SYNTHESIS, CHARACTERIZATION OF NOVEL 4-ARYLIDENE-2-PHENYL-5(4H) OXAZOLONES

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Abstract: The purpose of this research is to synthesize and characterize derivatives of the **mono oxazolones B(1-8).** These compounds were made in a single step. New oxazolone molecules were produced in a variety of ways. Method hippuric acid, Refluxed & Grinding in modest yields (53-92%). The structures of these **mono oxazolones B(1-8)** were determined using spectral data such as **IR, ^{1}H-NMR**, **^{13}C-NMR** and **Mass**

Keywords: oxazolones**,** hippuric acid**,** fused sodium acetate**,** porcelain mortar**,** ^{1}H-NMR ^{13}C NMR & Mass.

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INTRODUCTION

Oxazolones are oxygen and nitrogen-containing five-membered heterocyclic compounds. Oxazolone has the molecular formula $C_3H_3NO_2$[1] and is a chemical and functional group. **Fig 1.**

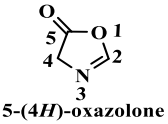


Figure 1. Structure of Oxazalone

Oxazolones are a class of small heterocyclic compounds that have gotten a lot of attention recently because of their pharmacological properties. Oxazolones are five- heterocyclic compounds containing nitrogen and oxygen. It was named using the Hantzsch–Widman nomenclature[2] and belongs to a large family of oxazole-based compounds. Oxazolone has five structural isomers: three for the carbonyl group and two for the doubly linked C=X (where X= N or C): **Fig2.**

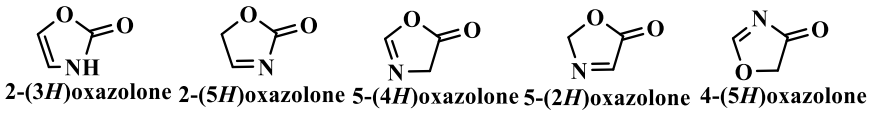


Figure 2. The five isomeric forms of oxazolone

The synthesis of oxazolone derivatives has been reported in the literature using a condensation process of aldehydes with benzoyl/N-acetyl glycine in the presence of several reagents and catalysts, including $ZnCl_2$, KF / NaOAc, Al_2O_3, H_3BO_3, Bi (III) salts, and Pb $(OAc)_2$[3]. A variety of catalysts have been created in recent years since the first report on the synthesis of azlactones was published in 1883. Lead acetate SO_3 in dimethylformamide, perchloric acid[4], polyphosphoric acid, carbodiimides, and anhydrous zinc chloride, for example. This condensation was carried out using $Bi(OAc)_3$, $Bi(OTf)_3$, $Ca(OAc)_2$, KF-alumina, $Yb(OTf)_3$, $POCl_3$, $H_3PW_{12}O_{40}$, Sm, $RuCl_3$, Al_2O_3, organic bases, K_3PO_4, and organic-inorganic hybrid polyoxometalates[5]. Some of these processes, however, have significant downsides, such as the employment of water-sensitive catalysts, noble metal/or salt catalysts, stringent conditions, and hazardous reagents[6]. Furthermore, several studies have found that aldehydes with electron-donating groups (EDGs, such as $-NR_2$, -NHR, $-NH_2$, -OH, -OR, -OCOR, and $-CH_3$) are more reactive than those with electron-withdrawing groups (EDGs, such as $-NO_2$, $-CF_3$, $-CCl_3$, -CN, -COOH, $-CO_2R$, and -F)[7]. Only a few reports suggest the reverse. The development of ecologically friendly procedures, such as solvent-free[8] conditions, nontoxic reagents, gentle reactions, simplified workup, and EDGs-active processes, is required[9].

MATERIALS AND METHODS.

General Experimental Information.

