CHAPTER – II

SYNTHESIS OF NOVEL IMIDAZO[1,2-a]PYRIDINE DERIVATIVES AND STUDIES ON THEIR ANTITUBERCULAR ACTIVITY
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SYNTHESIS OF NOVEL IMIDAZO[1,2-a]PYRIDINE DERIVATIVES
AND STUDIES ON THEIR ANTITUBERCULAR ACTIVITY

2.1 INTRODUCTION:-

In recent years heterocyclic compounds, analogues and derivatives have attracted wide attention due to their broad range of biological and pharmacological properties. The heterocycles are the versatile compounds existing in almost all natural products and synthetic organic compounds, usually associated with one or the other biological activity.

Heterocyclic compounds containing a bridge nitrogen atom represent important building blocks in both natural and synthetic bioactive compounds, which have been shown to possess various therapeutic activities. Imidazo[1,2-a]pyridine has significant importance in the pharmaceutical industry owing to the interesting biological activities displayed over a broad range of therapeutic classes, exhibiting anti-inflammatory, antiulcer, antibacterial, selective cyclin-dependant kinase inhibitors, GABA and benzodiazepine receptor agonists, cardiotonic, gastric anti secretory, hypnotic, and anti anxiety agents.

Among the heterocycles the thiazoles and benzothiazoles occupy a prominent position. They hold a broad range of biological activities and are found in many potent biologically active molecules and drugs.
such as vitamin thiamine, sulfathiazol (antimicrobial drug), ritonavir (antiretroviral drug), abafungin (antifungal drug) and tiazofurin (antineoplastic drug). Benzothiazole is among the usually occurring heterocyclic nuclei in many marine as well as natural plant products. It is a privileged bicyclic ring system with multiple applications. It is known to exhibit a wide range of biological properties including anticancer, antimicrobial, antidiabetic, anticonvulsant, anti-inflammatory, antiviral, antitubercular activities. A large number of therapeutic agents are synthesized with the help of benzothiazole nucleus. During recent years there have been some interesting developments in the biological activities of benzothiazole derivatives. These compounds have special significance in the field of medicinal chemistry due to their remarkable pharmacological potentialities.

Looking at the importance of these heterocyclic nuclei, it is thought of interest to accommodate Imidazo[1,2-a]pyridine and benzothiazole moieties in single molecular framework and screen them for their various biological activities. As a part of our current interest on the synthesis of novel imidazo[1,2-a]pyridine derivatives, we are presenting the synthesis of 2-benzothiazolyl-3-substituted acetamido imidazo[1,2-a]pyridine derivatives (Fig: a) and studied their antitubercular activity.
2.2 LITERATURE BACKGROUND

Kaplan\textsuperscript{10} et al reported the synthesis of hypnotic drug Zolpidem 1 starting from the reaction of toluene 2 with chloroacetylchloride 3 to produce 4. The compound 4, on condensation with 5 in IPA, gave imidazo[1,2-a]pyridine derivative 6. The compound 6 was further treated with dimethylamine and formaldehyde in the presence of acetic acid to give Mannich base 7. The compound 7 was treated with methyl iodide to produce quaternary salt 8, which was treated with Sodium cyanide to yield the corresponding nitrile derivative 9. The nitrile derivative was hydrolyzed with KOH in ethanol to give acid 10. The compound 10 on treatment with dimethylamine in presence of carbonyl diimidazole (CDI) to yield the corresponding amide 1.

(Scheme-2.1)
Danielle et al reported the synthesis of imidazo[1,2-a]quinoline derivatives by the reaction of 2-aminoquinoline with 4-chlorophenacylbromide in IPA to produce 14. The compound 14 was treated with DMF and oxalylchloride in presence of MDC to produce 15, which was reduced with sodium borohydride in ethanol to produce (2-(4-Chlorophenyl)imidazo[1,2-a]quinolin-1-yl)methanol 16. It was treated with PTSCl in pyridine followed by NaCN to give the corresponding nitrile derivative 17. The nitrile derivative was hydrolyzed using KOH in ethanol to give the acid derivative 18. Compound 18 was treated with pyrrolidine to give the corresponding amide 11 (Scheme-2.2)
Giuseppe et al. reported the synthesis of 2-(6,8-dichloro-2-(thiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N,N-dimethylacetamide 19 by the reaction of 2-(trimethylsilyl)thiazole with methyl 4-chloro-4-oxobutanate to produce 22, which was treated with pyridinium perbromide in THF to give the bromo derivative 23. The bromo derivative 23, on condensation with 24 in toluene gave 25, which was treated with dioxane in 1N HCl to produce an acid derivative 26. The acid derivative 26 was aminated with dimethylamine to give the corresponding amide 19 (Scheme-2.3).
Brun\textsuperscript{22} et al reported the synthesis of 2-(5-bromofuran-2-yl)imidazo[1,2-a]pyridin-6-carbonitrile \textbf{27} by the reaction of 2-bromo-1-(5-bromofuran-2-yl)ethanone \textbf{28} with 6-aminonicotinonitrile \textbf{29} in ethanol (\textbf{Scheme-2.4}).

Rousseau\textsuperscript{23} et al reported the synthesis of N-(2,6-dimethylphenyl)-2-p-tolylimidazo[1,2-a]pyridin-3-amine \textbf{32} by the reaction of 2-aminopyridine \textbf{30} with aldehyde \textbf{31} in presence of isocyanide \textbf{33} and catalyst to produce \textbf{32} (\textbf{Scheme-2.5}).
Jeremy\textsuperscript{24} et al reported the synthesis of ethyl 7-bromoimidazo[1,2-a]pyridin-5-carboxylate \textbf{36} by the reaction ethyl 6-amino-4-bromopicolinate \textbf{34}, with chloroacetaldehyde \textbf{35} in ethanol to produce \textbf{36} (Scheme-2.6).

J.V.Singh\textsuperscript{25} et al reported the synthesis of 2-(benzothiazol-2-yl)imidazo[1,2-a]pyridine \textbf{38} by the reaction of 2-aminopyridine \textbf{30} with 1-(benzothiazol-2-yl)-2-bromoethanone \textbf{37}, in IPA to produce \textbf{38} (Scheme-2.7).

Shankarappa\textsuperscript{26} et al reported the synthesis of 6-bromo-2-(3,4-
dichlorophenyl)imidazo[1,2-a]pyridine 41 by the reaction of 2-amino-5-bromopyridine 39 with 2-bromo-1-(3,4-dichlorophenyl) ethanone 40 in DMF to produce 41 (Scheme-2.8).

\[
\begin{align*}
\text{Br-} & \quad \text{Cl-} \\
\text{N} & \quad \text{N} \\
\text{O} & \quad \text{DMF} \\
\text{Microwave} \\
\text{39} & \quad \text{40} \\
\text{Cl} & \quad \text{Cl} \\
\text{Cl} & \quad \text{Cl} \\
\text{Br} & \quad \text{Br} \\
\end{align*}
\]

**2.3 PRESENT WORK:**

The present work involves the synthesis of Zolpidem analogues, containing benzothiazol-2-yl ring at second position, various acetamide derivatives at third position and different substituents in pyridine ring of imidazo[1,2-a]pyridine moiety and study of their anti tubercular activity.

\[
\begin{align*}
\text{R} & \quad \text{NH}_2 \\
\text{N} & \quad \text{N} \\
\text{S} & \quad \text{NaHCO}_3 \\
\text{Acetic acid} \\
\text{5(a-d)} & \quad \text{42} \\
\text{R} & \quad \text{N} \\
\text{N} & \quad \text{S} \\
\text{COOH} & \quad \text{KOH} \\
\text{KCN} & \quad \text{Ethanol} \\
\text{45(a-d)} & \quad \text{46(a-d)}
\end{align*}
\]
2.4 RESULTS AND DISCUSSION

The reaction of 2-aminopyridine 5a with (benzothiazol-2-yl)-2-chloroethanone 42 with sodium bicarbonate in isopropanol solvent at 80-85°C for 6h, gave a product which is different from the starting materials and homogeneous on the TLC. The product was characterized as 2-(benzothiazol-2-yl)imidazo[1,2-a]pyridine 38a (Scheme-2.10) on the basis of its analytical and spectral data. Its $^1$H NMR (CDCl$_3$/TMS) spectrum (Fig-2.1) showed signals as $\delta$ 6.99 (t, $J$ = 6.7 Hz, 1H aromatic -CH), 7.34 (t, $J$ = 8.5Hz, 1H aromatic -CH), 7.42 (d, $J$ = 7.5Hz, 1H aromatic -CH), 7.52 (t, $J$ = 7.8 Hz, 1H aromatic -CH), 7.65 (d, $J$ = 9.0 Hz, 1H aromatic -CH), 8.00 (d, $J$ = 8.0 Hz, 1H aromatic -CH), 8.01 (d, $J$ = 7.8 Hz, 1H aromatic -CH), 8.59 (d, $J$ =6.6 Hz, 1H aromatic -CH), 8.65 (s, 1H aromatic -CH). Its $^{13}$C NMR (CDCl$_3$/TMS): spectrum (Fig-2.2) showed signals at $\delta$ 112.25, 113.99, 117.54, 122.81, 123.00, 125.66, 126.92, 126.94, 128.02, 134.91, 139.16,
145.33, 154.24, 163.95 and its ESI mass spectrum (Fig-2.3) showed molecular ion peak at 252.9(M+1) corresponds to the molecular mass of 251.9 (M+).

\[
\begin{align*}
5(a-d) & \quad 42 & \quad 38(a-d) \\
\text{R = H} & \quad \text{R = 7-Methyl} \\
\text{R = 4-Methyl} & \quad \text{R = 6-Chloro} \\
\text{R = 5-Chloro} & \quad \text{R = 6-Methyl} \\
\text{R = 5-Methyl} & \quad \text{R = 6-Methyl}
\end{align*}
\]

(Scheme-2.10)

In similar manner, 2-amino-4-methylpyridine (5b), 2-amino-5-chloropyridine (5c), 2-amino-5-methylpyridine (5d) on condensation with (benzothiazol-2-yl)-2-chloroethanone 42 produced 38b, 38c and 38d correspondingly. Structures confirmed on the basis of their analytical and spectral data. (for details, please see experimental section)

