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Synthesis and Study the Anti-Bacterial Effect of New Oxazepine Derivatives

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Abstract*. in this study was preparation heterocyclic compounds of seven ring know Oxazepine compounds through reaction of schiff base compounds with cyclic anhydride (malic anhydride), schiff bases compounds synthesis by reaction between amins and different aldehyde compounds and the prepared compounds were identification by infrared (IR). The biological activity of the prepared compounds was studied and its effect on two bacteria (Escherichia coli)positive bacteria and (Staphylococcus aureus) negative bacteria*.

Keywords: *Biological Activity, Heterocyclic Compounds, Oxazepine, Schiff Base.*

1. INTRODUCTION

Heterocyclic compounds are organic compounds with a ringstructure that contains one carbon atom and at least one other element, such as S, N, or O. Heterocyclic rings can be either aromatic or nonaromatic many significant physical and chemical properties (Moldoveanu, 2010). A some of the heterocyclic compounds are be essential to life.

Various compounds such as vitamins, antibiotics essential amino acids and alkaloids. presence of hetero atom gives the heterocyclic compounds many significant physical and chemical properties (Aljamali, 2014). A Schiffs' base is a type of chemical compounds containing carbon nitrogen double bond in which nitrogen atom connected to alkyl or aryl group, these named Hugo Schiff (Chakraborti et al., 2004). Schiff bases have been reported to be used as analgesic, anticancer (Mohamed et al., 2012), antiviral, antifungal (Hussien, 2011), and antibacterial (Jarrahpour & Zarei, 2004). Schiff base ligands are essential in the field of coordination chemistry, especially in the development of complexes of Schiff bases because these compounds are potentially capable of forming stable complexes with metal ions (Naeimi et al., 2007).

Some of Schiff bases have been used as catalysts, components of thin-film organic solar cells and organic light emitting diodes thin-film organic solar cells, fluorescence properties are also known (Ibis & Zora, 2020). Oxazepines are important heterocyclic compounds found in many biologically active molecules (Zora et al., 2018). oxazepine ring which constitutes a class of- nitrogen and oxygen containing seven membered heterocyclics have been, investigated for their antibacterial activity. It is prepared by the pericyclic cycloaddition of schiff bases with succinic anhydrides, phthalic, nitrophthalic

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and maleic (Sunil et al., 2014). oxazepines has been studied in the last decades and still gain importance for their excitingmedicinal andbiological, like anticancer, antidepressant, antifungal, antipsychotic, anticonvlsant, antirombotic and telomeraseinhibitor. Oxazepine derivatives have medicinal and biological activities against different types bacteria (Abbas, 2016).

Preparation Of Imine (Schiff Bases) (How & Chinese, n.d.; Husein et al., 2020)

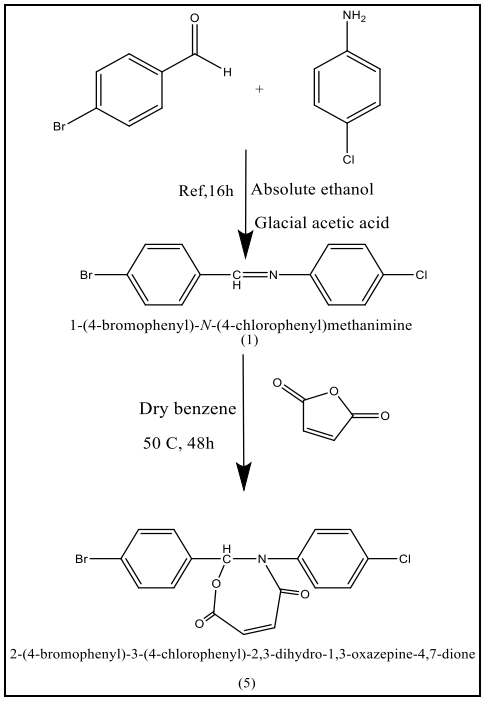
Four Schiff bases were prepared by dissolving specific quantities of amino compounds where the following amines were used(4-Chloro aniline, 4-Amino phenol, 4-Nitro aniline) with aldehyde compounds where the following aldehydes are used (4-Bromobenzaldehyde,4-chlorobenzaldehyde) in absolute Ethanol adding to the mixture 3 drops of Glacial acetic acid and the escalation process for the prepared mixtireat at atemperature of 79°C the process the reaction Was monitored by TLC through the use of the mobile phase (benzene-methanol) at a ratio of (1:4).

Preparation Of Oxazepine Compounds (Hassan & Kadhim, 2023; Sitepu et al., 2018)

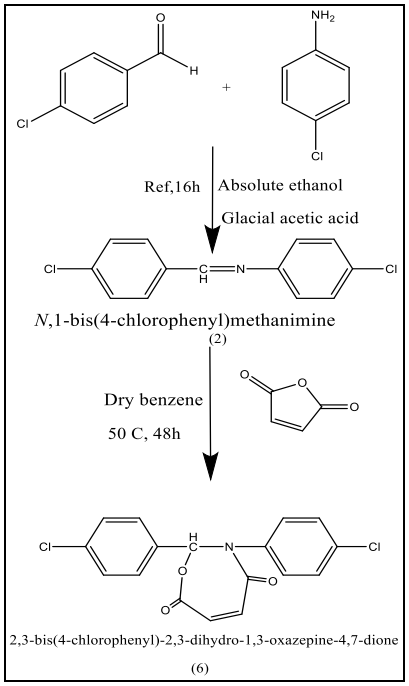
The oxazepine compounds were prepared using (Maleic anhydride) with the Schiff bases and the escalation of the mixture after dissolving both the Schiff base and the anhydride by dry benzene the mixture was escalated under 50 degrees the process the reaction Was monitored by TLC at a ratio of (1:4) from (benzene-methanol).

