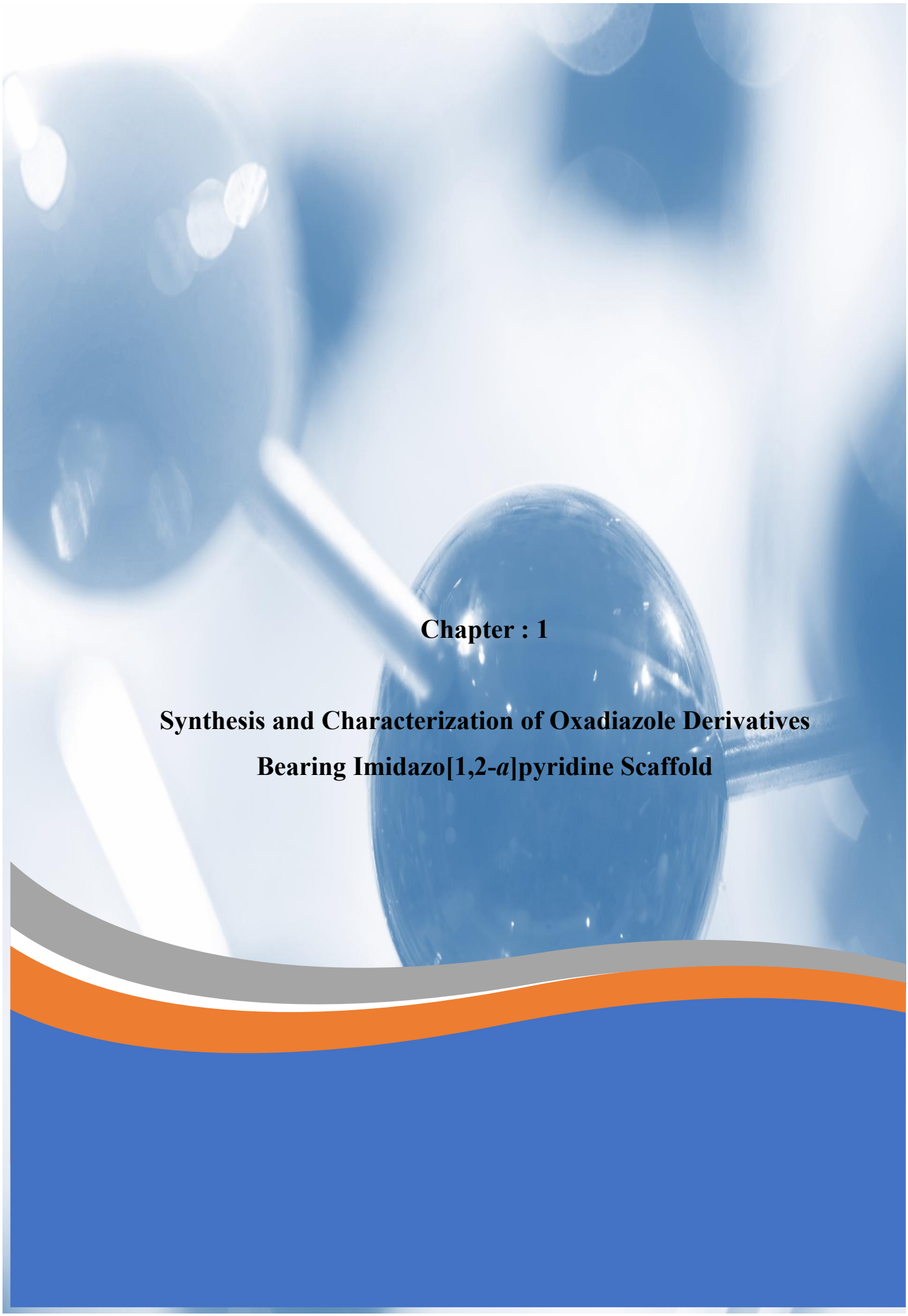


Chapter : 1

Synthesis and Characterization of Oxadiazole Derivatives Bearing Imidazo[1,2-*a*]pyridine Scaffold

1. Study on Oxadiazole:

1.1 Introduction:

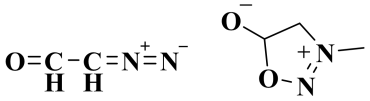
Oxadiazole is a five-membered heterocyclic compound consisting up of two carbon atoms, two nitrogen atoms, one oxygen atom, and two double bonds. It is additionally referred to as i.1,2,4-oxadiazole ii. 1,2,5-oxadiazole iii. 1,2,3-oxadiazole and iv. 1,3,4-oxadiazole. Oxadiazole comprises four isomers. Oxadiazole operates as the parent molecular structure for an extensive family of heterocyclic compounds.

i ii iii iv

1,2,4-oxadiazole 1,2,5-oxadiazole 1,2,3-oxadiazole 1,3,4-oxadiazole

Fig.1.1: Isomers of oxadiazole

The durability of oxadiazole isomers of has been assessed using their relative free Gibbs energy. 1,3,4-oxadiazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, and 1,2,5-oxadiazole all have free Gibbs energies of 0.0, 21.28, 8.64, and 40.61 kcal/mol, respectively. The 1,2,3-oxadiazole isomer is actually unstable and tends to transform into to a diazo-ketone linear structure. unexpectedly this transformation does not typically occur in the free state, but rather in an unusual mesoionic form known as sydnones.



Linear form Sydnones

The synthesis of 1,3,4-oxadiazole yields a more stable compound compared to its isomers. This enhanced stability is attributed to increased aromaticity, likely arising from its inherent symmetry. Notably, 1,3,4-oxadiazole demonstrates heightened

aromatic character. Beyond its structural advantages, 1,3,4-oxadiazole serves as a potent bio isostere for amide and ester functional groups. This compound plays a substantial role in pharmacological activity by actively participating in hydrogen bonding interactions with various receptors, thereby contributing significantly to its pharmacological efficacy.

Derivatives of 1,3,4-oxadiazole have been reported to have a diverse range of pharmacological, medicinal and biological actions. [1] Compounds having the 1,3,4-oxadiazole nucleus have a distinct place in medicinal chemistry and play an important role due to their high biological activity. [2] The tiny and simple 1,3,4-oxadiazole nucleus is found in compounds involved in research aimed at evaluating novel compounds with interesting pharmacological activities such as antimicrobial, [3][4]anticancer,[5][6]anti-inflammatory,[7][8]antituberculosis,[9]antidiabetic[10]and analgesic[11][12] agents.

- **Medications incorporating the 1,3,4-oxadiazole nucleus are currently available in the market:**

- Nesapidil as Anti-arrhythmic drug [13]
- Fenadiazole as Hypnotic drug [14]
- Raltegravir as Inhibits HIV replication [15]
- Tiodazosin as Antihypertensive drug[16]
- Zibotentan as Anticancer drug[17]

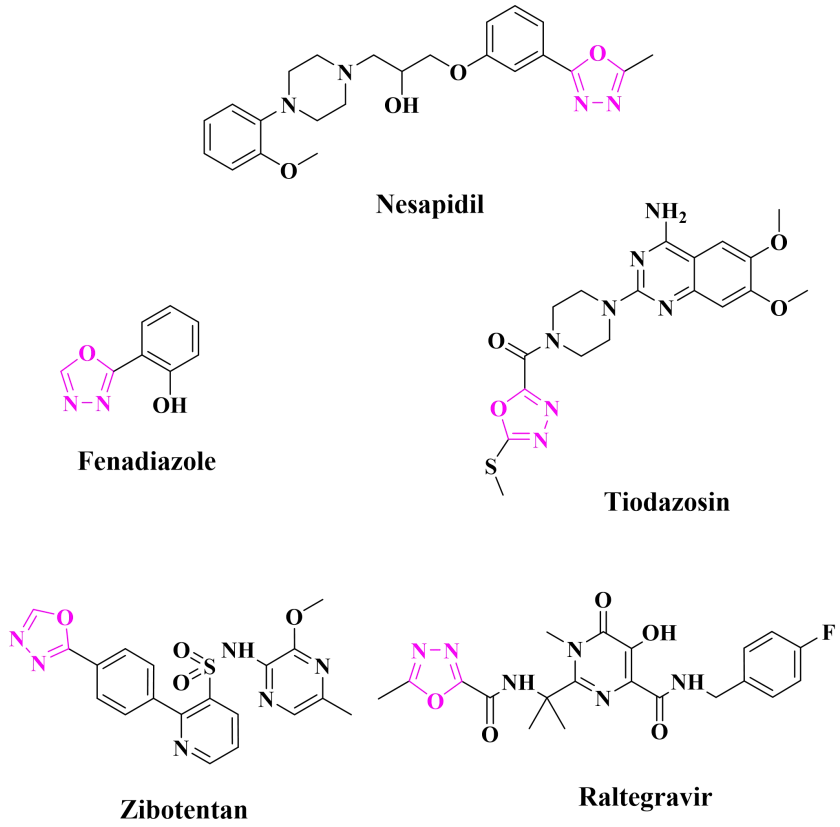
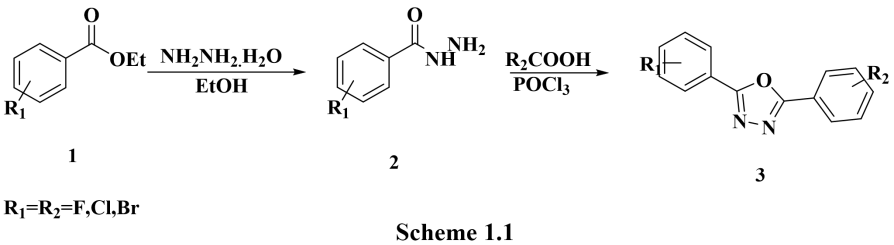


Fig.1.2: 1,3,4-oxadiazole nucleus are currently available in the market

1.2 Common Procedures for Oxadiazole Synthesis:

Zheng et al., [18] and Ke et al., [19] commonly used approach is to react substituted ethyl benzoate **1** in presence of hydrazine hydrate and ethanol to give substituted hydrazide **2**. **2** and substituted carboxylic acid in phosphorousoxychloride to yield 2,5-disubstituted oxadiazole **3**. The dehydrating agent is $POCl_3$. **(Scheme1.1)**



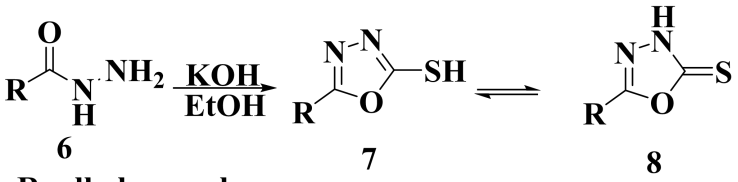
Scheme 1.1

Martin et al., [20] reported in order to produce 2,5-disubstituted 1,3,4-oxadiazole derivatives, *N*'-(4-hydroxybenzoyl)isonicotinohydrazide **4** is frequently cyclized with

thionyl chloride, another dehydrating agent to give 4-(5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl)phenol as product. **(Scheme1.2)**

Scheme 1.2

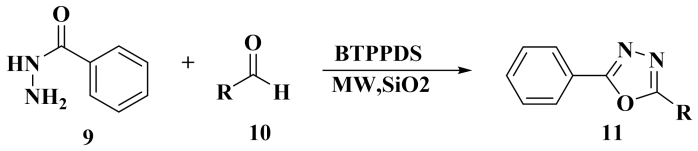
Koparir and Amir et al.,[21-22] reported different synthesis method for producing 5-aryl-1,3,4-oxadiazole-2-thiol **7** derivatives involves reacting acyl hydrazide **6** with carbon disulfide in a basic solution. Currently, the majority of the synthesized in this system, derivatives of oxadiazole were produced. **(Scheme1.3)**



R=alkyl or aryl

Scheme 1.3

Gorjizadeh et al.,[23] reported an environmentally friendly one-pot synthesis of 1,3,4-oxadiazoles **11** was achieved using 1,4-bis(triphenylphosphonium)-2-butene peroxodisulfate (BTPPDS) as the oxidation reagent. BTPPDS, known for its cost-effectiveness and environmental safety. Here is eco-friendly approach that utilizes BTPPDS immobilized on silica gel as an oxidant for the one-pot synthesis of benzohydrazide **9** and substituted aldehydes **10** conducted under solvent-free and microwave irradiation conditions. **(Scheme1.4)**

