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Synthesis and Characterization of New Oxazepine Compounds and Estimation its Biological Activity

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Abstract

This contribution, direct new azo compounds synthesis via coupling benzidine with 4-hydroxy or alkoxy benzaldehyde (A1-A7). Schiff`s bases (B1-B7) were synthesized by condensation of azo compounds (A1-A7) and 2-aminobenzothiazole. New seven compounds of oxazepines derivates (C1-C7) have synthesized via the reaction between phthalic anhydride and Schiff bases, which that previously prepared to produce seven organic compounds as heterocyclic. As well, the oxazepines synthesized have characterized via (FT-IR, and 1HNMR spectroscopy for several of them) and physical properties have recorded. Finally, oxazepine compounds have tested against bacteria two kinds as gram positive and gram negative.

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1. Introduction

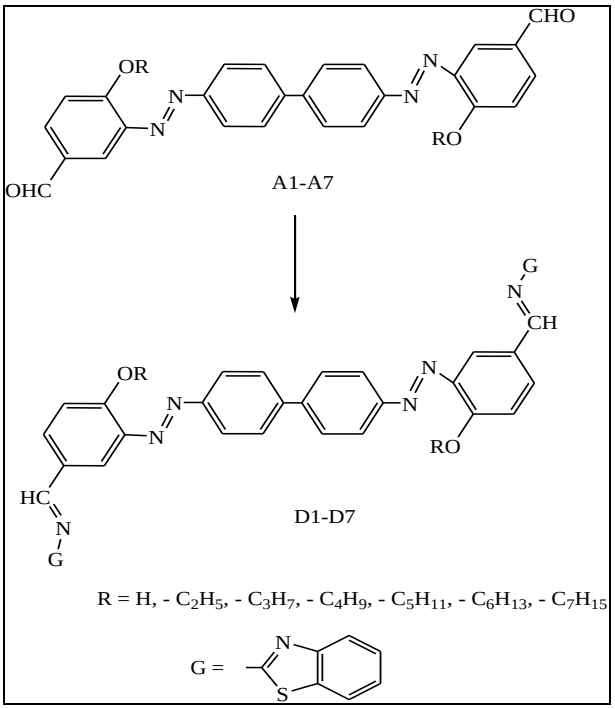
In 1965, Oxazepine (benzodiazepine) compounds used as in relief of the psychoneurosis characterized via anxiety and tension, oxazepine is seven membered ring which that included nitrogen atom and oxygen atom in his structure[(1)]. Oxazepines have been found to use as antibacterial[(2)], antifungal[(3)], antihistaimine[(4)], and anti-inflammatory[(5)].

Chemical compounds: such as, azo compounds is using in most scientific research[(6)], as a result highly rich attention. The aim of this research, synthesized and characterized of seven membered heterocycles that bearing azo compounds as 1,3-oxazepine rings with different aromatic moieties. These compounds has also been studied and characterized and then test their effectiveness against bacterial pathogenesis.

2. Experimental

Organic synthesis

The FTIR spectra recorded via using disc of the potassium bromide on FT-IR instrument. Model 8300 Shimadzu Spectrophotometer, Japan, Fourier-Transform Infrared Spectrophotometer of Perkins-Elmer. ^{1}HNMR spectra recorded on Brüker ACF 300 spectrometer at 300 MHz, the solvent is DMSO-d_6 with the internal standard TMS. In this research, all the chemicals that used are solid and liquid, gained from Fluka and BDH companies. The Schemes 1 and 2 below show the synthesis of compounds D1-D7.



Scheme 1. Synthesis of azo compounds D1-D7.

