

## MICROWAVE ASSISTED ONE –POT SYNTHESIS OF 3, 4-DIHYDRO-1-ARYL-(1, 3) OXAZINO (5, 6-H) QUINOLIN-3-ONE

### Abstract

In this book chapter, we have described an effective one-pot cyclocondensation reaction of 8-quinolinol, aromatic aldehydes, and urea under solvent-free condensation and microwave assisted conditions to produce 3, 4-dihydro-1-aryl-(1,3)oxazino(5,6h)quinolin-3-one derivatives (1-6). With our continuous investigation on the methodology of green synthesis we have described the synthesis, mass spectral analysis and biological activities of 3,4-dihydro-4-phenyl-(1,3)oxazino(5,6 h)quinolin-2-one (1), 3,4-dihydro-4-(4-nitrophenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (2), 3,4-dihydro-4-(hydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (3), 3,4-dihydro-4-(2,4-dihydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (4), 4-(3-ethoxy-2-hydroxyphenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one (5), 4-(4-(dimethylamino)phenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one (6).

**Keywords:**  $\rho$ -TSA, 3, 4-dihydro-1, 3-oxazin-2-one, Quinoline, Anti-Convulsant activity, pharmacologically active

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## I. INTRODUCTION

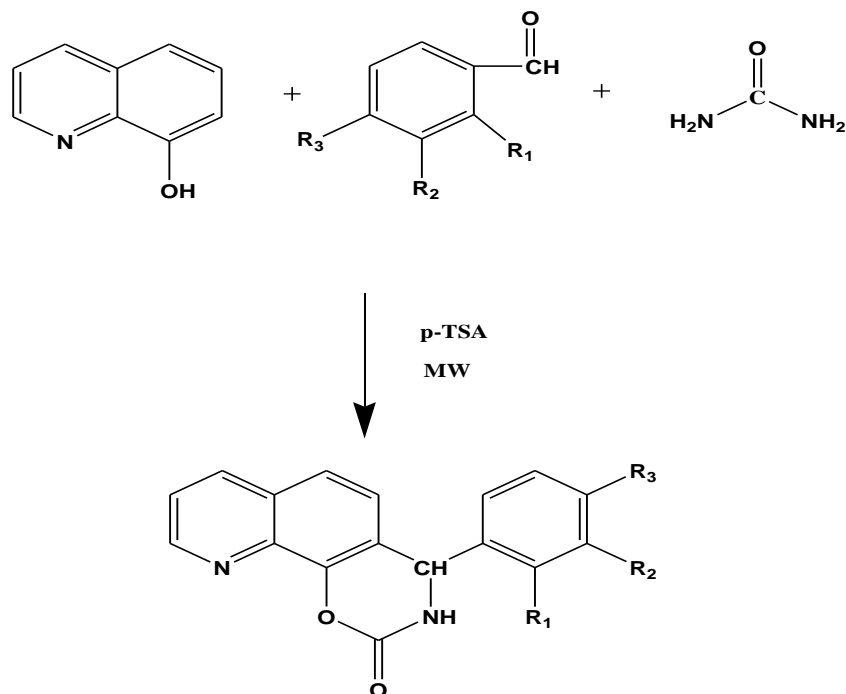
Since multicomponent reactions (MCRs) offer major advantages over traditional linear type synthesis, they are becoming more and more important in organic and medicinal chemistry. Since combining three or more small molecular weight building blocks in a single operation results in high combinatorial chemistry, MCRs that lead to interesting heterocyclic scaffolds are particularly helpful for the development of diverse chemical libraries of drug-like molecules for biological screening.

Organic synthesis involving environmentally friendly protocol under solvent free condition is being explored world wide due to stringent environment and economic regulation. The quinoline skeleton is present in the structures of pharmacologically active chemicals and natural products, which has sparked the creation of numerous synthesis methods. Quinoline derivatives have a lengthy history of being used as chemotherapeutic agents and for a variety of other biological activities<sup>1,2</sup> Additionally, they are utilised as photographic sensitizers and dyestuffs.<sup>3</sup> For the creation of nano and mesostructures with improved electrical and optical characteristics, they are useful reagents. They are valuable reagents for the synthesis of nano and mesostructures with enhanced electronic and photonic properties.<sup>4</sup> The quinoline nucleus is the backbone of many natural products and pharmacologically significant compounds displaying a broad range of biological activity. Many functionalized quinolines are widely used as antimalarial, antiasthmatic, anti-inflammatory agents, and antibacterial, antihypertensive and tyrosine kinase PDGF-RTK inhibiting agents.<sup>6</sup> Oxazinone derivatives have received considerable attention due to interesting pharmacological properties associated with this heterocyclic scaffold. Example - naphthooxazinone derivatives have been reported to acts as antibacterial agents, or Efavirenz (Sustiva), a benzoxazinone derivative, is a non-nucleoside reverse transcriptase inhibitor that has been approved by the FDA in 1998 and is presently in clinical use for the treatment of AIDS. As a result, there are many techniques in the literature for creating aromatic oxazinone derivatives. To the best of our knowledge, there are no studies in the literature describing the condensation of 6-quinolinol, aldehyde, and urea to produce 1, 2-dihydro (5, 6)-quinolin-3-one derivatives. Then, under solvent-free conditions utilising -TSA at 1500C, a number of aromatic aldehydes reacted to produce the desired compounds in good yields. Using aromatic aldehydes with electron-donating or electron-withdrawing substituents, high yields were attained. The yields of the reaction with aliphatic aldehydes significantly decreased under the same conditions (20% with butanal or hexanal), most likely as a result of a potential aldol condensation side reaction.