All of the materials were obtained from **Merck** (Germany), **Sigma-Aldrich** (USA), and **BDH** (UK). With the melting point device, the melting point was recorded. On a Shimadzu **FT-IR** (8300) spectrophotometer, FT-IR spectra were acquired using potassium bromide discs (4000-400) cm^{-1}. On a **Bruker** (400MHz) NMR spectrophotometer, **^{13}CNMR** and **^{1}HNMR** spectra were obtained using $CDCl_3$ and **DMSO-d_6** as solvents, Tetramethylsilane (TMS) as an internal reference, and chemical shift was measured in ppm relative to TMS. The GC-Mass spectra were obtained at 70 eV with an Agilent technologies

mass selective detector 5973 wett work at Technology Shareef University in Tehran, Iran.

Compounds' Preparation.

General Procedures for the preparations of Oxazolone[10,11]. Preparation method of Mono-oxazolone.

In general, mono-oxazolone is made by reactions derivative aromatic aldehyde (0.01 mol) was added to a swirling mixture of hippuric acid (0.01 mol), acetic acid (5 ml), and acetic anhydride (20 ml). Refluxed for 4 hours at 80^0C, with the temperature of the process reaching 80^0C. As the temperature rises, the combination becomes almost solid, then gradually liquefies and develops a bright yellow color. The reaction was allowed to cool once it was completed and monitored by TLC is used to monitor the reaction's progress. The eluent is hexane: ethyl acetate 3:7, and then the mixture was placed into crushed ice and agitated for 30 minutes. To obtain the desired chemical, the product was recovered and recrystallized in a suitable solvent. The oxazolone structures were validated by comparing their **m.p**., mixed. **m.p**., **TLC, IR, ^{1}H-NMR & ^{13}C-NMR** data to those in the literature. The physical data of **mono-oxazolone B(1-2)** as shown in **Table(1).** The following methods of **mono-oxazolone** preparations are:

4-(3-Ethoxy-4-methoxybenzylidene)-2-phenyloxazol-5(4*H*)-one(1B). It reactions were used to create. acetic acid(5ml), and acetic anhydride(20ml), 3-ethoxy-4-methoxybenzaldehyde(0.01mol, 1.80g), hippuric acid(0.01mol, 1.79g), **m.p**.= 201-202^{0}C. $\mathbf{R_f}$ = 0.6. **Yield**=72%, 1717 (C=O), 1668(C=N), 1595(C=C) **IR** ($\bar{\upsilon}$, cm^{-1}, KBr disk).

4-(3-Methoxy-5-methylbenzylidene)-2-phenyloxazol-5(4*H*)-one(2B). It reactions were used to create. acetic acid(5ml), and acetic anhydride(20ml), 3-methoxy-5-methylbenzaldehyde(0.01mol, 1.50g), hippuric acid(0.01mol, 1.79g), **m.p**.= 155-157^{0}C. $\mathbf{R_f}$ = 0.5. **Yield**=75%, 1699(C=O), 1636(C=N), 1605(C=C) **IR** ($\bar{\upsilon}$, cm^{-1}, KBr disk).

Table 1. Physical data of mono-oxazolone B(1-2)

No.	m.p ^{0}C	R_f	Yield %	Colour	Solvent of recrystalization
1B	201-202	0.6	72	White	Chloroform
2B	155-157	0.5	75	White	Chloroform

General Procedures for the preparations of Oxazolone[12,13]. Preparation method of Mono-oxazolone.