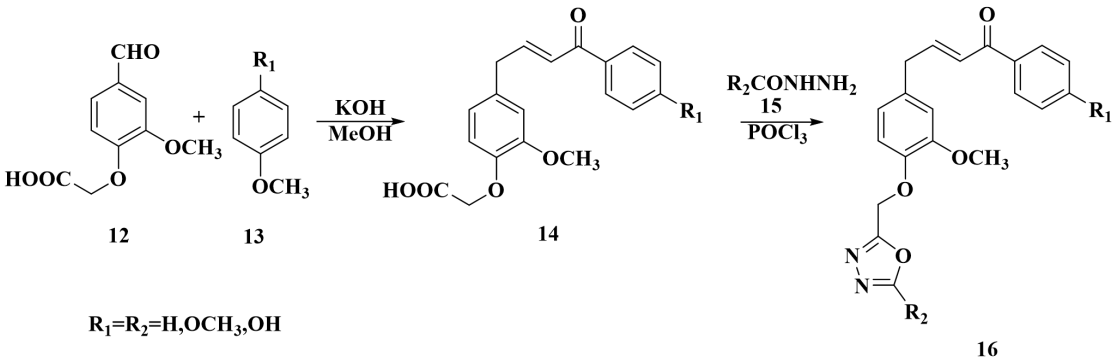


R=Ph,4-Cl-C_6H_4,4-CH_3-C_6H_4,4-OCH_3-C_6H_4,4-NO_2-C_6H_4

Scheme 1.4

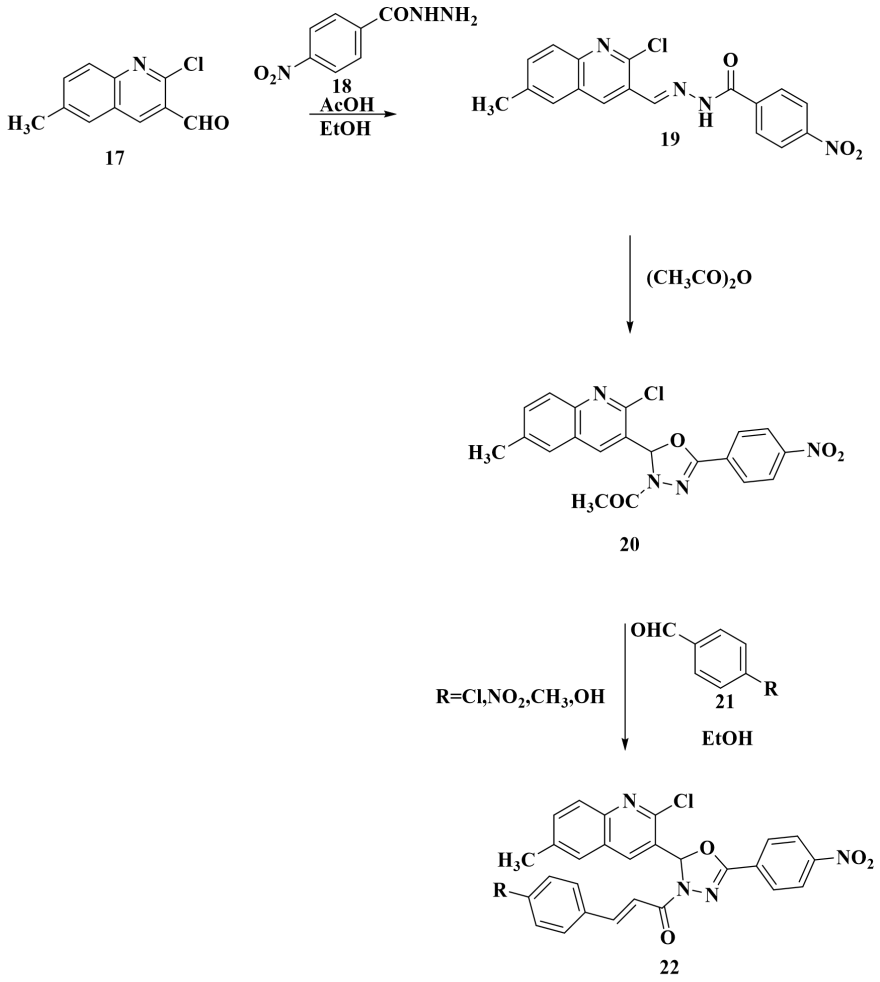
Bakht et al., [24] reported the synthesis of 1,3,4-oxadiazole derivatives begins with the formation of chalcones **14** through a standard Claisen-Schmidt condensation. This

process involves the interaction between 2-(4-formyl-2-methoxyphenoxy)acetic acid **12** and derivatives of acetophenone **13** in the presence of a KOH as base and methanol as solvent. Following the generation of chalcones **14**, these compounds undergo a subsequent reaction with an appropriate acid hydrazide **15** in the presence of phosphorus oxychloride ($POCl_3$), resulting in the successful production of (E)-4-(3-methoxy-4-((5-(p-substituted)-1,3,4-oxadiazol-2-yl)methoxy)phenyl)-1-phenylbut-2-en-1-one **16** with a favorable yield. **(Scheme1.5)**



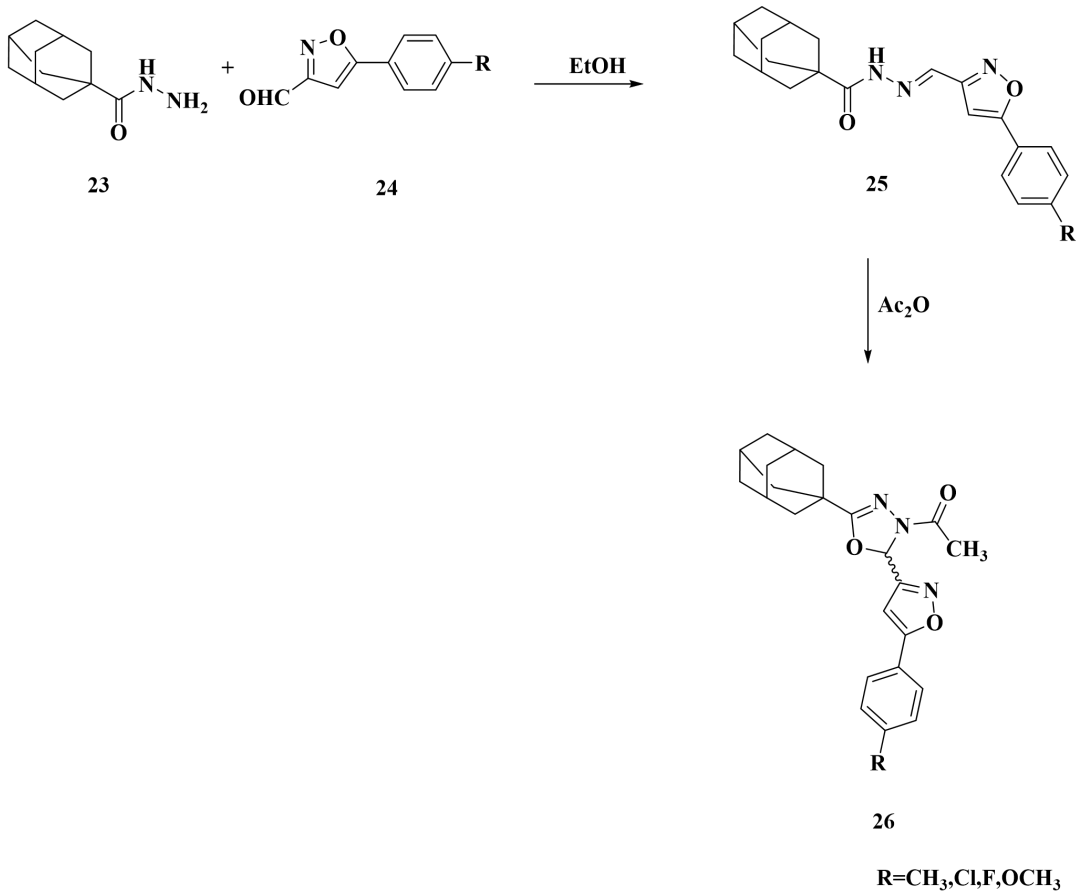
Scheme1.5

Desai et al., [25] reported the compound 2-chloro-6-methylquinoline-3-carbaldehyde **17** was reacted with 4-nitrophenyl hydrazide **18** in ethanol, using a catalytic amount of glacial acetic acid. This reaction produced (E)-*N*'-((2-chloro-6-methylquinolin-3-yl)methylene)-4-nitrobenzohydrazide **19**. Compound **19** was then cyclized by refluxing with an excess of acetic anhydride for six hours, yielding 1-(2-(2-chloro-6-methylquinolin-3-yl)-5-(4-nitrophenyl)-1,3,4-oxadiazol-3(2*H*)-yl)ethan-1-one **20**. In the final step, intermediate **20** was reacted with substituted aldehydes **21** in the presence of KOH in ethanol for 5-6 hours to produce derivatives of 1-[2-(2-chloro-6-methylquinolin-3-yl)-5-(4-substituted)-1,3,4-oxadiazol-3-yl]-3-(aryl)prop-2-en-1-ones **22**. while under MWI, the same reactions were completed in 3–5 min with excellent yield as compare to conventional method. Derivatives of **22** shows good antimicrobial activity against gram-positive and gram-negative bacteria.**(Scheme1.6)**



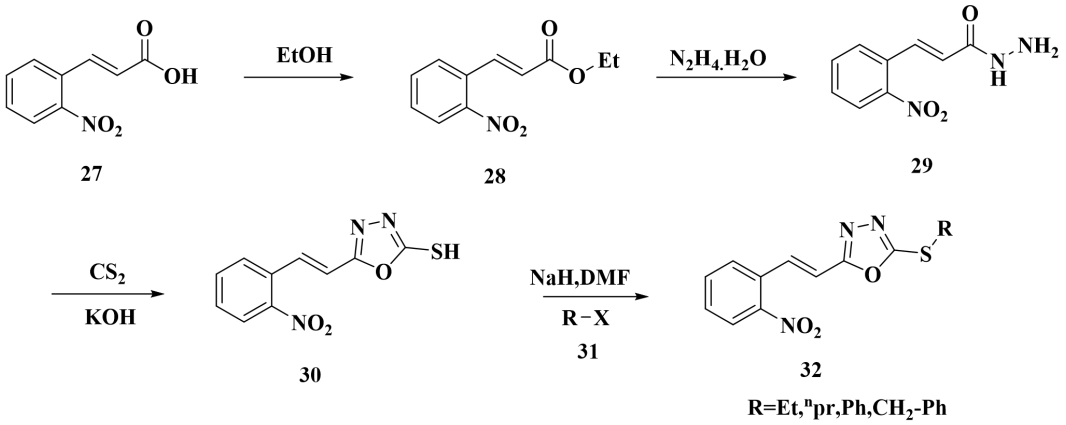
Scheme1.6

El-Emam et al., [26] reported Adamantane-1-carbohydrazide **23** was reacted with various substituted aldehydes **24** to form (E)-*N*'-((5-(p-substituted)isoxazol-3-yl)methylene)adamantane-1-carbohydrazide **25**. Compound 25, upon reaction with acetic anhydride, yielded 1-(5-(adamantan-1-yl)-2-(5-(p-substituted)isoxazol-3-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethan-1-one **26**. Compound **26** exhibited significant broad-spectrum antimicrobial activity. **(Scheme1.7)**



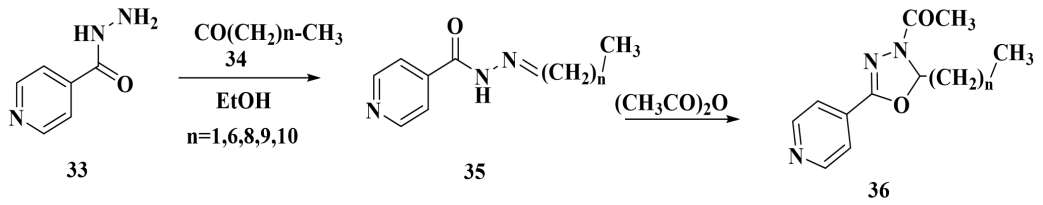
Scheme1.7

Athar Abbasi et al., [27] reported (E)-3-(2-Nitrophenyl)acrylic acid **27** was esterified with ethanol in the presence of concentrated H_2SO_4 to produce ethyl (E)-3-(2-nitrophenyl)acrylate **28**. This ester **28** was then reacted with hydrazine hydrate, forming (E)-3-(2-nitrophenyl)acrylohydrazide **29**. The acrylohydrazide **29** was treated with potassium hydroxide and carbon disulfide to yield (E)-5-(2-nitrostyryl)-1,3,4-oxadiazole-2-thiol **30**. Subsequently, compound **30** was reacted with sodium hydride in DMF and various halides **31**, resulting in the formation of (E)-2-(substituted thio)-5-(2-nitrostyryl)-1,3,4-oxadiazole derivatives **32**, which exhibited enzyme inhibition activity. **(Scheme1.8)**



