CHAPTER – 3
PART-I

Synthesis, Characterization and Antimicrobial Activity of New Biquinoline Derivatives from Ylidemalononitriles and Cyclic Enaminones.
Biquinolines are the versatile nitrogen containing heterocyclic compounds. Biquinolines are widely used as the parent compound in drug especially anti-malarial medicines, fungicides, biocides, alkaloids and dyes. Here we like to discuss synthesis of new biquinoline derivatives using ylidenemalononitriles as a versatile intermediate.

3.1.1 Synthetic and Biological Aspect

Various reactions of ylidenemalononitriles and cyclic enamiones have been already discussed in chapter 2 (section 2.2).

The available literature regarding the synthesis and reactivity of biquinoline derivatives has been discussed in chapter 1. The synthesis and reactivity of some 2,3′-biquinoline are given below

O. A. Antonova et al. has synthesized 1'-alkyl-2'-R-1',2'-dihydro-2,3'-biquinolines using organolithium compounds.\(^1\)

\[
\begin{array}{c}
\text{N} \\
\text{Li} \\
\text{R} \\
\text{R} \\
\text{R'} \\
\text{THF} \\
\text{R'}-\text{Li} \\
\end{array}
\]

Where: R=Me, Et; R’= Me, Et, Ph

D. A. Kovalev et. al. has proposed an unusual acylation reaction of 1'-alkyl-1',4'-dihydro-2,3'-biquinolines.\(^2\)

\[
\begin{array}{c}
\text{N} \\
\text{ClCOOEt} \\
\text{N} \\
\text{O} \\
\text{O} \\
\text{R} \\
\end{array}
\]

Where: R= Me, Et

V. V. Trifonov et. al. has proposed novel approach to synthesis 1',4'-dihydro-2,3'-biquinolines.\(^3\)
Where; R= H, Me, Ph

Only a few references are available for the synthesis and biologically active 3,4’-biquinoline derivative. J. Nirmal et. al. has synthesized following 3,4’-biquinoline derivatives.

Where: R= H, CH$_3$, OCH$_3$, Cl
R’= H, CH$_3$, OCH$_3$, Cl, COCH$_3$

As the thiazole is one of the substituent in our parent molecule it is worth here to brief here about the importance of this moiety.

Thiazole are familiar group of heterocyclic compounds possessing a wide variety of biological activities and their utility as medicaments is very much established$^{4-7}$ Thiazole nucleus is also integral part of all the available penicillin’s, which have revolutionized the therapy of bacterial diseases$^{8-13}$. They used as antiviral,
Antimycobacterial and showed antiproliferative\textsuperscript{14}. However, some of its derivatives proved as agent against constipation\textsuperscript{15}, as potent and selective human adenosine A3 receptor antagonists\textsuperscript{16-18}. Some new thiazole derivatives have been found to possess anti-inflammatory and analgesic\textsuperscript{19-21} as potent and selective acetyl CoA carboxylase 2 inhibitors\textsuperscript{22} and have potential as possible treatments of Alzheimer’s\textsuperscript{23} as noncovalent DNA-binding properties related to leinamycin\textsuperscript{24}. Many thiazole derivatives have positive inotropic activity of the novel histamine H2-receptor agonist, anthemion, on the human heart in vitro\textsuperscript{25} as antitumor agents\textsuperscript{26} as potent thrombin inhibitors\textsuperscript{27} against thrombocytopenia\textsuperscript{28}. Moreover, thiazole derivatives are also well known for their biological properties, antifungal activities\textsuperscript{29} and insecticidal activities\textsuperscript{30}. A literature survey\textsuperscript{31-32} reveal that number of thiazole derivatives containing other heterocyclic system have been designed, synthesized and evaluated for their antimicrobial activity involving several strains of bacteria, fungi and viruses\textsuperscript{33-35}.

3.I.2 Present Work

Quinolines and thiazoles with different functional groups exhibit a wide range of applications in the field of pharmaceuticals. Some of the quinoline and thiazole derivatives have been found to be associated with biological activities\textsuperscript{36}. There valid observations contemplated us to synthesize some biquinoline derivatives containing thiazole nucleus which have been synthesized from ylidemaloonitriles and cyclic enamiones containing thiazole moiety.

\[
\begin{align*}
\text{R}_1 = & \text{ H, Me, OMe, Cl,} \\
\text{R}_2 = & \text{ H, OH, Cl}
\end{align*}
\]

3.I.3 Experimental

This part of the chapter explores the synthesis of some new biquinoline compounds. The purity of the synthesized compounds including intermediates was checked by thin layer chromatography (TLC). TLC was runned using TLC aluminum
sheet silica gel 60 F_{254} (Merck) and chromatography was developed using a mixture of toluene:ethylacetate (7:3).


The title compounds were synthesized in following steps:

(i) Synthesis of 4-substituted acetanilide.

(ii) Synthesis of 6-substituted-2-chloro-3-formyl quinoline.

(iii) Synthesis of 6-substituted-2-chloro-3-quinozylidenemalononitriles.

(iv) Synthesis of 2-amino-5-substitutedphenyl thiazole.

(v) Synthesis of enaminone.


(a) Synthesis of 4-substituted acetanilide [I]

Synthesis of these compounds has been reported in the literature.\textsuperscript{37}

Table-2.I.1: Physical data for 4-substituted acetanilide (I a-d).

<table>
<thead>
<tr>
<th>Compd.</th>
<th>R</th>
<th>M.P. (°C)</th>
<th>Mol. Wt. (gm)</th>
<th>% yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>I a</td>
<td>Me</td>
<td>155</td>
<td>149.1</td>
<td>85</td>
</tr>
<tr>
<td>I b</td>
<td>OMe</td>
<td>123</td>
<td>165.1</td>
<td>70</td>
</tr>
<tr>
<td>I c</td>
<td>Cl</td>
<td>175</td>
<td>169.5</td>
<td>80</td>
</tr>
<tr>
<td>I d</td>
<td>Br</td>
<td>165</td>
<td>214.0</td>
<td>70</td>
</tr>
</tbody>
</table>

(b) Synthesis of 6-substituted-2-chloro-3-formyl quinoline [II]\textsuperscript{38}

Dimethylformamide (19.2 ml, 0.250 moles) was charged in a three-necked round-bottomed flask equipped with a thermometer, a drying tube and mechanical stirrer and cooled to 0°C. To it phosphorous oxychloride (64.4ml, 0.70 moles) was added drop wise with stirring at 0-10°C. To the solution, 4-substituted acetanilide (0.10 moles) was added and the mixture was heated under reflux for 6 hours at 75°C.
The reaction mass then cooled to room temperature and poured in crushed ice (300gm) with mechanical stirring. The product isolated was filtered and washed with water till neutral. The solid was crystallized from ethyl acetate to give light yellow compound.

Table-2.I.2: Physical data for compounds (II: a-d)

<table>
<thead>
<tr>
<th>Compd.</th>
<th>R</th>
<th>M.P. (°C)</th>
<th>Mol.Wt. (gm)</th>
<th>% yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>II a</td>
<td>H</td>
<td>145</td>
<td>191.6</td>
<td>70</td>
</tr>
<tr>
<td>II b</td>
<td>Me</td>
<td>125</td>
<td>205.7</td>
<td>73</td>
</tr>
<tr>
<td>II c</td>
<td>OMe</td>
<td>148</td>
<td>221.0</td>
<td>68</td>
</tr>
<tr>
<td>II d</td>
<td>Cl</td>
<td>165</td>
<td>226.0</td>
<td>37</td>
</tr>
</tbody>
</table>

(c) Synthesis of 6-(un)substituted-2-chloro-3-quinolidenemalononitriles (IIIa-d)

![Chemical structure of IIIa-d]

**Synthesis of 2-chloro-3-quinolizidenemalononitrile (III a)**

2-chloro-3-formyl quinoline (1.91gm, 0.01mole), malononitrile (0.70 ml, 0.01mole) and ethanol (10 ml) were charged in R.B. flask equipped with mechanical stirrer and condenser. The reaction mixture was slowly heated with stirring. When the entire compound was dissolved in mixture, 2-3 drops of piperidine was added to mixture and refluxed for 0.5 to 1 hr. After the completion of reaction (checked by TLC), the product was filtered and washed with chilled ethanol. The product was recrystallised with methanol. All the other compounds (III b-d) were synthesized following procedure using the respective substituted quinoline derivatives.
(d) Synthesis of 2-amino-5-(un)substitutedphenyl thiazole (IV a-c)

A mixture of 4-(un)substituted acetophenone (0.1 mole), thiourea (0.2 mole) and iodine (0.1 mole) was heated on a steam bath for 4 hrs. The crude hydro iodide, thus separated was filtered, washed with ether and dried. The product was dissolved in minimum quantity of hot water, filtered while hot and the clear solution was neutralized with a strong solution of ammonia. The solid separated was filtered, washed with water and dried.

\[
\text{H}_2\text{N}-\text{S}-\text{R}_1\text{H}_{\text{[IV]}}
\]

\[R_1 = \text{H, Cl, OH}\]

Table-3.I.3: Physical data for compounds (IV: a-c)

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>(R_1)</th>
<th>m.p. (^{(\degree C)})</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>H</td>
<td>132-133</td>
<td>50.12</td>
</tr>
<tr>
<td>4b</td>
<td>OH</td>
<td>197-199</td>
<td>52.36</td>
</tr>
<tr>
<td>4c</td>
<td>Cl</td>
<td>204-205</td>
<td>50.78</td>
</tr>
</tbody>
</table>

(e) Synthesis of enaminones (Va-c)

\[
\text{\text{O}}\text{-N-H-S}-\text{R}_1\text{H}_{\text{[V]}}
\]

\[R_1 = \text{H, OH, Cl}\]

