2.1 Introduction

Heterocycles make up an exceedingly important class of compounds due to their expansive range of applications. They are predominant among all types of pharmaceuticals, agrochemicals and veterinary products. Heterocycles containing nitrogen, sulfur and oxygen have been under investigation for a long time because of their important medicinal properties. The recent literature is enriched with progressive findings about the synthesis and pharmacological action of fused heterocycles. There has been increasing interest in the role played by benzimidazoles condensed with other heterocycles have shown their broad pharmacological activities.

Further, the therapeutic effects of 1,2,4-triazole containing compounds have been well studied for a number of pathological conditions. In addition, it was reported that 1,3,4-thiadiazoles exhibit various biological activities possibly due to the presence of the =N-C-S moiety. Moreover, the synthesis of triazoles fused to another heterocyclic ring has attracted widespread attention due to its diverse applications as pesticides, herbicides, dyes, lubricants, analytical reagents, antibacterials, antidepressants, antivirals, antitumorials and anti-inflammatory agents.

Among these, the triazoles fused to pyridines, pyridazines, pyrimidines, pyrazines and triazines, thiadiazines or thiadiazoles, a number of them have shown a broad spectrum of biological activities. Currently, benzimidazoles containing fused heterocycles are an object of sustained
interest due to the wide range of their biologically potent activities. Devising a systematic nomenclature system for heterocyclic compounds presented a formidable challenge, which has not been uniformly concluded. Many heterocycles, especially amines, were identified early, and received trivial names which are still preferred. The chemical reactivity of the saturated members of this class of heterocycles are tetrahydropyran, thiane and piperidine, resemble that of acyclic ethers, sulfides and 2º-amines. 1,3-Dioxanes and dithianes are cyclic acetals and thioacetals.

These units are commonly used as protective groups for aldehydes and ketones, as well as synthetic intermediates, and may be hydrolyzed by the action of aqueous acid. The reactivity of partially unsaturated compounds depends on the relationship of the double bond and the heteroatom (e.g. 3,4-dihydro-2H-pyran is an enol ether). Fully unsaturated six-membered nitrogen heterocycles, such as pyridine, pyrazine, pyrimidine and pyridazine, have stable aromatic rings. Oxygen and sulfur analogs are necessarily positive charged, as in the case of 2,4, 6-triphenylpyrylium tetrafluoroborate.
Some monocyclic and fused heterocyclic compounds of this kind are shown in the following chart.

Majority of DNA intercalating antitumor drugs have a common general structure comprising a planar tricyclic and tetra cyclic chromophore.\(^1\)\(^-\)\(^3\) Other side of the effectiveness of condensed heterocycles containing benzimidazole ring showed broad pharmacological activities.\(^4\)\(^-\)\(^8\) Further, synthesis of many 3-substituted bi heterocyclic coumarins with thiazoles and fused thiazoles exhibit promising biological activities.\(^9\),\(^10\) A large number of 3-chloromonocyclic 2-azetidinones having substitution at position 1 and 4 possess a broad spectrum of pharmacological activities.\(^11\)\(^-\)\(^14\)
On the other hand substituted Schiff’s bases also exhibit a wide range of biological and controlled therapeutic activities.\textsuperscript{15–18}

\section*{2.1.1 Thiazolo-benzimidazole derivatives}

The chemistry and biological activity of thiazolo-benzimidazole have been studied over several years ago.\textsuperscript{19–23} These derivatives are the analogues of tetramisole.\textsuperscript{24,25} Many literature protocols are available for the preparation of thiazolo-benzimidazole derivatives.\textsuperscript{26–31} These thiazolo-benzimidazole derivatives showed promising biological activities like antiprotozoal,\textsuperscript{32} anticonvulsant,\textsuperscript{33} antidepressants,\textsuperscript{34} anti-HIV,\textsuperscript{35} antitrichinellosis\textsuperscript{36} and hypoglycemic agents.\textsuperscript{37} It is well known that hetero aryl thio acetophenones can be prepared from the reaction of phenacyl halide derivatives with thiol compounds in alkaline medium.

\section*{2.2 Synthesis of Thiazolo-benzimidazole derivatives}

V.K. Chadha \textit{et al.}, synthesized derivatives of thiazolo [3,2-\textit{a}] benzimidazoles (1) by reacting 2-mercaptobenzimidazole with ketones in the presence of iodine.\textsuperscript{38}
1) RCH(Cl)COOH, 2) Ac₂O, Pyridine, 3) ArCHO, NaOAc, 4) Br₂, CHCl₃
R = H, CH₃

J.J. Wade³⁹ investigated 2- (Carbomethoxymethylene) -3-oxo-2H,3H-thiazolo [3,2-a] benzimidazole (2) by using dimethyl acetylenedicarboxylate (DMAD) with 2H- benzimidazole-2-thione.