2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridine 38a was treated with dimethylamine and paraformaldehyde in presence of acetic acid at 50-55°C for 5h to give a product and the compound was identified as (2-(benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N,N-dimethyl methanamine 43a (Scheme-2.11) on the basis of its analytical and spectral data. \textsuperscript{1}H NMR (CDCl\textsubscript{3}/TMS) spectrum (Fig-2.4) showed signals at \(\delta\) 2.37 (s, 6H, 2xCH\textsubscript{3} –N(CH\textsubscript{3})\textsubscript{2}), 4.48 (s, 2H –CH\textsubscript{2}N), 6.91
(t, $J = 6.7$ Hz, 1H aromatic -CH), 7.31 (t, $J = 8.9$ Hz, 1H aromatic -CH), 7.43 (d, $J = 7.5$ Hz, 1H aromatic -CH), 7.53 (t, $J = 7.7$Hz, 1H aromatic -CH), 7.72 (d, $J = 9.1$ Hz, 1H aromatic -CH), 8.00 (d, $J = 7.9$Hz, 1H aromatic -CH), 8.12 (d, $J = 8.1$ Hz, 1H aromatic -CH), 8.46 (d, $J = 6.8$Hz, 1H aromatic -CH). Its $^{13}$C NMR (CDCl$_3$/TMS) spectrum (Fig-2.5) showed signals at δ 45.29, 52.07, 112.85, 117.71, 121.04, 121.69, 123.15, 124.89, 125.68, 125.83, 125.96, 135.17, 137.50, 145.21, 154.55, 164.34 and its ESI mass spectrum (Fig-2.6) showed molecular ion peak at 309.2(M+1) corresponds to the molecular mass of 308.2(M$^+$).

\[
\text{Acetic acid} \quad \xrightarrow{(HCHO)_n} \quad \text{R} \quad \xrightarrow{\text{N}} \quad \text{38(a-d)} \quad \xrightarrow{\text{Acetic acid}} \quad \text{R} \quad \xrightarrow{\text{N}} \quad \text{43(a-d)}
\]

38a) $R = H$ \hspace{1cm} 43a) $R = H$

38b) $R = 7$-Methyl \hspace{1cm} 43b) $R = 7$-Methyl

38c) $R = 6$-Chloro \hspace{1cm} 43c) $R = 6$-Chloro

38d) $R = 6$-Methyl \hspace{1cm} 43d) $R = 6$-Methyl

(Scheme-2.11)

This general reaction was extended to other compounds such as 2-(benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridine (38b), 2-(benzothiazol-2-yl)-6-chloroimidazo[1,2-a]pyridine (38c) and 2-(benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridine (38d) and the
products were 43b, 43c and 43d on the basis of their analytical and spectral data. (for details, please see experimental section).

(2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N,N-dimethylmethanamine 43a was treated with methyl iodide in acetone at 10-15°C for 15h to give a product, which was different from the starting materials and homogeneous on the TLC. The compound was characterized as (2-(benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N,N,N-trimethylmethanammonium iodide 44a (Scheme-2.12) on the basis of its analytical and spectral data. Its $^{1}$H NMR (DMSO-d$_6$/TMS) spectrum (Fig-2.7) showed signals at $\delta$ 3.25 (s, 9H, 3xCH$_3$ –N$^\dagger$(CH$_3$)$_3$), 5.51 (s, 2H –CH$_2$-N), 7.26 (d, $J = 6.7$ Hz, 1H aromatic -CH), 7.61 (m, 3H aromatic -CH), 7.87 (d, $J = 9.0$ Hz, 1H aromatic -CH), 8.22 (t, $J = 8.8$ Hz, 2H aromatic -CH), 9.01 (d, $J = 6.8$ Hz, 1H aromatic -CH). Its $^{13}$C NMR (DMSO-d$_6$/TMS) spectrum (Fig-2.8) showed signals at $\delta$ 52.83, 57.38, 112.31, 115.10, 118.21, 122.79, 123.76, 126.29, 126.36, 127.07, 128.45, 134.90, 140.98, 146.55, 153.98, 163.73 and its ESI mass spectrum (Fig-2.9.) showed base peak at 265.5 corresponds to its fragment ion peak.
(2-(benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)-N,N-dimethylmethanamine (43b), (2-(benzothiazol-2-yl)-6-chloroimidazo[1,2-a]pyridine-3-yl)-N,N-dimethylmethanamine (43c) and (2-(benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridine-3-yl)-N,N-dimethylmethanamine (43d) reacted alike with methyliodide to produce compounds 44b, 44c and 44d respectively. All the products were confirmed the assigned structures on the basis of their analytical and spectral data. (for details, please see experimental section)

(2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N,N,N-trimethyl methanammonium iodide 44a was treated with potassium cyanide in dimethylimidazolidine and water at 95-100°C for 36h to yield 2-(2-(benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)acetonitrile (45a) (Scheme-2.13). The compound was characterized as on the basis of its analytical and spectral data. Accordingly the product in its IR (In KBr) spectrum (Fig-2.10) showed a peak at 2244cm⁻¹ as strong band corresponding to cyano group. ¹H NMR (CDCl₃/TMS) spectrum (Fig-2.11) showed signals at δ 5.00 (s, 2H -CH₂-CN), 7.07 (t, J = 6.7 Hz, 1H aromatic -CH), 7.35-7.41 (m, 2H aromatic -CH), 7.51 (t, J = 7.6 Hz, 1H aromatic -CH), 7.77 (d, J = 9.1 Hz, 1H aromatic -CH), 7.98 (d, J = 7.9 Hz, 1H aromatic -CH), 8.08 (d, J = 7.8 Hz, 1H aromatic -CH), 8.17 (d, J = 6.8 Hz, 1H aromatic -CH). Its ¹³C NMR (CDCl₃/TMS):
spectrum (Fig-2.12) showed signals as $\delta$ 32.65, 113.80, 114.07, 117.99, 118.20, 122.65, 124.50, 125.35, 126.04, 126.42, 134.91, 136.29, 139.19, 145.19, 153.76 and 165.02. Its ESI mass spectrum (Fig-2.13) showed molecular ion peak at 291.1(M+1) related to the molecular mass of product 290.1(M$^+$).

\[
\begin{align*}
44(a-d) & \quad \text{KCN} \quad \text{DMI, water} \\
\end{align*}
\]

\[
\begin{align*}
44(a-d) & \quad 45(a-d) \\
44a) R = H & \quad 45a) R = H \\
44b) R = 7-Methyl & \quad 45b) R = 7-Methyl \\
44c) R = 6-Chloro & \quad 45c) R = 6-Chloro \\
44d) R = 6-Methyl & \quad 45d) R = 6-Methyl \\
\end{align*}
\]

(Scheme-2.13)

Similar procedure extended to other derivatives. (2-(benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)-N,N,N-trimethyl methan ammonium iodide (44b), (2-(benzothiazol-2-yl)-6-chlorimidazo[1,2-a]pyridin-3-yl)-N,N,N-trimethylmethanammonium iodide (44c) and (2-(benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-N,N,N-trimethylmethanammonium iodide (44d) reacted with KCN and DMI to produce 45b, 45c and 45d. The products obtained were confirmed the assigned structure on the basis of their analytical and spectral data. (for details, please see experimental section).

2-(2-(Benzothiazol-2-yl)6-methylimidazo[1,2-a]pyridin-3-yl)acetonitrile 45a was hydrolyzed using potassium hydroxide in aqueous ethanol.
at 80-85°C for 24h to give a product, which was different from the starting materials. Obtained product confirmed as 2-(2-(benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)acetic acid 46a (Scheme-2.14) on the basis of its analytical and spectral data. The product in its IR (In KBr) spectrum (Fig-2.14) showed a peak at 1707 cm⁻¹ a strong band for carboxylic acid functional group. \(^1\)H NMR (DMSO-d\(_6\)/TMS) spectrum (Fig-2.15) showed signals at 4.66 (s, 2H –CH\(_2\)-CO), 7.02 (t, J = 6.6 Hz, 1H aromatic -CH), 7.41 (m, 2H aromatic -CH), 7.50 (t, J = 7.6 Hz, 1H aromatic –CH), 7.67 (d, J = 9.0 Hz, 1H aromatic -CH), 8.00 (d, J = 8.0 Hz, 1H aromatic -CH), 8.11 (d, J = 7.8 Hz, 1H aromatic -CH), 8.45 (d, J = 6.8 Hz, 1H aromatic -CH), 12.75 (s, 1H -COOH). Its \(^{13}\)C NMR (DMSO-d\(_6\)/TMS) spectrum (Fig-2.16) showed signals at \(\delta\) 29.87, 113.61, 117.53, 118.85, 122.63, 123.11, 125.65, 126.06, 126.57, 126.89, 134.58, 135.97, 144.72, 154.36, 164.85, 170.98 and its ESI mass spectrum (Fig-2.17) showed molecular ion peak at 310.0(M+1) corresponding to its molecular mass of 309.0(M⁺).

![Scheme-2.14](image-url)
This general procedure \textit{45a} hydrolysis with KOH in ethanol to produce \textit{46a} applied to preparation of other derivatives. 2-(2-(benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)acetonitrile \textit{(45b)}, 2-(2-(benzothiazol-2-yl)-6-chloroimidazo[1,2-a]pyridin-3-yl)acetonitrile \textit{(45c)} and 2-(2-(benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)acetonitrile \textit{(45d)} produced \textit{46b}, \textit{46c} and \textit{46d} respectively. Obtained products structures established on the basis of their analytical and spectral data. Details presented in experimental section.

2-(2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)aceticacid \textit{46a} was treated with pivaloyl chloride in dichloromethane solvent followed by morpholine at 0-5\(^{\circ}\)C for 1h to give the corresponding product, 2-(2-(benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-1-(morpholin-4-y1)ethanone \textit{(47aa)} \textbf{(Scheme-2.15)}. Compound structure confirmed on the basis of its analytical and spectral data. Its \textit{\textbf{1H NMR}} (CDCl\textsubscript{3}/TMS) spectrum \textbf{(Fig-2.18)} showed signals at \(\delta\) 3.54 (t, \(J = 4.4\) Hz, 2H morpholine-\textit{CH}\textsubscript{2}), 3.61 (s, 4H morpholine 2x-\textit{CH}\textsubscript{2}), 3.97 (t, \(J = 4.4\) Hz, 2H morpholine-\textit{CH}\textsubscript{2}), 4.81 (s, 2H -\textit{CH}\textsubscript{2}-CO), 6.92 (t, \(J = 8.0\) Hz, 1H aromatic -\textit{CH}), 7.29 (t, \(J = 7.2\) Hz, 1H aromatic -\textit{CH}), 7.41 (t, \(J = 7.6\) Hz, 1H aromatic -\textit{CH}), 7.50 (t, \(J = 7.2\) Hz, 1H aromatic -\textit{CH}), 7.60 (d, \(J = 8.8\) Hz, 1H aromatic -\textit{CH}), 7.97 (t, \(J = 8.8\) Hz, 2H aromatic -\textit{CH}), 8.62 (d, \(J = 6.8\) Hz, 1H aromatic -\textit{CH}). Its \textit{\textbf{13C NMR}} (CDCl\textsubscript{3}/TMS) spectrum \textbf{(Fig-2.19)} showed signals at \(\delta\) 30.5, 42.71, 46.90, 66.84, 66.94, 113.38, 117.30, 117.79, 121.96, 122.52, 125.14, 125.78,
125.99, 126.25, 134.97, 135.76, 145.40, 154.22, 164.71, 167.29 and its ESI mass spectrum (Fig-2.20) showed molecular ion peak at 379.3(M+1) related to the molar mass product 378.3(M+).

