5.1 **Introduction**

It was mentioned earlier in chapter 4 that the vast viable achievement of quinoline derivatives as potential medicinal agents\(^1\)\(^-\)\(^9\) and their benefits to society have led the chemistry of these materials to expand exponentially in the past few decades causing this subject to command a vast literature\(^10\)\(^-\)\(^17\). The study in this chapter was undertaken with a view to synthesize imino-5-substituted benzylidene-thiazolidin-4-one derivatives, which could easily obtained by the cyclocondensation of substituted imino-thiazolidinone derivatives. These studies culminated in the development of several clinically active substances containing aldehydes group in this molecules.

H. Zhou *et al.*\(^18\) synthesized 2-arylimino-5-arylidene-thiazolidin-4-one and screened them for their Cytoselective anticancer activity ([Fig-5.1](#)) and several compounds were shown to possess very good anti-viral efficacy with a good safety margin.

\[\text{Fig-5.1}\]

5.2 **SYNTHETIC ASPECTS OF BENZYLIDENE DERIVATIVES**

The wide spectrum of synthetic and pharmacological properties associated with these molecules has triggered the expansion of a variety of methods and has led to extraordinary armory of synthetic strategies to be devised in the literature for this class of compounds. In this context it seems necessary to present in the discussion to follow a brief outline of all the available literature methods, which have been employed to the synthesis of imino-benzylidene derivatives. Some of the reported methods for the synthesis of imino-benzylidene derivatives are described below.

D. Visagaperumal *et al.*\(^19\) have prepared 2-[3-(4-nitrophenyl)-1-(pyridin-4-ylcarbonyl) - 1H-pyrazol-4-yl]-3-substituted 1, 3-thiazolidin-4-one **5.004** form by the mixture of 2-mercaptoacetic acid with aromatic amine **5.002** in dry toluene were
stirred and irradiated in a microwave oven for 12 min. After cooling, ethyl acetate was added. **Scheme- 5.1**

**Scheme- 5.1**

D. Patel *et al.* synthesized 4-[(4-[(E)-phenylmethylidene]amino)phenyl]amino]-2H-chromen-2-one 5.006 form by the solution of 4-[(4-Aminophenyl)amino]-2H-chromen-2-one 5.005 with absolute ethanol containing a catalytic amount of piperidine, equimolecular amount of the appropriate aldehydes (for e.g. benzaldehyde) was added. The reaction mixture was heated under refluxed for 8-10 h. **Scheme- 5.2**

**Scheme- 5.2**

Jian-Feng Zhou *et al.* have synthesized 5-arylidene-2-imino-4-thiazolidinone 5.009 by the reaction of aromatic aldehyde 5.007, 1, 2-imino-4-thiazolidinone 5.008 and ammonium acetate was irradiated in a microwave. **Scheme- 5.3**

**Scheme- 5.3**
R. Mahendra and coworkers\textsuperscript{22} have prepared the 2-arylimino-5-(Z)-1-aryl methylidene-1,3-thiazolan-4-one \textbf{5.011} form the reaction of aromatic aldehyde, 2-arylimino-4-thiazolidenone \textbf{5.010} and fused sodium acetate with absolute alcohol and refluxed for 3 h. \textbf{Scheme- 5.4}

\begin{center}
\includegraphics[width=0.7\textwidth]{Scheme_5.4}
\end{center}

\textbf{Scheme- 5.4}

Z. Turgut and coworkers\textsuperscript{23} synthesized 5-benzylidene derivatives \textbf{5.014} by the reaction of 2-(3,4,5-Trimethoxyphenyl)-3-(4-methylphenyl)-4-thiazolidinone \textbf{5.012} with 4-chlorobenzaldehyde \textbf{5.013} and 4-dimethylaminobenzaldehyde in the presence of sodium ethoxide. \textbf{Scheme- 5.5}

\begin{center}
\includegraphics[width=0.7\textwidth]{Scheme_5.5}
\end{center}

\textbf{Scheme- 5.5}

K. H. Patel and A.G. Mehta\textsuperscript{24} have prepared 2-amino-6-naphthalenylthiazolo thiazole benzaldehyde derivative \textbf{5.017} in ethanol, 2-Aetylnaphthalene \textbf{5.015} to give 2-amino-4(2-naphthalenyl) thiazolo \textbf{5.016} were refluxed with aryl aldehyde for 5 hrs on water bath. \textbf{Scheme- 5.6}

\begin{center}
\includegraphics[width=0.7\textwidth]{Scheme_5.6}
\end{center}

\textbf{Scheme- 5.6}
D. Pareek et al.\textsuperscript{25} reported the 2-(Arylidinoceto)-6-substituted benzothiazoles \textsuperscript{5.019} from 2-amino-6 substituted benzothiazole \textsuperscript{5.018} and aromatic aldehyde (benzaldehyde, p-chlorobenzaldehyde, anisaldehyde, salicylaldehyde) with in absolute ethanol for 3 hrs. \textbf{Scheme- 5.7}

\begin{center}
\textbf{Scheme- 5.7}
\end{center}

M. K. Prajapati\textsuperscript{26} have prepared the 2-imino-3-(carboxamido hydroxyphenyl)-5-(phenyl)-4-thiazolidinones \textsuperscript{5.021} from the reaction of 2-imino-3-(carboxamido hydroxyphenyl)-4-thiazolidinones \textsuperscript{5.020}, benzaldehyde and anhydrous sodium acetate in glacial acetic acid. \textbf{Scheme- 5.8}