Microwave irradiation was utilised in the presence of several catalysts, including - TSA, HOAc, FeCl<sub>3</sub>, ZnCl<sub>2</sub>, and SnCl<sub>2</sub>, to shorten the reaction time. HOAc is the most productive catalyst in terms of yield, according to the study. It is evident that when a catalytic amount of HOAc was present, the reaction time employing microwave irradiation dropped from 2 to 2.5 hours to 4 minutes. In addition to decrease of reaction time, the yields in all cases are reasonable.<sup>12</sup> According to the findings, and as in several traditional multi-component reactions, acylamine intermediate<sup>14</sup> created in-situ by condensation reaction of aldehyde with urea can be mechanistically thought to go through.<sup>15</sup> Using aromatic aldehydes with electron-donating or electron-withdrawing substituents, high yields were achieved in excellent yields. The creation of this heterocyclic nucleus plays a significant role in chemical synthesis, and quinoline derivatives are known to exhibit a wide range of biological activities,

pharmacological and therapeutic qualities, such as antiviral, antibacterial, and anti-inflammatory activities.

In this chapter, In a three component cyclocondensation reaction of 8-quinolinol, aromatic aldehydes, and urea under solvent-free condensation and microwave assisted conditions, we have described an effective one-pot synthesis for the preparation of 3, 4-dihydro-1-aryl-(1,3)oxazino(5,6-h)quinolin-3-one derivatives (1-6).The following compounds are given below in Table 1.



**Table 1: Substituted Quinoline Derivatives are given below:**

COMPOUND NO	-R <sub>1</sub>	-R <sub>2</sub>	-R <sub>3</sub>
1	-H	-H	-H
2	-H	-H	-NO <sub>2</sub>
3	-H	-H	-OH
4	-OH	-H	-OH
5	-OH	-OC <sub>2</sub> H <sub>5</sub>	-H
6	-H	-H	-N(CH <sub>3</sub> ) <sub>2</sub>

**1. Synthesis of 3, 4-dihydro-4-phenyl-(1, 3) oxazino (5, 6-h) quinolin-2-one (1):** By cyclocondensing benzaldehyde, 8-quinolinol, and urea in a solvent-free environment with -TSA at 1500°C, the compound 3,4-dihydro-4-phenyl-(1,3)oxazino(5,6-h)quinolin-2-one (1) was created, giving rise to the desired products in good yields.

The mass spectrum of (1) has shown the molecular ion peak at m/e 276 (C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>). Other important peaks have been found at m/e 225(C<sub>14</sub>H<sub>11</sub>NO<sub>2</sub>), 200(C<sub>11</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>), 175(C<sub>10</sub>H<sub>9</sub>NO<sub>2</sub>), 149(C<sub>8</sub>H<sub>7</sub>NO<sub>2</sub>), 99(C<sub>4</sub>H<sub>5</sub>NO<sub>2</sub>). <sup>1</sup>HNMR spectrum of (1) has shown one singlet for NH proton at δ 8.0. One multiplet in the range of δ 7.06-7.14

for benzylic proton. One doublet has found at  $\delta$  6.16 for proton of heterocyclic ring adjacent to NH proton. One multiplet is also found in the range of  $\delta$  7.14-8.86 for protons of quinoline nucleus.

- 2. Synthesis of 3, 4-dihydro-4-(4-nitrophenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (2) :** 3,4-dihydro-4-(4-nitrophenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (**2**) has been synthesized by the cyclocondensation of 4-nitrobenzaldehyde, 8-quinolinol and urea under solvent free condition using  $\rho$ -TSA at 150<sup>0</sup>C reacted to afford the corresponding products in good yields. The mass spectrum of (**2**) has shown the molecular ion peak at m/e 321 (C<sub>17</sub>H<sub>11</sub>N<sub>3</sub>O<sub>4</sub>). Other important peaks have been found at m/e 276(C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>), 220(C<sub>10</sub>H<sub>8</sub>N<sub>2</sub>O<sub>4</sub>), 175(C<sub>10</sub>H<sub>9</sub>NO<sub>2</sub>), 149(C<sub>8</sub>H<sub>7</sub>NO<sub>2</sub>), 99(C<sub>4</sub>H<sub>5</sub>NO<sub>2</sub>). <sup>1</sup>HNMR spectrum of (**2**) has shown one singlet for NH proton at  $\delta$  8.0. One multiplet is found in the range of  $\delta$  7.32-8.07-for aromatic proton which is strongly deshielded by nitro group. One doublet has found at  $\delta$  6.16 for proton of heterocyclic ring adjacent to NH proton. One multiplet is also found for aromatic proton at  $\delta$  7.14-8.86 situated in quinoline nucleus.
- 3. Synthesis of 3,4-dihydro-4-(hydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (3) :** 3,4-dihydro-4-(hydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one has been synthesized by the cyclocondensation of 4-hydroxybenzaldehyde, 8-quinolinol and urea under solvent free condition using  $\rho$ -TSA at 150<sup>0</sup>C reacted to afford the corresponding products in good yields. The mass spectrum of (**3**) has shown the molecular ion peak at m/e 292 (C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>). Other important peaks have been found at m/e 276(C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>), 241(C<sub>14</sub>H<sub>11</sub>NO<sub>3</sub>), 200(C<sub>11</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>), 191(C<sub>10</sub>H<sub>9</sub>NO<sub>3</sub>), 175(C<sub>10</sub>H<sub>9</sub>NO<sub>2</sub>), 149(C<sub>8</sub>H<sub>7</sub>NO<sub>2</sub>), 99(C<sub>4</sub>H<sub>5</sub>NO<sub>2</sub>). <sup>1</sup>HNMR spectrum of (**3**) has shown one singlet for NH proton at  $\delta$  8.0. One multiplet is found in the range of  $\delta$  6.61-6.89 for aromatic proton which is strongly deshielded by hydroxyl group. One doublet has found at  $\delta$  6.16 for proton of heterocyclic ring adjacent to -NH proton. One multiplet is also found for aromatic proton at  $\delta$  7.14-8.86 situated in quinoline nucleus.
- 4. Synthesis of 3,4-dihydro-4-(2,4-dihydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (4) :** 3,4-dihydro-4-(2,4-dihydroxyphenyl)-(1,3)oxazino(5,6-H) quinolin-2-one has been synthesized by the cyclocondensation of 2,4-dihydroxybenzaldehyde, 8-quinolinol and urea under solvent free condition using  $\rho$ -TSA at 150<sup>0</sup>C reacted to afford the corresponding products in good yields. The mass spectrum of (**4**) has shown the molecular ion peak at m/e 309 (C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>4</sub>). Other important peaks have been found at m/e 292(C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>), 276(C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>), 207(C<sub>10</sub>H<sub>9</sub>NO<sub>4</sub>), 200(C<sub>11</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>), 175(C<sub>10</sub>H<sub>9</sub>NO<sub>2</sub>), 149(C<sub>8</sub>H<sub>7</sub>NO<sub>2</sub>), 99(C<sub>4</sub>H<sub>5</sub>NO<sub>2</sub>). <sup>1</sup>HNMR spectrum of (**4**) has shown one singlet for NH proton at  $\delta$  8.0. One multiplet in the range of  $\delta$  6.08-6.72 for aromatic proton. One doublet has found at  $\delta$  6.16 for proton of heterocyclic ring adjacent to NH proton. One multiplet is also found in the range of  $\delta$  7.14-8.86 for protons of quinoline nucleus. Another prominent singlet is observed at  $\delta$  5.0 for proton of hydroxyl group (-OH).
- 5. Synthesis of 4-(3-ethoxy-2-hydroxyphenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one(5) :** 4-(3-ethoxy-2-hydroxyphenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one has been synthesized by the cyclocondensation of 2-hydroxy-3-ethoxyhydroxybenzaldehyde, 8-quinolinol and urea under solvent free condition using  $\rho$ -

