2.1 INTRODUCTION

The heterocyclic systems with several atoms, ones considered as chemical oddities, are today just as easily obtained as five and six membered analogues and these compounds no longer remain the esoteric species, they were once considered to be. Hence, the pace of research and development in this area is witnessing immense acceleration due to the substantial advancement in the synthetic art that has been made in this field in the last few decades. As a result of that there seems to be virtually no limit to the number of interesting ring system that can be created in the laboratory today by the combination of initiative and perseverance. The vast commercial success of these medicinal agents and their benefits to society in the modern treatment of mental illnesses and other wide variety of disease have caused the chemistry of these systems to evolve in to a major area of research in the field of heterocyclic chemistry.

The heterocyclic compounds containing nitrogen have expanded exponentially in the past decades due to their unique physical properties, specific chemical reactivity and their remarkable potential biological activities.

It has been mentioned in chapter 1, that 4-thiazolidinone shows a varying degree of reactivity of its carbonyl group towards nucleophilic reagent and this property has been extensively used in the literature, in the synthesis of a wide variety of heterocyclic compounds of medicinal interest. Condensed heterocyclic systems containing the quinoline moieties have attracted the attention of the chemists owing to these nuclei having been identified in the literature as the most promising pharmacophores in drug design and synthesis. It has been observed that incorporation of certain bioactive pharmacophores in the existing drug molecules sometimes exert a profound influence on the biological profile of that molecule. With this idea in mind the aim in the present work has been to focus research on the synthesis of newer series of quinoline derivatives.

2.2 SYNTHETIC ASPECTS OF QUINOLINE

The structural core of quinoline has generally been synthesized by various classical named reactions such as Skraup, Daebner-Von Miller, friendlander,
pfitzinger, Cornard-Limpach, Combes, Paal-knorr, frequently used for the preparation of quinoline scaffold.

2.2.1 **Borsche synthesis**

The substituted quinolines have been obtained by the treatment of substituted ketones with (E)-N-(2-nitrobenzaldehyde)-4-methylbenzeneamine (scheme-2.1).

\[
\begin{align*}
\text{NO}_2 & \quad \text{NH}_2 \\
\text{CH}_3 & \quad \text{R}_1 \\
\text{R}_2 & \quad \text{R}_1 \\
\text{R}_2 & \quad \text{X} \\
\end{align*}
\]

Borsche synthesis

\[
\begin{align*}
\text{NO}_2 & \quad \text{NH}_2 \\
\text{R}_1 & \quad \text{R}_2 \\
\text{R}_1 & \quad \text{X} \\
\end{align*}
\]

Scheme-2.1

2.2.2 **Friedlander synthesis**

Friedlander synthesis of quinoline derivatives involves the condensation of substituted ketones with 1-(2-aminophenyl) ethanone (Scheme-2.1)

\[
\begin{align*}
\text{NO}_2 & \quad \text{NH}_2 \\
\text{R}_1 & \quad \text{R}_2 \\
\text{R}_1 & \quad \text{X} \\
\end{align*}
\]

Friedlander synthesis

\[
\begin{align*}
\text{NO}_2 & \quad \text{NH}_2 \\
\text{R}_1 & \quad \text{R}_2 \\
\text{R}_1 & \quad \text{X} \\
\end{align*}
\]

Niemantowski synthesis

\[
\begin{align*}
\text{R}_1 & \quad \text{R}_2 \\
\end{align*}
\]

Pfitzinger synthesis

2.2.3 **Niemantowski synthesis**

Substituted ketones reacted with 2-aminobenzoic acid and gave quinoline derivatives in this synthesis (Scheme-2.1).

2.2.4 **Pfitzinger reaction**

Pfitzinger synthesis offers an efficient route for the synthesis of quinoline derivatives. This reaction involves the condensation of substituted isatin with substituted ketone in presence of potassium hydroxide (Scheme-2.1).
2.2.5 Skraup synthesis

It is a version of the process in which glycerol is used. Glycerol reacts with aniline convert to acrolein under the strong acid condition used for the reaction (Scheme-2.2).

\[
\text{Scheme-2.2}
\]

2.2.6 Doebner-Von Miller synthesis

The most common method of preparing quinolines by condensing conjugated carbonyl derivatives with anilines in the presence of strong acid. This process most likely proceeds by conjugate addition of the amine to the unsaturated carbonyl compounds followed by electrophilic attack of the protonated carbonyl on the aromatic ring. The resulting 1, 2-dihydroquinoline is usually converted to quinoline during the course of the reaction by nitrobenzene which is commonly employed as the solvent, can act as the oxidizing agent (Scheme-2.3).