In general, **mono-oxazolone** is made by, 20 ml of (Ethanol+ Methanol), an equimolecular mixture of glycine(0.01mol) derivatives aromatic aldehyde(0.01mol) and derivatives benzoyl chloride(0.01mol) was refluxed with constant stirring for (4-12) hrs.' And sodium acetate(0.01mol). In the presence of a few drops of acetic anhydride. TLC is used to monitor the reaction's progress. The eluent is hexane: ethyl acetate 3:7, which evaporates and is then recrystallized from a suitable solvent. The oxazolone structures were validated by comparing their **m.p**, mixed. **m.p**, **TLC, IR, ^{1}H-NMR, ^{13}C-NMR & Mass** data to those in the literature. The physical data of **mono-oxazolone B(3-5)** as shown in **Table(2).** The following methods of **mono-oxazolone** preparations are:

(*E,Z*)-4-(3-Ethoxy-4-methoxybenzylidene)-2-(2-hydroxy-3-methoxyphe nyl)oxazol-5(4*H*)-one(3B). It reactions were used to create. A few drops of acetic anhydride, glycine(0.01mol, 0.75g), 3-ethoxy-4-methoxybenzaldehyde(0.01mol, 1.80g), 2-hydroxy-3-methoxybenzoylchloride(0.01mol, 1.85g) and sodium acetate (0.01mol, 0.8g). **m.p**.= 135-136^{0}C. $\mathbf{R_f}$ = 0.9. **Yield**= 86%, 1996(C=O), 1653(C=N), 1593(C=C) **IR** ($\bar{\upsilon}$, cm^{-1}, KBr disk).

4-(3-Methylbenzylidene)-2-(4-(trifluoromethyl)phenyl)oxazol-5(4*H*)-one (4B). It reactions were used to create. A few drops of acetic anhydride, glycine (0.01 mol, 0.75g), 3-methylbenzaldehyde(0.01mol, 1.20g, 1.17ml), 4-((trifluoromethyl)thio)benzoylchloride(0.01mol, 2.40g, 1.66ml) and sodium acetate (0.01mol, 0.8g). **m.p**.= 123-124^{0}C. $\mathbf{R_f}$ = 0.9. **Yield**= 89%, 1758(C=O), 1656(C=N), 1598(C=C) **IR** ($\bar{\upsilon}$, cm^{-1}, KBr disk).

4-(3-Methylbenzylidene)-2-(4-(trifluoromethyl)phenyl)oxazol-5(4*H*)-one (5B). It reactions were used to create. A few drops of acetic anhydride, glycine(0.01mol, 0.75g), 3-methylbenzaldehyde(0.01mol, 1.20g, 1.17ml), 4-((trifluor omethyl)benzoylchloride(0.01mol, 2.08g, 1.48ml) and sodium acetate (0.01mol, 0.8g). **m.p**.= 152-154^{0}C. $\mathbf{R_f}$ = 0.8. **Yield**= 92%, 1758(C=O), 1656(C=N), 1597(C=C) **IR** ($\bar{\upsilon}$, cm^{-1}, KBr disk).

Table 2. Physical data of mono-oxazolone B(3-5)

No.	m.p ^{0}C	R_f	Yield %	Colour	Solvent of recrystalization
3B	135-136	0.9	86	White	Benzene
4B	123-124	0.9	89	Yellow	Hexane
5B	152-154	0.8	92	Yellow	Chloroform

General Procedures for the preparations of Oxazolone[14,15]. Preparation method of Mono-oxazolone.

In general, mono-oxazolone is made by a porcelain mortar and pestle, glycine(0.01mol), derivatives aromatic aldehyde(0.01mol), derivatives benzoyl chloride(0.01mol), and fused sodium acetate(0.01mol) were combined for a few minutes in the presence of a few drops of acetic anhydride. The reaction mixture converted to solid after completion, as indicated by TLC, which was washed with cold water and recrystallized from ethanol to get the required azlactone. The oxazolone structures were validated by comparing their **m.p**., mixed. **m.p**., **TLC, IR, ^{1}H-NMR, ^{13}C-NMR & Mass** data to those in the literature. The physical data of **mono-oxazolone B(6-8)** as shown in **Table(3).** The following methods of **mono-oxazolone** preparations are:

(*E,Z*)-4-(4-Hydroxy-3-methoxybenzylidene)-2-(4-((trifluoromethyl)thio)phenyl)oxazol-5(4*H*)-one(6B). It reactions were used to create. A few drops of acetic anhydride, glycine(0.01mol, 0.75g), 4-hydroxy-3-methoxybenzaldehyde(0.01 mol, 1.52g), 4-