The reaction of 2-(2-(benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)aceticacid (46b), 2-(2-(benzothiazol-2-yl)-6-chloroimidazo[1,2-a]pyridin-3-yl)aceticacid (46c) and 2-(2-(benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)aceticacid (46d) with pivaloyl chloride and morpholine to produce the corresponding morpholinyl amides 47b, 47c and 47d respectively. Analytical and spectral data confirmed the structures.

In similar methods, we have prepared a series of compounds with various amines such as dimethylamine, diethylamine, tert butylamine, cyclo propylamine, cyclo hexylamine, piperidine and pyrrolidine and
different substituents at imidazo[1,2-a]pyridine ring such as 7-methyl, 6-methyl and 6-chloro. All the compounds are presented in Table 2.1.

Analytical and spectral data presented in experimental section.

Table 2.1: Various 2-(benzothiazol-2yl)-3-acetamideimidazo[1,2-a]pyridines derivatives.

<table>
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<tr>
<th>Entry</th>
<th>Product</th>
<th>R</th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
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<th>Yield</th>
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<td>morpholinyl</td>
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<td>2</td>
<td>47ab</td>
<td>-C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
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<td></td>
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<td>70%</td>
</tr>
<tr>
<td>18</td>
<td>47da</td>
<td>-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td></td>
<td>75%</td>
</tr>
<tr>
<td>19</td>
<td>47db</td>
<td>-C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>-C&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td></td>
<td>74%</td>
</tr>
<tr>
<td></td>
<td>47dc</td>
<td>Morpholinyl</td>
<td>78%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>------</td>
<td>-------------</td>
<td>-----</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>47dd</td>
<td>Piperdinyl</td>
<td>82%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>47de</td>
<td>pyrrolidinyl</td>
<td>68%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>47df</td>
<td>H</td>
<td>Tert-butyl</td>
<td>69%</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>47dg</td>
<td>H</td>
<td>Cyclohexyl</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>47dh</td>
<td>H</td>
<td>Cyclopropyl</td>
<td>81%</td>
<td></td>
</tr>
</tbody>
</table>

For further conformation of the structure of these compounds, we analyzed a typical compound of 47aa by single crystal X-Ray analysis. The structure of the compound confirmed unambiguously as depicted below.

![X-Ray crystal structure of compound 47aa](image)

X-Ray crystal structure of compound 47aa - 2-\{(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl\}-1-{morpholin-4-yl}ethanone.
Biological evaluation of prepared compounds

A total of 25 new compounds were screened for in vitro activity against M. tuberculosis H37Rv (ATCC 27294 strain) using the agar dilution method. The MIC (minimum inhibitory concentration) is defined as the minimum concentration of the compound required to completely inhibit bacterial growth. The MIC values (µg/mL) of all the synthesized compounds and three standard antitubercular drugs determined in triplicate at pH 7.40 are presented in Table 2.2. Several derivatives displayed MIC value of 6.25 µg/mL, a value postulated by the global program as an upper threshold for the evaluation of M. tuberculosis therapy and for the discovery of new antituberculosis drugs.

In-vitro MTB screening

Two-fold serial dilutions of each test compound/drug were prepared and incorporated into Middlebrook 7H11 agar medium with oleic acid, albumin, dextrose, and catalase (OADC) growth supplement to get final concentrations of 50, 25, 12.5, 6.25, 3.13, 1.56, and 0.78 µg/mL. Inoculum of M. tuberculosis H37Rv ATCC 27294 was prepared from fresh Middlebrook 7H11 agar slants with OADC (Difco) growth supplement adjusted to 1 mg/mL (wet weight) in Tween 80 (0.05%) saline diluted to 10⁻² to give a concentration of ~10⁷ cfu/mL. Five microliters of this bacterial suspension was spotted onto 7H11 agar tubes containing different concentrations of the drug as discussed above. The tubes were incubated at 37 °C, and final readings (as MIC in µg/mL) were determined after 28 days. This
method is similar to that recommended by the National Committee for Clinical Laboratory Standards for the determination of MIC in triplicate.
### Table 2.2: Antitubercular activity of the compounds.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Compound</th>
<th>MIC in ug/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47aa</td>
<td>12.5</td>
</tr>
<tr>
<td>2</td>
<td>47ab</td>
<td>3.13</td>
</tr>
<tr>
<td>3</td>
<td>47ac</td>
<td>1.56</td>
</tr>
<tr>
<td>4</td>
<td>47ad</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>47ae</td>
<td>6.25</td>
</tr>
<tr>
<td>6</td>
<td>47af</td>
<td>25</td>
</tr>
<tr>
<td>7</td>
<td>47ag</td>
<td>6.25</td>
</tr>
<tr>
<td>8</td>
<td>47ba</td>
<td>12.5</td>
</tr>
<tr>
<td>9</td>
<td>47bb</td>
<td>6.25</td>
</tr>
<tr>
<td>10</td>
<td>47bc</td>
<td>1.56</td>
</tr>
<tr>
<td>11</td>
<td>47bd</td>
<td>3.13</td>
</tr>
<tr>
<td>12</td>
<td>47be</td>
<td>12.5</td>
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<td>1.56</td>
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<td>47ca</td>
<td>3.13</td>
</tr>
<tr>
<td>15</td>
<td>47cb</td>
<td>25</td>
</tr>
<tr>
<td>16</td>
<td>47cc</td>
<td>1.56</td>
</tr>
<tr>
<td>17</td>
<td>47cd</td>
<td>25</td>
</tr>
<tr>
<td>18</td>
<td>47da</td>
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</tr>
<tr>
<td>19</td>
<td>47db</td>
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</tr>
<tr>
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<td>47dc</td>
<td>50</td>
</tr>
<tr>
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<td>47dd</td>
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</tr>
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<tr>
<td>27</td>
<td>Ethambutol</td>
<td>1.56</td>
</tr>
<tr>
<td>28</td>
<td>Pyrazinamide</td>
<td>6.25</td>
</tr>
</tbody>
</table>
2.5 EXPERIMENTAL SECTION:

General procedure for the preparation of 2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridine derivatives (38a-d)

A mixture of 2-aminopyridine 5a (8.9g, 94.7 mmol), 1-(benzothiazol-2-yl)-2-chloroethanone 42 (12.0g, 94.7 mmol) and sodium bicarbonate (12g, 14.3 mmol) in isopropanol was magnetically stirred in a RB flask fitted a condenser initially at room temperature and later at reflux temperature for 6h. The progress of the reaction was monitored by Thin layer chromatography. On completion, the reaction mixture was diluted with water (120 ml) and extracted with MDC (2 X 60 ml). The organic extract was washed with water (50 ml) dried over anhydrous sodium sulphate. The solution was filtered and concentrated to get brown colour solid 38a. Analytical and spectral data are given below.

38a: 2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridine.

![Chemical Structure](image)

**Description**: Brown colour solid.

**Melting point**: Up to 260.0°C (Not clear)

**IR (In KBr)**: 3412, 3118, 3046, 1502, 1450, 1433, 1361, 1314, 1183, 911, 756, 737, 725, 699 cm\(^{-1}\)

**\(^1\)H NMR (DMSO-d\(_6\)/TMS)**: \(\delta 6.99 (t, J = 6.7\ Hz, 1H), 7.34 (t, J = 8.5Hz, 1H)\)
1H), 7.42 (d, J = 7.5 Hz, 1H), 7.52 (t, J = 7.8 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 8.59 (d, J = 6.6 Hz, 1H), 8.65 (s, 1H).

**13C NMR (DMSO-d6/TMS):** δ 112.25, 113.99, 117.54, 122.81, 123.00, 125.66, 126.92, 126.94, 128.02, 134.91, 139.16, 145.33, 154.24, 163.95; **ESI-MS:** (m/z): 252.95 (M+1).

**38b: 2-(Benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridine.**

Description : Brown colour solid.

Melting point: Up to 260.0°C (Not clear).

IR (In KBr) : 3433, 3129, 3038, 1646, 1569, 1432, 1364, 1316, 1185, 1165, 1015, 917, 798, 756, 725, 694 cm⁻¹.

**1H NMR (CDCl₃/TMS):** δ 2.41 (s, 3H), 6.70 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 7.43 (s, 1H), 7.50 (d, J = 7.6 Hz, 1H), 7.96 (d, J = 9.2 Hz, 1H), 8.05 (d, J = 7.2 Hz, 2H), 8.25 (s, 1H).

**13C NMR (CDCl₃/TMS):** δ 21.49, 110.44, 116.28, 116.39, 121.85, 122.86, 124.94, 125.23, 126.20, 135.18, 136.87, 139.97, 146.11, 154.20, 163.77.

ESI-MS:** (m/z): 266.2 (M+1).
38c: 2-(Benzothiazol-2-yl)-6-chloroimidazo[1,2-a]pyridine.

Description : Brown colour solid.

Melting point: Up to 260.0°C (Not clear).

IR (In KBr) : 3421, 3125, 3035, 1183, 919, 796, 758, 726, 709 cm⁻¹.

¹H NMR (CDCl₃/TMS): δ 7.23 (d, J = 9.6 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.65 (d, J = 9.6 Hz, 1H), 7.97 (d, J = 7.9 Hz, 1H), 8.06 (d, J = 8.1 Hz, 1H), 8.22 (s, 1H), 8.29 (s, 1H).

¹³C NMR (CDCl₃/TMS): δ 112.35, 113.25, 117.54, 122.71, 123.00, 125.56, 126.82, 126.74, 128.12, 134.81, 139.36, 144.33, 153.24, 162.95.

ESI-MS: (m/z): 286.0(M+1).

38d: 2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridine.

Description : Brown colour solid.

Melting point: 245.1-247.2°C.

