY SULAIMANI

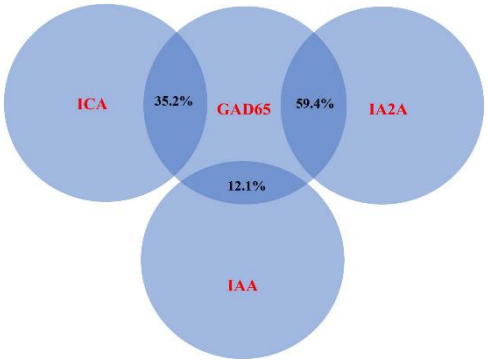
Part -A- (Pure and Applied Sciences)

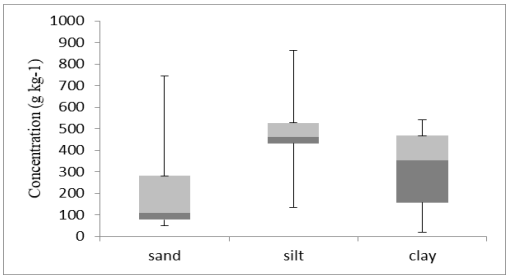
VOLUME 25 ISSUE 2 December 2023

ISSN: 1812-4100

www.jzs.univsul.edu.iq







Journal homepage www.jzs.univsul.edu.iq
Journal of Zankoy Sulaimani
Part-A- (Pure and Applied Sciences)
ISSN:1812-4100

Synthesis and Identification of Some New bis Oxazepinedione and bis Benzoxazepinedione Compounds via Cyclization Reaction for Some bis Schiff Bases

Shakhawan Beebany[1*], Saad Salem Jasim[1], Sevgi Samih Hidayet Arslan[2]

1 Department of Chemistry, College of Sciences, University of Kirkuk, Kirkuk, Iraq.

2 College of Dentistry, University of Kirkuk, Kirkuk, Iraq.

* Corresponding email: sh.beebany@uokirkuk.edu.iq

Article info

Original: 08/09/2023
Revised: 18/10/2023
Accepted: 25/10/2023
Published online: 20/12/2023

Keywords:
Oxazepinedione, Schiff base, Succinohydrazide, Schiff cyclization

Abstract

This study was involved synthesis of new bis oxazepinedione and bis benzoxazepinedione compounds, derived from Schiff bases **a(1-5)**. These Schiff bases were prepared from hydrazine and diethyl succinate using ethanol as solvent. The prepared Schiff bases have been undergone to reaction with maleic anhydride and phthalic anhydride to form bis oxazepinedione **b(1-5)** and bis benzoxazepinedione **b(6-10)** derivatives. The newly synthesized compounds were characterized using spectroscopic techniques such as Carbon, Hydrogen and Nitrogen (CHN) Elemental Analysis, Fourier transform infrared (FT-IR) spectroscopy and proton nuclear magnetic resonance (^{1}H-NMR). The molecular orbital package (MOPAC) method has been used to calculate heat of formation (HF) and steric Energy (SE) for all of the synthesized chemicals. The (SE) calculations were performed using the molecular modelling (MM2) method. The MOPAC and MM2 methods are available in CS- Chemoffice-version 6.0 contains. The results indicated that compounds (**a3**, **a4**, **b5** and **b9**) were shown high stability and less steric effect. This may relate to the presence of donating groups in the structure [OCH_3 and $N(CH_3)_2$].

Introduction

Heterocycle compounds exhibit diverse chemical and biological properties, making them an area of immense interest for researchers worldwide. Heterocyclic compounds have garnered significant attention in medicinal chemistry due to their remarkable pharmacological properties (1-3) including cancer, infectious diseases, and neurological disorders (4). Moreover, heterocyclic compounds serve as essential components in the development of dyes, pigments, and photoactive materials (5).

Oxazepines are a subset of heterocyclic compounds characterized by a heptagonal ring structure composed of five carbon atoms, one oxygen atom, and one nitrogen atom (6). This unique arrangement grants them distinctive properties, rendering them useful in various chemical transformations and biological activities (7). The structural diversity of oxazepines allows for numerous substitution patterns, expanding their potential

applications in organic synthesis and drug discovery (8). The core structure of oxazepines consists of a seven-membered ring, which imparts unique physicochemical properties to these compounds. The presence of heteroatoms, especially oxygen and nitrogen, introduces polarity and hydrogen-bonding capabilities, influencing their solubility and reactivity. The aromaticity of oxazepines is a critical structural feature that contributes to their stability and reactivity. Depending on the substitution pattern, oxazepines can exhibit both aromatic and non-aromatic characteristics (9). The synthesis of oxazepines involves variety of methods, each tailored to suit specific requirements based on the desired target compound. Some commonly employed strategies include: One of the primary approaches to obtain oxazepines is through ring expansion reactions of smaller heterocycles. For instance, the cyclization of γ-hydroxy-β-amino esters or amides can yield substituted oxazepines (10). These reactions are often catalyzed by Lewis acids or transition metal catalysts. Condensation reactions, particularly between 1,4-dicarbonyl compounds and 1,2-aminoalcohols, offer an efficient route to access oxazepine derivatives (11). The utilization of suitable catalysts and reaction conditions plays a crucial role in controlling regioselectivity and stereochemistry. Rearrangement reactions, such as the Beckmann rearrangement, have been employed to synthesize oxazepines from cyclic ketoximes (12). This transformation involves the migration of a substituent to generate the seven-membered oxazepine ring.

Understanding the synthesis and structural properties of oxazepines is essential for harnessing their potential fully and creating innovative solutions in the realm of organic chemistry. Ahmed et al (13) have synthesized a series of 1,3-oxazepine compounds via the microwave-assisted procedure, the reaction has been done by mixing 1,3,4-oxadiazole compounds with phthalic anhydride. The chemicals that had been synthesized were subjected to testing against two bacterial strains, namely *Escherichia coli* and *Staphylococcus aureus*. Another research group (14) have synthesized sulphathiadiazole Schiff bases and converted these bases into oxazepine compounds, the synthesized compounds were studied in terms of antibacterial, cytotoxicity, and antioxidant activities, as well as studying the molecular docking and the theory of density functional. Through a cycloaddition condensation procedure (2+5). New 1,3-oxazepine compounds have been synthesized (15), from the reaction of some acid anhydrides with Schiff bases. A study was conducted to synthesize oxazepine derivatives with their biological activity assessment (16), or to add different functional group to the molecular structure such as azo group (17). Furthermore, the microwave technique has been used to produce oxazepine derivatives (13).

This research is aimed to synthesize some of new bis oxazepinedione and bis benzoxazepinedione compounds from some Schiff bases derivatives containing succinamide mode. In addition to study (HF) and (SE) for the newly synthesized compounds using the MOPAC and MM2 methods. This will help to evaluate theoretically the structures and select those more stable and less steric effect to apply against bacteria and fungi for future works.

Materials and Methodology

Chemicals and Instrumentals

All compounds of this research work were used without further purification and supplied by Fluka, Scharlau and Merck. Melting points for the newly synthesized compounds were determined by using electrothermal melting point apparatus (Stuart SMP11). The products were characterized using Fourier transform infrared SHIMADZUFT-IR-8400S infrared spectrophotometer by KBr disc) with a range of (4000-400) cm^{-1} in Tikrit University. The ^{1}H-NMR and ^{13}C-NMR spectra have been recorded using Bruker AVANCEIII 400 MHz NMR spectrometer (^{1}H- NMR 400 MHz, ^{13}C -NMR 100 MHz) at Selçuk University, in Turkey. The DMSO-d_6 used as a solvent and TMS as an internal standard. The CHN Elemental Analysis was conducted by Eurovectro, EA 3000A, Italy at Al-Albayt University in Jordan.