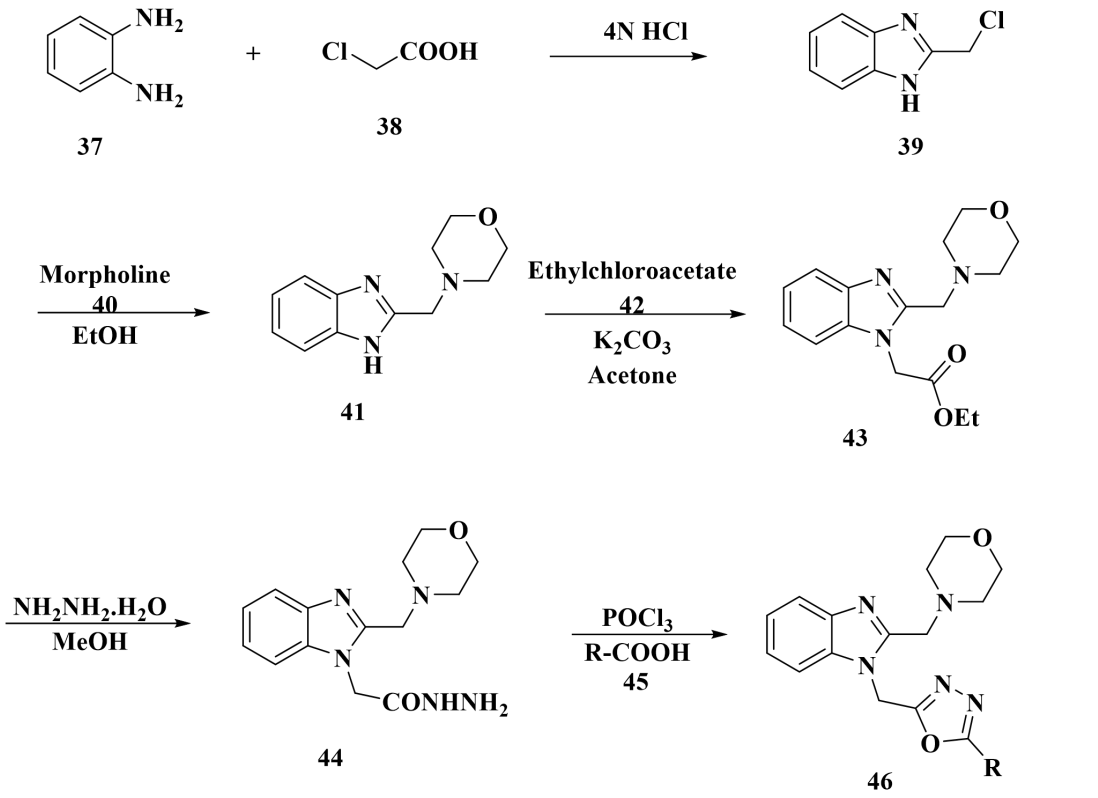
Scheme1.8

Mazurek et al., [28] reported a series on 1,3,4-oxadiazole derivative which initiated from Isonicotinohydrazide **33** was added to a solution of various aldehydes **34** in ethanol to form Schiff base derivatives of isonicotinoyl hydrazide **35**. These Schiff bases **35** were then subjected to reflux in the presence of excess anhydrous acetic anhydride for 4 hours, yielding 1-(2-substituted-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethan-1-one derivatives **36**. The synthesized compounds **36** were evaluated for their in vitro anti-mycobacterial activity. **(Scheme1.9)**



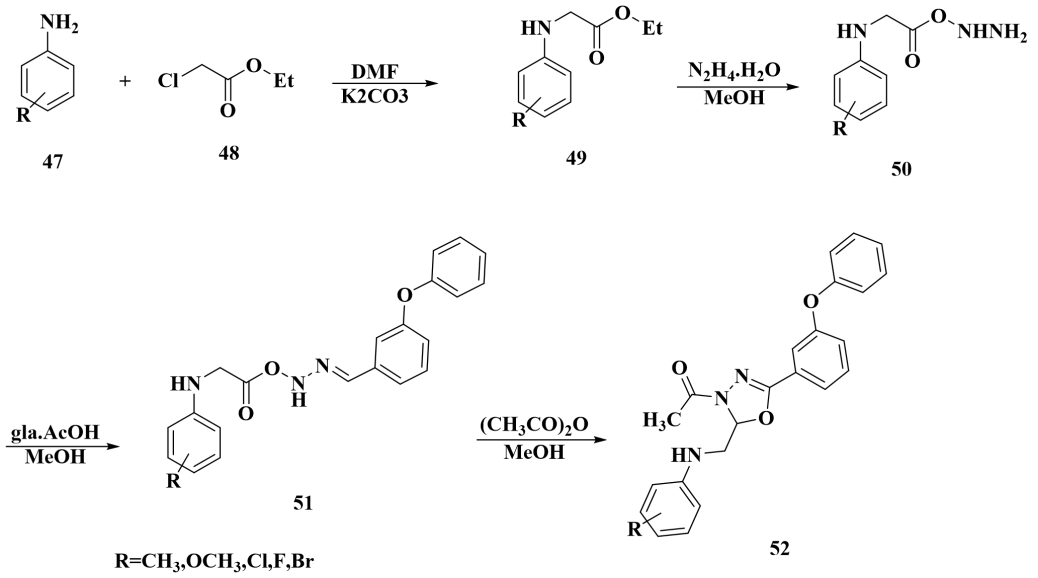
Scheme1.9

Rathore et al., [29] reported a series on 1,3,4-oxadiazole derivative which initiated from Benzene-1,2-diamine **37** and 2-chloroacetic acid **38** were reacted in the presence of HCl to produce 2-(chloromethyl)-1*H*-benzo[*d*]imidazole **39**. This compound **39** was then treated with morpholine **40** to yield 2-(morpholinomethyl)-1*H*-benzimidazole **41**. Compound **41** was subsequently treated with hydrazine hydrate, forming an ester intermediate **43** which was further processed to obtain 2-(2-(morpholinomethyl)-1*H*-benzimidazol-1-yl)acetohydrazide **44**. Cyclization of compound **44** with substituted carboxylic acids **45** resulted in the formation of 1-{(5-substituted-1,3,4-oxadiazol-2-yl)methyl}-2-(morpholinomethyl)-1*H*-benzimidazoles **46**, which exhibited in vivo anti-inflammatory activity. **(Scheme1.10)**



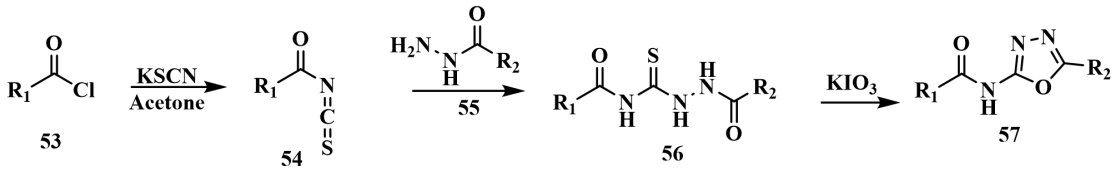
Scheme1.10

Ghaisas et al., [30] reported a series on 1,3,4-oxadiazole derivative which initiated from Substituted amine **47** was reacted with ethyl chloroacetate **48** in dry DMF in the presence of anhydrous potassium carbonate at 60°C to produce ethyl-2-(substituted amino)acetate **49**. Compound **49** was then treated with hydrazine hydrate to yield 2-(substituted amino)acetohydrazide **50**. This hydrazide **50** was subsequently reacted with m-phenoxybenzaldehyde and a few drops of glacial acetic acid to form (Z)-2-(substituted amino)-*N*'-(3-phenoxybenzylidene)acetohydrazide **51**. The intra cyclization of compound **51** in the presence of acetic anhydride produced 1-(2-(3-phenoxyphenyl)-5-((substituted-amino)methyl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone **52**, which exhibited in vitro antimicrobial activity against various pathogenic strains. **(Scheme1.11)**



Scheme1.11

Li et al.,[31] reported the synthesis of 2-acetylamino-substituted 1,3,4-oxadiazoles **57** was were evaluated for their antibacterial activity against B. subtilis and S. aureus. Which was synthesized in following method. Substituted acetyl chloride **53** was reacted with potassium thiocyanate in dry acetone at room temperature to yield substituted isothiocyanate **54**. This isothiocyanate **54** was then reacted with 4-substituted benzohydrazide **55** to form *N*-(2-(4-substituted benzoyl)hydrazine-1-carbonothioyl)benzamide derivatives **56**. These derivatives **56** were further treated with KIO_3 to produce 2-acetylamino-1,3,4-oxadiazole derivatives **57**.**(Scheme1.12)**

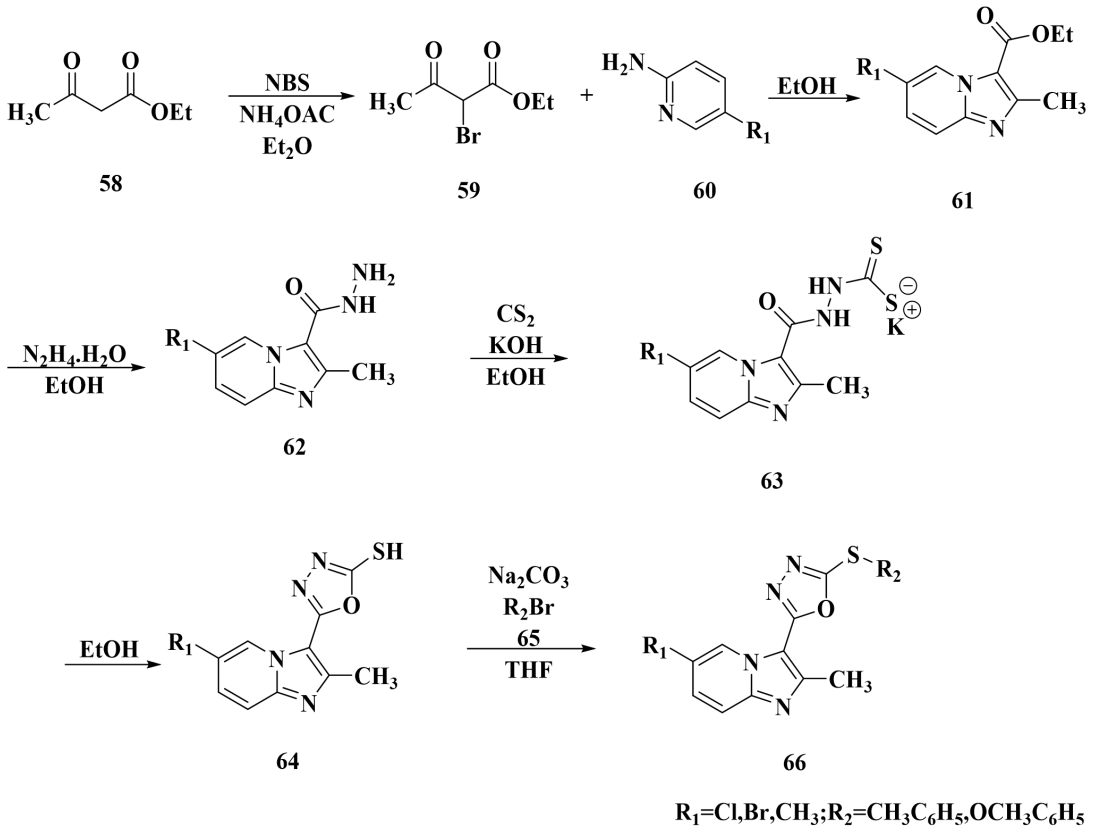


R_1=R_2=$CH_3C_6H_5$, $OCH_3C_6H_5$, ClC_6H_5, FC_6H_5,BrC_6H_5

Scheme1.12

Shyam Maurya et al., [32] reported the research focused on evaluating the activity against Mycobacterium tuberculosis H37Rv strains and in vitro anti-bacterial activity of synthesized hybrids containing 1,3,4-oxadiazole-substituted imidazo[1,2-*a*]pyridine **66**. This assessment was conducted following the specified methodology .Ethyl acetoacetate **58** was reacted with a mixture of ammonium acetate and NBS to yield

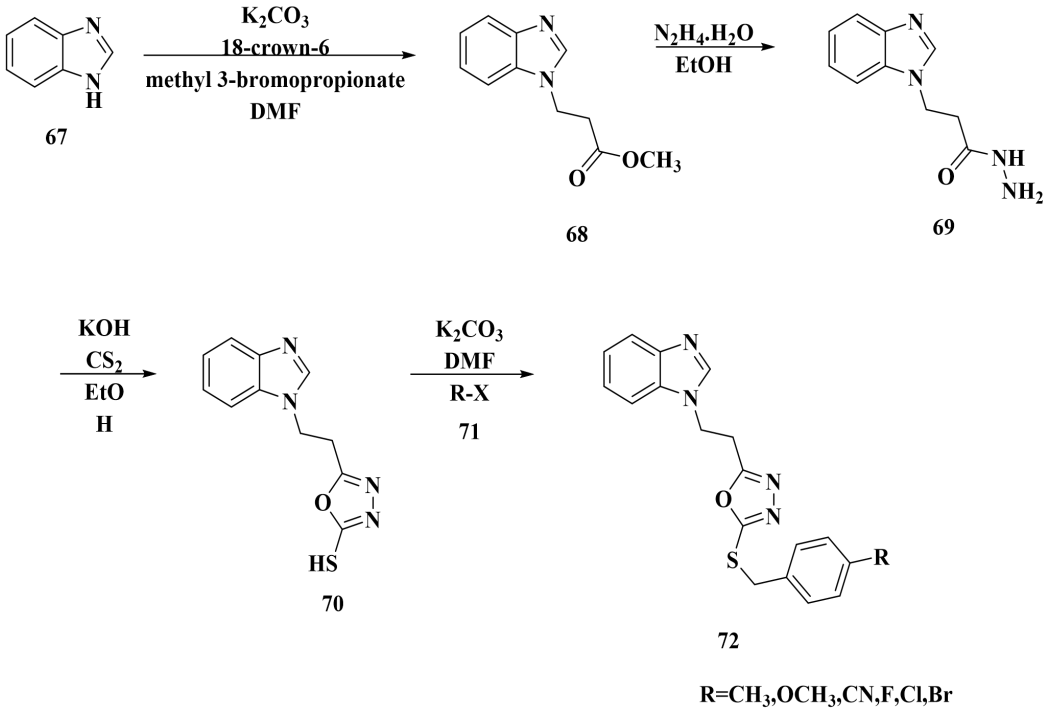
ethyl2-bromo-3-oxobutanoate **59**. This compound **59** was then reacted with substituted 2-aminopyridines **60** in ethanol, producing ethyl6-substituted-2-methylimidazo[1,2-*a*]pyridine-3-carboxylate **61**. Treating this ester **61** with hydrazine hydrate yielded 6-substituted-2-methylimidazo[1,2-*a*]pyridine-3-carbohydrazide **62**. This hydrazide was further reacted with carbon disulfide in the presence of potassium hydroxide to formation of salt 2-(6-substituted-2-methylimidazo[1,2-*a*]pyridine-3-carbonyl)hydrazine-1-carbodithioate **63**. **63** further reaction with ethanol led to the formation of 5-(6-substituted-2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazole-2-thiol **64**. Finally, reacting this compound with substituted halides **65** in THF produced 2-(6-substituted-2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-(substituted thio)-1,3,4-oxadiazole **66**. **(scheme1.13)**



Scheme1.13

Noureldin et al., [33] reported the synthesis process began with the formation of Methyl 3-(1*H*-benzo[*d*]imidazol-1-yl)propanoate **68** through a nucleophilic substitution reaction between benzimidazole **67** and methyl 3-bromopropionate in the presence of K_2CO_3 and 18-crown-6, enhancing K_2CO_3 ionization in DMF.