A mixture of 1,3-cyclohexanedione (0.01 mole) and substituted 2-amino thiazole (0.01 mole) was heated in an oil bath for 1 hr. and cooled to room temperature. The separated solid mass was filtered, washed with ether and dried.
Table-3.I.4: Physical data for compounds (V: a-c)

<table>
<thead>
<tr>
<th>Compd.</th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>M.P. (°C)</th>
<th>Mol.Wt. (gm)</th>
<th>% yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Va</td>
<td>H</td>
<td>212</td>
<td>270.5</td>
<td>85</td>
</tr>
<tr>
<td>Vb</td>
<td>OH</td>
<td>224</td>
<td>286.5</td>
<td>79</td>
</tr>
<tr>
<td>Vc</td>
<td>Cl</td>
<td>196-99</td>
<td>304.5</td>
<td>82</td>
</tr>
</tbody>
</table>


A mixture of enaminone (0.01mole), 2-((2-chloro-6-substitutedquinoline-3-yl)methylene)malononitrile (0.01mole) and ethanol (10 mL) were taken in R.B. flask with mechanical stirring and condenser. Piperidine (2-3 drops) was added as catalyst. The reaction mixture was refluxed with continuous stirring. The reaction was monitored by TLC, after the completion of reaction mixture was cooled to RT and stirred for 10-15 min., the resulting solid mass was filtered, washed with small amount of ethanol and dried. The crude product was purified by treating it in equimolar mixture of chloroform and methanol to obtain the pure solid sample.
3.I.3B Reaction Scheme:

Scheme: I

\[
\text{Scheme I}
\]

\[\text{R} - \text{NH}_2 + \text{Ac}_2\text{O/AcOH} \rightarrow \text{R} - \text{NHCOCH}_3 + \text{DMF/POCl}_3 \rightarrow \text{R} - \text{CHO} \]

Scheme: II

\[
\text{Scheme II}
\]

\[\text{N} + \text{CN} + \text{CN} + \text{Piperidine, EtOH} \rightarrow \text{R} \]

Scheme: III

\[
\text{Scheme III}
\]

\[\text{R} - \text{CN} + \text{R}_1 - \text{NH} \rightarrow \text{EtOH, Piperidine} \rightarrow \text{R} \]

Where: \( R = \text{H, Me, OMe, Cl; } R_1 = \text{H, OH, Cl} \)

3.1.4 Results and Discussion

Scheme-I and Scheme-II outline the synthesis of intermediates used for the preparation of final compounds. Scheme-III outlines the synthesis of new biquinoline derivatives (Bq1-12).

Substituted anilines, acetophenone and malononitrile are commercial products and were used without further purification. All the solvents were distilled before use.
All the melting points are uncorrected and expressed in °C. Elemental analysis (% C, H, N) was carried out by Perkin Elmer 2400 CHN analyzer. IR spectra of all the compounds have been recorded on a Schimadzu FT-IR 8401 spectrophotometer in KBr. The $^1$H-NMR and $^{13}$C-NMR spectra have been recorded on a Bruker AC 400F (400MHz) instrument using TMS as internal standard in DMSO-d$_6$ as a solvent.

The structures of the compounds were confirmed on the basis of elemental analysis and spectral data. As an example, the IR spectra of compound Bq$_5$ ($R_1$=H, $R_2$=H) shows band at 3440 cm$^{-1}$ for asym. N-H stretching, 3340 cm$^{-1}$ for sym. N-H stretching, 3040 cm$^{-1}$ for aromatic C-H stretching, 2205 cm$^{-1}$ for CN stretching, 1660 cm$^{-1}$ for C=O stretching of carbonyl group, 1518&1430 cm$^{-1}$ for C=C stretching of aromatic ring and 710 cm$^{-1}$ for C-Cl stretching. $^1$H-NMR spectra of Bq$_5$ showed multiplet signal at $\delta$ 1.85 -2.30 for three methylene group, two singlet at $\delta$ 5.08 and $\delta$ 6.16 for methine group and amine group respectively and a multiplet due to the aromatic protons around at $\delta$ 7.39-8.40. The $^{13}$C-NMR spectrum of Bq$_5$ was in good agreement with the structure assigned. The peak at $\delta$ peak at 21.24, 27.46 and 36.41 attributed to three methylene carbons, $\delta$ 35.48 is attributed to methine carbon. The peak at 60.42 is assigned to carbon of carbonitrile and the peaks at $\delta$ 113.67-156.05 are attributed to aromatic carbon. The peak at $\delta$ 195.77 is assigned to carbon of carbonyl carbon.

### Table-2.1.5: Physical data for ylideneomalononitrile derivatives [III a-e]

<table>
<thead>
<tr>
<th>Compd.</th>
<th>R</th>
<th>M.P. (°C)</th>
<th>Mol. Wt.</th>
<th>Mol. Formula</th>
<th>Yield %</th>
<th>Elemental Analysis Calculated (Found)</th>
</tr>
</thead>
<tbody>
<tr>
<td>III a</td>
<td>H</td>
<td>113</td>
<td>239</td>
<td>C$_{13}$H$_6$N$_3$Cl</td>
<td>96</td>
<td>65.15 (65.10) 2.52 (2.56) 17.53 (17.50)</td>
</tr>
<tr>
<td>III b</td>
<td>Me</td>
<td>182</td>
<td>253</td>
<td>C$_{14}$H$_8$N$_3$Cl</td>
<td>92</td>
<td>66.28 (66.24) 3.17 (3.20) 16.56 (16.55)</td>
</tr>
<tr>
<td>III c</td>
<td>OMe</td>
<td>172</td>
<td>269</td>
<td>C$_{14}$H$_8$ON$_3$Cl</td>
<td>91</td>
<td>62.35 (62.40) 2.99 (2.95) 15.58 (15.62)</td>
</tr>
<tr>
<td>III d</td>
<td>Cl</td>
<td>210</td>
<td>274</td>
<td>C$_{13}$H$_5$N$_3$Cl$_2$</td>
<td>89</td>
<td>56.96 (56.92) 1.83 (1.80) 15.33 (15.37)</td>
</tr>
</tbody>
</table>
Table 3.1.6: Physical data for biquinoline derivatives [Bq1-12]

<table>
<thead>
<tr>
<th>Compd.</th>
<th>R</th>
<th>R1</th>
<th>M.P. (°C)</th>
<th>Mol. Wt.</th>
<th>Mol. Formula</th>
<th>Yield %</th>
<th>Elemental Analysis Calculated (Found)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bq1</td>
<td>H</td>
<td>Cl</td>
<td>258</td>
<td>545</td>
<td>C28H19Cl2N3OS</td>
<td>85</td>
<td>61.77 (61.73) 3.52 (3.54) 12.86 (12.88)</td>
</tr>
<tr>
<td>Bq2</td>
<td>CH3</td>
<td>Cl</td>
<td>276</td>
<td>559</td>
<td>C29H21Cl2N5O2S</td>
<td>76</td>
<td>62.37 (62.35) 3.78 (3.74) 12.54 (12.50)</td>
</tr>
<tr>
<td>Bq3</td>
<td>OCH3</td>
<td>Cl</td>
<td>275</td>
<td>575</td>
<td>C29H21C2N5O2S</td>
<td>81</td>
<td>60.63 (60.66) 3.68 (3.65) 12.19 (12.15)</td>
</tr>
<tr>
<td>Bq4</td>
<td>Cl</td>
<td>Cl</td>
<td>271</td>
<td>579</td>
<td>C28H18Cl3N3OS</td>
<td>83</td>
<td>58.09 (58.12) 3.13 (3.16) 12.10 (12.14)</td>
</tr>
<tr>
<td>Bq5</td>
<td>H</td>
<td>H</td>
<td>260</td>
<td>510</td>
<td>C28H20ClN3OS</td>
<td>80</td>
<td>65.94 (65.90) 3.95 (3.90) 13.73 (13.79)</td>
</tr>
<tr>
<td>Bq6</td>
<td>CH3</td>
<td>H</td>
<td>262</td>
<td>524</td>
<td>C23H18ClN5OS</td>
<td>79</td>
<td>61.67 (61.64) 4.05 (4.11) 15.63 (15.67)</td>
</tr>
<tr>
<td>Bq7</td>
<td>OCH3</td>
<td>H</td>
<td>280</td>
<td>540</td>
<td>C29H22ClN5O3S</td>
<td>83</td>
<td>62.64 (62.68) 3.99 (3.95) 12.59 (12.54)</td>
</tr>
<tr>
<td>Bq8</td>
<td>Cl</td>
<td>H</td>
<td>279</td>
<td>545</td>
<td>C28H19Cl2N3OS</td>
<td>78</td>
<td>61.77 (61.71) 3.52 (3.56) 12.86 (12.83)</td>
</tr>
<tr>
<td>Bq9</td>
<td>H</td>
<td>OH</td>
<td>271</td>
<td>526</td>
<td>C28H20ClN5O2S</td>
<td>76</td>
<td>63.94 (63.90) 3.83 (3.79) 13.31 (13.34)</td>
</tr>
<tr>
<td>Bq10</td>
<td>CH3</td>
<td>OH</td>
<td>268</td>
<td>540</td>
<td>C29H22ClN5OS</td>
<td>87</td>
<td>66.47 (66.50) 4.23 (4.25) 13.36 (13.40)</td>
</tr>
<tr>
<td>Bq11</td>
<td>OCH3</td>
<td>OH</td>
<td>265</td>
<td>556</td>
<td>C23H18ClN5O2S</td>
<td>79</td>
<td>59.54 (59.60) 3.91 (3.95) 15.10 (15.02)</td>
</tr>
<tr>
<td>Bq12</td>
<td>Cl</td>
<td>OH</td>
<td>282</td>
<td>561</td>
<td>C28H19Cl2N3O2S</td>
<td>80</td>
<td>60.01 (60.06) 3.42 (3.48) 12.50 (12.54)</td>
</tr>
</tbody>
</table>

Spectral Analysis of Ylidenemalononitrile Derivatives

2-((2-chloroquinoline-3-yl)methylene)malanonitrile (III a)

IR (KBR): 3040(C-H str. of =CH-), 2240(-CN str.), 1570&1480(C=C str. of aromatic ring), 745(C-Cl str.)