TSA at 150<sup>0</sup>C reacted to afford the corresponding products in good yields. The mass spectrum of (5) has shown the molecular ion peak at m/e 336 (C<sub>19</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub>). Other important peaks have been found at m/e 320(C<sub>19</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub>), 292(C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>), 276(C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>), 287(C<sub>16</sub>H<sub>17</sub>NO<sub>4</sub>), 235(C<sub>12</sub>H<sub>13</sub>NO<sub>4</sub>), 200(C<sub>11</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>), 99(C<sub>4</sub>H<sub>5</sub>NO<sub>2</sub>). <sup>1</sup>HNMR spectrum of (5) has shown one singlet for NH proton at δ 8.0. One multiplet is found in the range of δ 6.41-6.59 for aromatic proton which is strongly deshielded by ethoxy group. One doublet has found at δ 6.16 for proton of heterocyclic ring adjacent to NH proton. One multiplet is also found for aromatic proton at δ 7.14-8.86 situated in quinoline nucleus, strongly deshielded by electronegative atom (N). Another prominent singlet is observed at δ 5.0 for proton of hydroxyl group (-OH). <sup>1</sup>HNMR spectrum shows that one quartet for methylene proton and one triplet for methyl proton at δ 3.98 and 1.33 respectively.

- 6. Synthesis of 4-(4-(dimethylamino)phenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one (6):** 4-(4-(dimethylamino)phenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one has been synthesized by the cyclocondensation of 4-dimethylaminobenzaldehyde, 8-quinolinol and urea under solvent free condition using ρ-TSA at 150<sup>0</sup>C reacted to afford the corresponding products in good yields. The mass spectrum of (6) has shown the molecular ion peak at m/e 319 (C<sub>19</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub>). Other important peaks have been found at m/e 276(C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>), 268(C<sub>16</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>), 200((C<sub>11</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>), 175(C<sub>10</sub>H<sub>9</sub>NO<sub>2</sub>), 149(C<sub>8</sub>H<sub>7</sub>NO<sub>2</sub>), 99(C<sub>4</sub>H<sub>5</sub>NO<sub>2</sub>). <sup>1</sup>HNMR spectrum of (6) has shown one singlet for NH proton at δ 8.0. One doublet has found at δ 6.16 for proton of heterocyclic ring adjacent to NH proton. The spectrum illustrates that two aryl proton are coupled to give a pair of doublets at δ 6.47-6.88 deshielded by dimethylamino group. One multiplet is also found for aromatic proton at δ 7.14-8.86 situated in quinoline nucleus.

## II. MASS SPECTRAL STUDIES

Electron impact is a method frequently used to determine an organic compound's mass spectrum. The techniques are used as for compounds which are volatile. The compound is introduced by vaporization followed by ionization by electron impact. Mass spectral studies of substituted quinoline derivatives 1-6, 3, 4-dihydro-4-phenyl-(1,3)oxazino(5,6-h)quinolin-2-one has been described in the Table 2.

**Table 2: Mass spectral fragmentation of substituted quinoline derivatives 3, 4-dihydro-4-phenyl-(1,3)oxazino(5,6-h)quinolin-2-one given below.**

Compound no:	-R <sub>1</sub>	-R <sub>2</sub>	-R <sub>3</sub>	-X	m/e
1	-H	-H	-H	-O	276,225,200,175,149,99
2	-H	-H	- NO 2	-O	321,276,270,220,200,175,149,99
3	-H	-H	- OH	-O	292,276,241,191,175,149,99
4	- OH	-H	- OH	-O	309,292,276,200,207,149,99

5	- OH	OC <sub>2</sub> H <sub>5</sub> -	-H	-O	336,320,292,276,287,235,20 0,99
6	-H	-H	- N( CH 3) <sub>2</sub>	-O	319,276,268,200,175,149,99

### III.RESULTS AND DISCUSSIONS

Although the molecular ion formed by the initial electron ionization usually undergoes extensive fragmentation but m/e value of ion is of course, molecular weight of compound.