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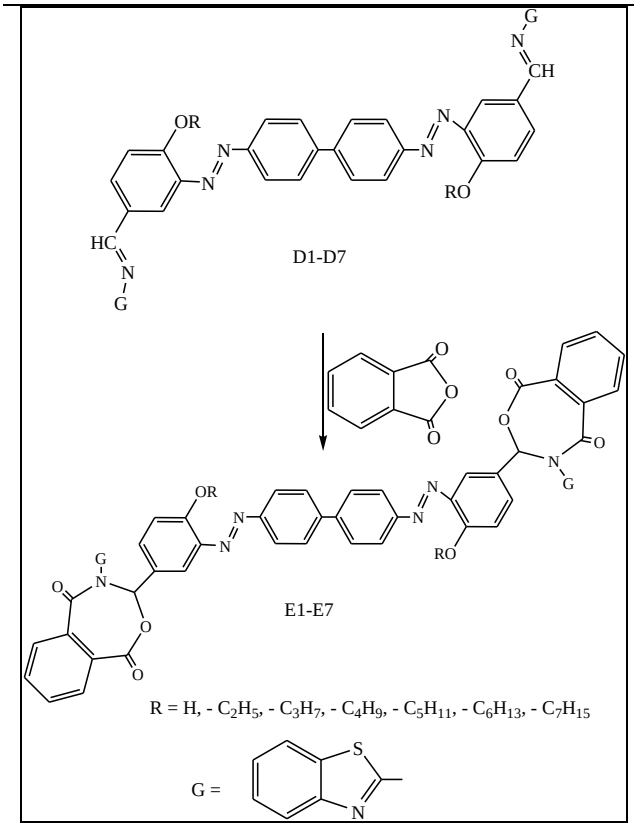

Scheme 2. Synthesis of 3-substituted [1,3] oxazepine-1,5-dione) E1-E7.

In cooling bath,added %10 HCl solution (5 ml) to Benzidine (0.01 mole, 1.84 g) then add (2-3) drops of Conc. HCl into test tube No.1. On the other hand, prepare $NaNO_2$ (0.02 mole, 1.379 g) in distilled water (5 ml) into test tube No.2. When the temperature of solution in test tube No.1 became (0-5 °C), added test tube No.2 to test tube No.1.

Prepare each the solution from 4-Hydroxybenzadehyde (0.02 mole, 2.44 g), 0.02 mole [D1-D7] in (10 ml) %10 NaOH into test tube No.3. Finally, added the mixture of solutions in to test tube No.3[7]. Then filtration the solution, and collected the precipitate that, gave the desired products, %yield and melting point are registered in Table 1.

Table 1. Physicalproperties of compounds A1-A7.

Comp No.	Yield %	Color	M.P.℃
A1	73	Dark Brown	241-242
A2	71	Brown	223-225
A3	72	Dark Brown	197-199
A4	71	Yellow	187-184
A5	70	Dark Yellow	171-173
A6	71	Yellow	161-163
A7	74	Yellow	155-158

Synthesis of schiff`s base compounds (D1-D7)

A mixture of each compounds (A1-A7) (0.01 mol) with 2-aminobenzothiazole (0.02 mole) in 20 ml of absolute ethanol as solvent with glacial acetic acid (3) drops. Then the solution mixture, refluxed (3) hrs. Finally, the precipitates were formed, collected by filtration, dried and recrystallized from ethanol.

Table 2. Physical properties of schiff`s base compounds (B1-B7).

Comp. No.	Yield %	Colour	M.P.℃
D1	74	Yellow	287-289
D2	73	Dark Yellow	245-248
D3	76	Yellow	261-264
D4	70	Light Yellow	277-280
D5	73	Yellow	248-251
D6	72	Yellow	230-232
D7	71	Light Yellow	222-225

Synthesis of Oxazepine compounds (E1-E7)

Each (D1-D7) (0.01 mol) and Phthalic anhydride (0.02 mol, 2.96 g) have mixture in benzene solvent (20 ml). Then, the mixture of reaction have refluxed. Finally, filtration of solution and collected the precipitate.

Table 3. Physical properties of 1,3-Oxazepine-4,7-Dione derivative(C1-C7).

Comp. No.	Yield %	Colour	M.P.℃
E1	74	Light Brown	321-324
E2	72	Brown	297-301
E3	72	Light Brown	284-287
E4	75	Dark Brown	265-267
E5	71	Light Brown	238-241
E6	72	Brown	214-217
E7	73	Light Brown	221-224

3. Results and Discussion

4-Alkoxybenzaldehyde were prepared from the reaction of 4-hydroxybenzaldehyde with appropriate alkyl halides[8].

Two chemical compounds to azo dye synthesis requires, a diazonium salt with a coupling component. The diazonium salt reacts as electrophile with rich electron in nitrogen atom coupling component, like 4-alkoxybenzaldehyde derivative through an electrophilic aromatic substitution mechanism. The aryl diazonium ion directed to the meta position respect to the carbonyl group and ortho site with respect to the hydroxyl or alkoxy group.