\[
\text{Scheme-2.3}
\]

2.2.7 Conrad-limpach synthesis

Condensation between beta ketonic ester and primary aromatic amines produces quinoline the nature of the product depending on condition e.g. aniline and ethylacetoxacetate react to give (Scheme-2.4).

\[
\text{Scheme-2.4}
\]
2.2.8 Knorr quinoline synthesis

Microwave assisted condensation between aniline $2.007$ and ethylacetoacetate $2.012$ with para-toluene-sulphonic acid as a catalysed, afforded a colourless solid, which was assigned as 4-methyl-2-hydroxyquinoline $2.014$ (Scheme-2.5).

$$\text{NH}_2 + \text{O} \quad \text{CH}_3 \quad \text{O} \quad \text{CH}_3 \quad \text{O} \quad \text{Et}$$

$$\text{N} \quad \text{O} \quad \text{CONHR}$$

Scheme-2.5

2.2.9 Microwave-assisted synthesis of quinoline

Solvent free one-pot synthesis of quinoline $2.017$ was achieved from ortho-nitrobenzaldehyde $2.015$ and enolizable ketones $2.016$ using SnCl$_2$.2H$_2$O by subjecting them to microwaves$^{17}$ (Scheme-2.6).

$$\text{O} \quad \text{CHO} \quad \text{NO}_2 \quad \text{SnCl}_2 \cdot 2\text{H}_2\text{O} \quad \text{MW}$$

Scheme-2.6

Jain and coworkers$^{18}$ synthesized the 3-acylamino-2-oxo-1, 2-dihydroquinoline-4-carboxamides $2.020$ by the reaction of isatin $2.005$ with acylaminoacids $2.018$ and isocyanate $2.019$ (Scheme-2.7).

$$\text{CONHR} \quad \text{NHCOAr}$$

Scheme-2.7

The method used for synthesizing the quinoline $2.023$ derivatives by pfitzinger reaction can be generalized as involving condensation in alkaline medium of an isatin to give 2-(2-aminophenyl)-2-oxoacetic acid $2.021$ with a ketone of the general formula RCOCH$_2$R $2.022$ (Scheme-2.8).
2.3 BIOLOGICAL ASPECTS OF QUINOLINE

Heterocyclic compounds containing one or two heteroatoms fused to quinoline ring are found in natural as well as in the synthetic compounds of biological interest\textsuperscript{19}. They are known to exhibit antiallergic\textsuperscript{20}, antifungal\textsuperscript{21-24}, hypocholesterolemic\textsuperscript{25}, antibacterial\textsuperscript{26}, hypolipidimic\textsuperscript{27}, and antiviral activities. Thienoquinolines and benzothienoquinoline have been shown to exhibit antimicrobial, antiviral, hypercholesterolemic, hypolipidimic and antifungal activities\textsuperscript{28-29}.

Quinoline moiety is present in many classes of biologically active compounds. A number of them have been clinically used as antibacterial, antifungal and antiprotozoic drugs\textsuperscript{30-31} as well as antituberculostatic agents\textsuperscript{32-33}. Some quinoline based compounds also shown antineoplastics activity\textsuperscript{34}. Styrylquinoline derivatives have gained strong attention recently due to their activity as perspective HIV integrase inhibitors\textsuperscript{35-37}.

The in vitro activity of ciprofloxacin was compared with various bacterial species as carbenicillin, azlocillin, ceftrulodin ceftazidine, tobramycin and amikacin in which ciprofloxacin found to have best activity against flavobacterium\textsuperscript{38}.

Substituted quinoline carboxylic acid was used to treat tumor against L1210 leukemia and B16 melanoma in the National Cancer Institute\textsuperscript{39}.

Pfolexacin and ciprofloxacin are two new quinoline carboxylic acid derivatives shown in vitro activity against a wide range of gram positive bacteria including pseudomonas aeruginosa.
Quinoline derivatives represent the major class of heterocyclic compounds and a number of preparations have been known since the late 1800s. The quinoline ring system occurs in various natural products, especially in alkaloids. The quinoline skeleton (2.024-2.30) is obtained used for the design of many pharmacological properties (Fig-2.1).