The mass spectrum of 3,4-dihydro-4-phenyl-(1,3)oxazino(5,6-h)quinolin-2-one (Figure 1) has shown major peaks at m/e 276, 225, 200, 175, 149 and 99. The most intense molecular ion peak is observed at m/e 276 (1). A characteristic fragmentation is cleavage of pyridine nucleus often leads to most abundant ion at m/e 225 (1.1) in the spectrum of compound. The most intense base peak is found at m/e 200(1.2). The typical peak found at m/e 175 (1.3) showing the loss of quinoline moiety. There is one more significant peak is found at m/e 99 (1.5) due to formation of 3, 4-dihydro-1, 3-oxazin-2-one nucleus which is more stable.

Fragmentation pattern of 3,4-dihydro-4-(4-nitrophenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (Figure 2) has shown molecular ion peak is observed at 321(2). Other important peaks are 321, 276, 200, 175, 149, 99. The spectrum also showed characteristic peak at m/e 276 showing nucleus of nitro group. Another ion at m/e 220 (2.2) is prominent in the mass spectrum of compounds, due to fragmentation of quinoline nucleus. The fragment at m/e 200(2.3) may be attributed to be formed due to cleavage of nitrobenzene nucleus, showing the loss of 123 units. The base peak has been observed at m/e 99(2.5) due to formation of 3, 4-dihydro-1, 3-oxazin-2-one nucleus.

The mass spectrum of 3,4-dihydro-4-(hydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (Figure 3) has shown the major peaks at m/e 292, 276, 241, 200, 191, 175, 149, 99. The most intense molecular ion peak is found at m/e 292 (3). A characteristic fragmentation is found at m/e 276 (3.1) due to loss of hydroxyl group showing the loss of 17 units. The typical peak is found at m/e 200 (3.3) showing the loss of -C<sub>6</sub>H<sub>5</sub>OH group. The peak at m/e 175 (3.5) comprises of fragmentation of quinoline nucleus. The most significant base peak is found at m/e 99 (3.7) due to formation of 3, 4-dihydro-1,3-oxazin-2-one nucleus which is more stable.

In the mass spectrum of 3,4-dihydro-4-(2,4-dihydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (Figure 4), the fragment molecular ion peak at m/e 309 together with ion peaks at m/e 292, 276, 200, 207, 149, 99 are suggestive of the presence of substituted benzaldehyde and 3,4-dihydro-1,3-oxazin-2-one nucleus. The most intense peak is found at m/e 309 (4). The other fragment at m/e 292 (4.1) confirms the removal of -OH group, showing the loss of 17 units. The spectrum also showed the characteristic peak at m/e 276 (4.2) showing the removal of both hydroxyl group substituted on benzaldehyde. Another ion at m/e 200 (4.3) is prominent in the mass spectrum of compounds, due to fragmentation of -C<sub>6</sub>H<sub>5</sub> (OH)<sub>2</sub>. The fragment at m/e 207 (4.4) may be attributed to be formed due to cleavage of

quinoline nucleus. The base peak has been observed at  $m/e$  99(4.6) due to formation of 3, 4-dihydro-1, 3-oxazin-2-one nucleus.

The mass spectrum of 4-(3-ethoxy-2-hydroxyphenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one (Figure 5) has shown the major peaks at  $m/e$  336, 320, 292, 287, 235, 200, 99. The most intense molecular ion peak is found at  $m/e$  336 (5). A characteristic fragmentation is found at  $m/e$  320 (5.1) due to loss of hydroxyl group showing the loss of 17 units. The typical peak is found at  $m/e$  292 (5.2) showing the loss of  $-OC_2H_5$  group. The peak at  $m/e$  276 (5.3) indicates fragmentation of hydroxyl and ethoxy group. The fragment at  $m/e$  235 (5.5) may be attributed to be formed due to cleavage of quinoline nucleus. The most significant base peak is found at  $m/e$  99 (5.7) due to formation of 3,4-dihydro-1, 3-oxazin-2-one nucleus which is more stable.

The mass spectrum of 4-(4-(dimethylamino)phenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one (Figure 6) has shown the molecular ion peak at  $m/e$  219 (6). Other important peaks are 268, 276, 200, 175, 149, 99. Fragmentation pattern has shown that dimethylamino group got fragmented showing the mass spectral peak at  $m/e$  276 (6.1). The peak at  $m/e$  200 (6.3) has shown that  $-C_6H_5(NCH_3)_2$  has been fragmented showing the loss of 121 units. The spectrum also showed the characteristic peaks at  $m/e$  175 (6.4) and 149(6.5). The most significant base peak is found at  $m/e$  99 (6.6) due to formation of 3,4-dihydro-1,3-oxazin-2-one nucleus which is more stable.