Methods

1- Preparation of succinohydrazide.

To make succinohydrazide, (0.02 mole) of ethyl succinate and (0.04 mole) of hydrazine were dissolved in (25 mL) of ethanol (100 %), allowed to reflux for 4.5–5 hours. The solution was concentrated and cooled to ambient temperature. The resulting precipitate was subjected to filtration, followed by rinsing with chilled distilled water. Afterwards underwent recrystallization using ethanol. The final substance is characterized by the presence of a white precipitate, which has a melting point at range of 170–171 °C (18).

2- Preparation of Schiff bases **a(1-5)**

Succinohydrazide (1.45 g, 0.01 mole) was mixed with different aldehydes (0.02 mole) in 25 mL of absolute ethanol. 3 drops of glacial acetic acid were added to the mixture and heated at reflux for 6 hours. The reaction mixture was cooled to precipitate. After filtration the solid product was dried and recrystallized from a mixture of absolute ethanol and methanol (19). Table 1 presents the physical characteristics for the synthesized chemicals.

3- Preparation of bis oxazepinedione compounds **b(1-5)**

Schiff bases **a(1-5)** (0.01 mole) and maleic anhydride (0.02 mole) dissolved in absolute ethanol (25 mL). The mixture was refluxed for 8 hours. After cooling, the precipitate was filtered and dried then crystallized from absolute ethanol (20). Table 2 summarizes some physical characteristics for the synthesized compounds.

Table 1: Physical characteristics of compounds **a(1-5).**

Comp. No.	X	compound name	Colour	M.P. ^{o}C	Yield %
a1	H	N1',N4'-dibenzylidenesuccinohydrazide	White	162-164	85
a2	4-Cl	N1',N4'-bis(4-chlorobenzylidene)succinohydrazide	White	255-257	70
a3	4-Br	N1',N4'-bis(4-bromobenzylidene)succinohydrazide	White	278-280	92
a4	4-OCH_3	N1',N4'-bis(4-methoxybenzylidene)succinohydrazide	Yellow	184-186	87
a5	4-N,N$(CH_3)_2$	N1',N4'-bis(4-(dimethylamino)benzylidene)succinohydrazide	Orange	79-80	56

4- Preparation of bis benzoxazepinedione compounds **b(6-10)**

The same procedure of oxazepinediones **b(1-5)** synthesis has been employed to synthesize benzoxazepinediones **b(6-10**) except using of phthalic anhydride instead of maleic anhydride (20). (Table 3) shows some physical features of the synthesized bis benzoxazepinediones.

Table 2: Physical characteristics of compounds **b(1-5)**.

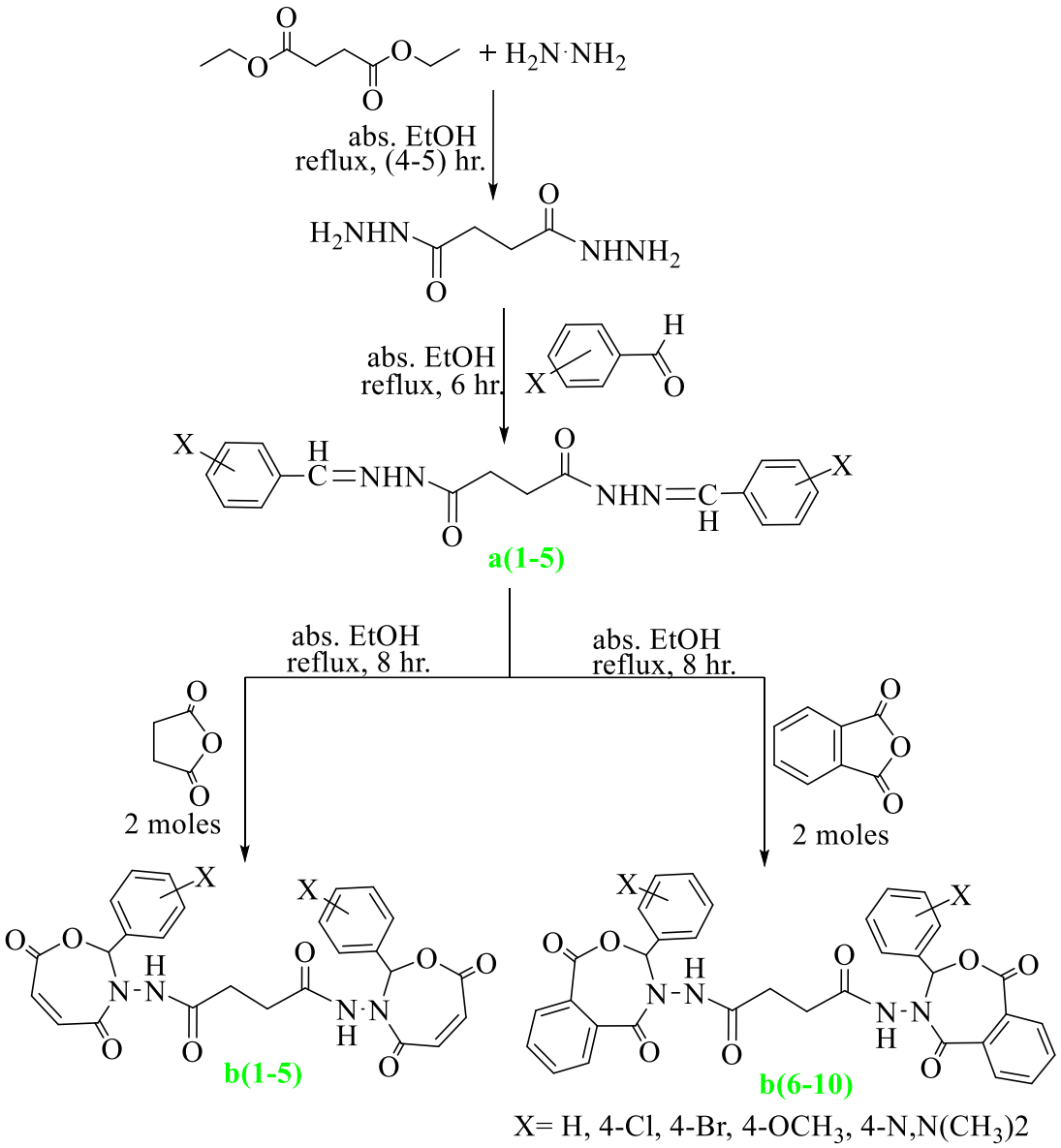
Comp. No.	X	compound name	Colour	M.P. °C	Yield %
b1	H	N1,N4-bis((Z)-4,7-(dioxo -2- phenyl-1,3-oxa-zepin-3(2H,,4H,,7H)-yl))succinamide	Light yellow	189-191	82
b2	4-Cl	N1,N4-bis((Z)-2-(4-chlorophenyl)-4,7-dioxo-1,3-oxazepin-3(2H,,4H,,7H)-yl)succinamide	Brown	235-237	89
b3	4-Br	N1,N4-bis((Z)-2-(4-bromophenyl)--4,7--di oxo-1,3-oxa zepin-3(2H,,4H,,7H)-yl)succinamide	Light brown	243-245	79
b4	4-OCH_3	N1,N4-bis((Z)-2-(4-methoxy phenyl)-4,7-di oxo-1,3-oxa-zepin-3(2H,,4H,,7H)-yl)succinamide	Deep red	172-174	95
b5	4-N,N$(CH_3)_2$	N1,N4-bis((Z)-2-(4-(dimethyl amino)phenyl)-4, 7-dioxo-1,3-oxa-zepin-3(2H,,4H,,7H)-yl)succinamide	Grey	208-210	67

Table 3: Physical characteristics of compounds **b(6-10)**.