Subsequently, 3-(1*H*-Benzo[*d*]imidazol-1-yl)propanehydrazide **69** was produced via hydrazinolysis of Methyl 3-(1*H*-benzo[*d*]imidazol-1-yl)propanoate **68** using excess hydrazine hydrate in EtOH. This hydrazide **69** intermediate underwent further reactions, including reflux with KOH and carbon disulfide to yield 2-(3-(1*H*-benzo[d]imidazol-1-yl)propanoyl)hydrazine-1-carbodithioate **70**. This intermediate **70** was then cyclized into 5-[2-(1*H*-benzo[*d*]imidazol-1-yl)ethyl)-1,3,4-oxadiazole-2-thiol **71**, 2-(2-(1*H*-benzo[*d*]imidazol-1-yl)ethyl)-5-((4-substitutedbenzyl)thio)-1,3,4-oxadiazole **72** obtained through the reaction of the cyclized products with various alkyl halides **71** in the presence of K_2CO_3. **(Scheme1.14)**



Scheme1.14

Upon reviewing the literature, it became evident that compounds containing 1,3,4-oxadiazole moieties hold a distinct significance in the realm of designing and synthesizing bioactive agents with noteworthy biological properties. Medicinal chemistry has highlighted the pivotal role of five-membered nitrogen-containing heterocycles, particularly 1,3,4-oxadiazole, in influencing biological systems. In light of this, our current research endeavors focus on the incorporation of aromatic groups at the 2 and 5 positions of the 1,3,4-oxadiazole scaffold.

1.3 Study on Imidazo[1,2-*a*]pyridine:

1.4 Introduction:

The pyridine ring-fused heterocycles, which have been created using a variety of techniques and are an important source of biologically significant compounds, are frequently built by attaching functionality around pyridine, a compound that is challenging to functionalize quickly and flexibly.[34]

One of the crucial fused bicyclic heterocycles is imidazopyridine. These are an important class of nitrogen-containing heterocyclic compounds that are physiologically active. It is recognized that the bicyclic imidazo heterocyclic scaffold formed by the imidazole moiety and the pyridine ring is a privileged structure. heterocycles with an imidazole ring that are fused at the bridgehead with nitrogen structural characteristics that are common.[35]

Imidazopyridine derivatives are very significant due to their exceptional biological characteristics. Due to their isomerism with indoles and azaindoles, two significant heterocyclics present in numerous alkaloids, they are of chemical and pharmacologicals, they are of chemical and pharmacological as pesticides, fungicides, herbicides, equine medications, and dyes.

The imidazopyridines comprise four important isomers. Imidazo[1,2-*a*]pyridine, Imidazo[1,5-*a*]pyridine, Imidazo[4,5-*b*]pyridine, Imidazo[4,5-*c*]pyridine.

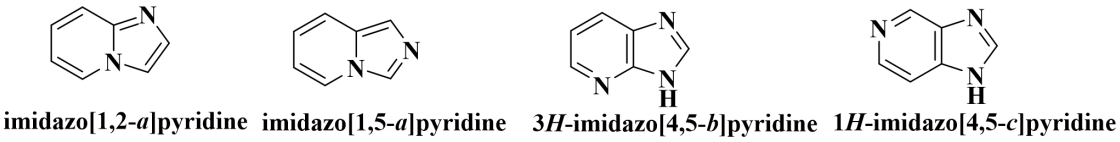


Fig.1.3: Isomers of Imidazopyridine

The imidazo[1,2-*a*]pyridine nucleus has been present in established drugs like Alpidem using in treatment of reduce anxiety, Zolpidem using in treatment of insomnia, Necopidem drug like Alpidem and Zolpidem using treatment of reduce anxiety, Saripidem drug using as sedative and anxiolytic agent, Zolimidine using in treatment of peptic ulcer, Olprinone is cardiotonic agent and Minodronic acid is third

generation bisphosphonate drug to treat osteoporosis.

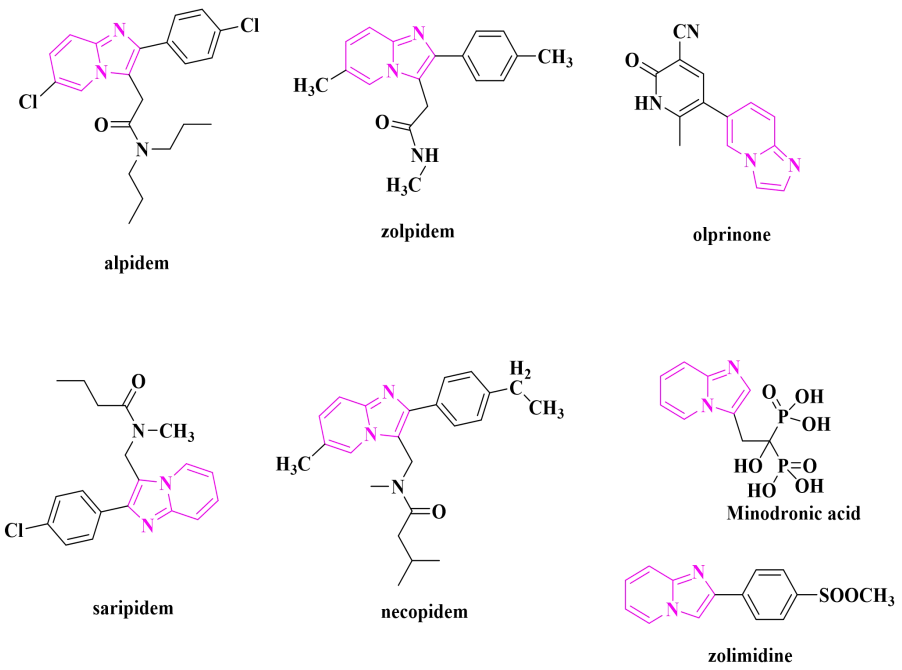


Fig.1.4: Drugs containing the imidazo[1,2-*a*]pyridine nucleus

A fused imidazopyridine heterocycle that has received a lot of attention is imidazo[1,2-*a*]pyridine. A useful scaffold present in a variety of natural compounds is imidazo[1,2-*a*]pyridine. physiologically active substances, including those with antimicrobial [36] , antibacterial [37] , antiprotozoal [38] , [39] , antitubercular [40] , anticancer[41], anti-inflammatory[42], anthelmintic[43], and antifungal[44] agents.

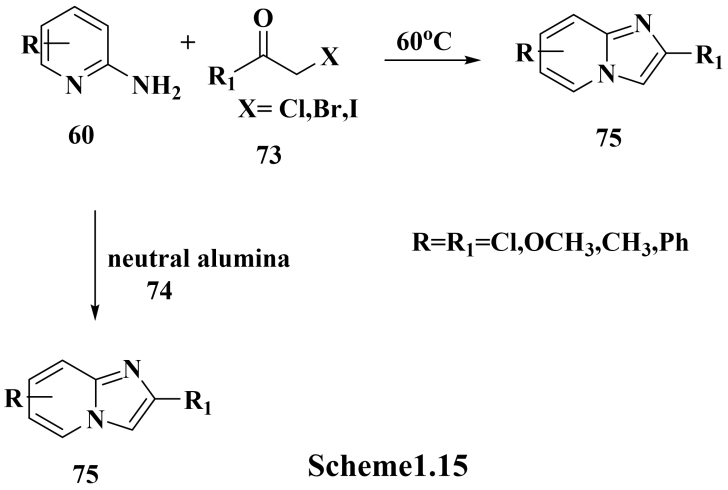
Imidazo[1,2-*a*]pyridines are aromatic organic compounds with a molecular formula $C_7H_6N_2$, a pyridine fused imidazole ring structure. Imidazo[1,2-*a*]pyridines have been proved to be useful precursors for the synthesis of a variety of medicinal agents.

1.5 Common Producers for Imidazo[1,2-*a*]pyridine:

A straightforward Beilstein search on the completely conjugated heterocycle turned up over 6000 hits during the previous ten years.

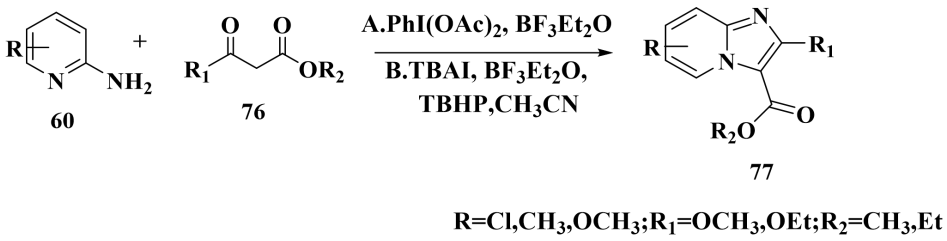
Ponnala et al., [45] reported conventional method for the formation of imidazo[1,2-*a*]pyridine derivatives **75** by condensation reaction of substituted haloketones **73** with substituted aminopyridines **60**. **(Scheme1.15)** In past decades, numerous catalytic and non-catalytic systems have been established by various groups. In this review, several

of them are discussed. At room temperature, the neutral alumina **74** serves as an effective mediator for this change in temperature.



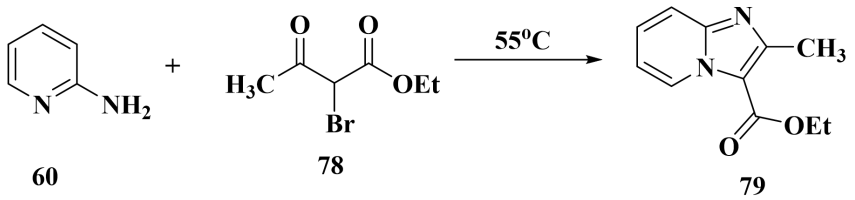
Scheme1.15

Ma et al.,[46] reported the direct oxidative C–N coupling of 2-aminopyridines **60** with β-keto esters **76**. 1,3-diones, leading to the formation of imidazo[1,2-*a*]pyridines **77**, was catalyzed by TBAI. The reaction was conducted under metal-free conditions, utilizing tert-butyl hydroperoxide (TBHP) as the oxidant. **(Scheme1.16)**

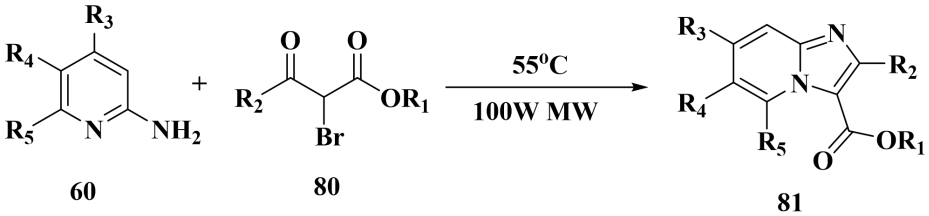


Scheme 1.16

Chunavala et al., [47] reported the synthesis of highly substituted imidazo[1,2-*a*]pyridine derivatives **79** and **81** were achieved through rapid processes employing both thermal and microwave assistance. This reaction involved the interaction between aminopyridines **60** and α-bromo-β-keto esters **78** and **80**, conducted under solvent-free conditions. **(Scheme1.17) (Scheme1.18)**



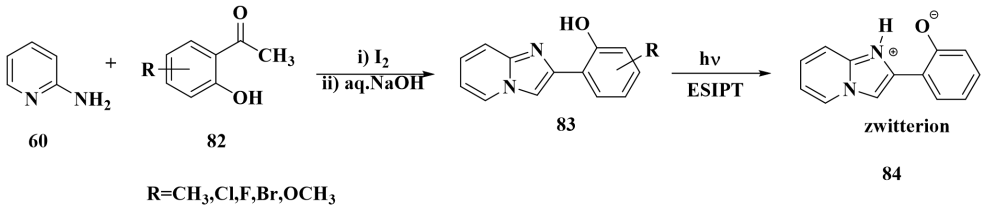
Scheme1.17



R_1=R_2=CH_3,CH_2CH_3;R_3=R_4=R_5=H,CH_3,Cl,Br

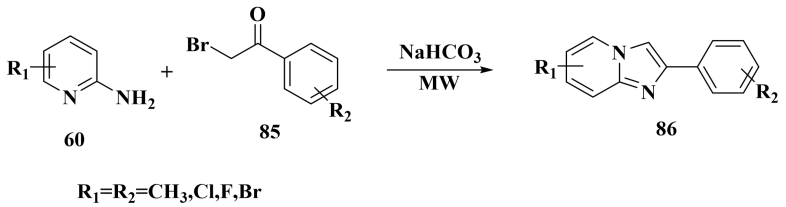
Scheme1.18

Stasyuk et al.,[48] reported a concise and effective pathway for synthesizing a diverse array of imidazo[1,2-*a*]pyridines **84** from 2-aminopyridines **60** and substituted acetophenones **82** is established through a streamlined, one-pot tandem process, initiated by an Orto leva-King reaction. **(Scheme1.19)**



