CHAPTER 5

Synthesis of imidazo pyridine derivatives containing morpholine nucleus
5.1. Introduction

Heterocyclic compounds hold a special place among pharmaceutically significant natural products and synthetic compounds [1, 2]. Nitrogen heterocycles are abundant in nature and are of great significance to life because their structural subunits exist in many natural products such as vitamins, hormones, antibiotics, and alkaloids as well as pharmaceuticals, herbicides and many more compounds. The remarkable ability of heterocyclic nuclei to serve both as biomimetics and reactive pharmacophores has largely contributed to their unique value as traditional key elements of numerous drugs. In both lead identification and lead optimization processes, there is an acute need for new small organic scaffolds.

Nitrogen bridgehead-fused heterocycles containing an imidazole ring are common structural motifs in pharmacologically important molecules, with activities spanning a diverse range of targets. Probably, the most widely used heterocyclic system from this group is imidazo-[1, 2-a] pyridine which contained in marketed drugs such as Zolpidem (1) benzodiazepine agonist, Olprinone (2) the PDE 3 inhibitor and Zolimidine(3) antiulcer drug as well as other experimental molecules [3-5].

The heterocyclic compounds play significant role in developing new antimicrobial, anticancer, antimalarial, anticonvulsant agents. Recent observations suggested that, heterocyclic compounds containing nitrogen as heteroatom are very
important class of organic heterocycles, because of their wide application in medicine, agriculture and technology aspects. Among these, 2-phenylimidazo[1,2-a]pyridine derivatives are of significant synthetic interest due to their diverse range of biological activities. Some of them showed pharmacological properties such as anti-inflammatory[6,7], aromatase inhibitors[8], antibacterial[9], antifungal[10], antiviral[11] and analgesic[12] activities. They have also been shown to be selective cyclin dependant kinase inhibitors[13], GABA[14], and benzodiazepine receptor agonists[15], and bradykinin B2 receptor antagonists[16]. The Mannich reaction [17] is an amino alkylation of an acidic proton with formaldehyde and any primary or secondary amine. Many literatures reveal that, enhancement of biological activity was found on inclusion of manich base into the parent moiety [18-21]. Literature shows the presence of morpholine moiety in the compounds is act as the building block in the preparation of Linezolid (4), an antibiotic [22] and anticancer agent [23].

Azole class of drugs particularly fused imidazoles occupy prominent place in medicinal chemistry because of their broad spectrum pharmacological activities such as anti-inflammatory, analgesic, anticancer, antimicrobial, antiviral, pesticidal cytotoxicity and anti-arrhythmic [19-23] activities. Omeprazole, Mebendazole, Pimobendan, and Albendazole are well known drugs in the market which contain fused imidazole as active core moiety.
The insertion of polar groups in the organic molecules leads to change in the absorption properties of the compound in the body. Cyclic secondary amines like morpholine are an important class of compounds due to their biological significance in the field of medicine and agriculture. Morpholines are the key pharmacophores in various important drugs and biologically significant molecules. Acylation or alkylation of morpholine enhances the original biological activity of the parent molecule. A number of N, O substituted morpholines have been found to possess interesting pharmacological properties. Many morpholine derivatives display varied activities like anti-bacterial, anti-viral, analgesic, anti-inflammatory, as local anesthetics and antiviral agents [24].

Morpholine, a six membered heterocyclic ring is hydrophilic in nature and it changes the properties of the compound to which it is attached. Morpholine has great industrial importance and a wide range of applications. It is used as solvent, corrosive inhibitor and fungicide. The morpholine ring also present in the antidepressant drug Reboxetine, anticonvulsant like Timonium methyl sulphate. It is also present in some drugs Phenmetrazine (7) a stimulant, Morazone (5) a nonsteroidal anti-inflammatory drug and Fenmetramide (6) an antidepressant drug.
Desai, C and their co-workers reported the synthesis of a series of novel imidazo-[1,2-a]pyridine derivatives 8(a-m) and studied their antimicrobial activity [24].

