6.1 Introduction

One of the main objectives of the organic and medicinal chemistry research has been the design, synthesis and development of molecules having value as therapeutic agents. There are numerous biologically active molecules with five membered rings containing two heteroatoms. Out of these thiazolidinone is an important scaffold known to be associated with several biological activities. It belongs to an important class of heterocyclic compounds containing sulphur and nitrogen in a five membered ring. Traditionally, thiazolidine, thiazolidinone and their spiro derivatives have been of great interest as sources of innovative drug candidates, with antimicrobial and antiviral effects.

Thiazolidinones represented an important class of heterocyclic motifs that are found as a core structure component in a variety of medicinally active agents. 4-Thiazolidinones are derivatives of thiazolidine with a carbonyl group at the 4 position. Substitutions are possible at 2, 3 and 5 position respectively\(^1\). The synthesis of thiazolidinone and their derivatives form major focus in medicinal chemistry\(^2\) on account of their ready accessibility, diverse chemical activity and profound multifarious biological medicinal properties such as analgesic\(^3\), anti-inflammatory\(^4\), antibacterial\(^5\), antifungal, tuberculo-static, and hormone receptor\(^6\), CNS stimulant\(^7\), antiproliferative\(^8\), anti-HIV\(^9\)-\(^10\) and anticonvulsant\(^11\), antihistaminic\(^12\) etc.

Spiro compounds are well known to possess various pharmacological activities (and hence there has been synthesis a challenge and attraction to organic chemists). They have possess very promising biological activities as anticancer, antibacterial, anticonvulsant, anti-tuberculosis, anti-Alzheimer, pain-relief, anti-dermatitis and antimicrobial agents. In addition to their medicinal uses, some spiro derivatives have found other uses in the agriculture, industrial field and they are also used as antifungal, pesticidal, laser dyes and electroluminescent devices. Recently spiro derivatives have used as antioxidants\(^13\). We were prompted by these findings to try to synthesize new spiro-thiazolidinone derivatives with potential anticonvulsant and antimicrobial properties.
Encouraged by the impressive bioactive potential of the thiazolidinone nucleus, we considered it of interest in the present work, to use acceptable protocols, to develop spiro analogues of this nucleus, on this premise that the presence of this nucleus in tandem with others, could contribute significantly to inherit a positive impact to the overall biological efficacy in the resulting molecules. I describe in this thesis, the preliminary results of our synthetic efforts focused in the direction of developing several novel spiro compounds, which could possibly be used as potential antimicrobial and anticonvulsant agents.

In this chapter we have described the synthesis of spiro-thiazolidinones derivatives with a view to verify this assumption that its incorporation could really produce an additive affect on the biological properties of the parent molecule.

6.2 SYNTHETIC ASPECTS OF SPIRO-THIAZOLIDINONES

Functionalized heterocycles are interesting scaffold for the preparation of diversity oriented compound libraries for medicinal and pharmaceutical applications. Of particular importance are the substituted spiro derivatives which are not only used for anti-oxidant, anti-inflammatory, antihypertensive agents but their novel application are continuously emerging. The recent demonstration that some of their derivatives can serve as potential agents in the control and treatment of convulsions has stimulated further interest in these compounds from yet another perspective.

B. P. Choudhari et al.\textsuperscript{14} have prepared N-[coumarin-6-ylamino] spiro-[3H-indole-(1H, 2H)-3, 2-(4H)-thiazolidine]-2, 4-diones by 1, 2-dihydro-3-[coumarin-6-ylhydrazono] indol-2-ones (6.002) by refluxed (6.001) with thioglycolic acid in the presence of catalyzed dry zinc chloride in 1, 4-dioxane for 6 hr. (Scheme-6.1)

\begin{center}
\includegraphics[width=\textwidth]{Scheme-6.1.png}
\end{center}

Scheme-6.1
A. Dandia and coworkers\textsuperscript{15} have prepared 5,7-Dimethyl-3-phenyl-spiro[3H-indole-3,2-thiazolidine]-2,4-(1H)-dithione (6.004) by spiro compound (6.003) and \( \text{P}_2\text{S}_5 \) was adsorbed on silica gel with the help of methanol. (Scheme-6.2)

\begin{center}
\includegraphics[width=\textwidth]{Scheme-6.2.png}
\end{center}

**Scheme-6.2**

H. Kaur and coworkers\textsuperscript{16} have synthesized 2-(benzo[d]thiazol-2-ylthio)-N-(2,4'-dioxospiro[indolin-3,2'-thiazolidin]-3'-yl) acetamides (6.006) by reaction of 2-(benzo[d]thiazol-2-ylthio)-N-(2-oxoindolin-3-ylidene)acetohydrazide (6.005) and mercaptoacetic acid in DMF containing anhyd. ZnCl\textsubscript{2} was heated under reflux for 6-8 h. (Scheme-6.3)

\begin{center}
\includegraphics[width=\textwidth]{Scheme-6.3.png}
\end{center}

**Scheme-6.3**

N. A. A. El-Kanzi et al.\textsuperscript{17} synthesized spiro thiazolidinone (6.008) by reaction of Schiff bases (6.007) was treated with mercaptoacetic acid in benzene and refluxed for 5 days. (Scheme-6.4)

\begin{center}
\includegraphics[width=\textwidth]{Scheme-6.4.png}
\end{center}

**Scheme-6.4**
D. Kaminskyy and coworkers\textsuperscript{18} have prepared spiro[3H-indole-3,2’-thiazolidine]-3’-aryl-2,4’(1H)-diones (6.012) by the reaction of isatin (6.009) amine (6.010) and acetic acid (6.011) in anhydrous benzene was refluxed for 2 hours. Thioglycolic acid was added refluxed with a Dean-Stark apparatus for 8 hours. (Scheme-6.5)

![Scheme-6.5](image)

Treatment of a solution\textsuperscript{19} (6.013) of in DMF was treated with mercaptoacetic acid in the presence of triethylamine catalyst refluxed for 16–18 h to give Spiro β-Lactam thiazolidinone derivatives\textsuperscript{15} (6.014). (Scheme-6.6)

![Scheme-6.6](image)

1-Carbaniloyl-2-oxo-3-pyrrolidinecarboxylates\textsuperscript{20} (6.015) were brominated to give (6.016). These underwent substitution and cyclization reactions with thiourea to give spiro[pyrrolidinethiazolidine] (6.017). (Scheme-6.7)

![Scheme-6.7](image)
The condensation between 4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)benzaldehyde (6.019) and pseudothiohydantoin (6.018) afforded (Z)-5-(4-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)benzylidene)-2-aminothiazol-4(5H)-one (6.014). Scheme-6.8

Scheme-6.8

O. Guzel and coworkers\textsuperscript{23} have synthesized 5-methyl-N-(3-oxo-1-thia-4-azaspiro[4.5]dec-4-yl)-3-phenyl-1\texttextit{H}-indole-2-carboxamide derivatives (6.023) by the reaction of 5-methyl-3-phenyl-1\texttextit{H}-indole-2-carboxyrazide (6.021) an appropriate cyclic ketone (6.022) and mercaptoacetic acid was refluxed in dry benzene for 5-6 h.

Scheme-6.9

M. M. Youssef and coworkers\textsuperscript{24} have synthesized 2-phenyl-5'-thioxo-1\texttextit{H}-spiro[isoquinoline-4,3' [1,2,4]triazolidine]-1,3(2\texttextit{H})-dione (6.026) by the reaction of 2-aryl-4,4-dibromoisoquinoline-1,3-(2\texttextit{H},4\texttextit{H})dione (6.024) reacted with thiosemicarbazide (6.025).