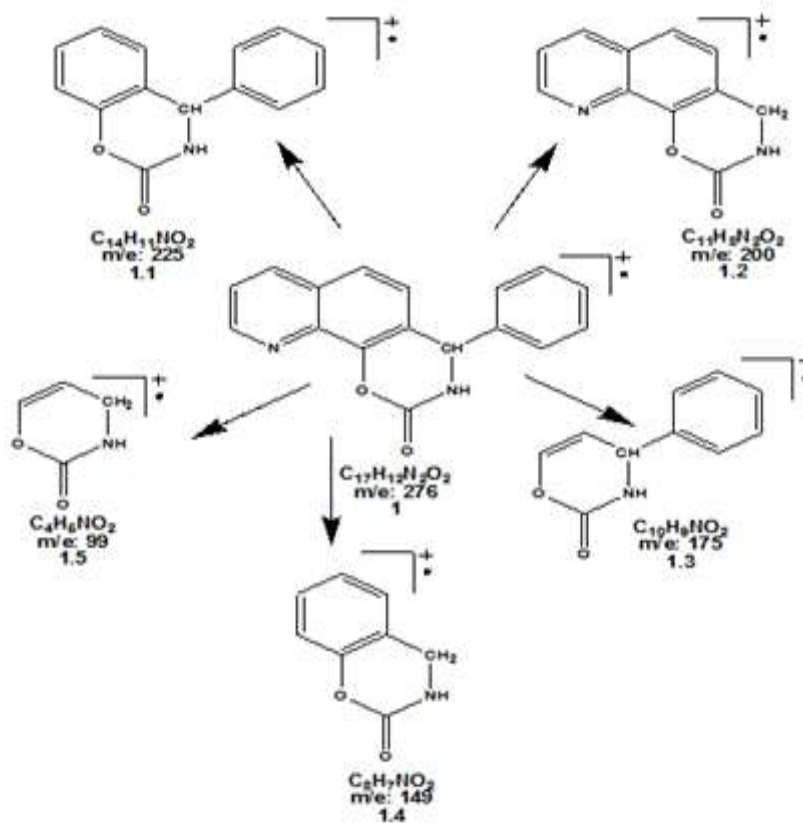


Figure 1

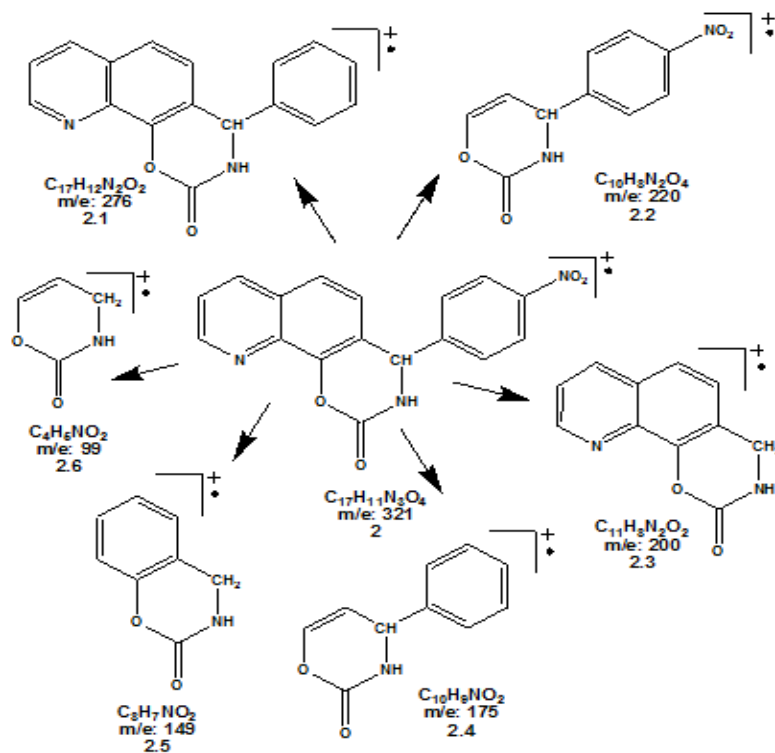


Figure 2

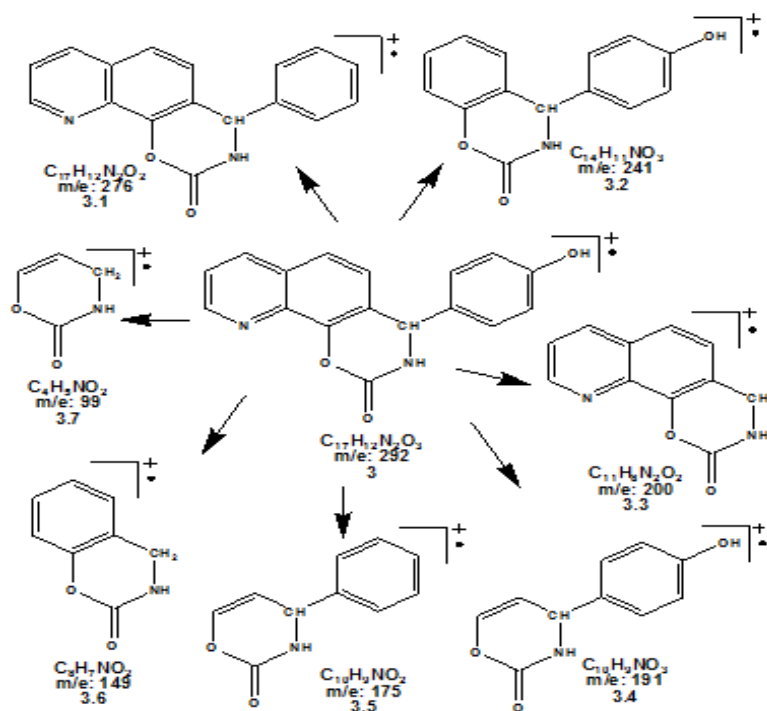


Figure 3



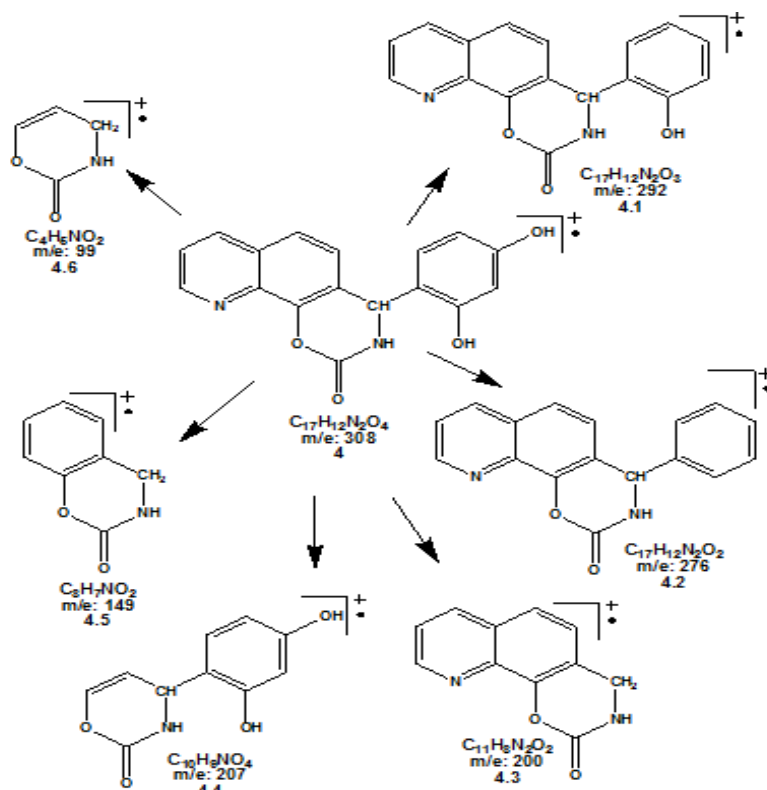


Figure 4

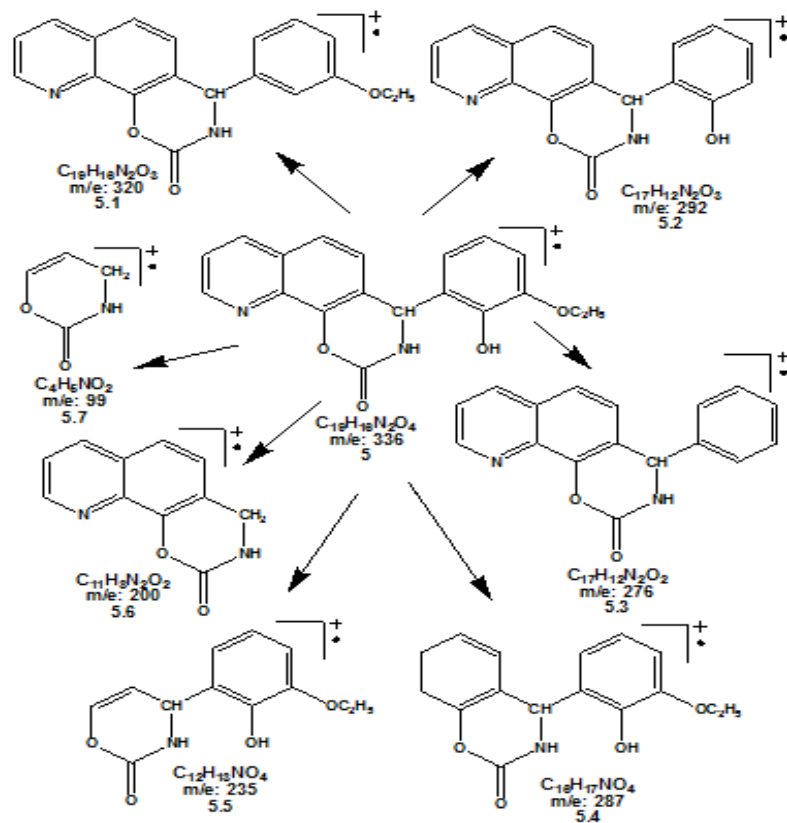


Figure 5

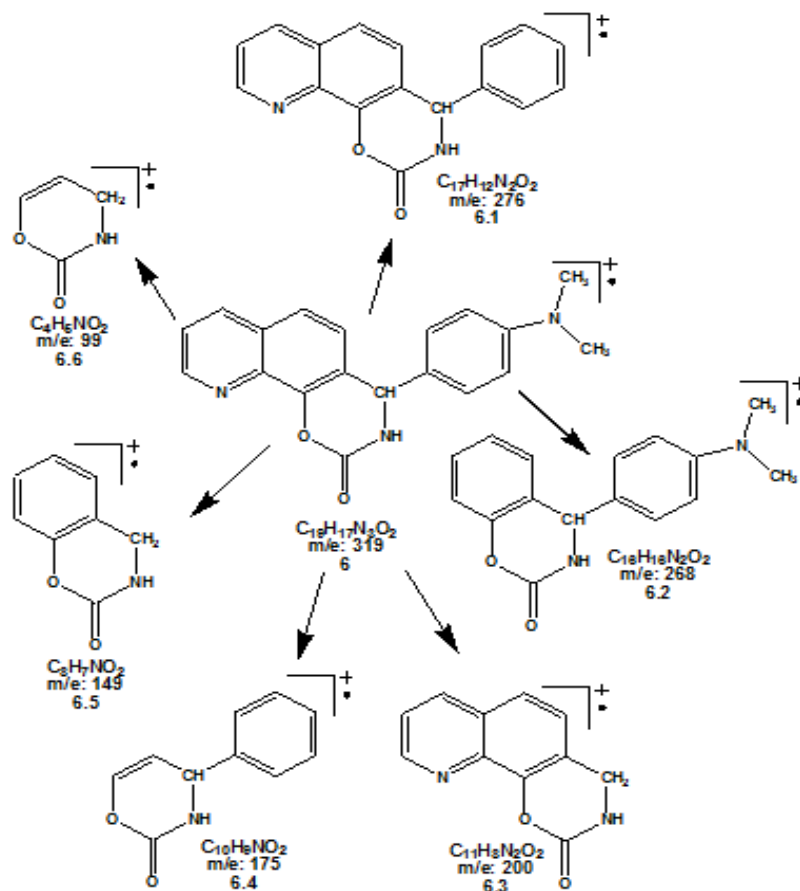


Figure 6

#### IV. EXPERIMENTAL

On silica gel TLC plates, compounds were routinely examined for purity, with spots being seen by iodine vapours. TMS was used as the internal reference while recording PMR spectra on the Bruker DRX 300 MHz FT NMR spectrometer, and chemical shift values were given in units. The signals had the following designations: s singlet, d doublet, t triplet, and m multiplet. On the Jeol SX-102 spectrometer, mass spectra were conducted. Thin layer chromatography was used to monitor each reaction over silica gel-G and basic alumina coated TLC plates. By using  $^1H$  NMR and mass spectra, the structures of products 1-6 were identified.