\begin{center}
\textbf{Scheme- 5.8}
\end{center}

T. Singh and coworkers\textsuperscript{27} have prepared 5-(2,4-dichlorobenzylidene)-2-(phenylamino) thiazolidin-4-one \textsuperscript{5.023} from 2-phenyliminothiazolidin-4-one \textsuperscript{5.022}, was reacted different aromatic aldehyde with fused sodium acetate in ethanol for 6-7 hr. \textbf{Scheme- 5.9}

\begin{center}
\textbf{Scheme- 5.9}
\end{center}
N. C. Desai et al.\textsuperscript{28} have synthesized N-[2-(4-hydroxyphenyl)-4-oxo-(1,3-thiazolidin-3-yl)]{4-[2-(4-methylphenyl)-4-oxo-(3-hydroquinazolin-3-yl)]phenyl} carboxamide 5.025 form by the cycloaddition of sodium methoxide solution of N-[2-(4-hydroxyphenyl)-4-oxo(1,3-thiazolidin-3-yl)]{4-[2-(4-methylphenyl)-4-oxo(3-hydroquinazolin-3 yl)]phenyl}carboxamide 5.024 and benzaldehyde in 1:4 dioxane and refluxed for 8 hr. \textbf{Scheme- 5.10}

\begin{center}
\includegraphics[width=0.5\textwidth]{Scheme_5.10.png}
\end{center}

\textbf{Scheme- 5.10}

S. Kasmi-Mir et al.\textsuperscript{18, 29} have prepared 2-Arylimino-5-arylidene-thiazolidin-4-ones 5.027 by reaction of 2-arylimino-thiazolidin-4-ones 5.026 react with benzaldehyde with absolute ethanol and piperidine. \textbf{Scheme- 5.11}

\begin{center}
\includegraphics[width=0.5\textwidth]{Scheme_5.11.png}
\end{center}

\textbf{Scheme- 5.11}

S. Verma et al.\textsuperscript{30} have synthesized 2-{2-(substitutedbenzyliden)-imino-5-methyl-1,3,4-thiadiazol}-imino-4-phenyl-1,3-thiazole 5.029 by the reaction of 5.028 and benzaldehyde in methanol with glacial acetic acid was refluxed on a water bath for about 2 hrs. \textbf{Scheme- 5.12}

\begin{center}
\includegraphics[width=0.5\textwidth]{Scheme_5.12.png}
\end{center}

\textbf{Scheme- 5.12}
T. Shu-Jiang et al.\textsuperscript{31} have reported benzo[e][1,4]thiazepin-2-(1H,3H,5H)-ones \textbf{5.033} form by the Emrys\textsuperscript{TM} reaction vial; aldehyde \textbf{5.030} reacted with aromatic amine \textbf{5.031} and mercaptoacetic acid \textbf{5.032} in water. \textbf{Scheme- 5.13}

\begin{center}
\begin{align*}
\text{H} & \text{C} \\
\text{N} & \text{H} \\
\text{O} & \text{C} \\
\text{H} & \text{A} \\
\text{R} & \text{S} \\
\end{align*}
\end{center}

\textbf{Scheme- 5.13}

\section*{5.3 BIOLOGICAL ASPECTS OF BENZYLIDENE DERIVATIVES}

Imino-benzylidene derivatives have a long and well-known history extending form the days of their discovery as important constituents of nucleus to their recent use in the medicinal chemistry and they have great medicinal significance. A huge array of Imino-benzylidene thiazolidin-4-one drugs possesses a multiplicity of medicinal properties including anticonvulsant, antiproliferative, anticancer anti-inflammatory, antimicrobial, analgesic and CNS-depressed activity. In view of the impressive biological activities shown by the molecules containing the thiazolidin-4-one ring, it seems appropriate in the account to follow, to highlight those features of these compounds which have inspired us to undertake this study. Some of the biological properties of imino-benzylidene derivatives are described below.

H. H. Parekh, K. A. Parikh and A. R. Parikh have synthesized\textsuperscript{32} some 4-thiazolidinone derivatives as antitubercular agents. \textbf{Fig-5.2}

\begin{center}
\begin{align*}
\text{S} & \text{N} \\
\text{O} & \text{C} \\
\text{H} & \text{A} \\
\text{R} & \text{S} \\
\end{align*}
\end{center}

\textbf{Fig-5.2}

T. Singh et al.\textsuperscript{33} have synthesized Substituted 5-ethylidene-2-(phenylimino) thiazolidin-4-one and their anticonvulsant activities. \textbf{Fig-5.3}
Synthesis of imino-5-substituted benzylidene-thiazolidin-4-one

V. Alagarsamy et al.\textsuperscript{34} reported 2-Mercapto-3-(2-oxo-1,2-dihydro-indol-3-ylideneamino)-5,6,7,8-tetrahydro-3Hbenzo [4,5]thieno[2,3-d]pyrimidin-4-one as analgesic and anti-inflammatory agents. \textbf{Fig-5.4}

P. N. Patel and H. S. Patel have synthesized\textsuperscript{35} 5’-(4-chlorobenzylidene)-3’-(4-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-ylsulfonyl)phenyl)spiro-[indoline-3,2’-thiazolidine]-2,4’-dione, showed that antimicrobial activity. \textbf{Fig-5.5}

O. M. Abd El-hafez \textit{et al.}\textsuperscript{36} reported N-arylidene coumarin-4-oxyacetic hydrazones. \textbf{Fig-5.6}
A. A. Chavan and N. R. Pai, have synthesized\(^{37}\) 2-\([2'\text{-(N'-(3-Bromobenzylidene) hydrazino)}\text{ acetylamino}]\text{ benzothiazole-6-carboxylic acid. Fig-5.7}\)