The titled compounds were synthesized from the reaction of previously synthesized compounds (A1 – A7) with 2-Hydroxy4-Aminotriazine through the condensation reaction.

Spectroscopic observation of the synthesized compounds includes the disappearance of the amino group,

and the appearance of new imine group in the range (1618-1632 cm^{-1}).

Figures 1 show the following characteristic absorption bands in FTIR spectroscopy: Broad band at (3272-3374) cm^{-1} that could be attributed to O – H stretching, all the synthesized compounds show bands at the range (3022-3084) cm^{-1} for the C – H aromatic stretching, (2932-2984) cm^{-1} and (2845-2889) cm^{-1} for asymmetrical and symmetrical C – H aliphatic stretching, (1618-1628) cm^{-1} which attributed to CH = N stretching, while the azo groups appear at (1511-1518) cm^{-1}, (1598-1602) cm^{-1} these bands range assign to C = C aromatic stretching.

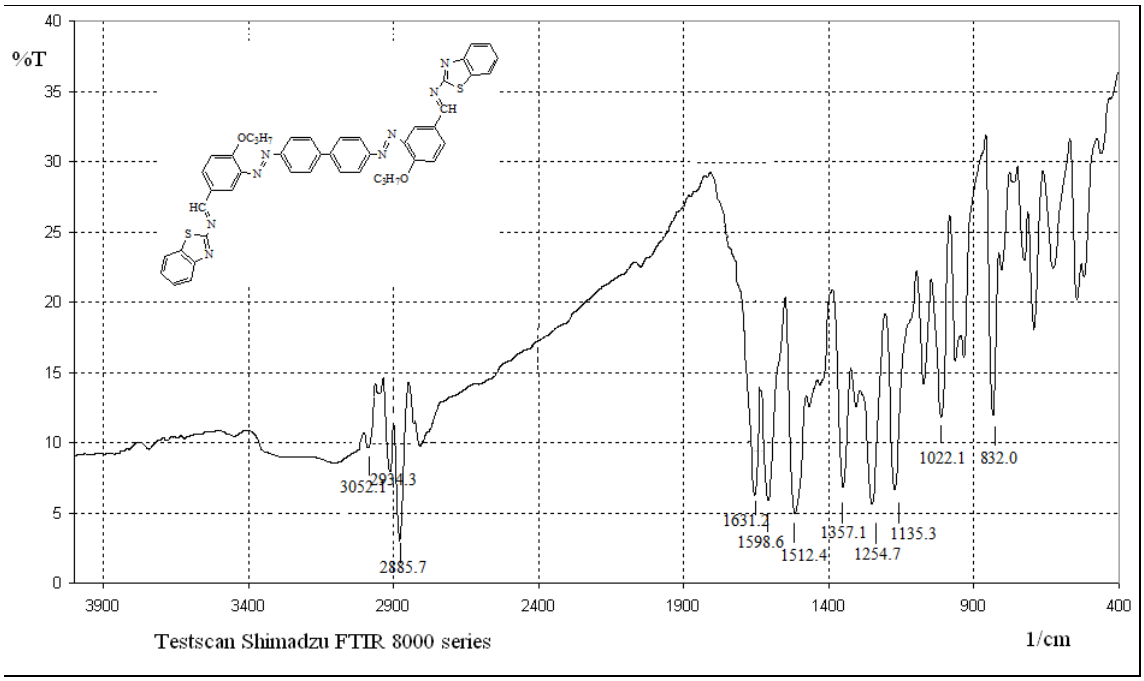

Figure 1. FTIR spectrum of compound D3.

Table 4. The FT-IR Characteristic absorption bans of D1-D7 compounds.

Comp. No.	C–H Alpha. (ASym.)	C–H Alpha. (Sym.)	N=N	O–H	C–H Ar.	CH=N	C=C Ar.
D1	–	–	1518	3281	3048	1628	1595
D2	2974	2832	1525	–	3082	1621	1600
D3	2934	2885	1518	–	3052	1631	1598
D4	2981	2842	1512	–	3087	1627	1589
D5	2964	2857	1512	–	3054	1632	1601
D6	2964	2841	1525	–	3084	1618	1598
D7	2908	2881	1510	–		1624	1587

Figure 2 shows the ^{1}H-NMR spectrum of compound [D1], the following characteristic chemical shifts (d_6-DMSO, ppm) were appeared: signal observed at 10.10 ppm due to the phenolic hydroxyl proton (2H), signal at 8.37 ppm could be assigned to the proton of imine group CH = N[9] (2H), the aromatic protons show three signals at 6.52 – 8.17 (22H).