(2)

B.R. Sharma and H.K. Pujari⁴⁰ prepared derivatives of thiazolo [3,2-a] benzimidazole-3 (2H)-ones (3) by using 2,4-dibromo-6- nitroaniline.

(3)

1) Raney Nickel, H₂NNH₂, H₂O, CS₂ 2) ClCH₂COOH
3) Ac₂O, Pyridine 4) BrCH₂CH₂Br
R¹ = Br, Cl, CH₃, NO₂  R² = H  R³ = Br, Cl, CH₃, H
A novel one pot synthesis of thiazolo [3,2-α] benzimidazoles (4) was described by A.A.O. Sarhan et al., by using α- haloketones.\(^{41}\)

\[
\begin{align*}
\text{a) AcOH/ H}_2\text{SO}_4 & \quad \text{b) NH}_4\text{OH} & \quad \text{c) PPA, 100 °C} \\
R = C_6\text{H}_5, p-\text{CH}_3C_6\text{H}_4, p-\text{OCH}_3C_6\text{H}_4, p-\text{ClC}_6\text{H}_4
\end{align*}
\]

A series of novel thiazolo [3,2-α] benzimidazole derivatives (5) were synthesized via the reaction of bis-hydrazoneoyl chloride with benzimidazole-2-thiol by K.M. Dawood et al.\(^{42}\)

\[
(5) \quad \text{Ar} = C_6\text{H}_5, p-\text{ICC}_6\text{H}_4
\]

M. Ochiai et al.\(^{43}\) showed domino Michael addition-carbene rearrangement-cyclization reaction of 1-alkynyl (aryl)-\(\lambda^3\)-bromanes with 2-mercapto benzimidazoles gives substituted thiazolo [3,2-α] benzimidazoles (6) in high yields.

\[
(6) \quad R = C_8\text{H}_{17}, \text{CH}_2-c-\text{C}_5\text{H}_9, t-\text{Bu}
\]
C. Roussel et al., showed new route for the preparation of 3-Alkyl-thiazolo [3,2-a] benzimidazole derivatives (7) in high yields via the corresponding 4-alkyl-N-3-(2-aminophenyl)-thiazoline-2-thiones which are easily prepared from 1,2-diaminobenzene, CS$_2$ and halogenoketones.$^{44}$

\[
\begin{align*}
\text{L} & \quad \text{R}^2 \\
\text{O} & \quad \text{R}^1
\end{align*}
\quad +
\quad \begin{array}{c}
\text{S} \\
\text{N} \\
\text{N} \\
\text{H} \\
\text{N} \\
\text{N} \\
\text{S}
\end{array}
\quad \xrightarrow{\text{(7)}}
\quad \begin{array}{c}
\text{N} \\
\text{S} \\
\text{N} \\
\text{N} \\
\text{O}
\end{array}
\]

\[
\text{R}^1 = \text{CH}_3, \quad \text{R}^2 = \text{H}
\]

Recently A. Kh. Khalil synthesized 7-methyl [1,3] thiazolo [3,2-a] benzimidazole-3 (2H)-one (8) by treating 5-methyl-2-mercaptobenzimidazole with chloro acetyl chloride afforded the desired product.$^{45}$

\[
\begin{array}{c}
\text{H}_3\text{C} \\
\text{N} \\
\text{N} \\
\text{S} \\
\text{H}
\end{array}
\quad \xrightarrow{\text{Chloroacetyl chloride}}
\quad \begin{array}{c}
\text{H}_3\text{C} \\
\text{N} \\
\text{S} \\
\text{N} \\
\text{O}
\end{array}
\]

2.3 Biologically active Thiazolo-benzimidazole derivatives

J.M. Singh synthesized thiazolo [3,2-a] benzimidazole mannich bases (9) and tested them for anticonvulsant activity.$^{32}$

\[
\begin{array}{c}
\text{N}(\text{R}^1\text{R}^2) = \text{Et}_2\text{N}, \text{Me}_2\text{N}, \text{ph}_2\text{N}, \text{phNEt}, \text{n-Pr}_2\text{N}, \text{n-Bu}_2\text{N}, \text{sec-Bu}_2\text{N}, \text{Piperidino}, \text{Morpholino}
\end{array}
\]
A. Chimirri and co-workers,\textsuperscript{46} prepared a series of novel 1-aryl-3-methyl-1\textit{H},3\textit{H}-thiazolo[3,4-\textit{a}]benzimidazoles, TBZ analogues (10) and investigated as anti-human immuno deficiency virus (HIV) agents in order to study the effects of structural modifications on antiviral activity and cytotoxicity.

\[
\begin{align*}
\text{R} & = \text{R}^1 = \text{H}, \text{Cl}, \text{F} \\
\end{align*}
\]