\[
\text{8(a-m)}
\]

\[
\begin{align*}
8(a-i) & = 2-\text{OH}; b=2,4\text{-}(\text{OH})_2; c=4-\text{OH}-3-\text{NO}_2; d=2,4\text{-}(\text{OH})_2-5-\text{NO}_2; e=3-\text{Cl}; f=3-\text{Cl}-4-\text{F}; g=2-\text{Br}; h=3-\text{Br}; i=3-\text{Br}-2\text{F}; j=2-\text{Br}-4\text{NO}_2; k=2,3(\text{F})_2; l,2,4(\text{F})_2; m=2,6(\text{F})_2
\end{align*}
\]

Said El Kazzouli et al reported the synthesis of 2-phenylimidazo [1, 2-a] pyridines (9) as a novel class of melatonin receptor ligands [25].

\[
\text{9}
\]

Miguel Angel and their coworkers synthesized 6-substituted 2-(N-trifluoroacetylamino) imidazo pyridines (10) and the synthesized compounds were evaluated for antiproliferative activity against a variety of cancer cell lines. Most of synthesized compounds displayed moderate cytotoxic activity [26].

\[
\text{10}
\]

Zhicai Wu and their coworkers designed series of 3, 7-diarylsubstituted imidazopyridines and developed as a new class of KDR kinase inhibitors. A variety of
imidazopyridines were synthesized and potent inhibitors of KDR kinase activity were identified with good aqueous solubility [27].

Sunil G. Sanghani and Kalpesh J. Ganatra prepared a series of manich bases (13) by the reaction of 7-methyl-2-(p-methylphenyl)imidazo[1,2-a]pyridine with secondary amines and p-formaldehyde in methanol and evaluated them for antimicrobial activities [28].

Wesley B Trotter synthesized imidazo morpholine derivatives (14&15) and studied their analgesic activities [29].
Masahiko Hayakawa et al synthesized series of imidazo[1,2-a]pyridine compounds (16), among which the thiazole derivative inhibited tumor cell growth [30].

Shrikanth Ulloora et al synthesized series of new imidazo [1,2-a]pyridines (17), among them many compounds exhibited prominent anticonvulsant activity [31].
Aldo Andreani et al synthesized imidazo [2, 1-b]thiazole guanyl hydrazones (18-19) which shows potent antitumor activities against breast cancer [32].

\[ \text{Imidazo pyridine derivatives containing morpholine nucleus} \]

Caroline Castera-Ducros et al synthesized series of imidazo [1, 2-a] pyridine derivatives (20) and evaluated them for antileishmanial activity [33].

\[ \text{Caroline Castera-Ducros et al} \]

Nurit Dahan-Farkas synthesized 6-substituted imidazo[1,2-a]pyridines among them the following two compounds (21-22) show the proteolytic phase of apoptosis [34].

\[ \text{Nurit Dahan-Farkas} \]

Kristjan S. Gudmundsson and Brian A. Johns synthesized imidazo [1,2-a]pyridine derivatives (23) which shows potent activity against herpes viruses [35].

\[ \text{Kristjan S. Gudmundsson and Brian A. Johns} \]
Yoshiyuki Sato, Yu Onozaki synthesized a novel class of imidazopyridines (24) derivatives which shows antitumor activity [36].

Said El Kazzouli et al synthesized a novel class of 2-phenylimidazo [1,2-a]pyridines (25) as melatonin receptor ligands [37].
5.2. Present work

Promoted by the above cited biological importance of imidazo pyridine derivatives, and in continuation of our efforts to explore biologically important new heterocyclic compounds, in the present investigation, an attempt was made to improve or modify its properties to get more potent analogues. The present work describes the synthesis of series of 4-((2-(4-chlorophenyl) imidazo [1,2-a] pyridin-3-yl) methyl) morpholine derivatives 29(a-o) by the reaction of substituted imidazo [1,2-a] pyridines derivatives 28(a-o) with morpholine and formaldehyde.