Scheme 1.19

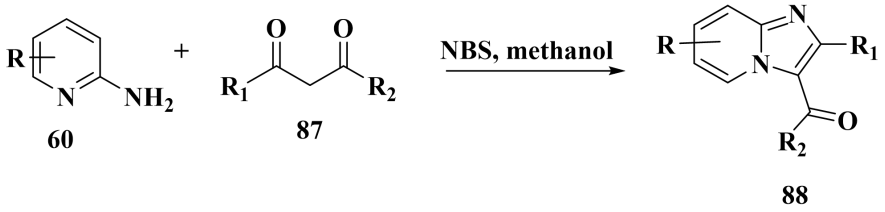
Hiebel et al., [49] reported highlights PEG400 as a fitting medium for the condensation of substituted 2-amino pyridines **60** with α-bromo ketones **85**. The synthesis of 2-substituted imidazo[1,2-*a*]pyridines **86** was efficiently achieved through microwave irradiation within a brief timeframe, resulting in excellent yields. **(Scheme1.20)**



R_1=R_2=CH_3,Cl,F,Br

Scheme 1.20

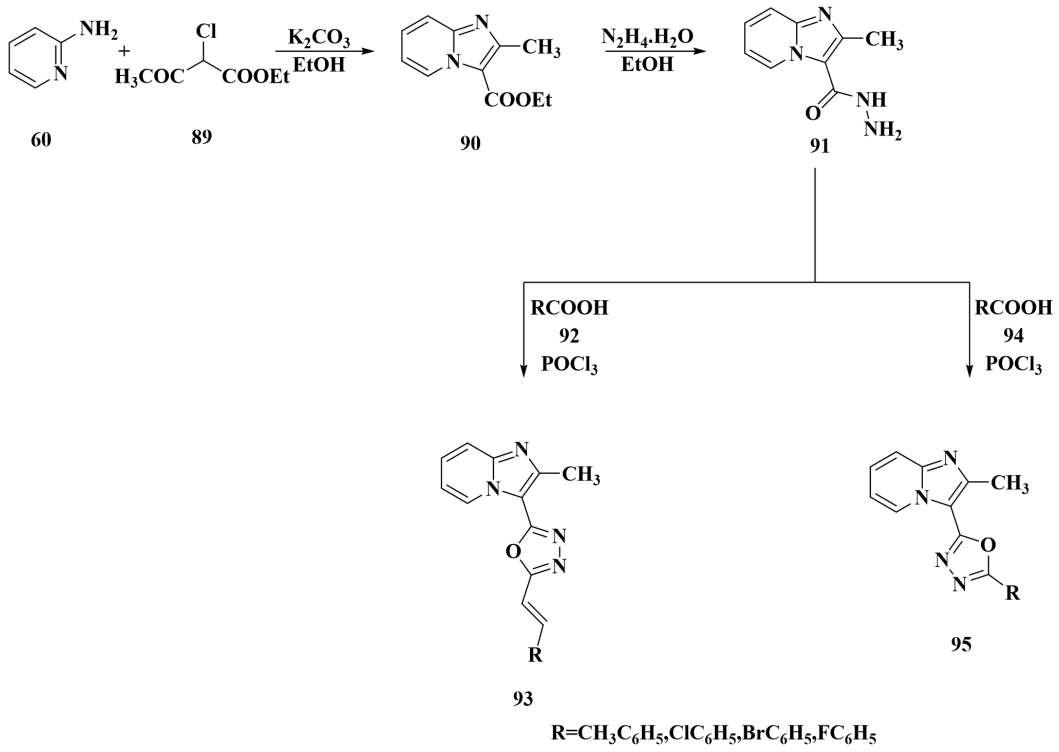
Bhagat et al., [50] reported the combination of 2-aminopyridine **60** with different β-keto esters **87** and 1,3-diketones **87** consistently produced excellent yields of 1-(2,7-substituted imidazo[1,2-*a*]pyridin-3-yl)substituted-1-one **88** in the resulting reactions. **(Scheme1.21)**



R=CH_3,Cl,Br,F;R_1=R_2=CH_3,CH_2CH_3,Ph

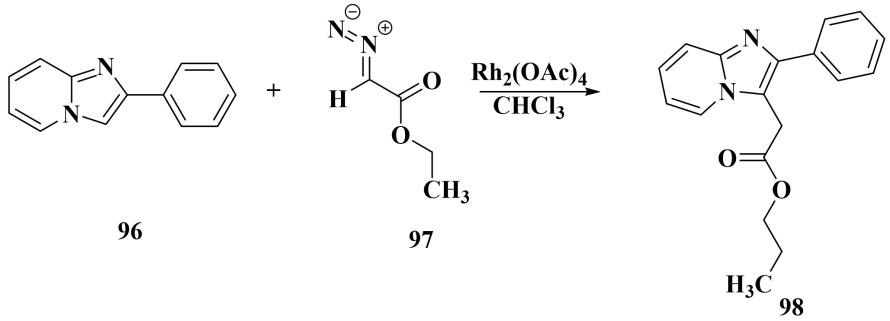
Scheme1.21

Raundal et al., [51] reported a set of novel derivatives of 2-(5-substituted)-1,3,4-oxadiazole-2-yl)-*H*-imidazo[1,2,*a*]pyridine **93** and **95** was evaluated for their antibacterial and antifungal properties, demonstrating significant antimicrobial activity. 2-Amino pyridine **60** was reacted with chloro-oxobutanoate **89** to produce ethyl 2-methylimidazo[1,2-*a*]pyridine-3-carboxylate **90**, which was then converted into 2-methylimidazo[1,2-*a*]pyridine-3-carbohydrazide **91** using hydrazinehydrate. This intermediate **91** was further reacted with either substituted benzoic acids **92** or cinnamic acids **94** in the presence of $POCl_3$, resulting in the target compounds (E)-2-(2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-substituted-1,3,4-oxadiazole **93** and 2-(2-methylimidazo[1,2-*a*]pyridin-3-yl)-5-substituted-1,3,4-oxadiazole **95**. **(Scheme1.22)**



Scheme1.22

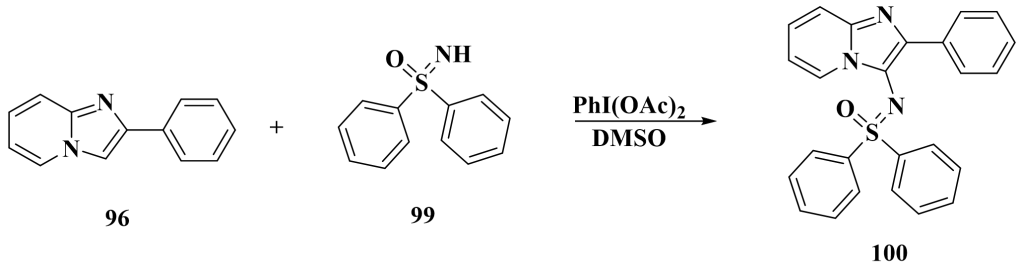
Huang et al., [52] reported a method for C3-ethoxycarbonylmethylation of imidazo[1,2-*a*]pyridines **98** using ethyl diazoacetate **97** in the presence of a Rh(II) catalyst has been successfully developed, demonstrating efficiency and environmental friendliness. Additionally, this innovative approach offers a means to produce synthetic intermediates for the synthesis of anticancer agents that exhibit cellular activity. **(Scheme1.23)**



Scheme1.23

Luan et al., [53] reported straightforward procedure for the direct oxidative coupling

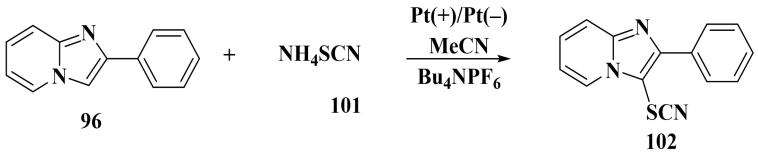
of Unactivated imidazo[1,2-*a*]pyridines **96** with NH-sulfoximines **99** have been revealed, employing sulfoximines as nitrogen sources in the presence of (diacetoxy)iodobenzene ($PhI(OAc)_2$). The reaction proceeds efficiently under atmospheric conditions without the need for any metal catalyst, yielding a range of regioselective C-3 sulfoximidoyl-functionalized imidazo[1,2-*a*]pyridines **100**. **(Scheme1.24)**



96 99 100

Scheme1.24

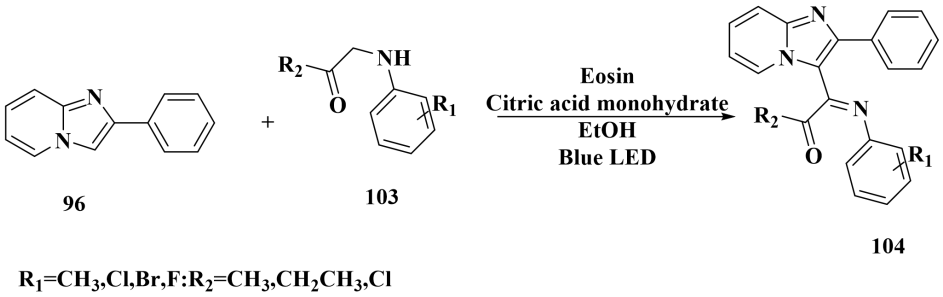
Cui et al.,[54] Achieving regioselective electrochemical oxidative C–H thiocyanation of imidazopyridines **96** has been successfully demonstrated using an undivided electrolytic cell. Notably, this protocol stands out for its transition-metal- and oxidant-free conditions. The synthesis of thiocyanated imidazopyridines **102**, accommodating a diverse array of functional groups, was accomplished with high yields. **(Scheme1.25)**



96 101 102

Scheme1.25

Zhu et al.,[55] reported a novel and efficient visible-light-promoted dehydrogenative cross-coupling reaction has been established for *N*-(4-substitutedphenyl)glycine ethyl ester **103** was reacted with 2-phenylimidazo[1,2-*a*]pyridine **96** in the presence of 10 mol% eosin Y as a catalyst in MeCN at room temperature, yielding substituted 2-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)-2-(substituted amino)acetate derivatives **104**. **(Scheme1.26)**

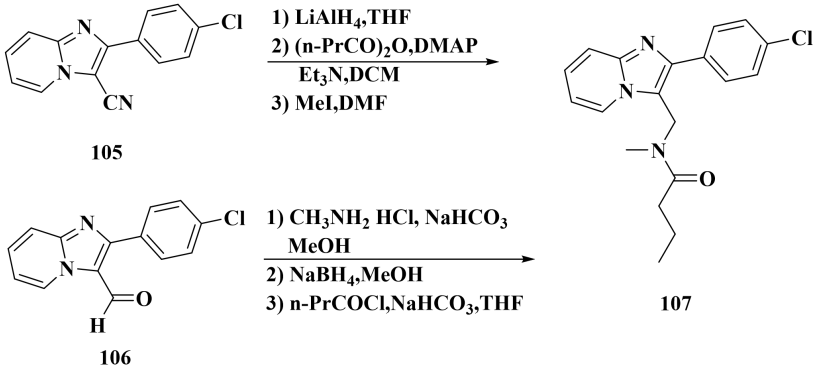


96 103 104

R_1=CH_3,Cl,Br,F:R_2=CH_3,CH_2CH_3,Cl

Scheme1.26

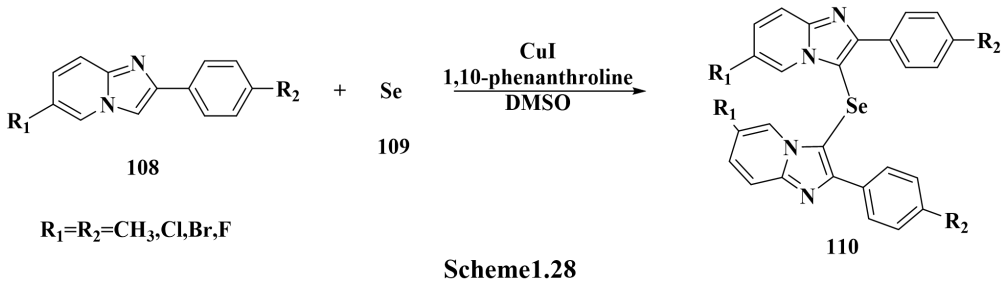
Li et al., [56] reported Cyanation and formylation procedures for 2-phenylimidazo[1,2-*a*]pyridine give 2-phenylimidazo[1,2-*a*]pyridine-3-carbonitrile **105** and 2-phenylimidazo[1,2-*a*]pyridine-3-carbaldehyde **106** respectively. **105** and **106** converted into *N*-((2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)methyl)-*N*-methylbutyramide **107**. This protocol serves as a convenient approach for the synthesis of Saripidem **107**, a clinically utilized compound. **(Scheme1.27)**