$^1$H NMR (DMSO-d$_6$): δ 7.56 -8.37 (s, 1H, -CH=CH- and m, 5H, Ar-H).

$^{13}$C-NMR (DMSO-d$_6$): 88.45, 105.35, 111.48, 113.80, 123.32, 127.59, 130.55, 137.38, 144.12, 145.24, 155.11, 159.07
IR SPECTRA

\[ \text{H}_3\text{C} - \text{N} - \text{Cl} - \text{CN} - \text{CN} \]

\[ \text{DMSO} \]

moisture of DMSO

1H-NMR SPECTRA
2-((2-chloro-6-methylquinoline-3-yl)methylene)malanonitrile (III b)

**IR (KBR):** 3048(C-H str. of =CH-), 2889(C-H str. of \( \text{CH}_3 \)), 2245(-CN str.), 1575&1485(C=C str. of aromatic ring), 737(C-Cl str.)

**\(^1\)H NMR (DMSO-d\(_6\)):** \( \delta \) 2.54(s, 3H, \( \text{CH}_3 \)), 7.82 -8.95(s, 1H, -\( \text{CH}=C- \) and m, 4H, Ar-H).

**\(^{13}\)C-NMR (DMSO-d\(_6\)):** 21.45, 88.14, 112.60, 113.67, 124.30, 128.08, 128.33, 136.34, 139.12, 140.04, 147.01, 147.36, 157.62

2-((2-chloro-6-methylquinoline-3-yl)methylene)malanonitrile (III c)

**IR (KBR):** 3038(C-H str. of =CH-), 2235(-CN str.), 1560&1465(C=C str. of aromatic ring), 2800(aromatic methoxy C-H str.), 1225&1038(C-O-C asym & sym str. of-O\( \text{CH}_3 \)), 747(C-Cl str.)

**\(^1\)H NMR (DMSO-d\(_6\)):** \( \delta \) 3.99 (s, 3H, \( \text{OCH}_3 \)), 7.85 -8.99 (s, 1H, -\( \text{CH}=C- \) and m, 4H, Ar-H).

**\(^{13}\)C-NMR (DMSO-d\(_6\)):** 55.51, 88.10, 112.63, 113.70, 124.14, 128.41, 128.53, 136.54, 139.12, 140.40, 147.08, 148.00, 1567.72

2-((2,6-dichloroquinoline-3-yl)methylene)malanonitrile (III d)

**IR (KBR):** 3046(C-H str. of =CH-), 2250(-CN str.), 1560&1465(C=C str. of aromatic ring), 732(C-Cl str.)

**\(^1\)H NMR (DMSO-d\(_6\)):** \( \delta \) 7.80 -8.91 (s, 1H, -\( \text{CH}=C- \) and m, 4H, Ar-H).

**\(^{13}\)C-NMR (DMSO-d\(_6\)):** 88.24, 112.25, 113.32, 124.14, 128.12, 128.32, 136.36, 139.65, 140.54, 147.47, 148.78, 1567.89
$\text{13C-NMR SPECTRA}$
Spectral Analysis of Biquinoline derivatives

2'-Amino-2-chloro-1'-(4-(4-chlorophenyl)thiazol-2-yl)-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carbonitrile (Bq1).

IR (KBR): 3445(asym.N-H str.), 3337(sym.N-H str.), 3010(aromatic C-H str.), 2215(-CN str.), 1685(C=O str.), 1512&1434(C=C str. of aromatic ring), 710(C-Cl str.).

$^1$H NMR (DMSO-d$_6$): $\delta$ 1.81-2.36 (m, 6H, 3xCH$_2$), 5.10 (s, 1H, -CH-), 6.14 (s, 2H, NH$_2$), 7.1 7-8.10 (m, 10H, Ar-H).

$^{13}$C-NMR (DMSO-d$_6$): $\delta$ 21.20, 27.21, 36.23, 35.18, 60.36, 114.65, 117.54, 117.47, 120.78, 125.89, 126.93, 127.32, 127.21, 128.17, 133.18, 137.49, 137.41, 137.50, 144.53, 149.74, 150.85, 151.96, 152.63, 153.52, 156.30, 195.65.

2'-Amino-2-chloro-1'-(4-(4-chlorophenyl)thiazol-2-yl)-6-methyl-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carbonitrile (Bq2).

IR (KBR): 3448(asym.N-H str.), 3340(sym.N-H str.), 3015(aromatic C-H str.), 2219(-CN str.), 1670(C=O str.), 1527&1423(C=C str. of aromatic ring), 710(C-Cl str.).

$^1$H NMR (DMSO-d$_6$): $\delta$ 1.82-2.31 (m, 6H, 3xCH$_2$), 2.36 (s, 3H, CH$_3$), 5.16(s, 1H, -CH-), 6.13 (s, 2H, NH$_2$), 6.85-8.36 (m, 9H, Ar-H).

$^{13}$C-NMR (DMSO-d$_6$): $\delta$ 21.98, 27.32, 36.82, 21.51, 35.90, 60.21, 114.14, 116.63, 116.92, 120.12, 125.14, 126.56, 127.12, 127.81, 128.01, 133.18, 137.49, 138.95, 142.50, 149.36, 150.85, 151.25, 152.12, 152.87, 153.90, 156.12, 195.45.
2'-Amino-2-chloro-1'-(4-(4-chlorophenyl)thiazol-2-yl)-6-methoxy-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carbonitrile (Bq₃).

**IR (KBR):**
- 3452 (asym. N-H str.), 3320 (sym. N-H str.),
- 3012 (aromatic C-H str.),
- 2228 (-CN str.),
- 1685 (C=O str.),
- 1520 & 1432 (C=C str. of aromatic ring),
- 1238 & 1040 (C-O-C asym & sym str. of OCH₃),
- 710 (C-Cl str.).

**¹H NMR (DMSO-d₆):**
- δ 1.79-2.36 (m, 6H, 3xCH₂), 3.82 (s, 3H, OCH₃), 5.36 (s, 1H, -CH-),
- 6.28 (s, 2H, NH₂), 6.85-8.29 (m, 9H, Ar-H).

**¹³C-NMR (DMSO-d₆):**
- δ 21.74, 27.45, 36.58, 21.72, 35.12, 60.23, 114.36,
- 116.54, 116.74, 121.12, 123.98, 125.87, 126.74,
- 127.41, 129.12, 132.42, 13645, 136.32, 138.99,
- 143.16, 148.82, 150.93, 151.00, 151.45, 154.74,
- 156.10, 195.65.

2'-Amino-2,6-chloro-1'-(4-(4-chlorophenyl)thiazol-2-yl)-5' -oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carbonitrile (Bq₄).

**IR (KBR):**
- 3447 (asym. N-H str.), 3318 (sym. N-H str.), 3010 (aromatic C-H str.),
- 2220 (-CN str.),
- 1665 (C=O str.),
- 1512 & 1435 (C=C str. of aromatic ring),
- 705 (C-Cl str.).

**¹H NMR (DMSO-d₆):**
- δ 1.79-2.30 (m, 6H, 3xCH₂), 5.52 (s, 1H, -CH-),
- 6.85 (s, 2H, NH₂), 7.07-8.81 (m, 9H, Ar-H).

**¹³C-NMR (DMSO-d₆):**
- δ 21.78, 26.23, 36.89, 35.36, 60.96, 114.65, 116.63,
- 117.41, 121.69, 122.98, 124.87, 126.74, 127.41,
- 129.12, 132.42, 136.45, 136.32, 138.99,
- 143.16, 148.82, 150.93, 151.00, 151.45, 154.74,
- 156.10, 195.54.
IR SPECTRA

\[ \text{NH}_2\text{N} \]
\[ \text{N} \quad \text{S} \quad \text{O} \quad \text{CN} \quad \text{N} \quad \text{Cl} \]

\[ \text{moisture of DMSO} \]  
\[ \text{DMSO} \]

\[ \text{1H-NMR SPECTRA} \]

\[ \text{14} \quad \text{13} \quad \text{12} \quad \text{11} \quad \text{10} \quad \text{9} \quad \text{8} \quad \text{7} \quad \text{6} \quad \text{5} \quad \text{4} \quad \text{3} \quad \text{2} \quad \text{1 ppm} \]
2’-Amino-2-chloro-1’-(4-phenylthiazol-2-yl)-5’-oxo-1’,4’,5’,6’,7’,8’-hexahydro-3,4’-biquinoline-3’-carbonitrile (Bq₅).

**IR** : 3440(asym.N-H str.), 3340(sym.N-H str.),
(KBR) 3040(aromatic C-H str.), 2205(-CN str.),
1660(C=O str.), 1518&1430(C=C str. of aromatic ring), 710(C-Cl str.).

**¹H NMR** : δ 1.85-2.30(m, 6H, 3xCH₂), 5.08(s, 1H, -CH-),
(DMSO-d₆) 6.16(s, 2H, NH₂), 7.39-8.40(m, 11H, Ar-H).

**¹³C-NMR** : δ 21.24, 27.46, 35.48, 36.41, 60.42, 113.67, 118.95,
(DMSO-d₆) 121.01, 127.00, 127.80, 127.97, 128.53, 129.13,
130.33, 131.55, 132.96, 134.06, 136.86, 137.81,
138.92, 139.09, 146.13, 150.03, 152.03, 152.63,
153.64, 156.05, 195.77.