The synthetic strategy involves the following steps:

1. Synthesis of intermediates substituted imidazo [1,2-a] pyridines derivatives as reported in chapter 2; 28(a-o)
2. Synthesis of series of 4-((2-(4-chlorophenyl) imidazo [1,2-a] pyridin-3-yl) methyl) morpholine 29(a-o) derivatives.

The schematic representation of imidazopyridine morpholine derivatives is given in the following Scheme-6.
5.2.1. Synthesis of substituted imidazo [1, 2-a] pyridine derivatives 28(a-o)

Substituted imidazo [1, 2-a] pyridine derivatives 28(a-o) have been synthesized according to the procedure which is described in chapter 2
5.2.2. Synthesis of 4-((2-(4-chlorophenyl) imidazo [1, 2-a] pyridin-3-yl) methyl) morpholine derivatives 29(a-o).

![Reaction diagram](image)

The structure of compounds 29(a-o) was confirmed by $^1$H NMR, $^{13}$C NMR and mass spectral studies. In $^1$H NMR spectrum, compound 29c showed two triplets at $\delta$ 2.41 and 3.52 ppm corresponds to four CH$_2$ protons of morpholine ring and a singlet at $\delta$ 4.00 ppm due to bridgehead CH$_2$ protons. The aromatic protons of the compound 29c were appeared between $\delta$ 7.43–8.85ppm. The $^{13}$CNMR spectrum of compound 29c showed a signals at $\delta$ 66.0 (2C) and 52 (2C) due to four morpholine carbons, a signal at $\delta$ 50.0 ppm corresponds to methylene carbon and other signals are in well agreement with the assigned structure. Compound 29c displayed a molecular ion peak M$^+$ at m/z 452 corresponding to the molecular mass of the compound and isotopic peak [M+2] at m/z 454.
Chapter 5

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^1^HNMR spectrum for the compound 29c
"\(^{13}\)CNMR spectrum for the compound 29c"
Imidazo pyridine derivatives containing morpholine nucleus

Sample Report:

Sample 1 Vial 2:22 ID B File B Description B

3: UV Detector: TIC

Mass spectrum for the compound 29c

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Imidazo pyridine derivatives containing morpholine nucleus

$^1$HNMR spectrum for the compound 29k
CHAPTER 5

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$^{13}$CNMR spectrum for the compound 29k

135
Imidazo pyridine derivatives containing morpholine nucleus

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**Data file:** \D:\DATA\MAY10\85017-136-17.D

**Vial No.:** Pi-P-03

**Injection Date:** 21/05/2010

**Injection vol:** 1.0ul

**Acq Method:** ASCENTIS_C18 NH4

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**Method info:**

Method info: a-10mM AMINONIC FORMATE:ACN[98:02]

MOBILE PHASE A: BUFFER:ACN[02:98]

FLOW: 1.0mL/min

Column: ASCENTIS EXPRESS C18 50X2.1mm 2.7μm

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**Mass spectrum for the compound 29k**

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</table>

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136
Mass spectrum for the compound 29k
5.3. Experimental protocol

5.3.1. Synthesis of substituted imidazo [1, 2-a] pyridines derivatives 28(a-o)

**General procedure:**

An equimolar mixture of substituted-2-aminopyridines 26(a-o) (1 mmol) and substituted phenacyl bromides 27 (1 mmol) was taken in dry ethanol (10 ml) and the reaction mixture was refluxed for about 10-12 h at the temperature of 85 °C. Completion of reaction was checked by TLC. The solvent was distilled off and the content was poured into crushed ice with uniform stirring. The product separated and filtered, dried and recrystallized using ethanol. The purification of compound was done by chromatography on silica gel using ethyl acetate and hexane as an eluent.