A. Rao \textit{et al.},\textsuperscript{47} described microwave-assisted synthesis of 1\textit{H},3\textit{H}-thiazolo[3,4-\textit{a}]benzimidazole derivatives (11) and tested them as HIV-1 RT inhibitors.

\[
\begin{align*}
\text{R}^1 & = \text{H}, 5\text{-CH}_3, 6\text{-CH}_3, 8\text{-CH}_3, \text{ R}^2 = \text{H}, 7\text{-CH}_3 \\
\text{R}^3 & = 2\text{-F}, 3\text{-NO}_2, \text{ R}^4 = \text{H}, 6\text{-F} \\
\end{align*}
\]

A.Ts. Mavrova \textit{et al.}, synthesized some 2-substituted- [1,3] thiazolo [3,2-\textit{a}] benzimidazole -3 (2\textit{H})-ones (12) which possessed significant antitrichinellosis activity against \textit{Trichinella spiralis}.\textsuperscript{36}

\[
\begin{align*}
\text{R}^1 & = \text{O} \begin{array}{c} \text{O} \\
\text{C} \end{array} \text{R}^1 = \text{O} \begin{array}{c} \text{O} \\
\text{C} \end{array} \text{R}^1 \\
\end{align*}
\]

\[
\begin{align*}
\text{R} & = \text{H}, \text{CH}_3, \text{NO}_2 \\
\end{align*}
\]
N.A. Hamdy et al.,\textsuperscript{48} have prepared 1,3-thiazole (13) and 1,3,4-thiadiazole (14) based on thiazolo [3,2-\textit{a}] benzimidazole moiety and they showed moderate activity against some bacterial and fungal species.

\begin{equation}
\text{(13)} \quad \text{R} = \text{CH}_3, \text{OEt} \\
\text{Ar} = \text{ph, 4-ClC}_6\text{H}_4, \text{4-CH}_3\text{C}_6\text{H}_4
\end{equation}

\begin{equation}
\text{(14)}
\end{equation}

### 2.4 Present work

The application of clean catalytic technologies, especially those with the use of heterogeneous catalysts, is becoming increasingly important for the development of environmentally benign chemical processes. Our approach reduces the use of organic solvents, which are potentially toxic, hazardous and uses simple and mild conditions with inherently lower costs. In the present study, our ongoing work devoted towards the development of environment friendly, rapid synthesis of heterocyclic molecules of biological interest, we explored the possibility of synthesizing Phenyl thiazolo benzimidazole derivatives (Scheme-1). The synthesis of Phenyl thiazolo benzimidazole compounds was performed according to the previously reported procedure.\textsuperscript{49,50} Working along these lines, we have introduced different substituents on to the benzimidazole to generate libraries of these compounds and screened them for potential biological activities.
The mixture of substituted \( \sigma \) phenylene diamine (1) (1.0 mmol) and substituted benzaldehyde (2) (1.2 mmol) were stirred in dry toluene under reflux condition followed by addition of mercaptoacetic acid (2.0 mmol). The reaction mixture was refluxed under stirring for an additional 24–48 h till the complete consumption of the amine component. The reaction mixture was concentrated to dryness under reduced pressure and the residue was taken up in ethyl acetate.

The organic layer was successively washed with 5% aq. citric acid, water, 5% aq. Sodium hydrogen carbonate and then finally with brine. The organic layer was dried over sodium sulphate and solvent was removed under reduced pressure to get a crude product 3(a-l) that was purified by column chromatography on silica gel using hexane-ethyl acetate as eluent.

All the reactions involved are highly efficient to give the desired compounds in high yield and high purity. And also, this adopted procedure is simple, rapid and eco-friendly due to easy experimental procedures. The versatility of this methodology can be extended to develop a stream-lined approach to synthesize bio active molecules. Yield and melting points of the synthesized compounds were tabulated in \textbf{(Table-1)}. 
Scheme-1

The one-pot synthesis of Phenyl thiazolo benzimidazoles

\[
\begin{align*}
R^1 & \text{NH}_2 \quad + \quad \text{HO-} \text{SH} \quad + \quad \text{H-} \text{CO} \\
\text{(1)} & \quad \text{R}^2 \\
\Delta & \quad \text{24-28 h} \quad \text{Toluene} \\
\rightarrow & \quad \text{R}^1 \text{N} \quad \text{S} \quad \text{R}^2 \\
\text{3(a-l)} & \quad 
\end{align*}
\]