2’-Amino-2-chloro-1’-(4-phenylthiazol-2-yl)-6-methyl-5’-oxo-1’,4’,5’,6’,7’,8’-
hexahydro-3,4’-biquinoline-3’-carbonitrile (Bq₆).

**IR** : 3445(asym.N-H str.), 3348(sym.N-H str.),
(KBR) 3022(aromatic C-H str.), 2220(-CN str.),
1655(C=O str.), 1530&1427(C=C str. of aromatic ring), 710(C-Cl str.).

**¹H NMR** : δ 1.83-2.33(m, 6H, 3xCH₂), 2.35(s, 3H, -CH₃),
(DMSO-d₆) 5.18(s, 1H, -CH-), 6.05(s, 2H, NH₂), 7.32-8.38(m, 10H, Ar-H).

**¹³C-NMR** : δ 20.24, 26.56, 35.48, 21.45, 36.36, 60.38, 114.77,
(DMSO-d₆) 118.05, 121.21, 126.99, 127.70, 128.97, 129.53,
129.93, 131.33, 131.55, 132.06, 134.46, 136.96,
138.81, 139.92, 140.09, 145.03, 149.13, 151.64,
151.93, 152.44, 156.55, 195.07.
$\text{13C-NMR SPECTRA}$
2'-Amino-2-chloro-1'-(4-phenylthiazol-2-yl)-6-methoxy-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carbonitrile (Bq₇).

**IR (KBR)**
- 3461 (asym. N-H str.), 3338 (sym. N-H str.),
- 3018 (aromatic C-H str.), 2212 (-CN str.),
- 1645 (C=O str.), 1529 & 1432 (C=C str. of aromatic ring), 1241 & 1020 (C-O-C asym & sym str. of OCH₃), 719 (C-Cl str.).

**¹H NMR (DMSO-d₆)**
- δ 1.81-2.36 (m, 6H, 3xCH₂), 3.83 (s, 3H, OCH₃),
- 5.28 (s, 1H, -CH-), 6.19 (s, 2H, NH₂), 7.31-8.30 (m, 10H, Ar-H).

**¹³C-NMR (DMSO-d₆)**
- δ 19.94, 26.40, 34.18, 36.36, 55.42, 60.11, 113.06,
- 117.65, 122.78, 125.01, 126.50, 127.17, 128.03,
- 129.00, 130.63, 131.95, 133.16, 135.06, 135.96,
- 137.18, 138.82, 139.84, 143.90, 146.67, 150.94,
- 151.28, 151.90, 155.01, 195.58.

2'-Amino-2,6-chloro-1'-(4-phenylthiazol-2-yl)-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carbonitrile (Bq₈).

**IR (KBR)**
- 3028 (aromatic C-H str.), 2218 (-CN str.),
- 1662 (C=O str.), 1520 & 1435 (C=C str. of aromatic ring), 714 (C-Cl str.).

**¹H NMR (DMSO-d₆)**
- δ 1.77-2.35 (m, 6H, 3xCH₂), 5.19 (s, 1H, -CH-),
- 6.79 (s, 2H, NH₂), 7.35-8.42 (m, 10H, Ar-H).

**¹³C-NMR (DMSO-d₆)**
- δ 19.25, 26.36, 34.10, 36.10, 60.25, 112.98, 118.00,
- 122.18, 124.41, 126.38, 127.87, 128.10, 129.29,
- 130.32, 132.01, 133.47, 135.45, 135.78, 137.20,
- 138.49, 139.78, 143.45, 146.18, 150.54, 151.08,
- 151.56, 155.79, 194.99.
IR SPECTRA

\[ \text{H}_3\text{C} - \text{N} - \text{C} = \text{N} - \text{Cl} - \text{CN} - \text{NH}_2 - \text{N} - \text{S} - \text{O} - \text{H} \]

\[ \text{HO} \]

\[ \text{DMSO} \]

moisture of DMSO

\[ \text{1H-NMR SPECTRA} \]
2’-Amino-2-chloro-1’-(4-(4-hydroxyphenyl)thiazol-2-yl)-5’-oxo-1’,4’,5’,6’,7’,8’-hexahydro-3,4’-biquinoline-3’-carbonitrile (Bq9).

**IR (KBR)**: 3459(asym.N-H str.), 3323(sym.N-H str.), 3037(aromatic C-H str.), 2223(-CN str.), 1668(C=O str.), 1510&1432 (C=C str. of aromatic ring), 713(C-Cl str.).

**$^1$H NMR (DMSO-d$_6$)**: δ 1.82-2.39(m, 6H, 3xCH$_2$), 5.16(s, 1H, -CH-), 6.07(s, 2H, NH$_2$), 7.07-8.12(m, 10H, Ar-H) 9.69(s, 1H, OH).

**$^{13}$C-NMR (DMSO-d$_6$)**: δ 21.21, 27.03, 36.48, 35.19, 60.25, 114.09, 117.08, 117.44, 120.79, 125.58, 125.31, 125.31, 127.45, 127.45, 128.13, 133.36, 137.19, 137.38, 137.79, 144.90, 149.00, 150.98, 151.81, 152.09, 153.78, 156.42, 156.62, 195.56.

2’-Amino-2-chloro-1’-(4-(4-hydroxyphenyl)thiazol-2-yl)-6-methyl-5’-oxo-1’,4’,5’,6’,7’,8’-hexahydro-3,4’-biquinoline-3’-carbonitrile (Bq10).

**IR (KBR)**: 3445(asym.N-H str.), 3345(sym.N-H str.), 3050(aromatic C-H str.), 2202(-CN str.), 1662(C=O str.), 1505&1430(C=C str. of aromatic ring), 710(C-Cl str.).

**$^1$H NMR (DMSO-d$_6$)**: δ 1.85-2.29(m, 6H, 3xCH$_2$), 2.33(s, 3H, -CH$_3$), 5.06(s, 1H, -CH-), 6.10(s, 2H, NH$_2$), 6.87-8.22(m, 9H, Ar-H) 9.72(s, 1H, OH).

**$^{13}$C-NMR (DMSO-d$_6$)**: δ 21.26, 27.43, 36.42, 21.59, 35.19, 60.81, 114.15, 116.01, 116.14, 120.69, 125.31, 126.95, 127.61, 127.89, 128.10, 133.06, 137.10, 137.38, 137.79, 144.96, 149.03, 151.48, 152.81, 152.89, 153.58, 156.62, 195.68.
$^{13}$C-NMR SPECTRA
2'-Amino-2-chloro-1'-(4-(4-hydroxyphenyl)thiazol-2-yl)-6-methoxy-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carbonitrile (Bq11).

**IR (KBR):** 3454 (asym. N-H str.), 3339 (sym. N-H str.), 3032 (aromatic C-H str.), 2218 (-CN str.), 1658 (C=O str.), 1509 & 1436 (C=C str. of aromatic ring), 1230 & 1032 (C-O-C asym & sym str. of OCH₃), 709 (C-Cl str.).

**¹H NMR (DMSO-d₆):** δ 1.80-2.33 (m, 6H, 3xCH₂), 3.80 (s, 3H, OCH₃), 5.26 (s, 1H, -CH-), 6.20 (s, 2H, NH₂), 6.85-8.29 (m, 9H, Ar-H) 9.70 (s, 1H, OH).

**¹³C-NMR (DMSO-d₆):** δ  21.20, 27.40, 36.40, 21.60, 35.20, 60.80, 114.10, 116.00, 116.10, 121.70, 123.30, 125.95, 126.86, 127.19, 129.18, 132.66, 136.00, 136.48, 138.99, 143.06, 148.33, 150.42, 151.44, 151.99, 154.08, 156.28, 195.60.

2'-Amino-2,6-chloro-1'-(4-(4-hydroxyphenyl)thiazol-2-yl)-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carbonitrile (Bq12).

**IR (KBR):** 3461 (asym. N-H str.), 3329 (sym. N-H str.), 3028 (aromatic C-H str.), 2214 (-CN str.), 1666 (C=O str.), 1513 & 1429 (C=C str. of aromatic ring), 712 (C-Cl str.).

**¹H NMR (DMSO-d₆):** δ 1.79-2.32 (m, 6H, 3xCH₂), 5.28 (s, 1H, -CH-), 6.19 (s, 2H, NH₂), 7.10-8.44 (m, 9H, Ar-H) 9.65 (s, 1H, OH).

**¹³C-NMR (DMSO-d₆):** δ 21.18, 26.98, 36.35, 35.28, 60.82, 114.87, 116.15, 117.25, 121.45, 122.47, 124.05, 126.80, 127.20, 129.78, 131.56, 136.08, 137.52, 138.01, 143.89, 146.33, 149.12, 150.42, 152.79, 154.68, 154.98, 195.96.
3.1.4B Antimicrobial activity

The methods used for antibacterial and antifungal activity are discussed in Chapter-2, 2.5B.

<table>
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<tr>
<th>Compd.</th>
<th>Inhibition zone (in mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>E. coli</em></td>
</tr>
<tr>
<td><strong>Bq1</strong></td>
<td>18</td>
</tr>
<tr>
<td><strong>Bq2</strong></td>
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<tr>
<td><strong>Bq3</strong></td>
<td>22</td>
</tr>
<tr>
<td><strong>Bq4</strong></td>
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</tr>
<tr>
<td><strong>Bq5</strong></td>
<td>16</td>
</tr>
<tr>
<td><strong>Bq6</strong></td>
<td>20</td>
</tr>
<tr>
<td><strong>Bq7</strong></td>
<td>25</td>
</tr>
<tr>
<td><strong>Bq8</strong></td>
<td>22</td>
</tr>
<tr>
<td><strong>Bq9</strong></td>
<td>20</td>
</tr>
<tr>
<td><strong>Bq10</strong></td>
<td>21</td>
</tr>
<tr>
<td><strong>Bq11</strong></td>
<td>22</td>
</tr>
<tr>
<td><strong>Bq12</strong></td>
<td>24</td>
</tr>
<tr>
<td><strong>Ampicillin</strong></td>
<td>28</td>
</tr>
<tr>
<td><strong>Ciprofloxacin</strong></td>
<td>35</td>
</tr>
<tr>
<td><strong>Griseofulvin</strong></td>
<td>---</td>
</tr>
</tbody>
</table>
Results of antimicrobial activity

All the synthesized compounds $\text{Bq}_{1-12}$ were tested against microorganism species at 1000 ppm concentration.