Scheme-6.10
K. M. Mistry and K. R. Desai\textsuperscript{25} have synthesized 2-[spiro-\{1-(4-methyl phenyl)-3-methyl\}-pyrazole]-3-(6-nitro benzothiazole)-5-methyl-4-thiazolidinone (6.028) from the reaction of schiff base 1-(4-Methyl phenyl)-3-methyl-5-(2-imino substituted benzothiazole)-pyrazole (6.027) with thiolactic acid in benzene refluxed for 15 - 16 hrs. Scheme-6.10

\[ \text{Scheme-6.10} \]

3-4-\{1-acetyl-5-(4-substituted phenyl)-2-pyrazoline-3-yl\} phenyl\}-1-N-ethoxy phthalimido-4'-1H- spiro [indole-3,2'-[1, 3]-thiazolidene]-2, 4'-1H-diones (6.030) from the reaction of 3-4-\{1-acetyl-5-(4-substituted phenyl)-2-pyrazoline-3-yl\} phenylimino) indole-2-one (6.029) reacted with 2-mercaptoacetic acid\textsuperscript{26}. Scheme-6.11

\[ \text{Scheme-6.11} \]

6.3 BIOLOGICAL ASPECTS OF SPIRO-THIAZOLIDINONES

Substituted spiro thiazolidinone derivatives showed a wide variety of biological activities viz; antibacterial\textsuperscript{27-28}, anticonvulsant agents\textsuperscript{29-31}, antituberculosis agents\textsuperscript{32}, anti-Alzheimer\textsuperscript{33}, pain-relief agent\textsuperscript{34-35}, antidermatitis\textsuperscript{36}, anticancer\textsuperscript{37-38}, antimicrobial\textsuperscript{39-40}, antifungal\textsuperscript{41} etc.

A large number of spiro thiazolidinone have been reviewed as an antibacterial agent\textsuperscript{42}. N. R. Pai et al. have synthesized N [naphtha [1,2b] pyrano3,4d]thiazol-8-yl]spiro-[3H-indole-(1H,2H)3,4-(2H)-3chloroazetidine- 2,2-diones and N[naphtha [1, 2b]pyrano[3,4-d]thiazol-8- yl]spiro-[3H- indole-(1H, 2
Synthesis of Spiro-thiazolidinone derivatives

H)-3,2-(4H)-thiazolidine]-2,4- dione, found to possess considerable antibacterial activity. (Fig. 6.1)

Fig. 6.1

G. L. Talesara et al.\textsuperscript{43} had synthesized 3'-[(4-acetate phenyl-1N-ethoxyphthalimido-6'-pyridin-2-yl]-3, 3a'-dihydro-6H-spiro [indole-3,5'-[1,3]-thiazo[4,5-c]isoxazol]-2(1H)-ones shows good antimicrobial activity. (Fig. 6.2)

Fig. 6.2

A. Kumar et al.\textsuperscript{44} had synthesized 3-Spiro[1', 3', 4'-oxa/thiadiazoly]2'-{5''-(substitutedphenyl-3''-amino)-4'-{5''- (substituted phenylisoxazolinyl})]-5'-indol-2-ones was showed anticonvulsant and antipsychotic activity. (Fig. 6.3)

Fig. 6.3

Singh et al.\textsuperscript{45} had synthesized a series of isatin-based spiroazetidinones was showed anticonvulsant activity. (Fig. 6.4)
3'-((p-chlorophenyl) 6'-Furyl-cis- 5'a, 6'- dihydro spiro [3H-indole 3, 4'- thiazolo(5', 1'-c) isoxazolo-2(1H)-one] possessed analgesic and anti-inflammatory activity. (Fig. 6.5)

R. K. Behera et al. have noticed antifungal and antibacterial activities of heterocyclic derivatives of spiro thiazolidinones. (Fig. 6.6)

Some fused spiro heterocyclic compounds have been tested against some bacterial and fungal strain. Synthesis of spiro-indolo-thiazolidinones has been carried out and bactericidal activities of these compounds have been evaluated. (Fig. 6.11)
Recently, a series of 4-thiazolidinones have been evaluated as selective inhibitors of the HIV-RT enzymes\textsuperscript{51}. Spiro thiazolidinone derivatives have found other uses in the agricultural and industrial fields. Spiro thiazolidinones are used as antifungal agents, pesticides\textsuperscript{52}, laser dyes\textsuperscript{53} and electroluminescent devices\textsuperscript{54}. Spiro compounds have also been recently used as antioxidants\textsuperscript{55-56}.

### 6.4 Present work

The present investigation was undertaken with a view to synthesize some novel spiro-thiazolidinones derivatives together with quinoline moieties.

Although the chemical literature is replete with great variety of synthetic methods which have been employed for the synthesis of these medicinally potent materials, but consideration of reactivity, compound availability, synthetic economy and simplicity in operation has led us to use the method which involving the reaction of corresponding imino-thiazolidinones with thioglycolic acid in dry benzene to yield spiro thiazolidinone derivatives.

### 6.5 Results and discussion

In view of the impressive pharmacodynamic applications shown by spiro thiazolidin-4-one derivatives, much attention has focused towards developing new synthetic routs to synthesized new spiro thiazolidin-4-one derivatives. The synthesis of this series of heterocycle was undertaken in the present work with this assumption.
that presence of spiro thiazolidin-4-one could result in the molecules with enhanced bio-activity. In the present work, the synthesis of spiro thiazolidin-4-one derivatives were carried out using condensation of substituted benzaldehydes (5.047-5.058) with thioglycolic acid in presence of dry benzene medium.

**Scheme of the proposed work**

![Scheme-6.12](image)

**Structures of compounds whose synthesis have been described in this chapter.**
Synthesis of Spiro-thiazolidinone derivatives

![Chemical structures](image)

Table-6.1 conditions used for the synthesis of substituted benzaldehydes (p-chloro, p-nitro and p-methoxy with thioglycolic acid)

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Substituted benzaldehyde</th>
<th>Thioglycolic acid</th>
<th>Solvent dry benzene</th>
<th>Temp.(°C)</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.052</td>
<td>0.18g (0.429mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.053</td>
<td>0.19g (0.439mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.054</td>
<td>0.18g (0.424mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.055</td>
<td>0.19g (0.443mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.056</td>
<td>0.21g (0.453mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.057</td>
<td>0.21g (0.453mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.058</td>
<td>0.21g (0.457mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.059</td>
<td>0.21g (0.467mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.060</td>
<td>0.21g (0.453mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.061</td>
<td>0.24g (0.487mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.062</td>
<td>0.25g (0.496mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
<tr>
<td>5.063</td>
<td>0.23g (0.481mol)</td>
<td>0.276g (0.03mol)</td>
<td>10ml</td>
<td>102-104</td>
<td>24h</td>
</tr>
</tbody>
</table>
### Table-6.2 Physical and analytical data of the compounds (6.049-6.060)