2. MATERIALS

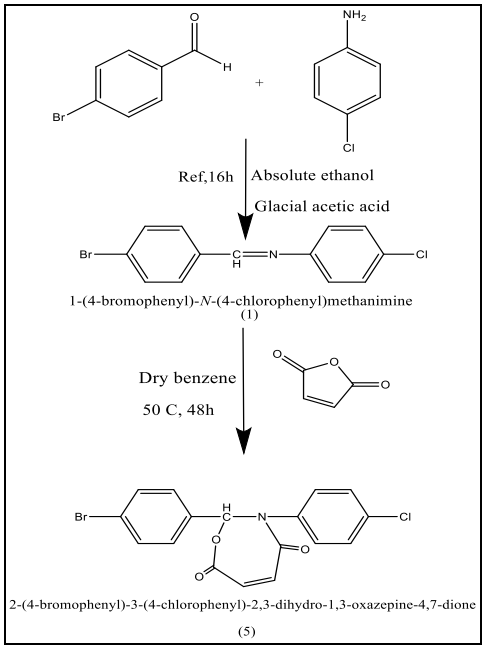
FT-IR spectra were recorded on a (SHIMADZU) FTIR-400 spectrophotometer (FTIR) Spectra (400-4000 cm-1) in KBr disk TLC was performed on glass plates coated with layer of silica-gel Compounds were detected by iodine vapor (Fluka).



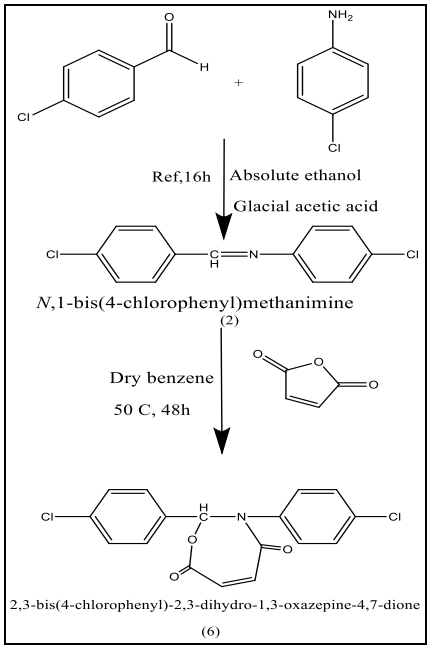
Scheme 1



Scheme 2



Scheme 3



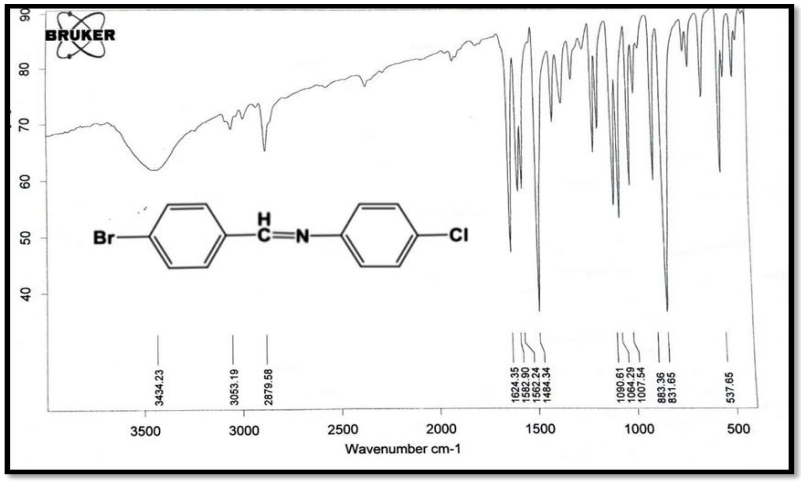
Scheme 4

Infrared spectra

Identification of compound (Moldoveanu, 2010)

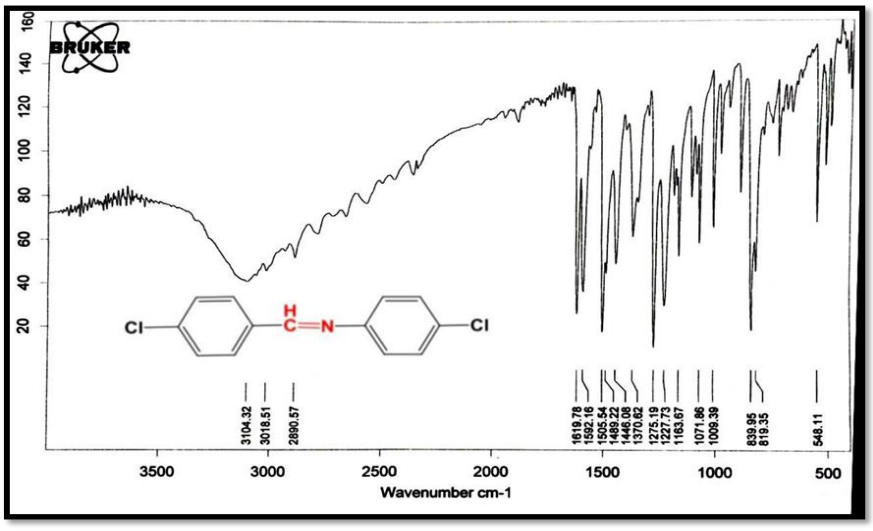
Show the infrared spectrum the appearance of an absorption beam at the (1620cm-1) due to chemical bond (C=N), the abearance of an absorption band at frequency (1064cm-1) is attributed to the chemical association to the bond (C-N). The absorption

band at frequency (2993cm-1) return to the aromatic (C-H) bond . the emergence of two absorbition beams at the frequency (1488cm-1) and in frequency (1581cm-1) returns to thearomatic (C=C) bonds, The absorption band at frequency (624cm- 1) belongs to the bond (C-Br), it was also observed that the NH2 absorption beams disappeared in the range (3533-3055 cm-1).