The observed results of antibacterial screening reported in Table, indicate that compounds $\text{Bq}_3$, $\text{Bq}_4$, $\text{Bq}_7$, $\text{Bq}_8$, $\text{Bq}_{11}$ and $\text{Bq}_{12}$ having the methoxy and halo group on quinoline nucleus show good activity against the bacterial species used.

From the antifungal assay it has been also observed that compounds having methoxy substituents on quinoline ring show the good activity against $F.\text{oxysporum}$, $A.\text{niger}$ and $R.\text{ oryzae}$. Rest of the compounds show significant activity but it could not reach the effectiveness of the conventional fungicidal Griseofulvin.
Figure 3.I.1: Antibacterial Chart
Figure 3.I.1: Antifungal Chart
REFERENCES


CHAPTER – 3
PART-II

Synthesis, Characterization and Antimicrobial Activity of Some New Biquinoline Derivatives from Ethyl Arylidene cyanocetoacetates and Cyclic enaminoones
Biquinoline derivatives having carboxylate group is also biologically important class of nitrogen containing heterocyclic compounds. Ethylarylidenecyanoacetates are the important intermediates to synthesize the biquinoline derivatives having carboxylate group. So, it is worth to give brief introduction about Ethylarylidenecyanoacetates.

3.II.1 Introduction

The ethylarylidenecyanoacetates are the versatile intermediates in organic chemistry to synthesize new biologically active compounds. The Knoevenagel condensation between active methylene group (ethyl cyanoacetate) and carbonyl compounds results the condensation product ethyl α-cyano-β-acrylates. The characteristic group present in the simple α,β-unsaturated system of acrylate is -COOCH₂CH₃.

Where R=R=' H, alkyl, aryl.

3.II.2 Synthetic and biological aspect

Knoevenagel condensation between ethyl cyanoacetate and various carbonyl compounds results into various ethylarylidenecyanoacetates.

A straightforward method for the synthesis of ethylarylidenecyanoacetates through proline-catalyzed Knoevenagel condensation has been reported by G. Cardillo and coworkers.¹

The efficient Knoevenagel condensation between ethyl cyanoacetate and various aromatic aldehydes containing electron donating groups such as methyl,
methoxy and hydroxy under microwave irradiation conditions has been reported by S. Kim and coworkers.\(^2\)

\[
\begin{array}{c}
\text{CHO} \\
\text{R} \\
\end{array} + \begin{array}{c}
\text{COOC}_2\text{H}_5 \\
\text{CN} \\
\end{array} \xrightarrow{\text{MW}} \begin{array}{c}
\text{CN} \\
\text{R} \\
\end{array}
\]

R= Me, OH, OCH\(_3\)

M. Gopalakrishnan et al have reported the synthesis of various ethylarylidenecyanoacetates by activated fly ash as catalyst\(^3\), Y. Hu and coworkers have reported this reaction by using ionic liquid ethyl ammonium nitrate (EAN) as catalyst\(^4\), W. Zuo and coworkers have reported condensation using ReBr(CO)\(_5\) as catalyst\(^5\), S. Wang et al have reported this condensation in the presence of CTMAB (cetyltrimethyl ammonium bromide) in water.\(^6\) Other reported methods have described in the literature.\(^7\)-\(^12\)

F. F. Abdel-Latif and R. M. Shaker have reported various pyran derivatives by using ethylarylidenecyanoacetates as intermediates.\(^13\)

The activity of parent moiety quinoline and thiazole is already discussed in part I of this chapter. Some author has reported the synthesis of biquinoline and the studies of their organometallic compounds which are given below.
### Structure of biquinoline derivatives

<table>
<thead>
<tr>
<th>Structure</th>
<th>Ref. No.</th>
</tr>
</thead>
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</tr>
<tr>
<td><img src="image15.png" alt="Structure 15" /></td>
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</tr>
<tr>
<td><img src="image16.png" alt="Structure 16" /></td>
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</tr>
<tr>
<td><img src="image17.png" alt="Structure 17" /></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>X</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>H, NO₂</td>
<td>H, Me</td>
</tr>
<tr>
<td>Me, Ph</td>
<td>Me, Et</td>
</tr>
<tr>
<td>Me, Ph</td>
<td>Me, Ph</td>
</tr>
</tbody>
</table>

### 3.II.3 Present Work

Quinoline represents one of the important classes of compounds having a broad spectrum of biological activities. Led by these considerations with an attempt to getting better therapeutic agents, the preparation of ethyl 2'-amino-2-chloro-1'-(4-(4-substitutedphenyl)thiazol-2-yl)-6-substituted-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carboxylate have been undertaken by the condensation of (E)-ethyl 2-cyano-3-(6-substitutedquinoline-3-yl)acrylate with various cyclic enaminone.
3.II.4 Experimental

This part of the chapter explores the synthesis of the synthesized compounds. The purity of the synthesized compounds including intermediates was checked by thin layer chromatography (TLC). TLC was run using TLC aluminum sheet silica gel 60 F_{254} (Merck) and chromatography was developed using a mixture of toluene:ethylacetate (7:3).


The title compounds were synthesized in following steps:

(i) Synthesis of 6-substituted-2-chloro-3-formyl quinoline.

(ii) Synthesis of (E)-ethyl 3-(2-chloro-6-substitutedquinolin-3-yl)-2-cyanoacrylate.

(iii) Synthesis of 2-amino-5-substitutedphenyl thiazole.

(iv) Synthesis of enaminone.


(i) Synthesis of substituted 2-chloro-3-formyl quinoline [I].

Synthesis and Physical data of these compounds are reported in Chapter-3; Part-I, 3.I.3 A.
(ii) Synthesis of (E)-ethyl 3-(2-chloro-6-substitutedquinolin-3-yl)-2-cyanoacrylate (II a-d).

![Diagram of II]

2-chloro-3-formyl quinoline (1.91gm, 0.01mole), ethyl cyanoacetate (1.10 ml, 0.01mole) and ethanol (10 ml) were charged in R.B. flask equipped with mechanical stirrer and condenser. The reaction mixture was slowly heated with stirring. When the entire compound dissolved in mixture, 2-3 drops of piperidine was added to mixture and refluxed for 2 to 3 hr. After the completion of reaction (checked by TLC), the product was filtered and washed with chilled ethanol. The product was crystallized with methanol. All the other compounds (II b-d) were synthesized by following procedure using the respective substituted quinoline derivatives.

(iii) Synthesis of 2-amino-5-substitutedphenyl thiazole.

Synthesis and Physical data of these compounds are reported in Chapter-3; Part-I, 3.I.3 A.

(iv) Synthesis of enamiones.

Synthesis and Physical data of these compounds are reported in Chapter-3; Part-I, 3.I.3 A.


![Diagram of R= H, Me, OMe, Cl, R2=H, OH, Cl]
A mixture of enaminone (0.01 mole), (E)-ethyl 3-(2-chloro-6-substitutedquinolin-3-yl)-2-cyanoacrylate (0.01 mole) and ethanol (10 mL) were taken in R.B. flask with mechanical stirring and condenser. Piperidine (2-3 drops) was added as catalyst. The reaction mixture was refluxed with continuous stirring. The reaction was monitored by TLC, after the completion of reaction mixture was cooled to RT and stirred for 10-15 min., the resulting solid mass was filtered, washed with small amount of ethanol and dried. The crude product was purified by treating it in equimolar mixture of chloroform and methanol to obtain the pure solid sample.

3.II.4B Reaction Scheme

Scheme: I

Scheme: II

Scheme: III

Where: R=H, CH₃, OCH₃, Cl; R₁=H, OH, Cl
3.II.5 Results and Discussion

Scheme-I and Scheme-II outline the synthesis of intermediates used for the preparation of final compounds. Scheme-III outlines the synthesis of new biquinoline derivatives (Ebq1-12).

Substituted anilines, acetophenone and ethyl cyanoacetate commercial products and were used without further purification. All the solvents were distilled before use. All the melting points are uncorrected and expressed in °C. Elemental analysis (% C, H, N) was carried out by Perkin Elmer 2400 CHN analyzer. IR spectra of all the compounds have been recorded on a Schimadzu FT-IR 8401 spectrophotometer in KBr. The $^1$H-NMR and $^{13}$C-NMR spectra have been recorded on a Bruker AC 400F (400MHz) instrument using TMS as internal standard in DMSO-d$_6$ as a solvent.