Comp. No.	X	compound name	Colour	M.P. °C	Yield %
b6	H	N1,N4-bis(1,5-dioxo-3-phenylbenzo[e][1,3]oxa-zepin-4(1H,,3H,, 5H)-yl)succinamide	Deep yellow	202-204	62
b7	4-Cl	N1,N4-bis(3-(4-chloro phenyl)-1,5-di oxo-benzo[e][1, 3]oxa-zepin-4(1H,,3H,,5H)-yl)succinamide	Grey	247-249	57
b8	4-Br	N1,N4-bis(3-(4-bromo phenyl)-1,5-dioxobenzo[e][1,3]oxa-zepin-4(1H,,3H,,5H)-yl)succinamide	Deep brown	268-270	84
b9	4-OCH_3	N1,N4-bis(3-(4-methoxyphenyl)-1,5-dioxobenzo[e][1,3]oxa-zepin-4(1H,, 3H,,b5H)-yl)succinamide	Deep yellow	229-231	86
b10	4-N,N$(CH_3)_2$	N1,N4-bis (3-(4-(di methylamino)phenyl)-1,5-di oxo-benzo[e][1,3]oxa-zepin-4(1H,, 3H,,5H)-yl)succinamide	Brown	244-245	92

Results and Discussion

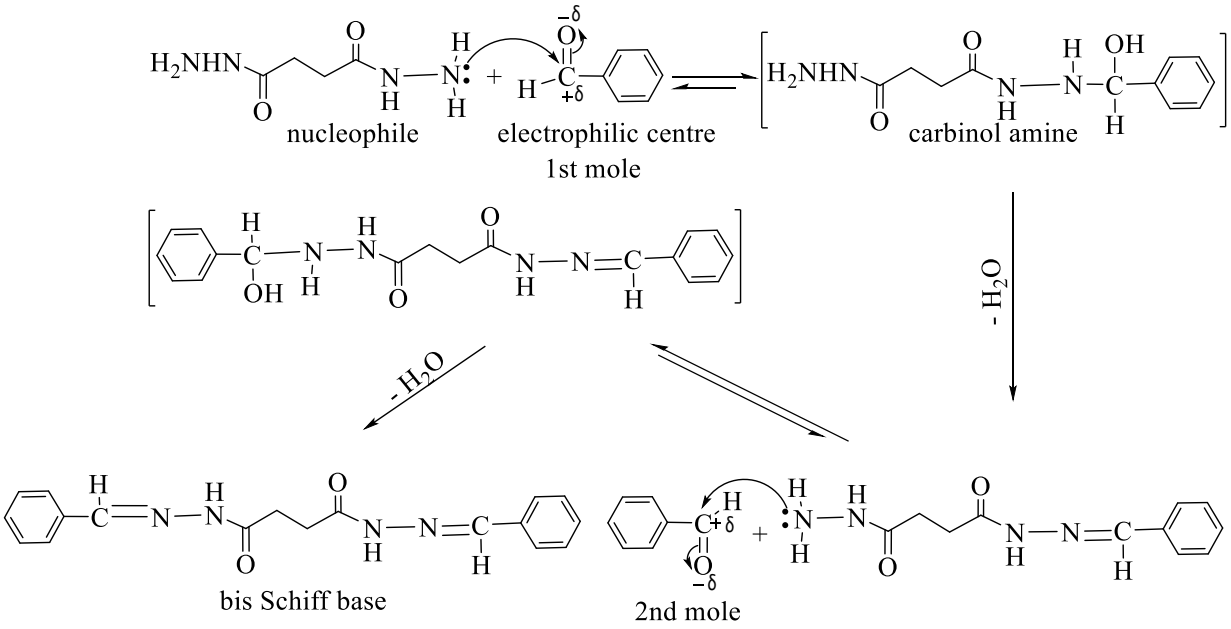
The prepared compounds were identified by some physical properties and spectroscopic techniques methods like infrared (FT-IR) spectroscopy, (C.H.N) elemental analysis, as well as the proton nuclear magnetic resonance (^{1}H-NMR). Scheme 1 includes all of the steps for this research work.



Scheme 1: Shows the preparation of bis Schiff bases (a1-5), bis oxazepine and bis benzoxazepine derivatives (b1-10).

Characterization of Schiff bases a(1-5)

Following the method of dibenzylidene succinohydrazide synthesis, succinohydrazide reacted with two moles of benzaldehyde or some of its replacements. The Schiff reaction undergoes a nucleophilic addition reaction mechanism to form a carbinol amine followed by release of water to form Schiff base as shown in Scheme 2. The IR and ^{1}H NMR spectrum of Schiff base **a4** will be taken as an example to discuss the spectral data for the series of **a(1-5)**.



Scheme 2: The reaction mechanism of Schiff base synthesis.

The FT-IR spectra of Schiff bases demonstrated the disappearance of the (O=C-H) stretching vibration in benzaldehyde derivatives and the (N-H) stretching vibration in succinic dihydrazide's primary amine group. The (N-H) stretching vibration appeared at (3369 cm^{-1}), and (C = N) stretching vibration observed within the range of (1605-1567 cm^{-1}) providing an indicator to the Schiff base forming, see Figure 1. The remaining packages were found in their expected positions. Table 4 shows the IR spectral data of series **a(1-5)** (21).

Figure 1: The IR spectrum of compound **a4**.

Table 4: FT-IR data of compounds **a(1-5)**.

Comp. No.	**X**	**str. N-H** cm^{-1}	**Str. C=N** cm^{-1}	**str. =C-H** cm^{-1}	**str.Ar C=C** cm^{-1}	**Other absorptions** cm^{-1}
a1	H	3295	1598	3023	1556 1503	asym.str. (C-H) 2923 sym.str. (C-H) 2854
a2	4-Cl	3246	1605	3067	1600 1495	str. (C- Cl) 737 asym.str. (C-H) 2934 sym.str. (C-H) 2867
a3	4-Br	3245	1567	3156	1556 1489	str. (C-Br) 750 asym.str. (C-H) 2987 sym.str. (C-H) 2839
a4	4-OCH_3	3369	1585	3080	1554 1500	str. (C-O-C) 1122 asym.str. (C-H) 2928 sym.str. (C-H) 2856
a5	4-N,Ndi$(CH_3)_2$	3239	1578	3112	1555 1499	asym.str. (C-H) 2915 sym.str. (C-H) 2843

The ^{1}H-NMR spectrum **a4**, indicated a singlet at (δ= 2.25) ppm referring to the 4 protons of the two methylene groups (CH_2). The single signal at (δ = 3.22) ppm corresponded to the six protons of the two methoxy groups (OCH_3). The multiple bands at (δ = 6.52 -7.65) ppm indicating the (eight protons for aromatic rings and two olefinic protons). Finally, the single signal appeared at (δ = 9.88) ppm belonging to the N-H proton as exhibited in Figure 2. Furthermore, a singlet observed at (δ = 8.30) ppm referring to the CH=N proton. These provide evidence to obtain the desired product. For the remaining spectra in the series see Table 5.