((trifluoromethyl)thio)benzoyl chloride(0.01mol, 2.40g, 1.66 ml), and fused sodium acetate(0.01mol, 0.8g). **m.p**.=110-112^{0}C. **R_f**= 0.6. **Yield**= 53%. 1748(C=O), 1648(C=N), 1585(C=C) **IR** ($\bar{\upsilon}$, cm^{-1}, KBr disk).

4-(2,4-Dichlorobenzylidene)-2-(4-hydroxyphenyl)oxazol-5(4*H*)-one(7B). It reactions were used to create. A few drops of acetic anhydride, glycine(0.01mol, 0.75g), 4-hydroxybenzoylchloride(0.01mol, 1.56g), 2,4-dichlorobenzaldehyde(0.01 mol, 1.75g), and fused sodium acetate (0.01mol, 0.8g). **m.p**.= 189-190^{0}C. **R_f** = 0.9. **Yield**= 66%. 1696(C=O), 1654(C=N), 1595(C=C) **IR** ($\bar{\upsilon}$, cm^{-1}, KBr disk).

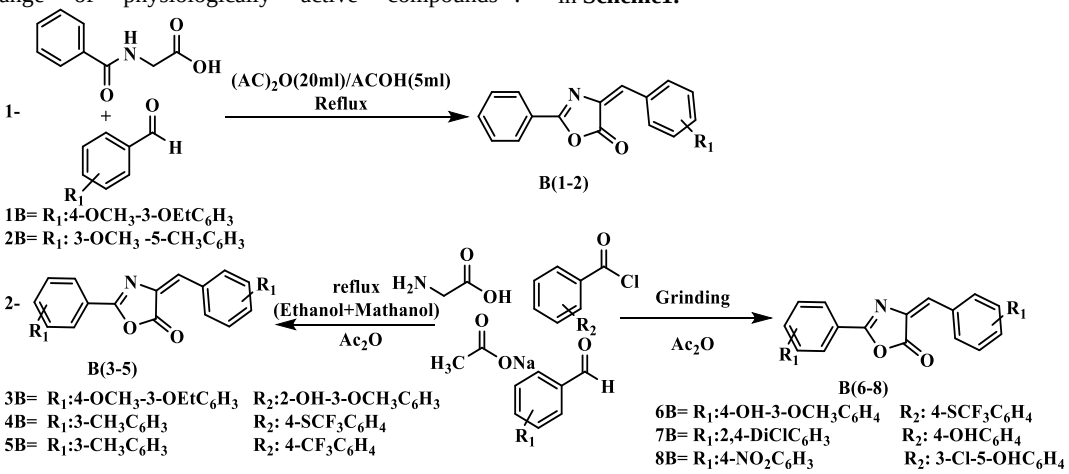
2-(3-Chloro-5-hydroxyphenyl)-4-(4-nitrobenzylidene)oxazol-5(4*H*)-one (8B). It reactions were used to create. A few drops of acetic anhydride, glycine(0.01mol, 0.75g), 4-nitrobenzaldehyde(0.01mol, 1.51g), 3-chloro-5-hydroxy benzoylchloride(0.01mol, 1.91g) and fused sodium acetate (0.01mol, 0.8g). m.p.= 202-201^{0}C. **R_f** = 0.6 Yield= 88%, 1717(C=O), 1668(C=N), 1600(C=C) **IR** ($\bar{\upsilon}$, cm^{-1}, KBr disk).