J. P. Sen and D. K. Shukla have synthesized\(^{38}\) 5-\([(2'-N\text{-sub. aryldiene hydrazinothioacetyl)-1-(methylene)-(1',3',4'-thiadiazole)}\text{-1,2,3 benzotriazole and sowed that antimicrobial activities. Fig-5.8}\)

B. Narasimhan \textit{et al.}\(^{39}\) synthesized several benzo[d]isothiazole hydrazones and evaluated for their potential antiretroviral activity. \textbf{Fig-5.9}
D. Pareek et al.\textsuperscript{40} have synthesized some bioactive 4-thiazolidinone derivatives incorporating benzothiazole moieties showed that antibacterial activity, antifeedant activity acaricidal activity, contact and stomach toxicity. \textbf{Fig-5.10}

\begin{center}
\includegraphics[width=0.5\textwidth]{5.4.png}
\end{center}

\textbf{Fig-5.10}

\section*{5.4 Present work}

It has been mentioned earlier in Chapter I that thiazolidinones are a versatile heterocyclic compound, and found to have variety of pharmacological properties, such as anticonvulsant, antibacterial, antiviral, hypnotic and anti-inflammatory activities etc. The present investigation was undertaken with a view to synthesize some novel benzylidene-thiazolidinones derivatives.

Considering the properties of benzylidene-thiazolidinone, present investigation was undertaken with a view to synthesize some novel benzylidene-thiazolidinone derivatives. Newer series of benzylidene-thiazolidinone derivatives have been synthesized by the condensation of imino-thiazolidinones and 4-substituted bezaldehydes by employing the strategy depicted in \textbf{scheme-5.14}.

\section*{5.5 Result and discussion}

Synthetic pathway depicted in \textbf{Scheme 5.14} outlines the chemistry of present work. In view of the impressive pharmacodynamic applications shown by conjugate substituted benzaldehyde derivatives, much attention has focused towards developing new synthetic routs to construct a system which carried quinoline, imino-thiazolidinone along with substituted benzaldehyde in same molecular framework. It was envisaged that the precursors which could fulfill this synthetic requirement could be imino-thiazolidinone derivatives (\textbf{4.076, 4.078, 4.080, and 4.082}) could be obtained easily. The syntheses of these molecules were conceived in this chapter following the strategy shown in \textbf{Scheme 5.14}. The synthesis of this series of heterocycle was undertaken in the present work with this assumption that
incorporation of more than one bioactive molecule could result in the molecules with enhanced activity. In the present work, the synthesis of substituted benzaldehydes was carried out using condensation of imino-thiazolidinone derivatives with substituted benzaldehydes in the presence of sodium acetate in dry benzene medium.

**Scheme of the proposed work**

\[
\begin{align*}
\text{X}=\text{Cl, OCH}_3, \text{ NO}_2 \\
an=n=2 \\
b=n=3 \\
c=n=4 \\
d=n=6
\end{align*}
\]

**Scheme-5.14**

### 5.6 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 and $^1$HNMR spectral data of all the compounds are given in **Table-5.1 Table-5.2** and the spectral graphs are presented in the form of **charts-5.1-5.10** at the end of this chapter.
5.6.1 Interpretation of spectral data of compound 5.047

**Infrared spectra**

Infrared spectrum of compound 5.047 using KBr standard exhibited two strong absorption str. at 3056 and 3040 cm\(^{-1}\) (CH str. arom.), 1706 cm\(^{-1}\) (C=O). Appearance of peak at 1606 cm\(^{-1}\) indicating formation of aldehyde derivative and 1585 cm\(^{-1}\) (N-H of imine), 1510 cm\(^{-1}\) (N-H of secondary amine), 1454 cm\(^{-1}\) (C-H bend CH\(_2\)), 1143 cm\(^{-1}\) (C-N str.), and 634 cm\(^{-1}\) (C-Cl str.) and 732 cm\(^{-1}\) indicating presence of chloro group which indicating the formation of compound 5.047.

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

\(^1\)HNMR spectra of compound of 5.047 in CDCl\(_3\) displayed signals for the presence of 16 protons of which 14 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 \(\delta\) 9.94 which exchanged with D\(_2\)O was assigned for NH group. Appearance a doublet at \(\delta\) 8.64 for the presence of protons in aromatic ring. The presence of one singlet which appeared at 8.00 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 \(\delta\) 7.64 assigned one C=H group. Two double doublet was observed at \(\delta\) 7.22 and \(\delta\) 7.24 assigned to four protons of aromatic ring. Three doublets which were appeared at \(\delta\) 7.43, \(\delta\) 7.61 and \(\delta\) 6.49 for the presence of protons in aromatic ring. Appearance a singlet at \(\delta\) 4.34 was assigned for NH group. The upfield, multiplet which was observed at \(\delta\) 1.42-1.25 for 4 protons was ascribed to the presence of aliphatic CH\(_2\).

Similar spectral interpretation established the formation of compound 5.050, 5.053 and 5.055.

5.6.2 Interpretation of spectral data of compound 5.048

**Infrared spectra**

Infrared spectrum of compound 5.048 using KBr standard exhibited two strong absorption str. at 3022 and 2981 cm\(^{-1}\) (CH str. arom.), 1700 cm\(^{-1}\) (C=O), 1669 cm\(^{-1}\) (N-H of imine). Appearance of peak at 1562 cm\(^{-1}\) indicating the formation of aldehyde derivative. Appearance of a peak at 1500 cm\(^{-1}\) (N-H of secondary amine),
1465 cm\(^{-1}\) (C-H bend CH\(_2\)), 1231 cm\(^{-1}\) (C-N str.), 1365 cm\(^{-1}\) indicating presence of nitro group which indicating the formation of compound 5.048 and 754 cm\(^{-1}\) (C-Cl str.).

