Chemistry and Materials Research
ISSN 2224- 3224 (Print) ISSN 2225- 0956 (Online)
Vol.7 No.2, 2015

Synthesis, Characterization and Biological Study of Some New 1,3-Oxazolone-5(4H)-one Derivatives

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Abstract
New 1,3-oxazol-5(4H)-one (oxazalone) have been synthesized by reaction 2-amino acid (glycine) with sebacoyl chloride. These compounds were characterized by CHN, IR and ^{1}HNMR spectroscopy.The present study showed that the our compounds more efficient than all antibiotics against gram positive bacteria *Staph. areus* and *E.coli* compared with all antibiotics except Gentamycin more efficient than compounds1&3 in against gram negative *E.coli* (18 mm).T- test shows signifying differences between our compounds of present study and antibiotics ($P<0.01$).
Keywords :oxazolone, Erlenmeyer Plochl reaction

Introduction

Oxazalones are five mannered heterocyclic compounds containing nitrogen and oxygen as hetero atoms Fig.1. The c-2 and c-4 position are crucial for their various biological activities [Aaglawe et al, 2003, Laue and Plgens, 2005] such:

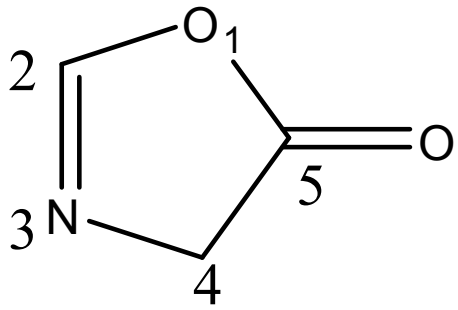
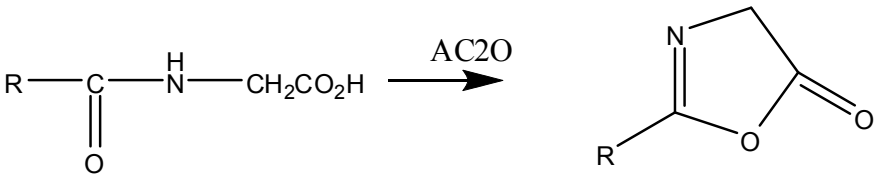


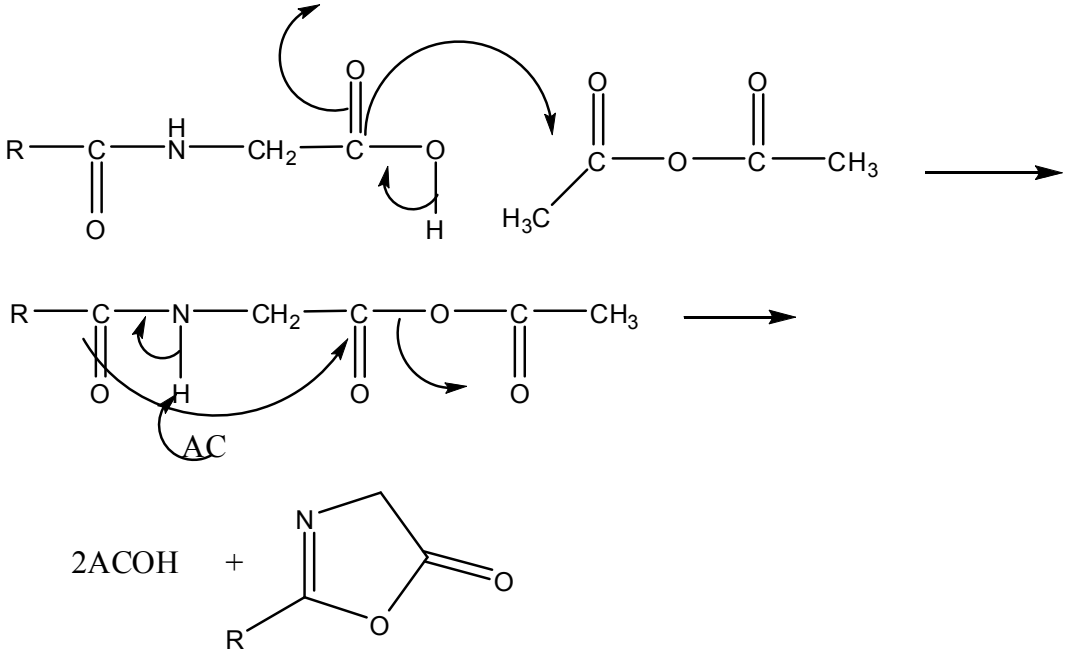
Fig.1: The structure of oxazalone (azolactons)

as anticancer [Ismailet al, 1991] antimicrobial [Desi et al, 2009] antitumor [Mesaik et al, 2004] antinplammatory [Argade et al, 2008]and herbicidal [Kennedy et al,1881].