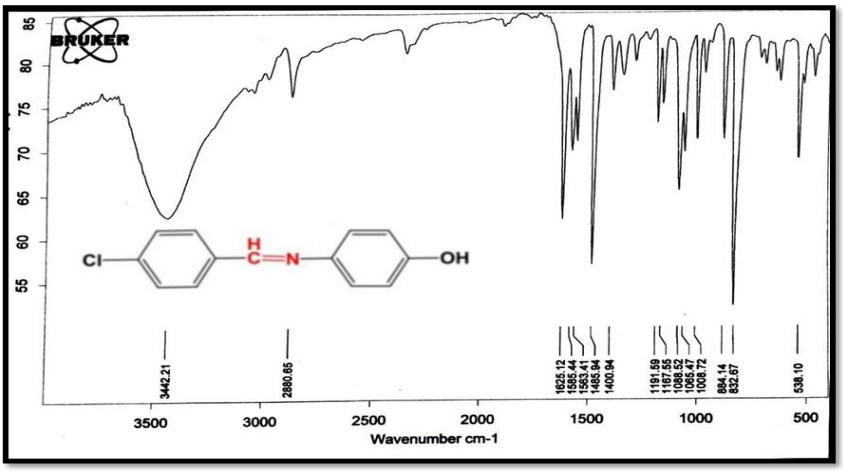
Identification of compound (Aljamali, 2014)

Show the infrared spectrum the appearance of an absorption beam at the (1620cm-1) due to chemical bond (C=N), the emergence of two absorbition beams at the frequency (1488cm-1) and in frequency (1581cm-1) returns to thearomatic (C=C) bonds, the abearance of infraredspectrum at (1064cm-1) is attributed to the chemical association to the bond (C-N). The absorption band at(2877cm-1) return to the aliphatic bond (C-H). The absorption band at frequency (624cm- 1) belongs to the (C-Cl) bond, it was also observed that the NH2 absorption beams disappeared in the range (3471-3200 cm-1).



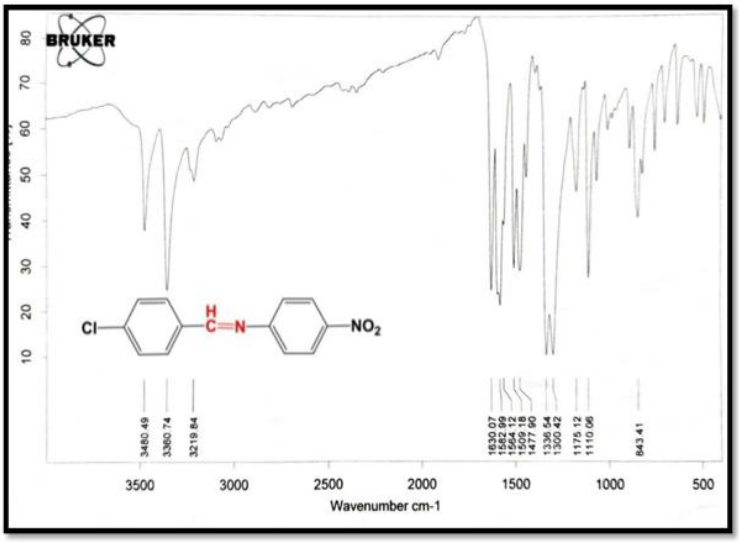
Identification of compound (Chakraborti et al., 2004)

Show the infrared spectrum the appearance of an absorption beam at the (1620cm-1) due to chemical bond (C=N), The absorption at (1589cm- 1) band returns to thearomatic (C=C) bonds, the abearance of an absorption band at (3101cm-1) is attributed to the chemical association to the bond (O-H). The absorption at (3016cm-1) band return to the aromatic (C-H) bond. The absorption band at (547cm- 1) belongs to the (C-Cl) bond.



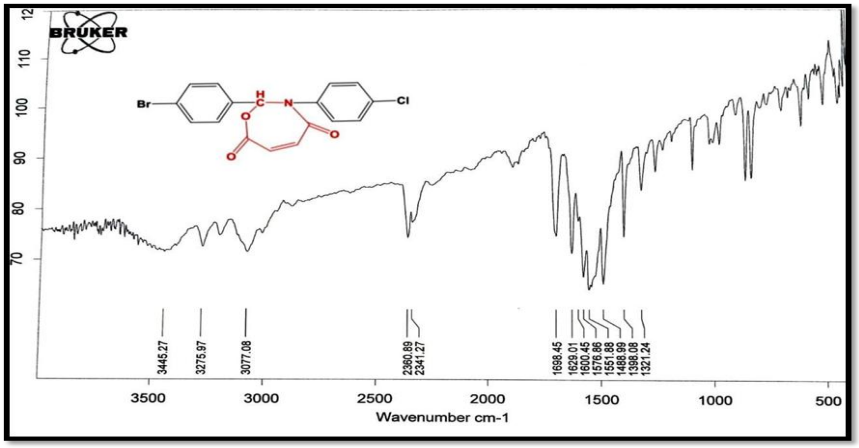
Identification of compound (Mohamed et al., 2012)

Show the infrared spectrum the appearance of an absorption beam at the (1627cm-1) due to chemical bond (C=N), The absorption band at (1581cm- 1) returns to thearomatic (C=C) bonds, the abearance of an absorption band at (1512cm-1) is attributed to the chemical association to the bond (N-O). The absorption at frequency (27796cm-1) band return to the aromatic (C-H) bond. The absorption band at frequency (524cm- 1) belongs to the bond (C-Cl).



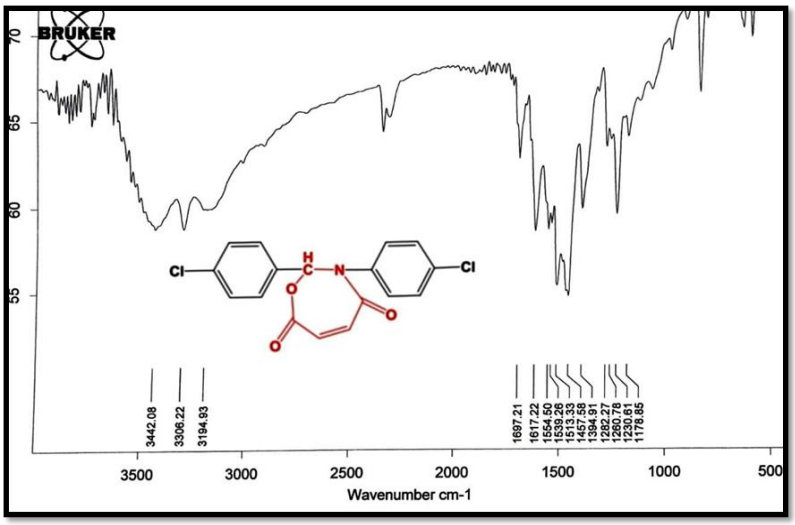
Identification of compound (Hussien, 2011)