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Comp.</th>
<th>Molecular wt.</th>
<th>Molecular formula</th>
<th>M. P. °C</th>
<th>Yield%</th>
<th>Elemental analysis % (cal/f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.049</td>
<td>517</td>
<td>C_{22}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>100-101</td>
<td>60</td>
<td>N 10.83/10.75, C 53.39/53.30, S 12.39/12.30</td>
</tr>
<tr>
<td>2</td>
<td>6.050</td>
<td>528</td>
<td>C_{22}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>154-155</td>
<td>55</td>
<td>N 13.26/13.20, C 52.32/52.25, S 12.15/12.10</td>
</tr>
<tr>
<td>3</td>
<td>6.051</td>
<td>513</td>
<td>C_{22}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>160-161</td>
<td>70</td>
<td>N 10.92/10.82, C 56.19/56.10, S 12.50/12.40</td>
</tr>
<tr>
<td>4</td>
<td>6.052</td>
<td>531</td>
<td>C_{22}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>170-171</td>
<td>60</td>
<td>N 10.54/10.45, C 54.24/54.18, S 12.09/12.03</td>
</tr>
<tr>
<td>5</td>
<td>6.053</td>
<td>542</td>
<td>C_{22}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>145-146</td>
<td>60</td>
<td>N 12.92/12.85, C 53.18/53.12, S 11.83/11.78</td>
</tr>
<tr>
<td>6</td>
<td>6.054</td>
<td>527</td>
<td>C_{22}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>157-158</td>
<td>70</td>
<td>N 10.63/10.55, C 56.97/56.91, S 12.17/12.10</td>
</tr>
<tr>
<td>7</td>
<td>6.055</td>
<td>545</td>
<td>C_{22}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>171-172</td>
<td>55</td>
<td>N 10.27/10.20, C 55.04/55.00, S 11.76/11.70</td>
</tr>
<tr>
<td>8</td>
<td>6.056</td>
<td>556</td>
<td>C_{22}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>156-157</td>
<td>60</td>
<td>N 12.59/12.51, C 54.00/53.99, S 11.53/11.48</td>
</tr>
<tr>
<td>9</td>
<td>6.057</td>
<td>541</td>
<td>C_{22}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>170-171</td>
<td>55</td>
<td>N 10.35/10.27, C 57.71/57.67, S 11.83/11.79</td>
</tr>
<tr>
<td>10</td>
<td>6.058</td>
<td>573</td>
<td>C_{27}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>180-181</td>
<td>55</td>
<td>N 9.77/9.70, C 56.54/56.46, S 11.18/11.12</td>
</tr>
<tr>
<td>11</td>
<td>6.059</td>
<td>584</td>
<td>C_{27}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>175-176</td>
<td>60</td>
<td>N 11.99/11.90, C 55.52/55.47, S 10.98/10.91</td>
</tr>
<tr>
<td>12</td>
<td>6.060</td>
<td>569</td>
<td>C_{27}H_{20}Cl_{2}N_{2}O_{2}S_{2}</td>
<td>165-166</td>
<td>70</td>
<td>N 9.84/9.80, C 59.09/59.01, S 11.27/11.20</td>
</tr>
</tbody>
</table>