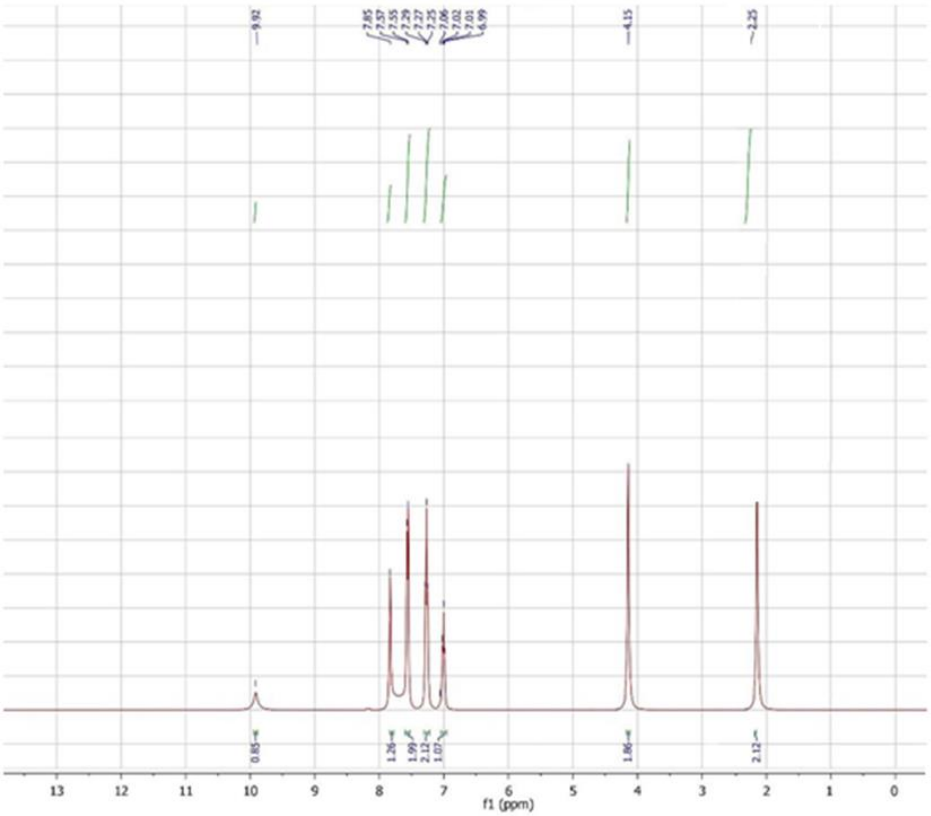
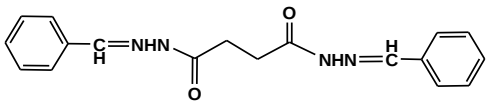
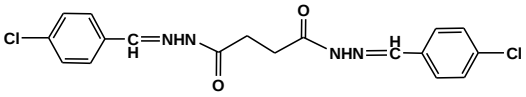
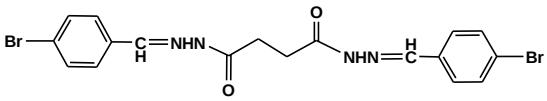
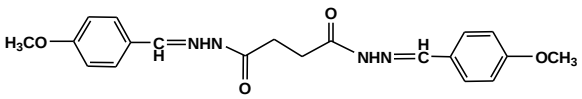
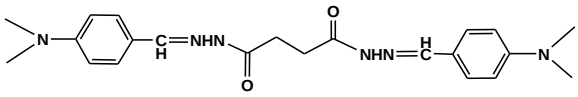


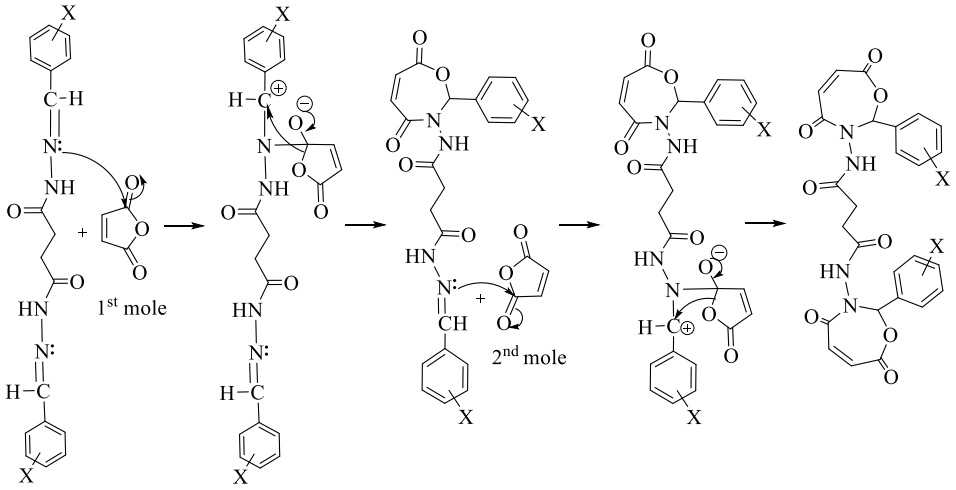
Figure 2: ^{1}H-NMR spectrum of compound **a4**.

Table 5: ^{1}H-NMR data of compounds **a(1-5)**.

Comp. No.	Structures	^{1}H NMR Spectral data (δ ppm)
a1		CH_2= 2.97 (4H, singlet) Ar + =C-H= 6.94 -8.29 (10H, multiple) N-H= 10.13(2H, singlet) CH=N=8.29 (2H, singlet)
a2		CH_2= 3.02 (4H, singlet) Ar + (=C-H)= 7.05 -8.15 (8H, multiple) N-H= 9.98(2H, singlet) CH=N=8.32 (2H, singlet)
a3		CH_2= 3.87 (4H, singlet) Ar + (=C-H)= 6.74 -8.05 (8H, multiple) N-H= 9.92(2H, singlet) CH=N=8.32 (2H, singlet)
a4		CH_2= 2.25 (4H, singlet) OCH_3= 3.22 (6H, singlet) Ar + (=C-H)= 6.52 -7.65 (8H, multiple) N-H= 9.88 (2H, singlet) CH=N=8.30 (2H, singlet)
a5		CH_2= 2.97 (4H, singlet) N,N-diCH_3= 3.45 (12H, singlet) Ar + (=C-H)= 6.89 -7.78 (8H, multiple) N-H= 10.15 (2H, singlet) CH=N=8.31 (2H, singlet)

Characterization of bis oxazepinedione compounds b(1-5)

The synthesis of bis oxazepinediones was achieved by Schiff bases **a(1-5)** reaction with maleic anhydride. This reaction proceeds via a mechanism involving nucleophilic assault by the succinohydrazide molecule on the carbon atom in the carbonyl group of anhydrous malic acid to give a polar compound. This leads to break and form bonds resulting in the oxazepine ring formation, see Scheme 3. The IR and ^{1}H NMR spectrum of bis oxazepinedione **b5** will be discussed as an example for the spectral data from the series of **b(1-5)**.



Scheme 3: The reaction mechanism of bis oxazepine synthesis.

The IR spectrum of bis oxazepinedione **b5** demonstrated the absence of the (C=N) bond stretching Schiff base derivatives, while the vibrational band appeared at (1612 cm^{-1}) as shown in (Figure 3). This belongs to the olefinic bond in oxazepine ring and it is evidence for Schiff cyclization reaction occurrence. The remaining packages were found in their expected locations. The remaining spectra of series **b(1-5)** collected in Table 6.