Axten et. al. have reported the preparation of quinolines (2.031) and screening of these synthesized derivatives showed a minimum inhibitory against bacteria. (Fig-2.2)

Synthesis of Indolequinolones, triazoloindoloquinolines, and its derivatives (2.032) have been given by Mulwad and Lohar (2003). Some of these compounds have been screened for antibacterial activity against both gram positive and gram negative bacteria. Among all the screened quinoline congeners the following congeners showed better efficacy in comparison to cephalosporin as standard drug. (Fig-2.3)
Liu et al.\textsuperscript{42} prepared substituted quinoline carboxylic acid derivatives (2.033) and evaluated them for antibacterial activity against \textit{S. aureus}, \textit{E. coli} and \textit{P. aeruginosa}. (Fig-2.4)

Preparations of 4(1H)-quinolone -3-carboxylic acid derivatives (2.034) as antimicrobial agents have been reported by Chen et al.\textsuperscript{43}. (Fig-2.5)

Takemura et al.\textsuperscript{44} reported the 1, 4-dihydro-4-oxoquinoline-3-carboxylic acid derivatives (2.035, 2.036) and evaluated them for potent antimicrobial agents. (Fig-2.6)
Synthesis of N-(7-Chloroquinolin-4-yl) substituted

Quinolines as antibacterial agents (2.037) have been reported by Sarvanan et al. (Fig-2.7)

Synthesis and pharmacological properties of substituted hydrazides of 2-chloro-5,6,7,8-tetrahydroquinoline-4-carboxylic acids (2.038) have been reported by Madapa et al. (Fig-2.8)

Preparation of quinolonecarboxylates (2.039) as antibacterial agents was given by Peterson et al. (Fig-2.9)
Maruyama et. al.\textsuperscript{48} have synthesized quinoline derivatives (2.040) and evaluated them for as antibacterial agent. (Fig-2.10)

![Fig-2.10](image)

Bahuguna et. al.\textsuperscript{49} synthesized substituted arylsulfonylbenzo [f] quinolines (2.041) and screened them for biological activity against gram positive and gram negative bacteria. (Fig-2.11)

![Fig-2.11](image)

Hiremath et. al.\textsuperscript{50} synthesized 5H and 6H evaluated 7H-indolo[2,3-c] isoquinoline-5- thiones (2.042) for antibacterial and antifungal activities. (Fig-2.12)

![Fig-2.12](image)

8-Ethynyl and 8-vinlyquinolonecarboxylates (2.043) have been synthesized by Peterson et. al.\textsuperscript{51}. Quinoline derivatives were found to posses antibacterial activity. (Fig-2.13)

![Fig-2.13](image)
Martynovskii et al.\textsuperscript{52} have prepared quinolines (2.044) and screened them for antibacterial activity. (Fig-2.14)

![Fig-2.14](image)

Synthesis of 6, 7-Dialkoxy-2, 2diakyl-3-hydroxy, ethyl-2,3,4-tetrahydroxyquinoline derivatives (2.045) have been reported by Dibyendu Benerjee et al.\textsuperscript{53}. The Synthesized compounds were evaluated for antibacterial activity. (Fig-2.15)

![Fig-2.15](image)

Quinolines (2.046) as antibacterial agents have also been reported by Bray\textsuperscript{54}. (Fig-2.16)

![Fig-2.16](image)

Lefevre et al.\textsuperscript{55} claimed substituted bridged-diazobicycloalkyl quinolone carboxylic acids (2.047) as bactericides. (Fig-2.17)

![Fig-2.17](image)
Quinoline bases (2.048) possessing potential bactericidal activity have been reported by Vurbanova and Chervenkov\textsuperscript{56}. (Fig-2.18)

![Fig-2.18](image)

Chauhan \textit{et. al.}\textsuperscript{57} have synthesized biologically active substituted chloroquinolines (2.049). (Fig-2.19)

![Fig-2.19](image)

Substituted oxoquinoline-3-carboxylic acid derivatives (2.050) was put forward by Uno \textit{et. al.}\textsuperscript{58}. They reported antibacterial activity in these derivatives. (Fig-2.20)

![Fig-2.20](image)

Antimicrobial activities in benzo heterocyclic compounds (2.051) were reported by Ishikawa \textit{et. al.}\textsuperscript{59} (1987) and found inhibitory action against \textit{E. coli}. (Fig-2.21)