### Table-6.3 Spectral data of compounds

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Compound</th>
<th>IR (KBr) cm⁻¹</th>
<th>¹HNMR (CDCl₃+DMSO-d₆) δ ppm &amp; MS m/z (% relative abundance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.049</td>
<td>3269 (NH amine), 3031, 2962 (C-H str.), 1715 (C=O str.), 1652 (C=CH), 1510 (NH amine), 1452 (C-H bend CH₂), 1336 (C-N str.), 762, 675 (C-Cl str. arom.)</td>
<td>8.8 (1H, s, NH), 8.18 (1H, d, ArH), 8.15 (1H, d, ArH), 8.01 (1H, s, ArH), 8.03 (1H, d, ArH), 7.8 (1H, d, ArH), 7.7-7.3 (2H, dd, ArH), 7.2-7.1 (1H, d, ArH), 6.8 (2H, s, C=CH), 4.0 (1H, s, NH), 3.6 (2H, s, CH₂), 1.5-1.2 (4H, m, CH₂). M/Z: 529 (33.7%), 527 (100.0%).</td>
</tr>
<tr>
<td>2</td>
<td>6.050</td>
<td>3242 (NH amine), 3021, 2931 (C-H str.), 1716 (C=O str.), 1658 (C=CH), 1509 (NH amine), 1459 (C-H bend CH₂), 1352 (N-O str.), 1315 (C-N str.), 764 (C-Cl str. arom.)</td>
<td>8.6 (1H, s, NH), 8.5 (1H, d, ArH), 8.1 (2H, dd, ArH), 8.0 (1H, s, ArH), 7.7 (2H, dd, ArH), 7.5 (2H, s, C=CH), 7.3 (1H, d, ArH), 6.3 (1H, d, ArH), 4.2 (2H, s, CH₂), 4.1 (1H, s, NH), 1.1-1.3 (4H, m, CH₂). M/Z: 512 (100.0%).</td>
</tr>
<tr>
<td>3</td>
<td>6.051</td>
<td>3295 (NH amine), 3062, 2945 (C-H str.), 1719 (C=O str.), 1657(C=CH), 1516 (NH amine), 1445 (C-H bend CH₂), 1321(C-N str.), 1298 (C-O str.), 8.6 (1H, s, NH), 8.0 (1H, s, ArH), 7.6 (1H, d, ArH), 7.4 (1H, d, ArH), 7.1 (2H, dd, ArH), 6.8 (2H, s, arom. CH₂), 6.7 (2H, dd, ArH), 6.4 (1H, d, ArH), 5.8 (2H, s, C=CH), 4.2 ((1H, s, NH), 3.2 (3H, s, CH₃), 1.3-1.4 (4H, m, CH₂). M/Z: 513 (26.3%), 512 (100.0%).</td>
<td></td>
</tr>
<tr>
<td>S. No.</td>
<td>Compound</td>
<td>IR (KBr) cm(^{-1})</td>
<td>(^{1})HNMR (CDCl(_3)+DMSO-d(_6)) &amp; MS m/z (% relative abundance)</td>
</tr>
<tr>
<td>-------</td>
<td>----------</td>
<td>------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>4.</td>
<td>6.052</td>
<td>785 (C-Cl str. arom.)</td>
<td>514 (41.4%).&lt;br&gt;8.56 (1H, s, NH), 8.55 (1H, d, ArH), 8.03 (1H, d, ArH), 8.01 (1H, s, ArH), 7.9 (1H, d, ArH), 7.5 (1H, d, ArH), 7.4 (1H, d, ArH), 6.6 (1H, d, ArH), 6.0 (2H, s, C=CH), 4.1 (1H, s, NH), 3.5 (2H, s, arom. CH(_2)), 1.4-1.0 (6H, m, CH(_2)).</td>
</tr>
<tr>
<td>5.</td>
<td>6.053</td>
<td>3295 (NH amine), 3012, 2972 (C-H str.), 1710 (C=O str.), 1658 (C=CH), 1505 (NH amine), 1466 (C-H bend CH(_2)), 1245(C-N str.), 786, 682 (C-Cl str. arom.).&lt;br&gt;8.6 (1H, d, ArH), 8.5 (1H, s, NH), 8.1 (2H, dd, ArH), 8.0 (1H, s, ArH), 7.6 (1H, d, ArH), 7.5 (2H, s, C=CH), 7.2 (1H, d, ArH), 6.5 (1H, d, ArH), 4.5 (1H, s, ArH), 4.2 (2H, s, arom. CH(_2)), 1.8-1.0 (6H, m, CH(_2)).</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>6.054</td>
<td>3263 (NH amine), 3043, 2987 (C-H str.), 1705(C=O str.), 1658 (C=CH), 1500 (NH amine), 1458 (C-H bend CH(_2)), 1350 (N-O str.), 1345(C-N str.), 767 (C-Cl str. arom.).&lt;br&gt;11.5 (1H, s, NH), 8.5 (1H, s, ArH), 8.0 (2H, dd, ArH), 7.7 (1H, d, ArH), 7.5 (1H, d, ArH), 7.3 (1H, d, ArH), 7.2 (2H, dd, ArH), 7.0 (1H, d, ArH), 6.6 (2H, s, C=CH), 4.1(1H, s, NH), 3.0 (2H, s, arom. CH(_2)), 2.4 (3H, s, CH(_3)), 1.8-1.0 (6H, m, CH(_2)).</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>6.055</td>
<td>3236 (NH amine), 3022, 3053 (C-H str.), 1708 (C=O str.), 1658 (C=CH), 1533 (NH amine), 1446 (C-H bend CH(_2)), 1284 (C-N str.), 765, 545 (C-Cl str. arom.).&lt;br&gt;9.5 (1H, s, NH), 8.6 (1H, d, ArH), 8.0 (1H, s, ArH), 7.6 (1H, d, ArH), 7.4 (1H, d, ArH), 7.3 (2H, dd, ArH), 7.2 (2H, dd, ArH), 6.4 (1H, d, ArH), 6.2 (2H, s, C=CH), 4.3 (2H, s, arom. CH(_2)), 4.0 (1H, s, NH), 1.5-1.2 (8H, m, CH(_2)).</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>6.056</td>
<td>3272 (NH amine), 3049, 2935 (C-H str.), 1705 (C=O str.), 1674 (C=CH), 1500 (NH amine), 1481(C-H bend CH(_2)), 1338 (N-O), 1288 (C-N str.), 763 (C-Cl str. arom.).&lt;br&gt;8.8 (1H, d, ArH), 8.3 (1H, s, NH), 8.2 (1H, s, ArH), 8.0 (1H, d, ArH), 7.9 (1H, d, ArH), 7.8 (1H, d, ArH), 7.6 (1H, d, ArH), 7.3 (1H, d, ArH), 7.2 (1H, d, ArH), 6.6 (1H, d, ArH), 6.4 (2H, s, C=CH), 4.4 (1H, s, NH), 3.1 (2H, s, arom. CH(_2)), 1.5-1.0 (8H, m, CH(_2)).</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>6.057</td>
<td>3272 (NH amine), 3049, 2998 (C-H str.), 8.6 (1H, d, ArH), 8.3 (1H, s, NH), 8.0 (1H, s, ArH), 7.6 (1H, d, ArH), 7.4</td>
<td></td>
</tr>
<tr>
<td>S. No.</td>
<td>Compound</td>
<td>IR (KBr) cm(^{-1})</td>
<td>(^1)HNM R (CDCl(_3)+DMSO-d(_6)) δ ppm &amp; MS m/z (% relative abundance)</td>
</tr>
<tr>
<td>-------</td>
<td>----------</td>
<td>----------------------</td>
<td>------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1719 (C=O str.), 1696 (C=CH), 1530 (NH amine), 1448 (C-H bend CH(_2)), 1290 (C-O str.), 1350 (C-N str.), 765 (C-Cl str. arom.)</td>
<td>(1H, d, ArH), 7.1 (2H, dd, ArH), 6.7 (2H, s, C=CH), 6.4 (1H, d, ArH), 4.3 (2H, s, arom. CH(_2)), 4.0 (1H, s, NH), 3.7 (3H, s, CH(_3)), 1.6-1.3 (8H, m, CH(_2)).</td>
</tr>
<tr>
<td>10.</td>
<td>6.058</td>
<td>3298 (NH amine), 3012, 2978 (C-H str.), 1711(C=O str.), 1657 (C=CH), 1500 (NH amine), 1462 (C-H bend CH(_2)), 1245(C-N str.), 761, 665 (C-Cl str. arom.)</td>
<td>8.8 (1H, s, NH), 8.7 (1H, d, ArH), 8.4 (1H, d, ArH), 8.2 (1H, d, ArH), 8.1 (1H, s, ArH), 8.0 (1H, d, ArH), 7.4-7.5 (3H, m, ArH), 6.9 (1H, d, ArH), 6.7 (2H, s, C=CH), 3.8 (1H, s, NH), 3.3 (2H, s, arom. CH(_2)), 1.5-1.0 (12H, m, CH(_2)).</td>
</tr>
<tr>
<td>11.</td>
<td>6.059</td>
<td>3221 (NH amine), 3022, 2941 (C-H str.), 1718 (C=O str.), 1659 (C=CH), 1505 (NH amine), 1485 (C-H bend CH(_2)), 1345 (N-O), 1232(C-N str.), 762 (C-Cl str. arom.)</td>
<td>8.8 (1H, s, NH), 8.6 (1H, d, ArH), 8.1 (2H, dd, ArH), 8.0 (1H, s, ArH), 7.6 (1H, d, ArH), 7.5 (2H, dd, ArH), 7.3 (1H, d, ArH), 6.4 (1H, d, ArH), 5.9 (2H, s, C=CH), 4.3 (2H, s, arom. CH(_2)), 4.1 (1H, s, NH), 2.9-1.5 (12H, m, CH(_2)).</td>
</tr>
<tr>
<td>12.</td>
<td>6.060</td>
<td>3246 (NH amine), 3027, 2978 (C-H str.), 1720 (C=O str.), 1333 (C-N str.), 1656 (C=CH), 1521, 1498 (NH amine), 1464 (C-H bend CH(_2)), 1300 (C-O str.), 766 (C-Cl str. arom.)</td>
<td>9.8 (1H, s, NH), 8.7 (1H, d, ArH), 8.2 (1H, d, ArH), 8.0 (1H, s, ArH), 7.8 (1H, d, ArH), 7.5 (1H, d, ArH), 7.2 (2H, s, C=CH), 6.8-7.1 (3H, m, ArH), 6.9 (1H, d, ArH), 4.2 (1H, s, NH), 3.8 (3H, s, CH(_3)), 3.1 (2H, s, CH(_2)), 1.6-1.1 (12H, m, CH(_2)).</td>
</tr>
</tbody>
</table>
Table 6.4 $^{13}$C NMR Spectral data

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon</td>
<td>calculated</td>
<td>found</td>
<td>calculated</td>
<td>found</td>
<td>calculated</td>
</tr>
<tr>
<td>1</td>
<td>116.8</td>
<td>113.0</td>
<td>151.4</td>
<td>152.0</td>
<td>151.4</td>
</tr>
<tr>
<td>2</td>
<td>122.5</td>
<td>123.7</td>
<td>121.8</td>
<td>123.75</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>127.1</td>
<td>127.3</td>
<td>127.5</td>
<td>126.5</td>
<td>127.3</td>
</tr>
<tr>
<td>4</td>
<td>134.9</td>
<td>136.9</td>
<td>134.6</td>
<td>134.45</td>
<td>134.9</td>
</tr>
<tr>
<td>5</td>
<td>129.4</td>
<td>129.4</td>
<td>128.1</td>
<td>128.24</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>119.3</td>
<td>119.3</td>
<td>119.7</td>
<td>119.7</td>
<td>119.7</td>
</tr>
<tr>
<td>7</td>
<td>46.1</td>
<td>45.7</td>
<td>43.3</td>
<td>46.2</td>
<td>39.5</td>
</tr>
<tr>
<td>8</td>
<td>38.3</td>
<td>38.8</td>
<td>-</td>
<td>38.3</td>
<td>46.1</td>
</tr>
<tr>
<td>9</td>
<td>76.3</td>
<td>76.4</td>
<td>76.3</td>
<td>76.9</td>
<td>40.4</td>
</tr>
<tr>
<td>10</td>
<td>174.2</td>
<td>170.7</td>
<td>171.2</td>
<td>170.8</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>33.8</td>
<td>33.4</td>
<td>-</td>
<td>38.3</td>
<td>64.1</td>
</tr>
<tr>
<td>12</td>
<td>-</td>
<td>-</td>
<td>138.8</td>
<td>136.0</td>
<td>76.3</td>
</tr>
<tr>
<td>13</td>
<td>169.7</td>
<td>165.0</td>
<td>165.0</td>
<td>162.1</td>
<td>39.2</td>
</tr>
<tr>
<td>14</td>
<td>124.1</td>
<td>124.0</td>
<td>124.1</td>
<td>123.6</td>
<td>160.0</td>
</tr>
<tr>
<td>15</td>
<td>127.4</td>
<td>128.2</td>
<td>127.4</td>
<td>126.9</td>
<td>124.1</td>
</tr>
<tr>
<td>16</td>
<td>-</td>
<td>-</td>
<td>127.6</td>
<td>127.12</td>
<td>-</td>
</tr>
<tr>
<td>17</td>
<td>-</td>
<td>-</td>
<td>128.8</td>
<td>128.67</td>
<td>-</td>
</tr>
<tr>
<td>18</td>
<td>-</td>
<td>-</td>
<td>133.0</td>
<td>132.01</td>
<td>-</td>
</tr>
<tr>
<td>19</td>
<td>-</td>
<td>-</td>
<td>128.8</td>
<td>128.37</td>
<td>-</td>
</tr>
<tr>
<td>20</td>
<td>-</td>
<td>-</td>
<td>127.5</td>
<td>128.6</td>
<td>-</td>
</tr>
<tr>
<td>21</td>
<td>-</td>
<td>-</td>
<td>55.8</td>
<td>64.4</td>
<td>55.9</td>
</tr>
<tr>
<td>22</td>
<td>-</td>
<td>-</td>
<td>127.6</td>
<td>-</td>
<td>59.8</td>
</tr>
<tr>
<td>23</td>
<td>55.8</td>
<td>64.4</td>
<td>64.6</td>
<td>-</td>
<td>55.9</td>
</tr>
<tr>
<td>24, 26, 28</td>
<td>55.8</td>
<td>64.4</td>
<td>64.6</td>
<td>-</td>
<td>55.9</td>
</tr>
</tbody>
</table>
6.6 Interpretation of spectral data for the elucidation of structure of compounds