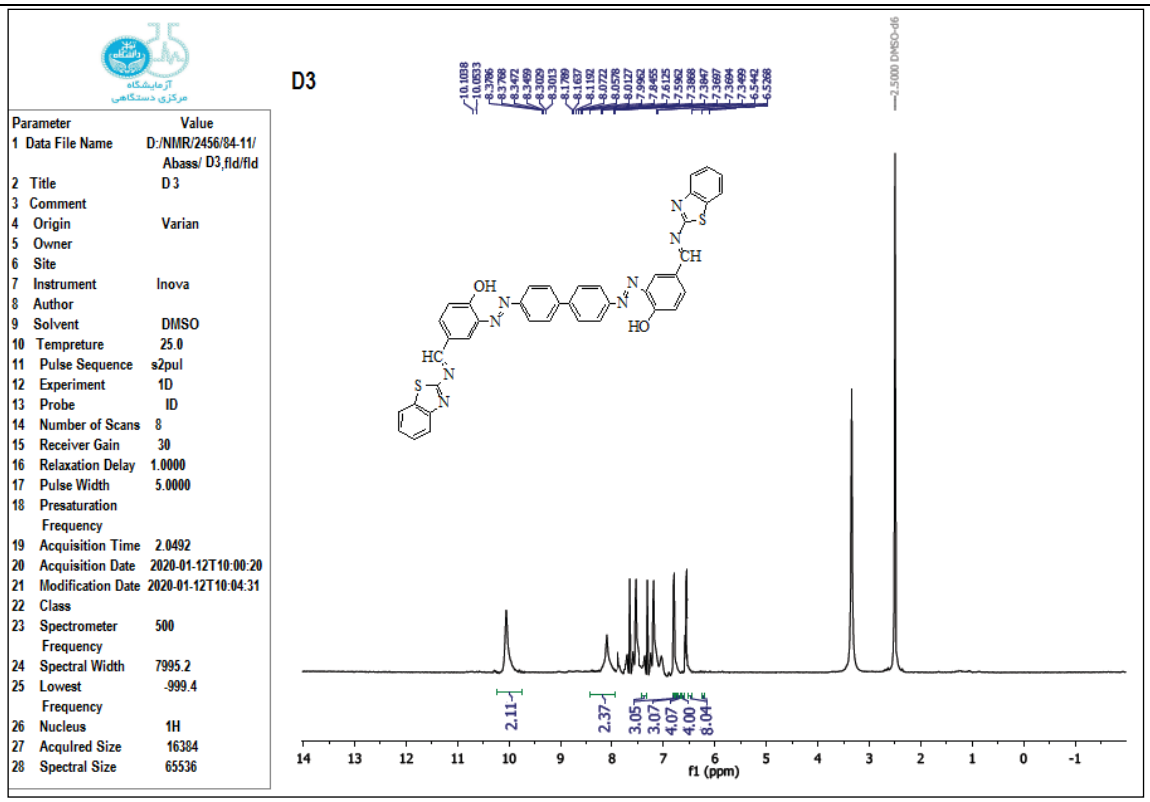

Figure 2. [1]HNMR spectrum of compound D1.

To produce Oxazepine compounds have required reaction between Schiff`s base compounds, phthalic anhydride, and benzene as solvent to produce 1,3-Oxazepine-4,7-dione derivatives. Cycloaddition reaction have finished via ring formation from the addition of π electrons, also formation of new δ bonds from δ π bonds[(10)].

The reaction mechanism involve two steps, firstly nucleophilic substitution (tetrahydral mechanism) by the addition of nucleophile (nitrogen of azo-methine group) to the carbon of the anhydride carbonyl group (ring opening), and secondly; nucleophilic addition of oxygen nucleophile to the carbon of the azo-methine group (ring closer).

Compounds E1-E7 Synthesized between the reaction of D1-D7 with phthalic anhydride and benzene as solvent to produced 1,3-Oxazepine-4,7-dione compounds.

The products structures have identified via using FT-IR and [1]H-NMR for one of them.