6-Bromo-2-(3, 4-dichlorophenyl) imidazo [1, 2-a] pyridine (28a)

m.p.: 155-158°C; $^1$H-NMR (400MHz, DMSO-d$_6$): 8.88 (s, 1H), 8.46 (s, 1H), 8.18 (s, 1H), 7.94-7.38 (m, 4H, Ar-H); Mol. Formula C$_{13}$H$_7$BrCl$_2$N$_2$

6-Bromo-2-(4-chlorophenyl) imidazo [1, 2-a] pyridine (28b)

m.p.: 168-170°C; $^1$H-NMR (400MHz DMSO-d$_6$); 9.18(s, 1H), 8.65 (s, 1H), 7.99-7.62 (m, 6H, Ar-H); Mol. Formula C$_{13}$H$_8$BrClN$_2$

6-Bromo-2-(4-bromophenyl) imidazo [1, 2-a] pyridine (28c)

m.p.; 202-204°C; $^1$HNMR (400MHz DMSO-d$_6$); 9.19 (s, 1H), 8.67 (s, 1H), 7.91-7.76(m, 6H, Ar-H); Mol. Formula C$_{13}$H$_8$BrClN$_2$

6-Bromo-2-(4-nitrophenyl) imidazo [1, 2-a] pyridine (28d)

m.p.; 163-165°C; $^1$HNMR (400MHz DMSO-d$_6$); 9.11 (s, 1H), 8.70 (s, 1H), 8.17-7.75 (m, 6H, Ar-H); Mol. Formula C$_{13}$H$_8$BrN$_3$O$_2$

4-(6-Bromoimidazo [1, 2-a] pyridin-2-yl) benzonitrile (28e)

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Imidazo pyridine derivatives containing morpholine nucleus

- **2-(3,4-Dichlorophenyl)-6-methylimidazo[1,2-a]pyridine (28f)**
  - m.p.: 193-195°C; 
  - $^1$HNMR (400MHz DMSO-d$_6$); 8.85 (s, 1H), 8.72 (s, 1H), 8.30 (s, 1H), 7.98-7.95 (m, 4H, Ar-H), 2.44 (s, 3H); 
  - Mol. Formula C$_{14}$H$_{10}$Cl$_2$N$_2$

- **2-(4-Chlorophenyl)-6-methylimidazo[1,2-a]pyridine (28g)**
  - m.p.: 188-190°C; 
  - $^1$HNMR (400MHz DMSO-d$_6$); 8.77 (s, 1H), 8.67 (s, 1H), 7.99-7.73 (m, 6H, Ar-H), 2.43 (s, 3H). 
  - Mol. Formula C$_{14}$H$_{11}$ClN$_2$

- **2-(4-Bromophenyl)-6-methylimidazo[1,2-a]pyridine (28h)**
  - m.p.: 176-178°C; 
  - $^1$HNMR (400MHz DMSO-d$_6$); 8.74 (s, 1H), 8.67 (s, 1H), 7.92-7.73 (m, 6H, Ar-H), 2.32 (s, 3H). 
  - Mol. Formula C$_{14}$H$_{11}$BrN$_2$

- **2-(4-Nitrophenyl)-6-methylimidazo[1,2-a]pyridine (28i)**
  - m.p.: 191-193°C; 
  - $^1$HNMR (400MHz DMSO-d$_6$); 8.91 (s, 1H), 8.73 (s, 1H), 8.17-7.81 (m, 6H, Ar-H), 2.41 (s, 3H). 
  - Mol. Formula C$_{14}$H$_{11}$N$_3$O$_2$

- **4-(6-Methylimidazo[1,2-a]pyridin-2-yl) benzonitrile (28j)**
  - m.p.: 168-170°C; 
  - $^1$HNMR (400MHz DMSO-d$_6$); 8.92 (s, 1H), 8.73 (s, 1H), 8.44-7.77 (m, 6H, Ar-H), 2.42 (s, 3H). 
  - Mol. Formula C$_{15}$H$_{11}$N$_3$

- **8-(Benzylxoy)-2-(3,4-dichlorophenyl) imidazo [1,2-a] pyridine (28k)**
  - m.p.: 199-201°C; 
  - $^1$HNMR (400MHz DMSO-d$_6$); 8.84 (s, 1H), 8.43-7.27 (m, 10H, Ar-H), 8.33 (s, 1H), 5.47 (s, 2H). 
  - Mol. Formula C$_{20}$H$_{14}$Cl$_2$N$_2$O