IR (In KBr) : 3434, 3126, 2924, 1569, 1349, 1312, 1184, 1159, 920, 784, 759, 728 cm⁻¹.
$^1$H NMR (CDCl$_3$/TMS): $\delta$ 2.32 (s, 3H), 7.09 (dd, $J = 1.0$Hz, $J = 9.2$Hz, 1H), 7.40 (t, $J = 7.6$Hz, 1H), 7.50 (t, $J = 7.6$Hz, 1H), 7.59 (d, $J = 6.8$Hz, 1H), 7.95 (m, 2H), 8.05 (d, $J = 8.70$Hz, 1H), 8.23, (S, 1H).

$^{13}$C NMR (CDCl$_3$/TMS): $\delta$ 18.04, 110.53, 117.25, 121.74, 122.70, 123.23, 123.55, 124.83, 126.09, 128.95, 135.07, 139.75, 144.56, 154.05, 163.67.

ESI-MS:($m/z$): : 266.1(M+1).

**General procedure for the preparation of 2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N,N-dimethylmethanamine derivatives (43a-d).**

A mixture of 2-(benzothiazol-2-yl)imidazo[1,2-a]pyridine 38a (1.9g, 7.54mmol), dimethylamine (40% in water) (1.27g, 11.3 mmol) and paraformaldehyde (0.29g, 9.81mmol) in acetic acid (40.0 ml) was stirred at 50-55°C for 4h and the progress of the reaction was monitored by TLC. After completion, acetic acid was distilled at reduced pressure and the residue diluted with water (25 ml). The solution was basified with sodium bicarbonate. Product was extracted with ethylacetate (2 x 25 ml) and the organic layer was washed with water 20 ml, dried over anhydrous sodium sulphate, filtered and concentrated. The residue was stirred in 10 ml of n-Hexane to give the product 43a. Analytical and spectral data are given below.
43a: (2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N,N-dimethylmethanamine.

Description: Pale brown colour solid.

Melting point: 173.5 - 174.9°C

IR (In KBr): 3435, 3036, 2935, 2822, 2775, 1374, 1346, 1253, 1235, 1044, 1014, 761, 751, 739, 691 cm⁻¹.

¹H NMR (CDCl₃/TMS): δ 2.37 (s, 6H, 2xCH₃), 4.48 (s, 2H), 6.91 (t, J = 6.7 Hz, 1H), 7.31 (t, J = 8.9 Hz, 1H), 7.43 (d, J = 7.5 Hz, 1H), 7.53 (t, J = 7.7 Hz, 1H), 7.72 (d, J = 9.1 Hz, 1H), 8.00 (d, J = 7.9 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 8.46 (d, J = 6.8 Hz, 1H).

¹³C NMR (CDCl₃/TMS): δ 45.29, 52.07, 112.85, 117.71, 121.04, 121.69, 123.15, 124.89, 125.68, 125.83, 125.96, 135.17, 137.50, 145.21, 154.55, 164.34.

ESI-MS: (m/z): 309.2(M+1).

43b: (2-(Benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)-N,N-dimethylmethanamine.
**Description**: Pale brown colour solid.

**Melting point**: 163.4-164.8°C.

**IR (In KBr)**: 3430, 3055, 2942, 2812, 2756, 1644, 1575, 1453, 1374, 1238, 1011, 963, 780, 757, 726, 609 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**:  δ 2.32 (s, 6H, 2xCH₃), 2.41 (s, 3H), 4.41 (s, 2H), 6.69 (t, J = 2.4 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.41 (s, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 6.8 Hz, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 21.51, 45.26, 52.07, 115.56, 115.96, 120.57, 121.66, 123.07, 124.77, 124.93, 125.90, 135.15, 136.70, 137.22, 145.67, 154.56, 164.56.

**ESI-MS**: (m/z): 323.3(M+1).

43c: (2-(Benzothiazol-2-yl)-6-chloroimidazo[1,2-a]pyridin-3-yl)-N,N-dimethylmethanamine.

**Description**: Pale brown colour solid.

**Melting point**: 193.5 – 196.8°C

**IR (In KBr)**: 3429, 3097, 2821, 2778, 1373, 1088, 965, 794, 758, 733, 682 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**:  δ 2.37 (s, 6H, 2xCH₃), 4.43 (s, 2H), 7.25 (m, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 8.08 (d, J = 8.1 Hz, 1H), 8.51 (s, 1H).
43d: (2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-N,N-dimethylmethanamine.

**Description**: Pale brown colour solid.

**Melting point**: 188.7 – 190.0°C.

**IR (In KBr)**: 3400, 3081, 2977, 2943, 2818, 2773, 1571, 1540, 1455, 1370, 1344, 1237, 1160, 1041, 1018, 965, 934, 793, 763, 728 cm⁻¹.

**1H NMR (CDCl₃/TMS)**: δ 2.35 (s, 6H, 2xCH₃), 2.37 (s, 3H), 4.42 (s, 2H), 7.12 (dd, J = 1.1 Hz, J = 9.3 Hz, 1H), 7.39 (t, J = 7.2 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.59 (d, J = 12 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 8.13 (s, 1H).

**13C NMR (CDCl₃/TMS)**: δ 18.46, 45.21, 51.85, 116.90, 120.59, 121.52, 122.51, 122.94, 124.66, 125.77, 128.82, 135.00, 137.26, 144.18, 154.43, 164.40.

**ESI-MS**: (m/z): 323.2(M+1).
General procedure for the preparation of (2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N,N,N-trimethyl methanammonium iodide derivatives (44a-d).

A solution of Mannich base 43a (1.4g,0.465 mmol) in 140 ml of acetone was stirred at 10-15°C for about 10-15 minutes and to this solution methyl iodide (1.98g 1.397mmol) was added. The reaction mixture was stirred for 16h at RT and the solid was filtered, washed with acetone (10 ml) to give the product 44a. Analytical and spectral data are given below.

44a: [2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl]-N,N,N-trimethylmethanammonium iodide.

Description : Pale brown colour solid.

Melting point: Up to 260.0°C (Not clear).

IR (In KBr) : 3428, 3067, 3033, 3007, 1488, 1359, 1192, 1148, 974, 926, 868, 752, 737, 727, 695 cm⁻¹.

¹H NMR (DMSO-d₆/TMS): δ 3.25 (s, 9H, 3xCH₃), 5.51 (s, 2H), 7.26 (d, J = 6.7 Hz, 1H), 7.61 (m, 3H), 7.87 (d, J = 9.0 Hz, 1H), 8.22 (t, J = 8.8 Hz, 2H), 9.01 (d, J = 6.8 Hz, 1H).

¹³C NMR (DMSO-d₆/TMS): δ 52.83, 57.38, 112.31, 115.10, 118.21,
122.79, 123.76, 126.29, 126.36, 127.07, 128.45, 134.90, 140.98, 146.55, 153.98, 163.73.

44b: \((2-\text{(Benzothiazol-2-yl)-7-methylimidazo}[1,2-a]\text{pyridin-3-yl})-\text{N,N,N-trimethylmethanammonium iodide.}\)

\[
\begin{align*}
\text{Description:} & \quad \text{Pale brown colour solid.} \\
\text{Melting point:} & \quad \text{Up to } 260.0^\circ C \text{ (Not clear).} \\
\text{IR (In KBr):} & \quad 3436, 3045, 2996, 2917, 1714, 1647, 1488, 1358, 925, 872, 780, 770, 735, 607 \text{ cm}^{-1}. \\
\text{\textsuperscript{1}H NMR (DMSO-d\textsubscript{6}/TMS):} & \quad \delta \ 2.42 \text{ (s, } 3H), \ 3.22 \text{ (s, } 9H, 3x\text{CH}_3), \ 5.45 \text{ (s, } 2H), \ 7.10 \text{ (d, } J = 6.8 \text{ Hz, } 1H), \ 7.50 \text{ (t, } J = 7.6 \text{ Hz, } 1H), \ 7.60 \text{ (t, } J = 7.6 \text{ Hz, } 2H), \ 8.19 \text{ (t, } J = 7.6 \text{ Hz, } 2H), \ 8.88 \text{ (d, } J = 6.8 \text{ Hz, } 1H). \\
\text{\textsuperscript{13}C NMR (DMSO-d\textsubscript{6}/TMS):} & \quad \delta \ 21.22, \ 52.79, \ 57.48, \ 111.64, \ 116.24, \ 117.53, \ 122.72, \ 123.70, \ 125.40, \ 126.22, \ 126.97, \ 134.83, \ 139.24, \ 140.84, \ 146.87, \ 153.96, \ 163.77. \\
\end{align*}
\]

44c: \((2-\text{(Benzothiazol-2-yl)-6-chloroimidazo}[1,2-a]\text{pyridin-3-yl})-\text{N,N,N-trimethylmethanammonium iodide.}\)

\[
\begin{align*}
\text{Description:} & \quad \text{Pale brown colour solid.} \\
\text{Melting point:} & \quad \text{Up to } 260.0^\circ C \text{ (Not clear).} \\
\text{IR (In KBr):} & \quad 3436, 3045, 2996, 2917, 1714, 1647, 1488, 1358, 925, 872, 780, 770, 735, 607 \text{ cm}^{-1}. \\
\text{\textsuperscript{1}H NMR (DMSO-d\textsubscript{6}/TMS):} & \quad \delta \ 2.42 \text{ (s, } 3H), \ 3.22 \text{ (s, } 9H, 3x\text{CH}_3), \ 5.45 \text{ (s, } 2H), \ 7.10 \text{ (d, } J = 6.8 \text{ Hz, } 1H), \ 7.50 \text{ (t, } J = 7.6 \text{ Hz, } 1H), \ 7.60 \text{ (t, } J = 7.6 \text{ Hz, } 2H), \ 8.19 \text{ (t, } J = 7.6 \text{ Hz, } 2H), \ 8.88 \text{ (d, } J = 6.8 \text{ Hz, } 1H). \\
\text{\textsuperscript{13}C NMR (DMSO-d\textsubscript{6}/TMS):} & \quad \delta \ 21.22, \ 52.79, \ 57.48, \ 111.64, \ 116.24, \ 117.53, \ 122.72, \ 123.70, \ 125.40, \ 126.22, \ 126.97, \ 134.83, \ 139.24, \ 140.84, \ 146.87, \ 153.96, \ 163.77. \\
\end{align*}
\]
**Description**: Pale brown colour solid.