Structures of all the compounds were established on the basis of elemental analysis, IR and $^1$HNMR spectral data. Physical data of all the compounds were found to be consistent to all structures assigned to these molecules.

The physical microanalyses, infrared, $^1$HNMR and $^{13}$C HNMR spectral data of all the compounds are given in Table-6.2, Table-6.3-6.4 and the spectral graphs are presented in the form of Chart- 6.1-6.16 at the end of chapter.

6.6.1 Interpretation of spectral data of compound 6.049

Infrared spectra

Infrared spectrum of compound 6.049 on KBr standard exhibited one strong absorption band at 3269 cm$^{-1}$ for secondary amine confirm formation of spiro ring. Appearance of two peak at 3031 cm$^{-1}$, 2962 cm$^{-1}$ (C-H str.) and one peak at 1715 cm$^{-1}$ (C=O str.), 1652 cm$^{-1}$ (C=CH), 1510 cm$^{-1}$ (NH amine), 1452 cm$^{-1}$ (C-H bend CH$_2$). Appearance of peak at 1336 cm$^{-1}$ (C-N str.),762 cm$^{-1}$ and 675 cm$^{-1}$ (C-Cl str. arom.) which established the compound 6.049.

$^1$HNMR spectrum

$^1$HNMR spectra of compound of 6.049 in CDCl$_3$ displayed signals for the presence of 18 protons of which 16 protons were bound to carbon atom and 2 protons were bound to nitrogen atom (the protons bound to nitrogen exchanged with D$_2$O). $^1$HNMR spectra display the downfield one singlet for one NH proton at $\delta$ 8.8 which exchanged with D$_2$O was assigned for NH group. The presence of one singlet which appeared at $\delta$ 8.1 was attributed C$_8$ quinoline proton (Meta to the chlorine function in the benzene ring at C$_7$). Four doublets which appeared at $\delta$ 8.03, $\delta$ 8.05, $\delta$ 8.01 and $\delta$ 7.8 for the presence of protons in aromatic chain. Presence of one singlet which appeared at $\delta$ 6.8 assigned one C=CH group. Appearance of singlet at $\delta$ 4.0 was assigned for NH group. Presence of singlet at $\delta$ 3.6 for two protons was ascribed to the presence of CH$_2$ in spiro ring. The upfield, multiplet which was observed at $\delta$ 1.5- $\delta$ 1.2 for 4 protons was ascribed to the presence of aliphatic CH$_2$. 
Similar spectral interpretation established the formation of compound 6.050, 6.053, 6.055 and 6.059.

6.6.2 Interpretation of spectral data of compound 6.050

Infrared spectra

Infrared spectrum of compound 6.050 on KBr standard exhibited one strong absorption band at 3242 cm\(^{-1}\) for secondary amine confirm formation of spiro ring. Appearance of two peak at 3021 cm\(^{-1}\), 2931 cm\(^{-1}\) (C-H str.) and one peak at 1716 cm\(^{-1}\) (C=O str.), 1658 cm\(^{-1}\) (C=CH), 1509 cm\(^{-1}\) (NH (amine)), 1459 cm\(^{-1}\) (C-H bend CH\(_2\)). Appearance of peak at 1352 cm\(^{-1}\) (C-N str.), 764 cm\(^{-1}\) (C-Cl str. arom.) which established the compound 6.050.

6.6.3 Interpretation of spectral data of compound 6.051

Infrared spectra

Infrared spectrum of compound 6.051 on KBr standard exhibited one strong absorption band at 3295 cm\(^{-1}\) for secondary amine confirm formation of spiro ring. Appearance of two peak at 3062 cm\(^{-1}\), 2945 cm\(^{-1}\) (C-H str.) and one peak at 1719 cm\(^{-1}\) (C=O str.), 1657 cm\(^{-1}\) (C=CH), 1516 cm\(^{-1}\) (NH amine), 1445 cm\(^{-1}\) (C-H bend CH\(_2\)). Appearance of peak at 1321 cm\(^{-1}\) (C-N str.), 1298 cm\(^{-1}\) (C-O str.), 785 cm\(^{-1}\) (C-Cl str. arom.) which established the compound 6.051

\(^1\)HNMR spectrum

\(^1\)HNMR spectra of compound of 6.051 in CDCl\(_3\) displayed signals for the presence of 21 protons of which 19 protons were bound to carbon atom and 2 protons were bound to nitrogen atom (the protons bound to nitrogen exchanged with D\(_2\)O). \(^1\)HNMR spectra display the downfield one singlet for one NH proton at \(\delta\) 8.6 which exchanged with D\(_2\)O was assigned for NH group. The presence of one singlet which appeared at \(\delta\) 8.0 was attributed C\(_8\) quinoline proton (Meta to the chlorine function in the benzene ring at C\(_7\)). Four doublets which appeared at \(\delta\) 8.7, \(\delta\) 7.6, \(\delta\) 7.4, and \(\delta\) 6.4 for the presence of protons in aromatic chain. A singlet at \(\delta\) 4.8 for two protons was ascribed to the presence of CH\(_2\) in spiro ring. Two double doublets were observed at \(\delta\) 7.1 and 6.7 assigned to two proton of aromatic ring. Presence of two singlet which appeared at \(\delta\) 6.8 assigned one C=CH group and other one is
appeared at \( \delta \) 4.2 for NH group. The upfield, multiplet which was observed at \( \delta \) 1.3-\( \delta \) 1.4 for 4 protons was ascribed to the presence of aliphatic CH. 

Similar spectral interpretation established the formation of compound 6.057.

### 6.6.4 Interpretation of spectral data of compound 6.052

#### Infrared spectra

Infrared spectrum of compound 6.052 on KBr standard exhibited one strong absorption band at 3281 cm\(^{-1}\) for secondary amine confirm formation of spiro ring. Appearance of two peak at 3012 cm\(^{-1}\), 2972 cm\(^{-1}\) (C-H str.) and one peak at 1710 cm\(^{-1}\) (C=O sr.), 1658 cm\(^{-1}\) (C=CH), 1505 cm\(^{-1}\) (C-H bend CH\(_2\)), 1489 cm\(^{-1}\) (NH amine), 1245 cm\(^{-1}\) (C-N str.), 786 cm\(^{-1}\), 682 cm\(^{-1}\) (C-Cl str. arom.) which established the compound 6.052.