Show the infrared spectrum the appearance of an absorption beam at the (1540cm-1) returns to thearomatic bond (C=C), the absorption band at frequency (3193 cm-1) return to the aromatic (C-H) bond, the absorption band at frequency (2851cm-1) return to the aliphatic bond (C-H), the absorption band at frequency (1697cm-1) return to the (C=O) in oxazepine ring, the absorption band at (1627cm-1) belongs to the (C=C) bond in oxazepine ring.



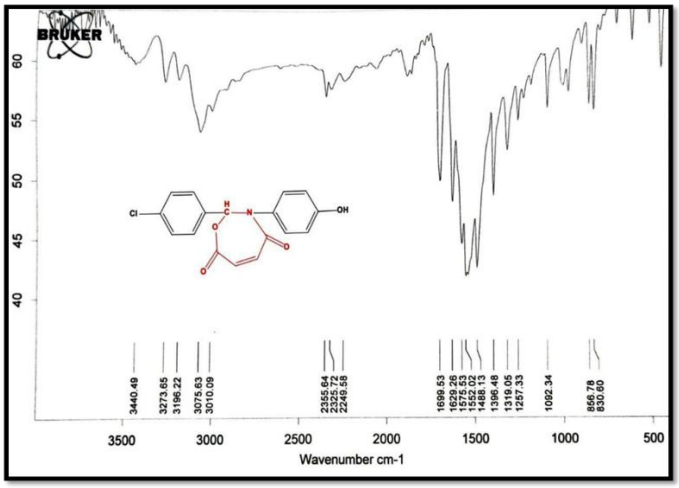
Identification of compound (Jarrahpour & Zarei, 2004)

Show the infrared spectrum the appearance of an absorption beam at the (1520cm-1) returns to thearomatic bond (C=C), the absorption at frequency (3300cm-1) band return to the aromatic (C-H) bond, the absorption band at frequency (2850cm-1) return to the aliphatic bond (C-H), the absorption band at frequency (1700cm-1) return to the (C=O) in oxazepine ring, the absorption at frequency (1558cm-1) band belongs to the (C=C) bond in oxazepine ring.



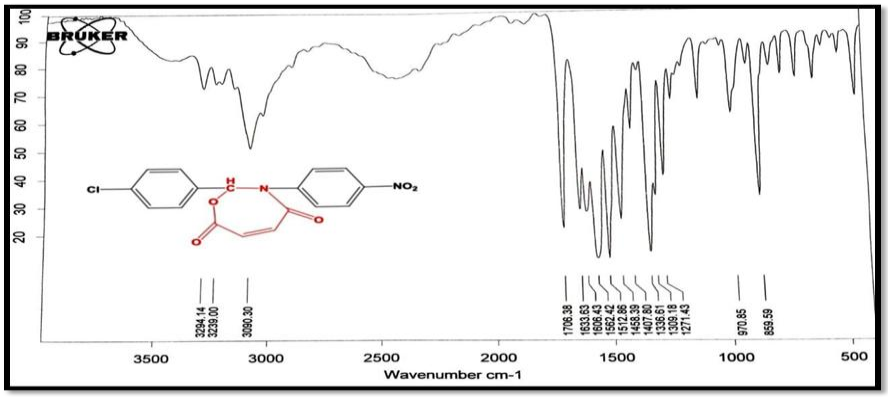
Identification of compound (Naeimi et al., 2007)

Show the infrared spectrum the appearance of an absorption beam at the (1500cm-1) returns to thearomatic bond (C=C), the absorption band at frequency (1697cm-1) return to the (C=O) in oxazepine ring, the absorption at frequency (3008cm-1) band return to the aromatic (C-H) bond, the absorption band at frequency (2877cm-1) return to the aliphatic bond (C-H), the absorption band at frequency (1250cm-1) return to the (C-O) in oxazepine ring, the absorption at frequency (1620cm-1) belongs to the band (C=C) bond in oxazepine ring.



Identification of compound (Ibis & Zora, 2020)

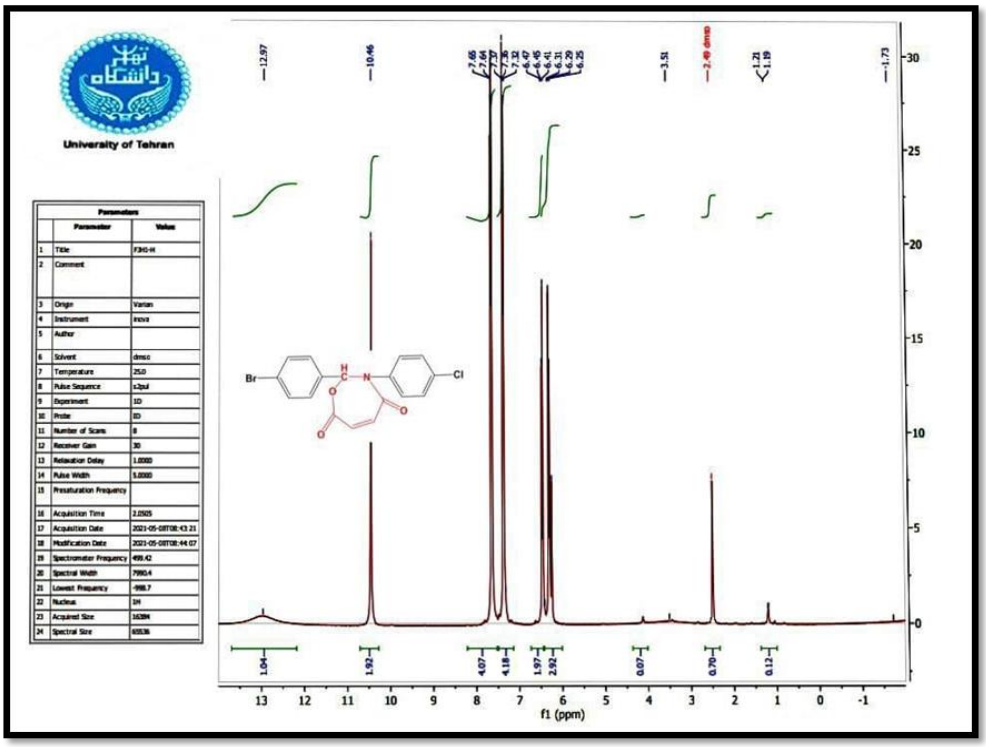
Show the infrared spectrum the appearance of an absorption beam at the (1635cm-1) returns to thearomatic bond (C=C), the absorption band at frequency (1272cm-1) return to the (C=O) in oxazepine ring, the absorption band at (3294cm-1) return to the aromatic (C-H) bond, the absorption band at frequency (2908cm-1) return to the aliphatic bond (C-H), the absorption band at frequency (1180cm-1) return to the (C-O) in oxazepine ring, the absorption at frequency (1704cm-1) band belongs to the (C=C) bond in oxazepine ring.