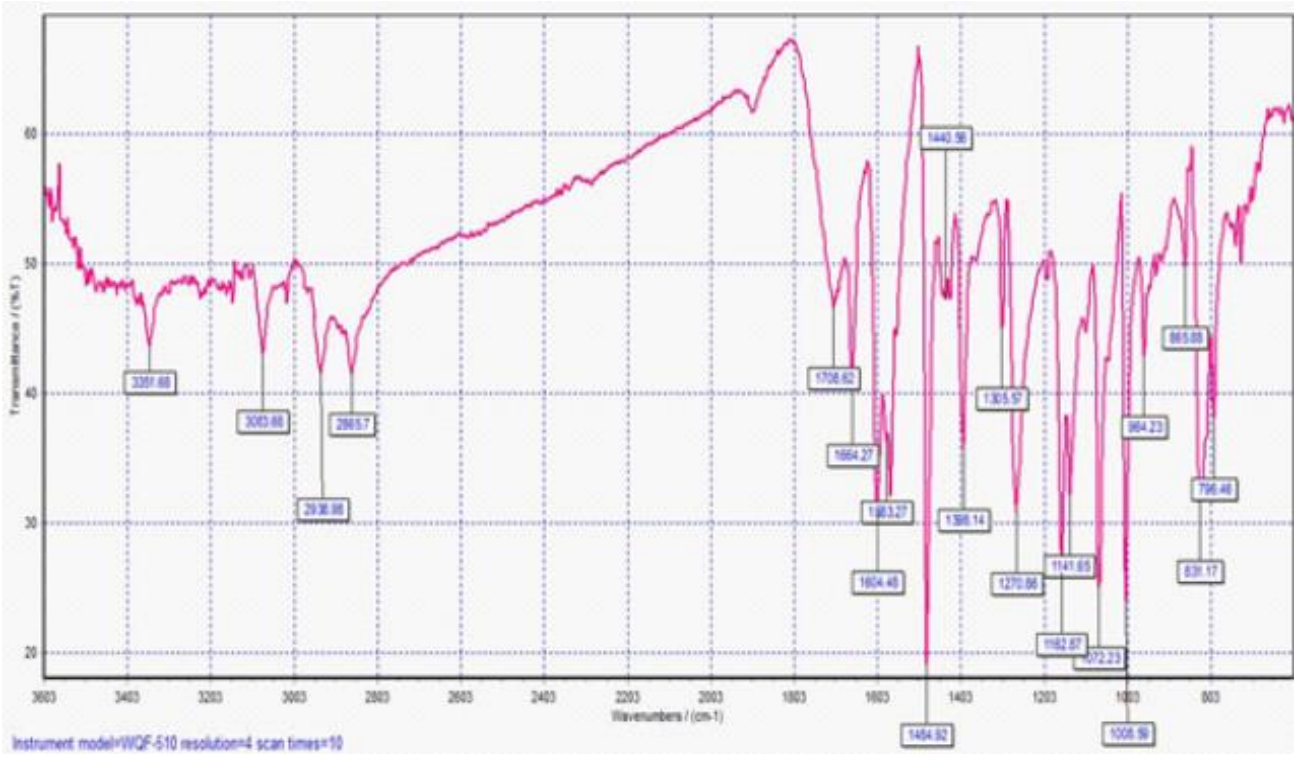


Figure 3: The IR spectrum of compound **b5**.

Table 6: FT- IR data of compounds **b(1-5)**.

Comp. No.	**X**	**str. C=O Lactone** cm^{-1}	**str. C=O Lactam** cm^{-1}	**str. =C-H** cm^{-1}	**str. C=C** cm^{-1}	**Other absorptions** cm^{-1}
b1	H	1673	1530	3052	1615	asym.str. (C-H) 2965 sym.str. (C-H) 2823
b2	4-Cl	1695	1555	3097	1600	str. (C- Cl) 725 asym.str. (C-H) 2983 sym.str. (C-H) 2821
b3	4-Br	1710	1667	3127	1595	str. (C-Br) 750 asym.str. (C-H) 2929 sym.str. (C-H) 2831
b4	4-OCH_3	1708	1664	3063	1604	str. (C-O-C) 1270 asym.str. (C-H) 2936 sym.str. (C-H) 2865
b5	4-N,$N(CH_3)_2$	1708	1627	3068	1612	asym.str. (C-H) 2965 sym.str. (C-H) 2838

The ^{1}H-NMR spectrum of bis oxazepine **b5** exhibited a singlet at (δ=1.70) ppm for the four protons of the two methylene groups (CH_2) and a singlet at (δ=3.53) ppm for the twelve protons of the four methyl groups (CH_3). Multiple bands observed at (δ=6.95-7.42) ppm belonging to the (eight protons for phenyl rings, two olefinic protons and the protons at the position 2 in the two oxazepine rings). Finally, the single signal appeared at (δ=9.35) ppm for the N-H protons, see Figure 4. These refer to achieve the rection of bis oxazepinediones **b(1-5)**. The remaining spectra in the series summarized in Table 7.

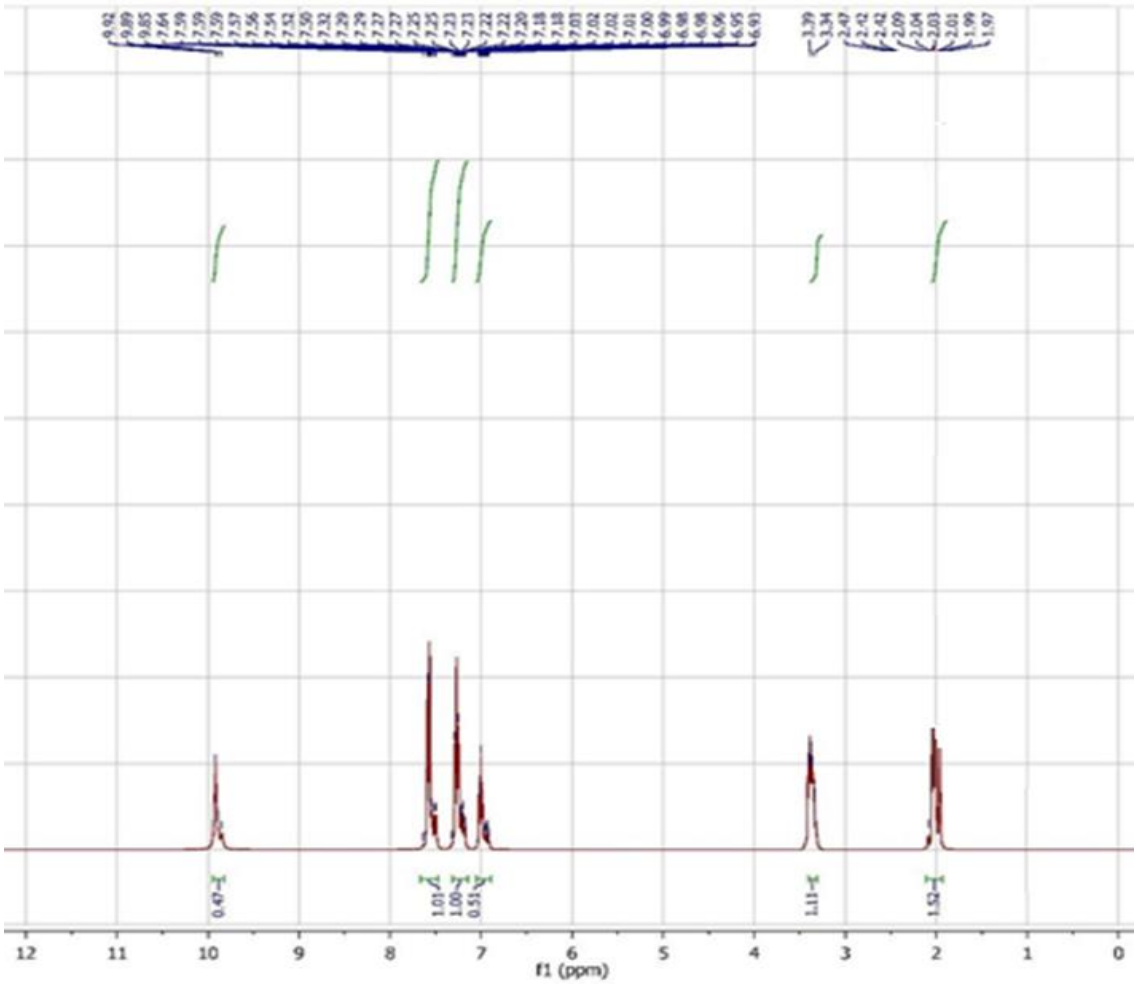


Figure 4: [1]H-NMR spectrum of compound **b5**.