105 106 107

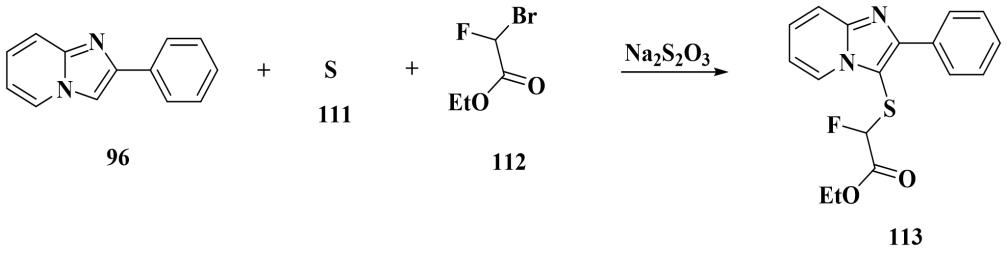
Scheme1.27

Matsumura et al.,[57] reported the selenides synthesized, featuring two imidazo[1,2-*a*]pyridine rings, are entirely novel compounds using substituted imidazo[1,2-*a*]pyridine **108** was reacted with selenium powder **109** in the presence of CuI and 1,10-phenanthroline in DMSO at 130 °C under aerobic conditions, resulting in the formation of bis(2,6-substituted-imidazo[1,2-*a*]pyridin-3-yl)selane **110**. Within the range of prepared selenides demonstrating cytotoxic effects against cancer cells, **110** exhibit outstanding anticancer activity with minimal cytotoxicity towards noncancerous cells. **(Scheme1.28)**



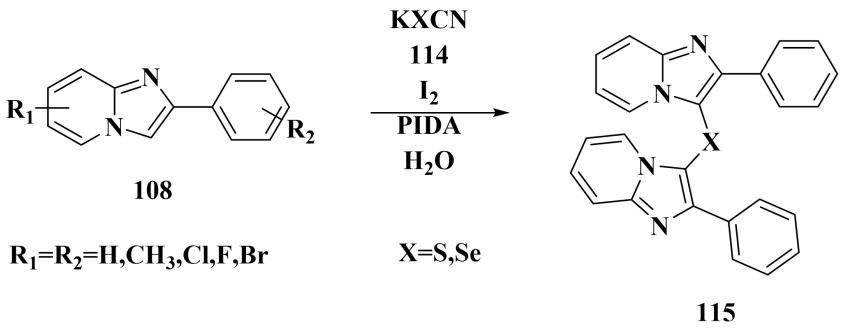
Scheme1.28

Gao et al.,[58] reported a novel transition-metal-free sulfite-assisted three-component C–H sulphuration process involving Sulfuration of 2-phenylimidazo[1,2-*a*]pyridine **96** was achieved by refluxing it with elemental sulfur **111**, ethyl bromofluoroacetate **112**, and sodium thiosulfate in dioxane. This reaction yielded ethyl 2-fluoro-2-((2-phenylimidazo[1,2-*a*]pyridin-3-yl)thio)acetate **113**. This method enables the swift incorporation of the synthetically valuable S-fluoroacetate group into imidazoheterocycles. **(Scheme1.29)**



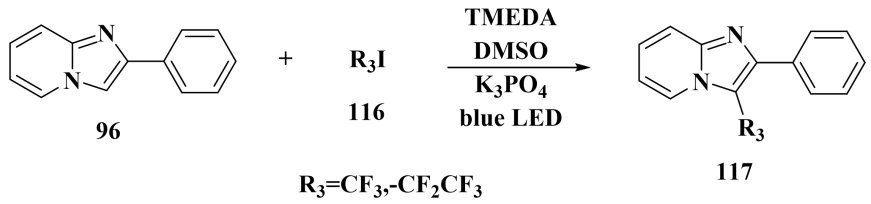
Scheme1.29

Zhu et al., [59] reported a series initiated with 2-Phenylimidazo[1,2-*a*]pyridine **108** was reacted with KXCN **114** (X = S or Se) in the presence of I_2 in water. This reaction resulted in the formation of bis(2-phenylimidazo[1,2-*a*]pyridin-3-yl)sulfane **115** and bis(2-phenylimidazo[1,2-*a*]pyridin-3-yl)selane **115**, respectively. **(Scheme1.30)**



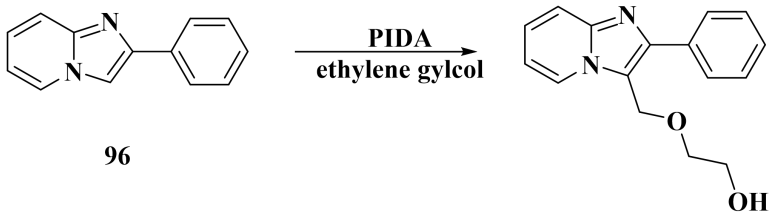
Scheme1.30

Huang et al., [60] reported a gentle and environmentally friendly approach utilizing visible-light-induced direct radical cross-coupling of 2-Phenylimidazo[1,2-*a*]pyridine **96** was reacted with perfluorobutyl iodide **116** in the presence of TMEDA (tetramethylethylenediamine) and tripotassium phosphate in DMSO. 1,1-Diphenylethene and hydroquinone were used as radical inhibitors. This reaction yielded 3-perfluoroalkyl-substitutedimidazo[1,2-*a*]pyridines **117** with excellent yields. **(Scheme1.31)**



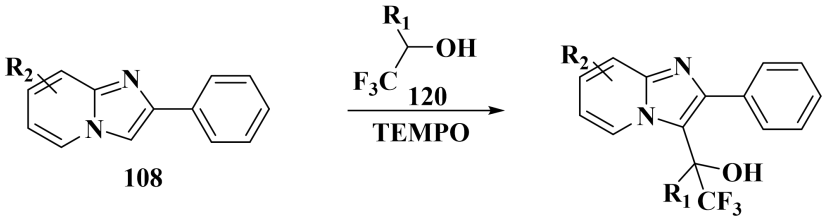
Scheme1.31

Kumar et al., [61] reported an effective and selective approach has been devised for the production of 2-phenylimidazo[1,2-*a*]pyridine **96** were reacted with ethylene glycol and (diacetoxyiodo)benzene (PIDA) as an oxidant to produce the product 2-(2-phenylimidazo-[1,2-*a*]pyridin-3-yl)ethan-1-ol **119**. **(Scheme1.32)**



Scheme1.32

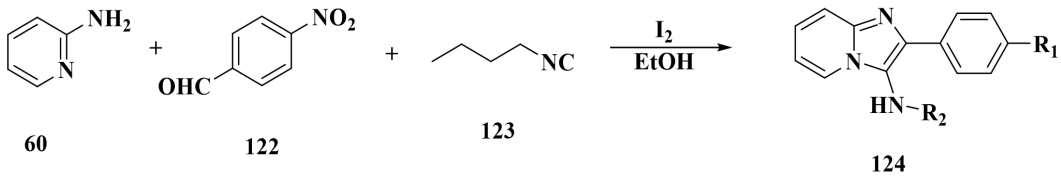
Nipate et al., [62] reported an uncomplicated and exceptionally effective metal-free approach has been established for the 7-methyl-2-phenylimidazo[1,2-*a*]pyridine **108** and 1,1,1,3,3,3-hexafluoropropan-2-ol **120** through TEMPO-mediated cross-dehydrogenative coupling of 1,1,1,3,3,3-hexafluoro-2-(7-methyl-2-phenylimidazo[1,2-*a*]pyridin-3-yl)propan-2-ol **121**. **(Scheme1.33)**



R_1=CF_3,C_2F_5;R_2=CH_3,Cl,F,Ph

Scheme1.33

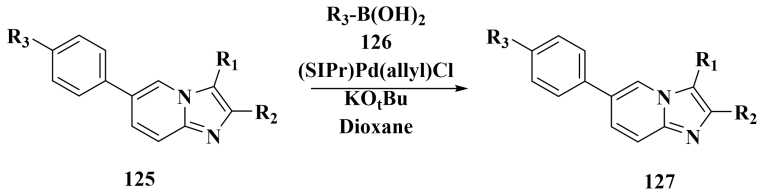
Krishnamoorthy et al., [63] reported a recent study has disclosed the synthesis of imidazo[1,2-*a*]pyridines **124** through one-pot three-component condensations. The product, formed in situ through the interaction between reaction involving 2-aminopyrazine **60**, 4-nitrobenzaldehyde **122**, tert-butyl isocyanide **123**, and I_2 as a catalyst was carried out at room temperature for 1-2 hr. Additionally, synthesized compounds **124** were subjected to evaluation for their anti-cancer activities against cancer cells. **(Scheme1.34)**



Scheme1.34

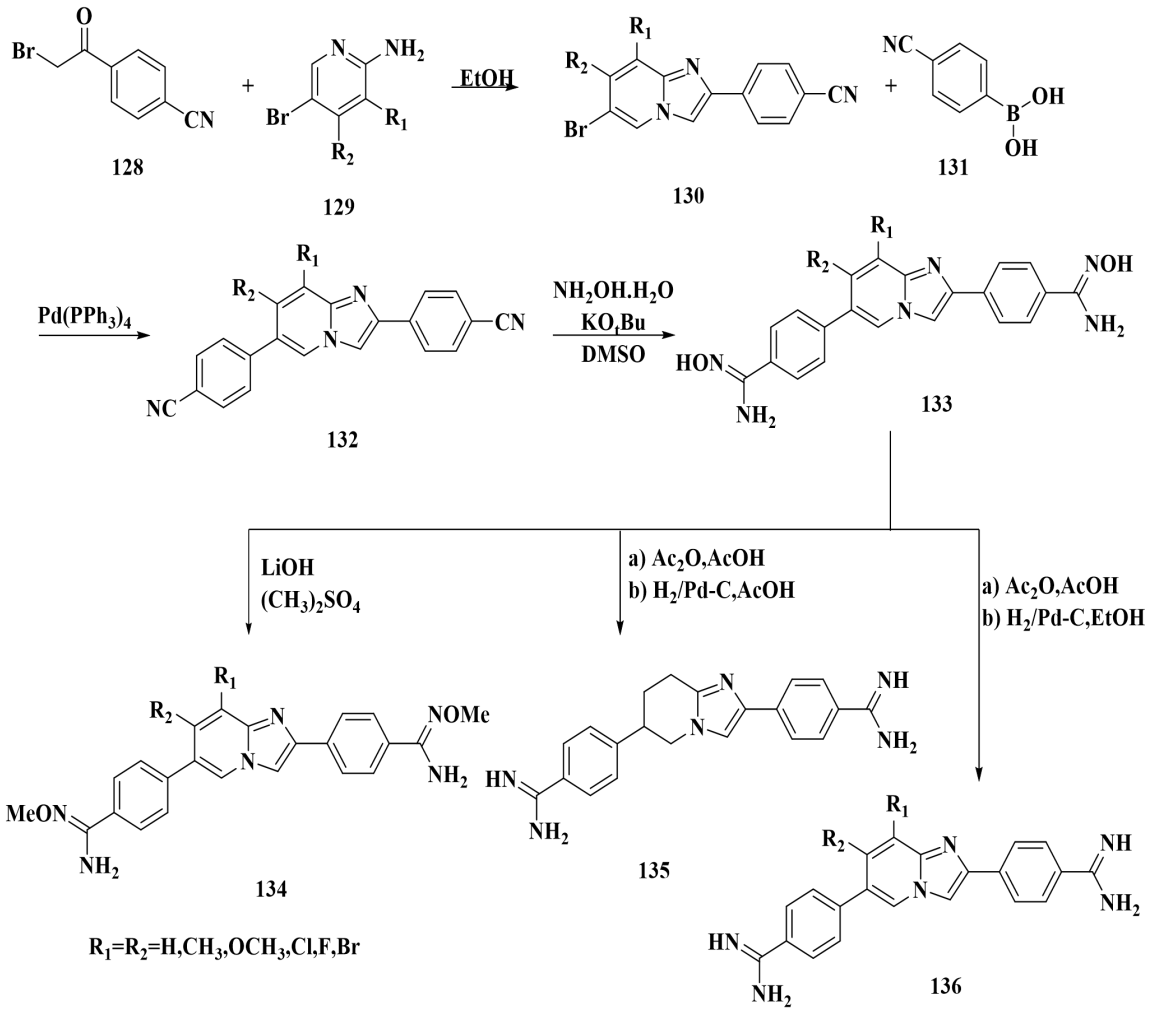
Abbouchi et al., [64] microwave-assisted C-H arylation and Suzuki-Miyara coupling reaction conditions. The coupling of imidazo[1,2-*a*]pyridine derivatives **125** with substituted halides and boronic acids **126** was accomplished in dioxane using potassium tert-butoxide (KO_tBu) as a base. This reaction utilized a phosphine-free catalyst, (SIPr)Pd(allyl)Cl, where SIPr represents *N*,*N*'-bis(2,6-diisopropylphenyl)-4,5-dihydroimidazol-2-ylidene. The (SIPr)Pd(allyl)Cl complex facilitated the formation of 3,6-disubstituted imidazo[1,2-*a*]pyridine **127** and 5-substituted imidazole

compounds with good to excellent yields within just hour. **(Scheme1.35)**



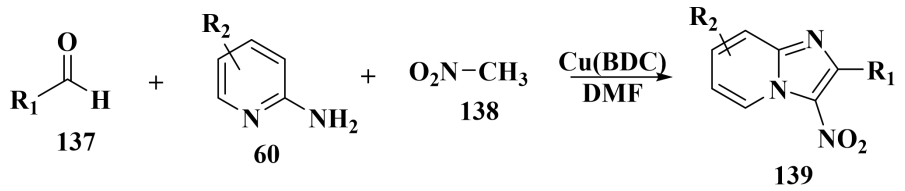
Scheme1.35

Ismail et al., [65] reported the synthesis commenced with the generation of crucial dinitrile intermediates through the reaction of substituted phenacyl bromide **128** with the appropriate 2-amino-5-bromopyridines **129**. Subsequent Suzuki coupling with 4-cyanophenylboronic acid **131** resulted in the formation of 2,6-bis(4-cyanophenyl)-imidazo[1,2-*a*]pyridine derivatives **132**. The bis-amidoximes **133**, obtained through the action of hydroxylamine, were transformed into bis-O-acetoxyamidoximes. Upon catalytic hydrogenation in a mixture of ethyl acetate in ethanol, this led to the acetate salts of 2,6-bis[4-(amidinophenyl)]-imidazo[1,2-*a*]pyridines **136**. In contrast, catalytic hydrogenation of the bis-O-acetoxyamidoxime in glacial acetic acid produced the saturated analogue 2,6-bis[4-(amidinophenyl)]-5,6,7,8-tetrahydro-imidazo[1,2-*a*]pyridine **134**. Finally, O-methylation of the amidoximes resulted in the formation of *N*-methoxyamidines **135**. **(Scheme1.36)**