<table>
<thead>
<tr>
<th>Compound</th>
<th>R$_1$</th>
<th>R$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-a</td>
<td>4-NO$_2$</td>
<td>H</td>
</tr>
<tr>
<td>3-b</td>
<td>4-NO$_2$</td>
<td>4-Cl</td>
</tr>
<tr>
<td>3-c</td>
<td>4-NO$_2$</td>
<td>4-OCH$_3$</td>
</tr>
<tr>
<td>3-d</td>
<td>4-NO$_2$</td>
<td>2-NO$_2$</td>
</tr>
<tr>
<td>3-e</td>
<td>4-NO$_2$</td>
<td>2-Cl</td>
</tr>
<tr>
<td>3-f</td>
<td>4-NO$_2$</td>
<td>4-NO$_2$</td>
</tr>
<tr>
<td>3-g</td>
<td>4-Br</td>
<td>H</td>
</tr>
<tr>
<td>3-h</td>
<td>4-Br</td>
<td>4-Cl</td>
</tr>
<tr>
<td>3-i</td>
<td>4-Br</td>
<td>4-OCH$_3$</td>
</tr>
<tr>
<td>3-j</td>
<td>4-Br</td>
<td>2-NO$_2$</td>
</tr>
<tr>
<td>3-k</td>
<td>4-Br</td>
<td>2-Cl</td>
</tr>
<tr>
<td>3-l</td>
<td>4-Br</td>
<td>4-NO$_2$</td>
</tr>
</tbody>
</table>
In summary, we have developed an efficient, facile and environmentally acceptable synthetic methodology for the synthesis of Phenyl thiazolo benzimidazole derivatives. The attractive features of this procedure are the mild reaction conditions, high conversions, ease of separation, inexpensive and environmentally friendly, excellent yields, all of which make it a useful and attractive strategy for the preparation of various Phenyl thiazolo benzimidazole derivatives simply by changing different substrates. The versatility of this methodology is suitable for library synthesis in drug discovery efforts.

2.5 Materials and methods

The melting points of the Phenyl thiazolo benzimidazole products were determined by open capillaries on a Buchi apparatus and are uncorrected. The IR spectra were recorded on a Nicolet Impact-410 FT-IR Spectrophotometer using KBr pellets. The $^1$H and $^{13}$C NMR spectras were recorded on a 300MHz Bruker-Avanace NMR instrument in CDCl$_3$ and the chemical shifts were expressed in parts per million (ppm) with tetramethylsilane (TMS) as an internal standard. Mass spectrometer with ionization energy maintained at 70eV using on Shimadzu mass spectrometer. The elemental analysis was carried out by using Heraus CHN rapid analyzer. All the compounds gave C, H and N analysis within ± 0.4% of the theoretical values. The homogeneity of the compounds was described by TLC on aluminum silica gel 60 F$_{254}$ (Merck) detected by U.V light (254 nm) and iodine vapours.
2.6 Experimental procedure

The mixture of substituted \( o \)- phenylene diamine (1.0 mmol) and substituted benzaldehyde (1.2 mmol) were stirred in dry toluene under reflux condition followed by addition of mercaptoacetic acid (2.0 mmol). The reaction mixture was refluxed under stirring for an additional 24–28 h till the complete consumption of the amine component. The reaction mixture was concentrated to dryness under reduced pressure and the residue was taken up in ethyl acetate. The organic layer was successively washed with 5% aq. citric acid, water, 5% aq. Sodium hydrogen carbonate and then finally with brine.

The organic layer was dried over sodium sulphate and solvent was removed under reduced pressure to get a crude product that was purified by column chromatography on silica gel using hexane-ethyl acetate as eluent. The product was purified by recrystallization. All the synthesized Phenyl thiazolo benzimidazole derivatives were characterized using analytical techniques like IR, \(^1\)H NMR, \(^{13}\)C NMR and mass spectroscopy. Melting points were measured for all synthesized Phenyl thiazolo benzimidazole derivatives and were compared with the corresponding reported melting points.
2.7 Results and discussion

The structures of newly synthesized 6-Nitro-1-phenyl-3H-benzo[4,5]imidazo[1,2-c]thiazole libraries 3(a-l) were supported by IR, $^1$H NMR, $^{13}$C NMR and Mass spectrometry. Physical and analytical data of the synthesized compounds were summarized in (Table-1).

The IR spectrum of all the compounds 3(a-l) had the characteristic C=N stretching band at 1628-1664 cm$^{-1}$ in Phenyl thiazolo Benzimidazole derivatives. The C=C stretching band at 1526-1593 cm$^{-1}$ was observed in all the compounds respectively. The -CH stretching band is observed at 2925-2940 cm$^{-1}$, The C-S stretching band noticed at 720 cm$^{-1}$ respectively. The $^1$H NMR spectrum displayed a characteristic signals at δ 3.72 for (s, 2H, CH$_2$), δ 6.02 for (s, 1H, CH-S) and δ 6.73-7.76 for (m, 8H, ArH and H-1). The $^{13}$C NMR spectra of all the compounds 3(a-l) displayed signals at δ 29.2 and δ 66.2 for (CH2-S) and (CH-S) carbon. These compounds showed sharp singlet signals at δ 141.5 ppm for imidazole carbon, at δ 110.5-146.8 ppm for aromatic carbon atoms, at δ 10-40 ppm saturated carbon atoms with DMSO solvent signals. The mass spectra of the same compounds showed peak corresponding to their molecular ion. The X-ray analysis of the compound(s) is under progress.