The structures of the compounds were confirmed on the basis of elemental analysis and spectral data. As an example, the IR spectra of compound Ebq8 ($R_1=Cl$ $R_2=H$) shows band at 3445 cm$^{-1}$ for asym. N-H stretching, 3345 cm$^{-1}$ for sym. N-H stretching, 3010 cm$^{-1}$ for aromatic C-H stretching, 1660 cm$^{-1}$ for C=O stretching of carbonyl group, 1558&1478 cm$^{-1}$ for C=C stretching of aromatic ring and 745 cm$^{-1}$ for C-Cl stretching. $^1$H-NMR spectra of Ebq8 showed signal at $\delta$1.01 for methyl group, a multiplet signal at $\delta$ 1.71 -2.25 for three methyl ene group, signal at 3.92 for OCH$_2$ group, one singlet at $\delta$ 5.30 and $\delta$ 8.45 for methine group and amine group respectively and a multiplet due to the aromatic protons around at $\delta$ 7.29-7.60. The $^{13}$C-NMR spectrum of Ebq8 was in good agreement with the structure assigned. The peak at $\delta$ 14.74 attributed to one methyl group, peak at 21.19, 27.46 and 36.58 attributed to three methylene carbons, $\delta$ 35.82 is attributed to methine carbon. The peak at 59.24 is assigned to carbon of carboxylate and the peaks at $\delta$ 113.67-156.98 are attributed to aromatic carbon. The peak at $\delta$ 168.99 and 195.77 are assigned to carbon of carbonyl carbon.
3.II.5A Characterization:

Table-3.II.1: Physical data for ethylarylidenecyanoacetates derivatives [II a-d]

<table>
<thead>
<tr>
<th>Compd.</th>
<th>R</th>
<th>R1</th>
<th>M.P. (°C)</th>
<th>Mol. Wt.</th>
<th>Mol. Formula</th>
<th>Yield %</th>
<th>Elemental Analysis Calculated (Found)</th>
</tr>
</thead>
<tbody>
<tr>
<td>II a</td>
<td>H</td>
<td></td>
<td>91</td>
<td>286</td>
<td>C₁₂H₁₇N₂O₂Cl</td>
<td>94</td>
<td>62.83 (62.87) 3.86 (3.83) 9.77 (9.74)</td>
</tr>
<tr>
<td>II b</td>
<td>Me</td>
<td></td>
<td>105</td>
<td>300</td>
<td>C₁₀H₁₆N₂O₂Cl</td>
<td>91</td>
<td>63.90 (63.95) 4.35 (4.31) 9.31 (9.28)</td>
</tr>
<tr>
<td>II c</td>
<td>OMe</td>
<td></td>
<td>154</td>
<td>316</td>
<td>C₁₀H₁₆N₂O₂</td>
<td>85</td>
<td>60.67 (60.65) 4.13 (4.10) 8.84 (8.80)</td>
</tr>
<tr>
<td>II d</td>
<td>Cl</td>
<td></td>
<td>119</td>
<td>321</td>
<td>C₁₅H₁₀N₂O₂Cl₂</td>
<td>80</td>
<td>56.09 (56.12) 3.13 (3.10) 8.72 (8.76)</td>
</tr>
</tbody>
</table>

Table-3.II.2: Physical data for biquinoline derivatives [Ebq₁-₁₂]

<table>
<thead>
<tr>
<th>Compd.</th>
<th>R</th>
<th>R₁</th>
<th>M.P. (°C)</th>
<th>Mol. Wt.</th>
<th>Mol. Formula</th>
<th>Yield %</th>
<th>Elemental Analysis Calculated (Found)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ebq₁</td>
<td>H</td>
<td>Cl</td>
<td>195-196</td>
<td>533</td>
<td>C₂₈H₂₂Cl₂N₄O₄S</td>
<td>87</td>
<td>63.04 (63.09) 4.16 (4.12) 10.50 (10.55)</td>
</tr>
<tr>
<td>Ebq₂</td>
<td>Me</td>
<td>Cl</td>
<td>208-209</td>
<td>547</td>
<td>C₂₉H₂₄Cl₂N₄O₂</td>
<td>81</td>
<td>63.62 (63.65) 4.42 (4.40) 10.23 (10.27)</td>
</tr>
<tr>
<td>Ebq₃</td>
<td>OMe</td>
<td>Cl</td>
<td>225-226</td>
<td>563</td>
<td>C₂₀H₂₄Cl₂N₄O₂</td>
<td>79</td>
<td>61.81 (61.83) 4.29 (4.32) 9.94 (9.98)</td>
</tr>
<tr>
<td>Ebq₄</td>
<td>Cl</td>
<td>Cl</td>
<td>198-199</td>
<td>568</td>
<td>C₂₈H₂₁Cl₃N₄O₄S</td>
<td>75</td>
<td>59.22 (59.25) 3.73 (3.76) 9.87 (9.90)</td>
</tr>
<tr>
<td>Ebq₅</td>
<td>H</td>
<td>H</td>
<td>245-246</td>
<td>499</td>
<td>C₂₈H₂₃Cl₂N₄O₄S</td>
<td>70</td>
<td>67.39 (67.35) 4.65 (4.61) 11.23 (11.20)</td>
</tr>
<tr>
<td>Ebq₆</td>
<td>Me</td>
<td>H</td>
<td>169-170</td>
<td>513</td>
<td>C₂₉H₂₃Cl₂N₄O₂</td>
<td>89</td>
<td>67.89 (67.85) 4.91 (4.87) 10.92 (10.90)</td>
</tr>
<tr>
<td>Ebq₇</td>
<td>OMe</td>
<td>H</td>
<td>221-222</td>
<td>529</td>
<td>C₂₀H₂₅Cl₂N₄O₂S</td>
<td>83</td>
<td>65.84 (65.87) 4.76 (4.80) 10.59 (10.55)</td>
</tr>
<tr>
<td>Ebq₈</td>
<td>Cl</td>
<td>H</td>
<td>232-233</td>
<td>533</td>
<td>C₂₉H₂₂Cl₂N₄O₄S</td>
<td>76</td>
<td>63.04 (63.10) 4.16 (4.13) 10.50 (10.52)</td>
</tr>
<tr>
<td>Ebq₉</td>
<td>H</td>
<td>OH</td>
<td>198-199</td>
<td>515</td>
<td>C₂₈H₂₃Cl₂N₄O₂S</td>
<td>73</td>
<td>65.30 (65.35) 4.50 (4.54) 10.88 (10.92)</td>
</tr>
<tr>
<td>Ebq₁₀</td>
<td>Me</td>
<td>OH</td>
<td>236-237</td>
<td>529</td>
<td>C₂₀H₂₅Cl₂N₄O₂S</td>
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<td>65.84 (65.87) 4.74 (4.71) 10.59 (10.63)</td>
</tr>
<tr>
<td>Ebq₁₁</td>
<td>OMe</td>
<td>OH</td>
<td>244-245</td>
<td>545</td>
<td>C₂₀H₂₅Cl₂N₄O₃S</td>
<td>81</td>
<td>63.90 (63.93) 4.62 (4.65) 10.28 (10.25)</td>
</tr>
<tr>
<td>Ebq₁₂</td>
<td>Cl</td>
<td>OH</td>
<td>256-257</td>
<td>549</td>
<td>C₂₀H₂₂Cl₂N₄O₂S</td>
<td>79</td>
<td>61.21 (61.19) 4.04 (4.00) 10.20 (10.24)</td>
</tr>
</tbody>
</table>
IR SPECTRA

\[
\begin{align*}
\text{MeO} & \quad \text{COOEt} \\
\text{Cl} & \quad \text{CN}
\end{align*}
\]

\text{\textbf{\textsuperscript{1}H-NMR SPECTRA}}

\[
\text{\textbf{\textsuperscript{1}H-NMR SPECTRA}}
\]
Spectral Analysis of ethylarylidenecyanoacetates Derivatives

(E)-ethyl 3-(2-chloro-quinolin-3-yl)-2-cyanoacrylate. (III a)

IR: 3042(C-H str. of =CH-), 2245(C≡N str.), 1720(C=O str. of aromatic ester), 1575 & 1484(C=C str. of aromatic ring), 750(C-Cl str.)

\( ^1H \text{ NMR} \): \( \delta 1.30-1.34 \) (t, 3H, CH\(_3\)), \( 4.31-4.39 \) (q, 3H, OCH\(_2\)), 7.52 - 8.91 (s, 1H, -CH=\(-C-\) and m, 5H, Ar-H).

\( ^{13}C \text{-NMR} \): \( 14.42, 62.12, 107.97, 108.25, 114.52, 124.01, 126.23, 127.36, 129.52, 139.76, 145.08, 146.99, 150.74, 158.35, 161.35. \)

(E)-ethyl 3-(2-chloro-6-methylquinolin-3-yl)-2-cyanoacrylate. (III b)

IR: 3048(C-H str. of =CH-), 2880(C-H str. of –CH\(_3\)), 2243(C≡N str.), 1725(C=O str. of aromatic ester), 1580 & 1485(C=C str. of aromatic ring), 754(C-Cl str.)

\( ^1H \text{ NMR} \): \( \delta 1.29-1.35 \) (t, 3H, CH\(_3\)), 2.41(s, 3H, CH\(_3\)), \( 4.33-4.39 \) (q, 3H, OCH\(_2\)), 7.58 - 8.95 (s, 1H, -CH=\(-C-\) and m, 4H, Ar-H).

\( ^{13}C \text{-NMR} \): \( 14.56, 21.45, 63.35, 107.98, 108.87, 114.47, \)

\( \text{DMSO-d}\(_6\) \): \( 124.58, 126.86, 127.53, 129.62, 138.41, 144.40, 146.71, 150.28, 158.93, 161.09. \)

(E)-ethyl 3-(2-chloro-6-methoxyquinolin-3-yl)-2-cyanoacrylate. (III c)

IR: 3035(C-H str. Of =CH-), 2235(C≡N str.), 1730(C=O str. of aromatic ester), 1563 & 1460(C=C str. of aromatic ring), 48(C-Cl str.)

\( ^1H \text{ NMR} \): \( \delta 1.33-1.36 \) (t, 3H, CH\(_3\)), \( 3.94 \) (s, 3H, OCH\(_3\)), \( 4.36-4.41 \) (q, 3H, OCH\(_2\)), 7.55 - 8.93 (s, 1H, -CH=\(-C-\) and m, 4H, Ar-H).