Scheme1.36

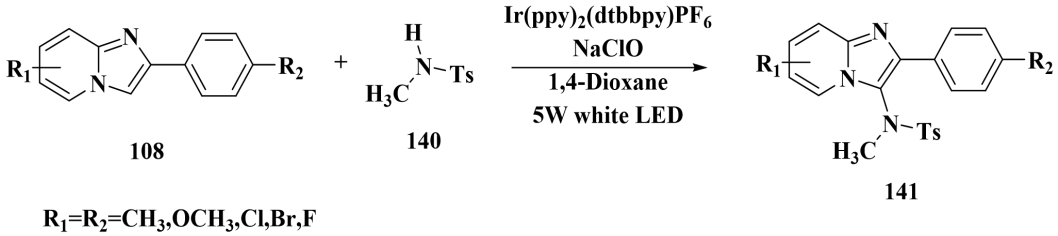
Puthiaraj et al., [66] An efficient and atom-economical one-pot synthesis of imidazo[1,2-*a*]pyridines were achieved through a three-component coupling reaction involving a substituted aldehyde **137**, 2-aminopyridine **60**, and nitromethane **138**. This process was catalyzed by copper terephthalate metal-organic framework (MOF) as a heterogeneous catalyst, resulting in the formation of 3-nitro-2-phenylimidazo[1,2-*a*]pyridine derivatives **139**.A metal–organic framework using copper terephthalate (Cu(BDC) MOF, where BDC stands for (1,4-benzenedicarboxylate) serves as an exceptionally effective heterogeneous catalyst. **(Scheme1.37)**



R_1=$CH_3C_6H_5$,$OCH_3C_6H_5$,FC_6H_5,ClC_6H_5;R_2=H,CH_3,Br,Cl,F

Scheme1.37

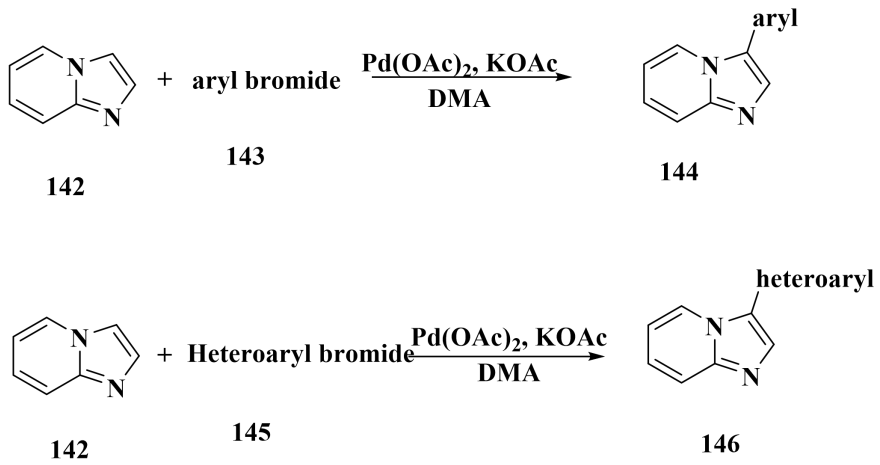
Gao et al., [67] reported the reaction of 2-phenylimidazo[1,2-*a*]pyridine derivatives **108** with *N*-methyl-p-toluenesulfonamide **140**, using Ir(ppy)2(dtbbpy)PF_6 as the photocatalyst and aqueous sodium hypochlorite (NaClO) as the oxidant, produced the C3-sulfonamidated product, *N*,4-dimethyl-*N*-(2-phenylimidazo[1,2-*a*]pyridin-3-yl)benzenesulfonamide derivatives **141**. This reaction was carried out in 1,4-dioxane at room temperature under the irradiation of 5W white LEDs. Additionally, the method proved effective for the sulfonamidation of other imidazoheterocycles. **(Scheme1.38)**



R_1=R_2=CH_3,OCH_3,Cl,Br,F

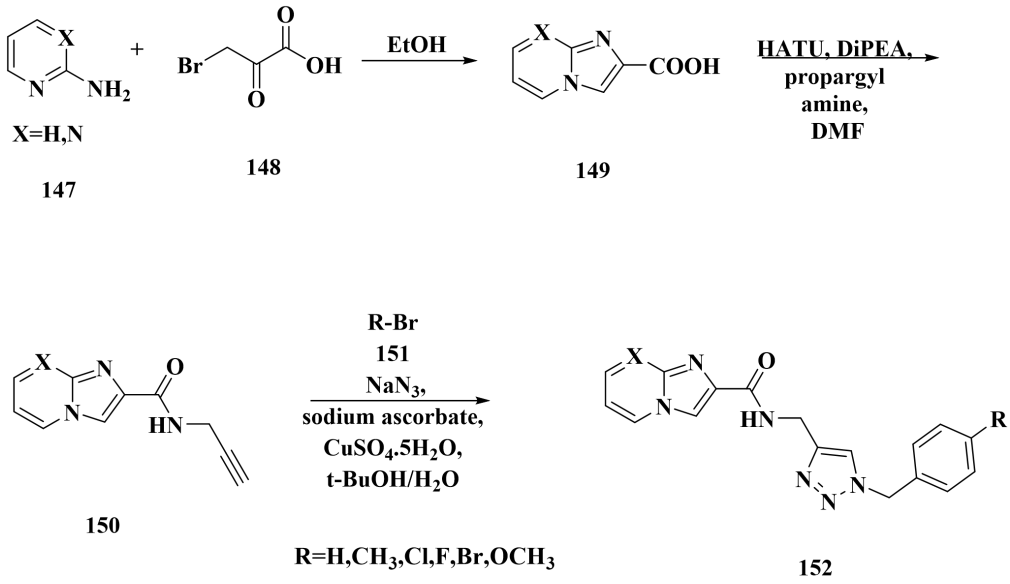
Scheme1.38

Karale et al.,[68] reported a straightforward ligand-free approach has been established for the $Pd(OAc)_2$ catalyzed decarboxylative arylation of imidazo[1,2-*a*]pyridine-3-carboxylic acids **144** and **146** using hetero(aryl) bromides **143** and **145**. This methodology is versatile and applicable to a wide range of (hetero)aryl bromides **143** and **145** as coupling partners. It demonstrates excellent tolerance to both electron-withdrawing and electron-donating groups on imidazo[1,2-*a*]pyridine-3-carboxylic acids **144** and **146** respectively.**(Scheme1.39)**



Scheme1.39

Reddyrajula et al., [69] reported a click synthesis based on 1,3,4oxadiazole which is initiated from Imidazo[1,2-a]pyridine-2-carboxylic acid **149** was synthesized by reacting 2-aminopyridine **147** with bromopyruvic acid **148** in ethanol at 80°C. This compound was then coupled with commercially available prop-2-yn-1-amine using the classical Hexafluorophosphate Azabenzotriazole Tetramethyl Uronium (HATU)-mediated reaction, resulting in the formation of the key intermediate *N*-(prop-2-yn-1-yl)imidazo[1,2-*a*]pyridine-2-carboxamide **149**. The intermediate underwent a click reaction with appropriately substituted benzyl bromides **150**, copper(II) sulfate pentahydrate ($CuSO_4.5H_2O$), and sodium ascorbate, yielding *N*-((1-aryl-1*H*-1,2,3-triazol-4-yl)methyl)imidazo[1,2-*a*]pyridine-2-carboxamide derivatives **152** in good yield. To investigate the importance of the pyridine ring in the antitubercular activity and antifungal activity of the compounds, pyrimidine analogues were synthesized by replacing the pyridine core with a pyrimidine ring, starting with 2-aminopyrimidine.**(Scheme1.40)**



Scheme1.40

Literature analysis underscores the significant pharmacological potential associated with the presence of the imidazo[1,2-*a*]pyridine nucleus, particularly in antimicrobial activities. Imidazo[1,2-*a*]pyridine derivatives serve as promising building blocks for synthesizing a diverse range of chemical compounds known for their wide-ranging biological and pharmacological applications. The field of imidazo[1,2-*a*]pyridine chemistry remains vibrant and presents ongoing challenges for further exploration and utilization. Interestingly, despite extensive research on imidazo[1,2-*a*]pyridines, there remains unexplored potential in both synthetic and biological investigations when combined with molecular moieties of various other biologically significant heterocyclic systems.

1.6 Result and Discussion:

The synthesis of the target molecules followed a systematic procedure outlined in the provided schematic diagram. The first step involved the reaction of 2-amino pyridine (1) with ethyl acetoacetate (2), facilitated by *N*-bromosuccinimide (NBS) in situ, resulting in an excellent yield of compound (3). Subsequently, compound (3) underwent transformation into its corresponding carbohydrazide (4) through a reaction with hydrazine hydrate. Further cyclization of compound (4) was achieved by

utilizing carbon disulfide (CS_2) in the presence of a basic medium, leading to the formation of a five-membered ring with heteroatoms oxygen and nitrogen, resulting in compound (5). The use of CS_2 as a cyclizing reagent proved highly effective, yielding the desired product efficiently. The next synthetic step involved the reaction of compound (5) with derivatives of 2-chloro-*N*-phenylacetamide in the presence of a basic medium, ultimately yielding the novel target compound (6a-6o). Notably, the overall synthetic pathway demonstrated efficient and high-yielding transformations at each step. All synthesized compounds were subjected to thorough spectral analysis to confirm their structural integrity and composition. The successful completion of this synthetic scheme underscores the effectiveness of the outlined methodology in producing the desired target molecule, highlighting its potential applicability in further studies or applications.

A novel series of 2-((5-(2-methylimidazo[1,2-a]pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)-N-phenylacetamide derivatives were synthesized and characterized using a combination of physical constants and spectral techniques including IR, ^{1}H NMR, ^{13}C NMR, MS, and elemental analysis. All synthesized compounds were isolated as oyster white solids with good to excellent yields (58–81%) and showed sharp melting points ranging from 206°C to 246°C, indicating high purity.

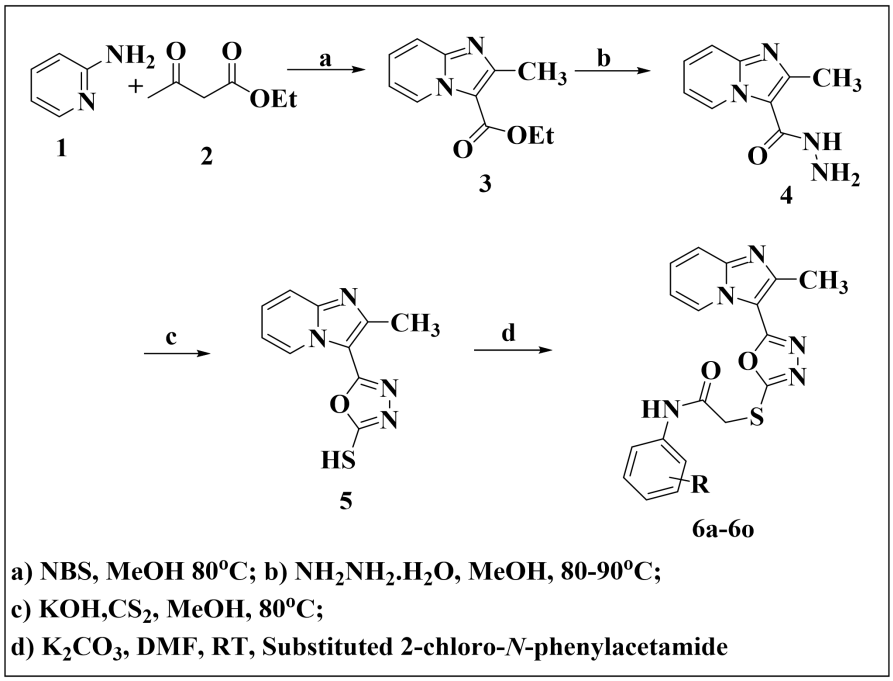
Infrared spectra confirmed the presence of essential functional groups. Broad absorptions near 3499–3352 cm^{-1} were attributed to NH stretching vibrations, while strong bands between 1728–1689 cm^{-1} corresponded to amide C=O stretching. Peaks between 1600–1660 cm^{-1} were assigned to C=N or aromatic C=C bonds, and C–H stretching (both aromatic and aliphatic) was evident near 3100–2980 cm^{-1}.