\(^1\)HNMR spectrum

\(^1\)HNMR spectra of compound of 5.048 in CDCl\(_3\) displayed signals for the presence of 16 protons of which 14 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 \(\delta\) 9.21 which exchanged with D\(_2\)O was assigned for NH group. One doublet which appeared at \(\delta\) 8.14 for the presence of protons in aromatic ring. 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\(_7\)). Presence of one singlet which appeared at \(\delta\) 7.77 assigned one C=H group. Two doublet was observed at \(\delta\) 7.61 and \(\delta\) 7.43 assigned to four proton of aromatic ring. Three doublets which appeared at \(\delta\) 7.56, \(\delta\) 7.43 and \(\delta\) 6.97 for the presence of protons in aromatic ring. Appearance of singlet at \(\delta\) 4.21 was assigned for NH group. The upfield, multiplet which was observed at \(\delta\) 1.51-1.42 for 4 protons was ascribed to the presence of aliphatic CH\(_2\).

Similar spectral interpretation established the formation of compound 5.051, 5.054 and 5.056.

5.6.3 Interpretation of spectral data of compound 5.049

Infrared spectra

Infrared spectrum of compound 5.049 using KBr standard exhibited two strong absorption str. at 3140 and 3021 cm\(^{-1}\) (CH str. arom.), 1704 cm\(^{-1}\) (C=O). Appearance of a peak at 1761 cm\(^{-1}\) indicating the formation of aldehyde derivative. Appearance of peak at 1652 cm\(^{-1}\) (N-H of imine), 1551 cm\(^{-1}\) (N-H of secondary amine), 1462 cm\(^{-1}\) (C-H bend CH\(_2\)) and 1300 cm\(^{-1}\) indicating presence of ester group and 1249 cm\(^{-1}\) (C-N str.), 751 cm\(^{-1}\) (C-Cl str.) which indicating the formation of compound 5.049.
1H NMR spectrum

1H NMR spectra of compound of 5.049 in CDCl₃ displayed signals for the presence of 19 protons of which 17 protons were bound to carbon atom, and 2 protons were bound to nitrogen atom (the protons bound to nitrogen exchanged with D₂O). 1H NMR spectra display the downfield one singlet for one NH proton at δ 9.84 which exchanged with D₂O was assigned for NH group. The presence of one singlet which appeared at δ 8.90 was attributed C₈ quinoline proton (Meta to the chlorine function in the benzene ring at C₇). Two doublets at δ 8.70 and δ 8.12 for the presence of protons in aromatic ring. One double doublet was observed at δ 8.01 assigned to two proton of aromatic ring. Presence of one singlet which appeared at δ 7.39 assigned one CH₂ group. four doublets which appeared at δ 6.70, δ 6.97, δ 7.41 and δ 7.80 for the presence of protons in aromatic ring. Appearance of singlet at δ 4.24 was assigned for NH group. The upfield, multiplet which was observed at δ 1.55-1.26 for 4 protons was ascribed to the presence of aliphatic CH₂.

Similar spectral interpretation established the formation of compound 5.052 and 5.055.

5.6.4 Interpretation of spectral data of compound 5.050

Infrared spectra

Infrared spectrum of compound 5.050 using KBr standard exhibited two strong absorption str. at 3187 and 2856 cm⁻¹ (CH str.arom.), 1700 cm⁻¹ (C=O), 1674 cm⁻¹ (N-H of imine), 1567 cm⁻¹ (N-H of secondary amine). Appearance of a peak at 1456 cm⁻¹ indicating formation of aldehyde derivative and 1389 cm⁻¹(C-H bend CH₂), 1277 cm⁻¹ (C-N str.), 767 cm⁻¹ and 678 cm⁻¹ (C-Cl str.) indicating presence of chloro group which indicating the formation of compound 5.050.

5.6.5 Interpretation of spectral data of compound 5.051

Infrared spectra

Infrared spectrum of compound 5.051 using KBr standard exhibited two strong absorption str. at 3196 and 2945cm⁻¹ (CH str.arom.), 1704 cm⁻¹ (C=O), 1589 cm⁻¹ (N-H of imine). Appearance of a peak at 1569 cm⁻¹ indicating formation of aldehyde derivative. Appearance of peak at 1500 cm⁻¹ indicating presence of nitro
group

1508 cm\(^{-1}\) (N-H of secondary amine), 1458 cm\(^{-1}\) (C-H bend CH\(_2\)), 1356 cm\(^{-1}\) (C-N str.) and 681 cm\(^{-1}\) (C-Cl str.) which indicating the formation of compound 5.051

5.6.6 Interpretation of spectral data of compound 5.052

**Infrared spectra**

Infrared spectrum of compound 5.052 using KBr standard exhibited two strong absorption str. at 3278 and 2876 cm\(^{-1}\) (CH str.arom.), 1710 cm\(^{-1}\) (C=O), 1678 cm\(^{-1}\) (N-H of imine), 1487 cm\(^{-1}\) (C-H bend CH\(_2\)). Appearance of a peak at 1578 cm\(^{-1}\) indicating formation of aldehyde derivative and 1545 cm\(^{-1}\) (N-H of secondary amine), 1329 cm\(^{-1}\) indicating presence of ester group and 1142 cm\(^{-1}\) (C-N str.), 772 cm\(^{-1}\) (C-Cl str.) which indicating the formation of compound 5.052.