The IR, $^1$H NMR, $^{13}$C NMR and Mass spectra of some compounds are enclosed as Spectrum No. 1 - 8.
Table 1
Physical and Analytical Data of the Phenyl thiazolo benzimidazole

<table>
<thead>
<tr>
<th>Product</th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>R&lt;sub&gt;2&lt;/sub&gt;</th>
<th>Reaction time (Hr) / Yield (%)</th>
<th>m. p (°C)</th>
<th>Mol. Formula/ Mol. Wt</th>
<th>Elem. Analysis (Cal./Found)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>H</td>
<td>24/ 60.02</td>
<td>174-176</td>
<td>C&lt;sub&gt;13&lt;/sub&gt;H&lt;sub&gt;12&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S&lt;sub&gt;2&lt;/sub&gt;  297</td>
<td>60.59 / 60.57  3.73 / 3.72  14.13 / 13.16</td>
</tr>
<tr>
<td>3b</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>4-Cl</td>
<td>25 / 59.84</td>
<td>187-189</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;3&lt;/sub&gt; 331</td>
<td>54.30 / 54.32  3.04 / 3.03  12.67 / 12.68</td>
</tr>
<tr>
<td>3c</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>4-OCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>24 / 68.46</td>
<td>182-184</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;12&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;3&lt;/sub&gt; 327</td>
<td>58.70 / 58.68  4.00 / 4.03  12.84 / 12.82</td>
</tr>
<tr>
<td>3d</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>2-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>26/ 65.00</td>
<td>197-198</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;2&lt;/sub&gt; 342</td>
<td>52.63 / 52.62  2.94 / 2.93  16.37 / 16.35</td>
</tr>
<tr>
<td>3e</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>2-Cl</td>
<td>25 / 64.48</td>
<td>162-164</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;3&lt;/sub&gt; 331</td>
<td>54.30 / 54.32  3.04 / 3.03  12.67 / 12.68</td>
</tr>
<tr>
<td>3f</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>27 / 54.34</td>
<td>183-185</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;3&lt;/sub&gt; 342</td>
<td>52.63 / 52.64  2.94 / 2.96  16.37 / 16.38</td>
</tr>
<tr>
<td>3g</td>
<td>4-Br</td>
<td>H</td>
<td>24 / 66.08</td>
<td>187-188</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;S&lt;sub&gt;3&lt;/sub&gt; 331</td>
<td>54.37 / 54.35  3.35 / 3.36  8.64 / 8.62</td>
</tr>
<tr>
<td>3h</td>
<td>4-Br</td>
<td>4-Cl</td>
<td>28 / 56.44</td>
<td>176-178</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;S&lt;sub&gt;3&lt;/sub&gt; 365</td>
<td>49.27 / 49.26  2.76 / 2.75  7.66 / 7.64</td>
</tr>
<tr>
<td>3i</td>
<td>4-Br</td>
<td>4-OCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>24 / 70.64</td>
<td>191-193</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;S&lt;sub&gt;3&lt;/sub&gt; 361</td>
<td>53.20 / 53.22  3.63 / 3.62  7.75 / 7.74</td>
</tr>
<tr>
<td>3j</td>
<td>4-Br</td>
<td>2-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>26 / 69.03</td>
<td>166-168</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;S&lt;sub&gt;3&lt;/sub&gt; 376</td>
<td>47.89 / 47.90  2.68 / 2.69  11.17 / 11.18</td>
</tr>
<tr>
<td>3k</td>
<td>4-Br</td>
<td>2-Cl</td>
<td>24 / 67.49</td>
<td>188-190</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;S&lt;sub&gt;3&lt;/sub&gt; 365</td>
<td>49.27 / 49.26  2.76 / 2.74  7.66 / 7.64</td>
</tr>
<tr>
<td>3l</td>
<td>4-Br</td>
<td>4-NO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>27 / 64.20</td>
<td>177-180</td>
<td>C&lt;sub&gt;15&lt;/sub&gt;H&lt;sub&gt;10&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;S&lt;sub&gt;3&lt;/sub&gt; 376</td>
<td>47.89 / 47.87  2.68 / 2.69  11.17 / 11.18</td>
</tr>
</tbody>
</table>

* Products were characterized by IR, NMR, MS and elemental analysis. b Isolated yields. c Melting points are uncorrected.
(3-a) 6-Nitro-1-phenyl-3H-benzo[4,5]imidazo[1,2-c]thiazole