- **8-(Benzylxoy)-2-(4-chlorophenyl) imidazo [1,2-a] pyridine (28l)**
  - m.p.: 212-213°C; 
  - $^1$HNMR (400MHz DMSO-d$_6$); 8.83 (s, 1H), 8.48-7.34 (m, 12H, Ar-H),
5.46 (s, 2H). Mol. Formula C_{20}H_{15}ClN_2O

8-(Benzyl oxy)-2-(4-bromophenyl) imidazo [1, 2-a] pyridine (28m)

m.p.; 203-205°C; $^1$HNMR (400MHz DMSO-d$_6$); 8.86 (s, 1H), 8.46-7.41(m, 12H, Ar-H), 5.49 (s, 2H). Mol. Formula C$_{20}$H$_{15}$BrN$_2$O

8-(Benzyl oxy)-2-(4-nitrophenyl) imidazo [1, 2-a] pyridine (28n)

m.p.; 177-179°C; $^1$HNMR (400MHz DMSO-d$_6$); 8.81(s, 1H), 8.38-6.9(m, 12H, Ar-H), 5.49 (s, 2H). Mol. Formula C$_{20}$H$_{15}$N$_3$O$_3$

4-(8-(Benzyl oxy) imidazo [1, 2-a] pyridin-2-yl) benzonitrile (28o)

m.p.; 186-188°C; $^1$HNMR (400MHz DMSO-d$_6$); 8.71 (s, 1H), 8.42-7.25 (m, 12H, Ar-H), 5.47(s, 2H). Mol. Formula C$_{21}$H$_{15}$N$_3$O

5.3.2. Synthesis of substituted 4-((2-phenylimidazo [1, 2-a] pyridin-3-yl) methyl) morpholine derivatives 29(a-o)

General procedure:

Compounds 28(a-o) (1 mmol), morpholine (1.2mmol), formaldehyde and catalytic amount of acetic acid was taken in round bottom flask in dry ethanol (8mL) and refluxed for 6-10 hr at 85°C, the progress of the reaction was monitored by T.L.C. After completion of reaction, excess of solvent was distilled off and the content was poured into crushed ice with uniform stirring. The product was separated, filtered, dried and recrystallized using ethanol. The purification of compound was done by chromatography on silica gel using a mixture of ethyl acetate and hexane as an eluent.

6-Bromo-2-(3,4-dichlorophenyl)-3-((morpholin-4-ylmethyl)imidazo[1,2-a]pyridine (29a)

White solid, Yield- 75 %, m.p. 185-187°C; $^1$HNMR (400MHz DMSO-d$_6$,δppm): 8.91 (s,
Imidazo pyridine derivatives containing morpholine nucleus

1H), 8.25 (s, 1H), 7.93-7.43 (m, 4H, Ar-H), 4.02 (s, 2H), 3.54 (bs, 4H), 2.47 (bs, 4H);

\textsuperscript{13}CNMR (400MHz DMSO-d\textsubscript{6}, \textdelta ppm): 145.1, 144.0, 136.2, 135.0, 133.8, 133.3, 132.5, 132.0, 130.7, 128.8, 127.0, 116.2, 112.1, 66.5, 53.1, 50.5; MS (LCMS): m/z 441 [M], 443 (M+2).

Mol. formula; C\textsubscript{18}H\textsubscript{18}BrC\textsubscript{2}N\textsubscript{3}O

\textbf{6-Bromo-2-(4-chlorophenyl)-3-(morpholin-4-ylmethyl)imidazo[1,2-a]pyridine (29b)}

White solid, Yield - 82 %, m.p.157-159°C; \textsuperscript{1}HNMR (400MHz DMSO-d\textsubscript{6}, \textdelta ppm): 8.84 (s, 1H), 7.93-7.42 (m, 6H, Ar-H), 4.01 (s, 2H), 3.52 (bs, 4H), 2.41 (bs, 4H); \textsuperscript{13}CNMR (400 MHz DMSO-d\textsubscript{6}, \textdelta ppm): 145.0, 144.0, 136.2, 134.3, 135.0, 132.2, 131.3, 129.8, 128.9, 121.3, 66.8, 53.4, 50.3; MS (LCMS): m/z 408 (M+2); Mol. formula; C\textsubscript{18}H\textsubscript{18}BrC\textsubscript{2}N\textsubscript{3}O.