Table 3. physical data of mono-oxazolone B(5-8)

No.	m.p ^{0}C	R_f	Yield %	Colour	Solvent of recrystalization
56	110-112	0.6	53	yellow	Ethanol
7B	189-190	0.9	66	yellow	Ethanol
8B	202-201	0.6	88	yellow	Ethanol

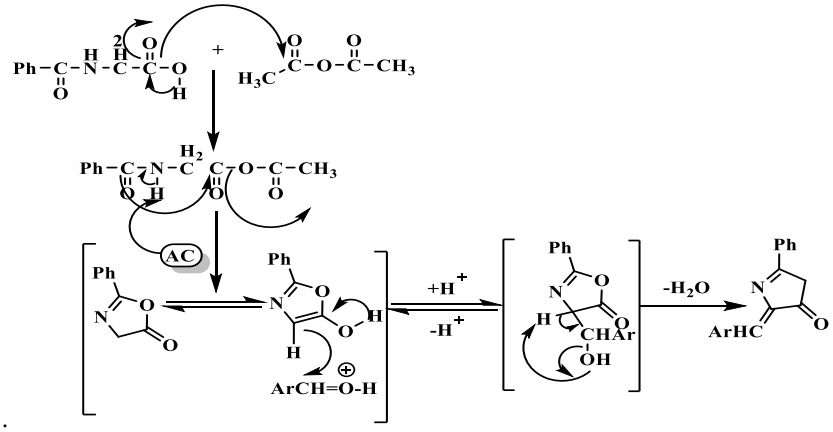
RESULTS AND DISCUSSION

Oxazolones are five-membered heterocyclic molecules that contain oxygen and nitrogen. Oxazolones are used to make a wide range of physiologically active compounds[16]. Antibacterial, antifungal, anti-diabetic, anti-cancer, and anti-inflammatory activities are among its many pharmacological qualities. are acquired In one step, **mono-oxazolone B(1-8)** is synthesized from glycine, aromatic aldehyde, benzoyl chloride, sodium acetate, and a few drops of acetic anhydride**.** As shown in **Scheme1.**



Scheme 1: Synthesis of Mono-oxazolone.

The suggested method for the synthesis of Mono-oxazolone was depicted in the **scheme2** below[17].



Scheme 2. Mechanism of formation of Mono-oxazolone

Infrared spectral IR-FT[18,19]

The structures of the **oxazalones B(1-8)** were established on the basis of spectral data, **IR**, **^{1}H-NMR, ^{13}C-NMR, Mass.**

Infrared spectral IR of **oxazalones B(1-8)**. Were characterized by (3218-3353)(OH stretching vibration), (3001-3119)(sp^2-CH stretching frequency), (2801-2907)(sp^3-CH stretching frequency), (1696-1758)(C=O stretching frequency of five membered ring lactone), (1636-1668)(C=N stretching frequency), (1585-1605)(C=C stretching frequency). cm^{-1} respectively. The IR spectrum of **oxazalones B(1-8)** data are gathered in **Table (4)**.

Table 4. FT-IR spectra of oxazolone B(1-8)

NO	OH ***Stretching cm^{-1}***	sp^3-CH ***Stretching cm^{-1}***	sp^2-CH ***Stretching cm^{-1}***	O-C=O ***Cyclic Stretching cm^{-1}***	O-C=N ***Cyclic Stretching cm^{-1}***	C=C ***Stretching cm^{-1}***
1B	-	3080&3119	2858&2907	1717	1668	1595
2B	-	3078&3109	2882&2938	1699	1636	1605
3B	3274	3001&3085	2862&2958	1996	1653	1593
4B	-	3031&3078	2801&2948	1758	1656	1598
5B	-	3077	2852&2922	1758	1656	1597
6B	3218	3005&3035	28450&293	1748	1648	1585
7B	3353	3080&3115	-	1696	1654	1595
8B	3351	3078&3109	-	1717	1668	1600

^{1}H-NMR Spectral Analysis[20,21]:

Some representative ^{1}H-NMR spectra of the **oxazalones B(1-8)**. The ^{1}H-NMR spectra of **4-(3-Ethoxy-4-methoxybenzylidene)-2-phenyloxazol-5(4*H*)-one(1B).** signal triplet δ(1.31-1.34ppm) (*t*, CH_3, 3H), signal singlet δ(3.89 ppm), (*s*, OCH_3, 3H), signal qurtate δ(4.31-4.37ppm), δ(*q*, OCH_2, 2H), singlet signal δ (8.26ppm) (*s*, C=CH, 1H), multiple signals δ(7.51-8.32ppm) δ(*m*, ArH, 8H). The^{1}H-NMR spectra of the **oxazalones B(1-8)** data are gathered in **Table (5)**.