Proton-1-Nuclear Magnetic resonance (^{1}H-NMR) spectrum

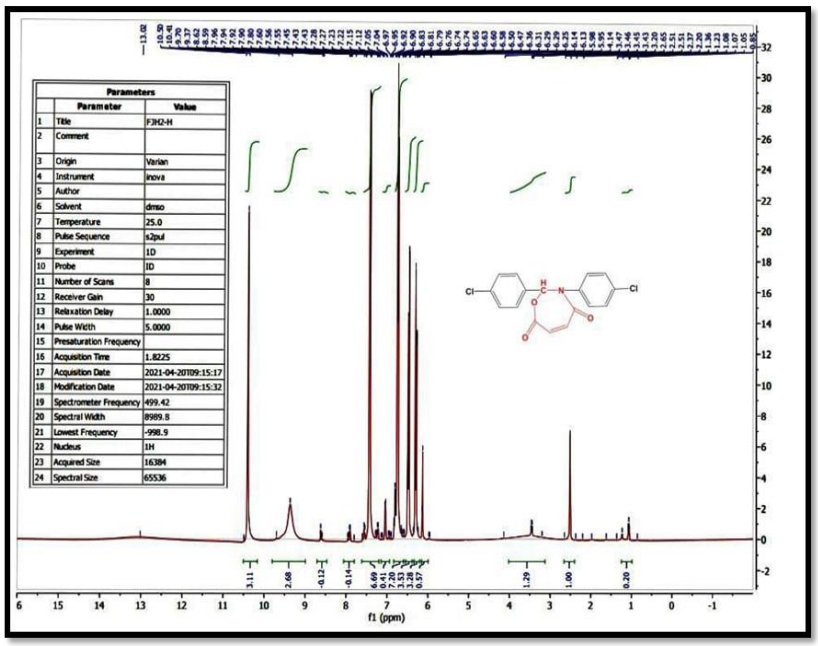
Identification of compound (5) by ^{1}H-NMR technique (Hassan & Kadhim, 2022)

By using the ^{1}H-NMR spectrum technique the identification of compound (Ibis & Zora, 2020) using DMSO was solved, the appearance a signal at the site (6,81 ppm) befonging to 2H in to (C=C) bond in oxazepine ring, the signal at the site(7,95ppm) befonging to 1H in to C-H, the signal at the sites (6,82-7,61 ppm) befonging to 10H in the aromatic rings, the signal at the location of (2,52ppm) returned to the solvent.



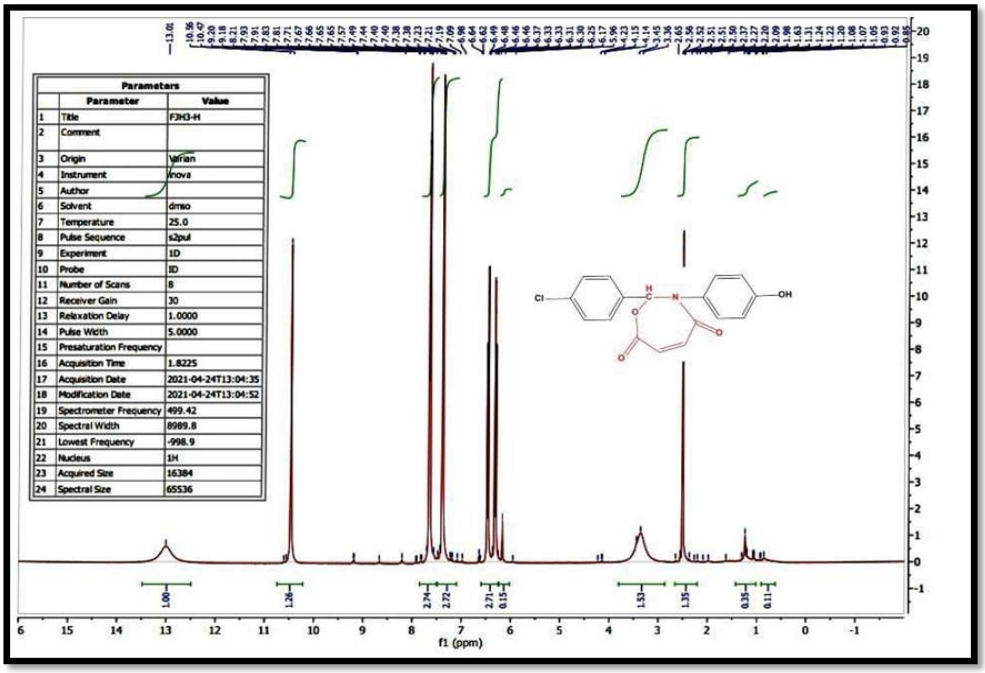
Identification of compound (Jarrahpour & Zarei, 2004) **by ^{1}H-NMR technique**

By using the ^{1}H-NMR spectrum technique the identification of compound (Jarrahpour & Zarei, 2004) using DMSO was solved, the appearance of a signal at the sites (6,4-7ppm) befonging to 10Hin the aromatic rings, a signal at the site (6,3ppm) befonging to 2H in to (C=C) bond in oxazepine ring,a signal at the site (7,45ppm) befonging to 1H in to C-H , a signal at the location of (2,5ppm) returned to the solvent.