Colorless solid, m.p; 174-176 °C; IR (KBr): \( \nu \) (cm\(^{-1}\)) 2924 (C-H), 1602 (C=N), 1510 (C=C), 725 (C-S); \(^1\)H NMR (DMSO, 300MHz): \( \delta \) ppm = 3.70 (s, 2H, CH\(_2\)), 6.72 (s, 1H, CH-S), 6.73-7.76 (m, 8H, ArH and H-1);

\(^{13}\)CNMR (75 MHz DMSO, \( \delta \) ppm): 29.2(CH2-S), 66.2(CH-S), 141.5(C=N), 110.5-146.8 (12, Ar-C); GCMS: \( m/z \) [M\(^+\)] = 297: Anal. Calcd. For C\(_{15}\)H\(_{11}\)N\(_3\)O\(_2\)S: C 60.59, H 3.73, N 14.13 %. Found: C 60.57, H 3.72, N 13.16 %.

(3-b) 1-(4-Chloro-phenyl)-6-nitro-3H-benzo[4,5]imidazo[1,2-c]thiazole

Light brown solid, m.p; 187-189°C; IR (KBr): \( \nu \) (cm\(^{-1}\)) 2924 (C-H), 1641 (C=N), 1610 (C=C), 714 (C-S);

\(^1\)H NMR (DMSO, 300MHz): \( \delta \) ppm = 3.36 (s, 2H, CH\(_2\)), 4.96 (s, 1H, CH-S), 6.76-7.78 (m, 7H, ArH and H-1); \(^{13}\)C NMR (75 MHz DMSO, \( \delta \) ppm): 29.6(CH2-S), 66.0 (CH-S), 146.5(C=N), 112.5-144.6 (12, Ar-C); GCMS: \( m/z \) [M\(^+\)] = 331: Anal. Calcd. For C\(_{15}\)H\(_{10}\)Cl N\(_3\)O\(_2\)S : C 54.30, H 3.04, N 12.67 %. Found: C 54.32, H 3.03, N 12.64 %.
(3-c) 1-(4-Methoxy-phenyl)-6-nitro-3H-benzo[4,5]imidazo[1,2-c]thiazole

Colorless solid, m.p; 182-184°C; IR (KBr): ν (cm⁻¹) 2924 (C-H), 1632 (C=N), 1518(C=C), 724 (C-S); ¹H NMR (DMSO, 300MHz): δ ppm = 3.74 (s, 2H, CH₂), 6.04 (s,1H, CH-S), 6.73-7.76 (m, 7H, ArH and H-1); ¹³C NMR (75 MHz DMSO, δ ppm): 29.6(CH₂-S), 66.8(CH-S),141.5(C=N), 112.5-148.8 (12, Ar-C); GCMS: m/z [M⁺]= 327: Anal. Calcd. For C₁₆H₁₃N₃O₃S: C 58.70, H 4.00, N 12.84 %. Found: C 58.68, H 4.03, N 12.82 %.

(3-d) 6-Nitro-1-(2-nitro-phenyl)-3H-benzo[4,5]imidazo[1,2-c]thiazole

Light yellow solid, m.p; 197-198 °C; IR (KBr): ν (cm⁻¹) 2924 (C-H), 1636 (C=N), 1516 (C=C), 724 (C-S); ¹H NMR (DMSO, 300MHz): δ ppm = 3.74 (s, 2H, CH₂), 6.08 (s,1H, CH-S), 6.73-7.76 (m, 7H, ArH and H-1); ¹³C NMR (75 MHz DMSO, δ ppm): 29.4(CH₂-S), 66.4(CH-S),141.2(C=N), 112.5-148.8 (12, Ar-C); GCMS: m/z [M⁺]= 342: Anal. Calcd. For C₁₅H₁₀N₄O₄S: C 52.63, H 2.94, N 16.37 %. Found: C 52.62, H 2.93, N 16.35 %.

(3-e) 1-(2-Chloro-phenyl)-6-nitro-3H-benzo[4,5]imidazo[1,2-c]thiazole

Light brown solid, m.p; 162-164 °C; IR (KBr): ν (cm⁻¹) 2925 (C-H), 1628 (C=N), 1516 (C=C), 720
(C-S); $^1$H NMR (DMSO, 300MHz): $\delta$ ppm = 3.72 (s, 2H, CH$_2$), 6.02 (s,1H, CH-S), 6.73-7.76 (m, 7H, ArH and H-1); $^{13}$C NMR (75 MHz DMSO, $\delta$ ppm): 29.2(CH2-S), 66.2(CH-S),141.5(C=N), 110.5-146.8 (12, Ar-C); GCMS: $m/z$ [M$^+$]= 331: Anal. Calcd. For: C$_{15}$H$_{10}$ClN$_3$O$_2$S: C 54.30, H 3.04, N 12.67 %. Found: C 54.32, H 3.03, N 12.68 %.