Characterization of bis benzoxazepinedione compounds b(6-10)

Synthesis of bis benzoxazepinediones **b(6-10)** is similar to bis oxazepinediones including the reaction conditions and its mechanism. The difference is only using phthalic anhydride instead of maleic anhydride. In Figure 5 the IR spectra of benzoxazepine compounds **b10** the (C=N) bond stretching vibration for Schiff base disappeared and another band appeared at (1500-1484 cm^{-1}) for the olefinic bond in benzoxazepine ring. The remaining packages were found in their expected positions as the same to the oxazepine situation. See (Table 8) for the remaining spectral data of series **b(6-10)**.

Table 7: ^{1}H-NMR data of compounds **b(1-5)**.

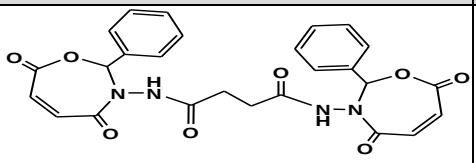
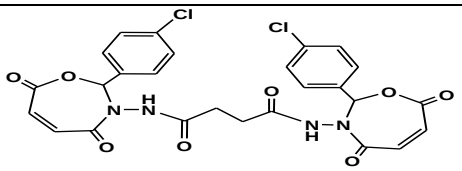
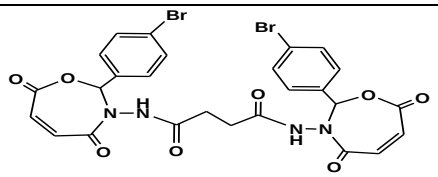
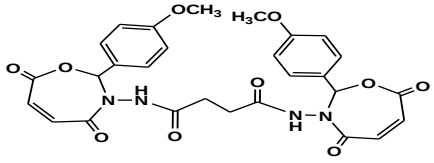
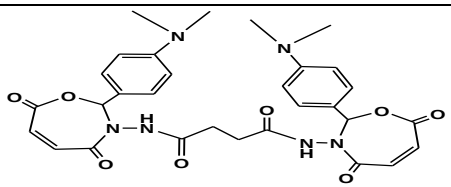
Comp. No.	Structures	^{1}H NMR Spectral data (δ ppm)
b1		CH_2= 2.05 (4H, singlet) Ar +(CH=CH) + (C_2-H)= 6.89-8.24 (16H, multiple) N-H= 8.55 (2H, singlet)
b2		CH_2= 1.98 (4H, singlet) Ar +(CH=CH) + (C_2-H)= 6.48-7.45 (14H, multiple) N-H= 8.31 (2H, singlet)
b3		CH_2= 2.76 (4H, singlet) Ar +(CH=CH) + (C_2-H)= 6.86 -8.12 (14H, multiple) N-H= 9.11 (2H, singlet)
b4		CH_2= 2.14 (4H, singlet) OCH_3= 3.26(6H, singlet) Ar +(CH=CH) + (C_2-H)= 6.31 -7.58 (14H, multiple) N-H= 8.75 (2H, singlet)
b5		CH_2= 1.70 (4H, singlet) CH_3= 3.53(12H, singlet) Ar +(CH=CH) + (C_2-H)= 6.95 -7.42 (14H, multiple) N-H= 9.35 (2H, singlet)

Figure 5: The IR spectrum of compound **b10**.

Table 8: FT- IR data of compounds **b(6-10)**.

Comp. No.	**X**	**Y C=O Lactone Cm^{-1}**	**υ C=O Lactam Cm^{-1}**	**Y =CH Cm^{-1}**	**υAr C=C Cm^{-1}**	**Other absorptions Cm^{-1}**
b6	H	1686	1546	3056	1535 1498	asym.υ (C-H) 2965 sym.υ (C-H) 2839
b7	4-Cl	1725	1595	3109	1527 1499	υ (C- Cl) 735 asym.υ (C-H) 2987 sym.υ (C-H) 2832
b8	4-Br	1699	1516	3037	1494 1465	υ (C-Br) 750 asym.υ (C-H) 2919 sym.υ (C-H) 2867
b9	4-OCH_3	1679	1618	3067	1532 1497	υ (C-O-C) 1204 asym.υ (C-H) 2935 sym.υ (C-H) 2898
b10	4-$N(CH_3)_2$	1664	1600	3062	1500 1488	asym.υ (C-H) 2925 sym.υ (C-H) 2858

The ^{1}H-NMR spectrum of bis benzoxazepinedione **b10** indicated a singlet band at (δ=2.81) ppm representing to the four protons of the two methylene groups (CH_2) and another singlet at (δ = 2.70) ppm for the twelve protons of the four methyl groups (CH_3). Multiple signals observed at (δ= 6.53-8.26) ppm belong to the (sixteen aromatic protons, and the protons at the position 2 for oxazepinediones). A singlet band also appeared at (δ=10.25) ppm belonging to the N-H proton, see Figure 6. These support the rection occurrence of bis benzoxazepinediones b6-10. The remaining spectra in the series mentioned in Table 9.