![Fig-2.21](image)
Oettiger et al.\textsuperscript{60} reported Mannich bases from nitroxoline (2.052). Which were screened for bactericidal activity. (Fig-2.22)

\begin{center}
\includegraphics[width=0.3\textwidth]{fig22}
\end{center}

Fig-2.22

8-Hydroxyquinolines (2.053) were prepared by Betageri, V. S. et al.\textsuperscript{61} which was found as potent antibacterial agent. (Fig-2.23)

\begin{center}
\includegraphics[width=0.3\textwidth]{fig23}
\end{center}

Fig-2.23

Synthesis of 2,3-Dihydrofuro [3,2-c] quinolines (2.054) have been prepared by Vaidya et al.\textsuperscript{62}. These compound was found as potent antibacterial agent. (Fig-2.24)

\begin{center}
\includegraphics[width=0.3\textwidth]{fig24}
\end{center}

Fig-2.24

Antibacterial activities of quinoline derivatives (2.055) proposed by Balenkaya et al.\textsuperscript{63}. (Fig-2.25)

\begin{center}
\includegraphics[width=0.3\textwidth]{fig25}
\end{center}

Fig-2.25
Agui et. al.\textsuperscript{64} have synthesized quinoline derivatives (2.056) and evaluated them for antimicrobial activities. (Fig-2.26)

![Fig-2.26](image1)

8,9-dihydro-7H-cyclopenta (h) quinolines (2.057) were prepared by Rhomberg et. al.\textsuperscript{65} (1994) and found useful as antimicrobial agents. (Fig-2.27)

![Fig-2.27](image2)

Kidwai\textsuperscript{66} have synthesized Indo-Hydroxyl quinoline derivative (2.058) and screened them against a wide range of pathogenic bacteria. (Fig-2.28)

![Fig-2.28](image3)

Synthesis of quinaldinium azomethine (2.059) and their biological properties such as antibacterial, antifungal were given by Shinohara et. al.\textsuperscript{67}. (Fig-2.29)

![Fig-2.29](image4)
Adolf H.\textsuperscript{68} has reported bactericidal fungicidal activities in quinoline derivates (2.060). (Fig-2.30).

![Fig-2.30]

10-Methoxy-1,2-methylenedioxy-7-oxo-dibenzo quinoline and 9-methoxy-1,2-methylenedioxy-7-oxodibenzo quinolines (2.061) have prepared by Govindachari \textit{et. al.}\textsuperscript{69} (1970), and these compounds showed antibacterial, anti-inflammatory and antifungal activities etc. (Fig-2.31)

![Fig-2.31]

Quinoline is an important structural feature in the antimalarial drugs. For instant quinine (2.062) is the well known antimalarial drug, which was earlier, obtained from cinchona barks (\textit{Solanum Xanthocarpum}) is a quinoline derivative and a natural alkaloid. It is not to mention that the drug had relieved more human suffering than any other drug in history. While it’s optical isomer quinoline is both more potent as an antimalarial and more toxic than quinine\textsuperscript{70}. (Fig-2.32)

![Fig-2.32]
Other quinoline based antimalarial drugs include chloroquine (2.063), pamaquine (2.064) and primaquine (2.065) which are readily available in the market. In addition to its antimalarial activity, chloroquine is effective in preventing the relapses of malaria\(^71\). Similar to pamaquine, primaquine destroys late hepatic stages and latent tissue forms of *plasmodium vivax* and *plasmodium ovale* and therefore is of great clinical value. (Fig-2.33-34)

![Fig-2.33](image)

Radical curve of vivax or ovale malarias can be achieved if the drugs is given either during the long-term latent period of infection or during an acute attack.

![Fig-2.34](image)

Numerous useful antibacterial drugs developed during the last four decades contain 4-quinolones-3-carboxylic acid moiety. For instance nalidixic acid (2.005), which is a none-fluorinated quinolones, is effective against most of the gram negative bacteria that commonly cause urinary tract infection\(^72\). (Fig-2.35)

![Fig-2.35](image)
Nalidixic acid is rapidly absorbed, extensively metabolized, and rapidly excreted after oral administration. Introduction of first fluorinate quinolones, norfloxacin (2.006) have been rapidly followed by new member of this class such as ciprofloxacin (2.007), ofloxacin (2.008) and lomefloxacin (2.009), which are effective against a large variety of gram-negative organisms. (Fig-2.36)

Norfloxacin (2.006) has broad-spectrum activity against both gram-negative (including *psuedomonas aeruginosa*) and gram-positive organism in treating various urinary tract infections. Ciprofloxacin (2.007) is used in the treatment of pseudomonas infections associated with cystic fibrosis for combating infections of the skins, soft tissues, bones and joints. (Fig-2.37)

Ofloxacin (2.069) resembles ciprofloxacin in its antibacterial spectrum and potency. It is primarily used in the treatment of prostatitis due to *Escherichia coli* and sexually transmitted disease with exception of syphilis. Lomefloxacin (2.070) is useful in the treatment of urinary tract infections in addition to bronchitis. (Fig-2.38)
Quinoline nucleus is an important structural moiety in a number of complex chemotherapeutic agents. Substituted quinoline and their benzo and hetero fused analogues signify an important class of heterocyclic compounds because their analogues have a wide variety of medicinal properties including antitumour, antiviral and antibacterial activities. Quinoline also exhibit antitumour activity due to the formation of highly stable complex with DNA molecule.