Figures 3 show the following characteristic absorption bands in FTIR spectroscopy: all the synthesized compounds show bands at the range (1728-1737) cm^{-1} (C = O of lactone stretching), (1687-1700) cm^{-1} (C = O of lactam stretching)[(11)], (3043-3081) (Ar – H), (2922-2965) cm^{-1} (*ν* C – H, aliphatic asymmetrical stretching), (2817-2881)) cm^{-1} (*ν* C – H, aliphatic symmetrical stretching), (1597-1604) cm^{-1} (*ν* C = C), (1512-1542) cm^{-1} (*ν* N = N), (1238-1554) cm^{-1} (*ν* C – O), (832-842) cm^{-1} (for *para*-substituted benzne ring of plane bending out). Table (3.5) shows all the characteristic absorption bands for the synthesized compounds (E1 – E7).

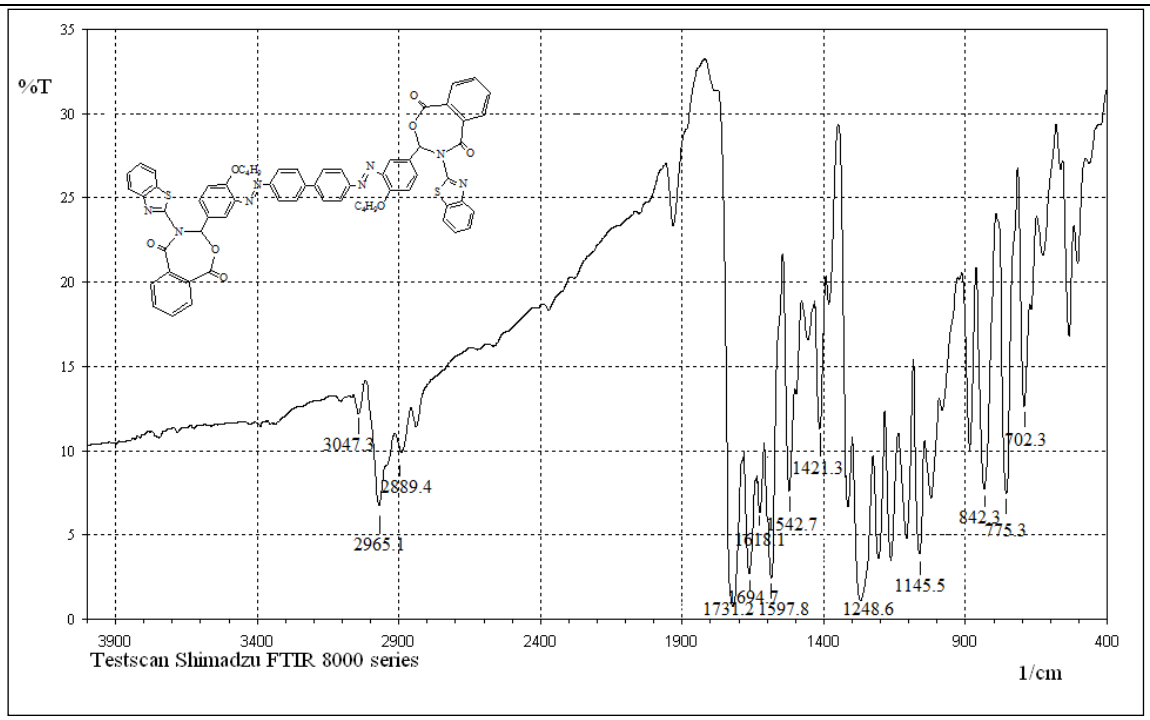

Figure 3. FTIR spectrum of compound E4.

Table 5. The FT-IR Characteristic absorption bans of E1-E7 compounds.

Comp. No.	C-H Alpha. (Asym.)	C-H Alpha. (Sym.)	N=N	Hydorxyl group	Carbonyl lacton	Carbonyl lacton	C=C Ar.
E1	–	–	1521	3387	1732	1687	1600
E2	2961	2822	1517	–	1737	1700	1604
E3	2957	2848	1512	–	1731	1688	1598
E4	2965	2881	1542	–	1731	1694	1597
E5	2942	2881	1522	–	1728	1688	1598
E6	2922	2817	1528	–	1731	1687	1598
E7	2931	2848	1521	–	1737	1687	1598

Figure 4 shows the ^{1}H-NMR spectrum of compound [E4], the following characteristic chemical shifts (d_6-DMSO, ppm) were appeared: Aromatic protons show signals at 6.46-7.48 (30H)[12]. Six protons appeared as triplet at δ 0.96-1.21 which could be assigned to $-CH_3$, protons appeared as multiplet at δ 1.64-1.81 which could be assigned to $-CH_2-CH_2$ (8 H). The $-OCH_2$ groups of butyl substituent appeared as triplet at δ 3.84-4.11 (4H).