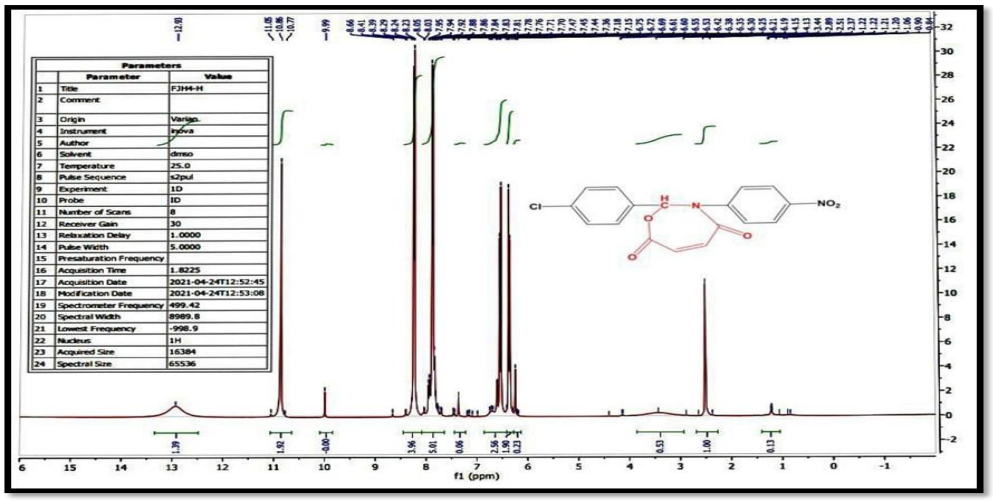
Identification of compound (Naeimi et al., 2007) **by ^{1}H-NMR technique**

By using the ^{1}H-NMR spectrum technique the identification of compound (Naeimi et al., 2007) using DMSO was solved, the appearance of a signal at the site (6,37ppm) befonging to 2H in to (C=C) bond in oxazepine ring, the signal at the sites (6,54-7,49 ppm) befonging to 10Hin the aromatic rings, the signal at the site (7,71 ppm) befonging to 1H in to C-H, the signal at the site (9,2ppm) befonging to 1H in to OH, the signal at the location of (2,52ppm) returned to the solvent.



Identification of compound (Ibis & Zora, 2020) **by ^{1}H-NMR technique**

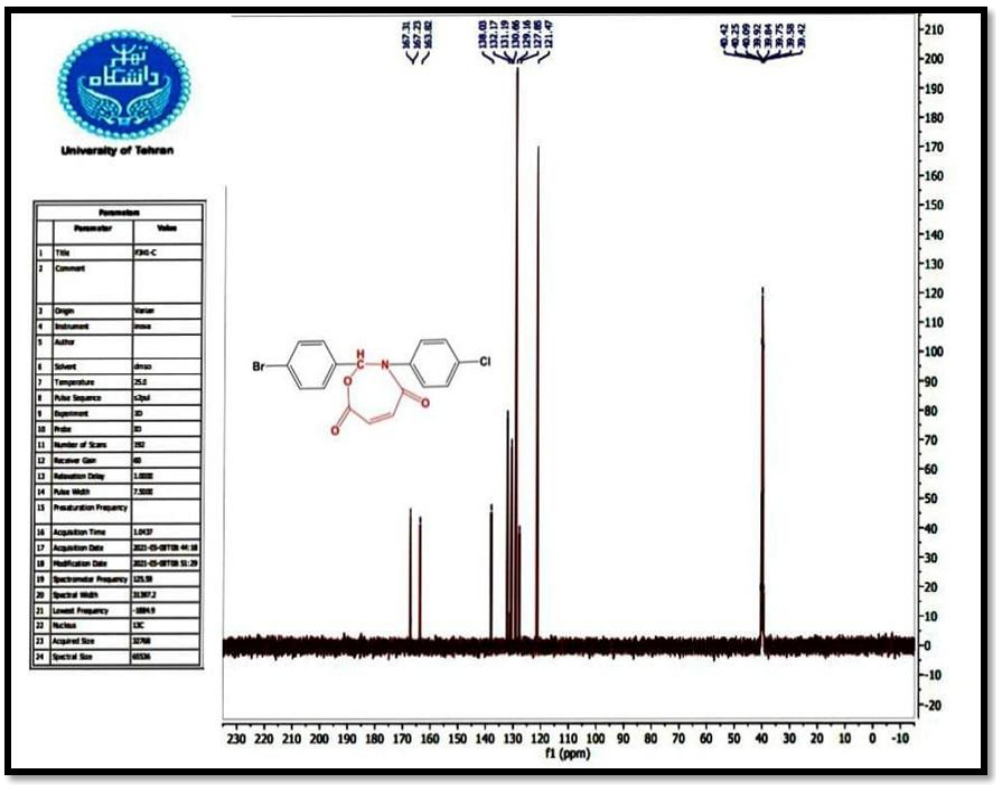
By using the ^{1}H-NMR spectrum technique the identification of compound (Ibis & Zora, 2020) using DMSO was solved, the appearance of a signal at the site(8,91ppm) befonging to 1H in to C-H, the signal at the sites (6,42-8,39ppm) befonging to 10Hin the aromatic rings, the signal at the site (6,38ppm) befonging to 2H in to (C=C) bond in oxazepine ring, the signal at the location of (2,51ppm) returned to the solvent.