Greatly encouraged by such a concept of drug design and synthesis of quinoline derivatives, it is aimed in the present work to synthesize some novel quinoline derivatives. The quinoline molecule has been selected with this idea in mind, that this molecule is biologically highly active. Several derivatives of the quinoline have been prepared in the literature in search of newer physiologically active materials from this nucleus. If their role to produce a positive impact on activity is established, such structures are likely to form interesting targets in synthesis and in biological evaluations. To test this hypothesis a series of novel compounds (Scheme-2.9) have been synthesized. While formulating this scheme of work, we envisioned that our proposed synthetic plan has to be such that requisite functionalities have to be present on appropriate positions for their elaboration to the desired heterocyclic scaffolds from this molecule. The strategies outlined in Scheme-2.9 have been designed in such a way so as to fit to this requirement.

2.4 Present work

In view of impressive synthetic application of 4, 7-dichloroquinoline in heterocyclic synthesis as discussed above in this chapter, it was considered worthwhile in the present work to prepare quinoline derivatives by employing the strategy shown in scheme-2.9. 4, 7-dichloroquinoline was used as a precursor in synthesis of compounds (2.072, 2.073, 2.074 and 2.075). (Scheme-2.9)

2.5 Results and discussion

In view of the impressive biological activities shown by quinoline, it was thought of interest in the present work to develop a system, which carried quinoline molecule incorporated with substituted diamines. The idea behind building such a system was to examine the effect of each other in the biological activities of these
well established molecule, when present together a single framework. To test this hypothesis the quinoline derivatives (2.072-2.075) were required to be obtained by the applying 4, 7-dichloroquinoline with substituted diamines refluxed in distilled ethanol. (Scheme-2.9)

Scheme of the proposed work

Structures of compounds whose synthesis have been described in this chapter.
Table 2.1: conditions used for the synthesis of quinoline with diamines

<table>
<thead>
<tr>
<th>S. No.</th>
<th>4,7-dichloroquinoline (g) and mol</th>
<th>Substituted diamines (g) and mol</th>
<th>Solvent (ml)</th>
<th>Temp. (°C)</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>2.97g (0.59mol) 0.720g (.05mol)</td>
<td>30ml</td>
<td>79-80</td>
<td>8h</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>2.97g(0.59mol) 0.89g (.07mol)</td>
<td>30ml</td>
<td>79-80</td>
<td>8h</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>2.97g(0.59mol) 1.06g (.09mol)</td>
<td>30ml</td>
<td>79-80</td>
<td>7h</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>2.97g(0.59mol) 1.3g (.15mol)</td>
<td>30ml</td>
<td>79-80</td>
<td>10h</td>
<td></td>
</tr>
</tbody>
</table>

Table 2.2: Physical and analytical data of the compounds

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Compound</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>2.072</td>
<td>221</td>
<td>C₁₁H₁₂ClN₃</td>
<td>111-112</td>
<td>50</td>
<td>N 18.95/18.89 C 59.60/59.50</td>
</tr>
<tr>
<td>2.</td>
<td>2.073</td>
<td>235</td>
<td>C₁₂H₁₄ClN₃</td>
<td>97-98</td>
<td>55</td>
<td>N 17.83/17.82 C 61.15/61.09</td>
</tr>
<tr>
<td>3.</td>
<td>2.074</td>
<td>249</td>
<td>C₁₃H₁₆ClN₄</td>
<td>98-99</td>
<td>55</td>
<td>N 6.83/16.76 C 62.52/62.48</td>
</tr>
<tr>
<td>4.</td>
<td>2.075</td>
<td>277</td>
<td>C₁₅H₂₀ClN₃</td>
<td>99-100</td>
<td>50</td>
<td>N 15.13/15.07 C 64.85/64.78</td>
</tr>
</tbody>
</table>