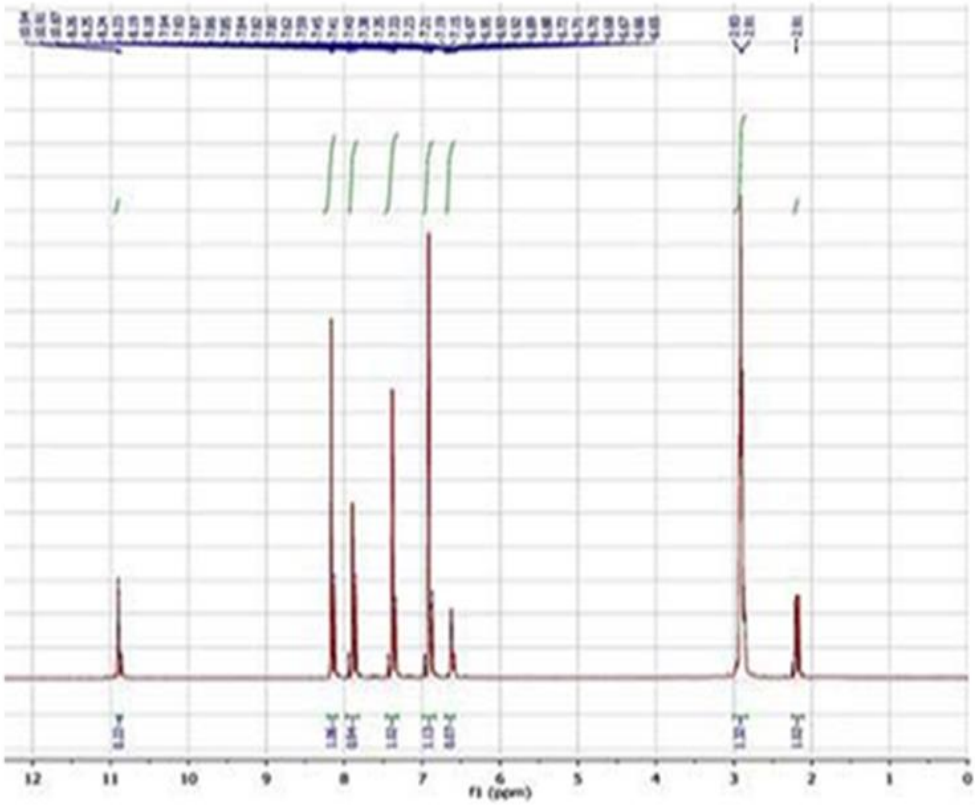
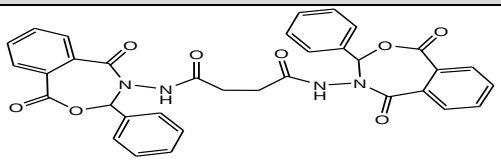
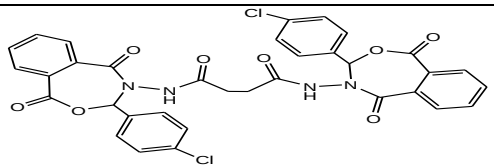
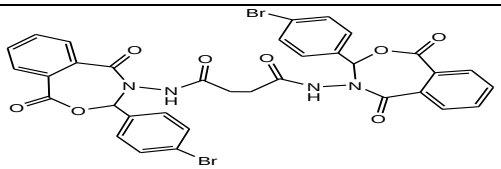
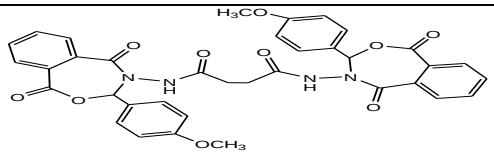
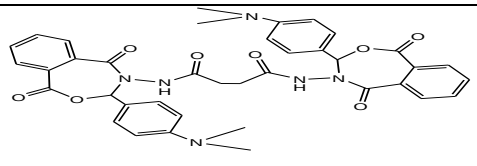


Figure 6: ^{1}H-NMR spectrum of compound **b10**.

Table 9: ^{1}H-NMR data of compounds **b(6-10)**.

Comp. No.	Structures	^{1}H NMR Spectral data(δ ppm)
b6		CH_2= 2.10 (4H, singlet) Ar + (C_2-H)= 6.43-8.75 (20H, multiple) N-H= 9.57 (2H, singlet)
b7		CH_2= 1.98 (4H, singlet) Ar + (C_2-H)= 6.48-7.45 (18H, multiple) N-H= 9.32 (2H, singlet)
b8		CH_2= 2.18 (4H, singlet) Ar + (C_2-H)= 6.86 -8.12 (18H, multiple) N-H= 9.11 (2H, singlet)
b9		CH_2= 2.56 (4H, singlet) OCH_3= 3.62(6H, singlet) Ar + (C_2-H)= 6.55 -8.62 (18H, multiple) N-H= 9.85 (2H, singlet)
b10		CH_2= 2.18 (4H, singlet) CH_3= 2.70 (12H, singlet) Ar + (C_2-H)= 6.53 -8.26 (18H, multiple) N-H= 10.25 (2H, singlet)

Elemental analysis (C.H.N) for all the synthesized compounds a(1-5) and b(6-10)

The elemental analysis measurements have been calculated for all the synthesized compounds. The results indicated that the structures for all of the synthesized derivatives were confirmed due to the too slight different in elements values. The different was within the permitted and accepted range for errors in weight calculations when the theoretical values compared to the practical values as shown in Table 10. The elemental analysis results were agreed with the spectral data (IR and HNMR) and this confirms the structure for the newly synthesized bis oxazepinedione and benzoxazepinedione derivatives in this research.

Table 10: The precise elemental analysis (C.H.N) of compounds a(1-5) and b(6-10)

Comp. NO.	Molecular Formula	Analysis		
		C	H	N
		Calculated	Calculated	Calculated
		Found	Found	Found
a1	$C_{18}H_{18}N_4O_2$	67.07	5.63	17.38
		67.09	5.60	17.35
a2	$C_{18}H_{16}Cl_2N_4O_2$	55.26	4.12	14.32
		55.28	4.10	14.31
a3	$C_{18}H_{16}Br_2N_4O_2$	45.03	3.36	11.67
		45.05	3.33	11.65
a4	$C_{20}H_{22}N_4O_4$	62.82	5.80	14.65
		62.72	5.77	14.6
a5	$C_{22}H_{28}N_6O_2$	64.68	6.91	20.57
		64.48	6.87	20.55
b1	$C_{26}H_{22}N_4O_8$	60.23	4.28	10.81
		60.21	4.27	10.79
b2	$C_{26}H_{20}Cl_2N_4O_8$	53.17	3.43	9.54
		53.15	3.41	9.51
b3	$C_{26}H_{20}Br_2N_4O_8$	46.18	2.98	8.28
		46.16	2.96	8.29
b4	$C_{28}H_{26}N_4O_{10}$	58.13	4.53	9.68
		58.12	4.50	9.70
b5	$C_{30}H_{32}N_6O_8$	59.60	5.33	13.90
		59.61	5.30	13.91
b6	$C_{34}H_{26}N_4O_8$	66.02	4.24	9.06
		66.00	4.21	9.05
b7	$C_{34}H_{24}Cl_2N_4O_8$	59.40	3.52	8.15
		59.42	3.51	8.12
b8	$C_{34}H_{24}Br_2N_4O_8$	52.60	3.12	7.22
		52.57	3.11	7.23
b9	$C_{36}H_{30}N_4O_{10}$	63.71	4.46	8.26
		63.73	4.43	8.25
b10	$C_{38}H_{36}N_6O_8$	64.76	5.15	11.93
		64.75	5.13	11.94

The heat of formation and steric energy of new synthesized compounds a(1-5) and b(6-10)

The heat of formation (HF) and steric energy (SE) for the synthesized compounds have been studied to assess the configuration stability. For the prepared Schiff bases, the most stable configurations formula in space are

compound a3 and a4 depending on their more less SE and HF values respectively. However, within bis oxazepinediones b1-5 and bis benzoxazepinediones b6-10, compounds b5 and b9 are the less or more negative value leading to make them to be the most stable formula as shown in (Tabe 10). This is could be related to the presence of releasing groups [OCH_3 and $N(CH_3)_2$]. D3 structures of compound (b9) is exhibited in Figure 7. The study of the heat of formation (HF) and steric energy (SE) helps to more and better understanding of the structure stability, atom's structure arrangements and its behavior toward biological activity effects for future research studies.

Table 11: Steric energy and heat of formation of compounds a(1-5) and b(6-10).