\( ^{13}C \text{-NMR} \): \( 14.40, 56.39, 63.34, 107.24, 108.37, 114.80, \)

\( \text{DMSO-d}\(_6\) \): \( 124.87, 126.16, 127.89, 129.75, 138.76, 144.18, 146.35, 150.45, 158.97, 161.35. \)
$^{13}$C-NMR SPECTRA
(E)-ethyl 3-(2-chloro-6-chloroquinolin-3-yl)-2-cyanoacrylate. (III d)

\[
\begin{align*}
\text{IR} & : \quad 3040(\text{C-H str. of } =\text{CH-}), \quad 2240(\text{C≡N str.}), \\
& \quad 1720(\text{C=O str. of aromatic ester}), \quad 1560\&1480(\text{C=C str. of aromatic ring}), \quad 758(\text{C-Cl str.}) \\
\text{KBR} & : \\
\text{H NMR} & : \quad \delta 1.34-1.38 (t, 3H, CH\textsubscript{3}), \quad 4.38-4.43 (q, 3H, OCH\textsubscript{2}) \\
& \quad 7.50 - 8.90 (s, 1H, -CH=\text{C-} \text{ and } m, 4H, \text{Ar-H}). \\
\text{C-NMR} & : \quad \delta 14.93, \quad 63.28, \quad 107.71, \quad 108.47, \quad 114.85, \quad 124.69, \\
& \quad 126.71, \quad 127.28, \quad 129.39, \quad 138.12, \quad 144.32, \quad 146.63, \\
& \quad 150.56, \quad 158.41, \quad 161.84.
\end{align*}
\]

Spectral Analysis of Biquinoline derivatives

Ethyl 2’-amino-2-chloro-1’-(4(4-chlorophenyl)thiazol-2-yl) -5’-oxo-1’,4’,5’,6’,7’,8’-hexahydro-3,4’-biquinoline-3’-carboxylate (Ebq\textsubscript{1})

\[
\begin{align*}
\text{IR} & : \quad 3441(\text{asym.N-H str.}), \quad 3260(\text{sym.N-H str.}), \\
& \quad 3005(\text{aromatic C-H str.}), \quad 1668(\text{C=O str.}), \\
& \quad 1542\&1470(\text{C=C str. of aromatic ring}), \quad 751(\text{C-Cl str.}) \text{ cm}\textsuperscript{-1} \\
\text{KBR} & : \\
\text{H NMR} & : \quad \delta 1.10(s, 3H, CH\textsubscript{3}), \quad 1.70-2.21(m, 6H, 3xCH\textsubscript{2}), \\
& \quad 3.94(s, 2H, OCH\textsubscript{2}), \quad 5.40(s, 1H, CH), \quad 6.40 (s, 2H, NH\textsubscript{2}), \quad 7.30-7.68(m, 11H, Ar-H). \\
\text{C-NMR} & : \quad \delta 14.98, \quad 21.78, \quad 26.54, \quad 35.45, \quad 36.12, \quad 57.98, \quad 78.32, \\
& \quad 113.87, \quad 117.36, \quad 119.74, \quad 126.65, \quad 126.45, \quad 128.54, \\
& \quad 129.56, \quad 129.74, \quad 131.36, \quad 131.70, \quad 133.12, \quad 140.56, \\
& \quad 144.78, \quad 150.23, \quad 150.45, \quad 152.65, \quad 152.85, \quad 152.03, \\
& \quad 156.19, \quad 168.23, \quad 195.98.
\end{align*}
\]
Ethyl 2’-amino-2-chloro-1’-(4-(4-chlorophenyl)thiazol-2-yl)-6-methyl-5’-oxo-1’,4’,5’,6’,7’,8’-hexahydro-3,4’-biquinoline-3’-carboxylate (Ebq₂).

**IR (KBR):**
- 3442 (asym.N-H str.)
- 3280 (sym.N-H str.)
- 3015 (aromatic C-H str.)
- 1678 (C=O str.)
- 1545 & 1476 (C=C str. of aromatic ring)
- 740 (C-Cl str.) cm⁻¹

**¹H NMR (DMSO-d₆):**
- δ 1.00-1.07 (t, 3H, CH₃)
- 1.72-2.45 (m, 6H, 3xCH₂)
- 2.93 (s, 3H, CH₃)
- 3.87 (s, 2H, OCH₂)
- 5.25 (s, 1H, CH)
- 6.87 (s, 2H, NH₂)
- 7.25 - 7.61 (m, 9H, Ar-H).

**¹³C-NMR (DMSO-d₆):**
- δ 14.12, 20.23, 21.39, 27.28, 35.17, 36.36, 59.65, 78.54, 105.47, 114.78, 116.89, 116.65, 122.54, 125.41, 128.10, 128.32, 129.21, 140.14, 141.74, 141.90, 147.12, 149.23, 152.36, 152.00, 156.03, 158.36, 158.96, 169.19, 195.37.


**IR (KBR):**
- 3445 (asym.N-H str.)
- 3285 (sym.N-H str.)
- 3012 (aromatic C-H str.)
- 1670 (C=O str.)
- 1548 & 1473 (C=C str. of aromatic ring)
- 1219 & 1023 (C-O-C asym & sym str. of OCH₃)
- 741 (C-Cl str.) cm⁻¹

**¹H NMR (DMSO-d₆):**
- δ 1.01-1.07 (t, 3H, CH₃)
- 1.75-2.41 (m, 6H, 3xCH₂)
- 3.85 (s, 2H, OCH₂)
- 3.95 (s, 3H, OCH₃)
- 5.32 (s, 1H, CH)
- 6.80 (s, 2H, NH₂)
- 7.29 - 7.60 (m, 9H, Ar-H).

**¹³C-NMR (DMSO-d₆):**
- δ 14.78, 21.89, 27.96, 35.65, 36.54, 56.41, 59.12, 78.23, 105.32, 114.21, 116.14, 116.45, 122.55, 125.65, 128.96, 128.85, 129.74, 140.17, 141.20, 141.39, 147.23, 149.11, 152.75, 152.85, 156.63, 158.74, 158.32, 169.32, 195.97.
**Ethyl 2'-amino-2-chloro-1'-(4-(4-chlorophenyl)thiazol-2-yl)-6-chloro-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carboxylate (Ebq₄).**

**IR (KBR):**
- 3439 (asym. N-H str.), 3281 (sym. N-H str.), 3010 (aromatic C-H str.), 1670 (C=O str.), 1540 & 1473 (C=C str. of aromatic ring), 748 (C-Cl str.) cm⁻¹

**¹H NMR (DMSO-d₆):**
- δ 1.00-1.06 (t, 3H, CH₃), 1.72-2.41 (m, 6H, 3xCH₂), 3.87 (s, 2H, OCH₂), 5.20 (s, 1H, CH), 6.24 (s, 2H, NH₂), 7.25-7.58 (m, 9H, Ar-H).

**¹³C-NMR (DMSO-d₆):**
- δ 14.98, 21.23, 27.45, 35.32, 36.89, 59.97, 78.56, 105.71, 114.82, 116.10, 116.98, 122.38, 125.30, 125.56, 128.91, 129.13, 140.17, 141.88, 141.99, 147.06, 149.12, 152.58, 152.30, 156.85, 158.06, 158.12, 169.87, 195.74.

**Ethyl 2'-amino-2-chloro-1'-(4-phenylthiazol-2-yl)-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carboxylate (Ebq₅)**

**IR (KBR):**
- 3425 (asym. N-H str.), 3280 (sym. N-H str.), 3018 (aromatic C-H str.), 1678 (C=O str.), 1555 & 1475 (C=C str. of aromatic ring), 751 (C-Cl str.) cm⁻¹

**¹H NMR (DMSO-d₆):**
- δ 1.11 (s, 3H, CH₃), 1.71-2.20 (m, 6H, 3xCH₂), 3.90 (s, 2H, OCH₂), 5.36 (s, 1H, CH), 6.24 (s, 2H, NH₂), 7.31-7.68 (m, 9H, Ar-H).

**¹³C-NMR (DMSO-d₆):**
- δ 14.45, 21.30, 26.82, 35.40, 36.12, 57.32, 78.25, 113.31, 117.78, 119.89, 126.96, 126.65, 128.54, 129.41, 129.12, 131.23, 131.30, 133.17, 140.28, 144.93, 150.41, 150.60, 152.53, 152.82, 152.73, 156.91, 168.75, 195.88.
Ethyl 2'-amino-2-chloro-1'-(4-phenylthiazol-2-yl)-6-methyl-5’-oxo-1’,4’,5’,6’,7’,8’-hexahydro-3,4’-biquinoline-3’-carboxylate (Ebq₆)

**IR (KBR):** 3437 (asym N-H str.), 3333 (sym N-H str.), 3008 (aromatic C-H str.), 1672 (C=O str.), 1550 & 1480 (C=C str. of aromatic ring), 752 (C-Cl str.) cm⁻¹

**¹H NMR (DMSO-d₆):** δ 1.09 (s, 3H, CH₃), 2.23 (s, 3H, CH₃), 2.71-2.20 (m, 6H, 3xCH₂), 3.93 (s, 2H, OCH₂), 5.31 (s, 1H, CH), 8.42 (s, 2H, NH₂), 7.29-7.65 (m, 10H, Ar-H).

**¹³C-NMR (DMSO-d₆):** δ 14.23, 20.14, 21.41, 26.02, 35.10, 36.32, 57.10, 78.74, 113.14, 117.14, 119.41, 126.41, 126.47, 128.25, 129.74, 129.45, 131.13, 131.15, 133.25, 140.47, 144.78, 150.41, 150.45, 152.13, 152.92, 152.71, 156.45, 168.79, 195.45.