(3-f) 6-Nitro-1-(4-nitro-phenyl)-3H-benzo[4,5]imidazo[1,2-c]thiazole

Colorless solid, m.p; 183-185 °C; IR (KBr): $\nu$ (cm$^{-1}$) 2922 (C-H), 1632 (C=N), 1514(C=C), 724(C-S); $^1$H NMR (DMSO, 300MHz): $\delta$ ppm = 3.74 (s, 2H, CH$_2$), 6.04 (s,1H, CH-S), 6.73-7.78 (m, 7H, ArH and H-1); $^{13}$C NMR (75 MHz DMSO, $\delta$ ppm): 29.2(CH2-S), 66.2(CH-S),141.5(C=N), 110.5-146.8 (12, Ar-C); GCMS: $m/z$ [M$^+$] = 342: Anal. Calcd. For C$_{15}$H$_{10}$N$_4$O$_4$S : C 52.63, H 2.94, N 16.37 %. Found: C 52.64, H 2.96, N 16.38 %.

(3-g) 6-Bromo-1-phenyl-3H-benzo[4,5]imidazo[1,2-c]thiazole

Colorless solid, m.p; 187-188 °C; IR (KBr): $\nu$ (cm$^{-1}$) 2924 (C-H), 1632 (C=N), 1518 (C=C), 726 (C-S); $^1$H NMR (DMSO, 300MHz): $\delta$ ppm = 3.74 (s, 2H, CH$_2$), 6.12 (s,1H, CH-S), 6.74-7.78(m, 8H, ArH and H-1); $^{13}$C NMR (75 MHz DMSO, $\delta$ ppm): 29.2(CH2-S), 66.2(CH-S),141.5(C=N), 110.5-146.8 (12, Ar-C); GCMS: $m/z$ [M$^+$]= 331 : Anal. Calcd. For C$_{15}$H$_{11}$BrN$_2$S: C 54.37, H 3.35, N 8.64 %. Found: C 54.35, H 3.36, N 8.62%.
(3-h) 6-Bromo-1-(4-chloro-phenyl)-3H-benzo[4,5]imidazo[1,2-c]thiazole

Light brown solid, m.p; 176-178 °C; IR (KBr): \( \nu (\text{cm}^{-1}) \)
2926 (C-H), 1628 (C=N), 1522 (C=C), 728 (C-S); \(^1\)H NMR (DMSO, 300MHz): \( \delta \text{ ppm} = 3.76 \) (s, 2H, CH\(_2\)),
6.14 (s,1H, CH-S), 6.74-7.80 (m, 7H, ArH and H-1); \(^{13}\)C NMR (75 MHz DMSO, \( \delta \text{ ppm} \)): 29.4(CH\(_2\)-S), 66.4(CH-S),141.8 (C=N), 110.6-146.4 (12, Ar-C); GCMS: \( m/z [\text{M}^+] = 365 \)
: Anal. Calcd. For \( \text{C}_{15}\text{H}_{10}\text{BrClN}_2\text{S} \): C 49.27, H 2.76, N 7.66 %. Found: C 49.26, H 2.75, N 7.64 %.

(3-i) 6-Bromo-1-(4-methoxy-phenyl)-3H-benzo[4,5]imidazo[1,2-c]

Light grey solid, m.p; 191-193 °C; IR (KBr): \( \nu (\text{cm}^{-1}) \)
2925 (C-H), 1628 (C=N), 1516 (C=C), 720 (C-S); \(^1\)H NMR (DMSO, 300MHz): \( \delta \text{ ppm} = 3.72 \) (s, 2H, CH\(_2\)),
6.02 (s,1H, CH-S), 6.73-7.76 (m, 7H, ArH and H-1); \(^{13}\)C NMR (75 MHz DMSO, \( \delta \text{ ppm} \)): 29.2(CH2-S), 66.2(CH-S),141.5(C=N), 110.5-146.8 (12, Ar-C); GCMS: \( m/z [\text{M}^+] = 361 \)
: Anal. Calcd. For \( \text{C}_{16}\text{H}_{13}\text{BrN}_2\text{OS} \): C 53.20, H 3.63, N 7.75 %. Found: C 53.22, H 3.62,N 7.74 %.