5.6.7 Interpretation of spectral data of compound 5.053

**Infrared spectra**

Infrared spectrum of compound 5.053 using KBr standard exhibited two strong absorption str. at 3249 and 2987 cm\(^{-1}\) (CH str.arom.), 1712 cm\(^{-1}\) (C=O), 1678 cm\(^{-1}\) (N-H of imine). Appearance of a peak at 1600 cm\(^{-1}\) indicating formation of aldehyde derivative, 1506 cm\(^{-1}\) (N-H of secondary amine), 1465 cm\(^{-1}\) (C-H bend CH\(_2\)), 1187 cm\(^{-1}\) (C-N str.) and 674 cm\(^{-1}\) (C-Cl str.), 767 cm\(^{-1}\) indicating presence of chloro group which indicating the formation of compound 5.053.

5.6.8 Interpretation of spectral data of compound 5.054

**Infrared spectra**

Infrared spectrum of compound 5.054 using KBr standard exhibited two strong absorption str. at 3150 and 2945 cm\(^{-1}\) (CH str.arom.), 1706 cm\(^{-1}\) (C=O), 1565 cm\(^{-1}\) (N-H of imine). Appearance of a peak in at 1545 cm\(^{-1}\) indicating formation of aldehyde derivative, 1500 cm\(^{-1}\) (N-H of secondary amine), 1473 cm\(^{-1}\) (C-H bend CH\(_2\)). Appearance of peak at 1345 cm\(^{-1}\) indicating presence of nitro group and 1000 cm\(^{-1}\) (C-N str.), 785 cm\(^{-1}\) (C-Cl str.) which indicating the formation of compound 5.054.
5.6.9  Interpretation of spectral data of compound 5.055

Infrared spectra

Infrared spectrum of compound 5.055 using KBr standard exhibited two strong absorption str. at 3010 and 2926 cm\(^{-1}\) (CH str. arom.), 1715 cm\(^{-1}\) (C=O). Appearance of a peak at 1616 cm\(^{-1}\) indicating formation of aldehyde derivative. Appearance of a peak at 1541 cm\(^{-1}\) (N-H of imine), 1529 cm\(^{-1}\) (N-H of secondary amine), 1487 cm\(^{-1}\) (C-H bend CH\(_2\)) and 1350 cm\(^{-1}\) indicating presence of ester group and 1222 cm\(^{-1}\) (C-N str.), 798 cm\(^{-1}\) (C-Cl str.) which indicating the formation of compound 5.055.

5.6.10  Interpretation of spectral data of compound 5.056

Infrared spectra

Infrared spectrum of compound 5.056 using KBr standard exhibited two strong absorption str. at 3299 and 2924 cm\(^{-1}\) (CH str. arom.), 1705 cm\(^{-1}\) (C=O). Appearance of a peak at 1600 cm\(^{-1}\) indicating formation of aldehyde derivative. Appearance of a peak at 1551 cm\(^{-1}\) (N-H of imine), 1510 cm\(^{-1}\) (N-H of secondary amine), 1448 cm\(^{-1}\) (C-H bend CH\(_2\)), 1200 cm\(^{-1}\) (C-N str.) and 767 cm\(^{-1}\) indicating presence of chloro group which indicating the formation of compound 5.056.

5.6.11  Interpretation of spectral data of compound 5.057

Infrared spectra

Infrared spectrum of compound 5.057 using KBr standard exhibited two strong absorption str. at 3058 and 2945 cm\(^{-1}\) (CH str. arom.), 1700 cm\(^{-1}\) (C=O), 1695 cm\(^{-1}\) (N-H of imine). Appearance of a peak at 1569 cm\(^{-1}\) indicating formation of aldehyde derivative. Appearance of peak at 1494 cm\(^{-1}\) (N-H of secondary amine), 1446 cm\(^{-1}\) (C-H bend CH\(_2\)), 1307 cm\(^{-1}\) (C-N str.) and 1359 cm\(^{-1}\) peak is presence of nitro group and 730 cm\(^{-1}\) (C-Cl str.) which indicating the formation of compound 5.057.

5.6.12  Interpretation of spectral data of compound 5.058

Infrared spectra

Infrared spectrum of compound 5.058 on KBr standard exhibited two strong absorption str. at 3278 and 2876 cm\(^{-1}\) (CH str. arom.), 1720 cm\(^{-1}\) (C=O), 1690 cm\(^{-1}\)
(N-H of secondary amine). Appearance of a peak at 1650 cm\(^{-1}\) indicating formation of aldehyde derivative. Appearance of peak at 1545 cm\(^{-1}\) (N-H of imine), 1468 cm\(^{-1}\) (C-H bend CH\(_2\)), 1355 cm\(^{-1}\) (C-N str.) and 1245 cm\(^{-1}\) indicating presence of ester group and 745 cm\(^{-1}\) (C-Cl str.) which indicating the formation of compound 5.058.

\(^1\)HNMR spectrum

\(^1\)HNMR spectra of compound of 5.058 in CDCl\(_3\) displayed signals for the presence of 27 protons of which 25 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 \(\delta\) 10.01 which exchanged with D\(_2\)O was assigned for NH group. Four doublets which appeared at \(\delta\) 8.78, \(\delta\) 8.49, \(\delta\) 8.18 and \(\delta\) 8.15 for the presence of protons in aromatic ring. The presence of one singlet which appeared at \(\delta\) 8.12 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 \(\delta\) 7.71 assigned to one C=H group. Four doublets which appeared at \(\delta\) 7.84, \(\delta\) 7.65, \(\delta\) 7.48, \(\delta\) 6.98 for the presence of protons in aromatic ring. Two singlets at 4.69 were assigned for NH group and \(\delta\) 3.3 for three protons was ascribed to the presence of CH\(_3\) group. The upfield, multiplet which was observed at \(\delta\) 1.7-1.2 for 12 protons was ascribed to the presence of aliphatic CH\(_2\).