**Melting point**: Up to 260.0°C (Not clear).

**IR (In KBr)**: 3438, 3006, 1707, 1488, 1362, 1088, 877, 794, 765, 732 cm$^{-1}$.

**$^1$H NMR (DMSO-$d_6$/TMS)**: δ 3.20 (s, 9H, 3xCH$_3$), 5.43 (s, 2H) 7.49 (t, $J$ = 7.6 Hz, 1H), 7.60 (m, 2H), 7.89 (d, $J$ = 9.5 Hz, 1H), 8.19 (t, $J$ = 7.8 Hz, 2H), 9.24 (s, 1H).

**$^{13}$C NMR (DMSO-$d_6$/TMS)**: δ 52.83, 57.15, 113.05, 119.08, 122.33, 122.81, 123.83, 124.29, 126.45, 127.12, 129.34, 134.96, 141.90, 145.09, 153.92, 163.22.

**44d**: (2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-N,N,N-trimethylmethanammonium iodide.

![Structural formula of 44d]

**Description**: Pale brown colour solid.

**Melting point**: Up to 260.0°C (Not clear).

**IR (In KBr)**: 3437, 3030, 3005, 1485, 1380, 1361, 1317, 1157, 973, 943, 875, 802, 758, 728 cm$^{-1}$.

**$^1$H NMR (DMSO-$d_6$/TMS)**: δ 2.38 (s, 3H), 3.25 (s, 9H, 3xCH$_3$), 5.46 (s, 2H) 7.40 (d, $J$ = 9.1 Hz, 1H), 7.49 (t, $J$ = 7.5 Hz, 1H), 7.59 (t, $J$ = 7.5 Hz, 1H), 7.74 (d, $J$ = 9.1 Hz, 1H), 8.14-8.19 (m, 2H), 8.84 (s, 1H).
$^{13}$C NMR (DMSO-d$_6$/TMS): δ 18.20, 52.75, 57.37, 111.10, 117.37, 122.62, 123.41, 123.57, 124.71, 126.14, 126.89, 131.20, 134.74, 140.70, 145.45, 153.85, 163.71.

**General procedure for the preparation of 2-(2-(Benzothiazol-2-yl)imidazo [1,2-a] pyridin-3-yl)acetonitrile derivatives (45a-d).**

A mixture of the quaternary salt 44a (1.5g, 3.3 mmol) and potassium cyanide (1.08g, 16.7mol) in 15 ml of water and 7.5ml of DMI was stirred at reflux temperature for 30-36h. The progress of the reaction was monitored by TLC and on completion, cooled to room temperature and stirred for 30 minutes. Formed solid was filtered, washed with water, dried in the oven. Obtained solid further purified by silica gel column chromatography using MDC as eluent to give the product 45a. Analytical and spectral data are given below.

**45a: 2-(2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)acetonitrile.**

**Description** : Off-white solid

**Melting point:** 238.0 - 240.0°C

**IR (In KBr)** : 3434, 2944, 2924, 2244, 1364, 1317, 1240, 1143, 925, 759, 747, 736 cm$^{-1}$.

**$^1$H NMR (CDCl$_3$/TMS):** δ 5.00 (s, 2H), 7.07 (t, $J = 6.7$ Hz, 1H), 7.35-7.41 (m, 2H), 7.51 (t, $J = 7.6$ Hz, 1H), 7.77 (d, $J = 9.1$ Hz, 1H), 7.98 (d,
\( J = 7.9 \ \text{Hz, 1H}) \), 8.08 (d, \( J = 7.8 \ \text{Hz, 1H}) \), 8.17 (d, \( J = 6.8 \ \text{Hz, 1H}) \).

\textbf{\( ^{13}C\) NMR (CDCl}_3/TMS\):  \( \delta \) 32.65, 113.80, 114.07, 117.99, 118.20, 122.65, 124.50, 125.35, 126.04, 126.42, 134.91, 136.26, 139.29, 145.19, 153.76, 165.02,}

\textbf{ESI-MS: (m/z): 291.1(M+1).}

\textbf{45b:} \( 2-(2-(\text{Benzothiazol-2-yl})-7\text{-methylimidazo[1,2-a]pyridin-3-yl})\text{acetonitrile}. \)

\textbf{Description:} Off-white solid

\textbf{Melting point:} Up to 260.0°C (Not clear).

\textbf{IR (In KBr):} 3436, 3053, 2921, 2245, 1645, 1361, 1316, 1262, 1243, 1166, 919, 755, 728, 706, 511 cm\(^{-1}\).

\textbf{\( ^1H\) NMR (CDCl}_3/TMS\):  \( \delta \) 2.46 (s, 3H), 4.96 (s, 2H), 6.87 (t, \( J = 6.0 \ \text{Hz, 1H}) \), 7.42 (t, \( J = 7.2 \ \text{Hz, 1H}) \), 7.52 (t, \( J = 6.4 \ \text{Hz, 2H}) \), 7.97 (d, \( J = 8.0 \ \text{Hz, 1H}) \), 8.05 (t, \( J = 8.0 \ \text{Hz, 2H}) \).

\textbf{\( ^{13}C\) NMR (CDCl}_3/TMS\):  \( \delta \) 13.31, 21.51, 110.42, 115.04, 116.77, 117.04, 121.85, 122.41, 123.14, 125.29, 126.31, 134.90, 137.02, 137.51, 146.04, 154.18, 163.46.

\textbf{ESI-MS:(m/z):} 305.4(M+1).
45c: 2-(2-(Benzothiazol-2-yl)-6-chloroimidazo[1,2-a]pyridin-3-yl)acetonitrile.

**Description**: Off-white solid

**Melting point**: Up to 260.0°C (Not clear).

**IR (In KBr)**: 3422, 3060, 2920, 2245, 1680, 1375, 1144, 944, 796, 759, 729, 706 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 5.41 (s, 2H), 7.47 (t, J = 8.4 Hz, 2H), 7.55 (t, J = 7.6 Hz, 1H), 7.77 (d, J = 9.6 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 7.8 Hz, 1H), 8.17 (s, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 30.83, 118.40, 120.40, 120.92, 122.67, 123.17, 124.19, 125.75, 126.92, 127.30, 134.62, 136.75, 140.90, 154.35, 164.47, 170.07.

**ESI-MS:** (m/z): 326.0(M⁺).

45d: 2-(2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)acetonitrile.
**Description**: Off-white solid

**Melting point**: Up to 260.0°C (Not clear).

**IR (In KBr)**: 3424, 3060, 2921, 2246, 1684, 1375, 1144, 944, 796, 759, 729, 706 cm⁻¹.

**₁H NMR (CDCl₃/TMS)**: δ 2.44 (s, 3H), 4.98 (s, 2H), 7.24 (m, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 7.2 Hz, 1H), 7.67 (d, J = 9.2 Hz, 1H), 7.91 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H).

**₁³C NMR (CDCl₃/TMS)**: δ 13.19, 18.41, 110.50, 114.88, 117.64, 120.66, 121.70, 123.01, 124.30, 125.16, 126.18, 129.38, 134.76, 136.94, 144.54, 154.06, 163.34.

**ESI-MS (m/z)**: 305.3(M+1).

**General procedure for the preparation of 2-(2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)acetic acid derivatives (46a-d).**

The acetonitrile derivative **45a** (1.22g, 4.22 mmol) was dissolved in aqueous ethanol (50 ml), containing potassium hydroxide 1.4g and the reaction mixture was stirred under reflux for 24h. The progress of the reaction was monitored by TLC and on completion; the reaction mixture was filtered and acidified with acetic acid. Solid formed was filtered and recrystallized from water to give the product **46a**. Analytical and spectral data are given below.
46a: 2-{2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl}acetic acid.

![Image of 46a](image)

**Description**: Pale brown colour solid.

**Melting point**: Up to 260.0°C (Not clear).

**IR (In KBr)**: 3423, 3055, 2861, 2776, 1707, 1372, 1315, 1236, 1196, 938, 763, 747, 739, 698 cm\(^{-1}\).

**\(^1\)H NMR (DMSO-\(d_6\)/TMS)**: \(\delta\) 4.66 (s, 2H), 7.02 (t, \(J = 6.6\) Hz, 1H), 7.41 (m, 2H), 7.50 (t, \(J = 7.6\) Hz, 1H), 7.67 (d, \(J = 9.0\) Hz, 1H), 8.00 (d, \(J = 8.0\) Hz, 1H), 8.11 (d, \(J = 7.8\) Hz, 1H), 8.45 (d, \(J = 6.8\) Hz, 1H), 12.75 (s, 1H).

**\(^{13}\)C NMR (DMSO-\(d_6\)/TMS)**: \(\delta\) 29.87, 113.61, 117.53, 118.85, 122.63, 123.11, 125.65, 126.06, 126.57, 126.89, 134.58, 135.97, 144.72, 154.36, 164.85, 170.98.

**ESI-MS: [m/z]**: 310.0(M+1).

46b: 2-{2-(Benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl}acetic acid.

![Image of 46b](image)
Description : Pale brown colour solid.

Melting point: 182.2 - 183.5°C.

IR (In KBr) : 3430, 3063, 2910, 2459, 1905, 1710, 1646, 1257, 936, 885, 783, 755, 726, 670 cm⁻¹.

¹H NMR (DMSO-d₆/TMS): δ 2.38 (s, 3H), 4.67 (s, 2H), 6.89 (d, J = 7.2 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 8.35 (d, J = 7.2 Hz, 1H).

¹³C NMR (DMSO-d₆/TMS): δ 21.29, 29.84, 115.56, 116.14, 118.33, 122.58, 123.03, 125.19, 125.55, 126.84, 134.54, 135.68, 137.20, 145.12, 154.37, 165.01, 171.03.

ESI-MS: (m/z): 324.1(M+1).

46c: 2-(2-(Benzothiazol-2-yl)-6-chlorimidazo[1,2-a]pyridin-3-yl)aceticacid.

Description : Pale brown colour solid.

Melting point: 231.0 - 234.2 °C (Decomposed).

IR (In KBr) : 3434, 3052, 2920, 1708, 1315, 1245, 1187, 946, 802, 762, 730, 723, 666 cm⁻¹.

¹H NMR (DMSO-d₆/TMS): δ 4.71 (s, 2H), 7.46 (d, J = 7.5 Hz, 2H), 7.55 (t, J = 7.6 Hz, 1H), 7.76 (d, J = 9.5 Hz, 1H), 8.03 (d, J = 7.9 Hz, 1H), 8.14 (d, J = 7.76 Hz, 1H), 8.84 (s, 1H).
13C NMR (DMSO-d<sub>6</sub>/TMS): δ 29.98, 118.41, 119.86, 120.69, 122.68, 123.21, 124.26, 125.81, 126.97, 127.47, 134.58, 136.85, 143.13, 154.31, 164.31, 170.82.