Table 2.3: Spectral data of compounds

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Compound</th>
<th>IR (KBr) cm⁻¹</th>
<th>¹HNMR (CDCl₃) δ ppm &amp; MS m/z (% relative abundance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>2.072</td>
<td>3325, 3200 (NH str.), 3048, 2999 (C-H str.), 1510 (NH str.), 1465 (C-H bend), 1350 (C-N str.), 776 (C-Cl str.)</td>
<td>8.6 (1H, d, CH), 8.0 (1H, s, CH), 7.4 (1H, d, CH), 7.2 (1H, d, CH), 6.3 (1H, d, CH), 4.0 (1H, s, NH), 2.8-3.34 (4H, m, CH₂), 2.3 (2H, s, NH₂). M/Z : 223 (32.01%), 221 (100.0%), 222 (12.0 %).</td>
</tr>
<tr>
<td>2.</td>
<td>2.073</td>
<td>3272, 3070 (NH str.), 2968, 2905 (C-H str.), 1552 (NH str.), 1485 (C-H bend), 1290 (C-N str.), 769 (C-Cl str.)</td>
<td>8.9 (1H, d CH), 8.0 (1H, s, CH), 7.8 (1H, d, CH), 7.4 (1H, d, CH), 6.4 (1H, d, CH), 4.2 (1H, s, NH), 2.3 (2H, s, NH₂), 1.7-3.4 (6H, m, CH₂). M/Z : 237 (32.08%), 235 (100.0%), 236 (13.9 %).</td>
</tr>
<tr>
<td>3.</td>
<td>2.074</td>
<td>3272, 3049 (NH str.), 2935, 2860 (C-H str.), 1548 (NH str.), 1481 (C-H bend), 1288 (C-N str.), 763 (C-Cl str.)</td>
<td>8.8 (1H, d, CH), 8.6 (1H, s, CH), 8.0 (1H, d, CH), 7.4 (1H, d, CH), 7.3 (1H, d, CH), 4.3 (1H, s, NH), 3.7-3.5 (8H, m, CH₂), 2.3 (2H, s, NH₂). M/Z : 251 (32.10%), 249 (100.0%).</td>
</tr>
<tr>
<td>4.</td>
<td>2.075</td>
<td>3457, 3225 (NH str.), 3150, 2928 (C-H str.), 1485 (C-H bend), 1559 (NH), 1200 (C-N str.), 786 (C-Cl str.)</td>
<td>8.1 (1H, d, CH), 8.1 (1H, s, CH), 7.8 (1H, d, CH), 7.4 (1H, d, CH), 6.0 (1H, d, CH), 4.9 (1H, s, NH), 2.4 (2H, s, NH₂), 1.5-3.7 (12H, m, CH₂). M/Z : 279 (32.1%), 277 (100.0%), 278 (16.5 %).</td>
</tr>
</tbody>
</table>
2.6 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, $^1$HNMR and MS 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 MS spectral data of all the compounds are given in Table-2.1, Table-2.2 and Table-2.3 and the spectral graphs are presented in the form of charts-2.1-2.8 at the end of this chapter.

2.5.1 Interpretation of spectral data of compounds (2.072)

Infrared Spectra

Infrared spectrum of compound 2.072 using KBr standard exhibited two strong absorption band at 3325, 3200 cm$^{-1}$ (NH str.), 3048, 2999 cm$^{-1}$ (aromatic ring, C-H str.). Appearance of peak 1510 cm$^{-1}$ (NH str.) for secondary amine, and 1350 (C-N str.), 776 (C-Cl str.). Appearance of peak at 3325, 3200 cm$^{-1}$ for primary amine and peak at 1510 cm$^{-1}$ for secondary amine indication for the formation of compound 2.072.

$^1$HNMR Spectrum

$^1$HNMR spectrum of compound 2.072 at 300 MHz in CDCl$_3$ displayed characteristic signals for the presence of 12 protons of which 9 protons were bound to carbon atom, and 3 protons bound to the nitrogen atom. Appearance of four doublets for 4H at $\delta$ 8.6, $\delta$ 7.4, $\delta$ 7.2 and $\delta$ 6.3 were attributed to (CH) protons of quinoline ring. The presence of one singlet which appeared at $\delta$ 8.0 was attributed C$_8$ aromatic proton (Meta to the chlorine function in the benzene ring at C$_7$). Appearance of a singlet for 1H at $\delta$ 4.0 was assigned to aliphatic (NH) group attached to the quinoline chain and a singlet at $\delta$ 2.3 was assigned for NH$_2$ group. A multiplet signal for 4H at $\delta$ 1.8-2.3 was assigned to (CH$_2$) protons of aliphatic ring.
Interpretation of spectral data of compounds (2.073)

Infrared Spectra

Infrared spectrum of compound 2.073 using KBr standard exhibited two strong absorption band at 3272, 3070 cm\(^{-1}\) (NH str.), 2968, 2905 cm\(^{-1}\) (aromatic ring, C-H str.). Appearance of peak 1552 cm\(^{-1}\) (NH str.) for secondary amine, and 1485 cm\(^{-1}\) (CH ben.), 1290 cm\(^{-1}\) (C-N str.), 769 cm\(^{-1}\) (C-Cl str.). Appearance of peak at 3325, 3200 cm\(^{-1}\) for primary amine and a peak at 1510 cm\(^{-1}\) for secondary amine indication for the formation of compound 2.073.