(3-j) 6-Bromo-1-(2-nitro-phenyl)-3H-benzo[4,5]imidazo[1,2-c]thiazole

Colorless solid, m.p; 166-168 °C; IR (KBr): \( \nu (\text{cm}^{-1}) \)
2922 (C-H), 1634 (C=N), 1520 (C=C), 724 (C-S); \(^1\)H NMR (DMSO, 300MHz): \( \delta \text{ ppm} = 3.74 \) (s, 2H, CH\(_2\)), 6.08 (s,1H, CH-S), 6.74-7.78 (m, 7H, ArH and H-1); \(^{13}\)C NMR (75 MHz
DMSO, δ ppm: 29.4(CH2-S), 66.8(CH-S), 142.5(C=N), 112.5-148.6 (12, Ar-C); GCMS: m/z [M+] = 376: Anal. Calcd. For C15H10BrN3O2S: C 47.89, H 2.68, N 11.17 %. Found: C 47.90, H 2.69, N 11.18 %.

(3-k) 6-Bromo-1-(2-chloro-phenyl)-3H-benzo[4,5]imidazo[1,2-c]thiazole

Light yellow solid, m.p; 188-190 °C; IR (KBr): ν (cm⁻¹) 2925 (C-H), 1628 (C=N), 1516 (C=C), 720 (C-S); ¹H NMR (DMSO, 300MHz): δ ppm = 3.72 (s, 2H, CH2), 6.02 (s, 1H, CH-S), 6.73-7.76 (m, 7H, ArH and H-1); ¹³C NMR (75 MHz DMSO, δ ppm): 29.2(CH2-S), 66.2(CH-S), 141.5(C=N), 110.5-146.8 (12, Ar-C); GCMS: m/z [M+] = 365: Anal. Calcd. For C15H10BrClN2S: C 49.27, H 2.76, N 7.66 %. Found: C 49.26, H 3.74, N 7.64 %.

(3-l) 6-Bromo-1-(4-nitro-phenyl)-3H-benzo[4,5]imidazo[1,2-c]thiazole

Colorless solid, m.p; 177-180 °C; IR (KBr): ν (cm⁻¹) 2924 (C-H), 1643 (C=N), 1518 (C=C), 724 (C-S); ¹H NMR (DMSO, 300MHz): δ ppm = 3.76 (s, 2H, CH2), 6.12 (s, 1H, CH-S), 6.74-7.78 (m, 7H, ArH and H-1); ¹³C NMR (75 MHz DMSO, δ ppm): 29.4(CH2-S), 66.4(CH-S), 141.8(C=N), 112.5-146.6 (12, Ar-C); GCMS: m/z [M+] = 376: Anal. Calcd. For C15H10BrN3O2S: C 47.89, H 2.68, N 11.17 %. Found: C 47.87, H 2.69, N 11.18 %.
Spectrum 1: IR Spectrum of compound (3a) (Code-TH-BZ)

Spectrum 2: \(^1\)H NMR (300MHz) Spectrum of compound (3a)
Spectrum 3: $^{13}$C NMR (75MHz) Spectrum of compound (3a)

Spectrum 4: Mass Spectra of compound (3a)
Chapter-2  
Chemistry of Thiazolo-benzimidazoles

Spectrum 5: IR Spectrum of compound (3b)

Spectrum 6: $^1$H NMR (300MHz) Spectrum of compound (3b)
Chapter 2

Chemistry of Thiazolo-benzimidazoles

Spectrum 7: $^{13}$C NMR (75MHz) Spectrum of compound (3b)

Spectrum 8: Mass Spectra of compound (3b)
2.8 References


13. T. Komori, O. Nakaguti, T. Oku and Y. Shiokawa, 


15. A.H. El-Masry, H.H. Fabmy and S.H.A. Abdelwahed, 
*Molecules*, 2000, **5**, 1429.


*Il farmaco*, 1999, **54**, 624.

19. H. Ogura, T. Itoh and T. Tajika, 
*J. Heterocyclic Chem.*, 1968, **5**, 319.

20. H. Ogura, T. Itoh, and Y. Shimada, 

21. A.N. Krasovskii, and P.M. Kochergin, 

22. J.J. D’Amico, R.H. Compbell, and E.C. Gunn, 

23. A.E. Alper, and A. Taurins, 


26. A.E. Alper, and A. Taurins,  
27. H. Alper, A.E. Alper, and A. Taurins,  
28. H. Alper, E.C.H. Keung, and R.A. Parts,  
29. V.K. Chadha, K.S. Sharma, and H.K. Pujari,  
30. H. Singh, and S. Singh,  
31. H. Singh, and S. Singh,  
32. J.M. Singh,  
33. C.J. Sharpe, R.S. Shadbolt, A. Ashfered and J.W. Ross,  
34. I.F. Miller and R.E. Bambury,  
35. A. Chimirri, S. Grasso, A.M. Monforte, P. Monforte and M. Zappala,  
37. D.E. Kuhla,  
   *U.S. Pat.*, 3,860,718.  
   *Chem. Abstr.*, 1975, 82, 140133.
38. V.K. Chadha, H.S. Chaudhary and H.K. Pujari,  
39. J.J. Wade,  