#### \textsuperscript{1}HNMR spectrum

\textsuperscript{1}HNMR spectra of compound of 6.052 in CDCl\(_3\) displayed signals for the presence of 20 protons of which 18 protons were bound to carbon atom, and 2 protons were bound to nitrogen atom (the protons bound to nitrogen exchanged with D\(_2\)O). \textsuperscript{1}HNMR spectra display the downfield one singlets for one NH proton at \( \delta \) 8.5 which exchanged with D\(_2\)O was assigned for NH group. The presence of one singlet which appeared at 8.0 was attributed C\(_8\) quinoline proton (Meta to the chlorine function in the benzene ring at C\(_7\)). Five doublets which appeared at \( \delta \) 8.55, \( \delta \) 8.03, \( \delta \) 7.9, \( \delta \) 7.5 and \( \delta \) 7.4 for the presence of protons in aromatic chain. One double doublet was observed at \( \delta \) 7.2 assigned to two proton of aromatic ring. Presence of one singlet which appeared at \( \delta \) 6.0 assigned one C=CH group. Two singlets at \( \delta \) 3.5 for two protons were ascribed to the presence of CH\(_2\) in spiro ring and \( \delta \) 4.1 was assigned for NH group. The upfield, multiplet which was observed at \( \delta \) 1.4- \( \delta \) 1.0 for 6 protons was ascribed to the presence of aliphatic CH\(_2\).

### 6.6.5 Interpretation of spectral data of compound 6.053

#### Infrared spectra

Infrared spectrum of compound 6.053 on KBr standard exhibited one strong absorption band at 3232 cm\(^{-1}\) for secondary amine confirm formation of spiro ring.
Appearance of two peak at 3028 cm\(^{-1}\), 2951 cm\(^{-1}\) (C-H str.), 1715 cm\(^{-1}\) (C=O str.), 1659 cm\(^{-1}\) (C=CH), 1519 cm\(^{-1}\) (NH amine), 1445 cm\(^{-1}\) (C-H bend CH\(_2\)), and 1350 cm\(^{-1}\) (N-O str.), 1345 cm\(^{-1}\) (C-N str.), 767 cm\(^{-1}\) (C-Cl str. arom.) which established the compound 6.053.

6.6.6 Interpretation of spectral data of compound 6.054

**Infrared spectra**

Infrared spectrum of compound 6.054 on KBr standard exhibited one strong absorption band at 3263 cm\(^{-1}\) for secondary amine confirm formation of spiro ring. Appearance of two peak at 3043 cm\(^{-1}\), 2987 cm\(^{-1}\) (C-H str.), 1705 cm\(^{-1}\) (C=O str.) 1658 cm\(^{-1}\) (C=CH), 1500 cm\(^{-1}\) (NH amine), 1458 cm\(^{-1}\) (C-H bend CH\(_2\)), and 1311 cm\(^{-1}\) (C-O str.), 1278 cm\(^{-1}\) (C-N str.), 750 cm\(^{-1}\) (C-Cl str. arom.) which established the compound 6.054.

**\(^1\)HNMR spectrum**

\(^1\)HNMR spectra of compound 6.054 in CDCl\(_3\) displayed signals for the presence of 23 protons of which 21 protons were bound to carbon atom and 2 protons were bound to nitrogen atom (the protons bound to nitrogen exchanged with D\(_2\)O). \(^1\)HNMR spectra display the downfield one singlet for one NH proton at \(\delta\) 11.5 which exchanged with D\(_2\)O was assigned for NH group. The presence of one singlet which appeared at \(\delta\) 8.5 was attributed C\(_8\) quinoline proton (Meta to the chlorine function in the benzene ring at C\(_7\)). Two double doublets were observed at \(\delta\) 8.0 and \(\delta\) 7.2 assigned to four protons of aromatic ring. Four doublets which appeared at \(\delta\) 7.7, \(\delta\) 7.5, \(\delta\) 7.3, \(\delta\) 7.2 and \(\delta\) 7.0 for the presence of protons in aromatic ring. Presence of one singlet which appeared at \(\delta\) 6.6 assigned one C=CH group. Two singlets at \(\delta\) 4.1 were assigned for NH group and \(\delta\) 3.0 for two protons was ascribed to the presence of CH\(_2\) in spiro ring. The upfield, multiplet which was observed at \(\delta\) 1.8- \(\delta\) 1.0 for 6 protons was ascribed to the presence of aliphatic CH\(_2\).

6.6.7 Interpretation of spectral data of compound 6.055

**Infrared spectra**

Infrared spectrum of compound 6.055 on KBr standard exhibited one strong absorption band at 3236 cm\(^{-1}\) for secondary amine confirm formation of spiro ring.
Appearance of two peak at 3022 cm\(^{-1}\), 3053 cm\(^{-1}\) (C-H str.) and 1708 cm\(^{-1}\) (C=O str.), 1658 cm\(^{-1}\) (C=CH), 1533 cm\(^{-1}\) (NH amine)), 1446 cm\(^{-1}\) (C-H bend CH\(_2\)), 1284 cm\(^{-1}\) (C-N str.), 765 cm\(^{-1}\), 545 cm\(^{-1}\) (C-Cl str. arom.) which established the compound \textbf{6.055}.

\textbf{6.6.8 Interpretation of spectral data of compound 6.056}

\textbf{Infrared spectra}

Infrared spectrum of compound \textbf{6.056} on KBr standard exhibited one strong absorption band at 3272 cm\(^{-1}\) for secondary amine confirm formation of spiro ring. Appearance of two peak at 3049 cm\(^{-1}\), 2935 cm\(^{-1}\) (C-H str.), 1705 cm\(^{-1}\) (C=O str.), 1674 cm\(^{-1}\) (C=CH), 1500 cm\(^{-1}\) (NH amine), 1481 cm\(^{-1}\) (C-H bend CH\(_2\)), and 1338 cm\(^{-1}\) (N-O), 1288 cm\(^{-1}\) (C-N str.), 763 cm\(^{-1}\) (C-Cl str. arom.) which established the compound \textbf{6.056}.

\textbf{\textsuperscript{1}HNMR spectrum}

\textsuperscript{1}HNMR spectra of compound \textbf{6.056} in CDCl\(_3\) displayed signals for the presence of 22 protons of which 20 protons were bound to carbon atom and 2 protons were bound to nitrogen atom (the protons bound to nitrogen exchanged with D\(_2\)O). \textsuperscript{1}HNMR spectra display the downfield one singlets for one NH proton at \(\delta\) 8.3 which exchanged with D\(_2\)O was assigned for NH group. Eight doublets which appeared at \(\delta\) 8.8, \(\delta\) 8.0, \(\delta\) 7.9, \(\delta\) 7.8, \(\delta\) 7.6, \(\delta\) 7.3, \(\delta\) 7.2 and \(\delta\) 6.6 for the presence of protons in aromatic chain. The presence of one singlet which appeared at \(\delta\) 8.2 was attributed C\(_8\) quinoline proton (Meta to the chlorine function in the benzene ring at C\(_7\)). Presence of one singlet which appeared at \(\delta\) 6.4 assigned one C=CH group. Two singlets at \(\delta\) 4.4 were assigned for NH group and \(\delta\) 3.1 for two protons was ascribed to the presence of CH\(_2\) in spiro ring. The upfield, multiplet which was observed at \(\delta\) 1.5- \(\delta\) 1.0 for 8 protons was ascribed to the presence of aliphatic CH\(_2\).