MS spectral data also provided the evidence for the formation of compounds 5.044-5.055.

5.7 Mechanism of formation of compounds (5.047-5.058).

![Mechanism diagram](image)

Structures of compounds whose synthesis have been described in this chapter.

![Structures](image)
Synthesis of imino-5-substituted benzylidene-thiazolidin-4-one
Table-5.1 Physical and analytical data of the compounds (5.047-5.058)

<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>
<th>N</th>
<th>C</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.047</td>
<td>443</td>
<td>C_{2}H_{8}Cl_{2}N_{2}O_{5}</td>
<td>115-116</td>
<td>60</td>
<td>12.64/12.58</td>
<td>56.89/56.80</td>
<td>7.23/7.22</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5.048</td>
<td>453</td>
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<td>7.31/7.28</td>
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<td>457</td>
<td>C_{2}H_{9}Cl_{2}N_{2}O_{5}</td>
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<td>6.85/6.80</td>
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<td>61.73/61.66</td>
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<td>133-134</td>
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<td>11.32/11.25</td>
<td>63.08/63.02</td>
<td>6.48/6.42</td>
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Table-5.2 Spectral data of compounds (5.047-5.058)

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<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>
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<td>1</td>
<td>5.047</td>
<td>3056, 3040 (CH str.), 1706 (C=O), 1606 (C=C str.), 1585 (NH str. imine), 1510 (NH sec. amine), 1454 (CH₂ ben.), 1143 (C-N), 732-689 (C-Cl).</td>
<td>9.0 (1H, s, NH), 8.6 (1H, d, CH), 8.8 (1H, s, NH), 8.0 (1H, s, CH), 7.6 (2H, s, C=H), 7.6 (1H, d, CH), 7.4 (1H, d, CH), 7.2 (2H, dd, CH), 6.4 (1H, d, CH), 4.3 (1H, s, NH), 1.4-1.2 (4H, m, CH₂).</td>
</tr>
<tr>
<td>2</td>
<td>5.048</td>
<td>3022, 2981 (CH str.), 1700 (C=O), 1669 (NH), 1562 (C=C str.), 1500 (NH sec. amine), 1465 (CH₂ ben.), 1365 (N-O str.), 1231 (C-N), 754 (C-Cl).</td>
<td>9.2 (1H, s, NH), 8.6 (1H, d, CH), 8.0 (1H, s, CH), 8.1 (1H, d, CH), 7.7 (2H, s, C=H), 7.5 (2H, dd CH), 7.6 (2H, dd, CH), 7.4 (2H, dd, CH), 7.6 (2H, dd, CH), 4.2 (1H, s, NH), 1.5-1.4 (4H, m, CH₂).</td>
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M/Z : 455 (36.5%), 453 (100.0%), 454 (23.8.0%).
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<td>3187, 2856 (CH str.), 1700 (C=O), 1674 (NH str. imine), 1567 (NH sec. amine), 1456 (C=C str.), 1389 (CH₂ ben.), 1277 (C-N), 767-678 (C-Cl).</td>
<td>3196, 2945 (CH str.), 1710 (C=O), 1586 (NH str. imine), 1569 (C=C), 1508 (NH sec. amine), 1500 (N-O str.), 1458 (CH₂ ben.), 1356 (C-N str.), 781 (C-Cl str.).</td>
<td>3196, 2945 (CH str.), 1712 (C=O), 1586 (NH str. imine), 1569 (C=C), 1508 (NH sec. amine), 1500 (N-O str.), 1458 (CH₂ ben.), 1356 (C-N str.), 781 (C-Cl str.).</td>
<td>3249, 2987 (CH₂ str.), 1706 (C=O), 1678 (NH str. imine), 1600 (C=C), 1506 (NH sec. str. amine), 1465 (CH₂ ben.), 1185 (C-N str.), 767, 674 (C-Cl str.).</td>
<td>3150, 2945 (CH₂ Str.), 1705 (C=O), 1565 (NH str. imine), 1545 (C=C),</td>
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<td>9.8 (1H, s, NH), 8.9 (1H, s, CH), 8.7 (1H, d, CH), 8.1 (1H, d, CH), 8.0 (2H, dd, CH), 7.4 (1H, d CH), 7.3 (2H, s, C=H), 6.9 (1H, d, CH), 6.7 (1H, d, CH), 4.2 (1H, s, NH), 3.8 (3H, s, CH₃), 1.5-1.2 (4H, m, CH₂).</td>
<td>9.2 (1H, s, NH), 8.6 (2H, dd, CH), 8.2 (1H, s, CH), 7.5 (1H, d, CH), 7.2 (1H, s, CH), 7.2 (2H, dd, CH), 7.4 (1H, d, CH), 6.2 (1H, d, CH), 4.3 (1H, s, NH), 1.48-2.7 (6H, m, CH₂).</td>
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<td>8.6 (1H, d, CH), 8.4 (1H, s, NH), 8.4 (1H, s, NH), 8.1 (1H, s, CH), 7.4 (1H, d, CH), 7.4 (2H, s, C=H), 7.6 (2H, dd, CH), 6.4 (1H, d, CH), 6.7 (2H, dd, CH), 4.1 (1H, s, NH), 1.8-2.1 (6H, m, CH₂).</td>
<td>10.2 (1H, s, NH), 8.5 (1H, d, CH), 8.0 (1H, s, CH), 7.7 (2H, s, C=H), 7.65 (2H, dd, CH), 7.24 (1H, dd, CH), 7.22 (2H, dd, CH), 6.3 (1H, d, CH), 4.2 (1H, s, NH), 1.5-2.9 (8H, m, CH₂).</td>
<td>10.3 (1H, s, NH), 8.6 (2H, dd, CH), 8.0 (1H, s, CH), 7.6 (2H, s, C=H), 7.5 (2H, dd, CH), 6.4 (1H,</td>
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<td>M/Z : 438 (100.0%), 439 (24.1%).</td>
<td>M/Z : 472 (68.8%), 470 (100.0%), 471 (25.1%).</td>
<td>M/Z : 472 (68.8%), 470 (100.0%), 471 (25.1%).</td>
<td>M/Z : 472 (68.8%), 470 (100.0%), 471 (25.1%).</td>
<td>M/Z : 472 (68.8%), 470 (100.0%), 471 (25.1%).</td>
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<td>11.2 (1H, s, NH), 8.6 (2H, dd, CH), 8.0 (1H, s, CH), 7.6 (2H, s, C=H), 7.1 (2H, dd, CH), 7.2 (1H, d, CH), 6.5 (1H, d, CH), 4.2 (1H, s, NH), 1.4-2.7 (8H, m, CH₂).</td>
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<td>5.056</td>
<td>3299, 2924 (CH₂ str.), 1700 (C=O), 1600 (C=C), 1551 (NH str. imine), 1510 (NH sec. str. amine), 1448 (CH₂ ben.), 1200 (C-N str.), 795 (C-Cl str.).</td>
<td>11.3 (1H, s, NH), 8.6 (2H, dd, CH), 8.0 (1H, s, CH), 7.5 (2H, s, C=H), 7.2 (1H, d, CH), 7.2 (1H, dd, CH), 6.3 (1H, d, CH), 4.3 (1H, s, NH), 1.2-2.8 (12H, m, CH₂).</td>
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<tr>
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<td>3058, 2945 (CH₂ str.), 1720 (C=O), 1695 (NH str. imine), 1569 (C=C), 1494 (NH sec. str. amine), 1446 (CH₂ ben.), 1359 (N-O str.), 1307 (C-N str.), 730 (C-Cl str.).</td>
<td>10.3 (1H, s, NH), 8.7 (1H, d, CH), 8.4 (1H, s, CH), 7.7 (2H, s, C=H), 7.5 (1H, dd, CH), 7.6 (1H, dd, CH), 7.4 (1H, d, CH), 6.4 (1H, d, CH), 4.1 (1H, s, NH), 1.1-2.8 (12H, m, CH₂).</td>
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</table>