ESI-MS:(m/z): 344.1(M+1).

46d: 2-(2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)acetic acid.

![Chemical Structure](Image)

Description : Pale brown colour solid.

Melting point: 221.0 - 222.0°C (Decomposed).

IR (In KBr) : 3429, 3061, 2922, 1710, 1315, 1239, 1187, 946, 802, 762, 734, 723, 662 cm<sup>-1</sup>.

1H NMR (DMSO-d<sub>6</sub>/TMS): δ 2.34 (s, 3H), 4.63 (s, 2H), 7.22 (d, J= 8.0 Hz, 1H), 7.42 (t, J= 7.6 Hz, 1H), 7.51 (t, J= 7.2 Hz, 1H), 7.58 (d, J= 9.2 Hz, 1H), 7.99 (d, J= 8.0 Hz, 1H), 8.10 (d, J= 8.0 Hz, 1H), 8.23 (s, 1H).

13C NMR (DMSO-d<sub>6</sub>/TMS): δ 18.08, 30.11, 116.74, 118.88, 122.44, 122.80, 122.90, 123.07, 125.42, 126.70, 129.36, 134.40, 135.63, 143.60, 154.27, 164.94, 170.93.

ESI-MS:(m/z): 324.1(M+1).
Typical procedure for the preparation of 2-{2-[Benzothiazol-2-yl]imidazo[1,2-a]pyridin-3-yl}acetamide derivatives.

In a RB flask was charged acid derivative (46a), dichloromethane and triethylamine. It was cooled to 0-5°C and pivaloyl chloride was added under stirring. After the addition, the reaction mixture was stirred at 0-5°C for about 30 min. Reaction progress was monitored by TLC and after mixed anhydride formation was completed, amine base was added at 0-5°C. The reaction mixture was stirred at 0-5°C for 1h and monitored the reaction by TLC for completion of reaction. The reaction mixture quenched in water and extracted with MDC. The MDC layer was distilled under reduced pressure and further purified by the silica gel column chromatography. All the obtained compounds analysed by their spectral data and given below.

47aa: 2-{2-[Benzothiazol-2-yl]imidazo[1,2-a]pyridin-3-yl}-(1-(morpholin-4-yl)ethanone.

![Chemical structure](image)

**Description** : Off-white solid

**Melting point**: 253.0 - 256.5°C.

**IR (In KBr)** : 3326, 3037, 2894, 2851, 1650, 1599, 1571, 1451,
1434, 1358, 1232, 1216, 1114, 928, 772, 747, 737, 429 cm⁻¹.

**¹H NMR (CDCl₃/TMS):**  δ 3.54 (t, J = 4.4 Hz, 2H), 3.61 (s, 4H), 3.97 (t, J = 4.4 Hz, 2H), 4.81 (s, 2H), 6.92 (t, J = 8.0 Hz, 1H), 7.29 (t, J = 7.2 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 7.2 Hz, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.97 (t, J = 8.8 Hz, 2H), 8.62 (d, J = 6.8 Hz, 1H).

**¹³C NMR (CDCl₃/TMS):**  δ 30.05, 42.71, 46.90, 66.84, 66.94, 113.38, 117.30, 117.79, 121.96, 122.52, 125.14, 125.78, 125.99, 126.25, 134.97, 135.76, 145.40, 154.22, 164.71, 167.29.

**ESI-MS:** (m/z):  379.3(M+1).

**47ab:**  2-(2-(Benzothiazol-2-yl)imidazo[1-2-a]pyridin-3-yl)-N,N-diethylacetamide.

![](image)

**Description:** Off-white solid

**Melting point:** 182.2 - 184.5°C.

**IR (In KBr):**  3324, 2971, 2930, 1633, 1573, 1450, 1435, 1362, 935, 754, 735, 430 cm⁻¹.

**¹H NMR (CDCl₃/TMS):**  δ 1.11 (t, J = 7.2 Hz, 3H), 1.21 (t, J = 7.2 Hz, 3H), 3.40 (m, 2H), 3.64 (m, 2H), 4.48 (s, 2H), 6.90 (t, J = 6.4 Hz, 1H), 7.28 (s, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.99 (t, J = 7.2 Hz, 2H), 8.64 (d, J = 6.8 Hz, 1H).
**47ac: 2-(2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-1-(piperidin-1-yl)ethanone.**

**Description**: Off-white solid

**Melting point**: up to 260.0°C (Not clear).

**IR (In KBr)**: 3060, 3037, 2938, 2917, 1644, 1599, 1572, 1437, 1353, 1252, 1238, 1226, 1123, 1011, 930, 769, 747, 736, 429 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 1.37 (m, 2H), 1.47 (m, 2H), 1.55 (m, 2H), 3.54 (t, J = 5.2 Hz, 2H), 3.78 (t, J = 5.1 Hz, 2H), 4.82 (s, 2H), 6.89 (t, J = 6.7 Hz, 1H), 7.27 (t, J = 9.1 Hz, 1H), 7.4 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.66 (d, J = 9.0 Hz, 1H), 7.99 (t, J = 8.6 Hz, 2H), 8.62 (d, J = 6.7 Hz, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 13.09, 14.48, 30.66, 40.84, 42.62, 113.17, 117.62, 118.10, 121.86, 122.68, 124.97, 125.84, 126.00, 126.09, 135.04, 135.78, 145.39, 154.37, 164.70, 167.68.

**ESI-MS: (m/z)**: 365.3 (M+1).

**ESI-MS: (m/z)**: 377.3(M+1).
47ad: 2-(2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-1-(pyrrolidin-1-yl)ethanone.

**Description**: Off-white solid

**Melting point**: 244.0 - 249.0°C.

**IR (In KBr)**: 3431, 3052, 2970, 2871, 1655, 1634, 1439, 1391, 1363, 1259, 1242, 934, 746, 732, 726, 432 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 1.87 (m, 2H), 1.95 (m, 2H), 3.48 (t, ³J = 6.7 Hz, 2H), 3.79 (t, ³J = 6.7 Hz, 2H), 4.80 (s, 2H), 6.90 (t, ³J = 6.7 Hz, 1H), 7.28 (t, ³J = 9.1 Hz, 1H), 7.41 (t, ³J = 7.3 Hz, 1H), 7.50 (t, ³J = 7.6 Hz, 1H), 7.67 (d, ³J = 9.0 Hz, 1H), 7.99 (t, ³J = 8.1 Hz, 2H), 8.60 (d, ³J = 6.8 Hz, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 24.37, 26.26, 31.45, 46.19, 47.20, 113.13, 117.68, 121.87, 122.68, 124.93, 125.79, 125.87, 126.04, 135.08, 145.37, 154.42, 167.03.

**ESI-MS** (m/z): 363.1(M+1).
47ae: 2-(2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N-tert-butylacetamide.

Description: Off-white solid

Melting point: 179.0 - 181.2°C.

IR (In KBr): 3277, 3222, 3068, 3046, 2959, 2929, 1675, 1360, 1313, 1254, 1240, 1227, 1032, 754, 733, 728, 430 cm⁻¹.

¹H NMR (CDCl₃/TMS): δ 1.26 (s, 9, 3xCH₃), 4.19 (s, 2H), 6.95 (t, J = 6.5 Hz, 1H), 7.30 (t, J = 8.6 Hz, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.67 (d, J = 9.0 Hz, 1H), 8.01 (t, J = 7.5 Hz, 2H), 8.20 (s, 1H), 8.49 (d, J = 6.6 Hz, 1H).

¹³C NMR (CDCl₃/TMS): δ 28.71, 34.10, 51.12, 113.73, 117.85, 119.35, 122.13, 122.38, 124.73, 125.24, 126.01, 126.46, 134.95, 135.89, 145.09, 153.68, 165.07, 167.85.

ESI-MS: [m/z]: 365.3(M+1).
47af: 2-(2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N-cyclohexylacetamide.

**Description**: Off-white solid.

**Melting point**: up to 260.0°C (Not clear).

**IR (In KBr)**: 3311, 2930, 2853, 1633, 1539, 1364, 1344, 1139, 1124, 929, 756, 745, 729, 431 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 1.13 (m, 2H), 1.29 (m, 2H), 1.66 (m, 4H), 1.81 (m, 2H), 3.70 (m, 1H), 4.26 (s, 2H), 6.96 (t, J = 6.7 Hz, 1H), 7.30 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.56 (t, J = 7.7 Hz, 1H), 7.67 (d, J = 9.0 Hz, 1H), 8.03 (t, J = 7.9 Hz, 2H), 8.27 (d, J = 7.3 Hz, 1H), 8.50 (d, J = 6.8 Hz, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 24.50, 25.48, 32.82, 33.12, 48.27, 113.70, 117.89, 119.15, 122.13, 122.37, 124.71, 125.26, 125.66, 126.49, 135.00, 136.03, 145.10, 153.71, 165.07, 167.75.

**ESI-MS:** [m/z]: 391.4(M+1).
47ag: 2-(2-(Benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)-N-cyclopropylacetamide.

**Description**: Off-white solid.

**Melting point**: up to 260.0°C (Not clear).

**IR (In KBr)**: 3277, 3053, 2925, 1644, 1537, 1364, 1256, 1238, 1033, 927, 757, 747, 731, 432 cm\(^{-1}\).

**\(^1\)H NMR (CDCl\(_3\)/TMS)**: \(\delta\) 0.458 (m, 2H), 0.718 (m, 2H), 2.71 (m, 1H), 4.24 (s, 2H), 6.96 (t, \(J = 6.7\) Hz, 1H), 7.30 (t, \(J = 7.3\) Hz, 1H), 7.46 (t, \(J = 7.3\) Hz, 1H), 7.56 (t, \(J = 7.8\) Hz, 1H), 7.67 (d, \(J = 9.0\) Hz, 1H), 8.00 (d, \(J = 8.0\) Hz, 2H), 8.48 (d, \(J = 6.3\) Hz, 2H).

**\(^{13}\)C NMR (CDCl\(_3\)/TMS)**: \(\delta\) 6.18, 22.49, 33.85, 113.63, 117.78, 118.57, 122.00, 122.17, 124.52, 125.21, 125.92, 126.40, 134.80, 135.94, 145.00, 153.47, 164.97, 169.81.

**ESI-MS**: (m/z): 349.3(M+1).
47ba: 2-(2-(Benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)-N,N-diethylacetamide.