\textbf{6-Bromo-2-(4-bromophenyl)-3-(morpholin-4-ylmethyl) imidazo[1,2-a]pyridine (29c)}

Off white solid, Yield - 78 %, m.p.176-178°C; \textsuperscript{1}HNMR (400MHz DMSO-d\textsubscript{6}, \textdelta ppm): 8.85 (s, 1H), 7.86-7.84 (d, 2H), 7.69-7.66 (d, 2H), 7.61-7.59 (d, 1H), 7.44-7.41 (d, 1H), 4.00 (s, 2H), 3.52 (bs, 4H), 2.41 (bs, 4H); \textsuperscript{13}C NMR (400MHz DMSO-d\textsubscript{6}, \textdelta ppm): 145.2, 144.1, 136.2, 135.3, 133.0, 132.4, 129.4, 123.6, 121.3, 66.8, 53.4, 50.6; MS (LCMS): m/z 451 (M+1), 454 (M+2), Mol. formula; C\textsubscript{18}H\textsubscript{18}BrN\textsubscript{3}O.

\textbf{6-Bromo-3-(morpholin-4-ylmethyl)-2-(4-nitrophenyl)imidazo[1,2-a]pyridine (29d)}

White solid, Yield - 80 %, m.p.188-190°C; \textsuperscript{1}HNMR (400MHz DMSO-d\textsubscript{6}, \textdelta ppm): 8.89 (s, 1H), 8.12 -7.44 (m, 6H, Ar-H), 4.04 (s, 2H), 3.52 (bs, 4H), 2.43 (bs, 4H); \textsuperscript{13}C NMR (400MHz DMSO-d\textsubscript{6}, \textdelta ppm): 146, 143, 139, 132, 129, 128, 126, 119, 118, 110, 106,
66.7, 52.8, 50.5; MS (LCMS); m/z-416 [M+] Mol. formula; C_{16}H_{17}BrCl_{2}N_{4}O_{3}

4-[6-Bromo-3-(morpholin-4-ylmethyl)imidazo[1,2-a]pyridin-2-yl]benzonitrile (29e)

White solid, Yield- 74% m.p. 223-225°C; \(^1\)HNMR (400MHz DMSO-d_6, \(\delta\) ppm): 8.91 (s, 1H), 8.35-8.33 (m, 6H, Ar-H) 4.07 (s, 2H), 3.53 (bs, 4H), 2.45 (bs, 4H); \(^1^3\)C NMR (400MHz DMSO-d_6, \(\delta\) ppm): 145.3, 144.1, 136.6, 135.0, 132.7, 132.5, 132.1, 128.3, 121.4, 116.8, 115.3, 112.4, 66.8, 53.2, 50.4; MS(LCMS)-397[M], Mol. formula; C_{16}H_{17}BrN_{4}O.

2-(3, 4-Dichlorophenyl)-6-methyl-3-(morpholin-4-ylmethyl)imidazo[1,2-a]pyridine (29f)

Off white solid. Yield- 76 %, m.p. 157-159°C; \(^1\)HNMR (400MHz DMSO-d_6, \(\delta\) ppm): 8.42 (s, 1H), 8.28 (s, 1H), 7.95-7.18 (m, 4H), 3.95 (s, 2H), 3.56 (bs, 4H), 2.50 (bs, 4H), 2.35 (s, 3H); \(^1^3\)C NMR (400MHz DMSO-d_6, \(\delta\) ppm): 143, 141, 135, 131.6, 131.1, 130, 128.6, 128.1, 123, 122, 117, 116, 66, 52, 50, 18; MS(LCMS):m/z 376[M]. Mol. formula; C_{19}H_{19}Cl_{2}N_{3}O.