### 5.8 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 5.1 and Table 5.2.
7. Substituted benzaldehydes were used in the synthesis without further purification.

5.8.1 Synthetic procedures

1. **Preparation of 3-[2-(7-chloroquinolin-4-ylamino) ethyl-2-imino-5-(4-chloro benzylidene)] thiazolidin-4-one. (5.047)**

   A mixture of compound (4.075) 0.30 gm (0.12 mmol) and sodium acetate (0.10gm) respectively mixed with $\beta$-chloro benzaldehyde 0.127 gm (0.171mmol) in dry benzene (20ml) medium. The reaction mixture was refluxed on water bath for 8 hr at 110 $^\circ$C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction, it was cooled and solvent evaporate. The product was recrystallized with EtOH. **Scheme-5.14**

2. **Preparation of 3-[2-(7-chloroquinolin-4-ylamino) ethyl-2-imino-5-(4-nitro benzylidene)] thiazolidin-4-one. (5.048)**

   A mixture of (4.075) 0.30 gm (0.13 mmol) and sodium acetate (0.10gm) respectively mixed with $\beta$-nitro benzaldehyde 0.37 gm (0.038 mmol) in dry benzene (20ml) medium. The reaction mixture was refluxed on water bath for 8 hr at 110 $^\circ$C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction, it was cooled and solvent evaporate. The product was recrystallized with EtOH. **Scheme-5.14**

3. **Preparation of 3-[2-(7-chloroquinolin-4-ylamino) ethyl-2-imino-5-(4-methoxy benzylidene)] thiazolidin-4-one. (5.049)**

   A mixture of (4.076) 0.30 gm (0.12 mmol) and zinc chloride (0.50 mg) respectively mixed with $\beta$-methoxy benzaldehyde 0.127 gm (0.017mmol) in glacial acetic acid (20ml) medium. The reaction mixture was refluxed on sand bath for 8 hr
at 120 °C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction it was cooled and solvent evaporate. The product was neutralized NaHCO₃, white precipitate comes occur which pour in the water and filtered it. The compound recrystallized with methanol and water. The obtained solid purified by column chromatography the product were recrystallized with ethanol. **Scheme-5.14**

4. **Preparation of 3-[3-(7-chloroquinolin-4-ylamino) propyl-3-imino-5-(4-chloro benzylidene)] thiazolidin-4-one. (5.050)**

A mixture of (4.078) 0.30 gm (0.13 mmol) and sodium acetate (0.10gm) respectively mixed with β-chlorobenzaldehyde 0.127 gm (0.017mmol) in dry benzene (20ml) medium. The reaction mixture was refluxed on water bath for 8 hr. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction, it was cooled and solvent evaporate. The product was recrystallized with EtOH. **Scheme-5.14**

5. **Preparation of 3-[3-(7-chloroquinolin-4-ylamino) propyl-3-imino-5-(4-nitro benzylidene)] thiazolidin-4-one. (5.051)**

A mixture of (4.078) 0.30 gm (0.13 mmol) and sodium acetate (0.10gm) respectively mixed with β-nitrobenzaldehyde 0.37 gm (0.038 mmol) in dry benzene (20ml) medium. The reaction mixture was refluxed on water bath for 8 hr at 110 °C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction, it was cooled and solvent evaporate. The product was recrystallized with EtOH. **Scheme-5.14**