Ethyl 2'-amino-2-chloro-1'-(4-phenylthiazol-2-yl)-6-methoxy-5’-oxo-1’,4’,5’,6’,7’,8’-hexahydro-3,4’-biquinoline-3’-carboxylate (Ebq₇)

**IR (KBR):** 3446 (asym N-H str.), 3240 (sym N-H str.), 3015 (aromatic C-H str.), 1668 (C=O str.), 1562 & 1478 (C=C str. of aromatic ring), 1222 & 1030 (C-O-C asym & sym str. of OCH₃), 748 (C-Cl str.) cm⁻¹

**¹H NMR (DMSO-d₆):** δ 1.01 (s, 3H, CH₃), 1.71-2.25 (m, 6H, 3xCH₂), 3.90 (s, 2H, OCH₂), 3.89 (s, 3H, OCH₃), 5.35 (s, 1H, CH), 8.43 (s, 2H, NH₂), 7.29-7.65 (m, 10H, Ar-H).

**¹³C-NMR (DMSO-d₆):** δ 14.64, 21.23, 27.12, 35.14, 36.00, 57.23, 59.10, 77.74, 114.41, 117.12, 119.32, 126.40, 126.84, 128.23, 129.18, 129.78, 131.41, 131.97, 133.41, 140.40, 144.68, 150.74, 150.92, 152.44, 152.64, 152.90, 156.01, 168.14, 195.38.
IR SPECTRA

mass of DMSO

DMSO

^1H-NMR SPECTRA
Ethyl 2'-amino-2-chloro-1'-(4-phenylthiazol-2-yl)-6-chloro-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carboxylate (Ebq8)

**IR (KBR)**: 3445 (asym. N-H str.), 3265 (sym. N-H str.), 3010 (aromatic C-H str.), 1660 (C=O str.), 1558 & 1478 (C=C str. of aromatic ring), 745 (C-Cl str.) cm$^{-1}$

**$^1$H NMR (DMSO-d$_6$)**: δ 1.01 (s, 3H, CH$_3$), 1.71-2.25 (m, 6H, 3xCH$_2$), 3.92 (s, 2H, OCH$_2$), 5.30 (s, 1H, CH), 8.45 (s, 2H, NH$_2$), 7.29-7.60 (m, 10H, Ar-H).

**$^{13}$C-NMR (DMSO-d$_6$)**: δ 14.74, 21.19, 27.46, 35.82, 36.58, 59.24, 77.93, 114.17, 117.70, 119.34, 126.61, 126.85, 128.22, 129.37, 129.87, 131.05, 131.81, 133.95, 140.70, 144.35, 150.66, 150.93, 152.55, 152.76, 152.87, 156.98, 168.99, 195.87.

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Ethyl 2'-amino-2-chloro-1'-(4-(4-hydroxyphenyl)thiazol-2-yl)-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carboxylate (Ebq9)

**IR (KBR)**: 3439 (asym. N-H str.), 3295 (sym. N-H str.), 3020 (aromatic C-H str.), 1675 (C=O str.), 1550 & 1470 (C=C str. of aromatic ring), 740 (C-Cl str.) cm$^{-1}$

**$^1$H NMR (DMSO-d$_6$)**: δ 1.05-1.07 (t, 3H, CH$_3$), 1.68-2.44 (m, 6H, 3xCH$_2$), 3.90 (s, 2H, OCH$_2$), 5.21 (s, 1H, CH), 6.78 (s, 2H, NH$_2$), 7.20-7.61 (m, 10H, Ar-H), 9.65 (s, 1H, OH).

**$^{13}$C-NMR (DMSO-d$_6$)**: δ 14.11, 20.92, 27.14, 35.47, 36.85, 59.52, 78.36, 105.36, 114.69, 116.78, 116.92, 122.12, 125.98, 128.32, 128.87, 129.40, 140.71, 141.43, 141.61, 147.91, 149.73, 152.82, 152.49, 156.93, 158.71, 158.25, 169.61, 195.40.
$^{13}$C-NMR SPECTRA
IR SPECTRA

H-NMR SPECTRA

\[
\begin{align*}
\text{MeO} & \quad \text{Cl} \\
\text{O} & \quad \text{COOC}_2\text{H}_5 \\
\text{N} & \quad \text{NH}_2 \\
\text{S} & \\
\text{N} & \\
\text{Cl} & \\
\text{COOC}_2\text{H}_5 & \\
\text{OH} & \\
\text{MeO} & 
\end{align*}
\]

\[
\begin{align*}
\text{Moisture of DMSO} \\
\text{DMSO} & 
\end{align*}
\]

\[^1\text{H-NMR SPECTRA}\]
Ethyl 2'-amino-2-chloro-1'-(4-(4-hydroxyphenyl)thiazol-2-yl)-6-methyl-5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carboxylate (Ebq_{10}).

IR (KBR) : 3442 (asym.N-H str.), 3280 (sym.N-H str.), 3009 (aromatic C-H str.), 1678(C=O str.), 1556&1475 (C=C str. of aromatic ring), 740(C-Cl str.). cm\(^{-1}\)

\(^1\)H NMR (DMSO-d\(_6\)) : \(\delta\) 1.03-1.06(t, 3H, \(\text{CH}_3\)), 1.70-2.41(m, 6H, 3x\(\text{CH}_2\)), 2.91(s, 3H, \(\text{CH}_3\)), 3.89(s, 2H, O\(\text{CH}_2\)), 5.24(s, 1H, \(\text{CH}\)), 6.87 (s, 2H, \(\text{NH}_2\)), 7.25 -7.61(m, 9H, Ar-H), 9.62 (s, 1H, \(\text{OH}\)).

\(^{13}\)C-NMR (DMSO-d\(_6\)) : \(\delta\) 14.23, 20.98, 21.12, 27.78, 35.45, 36.98, 59.56, 78.89, 105.54, 114.32, 116.36, 116.52, 122.00, 125.35, 128.34, 128.47, 129.10, 140.87, 141.71, 141.99, 147.40, 149.59, 152.81, 152.99, 156.63, 158.25, 158.86, 169.10, 195.32.

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Ethyl 2'-amino-2-chloro-1'-(4-(4-hydroxyphenyl)thiazol-2-yl)-6-methoxy -5'-oxo-1',4',5',6',7',8'-hexahydro-3,4'-biquinoline-3'-carboxylate (Ebq_{11}).

IR (KBR) : 3445(asym.N-H str.), 3260(sym.N-H str.), 3012 (aromatic C-H str.), 1680(C=O str.), 1562&1472 (C=C str. of aromatic ring), 1215&1018(C-O-C asym & sym str. of-\(\text{OCH}_3\)), 741(C-Cl str.). cm\(^{-1}\)

\(^1\)H NMR (DMSO-d\(_6\)) : \(\delta\) 1.01-1.05(t, 3H, \(\text{CH}_3\)), 1.70-2.41 (m, 6H, 3x\(\text{CH}_2\)), 3.91(s, 2H, O\(\text{CH}_2\)), 3.89(s, 3H, O\(\text{CH}_3\)), 5.24(s, 1H, \(\text{CH}\)), 6.87(s, 2H, \(\text{NH}_2\)), 7.29-7.61(m, 9H, Ar-H), 9.72(s, 1H, \(\text{OH}\)).

\(^{13}\)C-NMR (DMSO-d\(_6\)) : \(\delta\) 14.72, 21.26, 27.47, 35.63, 36.60, 56.08, 59.13, 78.35, 105.79, 114.48, 116.04, 116.25, 122.99, 125.28, 128.09, 128.59, 129.14, 140.27, 141.20, 141.90, 147.47, 149.01, 152.69, 152.91, 156.73, 158.10, 158.38, 169.06, 195.81.
\(^{13}\)C-NMR SPECTRA

**IR**  
(KBR) 3440 (asym.N-H str.), 3275 (sym.N-H str.), 3005 (aromatic C-H str.), 1675(C=O str.), 1555 & 1480 (C=C str. of aromatic ring), 742 (C-Cl str.) cm$^{-1}$

**$^1$H NMR**  
(DMSO-d$_6$) $\delta$ 1.00-1.07(t, 3H, CH$_3$), 1.70-2.41(m, 6H, 3xCH$_2$), 3.91(s, 2H, OCH$_2$), 5.25(s, 1H, CH), 6.24(s, 2H, NH$_2$), 7.25-7.55(m, 9H, Ar-H), 9.70(s, 1H, OH).

**$^{13}$C-NMR**  
(DMSO-d$_6$) $\delta$ 14.12, 21.23, 27.36, 35.32, 36.21, 59.45, 78.56, 105.65, 114.23, 116.10, 116.98, 122.34, 125.30, 128.23, 128.87, 129.13, 140.17, 141.78, 141.99, 147.56, 149.32, 152.23, 152.30, 156.30, 158.96, 158.32, 169.87, 195.96.
3.II.5B Antimicrobial activity

The methods used for antibacterial and antifungal activity are discussed in Chapter-2, 2.5B.

Table 3.II.3: Antimicrobial activity of compound (Bq₁₋₁₂)

<table>
<thead>
<tr>
<th>Compd.</th>
<th>E.coli</th>
<th>B.subtilis</th>
<th>S.aureus</th>
<th>F.oxysporum</th>
<th>A.niger</th>
<th>R.oryzae</th>
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</table>
**Results of antimicrobial activity**

All the synthesized compounds Ebq_{1-12} were tested against microorganism species at 1000 ppm concentration.

The observed results of antibacterial screening reported in Table-3.II.3, indicate that compounds Ebq_4, Ebq_5, Ebq_7, Ebq_8, Ebq_{11} and Ebq_{12} having the methoxy and halo group on quinoline nucleus shows good activity against the bacterial species used.

From the antifungal assay it has been also observed that compounds having methoxy substituents on quinoline ring show the highest activity against *F. oxysporum*, *A. niger* and *R. oryzae*. Rest of the compounds show significant activity but it could not reach the effectiveness of the conventional fungicidal Griseofulvine.
Figure 3.II.1: Antibacterial Chart
Figure 3.II.2: Antifungal Chart
REFERENCES