\textbf{6.6.9 Interpretation of spectral data of compound 6.057}

\textbf{Infrared spectra}

Infrared spectrum of compound \textbf{6.057} on KBr standard exhibited one strong absorption band at 3272 cm\(^{-1}\) for secondary amine confirm formation of spiro ring. Appearance of two peaks at 3049 cm\(^{-1}\), 2998 cm\(^{-1}\) (C-H str.), 1719(C=O str.), 1696
Synthesis of Spiro-thiazolidinone derivatives

193 cm\(^{-1}\) (C=CH), 1530 cm\(^{-1}\) (NH amine), 1448 cm\(^{-1}\) (C-H bend CH\(_2\)), 1350 cm\(^{-1}\) (C-N str.) and 1290 cm\(^{-1}\) (C-O str.), 765 cm\(^{-1}\) (C-Cl str. arom.) which established the compound 6.057.

6.6.10 Interpretation of spectral data of compound 6.058

Infrared spectra

Infrared spectrum of compound 6.058 on KBr standard exhibited one strong absorption band at 3298 cm\(^{-1}\) for secondary amine confirm formation of spiro ring. Appearance of two peaks at 3012 cm\(^{-1}\), 2978 cm\(^{-1}\) (C-H str.) and 1711 cm\(^{-1}\) (C=O), 1657 cm\(^{-1}\) (C=CH), 1500 cm\(^{-1}\) (NH amine), 1462 cm\(^{-1}\) (C-H bend CH\(_2\)), 1245 cm\(^{-1}\) (C-N str.), 761 cm\(^{-1}\), 665 cm\(^{-1}\) (C-Cl str. arom.) which established the compound 6.058.

\(^1\)HNMR spectrum

\(^1\)HNMR spectra of compound of 6.058 in CDCl\(_3\) displayed signals for the presence of 26 protons of which 24 protons were bound to carbon atom and 2 protons were bound to nitrogen atom (the protons bound to nitrogen exchanged with D\(_2\)O). \(^1\)HNMR spectra display the downfield one singlets for one NH proton at \(\delta\) 8.8 exchanged with D\(_2\)O was assigned for NH group. Six doublets which appeared at \(\delta\) 8.0, \(\delta\) 8.7, \(\delta\) 8.4, \(\delta\) 8.2, \(\delta\) 8.1 and \(\delta\) 6.9 for the presence of protons in aromatic ring. The presence of one singlet which appeared at \(\delta\) 8.1 was attributed C\(_8\) quinoline proton (Meta to the chlorine function in the benzene ring at C\(_7\)). One multiplet was observed at \(\delta\) 7.4- \(\delta\) 7.5 assigned to three proton of aromatic chain. Presence of one singlet which appeared at \(\delta\) 6.7 assigned one C=CH group. Two singlets at \(\delta\) 3.8 were assigned for NH group and \(\delta\) 3.3 for two protons was ascribed to the presence of CH\(_2\) in spiro ring. The upfield, multiplet which was observed at \(\delta\) 1.5- \(\delta\) 1.0 for 12 protons was ascribed to the presence of aliphatic CH\(_2\).

6.6.11 Interpretation of spectral data of compound 6.059

Infrared spectra

Infrared spectrum of compound 6.059 on KBr standard exhibited one strong absorption band at 3221 cm\(^{-1}\) for secondary amine confirm formation of spiro ring. Appearance of two peak at 3022 cm\(^{-1}\), 2941 cm\(^{-1}\) (C-H str.), 1718 cm\(^{-1}\) (C=O str.)
1659 cm\(^{-1}\) (C=CH), 1505 cm\(^{-1}\) (NH amine), 1485 cm\(^{-1}\) (C-H bend CH\(_2\)) and 1345 cm\(^{-1}\) (N-O), 1232 cm\(^{-1}\) (C-N str.), 762 cm\(^{-1}\) (C-Cl str. arom.) which established the compound 6.059.

### 6.6.12 Interpretation of spectral data of compound 6.060

#### Infrared spectra

Infrared spectrum of compound 6.060 on KBr standard exhibited one strong absorption band at 3246 cm\(^{-1}\) for secondary amine confirm formation of spiro ring. Appearance of two peak at 3027 cm\(^{-1}\), 2978 cm\(^{-1}\) (C-H str.), 1720 cm\(^{-1}\) (C=O str.), 1656 cm\(^{-1}\) (C=CH), 1521 cm\(^{-1}\) (NH amine), 1464 cm\(^{-1}\) (C-H bend CH\(_2\)), 1333 cm\(^{-1}\) (C-N str.), 1300 cm\(^{-1}\) (C-O str.), 766 cm\(^{-1}\) (C-Cl str. arom.) which established the compound 6.060.

#### \(^1\)HNMR spectrum

\(^1\)HNMR spectra of compound of 6.060 in CDCl\(_3\) displayed signals for the presence of 29 protons of which 27 protons were bound to carbon atom and 2 protons were bound to nitrogen atom (the protons bound to nitrogen exchanged with D\(_2\)O). \(^1\)HNMR spectra display the downfield one singlet for one NH proton at \(\delta\) 9.8 which exchanged with D\(_2\)O was assigned for NH group. Five doublets which appeared at \(\delta\) 8.7, \(\delta\) 8.2, \(\delta\) 7.8, \(\delta\) 7.5 and \(\delta\) 6.8 for the presence of protons in aromatic ring. The presence of one singlet which appeared at \(\delta\) 8.0 was attributed C\(_8\) quinoline proton (Meta to the chlorine function in the benzene ring at C\(_7\)). Presence of one singlet which appeared at \(\delta\) 7.2 assigned one C=CH group. One multiplet was observed at \(\delta\) 6.8- \(\delta\) 7.2 assigned to three proton of aromatic ring. Two singlets at \(\delta\) 3.1 for two protons were ascribed to the presence of CH\(_2\) in spiro ring and \(\delta\) 4.0 was assigned for NH group. The upfield, multiplet which was observed at \(\delta\) 1.6-1.1 for 12 protons was ascribed to the presence of aliphatic CH\(_2\).

MS spectral data also provided the evidence for the formation of compounds 6.050.
6.7  Mechanism of formation of compounds (6.049-6.060).

6.8  Experimental section
1.  Melting points were determined in open glass capillaries and are uncorrected.
2.  The purity of the compounds was checked by TLC on silica gel ‘G’ plates in solvent system benzene: methanol (9:1) as eluent. Iodine was used as visualizing agents.
3.  IR spectra on KBr were recorded on FTIR-8400S, CE (SHIMADZU).
4.  $^1$HNMR spectra were recorded on model A-300F (BRUKER) using CDCl$_3$ as solvent internal reference. Chemical shift are expressed in $\delta$ ppm.
5.  Before analysis all sample were dried for one hour under reduced pressure.
6. Physical and analytical data for all compounds are given Table 6.1, Table 6.1 and Table 6.3.