2-(4-Chlorophenyl)-6-methyl-3-(morpholin-4-ylmethyl)imidazo[1,2-a]pyridine (29g)

White solid, Yield- 78% m.p. 139-137°C; \(^1\)HNMR (400MHz DMSO-d_6, \(\delta\) ppm): 8.36 (s, 1H), 7.94-7.15 (m, 6H, Ar-H) 3.94 (s, 1H), 3.53 (bs, 4H), 2.43 (bs, 4H), 2.34 (s, 3H); \(^1^3\)CNMR (400MHz DMSO-d_6, \(\delta\) ppm): 143, 142, 139, 132, 130, 129, 128, 123, 121, 117, 116, 67, 53, 21; MS(LCMS)m/z 341[M], Mol. formula; C_{16}H_{20}ClN_{3}O.

2-(4-Bromophenyl)-6-methyl-3-(morpholin-4-ylmethyl)imidazo[1,2-a]pyridine (29h)

Off white solid, Yield- 76%, m.p. 175-177°C; \(^1\)HNMR (400MHz DMSO-d_6, \(\delta\) ppm): 8.37 (s, 1H), 7.88-7.15 (m, 6H, Ar-H), 3.94 (s, 1H), 3.53 (bs, 4H), 2.43 (bs, 4H), 2.34 (s,
3H); $^{13}\text{C NMR}$ (400MHz DMSO-d$_6$, δppm): 145.2, 144.1, 135.0, 134.3, 133.8, 132.0, 131.9, 129.1, 124.3, 122.1, 66.7, 53.2, 50.5, 24.7; MS (LCMS): m/z 388[M+2], Mol. Formula; C$_{19}$H$_{20}$BrN$_3$O.

6-Methyl-3-(morpholin-4-ylmethyl)-2-(4-nitrophenyl) imidazo[1,2-a]pyridine (29i)

Pale Yellow solid, Yield-85 % m.p.; 1H NMR (400MHz DMSO-d$_6$, δ ppm): 8.41 (s, 1H), 8.15-7.19 (m, 6H, Ar-H) 3.98 (s, 2H), 3.32 (bs, 4H), 2.43 (bs, 4H), 2.35 (s, 3H); $^{13}\text{C NMR}$ (400MHz DMSO-d$_6$, δppm): 147.9, 145.4, 144.1, 139.2, 135.0, 134.1, 133.5, 128.4, 124.2, 122.1, 114.6, 66.7, 53.1, 50.4, 24.2; MS (LCMS): m/z 352[M]. Mol. formula C$_{19}$H$_{20}$N$_4$O$_3$.

4-(6-Methyl-3-(morpholinomethyl) imidazo [1,2-a] pyridin-2-yl) benzonitrile (29j)

Off white solid, Yield- 80%, m.p. 199-203°C; 1H NMR (400MHz DMSO-d$_6$, δ ppm): 8.44 (s, 1H), 8.35-7.21 (m, 6H, Ar-H), 4.02 (s, 2H), 3.55 (bs, 4H), 2.48 (bs, 4H), 2.36 (s, 3H); $^{13}\text{C NMR}$ (400MHz DMSO-d$_6$, δppm): 145.3, 144.1, 137.3, 135.1, 134.2, 133.6, 132.2, 128.1, 122.2, 115.6, 114.7, 112.2, 66.5, 53.6, 24.4; MS (LCMS): m/z 332[M+]. Mol. formula; C$_{20}$H$_{20}$N$_4$O.