#### V. GENERAL PROCEDURE

Finally, urea (1.5 mmol), aldehyde (1.0 mmol), and 8 quinolinol (1.0 mmol) were combined with -TSA. In a Pyrex test tube, the reaction mixture was put, and it was exposed to a 700W irradiation source for 4 minutes. To obtain pure product, the reaction mixture was cooled, washed with water, and then recrystallized from EtOH or hexane. According to the findings, and as in numerous traditional multicomponent reactions, the acylamine intermediate created in-situ by the condensation reaction of aldehyde with urea can be

mechanistically thought of as the pathway through which the process proceeds. After adding 8-quinolinol to the acylamine, the intermediate underwent cyclization to produce cyclization products.

- 1. Synthesis of 3, 4-dihydro-4-phenyl-(1,3)oxazino(5,6-h)quinolin-2-one (1) :** 3,4-dihydro-4-(hydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one has been synthesized by the cyclocondensation of hydroxybenzaldehyde (106mg), 8-quinolinol (145mg) and urea(60mg) under solvent free condition using  $\rho$ -TSA at 150 °C reacted to afford the corresponding products in good yields. White power, Yield: 143mg. mp: above 200 °C  $^1\text{HNMR}$  (DMSO $_d_6$ )  $\delta$  8.0 (s, 1H,  $\text{NH}$ ), 7.25-8.86 (m, 5H,  $\text{ArH}$ ), 7.06-7.14(m, 5H,  $\text{ArH}$ ), 6.16 (d, 1H,  $\text{CH}$ ).MS(m/e): 276(C $_{17}$ H $_{12}$ N $_2$ O $_2$ ), 225(C $_{14}$ H $_{11}$ NO $_2$ ), 200(C $_{11}$ H $_8$ N $_2$ O $_2$ ), 175(C $_{10}$ H $_9$ NO $_2$ ), 149(C $_8$ H $_7$ NO $_2$ ), 99(C $_4$ H $_5$ NO $_2$ ). Anal.: (C $_{17}$ H $_{12}$ N $_2$ O $_2$ ) Calc:C, 73.90; H, 4.30; N, 10.14.Found: C, 73.84; H, 4.26; N, 10.10 %
- 2. Synthesis of 3,4-dihydro-4-(4-nitrophenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (2):** 3,4-dihydro-4-(4-nitrophenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (2) has been synthesized by the cyclocondensation of 4-nitrobenzaldehyde(151mg), 8-quinolinol(145mg) and urea(60mg) under solvent free condition using  $\rho$ -TSA at 150°C reacted to afford the corresponding products in good yields. White power, Yield: 143mg. mp: above 200 °C  $^1\text{HNMR}$ (DMSO $_d_6$ )  $\delta$  8.0(s, 1H,  $\text{NH}$ ), 7.32-8.02(m, 4H,  $\text{ArH}$ ), 7.25-8.86 (m, 5H,  $\text{ArH}$ ), 6.16 (d, 1H,  $\text{CH}$ ). MS (m/e): 321 (C $_{17}$ H $_{11}$ N $_3$ O $_4$ ), 276(C $_{17}$ H $_{12}$ N $_2$ O $_2$ ), 270(C $_{14}$ H $_{10}$ N $_2$ O $_4$ ), 220(C $_{10}$ H $_8$ N $_2$ O $_4$ ), 200(C $_{11}$ H $_8$ N $_2$ O $_2$ ), 175(C $_{10}$ H $_9$ NO $_2$ ), 149(C $_8$ H $_7$ NO $_2$ ), 99(C $_4$ H $_5$ NO $_2$ ). Anal.: (C $_{17}$ H $_{11}$ N $_3$ O $_4$ )Calc: C, 63.55; H, 3.45; N, 13.08.Found: C, 63.14; H, 3.26; N, 13.00 %
- 3. Synthesis of 3,4-dihydro-4-(hydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one :** 3,4-dihydro-4-(hydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one has been synthesized by the cyclocondensation of 4-hydroxybenzaldehyde(122mg), 8-quinolinol(145mg) and urea(60mg) under solvent free condition using  $\rho$ -TSA at 150° C reacted to afford the corresponding products in good yields. White power, Yield: 143mg. mp: above 200 °C  $^1\text{HNMR}$ (DMSO $_d_6$ )  $\delta$  8.0(s, 1H, $\text{NH}$ ), 7.14-8.86 (m, 5H,  $\text{ArH}$ ), 6.61-6.89(m, 4H,  $\text{ArH}$ ), 6.16 (d,1H,  $\text{CH}$ ), 5.0(s, 1H,  $\text{OH}$ ) MS(m/e): 292 (C $_{17}$ H $_{12}$ N $_2$ O $_3$ ), 276(C $_{17}$ H $_{12}$ N $_2$ O $_2$ ) , 241(C $_{14}$ H $_{11}$ NO $_3$ ), 200(C $_{11}$ H $_8$ N $_2$ O $_2$ ), 175(C $_{10}$ H $_9$ NO $_2$ ), 149(C $_8$ H $_7$ NO $_2$ ), 99(C $_4$ H $_5$ NO $_2$ ). Anal.: (C $_{17}$ H $_{12}$ N $_2$ O $_3$ ) Calc:C, 69.86; H, 4.14; N, 9.58.Found C, 69.14; H, 4.12; N, 9.50%
- 4. Synthesis of 3,4-dihydro-4-(2,4-dihydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one (4):** 3,4-dihydro-4-(2,4-dihydroxyphenyl)-(1,3)oxazino(5,6-h)quinolin-2-one has been synthesized by the cyclocondensation of 2,4-dihydroxybenzaldehyde(138mg), 8-quinolinol(145mg) and urea (60mg)under solvent free condition using  $\rho$ -TSA at 150 °C reacted to afford the corresponding products in good yields. White power, Yield: 143mg. mp: above 200 °C  $^1\text{HNMR}$  (DMSO $_d_6$ )  $\delta$  8.0(s, 1H,  $\text{NH}$ ), 7.14-8.86 (m, 5H,  $\text{ArH}$ ), 6.16 (d, 1H,  $\text{CH}$ ), 6.08-6.72(m, 3H,  $\text{ArH}$ ), 5.0(s, 1H,  $\text{OH}$ ). MS (m/e): 336(C $_{19}$ H $_{16}$ N $_2$ O $_4$ ), 292 (C $_{17}$ H $_{12}$ N $_2$ O $_3$ ), 276(C $_{17}$ H $_{12}$ N $_2$ O $_2$ ), 207(C $_{10}$ H $_9$ NO $_4$ ), 200(C $_{11}$ H $_8$ N $_2$ O $_2$ ), 175(C $_{10}$ H $_9$ NO $_2$ ), 149(C $_8$ H $_7$ NO $_2$ ), 99(C $_4$ H $_5$ NO $_2$ ). Anal.: (C $_{17}$ H $_{12}$ N $_2$ O $_4$ )Calc: C, 66.23; H, 3.92; N, 9.09. Found C, 66.14; H, 3.89; N, 9.00%
- 5. Synthesis of 4-(3-ethoxy-2-hydroxyphenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one(5):** 4-(3-ethoxy-2-hydroxyphenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one