6. **Preparation of 3-[3-(7-chloroquinolin-4-ylamino) propyl-3-imino-5-(4-methoxy benzylidene)] thiazolidin-4-one. (5.052)**

A mixture of (4.078) 0.30 gm (0.13 mmol) and zinc chloride (0.50 mg) respectively mixed with β-methoxybenzaldehyde 0.127 gm (0.017mmol) in glacial acetic acid (20ml) medium. The reaction mixture was refluxed on sand bath for 8 hr at 120 °C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction it was cooled and solvent evaporate. The product was neutralized NaHCO₃, white precipitate comes
occur which pour in the water and filtered it. The compound recrystallized with methanol and water. The obtained solid purified by column chromatography the product were recrystallized with ethanol. **Scheme-5.14**

7. **Preparation of 3-[4-(7-chloroquinolin-4-ylamino) butyl-4-imino-5-(4-chloro benzylidene)] thiazolidin-4-one. (5.053)**

A mixture of (4.080) 0.30 gm (0.13 mmol) and sodium acetate (0.10gm) respectively mixed with p-chlorobenzaldehyde 0.127 gm (0.017mmol) in dry benzene (20ml) medium. The reaction mixture was refluxed on water bath for 8 hr at 80-100 °C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction, it was cooled and solvent evaporate. The product was recrystallized with EtOH. **Scheme-5.14.**

8. **Preparation of 3-[4-(7-chloroquinolin-4-ylamino) butyl-4-imino-5-(4-nitro benzylidene)] thiazolidin-4-one. (5.054)**

A mixture of (4.080) 0.30 gm (0.13 mmol) and sodium acetate (0.10gm) respectively mixed with p-nitrobenzaldehyde 0.37 gm (0.038 mmol) in dry benzene (20ml) medium. The reaction mixture was refluxed on water bath for 8 hr at 80-100 °C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction, it was cooled and solvent evaporate. The product was recrystallized with EtOH. **Scheme-5.14**

9. **Preparation of 3-[4-(7-chloroquinolin-4-ylamino) butyl-4-imino-5-(4-methoxy benzylidene)] thiazolidin-4-one. (5.055)**

A mixture of (4.080) 0.30 gm (0.13 mmol) and zinc chloride (0.50 mg) respectively mixed with p-methoxybenzaldehyde 0.127 gm (0.017mmol) in glacial acetic acid (20ml) medium. The reaction mixture was refluxed on sand bath for 8 hr at 120 °C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction it was cooled and solvent evaporate. The product was neutralized NaHCO₃, white precipitate comes occur which pour in the water and filtered it. The compound recrystallized with methanol and water. The obtained solid purified by column chromatography the product were recrystallized with ethanol. **Scheme-5.14**
10. **Preparation of 3-[6-(7-chloroquinolin-4-ylamino) hexyl-6-imino-5-(4-chloro benzylidene)] thiazolidin-4-one. (5.056)**

A mixture of (4.082) 0.30 gm (0.14 mmol) and sodium acetate (0.10gm) respectively mixed with \( \beta \)-chlorobenzaldehyde 0.127 gm (0.017mmol) in dry benzene (20ml) medium. The reaction mixture was refluxed on water bath for 8 hr at 80-100 \(^{\circ}\)C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction, it was cooled and solvent evaporate. The product was recrystallized with EtOH. **Scheme-5.14**

11. **Preparation of 3-[6-(7-chloroquinolin-4-ylamino) hexyl-6-imino-5-(4-nitro benzylidene)] thiazolidin-4-one. (5.057)**

A mixture of (4.082) 0.30 gm (0.14 mmol) and sodium acetate (0.10gm) respectively mixed with \( \beta \)-nitrobenzaldehyde 0.37 gm (0.038mmol) in dry benzene (20ml) medium. The reaction mixture was refluxed on water bath for 8 hr at 80-100 \(^{\circ}\)C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction, it was cooled and solvent evaporate. The product was recrystallized with EtOH. **Scheme-5.14**

12. **Preparation of 3-[6-(7-chloroquinolin-4-ylamino) hexyl-6-imino-5-(4-methoxy benzylidene)] thiazolidin-4-one. (5.058)**

A mixture of (4.082) 0.30 gm (0.14 mmol) and zinc chloride (0.50 mg) respectively mixed with \( \beta \)-methoxybenzaldehyde 0.127 gm (0.017mmol) in glacial acetic acid (20ml) medium. The reaction mixture was refluxed on sand bath for 8 hr at 120 \(^{\circ}\)C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction it was cooled and solvent evaporate. The product was neutralized NaHCO\(_3\), white precipitate comes occur which pour in the water and filtered it. The compound recrystallized with methanol and water. The obtained solid purified by column chromatography the product were recrystallized with ethanol. **Scheme-5.14**
Synthesis of imino-5-substituted benzylidene-thiazolidin-4-one

Chart 5.1-IR spectra of compound no. (5.053)

Chart 5.2-IR spectra of compound no. (5.055)
Synthesis of imino-5-substituted benzylidene-thiazolidin-4-one

Chart 5.3-IR spectra of compound no. (5.056)

Chart 5.4-Mass spectra of compound no. (5.048)
Chart 5.5-$^1$HNMR spectra of compound no. (5.049)

Chart 5.6- Mass spectra of compound no. (5.049)
Chart 5.7- Mass spectra of compound no. (5.055)

Chart 5.8- $^1$HNMR spectra of compound no. (5.058)
Chart 5.9- Mass spectra of compound no. (5.056)HC

Chart 5.10- Mass spectra of compound no. (5.057)
5.9 References