4-((8-(Benzyloxy)-2-(3,4-dichlorophenyl) imidazo [1,2-a] pyridin-3-yl) methyl) morpholine (29k)

Off white solid, Yield-82 % , m.p. 187-189°C; 1H NMR (400MHz DMSO-d$_6$, δppm): 8.22 (s, 2H), 7.92-7.90 (m, 9H, Ar-H), 5.33 (s, 2H), 3.54 (s, 2H), 3.32 (bs, 4H), 2.44 (bs, 4H); $^{13}\text{C NMR}$ (DMSO-d$_6$, δppm): 147, 140, 139, 136, 135, 31.6, 131.1, 130, 129, 128, 119, 118, 112, 104, 70, 66, 52, 50; MS (LCMS): m/z 468[M+]; Mol. Formula;
C_{25}H_{23}Cl_2N_3O_2.

4-((8-(Benzyloxy)-2-(4-chlorophenyl) imidazo [1, 2-a] pyridin-3-yl) methyl) morpholine (29i)

Off white solid, Yield-80%, m.p. 178-180°C; \(^1^H\)NMR (400MHz DMSO-d_6, δ ppm): 8.20-6.8 (m, 12H, Ar-H), 5.32 (s, 2H), 3.95 (s, 2H), 3.52 (bs, 4H), 2.41 (bs, 4H); \(^1^H\)NMR (400MHz DMSO-d_6, δ ppm): 147, 136, 133, 132, 130, 128.9, 128.6, 119, 118, 112, 103, 70, 66, 53, 51; MS(LCMS): m/z 436 (M+1), 435 (M+2); Mol. formula; C_{25}H_{24}ClN_3O_2.

4-(8-(Benzyloxy)-2-(4-bromophenyl) imidazo [1,2-a] pyridin-3-yl) methyl) morpholine (29m)

White solid, Yield-70%, m.p. 224-226°C; \(^1^H\)NMR (400MHz DMSO-d_6, δ ppm): 8.21-6.82 (m, 12H, Ar-H), 5.36 (s, 2H), 3.95 (s, 2H), 3.52 (bs, 4H), 2.41 (bs, 4H); \(^1^C\)NMR (400MHz DMSO-d_6, δ ppm): 145.3, 143.2, 141.6, 137.1, 135.0, 132.2, 132.1, 129.7, 129.0, 127.7, 127.1, 124.2, 123.1, 70.8, 66.4, 53.8, 50.2; MS(LCMS): m/z 478[M+]; Mol. formula; C_{25}H_{24}BrN_3O_2.

4-((8-(Benzyloxy)-2-(4-nitrophenyl) imidazo [1,2-a] pyridin-3-yl) methyl) morpholine (29n)

Light yellow solid, Yield-72%, m.p. 236-238°C; \(^1^H\)NMR (400MHz DMSO-d_6, δ ppm): 8.22-6.83 (m, 12H, Ar-H), 5.33 (s, 2H), 3.99 (s, 2H), 3.52 (bs, 4H), 2.43 (bs, 4H); \(^1^C\)NMR (400MHz DMSO-d_6, δ ppm): 147.6, 145.3, 143.8, 141.3, 139.1, 137.4, 135.0, 129.0, 128.4, 128.7, 127.9, 124.4, 124.0, 70.8, 65.1, 52.9, 50.6; MS(LCMS): m/z 444[M]. Mol. Formula; C_{25}H_{24}N_4O_4
4-(8-(Benzyloxy)-3-(morpholinomethyl)imidazo[1,2-a]pyridin-2-yl)benzonitrile

(29o)

Off white solid, Yield-76%, m.p. 203-205°C; Yield-79%; $^1$HNMR (400MHz DMSO-d$_6$, δ ppm): 8.34-6.85 (m, 12H, Ar-H), 5.33 (s, 2H), 4.02 (s, 2H), 3.31 (bs, 4H), 2.45 (bs, 4);

$^{13}$CNMR (400MHz DMSO-d$_6$, δ ppm): 145.5, 143.4, 141.2, 137.3, 132.5, 129.0, 128.2, 127.7, 127.1, 124.0, 71.0, 66.6, 53.4, 50.8; MS (LCMS): m/z=444 [M+2], Mol. Formula; C$_{26}$H$_{24}$N$_4$O$_2$. 
References