**Description**: Off-white solid.

**Melting point**: 212.0 - 214.5°C.

**IR (In KBr)**: 3436, 3070, 2974, 1638, 1454, 1434, 1260, 1034, 935, 753 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 1.09 (t, J = 7.0 Hz, 3H), 1.15 (t, J = 7.0 Hz, 3H), 2.40 (s, 3H), 3.38 (m, 2H), 3.61 (m, 2H), 4.79 (s, 2H), 6.70 (d, J = 6.4 Hz, 1H), 7.39 (t, J = 8.0 Hz, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.97 (t, J = 7.3 Hz, 2H), 8.52 (d, J = 7.0 Hz, 1H).

**¹³C (CDCl₃/TMS)**: δ 13.09, 14.47, 21.49, 30.83, 40.79, 42.58, 115.86, 115.88, 117.54, 121.85, 122.61, 124.85, 125.19, 126.04, 135.04, 135.46, 136.87, 145.85, 154.40, 164.94, 167.79.

**ESI-MS**: (m/z) 379.2(M+1).
47bb: 2-(2-(Benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)-1-(morpholin-4-yl)ethanone.

**Description**: Off-white solid.

**Melting point**: Up to 260.0°C (Not Clear).

**IR (In KBr)**: 3436, 3052, 2982, 2856, 1648, 1434, 1359, 1235, 1120, 1028, 933, 756 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 2.41 (s, 3H), 3.51 (t, J = 4.6 Hz, 2H), 3.6 (s, 4H), 3.95 (t, J = 4.7 Hz, 2H), 4.77 (s, 2H), 6.73 (d, J = 7.1 Hz, 1H), 7.40 (t, J = 7.4 Hz, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.96 (t, J = 10.2 Hz, 2H), 8.49 (d, J = 7.0 Hz, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 21.49, 30.15, 42.70, 46.38, 115.99, 116.09, 116.75, 121.92, 122.45, 124.90, 125.02, 126.18, 134.93, 135.41, 137.07, 145.91, 154.22, 164.88, 167.39.

**ESI-MS**(m/z): 393.2(M+1).
47bc: 2-(2-(Benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)-1-(piperidin-1-yl)ethanone.

**Description**: Off-white solid

**Melting point**: 172.3 - 174.2°C.

**IR (In KBr)**: 3327, 2928, 2851, 1622, 1571, 1454, 1437, 1360, 1242, 1088, 930, 725 cm⁻¹.

**¹H (CDCl₃/TMS)**: δ 1.34 (m, 2H), 1.53 (m, 4H), 2.42 (s, 3H), 3.54 (t, J = 5.5 Hz, 2H), 3.77 (t, J = 5.3 Hz, 2H), 4.79 (s, 2H), 6.71 (d, J = 6.4 Hz, 1H), 7.39 (t, J = 7.4 Hz, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.98 (t, J = 8.2 Hz, 2H), 8.51 (d, J = 7.0 Hz, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 21.48, 24.45, 25.77, 26.54, 30.66, 43.53, 47.54, 115.90, 115.95, 117.45, 121.83, 122.63, 124.86, 125.08, 126.04, 134.98, 135.33, 136.87, 145.81, 154.39, 164.87, 166.85.

**ESI-MS**: (m/z): 391.3(M+1).
47bd: 2-(2-(Benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)-1-(pyrrolidin-1-yl)ethanone.

**Description**: Off-white solid

**Melting point**: Up to 260.0°C (Not clear).

**IR (In KBr)**: 3435, 2970, 2870, 1655, 1437, 1394, 1359, 1164, 1033, 934, 754 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 1.84 (m, 2H), 1.95 (m, 2H), 2.39 (s, 3H), 3.46 (t, $J = 6.9$ Hz, 2H), 3.75 (t, $J = 6.8$ Hz, 2H), 4.74 (s, 2H), 6.70 (d, $J = 6.8$ Hz, 1H), 7.38 (t, $J = 8.5$ Hz, 2H), 7.48 (t, $J = 7.7$ Hz, 1H), 7.97 (t, $J = 7.6$ Hz, 2H), 8.45 (d, $J = 7.0$ Hz, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 21.48, 24.35, 26.25, 31.52, 46.18, 47.15, 115.86, 117.15, 121.84, 122.61, 124.82, 124.99, 125.99, 135.03, 135.79, 136.87, 145.80, 154.42, 164.89, 167.15.

**ESI-MS: [m/z]**: 377.2 (M+1).
47be: 2-(2-(Benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)-N-tert-butylacetamide.

**Description**: Off-white solid.

**Melting point**: 230.5 - 233.8°C.

**IR (In KBr)**: 3434, 3294, 2962, 1680, 1566, 1359, 1314, 1243, 1032, 941, 754 cm\(^{-1}\).

**\(^1\)H NMR (CDCl\(_3\)/TMS)**: \(\delta\) 1.26 (s, 9H, 3xCH\(_3\)), 2.42 (s, 3H), 4.15 (s, 2H), 6.77 (d, \(J = 6.4\) Hz, 1H), 7.43 (d, \(J = 7.8\) Hz, 2H), 7.53 (t, \(J = 7.6\) Hz, 1H), 8.00 (m, 2H), 8.20 (s, 1H), 8.36 (d, \(J = 7.0\) Hz, 1H).

**\(^{13}\)C NMR (CDCl\(_3\)/TMS)**: \(\delta\) 21.49, 28.70, 34.10, 51.07, 116.05, 116.42, 118.88, 122.08, 122.19, 123.83, 125.09, 126.37, 134.94, 135.61, 137.09, 145.55, 153.70, 165.26, 167.97.

**ESI-MS**: (m/z): 379.2(M+1).
**47bf**: 2-(2-(Benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridin-3-yl)-N-cyclohexylacetamide.

**Description**: Off-white solid.

**Melting point**: 236.8 - 237.9°C.

**IR (In KBr)**: 3326, 2928, 2851, 1657, 1575, 1541, 1312, 1244, 1069, 928, 753 cm\(^{-1}\).

**\(^1\)H NMR (CDCl\(_3\)/TMS)**: \(\delta\) 1.12 (m, 2H), 1.28 (m, 2H), 1.60 (m, 4H), 1.80 (m, 2H), 2.48 (s, 3H), 3.69 (m, 1H), 4.22 (s, 2H), 6.78 (d, \(J = 6.8\) Hz, 1H), 7.44 (m, 2H), 7.55 (t, \(J = 7.6\) Hz, 1H), 8.01 (t, \(J = 6.8\) Hz, 2H), 8.26 (d, \(J = 7.4\) Hz, 1H), 8.36 (d, \(J = 7.0\) Hz, 1H).

**\(^{13}\)C NMR (CDCl\(_3\)/TMS)**: \(\delta\) 21.54, 24.52, 25.48, 32.82, 33.10, 48.24, 116.04, 116.46, 118.70, 122.13, 122.30, 123.80, 125.17, 126.46, 134.95, 145.52, 153.68, 167.91.

**ESI-MS**: (m/z) 405.3(M+1).
47ca: 2-(2-(Benzothiazol-2-yl)-6-chloroimidazo[1,2-a]pyridin-3-yl)-N,N-diethylacetamide.

**Description**: Off-white solid.

**Melting point**: 182.2 - 186.5°C.

**$^1$H NMR (CDCl$_3$/TMS)**: δ 1.13 (t, $J = 7.0$ Hz, 3H), 1.28 (t, $J = 7.0$ Hz, 3H), 3.42 (m, 2H), 3.67 (m, 2H), 4.79 (s, 2H), 7.22 (d, $J = 9.5$ Hz, 1H), 7.41 (t, $J = 7.4$ Hz, 1H), 7.50 (t, $J = 7.6$ Hz, 1H), 7.60 (d, $J = 9.5$ Hz, 1H), 7.97 (d, $J = 7.8$ Hz, 2H), 8.68 (s, 1H).

**$^{13}$C NMR (CDCl$_3$/TMS)**: δ 13.10, 14.57, 31.93, 40.93, 42.71, 117.97, 118.75, 121.43, 121.87, 122.73, 123.89, 125.10, 126.15, 127.28, 135.07, 136.79, 141.73, 154.32, 164.28, 167.37.

**ESI-MS**: (m/z): 399.3(M+1).
47cb: 2-(2-(Benzothiazol-2-yl)-6-chloroimidazo[1,2-a]pyridin-3-yl)-1-(morpholin-4-yl)ethanone.

**Description**: Off-white solid.

**Melting point**: Up to 260.0°C (Not Clear).

**IR (In KBr)**: 3437, 3052, 2906, 2861, 1651, 1434, 1238, 1117, 945, 755, 563 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 3.62 (t, J = 4.6 Hz, 2H), 3.69 (s, 4H), 4.01 (t, J = 4.6 Hz, 2H), 4.79 (s, 2H), 7.24 (m, 1H), 7.43 (t, J = 7.4 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H), 7.98 (m, 2H), 8.69 (s, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 29.48, 42.70, 46.96, 66.81, 66.96, 117.97, 118.08, 121.68, 121.98, 122.55, 123.65, 125.30, 126.34, 127.51, 134.95, 136.71, 143.78, 154.15, 164.20, 166.98.

**ESI-MS (m/z)**: 413.2(M+1).
47cc: 2-(2-(Benzothiazol-2-yl)-6-chlorimidazo[1,2-a]pyridin-3-yl)-1-(piperidin-1-yl)ethanone.

![Chemical Structure](image)

**Description**: Off-white solid.

**Melting point**: 182.2 - 186.5°C.

**$^1$H NMR (CDCl$_3$/TMS)**: \( \delta 1.51\ (m,\ 4H),\ 1.60\ (t,\ J = 5.4\ Hz,\ 2H),\ 3.57\ (t,\ J = 5.4\ Hz,\ 2H),\ 3.83\ (t,\ J = 5.2\ Hz,\ 2H),\ 4.79\ (s,\ 2H),\ 7.23\ (m,\ 1H),\ 7.41\ (t,\ J = 7.5\ Hz,\ 1H),\ 7.50\ (t,\ J = 7.6\ Hz,\ 1H),\ 7.60\ (d,\ J = 9.5\ Hz,\ 1H),\ 7.98\ (m,\ 2H),\ 8.68\ (s,\ 1H)\).

**$^{13}$C NMR (CDCl$_3$/TMS)**: \( \delta 24.45,\ 25.68,\ 26.67,\ 29.88,\ 43.54,\ 47.64,\ 117.99,\ 118.70,\ 121.51,\ 121.89,\ 122.75,\ 123.79,\ 125.14,\ 126.18,\ 127.34,\ 134.99,\ 136.65,\ 143.69,\ 154.30,\ 164.18,\ 166.43\).