The synthesis of oxazolone involve the intermolecular condensation (perkin condensation) of N-acetyl glycine with aromatic aldehyde in the presence of acetic anhydride is known as Erlemeyer-Plochi azolacaton synthesis [Kudair, 2012]



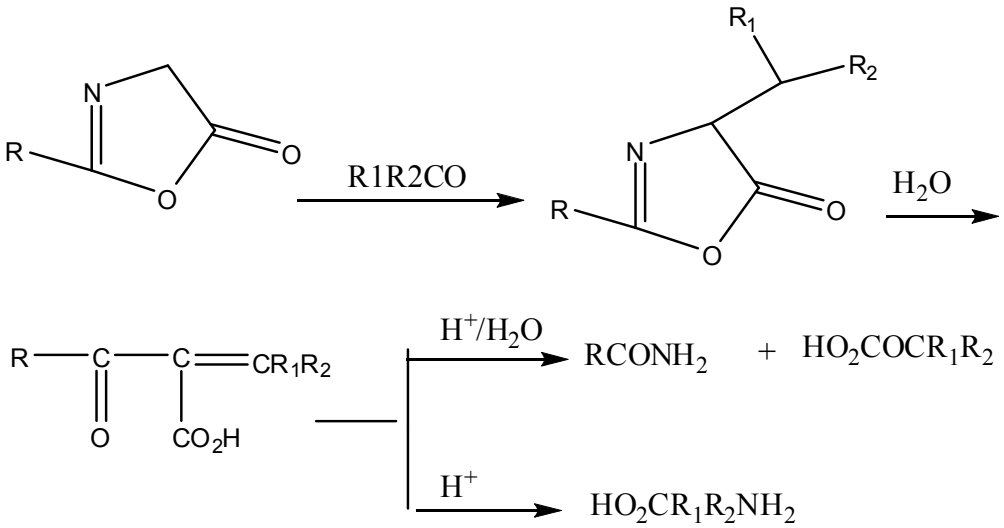
Mechanism:



Eq.1:Erlemeyer-Plochi oxazalone synthesis

The methods is away to important intermediate products used in synthesis of amino acid [Lamb, 1931] peptides [Gottwald, 1999]and related compounds [Erlenmeyer, 1893].

The aldol condensation reaction of azolactons with carbonyl compounds is often followed by hydrolysis to provide unsaturated α-amino acid, while drastic hydrolysis gives α -oxo acid [Schmid et al, 1944]



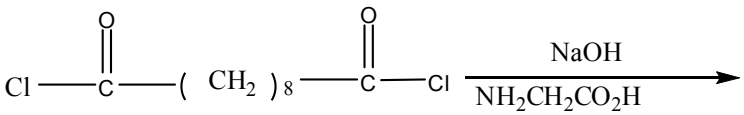
There are many methods to synthesis oxazolone [Suman et al , 2011] involving the use zinc oxide [Pasha et al, 2007], sodium acetate [Cleary et al, 2010], calcium acetate [Paul et al, 2004] basic ionic liquid (bimlue) OH [Patil et al, 2011] and K_2PO4 [Zturk et al, 2007].

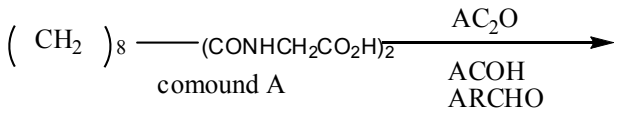
Oxazolones are important role in photochemical activities, so they are used in semiconductor devices [Gottwald, 1999]or photosensitive composition devices for protein [Tikdari et al, 2008].

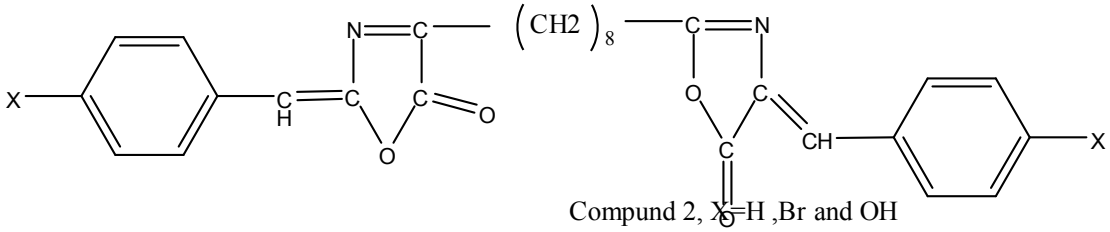
Oxazolones show interesting behavior towards polymerization and condensation leading to photopolymers, telomeres condensation [Mendozaet al, 2005].