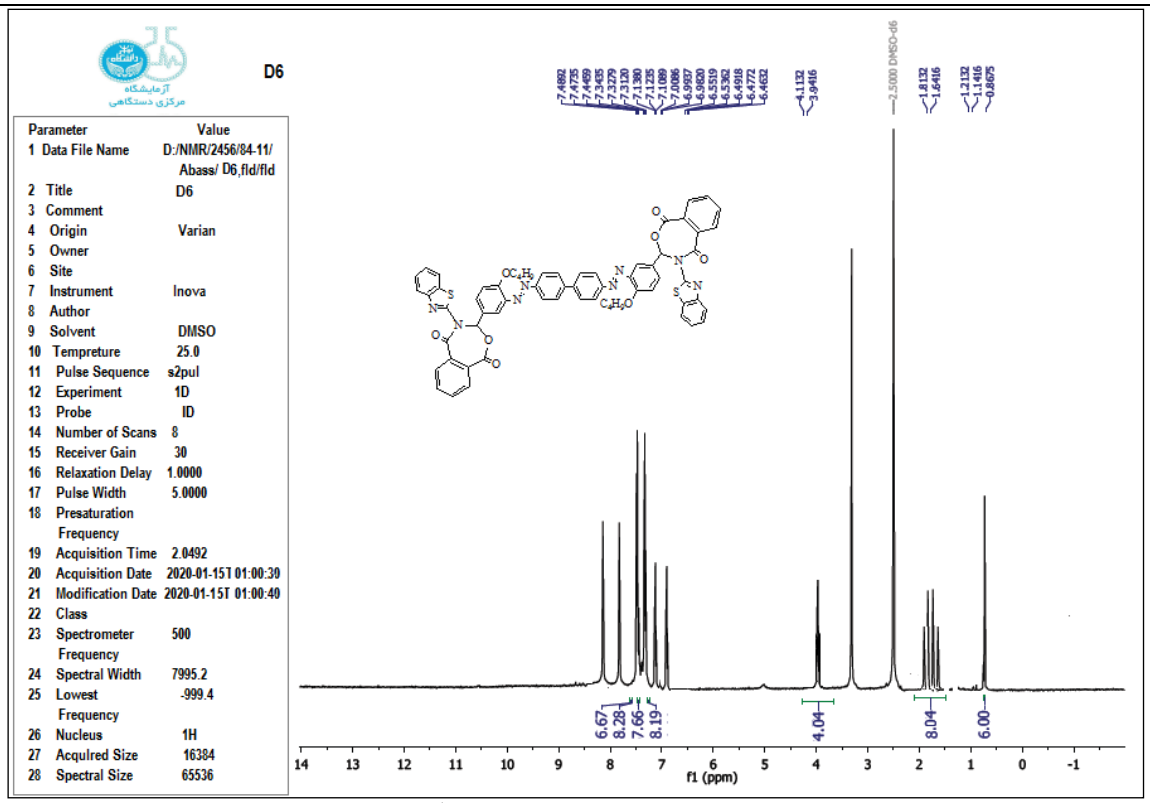

Figure 4. [1]HNMR spectrum of compound E4.

4. Biological Activity

The prepared oxazepine compounds has tested against different types of bacteria gram positive and gram negative; such as, *Staphylococcus aureus* and *E.Coli*. All these results are shown in Table 6.

Table 6. Antibacterial activities of the compounds (E1-E4).

Compound No.	*E.coli*	*Staphylococcus*
E1	++	++
E2	+	+
E3	+	–
E4	–	+

Note. (–): No inhibition, (+) =10-14 mm, (++): 15-22 mm.

5. Conclusion

In conclusion, we have synthesized a new 1,3-oxazepine compounds using a schiff's bases synthesis. In addition, all newly synthesized 1,3-oxazepine compounds role as inhibitors to bacterial which include bacteria (*Staphylococcus aureus*), and bacteria (*Escherichia coli*).

Acknowledgments

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