**ESI-MS: (m/z)**: 411.3(M+1).
47cd: 2-(2-(Benzothiazol-2-yl)-6-chlorimidazo[1,2-a]pyridin-3-yl)-1-(pyrrolidin-1-yl)ethanone.

Description: Off-white solid.

Melting point: 182.2-186.5°C.

$^1$H NMR (CDCl$_3$/TMS): $\delta$ 1.90 (m, 2H), 2.01 (m, 2H), 3.49 (t, $J = 6.8$ Hz, 2H), 3.85 (t, $J = 6.8$ Hz, 2H), 4.73 (s, 2H), 7.21 (d, $J = 9.4$ Hz, 1H), 7.40 (t, $J = 7.4$ Hz, 1H), 7.49 (t, $J = 7.4$ Hz, 1H), 7.59 (d, $J = 9.5$ Hz, 1H), 7.97 (t, $J = 4.7$ Hz, 2H), 8.62 (s, 1H).

$^{13}$C NMR (CDCl$_3$/TMS): $\delta$ 24.42, 26.24, 31.00, 46.18, 47.32, 117.97, 118.47, 121.41, 121.88, 122.72, 123.74, 125.09, 126.09, 127.29, 135.06, 137.00, 143.69, 154.33, 164.22, 166.68.

ESI-MS: (m/z): 397.3(M+1).
47da: 2-(2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-N,N-dimethylacetamide.

**Description**: Off-white solid.

**Melting point**: Up to 260.0°C (Not Clear).

**IR (In KBr)**: 3436, 3070, 2923, 1645, 1634, 1391, 1265, 1142, 941, 773 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 2.36 (s, 3H), 2.96 (s, 3H), 3.27 (s, 3H), 4.80 (s, 2H), 7.11 (d, J = 8.7 Hz, 1H), 7.39 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 7.2 Hz, 1H), 7.57 (d, J = 8.8 Hz, 1H), 7.99 (m, 2H), 8.30 (s, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 18.43, 30.21, 35.86, 37.84, 116.86, 117.33, 121.69, 122.53, 122.84, 123.02, 124.74, 125.87, 128.93, 134.85, 135.63, 144.35, 154.24, 164.77, 168.59.

**ESI-MS: (m/z)**: 351.2(M+1).
47db: 2-(2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-N-N-diethylacetamide.

**Description**: Off-white solid.

**Melting point**: 211.0 - 213.8°C.

**IR (In KBr)**: 3436, 3055, 2976, 2926, 1656, 1452, 1434, 1260, 1143, 948, 793, 755 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 1.12 (t, J = 6.9 Hz, 3H), 1.20 (t, J = 6.8 Hz, 3H), 2.37 (s, 3H), 3.40 (m, 2H), 3.65 (m, 2H), 4.80 (s, 2H), 7.12 (d, J = 9.1 Hz, 1H), 7.40 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.4 Hz, 1H), 7.57 (d, J = 9.1 Hz, 1H), 7.98 (m, 2H), 8.39 (s, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 13.01, 14.39, 18.47, 30.52, 40.73, 42.51, 116.82, 117.73, 121.73, 122.49, 122.81, 123.22, 124.74, 125.92, 128.96, 134.88, 135.53, 144.36, 154.28, 164.82, 167.66.

**ESI-MS** (m/z): 379.3(M+1).
**47dc**: 2-(2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-1-(morpholin-4-yl)ethanone.

**Description**: Off-white solid.

**Melting point**: Up to 260.0°C (Not Clear).

**IR (In KBr)**: 3437, 3052, 2906, 2861, 1651, 1356, 1238, 1117, 1033, 945, 755 cm\(^{-1}\).

**\(^1\)H NMR (CDCl\(_3\)/TMS)**: \(\delta\) 2.73 (s, 3H), 3.56 (t, \(J = 4.6\) Hz, 2H), 3.62 (s, 4H), 3.98 (t, \(J = 4.6\) Hz, 2H), 4.77 (s, 2H), 6.13 (d, \(J = 9.2\) Hz, 1H), 7.40 (t, \(J = 7.5\) Hz, 1H), 7.50 (t, \(J = 7.4\) Hz, 1H), 7.58 (d, \(J = 9.2\) Hz, 1H), 8.49 (m, 2H), 8.36 (s, 1H).

**\(^{13}\)C NMR (CDCl\(_3\)/TMS)**: \(\delta\) 18.57, 29.98, 42.73, 46.90, 66.84, 66.95, 117.04, 117.08, 121.91, 122.42, 123.11, 123.16, 125.01, 126.16, 129.21, 134.95, 135.63, 144.57, 154.25, 164.92, 167.39.

**ESI-MS**: (m/z): 393.2(M+1).
47dd: 2-(2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-1-(piperidin-1-yl)ethanone.

Description : Off-white solid.

Melting point: 227.1 - 229.6°C.

IR (In KBr): 3436, 2927, 2855, 1635, 1452, 1439, 1355, 1227, 1136, 943, 766 cm⁻¹.

¹H NMR (CDCl₃/TMS): δ 1.45 (d, J = 3.8 Hz, 2H), 1.54 (t, J = 6.1 Hz, 2H), 1.60 (d, J = 5.0 Hz, 2H), 2.42 (s, 3H), 3.59 (t, J = 5.4 Hz, 2H), 3.84 (t, J = 5.4 Hz, 2H), 4.83 (s, 2H), 7.15 (d, J = 9.3 Hz, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.60 (d, J = 9.2 Hz, 1H), 8.01 (t, J = 7.0 Hz, 2H), 8.41 (s, 1H).

¹³C NMR (CDCl₃/TMS): δ 18.60, 24.47, 25.75, 26.59, 30.40, 43.55, 47.56, 116.98, 117.76, 121.83, 122.62, 122.98, 123.26, 124.87, 126.03, 129.08, 134.96, 135.54, 144.45, 154.39, 164.89, 166.85.

ESI-MS:(m/z): 391.4(M+1).
**47de: 2-(2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-1-(pyrrolidin-1-yl)ethanone.**

![47de](image)

**Description**: Off-white solid.

**Melting point**: 248.0 - 249.2°C.

**IR (In KBr)**: 3435, 3053, 2974, 1654, 1633, 1439, 1396, 1242, 1143, 947, 793, 754 cm⁻¹.

**¹H NMR (CDCl₃/TMS)**: δ 1.87 (m, 2H), 1.97 (m, 2H), 2.36 (s, 3H), 3.49 (t, J = 6.8 Hz, 2H), 3.80 (t, J = 6.8 Hz, 2H), 4.76 (s, 2H), 7.12 (d, J = 9.2 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.4 Hz, 1H), 7.57 (d, J = 9.2 Hz, 1H), 7.98 (t, J = 6.6 Hz, 2H), 8.34 (s, 1H).

**¹³C NMR (CDCl₃/TMS)**: δ 18.54, 24.37, 26.26, 31.42, 46.18, 47.18, 116.99, 117.43, 121.83, 122.58, 122.87, 123.22, 124.82, 125.97, 129.04, 135.05, 136.01, 144.48, 154.44, 164.97, 167.15.

**ESI-MS:(m/z)**: 377.3(M+1).
47df: 2-(2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-N-tert-butylacetamide.

Description : Off-white solid.

Melting point: 223.2 - 226.1°C.

IR (In KBr): 3435, 3296, 2969, 2925, 1672, 1548, 1313, 1244, 1225, 1123, 947, 764 cm⁻¹.

¹H NMR (CDCl₃/TMS): δ 1.31 (s, 9H, 3xCH₃), 2.42 (s, 3H), 4.20 (s, 2H), 7.18 (d, J = 9.0 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.61 (d, J = 9.2 Hz, 1H), 8.04 (m, 2H), 8.29 (s, 2H).

¹³C NMR (CDCl₃/TMS): δ 18.55, 28.72, 34.06, 51.08, 117.12, 119.03, 122.09, 122.27, 123.57, 125.13, 126.40, 129.33, 134.86, 135.69, 144.19, 153.65, 165.27, 168.01.

ESI-MS:(m/z): 379.2(M+1).
47dg: 2-(2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-N-cyclohexylacetamide.

Description : Off-white solid.

Melting point: Up to 260.0°C (Not Clear).

IR (In KBr) : 3434, 3288, 2928, 2853, 1631, 1543, 1352, 1129, 943, 755 cm⁻¹.

¹H NMR (CDCl₃/TMS): δ 1.17 (m, 2H), 1.32 (m, 2H), 1.55 (m, 2H), 1.64 (m, 2H), 1.85 (m, 2H), 2.42 (s, 3H), 3.71 (m, 1H), 4.27 (s, 2H), 7.18 (d, ²J = 9.2 Hz, 1H), 7.30 (s, 1H), 7.49 (t, ²J = 7.6 Hz, 1H), 7.61 (m, 2H), 8.05 (t, ²J = 7.4 Hz, 2H), 8.29 (s, 1H).

¹³C NMR (CDCl₃/TMS): δ 18.48, 24.53, 25.48, 32.83, 33.10, 48.29, 117.15, 118.84, 122.11, 122.29, 123.63, 125.18, 126.47, 129.33, 134.93, 135.83, 144.20, 153.67, 165.25, 167.93.

ESI-MS:(m/z): 405.2(M+01).
47dh: 2-(2-(Benzothiazol-2-yl)-6-methylimidazo[1,2-a]pyridin-3-yl)-N-cyclopropylacetamide.

**Description**: Off-white solid.

**Melting point**: 255.8 - 257.0°C.

**IR (In KBr)**: 3301, 3052, 2923, 1639, 1538, 1337, 1127, 1002, 941, 796, 754 cm\(^{-1}\).

**\(^1\text{H NMR (CDCl}_3/\text{TMS)}\)**: δ 0.45 (m, 2H), 0.71 (m, 2H), 2.39 (s, 3H), 2.71 (m, 1H), 4.22 (s, 2H), 7.15 (m, 1H), 7.45 (t, \(J= 7.2\) Hz, 1H), 7.58 (m, 2H), 8.00 (m, 2H), 8.25 (s, 1H), 8.53 (s, 1H).

**\(^{13}\text{C NMR (CDCl}_3/\text{TMS)}\)**: δ 6.26, 6.29, 18.45, 22.60, 32.78, 117.18, 118.37, 122.06, 122.10, 122.21, 123.67, 125.23, 126.48, 129.35, 134.88, 135.90, 144.24, 153.59, 165.31, 170.16.

**ESI-MS:(m/z)**: 363.2(M+1).
REFERENCES:


10) Kaplan, J. P.; George, P. *Eur. Patent* 0050563, **1982**.