In the present work, we report the synthesis, characterization and biological study of some new oxazolone

compounds by reaction sebasoyl chloride with glycine as show in equation:







Compund 2, X=H ,Br and OH

Experiment work

1-A:preparation bis (2-acetamido acetic acid octane: compound (A)

To a string solution of glycine (1mg, 0.02mol) and sodium hydroxide (1 ml, 10% solution), sebasoyl chloride (0.01 mol) was added, then the reaction mixture was shacked vigorously for 1 hr., a few grams of ice was added with string. After that, the solution was acidified with con. HCl and the product was collected and recrystallized from ethanol, yield 70%, m.p. 236-238^{0}C.

2-B:preparation (4-x-benzylidine) sebasoyl bis 1,3-oxazol 5(4H)-one (compound2):

To a string mixture of compound (0.01 mol) acetic acid (5 ml) acetic anhydride (20 ml), p-x-benzaldehyde (0.02 mol) was added. The temperature of reaction was reached to 70^0 C for 10 min., the mixture was poured into crushed ice and stirred for 30 min., and the product was collected and recrystallized from ethanol to give products. Table 1. Show the physical properties for the prepared compounds

Table 1: The physical properties for prepared compounds

No.	X	Mw	Yield%	Coluor
1	H	458	71	Paleyellow
2	P-Br	616	80	Yellow
3	P-OH	476	75	Pale yellow

Physical Measurements

IR spectra as KBr discs in the range (200-4000) cm-1 were recorded on a Pye-Unicam SP3-300s IR spectrometer. Electronic spectra were recorded on a Pye-Unicam SP8-100 spectrophotometer in DMSO solution. 1HNMR spectra in DMSO-d6 were recorded on Joel EX-90 FT using TMS as an internal standard. Melting point was measured on Gallenkamp melting point apparatus and is uncorrected. The carbon hydrogen and nitrogen analyses were carried out with Perkin-Elmer 240M elemental analyzer.

Evaluation biological activity of compounds

Two species' of pathogenic bacteria (*E.coli &Staphalyococcus aureus*) were used in present study which isolated from clinical patients, biochemical & laboratory tests were used to diagnose those bacteria (Boron et al, 1999). Plate agar diffusion method to measure growth inhibition zone (mm). To evaluate biological activity of our compounds were compared with standard antibiotics, Penicillin(p), Ampicillin (Amp), Carbencllin(CR), Chloramphenicol (C), Nitrofurantoin(F), Nalidixic acid (NA), Cphalexin(CP), Tetracyclin (TE), Kanamycin(K), Erythromycin(E), Gentamicyin(GN) and Neomycin (N).

T- test was used for statistical analysis to compare between our compounds with antibiotic.

Result and Discussion

1.Infra-Red (IR)

Compound (1) have been synthesized by nucleophilic displacement mechanism SN_2 in the presence of sodium hydroxide. IR spectra of compound (1) showed absorption hand forυCO2H at 3200 cm^{-1} and υN-H at 3250 cm^{-1},while υC=O acid and υC=O amide at 1700 cm^{-1} and 1600 cm^{-1} respectively, υC-H aliphatic appears at 2980 cm^{-1}. New absorption in band at 3250 cm^{-1} due to υN-H was evidence to form compound (1). The treatment of compound (1) with P-X-arylaldehyde in the presence of acetic acid and acetic anhydride lead to compound (2) (4-X-benzylidine) sebasoyl bis (1,3-oxazol 5(4H)-one) have been characterized by IR spectrum which it showed appearance characteristic absorption band at 1700.1699cm^{-1} which belonged to the oxazol-5(4H) one carbonyl group (oxazol, υC=O and at 3091.68- 3090.55 cm^{-1} due to υC-N at 1600- 1500 cm^{-1}. CH_2sym. and asym. shows at 2945- 2950 cm^{-1} and 2652-2880 cm^{-1} respectively. Absorption band of C=C aromatic appears at 1587-1548 cm^{-1}.

2-Elemental analysis CHN

The elemental analysis of measured percentages are in good agreement with calculated values as show in Table 2:

Table 2: CHN results of prepared compounds

No.	X	Molecular formula	Calculated			Formed		
			%C	%H	%N	%C	%H	%N
1	H	C28H30N2O4	37.36	6.55	6.11	73.32	6.53	6.11
2	P-Br	C28H26Br2N2O4	54.54	4.22	4.54	54.53	4.21	4.53
3	P-OH	C28H30N2O6	70.58	6.30	5.88	70.57	6.30	5.87

3-^{1}HNMR

^{1}HNMR spectra in DMSO-d6 solvent, Fig.2 illustrated the structure of compound.