has been synthesized by the cyclocondensation of 2-hydroxy-3-ethoxyhydroxybenzaldehyde(166mg), 8-quinolinol(145mg) and urea(60mg) under solvent free condition using p-TSA at 150 °C reacted to afford the corresponding products in good yields. White power, Yield: 143mg. mp: above 200 °C. <sup>1</sup>HNMR (DMSO<sub>d</sub><sub>6</sub>) δ 8.0(s, 1H, NH), 6.41-6.59(m, 3H, ArH), 7.14-8.86 (m, 5H, ArH), 6.16 (d, 1H, CH), 5.0(s, 1H, OH) 3.98(q, 2H, CH<sub>2</sub>), 1.33(t, 3H, CH<sub>3</sub>). MS (m/e): 336(C<sub>19</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub>) 292 (C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>), 276(C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>), 287(C<sub>16</sub>H<sub>17</sub>NO<sub>4</sub>), 200(C<sub>11</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>), 235(C<sub>12</sub>H<sub>13</sub>NO<sub>4</sub>), 149(C<sub>8</sub>H<sub>7</sub>NO<sub>2</sub>), 99(C<sub>4</sub>H<sub>5</sub>NO<sub>2</sub>). Anal.: (C<sub>19</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub>) Calc:C, 67.85; H, 4.79; N, 8.33. Found C, 67.14; H, 4.69; N, 8.20 %.

- 6. Synthesis of 4-(4-(dimethylamino)phenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one (6):** 4-(4-(dimethylamino)phenyl)-3,4-dihydro-(1,3)oxazino(5,6-h)quinolin-2-one has been synthesized by the cyclocondensation of 4-dimethylaminobenzaldehyde(149mg), 8-quinolinol(145mg) and urea(60mg) under solvent free condition using p-TSA at 150 °C reacted to afford the corresponding products in good yields. White power, Yield: 133mg. mp: above 200°C. (<sup>1</sup>HNMR DMSO<sub>d</sub><sub>6</sub>)δ 8.0(s, 1H, NH), 7.14-8.86 (m, 5H, ArH), 6.47-6.88(m, 4H, ArH), 6.16 (d, 1H, CH), 2.85(s, 3H, CH<sub>3</sub>). MS (m/e): 319 (C<sub>19</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub> m/e 276(C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>), 268(C<sub>16</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>), 200((C<sub>11</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>), 175(C<sub>10</sub>H<sub>9</sub>NO<sub>2</sub>), 149(C<sub>8</sub>H<sub>7</sub>NO<sub>2</sub>), 99(C<sub>4</sub>H<sub>5</sub>NO<sub>2</sub>). Anal.: (C<sub>19</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub>)Calc: C, 81.46; H, 5.37; N, 13.16. Found: C, 81.44; H, 5.29; N, 13.10; %

## VI. BIOLOGICAL ACTIVITY

- 1. Anti-Inflammatory Activity:** By using the described method, compounds (1- 6) anti-inflammatory activity was carried out. Table 3 displays these chemicals' action profile.

**Table 3: Compounds of 3, 4,dihydro-4-phenyl(1,3)oxazino(5,6-h)quinolin-2-one with anti-inflammatory properties.**

No. of Compounds	Difference in Mean	(%)Activity(100mg/Kg)
1	22.01	45
2	24.35	39
3	21.19	32
4	17.73	49
5	23.18	40
6	25.63	37

- 2. Anti-Convulsant Activity:** By using the described method, compounds (1- 6) anti-convulsant activity was carried out. Table 4 displays these chemicals' action profile.

**Table 4: Anti-Convulsant activity of substituted 3, 4-dihydro-4-phenyl-(1,3)oxazino(5,6-h)quinolin-2-one derivatives.  
 (Dose 60mg/Kg)**

Sl. No	Protection (%) After 2 hours
Positive control <i>Carbamazepine</i>	80
<b>1</b>	40
<b>2</b>	0
<b>3</b>	60
<b>4</b>	20
<b>5</b>	0
<b>6</b>	60

**3. Cardiovascular Activity:** The anti-inflammatory activity of compounds (1 – 6) was carried out by the procedure described. The activity profile of these compounds is reported in *Table 5*.

**Table 5: Cardiovascular Activity of substituted 3, 4-dihydro-4-phenyl-(1,3)oxazino(5,6-h)quinolin-2-one derivatives.**

Sl. No.	Resting BP (mmHg)	Change in BP		Change in HR	CO
		Immediate	Delayed		
<b>1</b>	130	-50	-3	-20	↓
<b>2</b>	165	-40	20	-6	↓
<b>3</b>	105	-30	-12	No change	↓
<b>4</b>	115	-20	-52	No change	↓
<b>5</b>	170	-60	60	-8	↓
<b>6</b>	130	-40	-12	-24	↓

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