Table 5. ^{1}H-NMR spectra of oxazolones B(1-8)

Chemical shift ppm		
NO	***Aliphatic Protons***	***Aromatic protons***
1B	1.31-1.34 δ(*t*, CH_3,3H), 3.89 δ(*s*, OCH_3, 3H) 3.37-4.31 δ(*q*,OCH_3, 2H)	7.51-8.32 δ(*m*, ArH, 8H) 8.26 δ(*s*, C=CH 1H)
2B	2.30 δ(*s*, CH_3, 3H), 3.88 δ(*s*, OCH_3, 3H)	7.25-8.17 δ(*m*, ArH, 8H) 7.36 δ(*s*, C=CH, 1H)
3B	1.31-1.35 δ(*t*, CH_3, 3H), 3.83 δ(*s*, OCH_3, 3H) 3.89 δ(*s*, OCH_3,3H), 4.32-4.37 δ(*q*, OCH_2, 3H)	*Z*-isomer(40%), 7.35(*s*, C=CH, 1H) *E*-isomer(60%), 7.36(*s*, C=CH, 1H) 6.93-7.41 δ(*dd*,*dd*,*dd*, *J*=4,4,9, ArH, 3H), δ(*m*, 8.12-8.34ppm, 3H)9.74 δ(*s*, OH,1H)
4B	2.31 δ(*s*, CH_3,3H)	7.30-7.32δ(*dd*, *J*=8, 2H), 8.35-8.37 δ(*dd*, *J*=8, 2H), Para Para System, 7.62-8.14 δ(*m*, ArH,3H), 7.38 δ(*s*, C=CH, 1H)
5B	2.31 δ(*s*, CH_3, 3H)	7.31-7.33 δ(*dd*, *J*=8, 2H), 8.35-8.37 δ(*dd*, , *J*=8, 2H), Para Para System, 7.63-8.15δ(*m*, ArH, 3H), 7.38ppm δ(*s*, C=CH,1H)
6B	3.83ppm,δ(*s*, OCH_3, 3H)	6.81-6.83 δ(*dd*, *J*=8, 2H), 7.78-7.80ppm δ(*dd*, , *J*=8, 2H), Para Para System, *Z*-isomer(30%) 7.37(*s*, C=CH, 1H,) *E*-isomer(70%) 7.38(*s*, C=CH, 1H,) 6.95-7.43 δ(*dd*,*dd*,*dd*, *J*=4,4,9, ArH, 3H), 9.76 δ(*s*, OH 1H)
7B	-	8.15-8.17δ(*dd*, , *J*=8, 2H), 8.30-8.32ppm, δ(*dd*, *J*=8, 2H) Para Para System 7.56-7.94δ(*m*, ArH, 3H), 7.68δ(*s*, C=CH 1H), 9.99δ(*s*, OH, 2H)
8B	-	8.15-8.17 δ(*dd*, *J*=8, 2H), 8.30-8.32ppm, δ(*dd*, *J*=8, 2H) Para Para System 6.91-7.77 δ(*m*, ArH, 3H), 7.74δ(*s* C=CH, 1H), 9.78δ(*s*, OH,1H)

^{13}C-NMR Spectral Analysis[22,23].