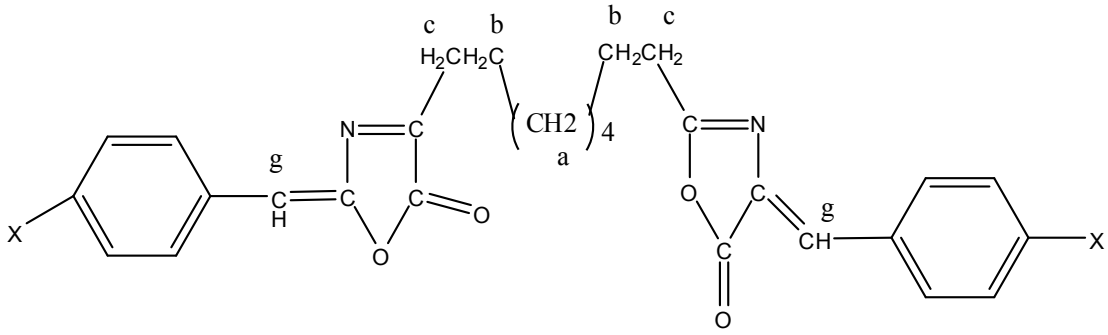


Fig.2: The structure of prepared compounds

Aromatic protons showed multiple signals at 6.5- 7.5 ppm while H olefin protons (g) appears at 9- 9.3 ppm as a singlet peaks [Silverstein, 2005].

Protons (a) appear a single singlet at 1.3- 1.2 ppm while protons (b)appears at 1.8- 1.9 ppm as multiple peaks. Protons(c)appears at 2.1- 2.3 ppm as a triplet due to couple interaction between protons c and b. Table 3 illustrated the of^{1}HNMR.

Table 3: ^{1}HNMR of prepared compounds

No.	X	Harom.	Holi.	Ha	Hb	Hc
1	H	6.55-7.5 m	9-9.25	1.25	1.8-1.9 m	2.1-2.3 t
2	P-Br	6.6-7.4 m	9.1-9.315	1.35	1.8-1.9 m	2.1-2.2 t
3	P-OH	6.5-7.4 m	9-9.215	1.25	1.8-1.9 m	2.1-2.3 t

4-Biological activity

Table 4 shows the results of the biological activity of our compounds against bacteria to of this study can be summarized that the compound 3 more efficient than the compound 2 and compound 1 in against gram positive bacteria *Staph. areus* has reached 30 mm compared to the compound 3 (28 mm), while the compound1 has report diameter of 20 mm.

Table 4: The antibacterial activity of the prepared compounds against *E.coli* &*Stap. aureus*.

No.	Name of compound	Inhibition diameters mm	
		Staphylococcusaureus	*Escherichiacoli*
1	H	20	15
2	P-Br	28	25
3	P-OH	30	15

The present study recorded the biological activity of that compound 2 more efficient than the two compounds 1 and compound 3 against gram negative bacteria *Ecoli*, has announce 25 mm while the both compounds 3&1 were recorded (15mm)

The present study showed that the compounds more efficient than all antibiotics against gram-positive bacteria Staph. *areus* and *E.coli* compared with all antibiotics except Gentamycin more efficient than compounds1&3 in against gram negative E.coli (18 mm).

The statistical analysis (T –test) shows there are significant differences between inhibition zone(I .Z) of our compounds of present study in comparison with all antibiotics($P< 0.01$) Table 5.

Table 5: Antibiotic activity, diameter of inhibition zone I.Z (mm)

Bacteria types	Penc illin P)I. Z(	Ampi cillin (Amp) I.Z	Carbe ncillin (CR)I. Z	Chloram phnicol (C) I.Z	NItrofura ntion(F) I.Z	Nalid ixic Acid(NA) I.Z	Ceph alxin (CP) I.Z	Tetrac yclin (TE) I.Z	Kana mycin (K) I.Z	Erythro mycin (E) I.Z	Genta micin (CN) I.Z	Neo mycin (N) I.Z
E.coli	8	6	10	12	11	13	9	9	10	11	18	15
Staph. areus	9	9	6	9	10	9	21	8	11	8	14	16

The result of this study are agree with the study of Al-Masoudi et al, 1994 and Al-Saimary et al, 2006 . Regarding the impact of 6–Azaruracil nucleoside and isatins series respectively against bacteria Staph. aurous and E. Coli.

The reason for the biological activity of compounds of present study against bacteria is due to the presence of functional groups (CO, Cl, and OH).

CONCLUSION

1-The present study recorded New compounds 1,3-oxazol-5(4H)-one (oxazalone) have been synthesized by Erlenmeyer-Plochl azlactone

2.The present study proved that the our new compounds more efficient than all antibiotics against gram positive bacteria *Staph. areus* and *E.coli* compared with all antibiotics except Gentamycin more so that we are propose to use these compounds as bactericidal (antibiotics) against pathogenic bacteria.

Acknowledgements

We are thankful the worker in Faculty of Pharmacy, University of Tabriz (IRAN) for NMR analysis.

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