Carbon-1-Nuclear Magnetic resonance (^{13}C-NMR) spectrum

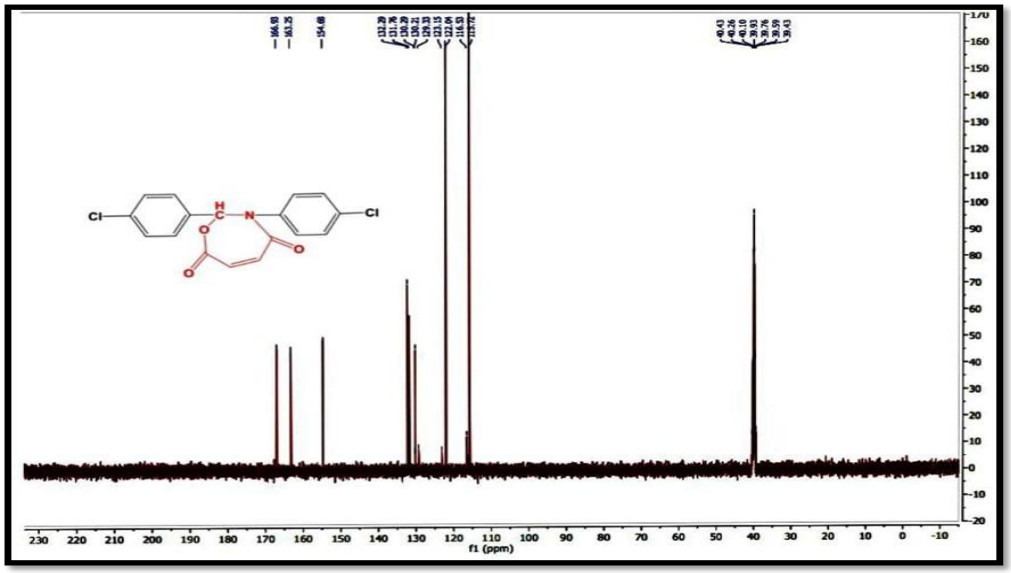
Identification of compound (Hussien, 2011) **by ^{13}C-NMR technique**

By using the ^{13}C -NMR technology and by using DMSO as a solvent this compound has been identification, the signal at (168ppm) at C_{10} in to C=O, the signal at (161ppm) at C_7 in to C=O, the signal at (128-135ppm) at C $_{(1,2,3,4,5,6,12,13,14,15,16,17)}$ in the aromatic rings , the signal at (123ppm) at C_{11} in to C-H, the signal at (133ppm) at C_8,C_9 in to (C=C) bond in oxazepine ring , the signal at (39,8ppm) at solvent.



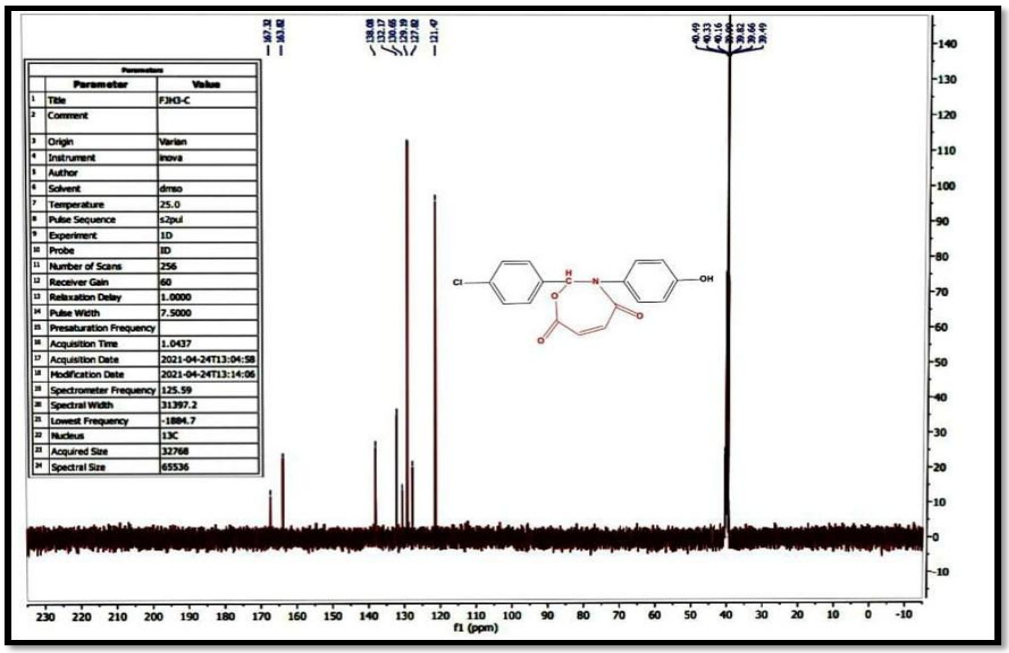
Identification of compound (Jarrahpour & Zarei, 2004) **by ^{13}C-NMR technique**

By using the ^{13}C -NMR technology and by using DMSO as a solvent this compound has been identification, the signal at (166ppm) at C_{10} in to C=O, the signal at (163ppm) at C_7 in to C=O, the signal at (123-130ppm) at C $_{(1,2,3,4,5,6,12,13,14,15,16,17)}$ in the aromatic rings , the signal at (155ppm) at C_{11} in to C-H, the signal at (122ppm) at C_8,C_9 in to (C=C) bond in oxazepine ring , the signal at (39,9ppm) at solvent.