\(^1\)HMNR Spectrum

\(^1\)HNMR spectrum of compound 2.073 at 300 MHz in CDCl\(_3\) displayed characteristic signals for the presence of 14 protons of which 11 protons were bound to carbon atom, and 3 protons bound to the nitrogen atom. Appearance of four doublets for 4H at \(\delta\ 8.9,\ 7.8,\ 7.4\) and \(\delta\ 6.4\) was attributed to (CH) protons of quinoline ring. The presence of one singlet which appeared at \(\delta\ 8.0\) was attributed C\(_8\) aromatic proton (Meta to the chlorine function in the benzene ring at C\(_7\)). Appearance of a singlet for 1H at \(\delta\ 4.2\) was assigned to aliphatic (NH) group attached to the quinoline chain and a singlet at \(\delta\ 2.3\) was assigned for NH\(_2\) group. A multiplet signal for 6H at \(\delta\ 1.7-3.4\) was assigned to (CH\(_2\)) protons of aliphatic ring.

Interpretation of spectral data of compounds (2.074)

Infrared Spectra

Infrared spectrum of compound 2.074 using KBr standard exhibited two strong absorption band at 3272, 3049 cm\(^{-1}\) (NH str.), 2935, 2860 cm\(^{-1}\) (aromatic ring, C-H str.). Appearance of peak 1548 cm\(^{-1}\) (NH str.) for secondary amine, and 1481 cm\(^{-1}\) (CH ben.), 1288 cm\(^{-1}\) (C-N str.), 763 cm\(^{-1}\) (C-Cl str.). Appearance of peak at 3272, 3049 cm\(^{-1}\) for primary amine and a peak at 1548 cm\(^{-1}\) for secondary amine indication for the formation of compound 2.074.

\(^1\)HMNR Spectrum

\(^1\)HNMR spectrum of compound 2.074 at 300 MHz in CDCl\(_3\) displayed characteristic signals for the presence of 16 protons of which 13 protons were bound to carbon atom, and 3 protons bound to the nitrogen atom. Appearance of a doublet
for 1H at δ 8.8, δ 8.6, δ 7.4 and δ 7.3 were attributed to (CH) protons of quinoline ring. The presence of one singlet which appeared at δ 8.0 was attributed C₈ aromatic proton (Meta to the chlorine function in the benzene ring at C₇). Appearance of a singlet for 1H at δ 4.3 was assigned to aliphatic (NH) group attached to the quinoline chain and a singlet at δ 2.3 was assigned for NH₂ group. A multiplet signal for 8H at δ 3.7-3.5 was assigned to (CH₂) protons of aliphatic ring.

**Interpretation of spectral data of compounds (2.075)**

**Infrared Spectra**

Infrared spectrum of compound 2.075 using KBr standard exhibited two strong absorption band at 3457, 3225 cm⁻¹ (NH str.), 3150, 2928 cm⁻¹ (aromatic ring, C-H str.). Appearance of peak 1559 cm⁻¹ (NH str.) for secondary amine, and 1485 cm⁻¹ (CH ben.), 1200 cm⁻¹ (C-N str.), 786 cm⁻¹ (C-Cl str.). Appearance of peak at 3457, 3225 cm⁻¹ for primary amine and a peak at 1559 cm⁻¹ for secondary amine indication for the formation of compound 2.075.

**¹H NMR Spectrum**

¹H NMR spectrum of compound 2.075 at 300 MHz in CDCl₃ displayed characteristic signals for the presence of 20 protons of which 17 protons were bound to carbon atom, and 3 protons bound to the nitrogen atom. Appearance of a doublet for 1H at δ 8.1, δ 7.8, δ 7.4 and δ 6.0 were attributed to (CH) protons of quinoline ring. The presence of one singlet which appeared at δ 8.0 was attributed C₈ aromatic proton (Meta to the chlorine function in the benzene ring at C₇). Appearance of a singlet for 1H at δ 4.9 was assigned to aliphatic (NH) group attached to the quinoline chain and a singlet at δ 2.5 was assigned for NH₂ group. A multiplet signal for 12H at δ 1.5-3.7 was assigned to (CH₂) protons of aliphatic ring.