Comp. NO.	Molecular Formula	HF. Kcal / mol	SE. Kcal /mol
a1	$C_{18}H_{18}N_4O_2$	55.62	56.40
a2	$C_{18}H_{16}Cl_2N_4O_2$	38.89	32.58
a3	$C_{18}H_{16}Br_2N_4O_2$	65.95	30.48
a4	$C_{20}H_{22}N_4O_4$	-20.29	46.74
a5	$C_{22}H_{28}N_6O_2$	69.45	49.98
b1	$C_{26}H_{22}N_4O_8$	1218.13	1285.68
b2	$C_{26}H_{20}Cl_2N_4O_8$	1355.83	1285.51
b3	$C_{26}H_{20}Br_2N_4O_8$	1033.21	1285.60
b4	$C_{28}H_{26}N_4O_{10}$	1031.47	1301.90
b5	$C_{30}H_{32}N_6O_8$	1031.18	-67.72
b6	$C_{34}H_{26}N_4O_8$	-64.80	189.21
b7	$C_{34}H_{24}Cl_2N_4O_8$	-73.24	189.47
b8	$C_{34}H_{24}Br_2N_4O_8$	-62.09	189.73
b9	$C_{36}H_{30}N_4O_{10}$	-136.81	196.67
b10	$C_{38}H_{36}N_6O_8$	-47.47	210.56

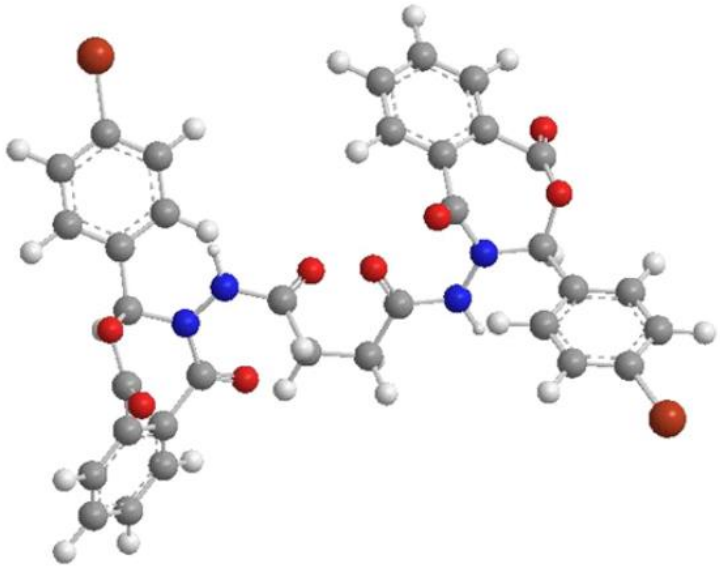


Figure 7: 3D structure of compound **b9**.

Conclusions

This study successfully synthesized some new substituted bis oxazepinediones and benzoxazepinediones derivatives, from Schiff's bases as the initial step followed by the cyclization reaction. The results of the characterization process introduce strong confirmational to the structure of the desired products. Theatrical characteristics were studied to calculate HF and steric energy SE, in which compounds (**a3, a4, b5 and b9**) are possess high stability and less steric effect. This may be attributed with the presence of donating groups in the structure [OCH_3 and $N(CH_3)_2$]. The study of the HF and SE should be considered and given more interest especially before running biological effect tests as it provides information about understanding of the structure stability and atoms arrangements. This can predict the behavior of compounds toward biological activity assessments. The results suggest to evaluate biological activity for the newly synthesized compounds in future works.

Acknowledgements

The author would like to acknowledge who helping in achieving this research.

Conflict of interest

The authors confirm that they are not affiliated with or involved in any organization or entity with financial interests.

References

1. Kapoor, K., Singh, P., & Gautam, D. (2018). Heterocyclic scaffolds: A key tool in modern drug discovery. Current Topics in Medicinal Chemistry, 18(5), 349-358.
2. J.S. Salem, J.H. Abdulwahid, S. Beebany, B. Mohammed, Synthesis, Identification, and Antibacterial Effect Assessment of Some New 1, 4-Thiazepines, Derived from Substituted Diphenyl Acrylamides and Diphenyl Dienones, Chemical Methodologies, 7 (2023) 509-523.
3. Daina,A., Michielin, O., & Zoete, V. (2017).Swiss ADME: A Free Web Tool to Evaluate Pharmacokinetics, Drug-likeness and Medicinal Chemistry Friendliness of Small Molecules. Scientific Reports,7, 42717.
4. Li, W., Tian, W., Yuan, G., Pan, W., He, Y., Chen, C., & Chen, Y. (2020). Recent Advances in the Discovery of Small-Molecule Drug Candidates Targeting MicroRNAs in Cancer. Journal of Medicinal Chemistry, 63(4), 1545-1568.
5. Chen, Q., Wu, Y., & Cao, W. (2018). Advances in heterocyclic dyes for dye-sensitized solar cells. Chemical Society Reviews, 47(9), 3453-3488.
6. Anastas, P. T., & Kirchhoff, M. M. (2002). Origins, Current Status, and Future Challenges of Green Chemistry. Accounts of Chemical Research, 35(9), 686-694.
7. Katritzky, A. R., Poznanski, A. F., & Karelson, M. (2006). Handbook of Heterocyclic Chemistry (3rd ed.). Elsevier.
8. Zhang, Y., Guo, J., & Wang, H. (2016). Strategies for constructing oxazepines: recent advances. Tetrahedron Letters, 57(4), 365-372.
9. Reichardt, C., Saller, A., Geibler, F., & Verhoefen, S. (2014). Heterocyclic amides: An easy way to prepare oxazepine derivatives. Tetrahedron Letters, 55(45), 6186-6189.
10. Buchta, W. M., & Chandler, B. D. (2012). Advances in the Beckmann Rearrangement. Tetrahedron, 68(27-28), 5355-5412.
11. Ahmed, A., Mahdi, S., Hussein, A., Hamed, A., & Yousif, E. (2015). Antibacterial study of some oxazepine derivatives. Al-Nahrain Journal of Science, 18(4), 22-26.
13. Hassan, S. A., Aziz, D. M., Abdullah, M. N., Bhat, A. R., Dongre, R. S., Ahmed, S., ... & Jamalis, J. (2023). Design and Synthesis of Oxazepine Derivatives from Sulfonamide Schiff bases as Antimicrobial and Antioxidant agents with low Cytoxicity and Hemolytic Prospective. Journal of Molecular Structure, 136121.
14. Abid, O. H., & Ahmed, K. R. (2018). Preparation and identification of 1, 3-oxazepine derivatives from selected carboxylic acid anhydrides with imines derived from 4-methyl aniline. Al-Must J Sci, 29(2), 93-100.
15. Abbas, A. K., & Jber, N. R. (2020). Synthesis and Estimation of Biological Activity of New Oxazepine Derivatives. International Journal of Pharmaceutical Research, 12(2), 3750-3758.
16. Sallal, Z. A., & Ghanem, H. T. (2018). Synthesis and Identification of New Oxazepine Derivatives bearing

Azo group in their structures. Iraqi Journal of Science, 1-8.
17. Kapur S, Cho R, Jones C, Mckay G, Zipursky, Biol Psychiatry, 45, 1217-1220 (1999).
Saad Salim Jasim, Ghazwan Hasan Al-Somaidaie, Siham Shakor Obid, Hiro Mohammed Obaid, Journal of Babylon University/Pure and Applied Sciences, Vol.(24), No.(7),1836-1847 (2016).
18. N.M. Aljamali, Synthesis and identification of oxazipene, diazipene compounds via peri cyclic reactions, J Chem & Cheml Sci, 3 (2013) 64-69.
19. S.I.C. AL-Khazraji, Synthesis of and characterization of some Heterocyclic Compounds derived from Thiophenol, Egyptian Journal of Chemistry, 64 (2021) 5655-5662.
20. R. M. Silverstein, G.C.Bassler and T.C. Morrill, Spectrometric identification of organic compounds. 3rdEdu. John Wiley and sons, Inc, New York, (1974), 25, pp.100
21. R.I. Al-bayati,A. A Hussain Al-Amiery and. Y. K. Al-Majedy, African J. of pure and Applied Chemistry, Vol. 4(6), pp.74-86 (2010).