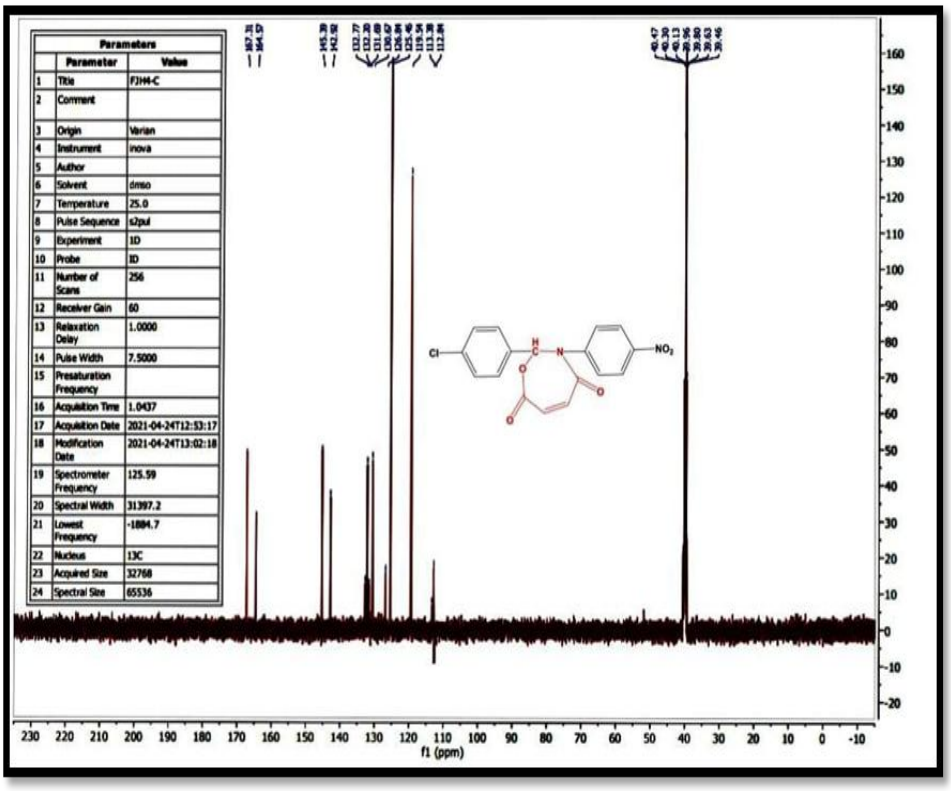
Identification of compound (Naeimi et al., 2007) **by ^{13}C-NMR technique**

By using the ^{13}C -NMR technology and by using DMSO as a solvent this compound has been identification, the signal at (121ppm) at C_{11} in to C-H, the signal at (132ppm) at C_8, C_9 in to (C=C) bond in oxazepine ring , the signal at (127-130ppm) at $C_{(1,2,3,4,5,6,12,13,14,15,16,17)}$ in the aromatic rings, the signal at (167ppm) at C_{10} in to C=O, the signal at (163ppm) at C_7 in to C=O, the signal at (39,99ppm) at solvent.



Identification of compound (Ibis & Zora, 2020) **by ^{13}C-NMR technique**

By using the ^{13}C -NMR technology and by using DMSO as a solvent this compound has been identification, the signal at (112ppm) at C_{11} in to C-H, the signal at (132ppm) at C_8, C_9 in to (C=C) bond in oxazepine ring , the signal at (110-131ppm) at $C_{(1,2,3,4,5,6,12,13,14,15,16,17)}$ in the aromatic rings, the signal at (167ppm) at C_{10} in to C=O, the signal at (164ppm) at C_7 in to C=O, the signal at (39,96ppm) at solvent.



Biological activity (Alfarhani et al., 2019; Dur et al., 2020; Hassan & Kadhim, 2023; H. A. A.-A. Humood & Kadhim, 2020; H. A. Humood & Kadhim, 2020; Husein et al., 2020; Jabbar et al., 2019; Jabbar & Al-azawi, 2020; Jabbar & Al-Azawi, 2020; JABBAR & AL-AZAWI, 2020; Kadhim, 2015; Kadhim et al., 2020; Kadhim & Al-fatahi, 2012; Kadhim & Husein, 2020; Kadhim & Jabbar, 2020; Kadhim & Shanshal, 2012; Karam et al., 2015; Lamondo et al., 2021; Luaibi et al., 2018; Mohammed et al., 2019; Walli et al., 2020)

Biological activity was studied examined in this work against two type of bacteria gram negative bacteria (Escherichia coli) and gram–positive bacteria (Staphylococcus aureus) of synthesized compounds 1,2,3,4 compounds result were recorded as shown in Table:

Table 1. The effectiveness of the prepared compounds on two types of bacteria (*Staphylococcus aureus*, *Escherichia coli*).

Escherichiacoli		Concentration aureus		Compound
Concentration 75mg/ml	Concentration 100mg/ml	Concentration 75mg/ml	Concentration 100mg/ml	
+	+	+	+	1
++	+	+	++	2
+	++	+	+++	3
++	+	+++	+	4
+++	+	++	++	5
+++	+	+	++	6
+	++	+	+	7
+	+++	+	++	8

There is no bacterial suppression, cm in diameter (0.1-1Inhibition of = (+) cm in diameter (1-1.5Inhibition of = (++) cm in diameter 5(1.5-2) Inhibition of = (+++).

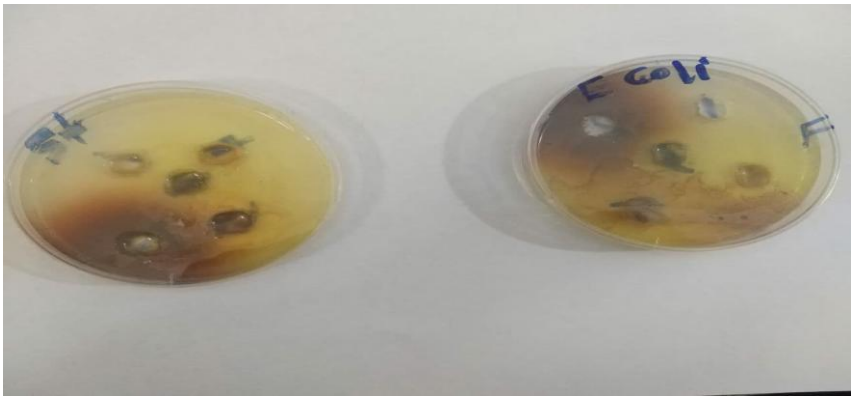


Figure 1. shows the effect of the 8 compounds against the *(Staphylococcus aureus*, *Escherichia coli*)

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