Some representative **^{13}C-NMR** spectra of the **oxazalones B(1-8).** The **^{13}C-NMR** spectra of **4-(3-Ethoxy-4-methoxybenzylidene)-2-phenyloxaz ol-5(4*H*)-one(1B).** Show singlet signal at δ(14.05ppm) for (-CH_3-), Show singlet signal at δ (52.88ppm) for (-OCH_3) Show singlet signal at δ(66.73ppm) for (-OCH_2-) at δ(124.04-137.79ppm) aromatic carbon show singlet signal at δ(166.57), for **(**C=O) δ(164.30ppm) for (C=N) δ(150.20ppm) for (C=CH). The **^{13}C-NMR** spectra of the **oxazalones B(1-8)** data are gathered in **Table (6)**.

Table 6. ^{13}C-NMR spectra of oxazolones B(1-8)

Chemical shift ppm						
NO	**CH_3**	**OCH_3**	**Aromatic Carbons**	C=O	**C=N**	**C=C**

1B	14.0	52.88, 66.73	124.04-137.79	166.57	164.30	150.20
2B	20.49	55.89	116.17-166.93	165.42	163.19	151.02
3B	14.07	52.90, 55.60, 61.74	110.66-153.10	165.91	164.32	150.22
4B	20.97	-	125.43-166.95	169.00	163.16	152.49
5B	20.01	-	125.43-166.99	169.07	163.22	152.54
6B	-	55.66	110.73-148.26	167.43	161.72	153.13
7B	-	-	124.18-138.85	166.22	165.45	139.45
8B	-	-	115.69-136.45	165.90	163.38	150.07

Analysis of mass spectra[24,25]:
The mass spectrum of **(*E,Z*)-4-(3-Ethoxy-4-methoxybenzylidene)-2-(2-hydr oxy-3-methoxyphenyl)oxazol-5(4*H*)-one(3B).** showed the molecular ion peak at m/z=369, and shown the important fragmentation peaks in 65.2m/z, 82.2m/z, 104.1m/z, 121.1m/z, 150.1m/z, 167.1m/z. The mass spectrum of **4-(3-Methylbenzyli dene)-2-(4-(trifluoromethyl)phenyl)oxazol-5(4*H*)-one(5B).** showed the molecular ion peak at m/z =331 shown the important fragmentation peaks in 65.1m/z, 92.1 m/z, 119.1m/z, 165.1m/z, 190.1m/z, 214.1m/z, 257.1m/z, 281.0m/z, 304.1m/z. The mass spectrum of **2-(3-Chloro-5-hydroxy phenyl)-4-(4-nitrobenzylidene)oxazol-5(4*H*)-one(8B).**
showed the molecular ion peak at m/z=344 shown the important fragmentation peaks in 57.1m/z, 77.1m/z, 105.1m/z, 121.1m/z, 149.0m/z, 167.0m/z, 185.1m/z, 207.1m/z , 225.1m/z, 241.1m/z, 265.1 m/z, 281.1 m/z, 307.1 m/z.
TLC was used to determine the end point of each step in the synthesis of oxazolone analogs. Every 30 minutes, The value of R_f was calculated. Each reaction is through one clear place.

CONCLUSION

The newly composition Mono-oxazolone's and structure were synthesized in high yields (53-92%). Analytical and physicochemical properties were used to confirm the findings. and the chemical structure of the generated compounds was determined using **FT-IR, ^{1}HNMR** & **^{13}CNMR**.

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COMPLIANCE WITH ETHICAL STANDARDS STATEMENTS

I. Ethical approval: The manuscript is written in original and all the data, results pertaining to this manuscript are original according to the research performed. The authors followed academic integrity and have not copied any content/results from another source.
II. Funding details (In case of Funding): The authors of this manuscript did not receive any funding to perform the present research
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V. All the authors of this study contributed equally in terms of performing the research as well as in preparing the manuscript. All the authors of the study followed the guidelines of the corresponding author. Any query/suggestion related to the manuscript can be reached to the corresponding author

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