MS spectral data also provided the evidence for the formation of compounds 2.072-2.075.
Synthesis of N (7-Chloroquinolin-4-yl) substituted

2.7 Mechanism of formation of compounds (2.072-2.075).

\[ \text{N} \begin{array}{c} \text{Cl} \\ Cl \end{array} \text{N} \begin{array}{c} \text{Cl} \\ \text{Cl} \end{array} + \text{NH}_2(\text{CH}_2)_n\text{NH}_2 \xrightarrow{\text{dist. ethanol}} \text{NH}_2(\text{CH}_2)_n\text{NH}_2^{-}\text{HCl} \]

n=1, 2-diamino ethane
n=1, 3-diamino proane
n=1, 4-diamino butane
n=1, 6-diamino hexane

2.8 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 Spectral data for all compounds are given Table 2.1, Table 2.2 and Table 2.3.
7. 4, 7-dichloroquinoline was used in the synthesis without further purification.

2.8.1 Synthetic procedure
1. Preparation of N-(7-Chloroquinolin-4-yl) ethane-1, 2-diamine (2.072)

A mixture of 2.97g (0.59mol) 4,7-dichloroquinoline (2.071), 0.89g (0.07mole) of 1-2-diaminoethane was dissolve in 30 ml ethanol in a 250 ml round bottom flask and refluxed for 8h., the solid obtained was extracted with DCM in presence of brine solution. Organic layer was separated and dried with Na$_2$SO$_4$. The solvent was evaporated under reduced pressure, and the resultant solid obtained. The solid obtained was recrystelized from EtOH. (Scheme-2.9)
2. Preparation of N-(7-Chloroquinolin-4-yl) propane-1, 3-diamine (2.073)

A mixture of 2.97 g (0.59 mol) 4,7-dichloroquinoline (2.071), 0.89 g (0.07 mole) of 1-2-diaminopropane was dissolved in 30 ml ethanol in a 250 ml round bottom flask and refluxed for 8 h., the solid obtained was extracted with DCM in presence of brine solution. Organic layer was separated and dried with Na$_2$SO$_4$. The solvent was evaporated under reduced pressure, and the resultant solid obtained. The solid obtained was recrystallized from EtOH. (Scheme-2.9)

3. Preparation of N-(7-Chloroquinolin-4-yl) butane-1, 4-diamine (2.074)

A mixture of 2.97 g (0.59 mol) 4,7-dichloroquinoline (2.071), 1.06 g (0.09 mole) of 1-2-diaminobutane was dissolved in 30 ml ethanol in a 250 ml round bottom flask and refluxed for 7 h., the solid obtained was extracted with DCM in presence of brine solution. Organic layer was separated and dried with Na$_2$SO$_4$. The solvent was evaporated under reduced pressure, and the resultant solid obtained. The solid obtained was recrystallized from EtOH. (Scheme-2.9)

4. Preparation of N-(7-Chloroquinolin-4-yl) hexane-1, 6-diamine (2.075)

A mixture of 2.97 g (0.59 mol) 4,7-dichloroquinoline (2.071), 1.39 g (0.015 mole) of 1-2-diaminohexane was dissolved in 30 ml ethanol in a 250 ml round bottom flask and refluxed for 10 h., the solid obtained was extracted with DCM in presence of brine solution. Organic layer was separated and dried with Na$_2$SO$_4$. The solvent was evaporated under reduced pressure, and the resultant solid obtained. The solid obtained was recrystallized from EtOH. (Scheme-2.9)
Synthesis of N (7-Chloroquinolin-4-yl) substituted

Chart 2.1-Mass spectra of compound no. 2.072

Chart 2.2-IR spectra of compound no. 2.073
Synthesis of N (7-Chloroquinolin-4-yl) substituted

Chart 2.3-Mass spectra of compound no. 2.073

Chart 2.4-IR spectra of compound no. 2.074
Chart 2.5-$^1$HNMR spectra of compound no. 2.074
Synthesis of N-(7-Chloroquinolin-4-yl) substituted

Chart 2.6-IR spectra of compound no. 2.074

Chart 2.7-IR spectra of compound no. 2.075
Synthesis of N (7-Chloroquinolin-4-yl) substituted

Chart 2.8-Mass spectra of compound no. 2.075

2.9 REFERENCES


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