7. Thioglycolic acid was used in the synthesis without further purification.

6.8.1 Synthetic procedures

1. **2-(4-substituted benzylidene)-4-(2-[7-chloroquinolin-4-ylamine] ethyl) 1,6-dithia-4,9-diazaspiro [4,4]nonane-3,8-dione (6.049-6.051)**

   A mixture of substituted benzylidene derivatives (5.047-5.049) 0.18g (0.429mol) dissolved in dry benzene (10ml) with thioglycolic acid 0.276g (0.03mol) was refluxed on water bath for about 24 hr. The progress of the reaction was checked by TLC using methanol-benzene (2:8) as an eluent. After completion of the reaction, it was cooled and neutralized with aqueous standard solution of sodium bicarbonate (NaHCO$_3$) and water successively and purified by column chromatography to give compound (6.049-6.051). (Scheme-6.12)

   **Microwave assisted method**

   A mixture of substituted benzylidene derivatives 0.18g (0.429mol) dissolved in dry benzene (10ml) with thioglycolic acid 0.276g (0.03mol), was placed in a 100 ml borosil flask with ice fitted with a funnel as a loose top. The reaction mixture was subjected to microwave irradiation, at 20% (360W) microwave power for 10-15 min, overheating of the solution had to be avoided. The completion of the reaction was checked by TLC and UV. The reaction mixture was cooled and the resulting solid was filtered, washed with ethanol dried and recrystallized from ethanol to give compound (6.049-6.051) yield 40.55%.

2. **2-(4-substituted benzylidene)-4-(3-[7-chloroquinolin-4-ylamine] propyl) 1,6-dithia-4,9-diazaspiro [4,4]nonane-3,8-dione (6.052-6.054)**

   A mixture of substituted benzylidene derivatives (5.050-5.052) 0.18g (0.429mol) dissolved in dry benzene (10ml) with thioglycolic acid 0.276g (0.03mol) was refluxed on water bath for about 24 hr. The progress of the reaction was checked by TLC using methanol-benzene (2:8) ratio as an eluent. After completion of the reaction, it was cooled and neutralized with aqueous standard solution of
sodium bicarbonate (NaHCO₃) and water successively and purified by column chromatography to give compound (6.052-6.054).

**Microwave assisted method**

A mixture of substituted benzylidene derivatives 0.18g (0.429mol) dissolved in dry benzene (10ml) with thioglycolic acid 0.276g (0.03mol), was placed in a 100 ml borosil flask with ice fitted with a funnel as a loose top. The reaction mixture was subjected to microwave irradiation, at 20% (360W) microwave power for 10-15 min, overheating of the solution had to be avoided. The completion of the reaction was checked by TLC and UV. The reaction mixture was cooled and the resulting solid was filtered, washed with ethanol dried and recrystallized from ethanol to give compound (6.052-6.054) yield 40.55%. **Scheme -6.12**

3. 2-(4-substituted benzylidene)-4-(4-[7-chloroquinolin-4-ylamine] butyl) 1,6-dithia-4,9-diazaspiro [4,4]nonane-3,8-dione (6.055-6.057)

A mixture of substituted benzylidene derivatives (5.053-6.055) 0.24g (0.487mol) dissolved in dry benzene (10ml) with thioglycolic acid 0.276g (0.03mol) was refluxed on water bath for about 24 hr. The progress of the reaction was checked by TLC using methanol-benzene (2:8) as an eluent. After completion of the reaction, it was cooled and neutralized with aqueous standard solution of sodium bicarbonate (NaHCO₃) and water successively and purified by column chromatography. **(Scheme-6.12)**

4. 2-(4- substituted benzylidene)-4-(6-[7-chloroquinolin-4-ylamine] hexyl) 1,6-dithia-4,9-diazaspiro [4,4]nonane-3,8-dione (6.058-6.060)

A mixture of substituted benzylidene derivatives (5.056-5.058) 0.25g (0.496mol) dissolved in dry benzene (10ml) with thioglycolic acid 0.276g (0.03mol) was refluxed on water bath for about 24 hr. The progress of the reaction was checked by TLC using methanol-benzene (2:8) as an eluent. After completion of the reaction, it was cooled and neutralized with aqueous standard solution of sodium bicarbonate (NaHCO₃) and water successively and purified by column chromatography to give compound (6.058-6.060).
Microwave assisted method

A mixture of substituted benzylidene derivatives 0.18g (0.429mol) dissolved in dry benzene (10ml) with thioglycolic acid 0.276g (0.03mol), was placed in a 100 ml borosil flask with ice fitted with a funnel as a loose top. The reaction mixture was subjected to microwave irradiation, at 20% (360 W) microwave power for 10-15 min, overheating of the solution had to be avoided. The completion of the reaction was checked by TLC and UV. The reaction mixture was cooled and the resulting solid was filtered, washed with ethanol dried and recrystallized from ethanol to give compound (6.058-6.060) yield 40.55%.
Chart 6.1-$^1$HNMR spectra of compound no. 6.049

Chart 6.2-MS spectra of compound no. 6.049
Chart 6.3-\textsuperscript{13}CNMR spectra of compound no. 6.049

Chart 6.4-\textsuperscript{1}HNMR spectra of compound no. 6.050
Chart 6.5-^1^HNMR spectra of compound no. 6.051

Chart 6.6-^13^CNMR spectra of compound no. 6.051
Chart 6.7- $^1$HNMR spectra of compound no. 6.052

Chart 6.8- IR spectra of compound no. 6.054
Chart 6.9-$^1$HNMR spectra of compound no. 6.054

Chart 6.10-IR spectra of compound no. 6.056
Chart 6.11-$^1$HNMR spectra of compound no. 6.056

Chart 6.12-IR spectra of compound no. 6.057
Synthesis of Spiro-thiazolidinone derivatives

Chart 6.13 - Mass spectra of compound no. 6.057

Chart 6.14 - $^{13}$CNMR spectra of compound no. 6.057
Chart 6.15-\textsuperscript{1}HNMR spectra of compound no. 6.060

Chart 6.16-\textsuperscript{13}CNMR spectra of compound no. 6.060
6.9 References


39. Pawar, M. J., Burungale, A. B., Karale, B. K., Synthesis and antimicrobial activity of spiro(chromeno[4,3-d][1,2,3]thiadiazole-4,1'-cyclohexanes),
spiro(chromeno-[4,3-d][1,2,3]-selenadiazole-4,1'-cyclohexanes) and (spiro-
chroman-2,1'-cyclohexan-4-one)-5-spiro-4-acetyl-2-(acetylamino)-\(\Delta 2\)-1,3,4-

40. Thadhaney, B., Sain, D., Pernawat, G., Talesara, G. L., Synthesis and 
antimicrobial evaluation of ethoxyphthalimide derived from spiro[indole-
3,5'-(1,3)thiazole(4,5-c)isoxazol]-2(1H)-ones via ring closure metathesis, 

41. Hejiao, H., Huijuan, G., Erwei, L., Xingzhong, L., Yuguang, Z., Yongsheng, 
C., Decaspirones F-I, bioactive secondary metabolites from the saprophytic 

42. Pai, N. R., Suryanvansi, J. P., Synthesis and antibacterial screening of N-
[Naphtho[1,2-b]pyrano[3,4-d]thiazol-8-yl]spiroindoloazetidin-2 

43. Talesara, G. L., Thadhaney, B., Sain, D., Pemawat, G., Synthesis and 
antimicrobial evalution of ethoxyphthalimide derivatized spiro (indole-3, 5-
(1, 3) thiazolo (4, 5-C) isoxazol]-2 (1H)-ones via ring closure metathesis, 

44. Kumar, A., Kaur, H., Kumar, S., Synthesis, Antipsychotic and 
Anticonvulsant Activity of some new pyrazolinyl/isoxazolylindol-2-ones, 

45. Singh, G. S., Singh, T., Lakhan, R., Synthesis 13C-NMR and anticonvulsant 
951-954.

46. Mana, S., Sharma, N. K., Pahari, N., Priyanka, Synthesis and 
characterization of novel thiazolo-isoxazole fused isatin as analgesic and 

47. Behera, R. K., Behera, A. K., Pradhan, R., and Patra, M., Studies on spiro 
heterocycles part-I: Installation of biologically active heterocyclic nuclei into 
spiro compounds derived from cyclohexanone and biphenyl thioborbituric 