^{1}H NMR spectra (400 MHz, DMSO-d_6) showed characteristic singlets for methyl groups (~2.37–2.60 ppm) and methylene linkers (~4.20–4.35 ppm). Multiple signals between 7.0–7.7 ppm corresponded to aromatic and heteroaromatic protons, and downfield singlets/doublets around 9.1–10.5 ppm were assigned to NH and imidazole protons. These patterns confirmed the substitution and connectivity of the functional groups.

^{13}C NMR spectra (101 MHz, DMSO-d^6) further supported the structural identity, displaying expected signals for methyl, methylene, aromatic, heteroaromatic, and carbonyl carbons within their respective ranges. Mass spectra showed molecular ion

peaks consistent with their respective molecular weights, confirming molecular composition. Additionally, elemental analysis data were in close agreement with theoretical values, supporting compound purity.

1.7 Reaction Scheme:



1.8 Physical Characteristics:

Table 1.1: Physical characteristics of the synthesized compounds.

Entry	Compound code	R	Molecular weight	Molecular formula	M.P. in °C	Yield (%)
1	6a	4-CH_3	379.11	$C_{18}H_{17}O_2N_5S$	213-215	78
2	6b	4-F	383.09	$C_{18}H_{14}O_2N_5SF$	206-208	62
3	6c	4-Cl	399.06	$C_{18}H_{14}O_2N_5SCl$	228-230	60
4	6d	4-Br	443.01	$C_{18}H_{14}O_2N_5SBr$	244-246	58
5	6e	H	365.09	$C_{18}H_{15}O_2N_5S$	207-209	81

6	6f	4-OCH_3	395.44	$C_{20}H_{19}O_3N_5S$	219-221	42
7	6g	2,4-CH_3	393.13	$C_{20}H_{19}O_2N_5S$	210-212	61
8	6h	3-Cl	399.06	$C_{18}H_{14}O_2N_5SCl$	224-226	41
9	6i	2-OCH_3	395.44	$C_{20}H_{19}O_3N_5S$	201-203	40
10	6j	2-CH_3	379.11	$C_{18}H_{17}O_2N_5S$	199-201	46
11	6k	3-CH_3	379.11	$C_{18}H_{17}O_2N_5S$	202-204	49
12	6l	3-OCH_3	395.44	$C_{20}H_{19}O_3N_5S$	226-228	42
13	6m	3-Cl,4-F	417.05	$C_{18}H_{13}O_2$ $ClFN_5S$	222-224	43
14	6n	2,4-F	401.08	$C_{18}H_{13}O_2F_2N_5S$	186-188	51
15	6o	3,4-Cl	433.02	$C_{18}H_{13}O_2Cl_2N_5S$	231-233	53

All compounds are amorphous Oyster white solid.

1.9 Conclusion:

In this study, a series of 2-((5-(2-methylimidazo[1,2-a]pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)-N-phenylacetamide derivatives were successfully synthesized using an efficient and reliable multistep synthetic route. Each transformation proceeded with good to excellent yields, highlighting the robustness and versatility of the methodology employed. Comprehensive spectral analysis, including ^{1}H NMR, ^{13}C NMR, and mass spectrometry, confirmed the structural identities and purity of the synthesized compounds.

The incorporation of the oxadiazole ring into the imidazo[1,2-a]pyridine framework introduced structural diversity and opened new avenues for potential bioactivity. The ability to easily modify functional groups further enhances the relevance of these molecules for medicinal chemistry.

Overall, the synthesis and detailed characterization of these novel compounds underscore their potential as promising candidates for future drug development.

Further exploration of their biological properties is anticipated to reveal new therapeutic possibilities.

1.10 Experimental Section:

1.10.1 Materials and Methods:

In our experiment, we utilized reagents sourced from reputable suppliers such as Sigma-Aldrich and Spectrochem chemicals, ensuring the reliability and quality of our materials. These reagents were employed directly without purification, maintaining the integrity of our experimental process while saving time and resources. To monitor the progress of our reactions, we employed thin-layer chromatography (TLC) using silica gel-G plates (G60 F254, E-Merck Co.). Visualization under UV light allowed for real-time observation of reaction progress, facilitating efficient optimization of reaction conditions. Melting points of synthesized compounds were determined in open capillaries, providing initial insights into their purity and identity. While these melting points remained uncorrected, they served as valuable indicators of compound characteristics. Infrared (IR) spectra were recorded using an FT-IR-8400 instrument with potassium bromide (KBr) as the matrix, enabling the identification of functional groups present in the synthesized compounds based on their absorption patterns. Nuclear magnetic resonance (NMR) spectroscopy, including both ^{1}H and ^{13}C NMR, was performed on a Bruker Avance 400MHz spectrometer and 101 MHz spectrometer respectively. Chemical shifts were reported in δ ppm relative to the solvent DMSO-d^6, with tetramethylsilane (TMS) serving as the internal reference. This provided detailed structural information essential for compound characterization. mass spectra were obtained using ultraperformance liquid chromatography coupled with mass spectrometry (LC/MS), employing electrospray ionization in positive ion mode. Covering a mass range from 100 to 1500 Da with a cone voltage set at 30 V, LC/MS analysis facilitated the determination of molecular weights and fragmentation patterns of the synthesized compounds, enhancing our understanding of their chemical composition.

1.10.2 General Procedures:

General procedure for ethyl 2-methylimidazo[1,2-*a*]pyridine-3-carboxylate(3):

Ethyl acetoacetate (10 mmol) was dissolved in 40 mL of methanol and cooled to 0-5°C with stirring for 10-15 minutes. *N*-Bromo succinimide (NBS) (10 mmol) was added portion-wise and the reaction mixture was stirred at the same temperature for 15-20 minutes. Subsequently, the mixture was stirred at room temperature for 45-50 minutes until it became clear. 2-Aminopyridine (10 mmol) was then added portion-wise, and the reaction mixture was refluxed for 2-3 hours at 80°C. The progress of the reaction was monitored via TLC until the starting material was fully consumed. Upon completion, the solvent was evaporated under reduced pressure, and the residue was poured onto crushed ice. The resulting solid was recrystallized using methanol to afford the desired product.[70]

General procedure for 2-methylimidazo-[1,2-*a*]pyridine-3-carbohydrazide(4):

Ethyl 2-methylimidazo[1,2-*a*]pyridine-3-carboxylate (10 mmol) was dissolved in 10 mL of methanol. Hydrazine hydrate (80%) (10 mmol) was added dropwise, and the reaction mixture was refluxed for 2-3 hours at 80°C. The progress of the reaction was monitored via TLC until the starting material was fully consumed. After completion, the reaction mixture was cooled to room temperature and poured into ice-cold water. The resulting solid was collected and recrystallized using ethyl acetate to obtain the product.[71]

General procedure for 5-(2-methylimidazo-[1,2-*a*]pyridine-3-yl)-1,3,4-oxadiazole-2-thiol(5):

A mixture of 2-methylimidazo-[1,2-*a*]pyridine-3-carbohydrazide (10 mmol) and potassium hydroxide (KOH) (10 mmol) in 20 mL of methanol was stirred at 0°C until the solution became clear. Carbon disulfide (CS_2) (10 mmol) was then added dropwise. After the addition of CS_2, the reaction mixture was refluxed at 80°C for 6-7 hours. The progress of the reaction was monitored via TLC until the starting material was fully consumed. Upon completion, the reaction mixture was cooled to room temperature and poured into ice-cold water. The resulting mixture was then acidified with 1N aqueous hydrochloric acid (HCl). The solid product was collected by

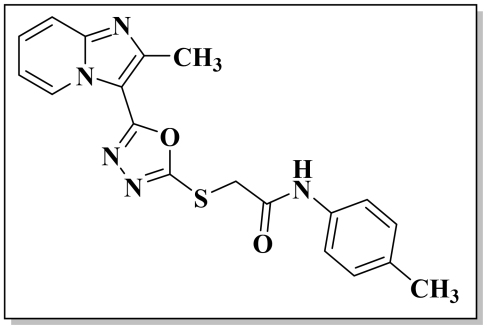
filtration, washed with water, and dried at room temperature overnight. It is noted that the compound exists in thione-thiol tautomeric forms, but our investigation revealed a specific tautomeric form in this case. [72] The material obtained was utilized in the subsequent step without undergoing additional purification.

General procedure for 2-((5-2-methylimidazo[1,2-*a*]pyridine-3-yl)-1,3,4-oxadiazol-2-yl)thio)-*N*-phenylacetamide(6a-6o):

A mixture of 5-(2-methylimidazo[1,2-*a*]pyridine-3-yl)-1,3,4-oxadiazole-2-thiol (**5**, 1 gm, 0.004 mol, 1 eq) and potassium carbonate (K_2CO_3) (1.19 gm, 0.004 mol, 2 eq) in 10 mL of dimethylformamide (DMF) was stirred for 15-30 minutes until a color change was observed. Subsequently, 2-chloro-*N*-phenylacetamide derivative (0.75 gm, 0.004 mol, 1.1 eq) appears portion-wise, When the mixture of reactions was agitated for 2-3 hours at ambient temperature. The progress of the reaction was monitored via TLC until completion. Upon completion, Ice was used to contain the reaction mixture, resulting in a hazy solution. A few drops of aqueous hydrochloric acid (HCl) were mixed into the solution. The substantial goods were gathered by vacuum filtration and dried overnight in a refrigerator. The newly formed The compounds were refined by means of recrystallization using either methanol or ethanol as solvents. The reactions proceeded smoothly, yielding goods with yields that range from 40% to 81%. (6a-6o)

1.10.3 Spectral Characterization:

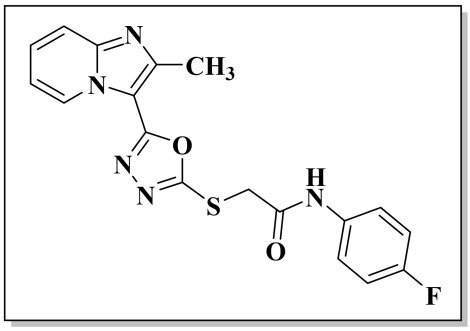
2-((5-(2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)-*N*-(p-tolyl)acetamide(6a):



Oyster white; yield:78%; M.P.:213-215°C; IR(KBr,υ_{max},cm^{1}): 3309.96, 3140.22, 2974.33, 1716.70, 1662.69, 1600.97, 1504.53, 1446.66, 860.28; ^{1}H NMR (400 MHz,

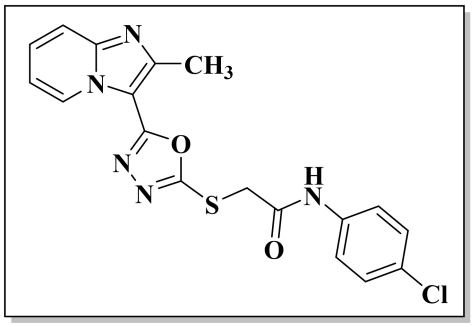
DMSO-d^6) δ 2.37 (s, 3H), 2.62 (s, 3H), 4.20 (s, 2H), 7.02 (t, J = 6.9 Hz, 1H), 7.25 (d, J = 7.9 Hz, 2H), 7.32-7.41 (m, 4H), 7.60 (d, J = 8.9 Hz, 1H), 8.90 (d, J = 7.0 Hz, 1H), 10.31 (s, 1H); ^{13}C NMR (101 MHz, DMSO-d^6) δ 16.33, 21.23, 33.34, 49.08, 113.57, 115.39, 116.68, 127.24, 127.38, 128.44, 130.06, 132.80, 138.72, 145.68, 146.63, 159.23, 171.93; MS(*m/z*):380.3 (m^+); Anal. Calcd. For $C_{19}H_{17}N_5O_2S$: C, 60.14; H, 4.52; N, 18.46; found: C, 60.12; H, 4.51; N, 18.45.

_N_-(4-fluorophenyl)-2-((5-(2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)acetamide(6b):



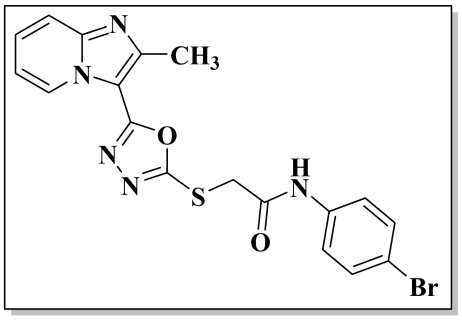
Oyster white; yield:62%; M.P.:206-208°C; IR(KBr,υ_{max},cm^{-1}): 3498.99, 3147.93, 3070.78, 1728.28, 1658.84, 1612.54, 1573.97, 1481.38, 837.13, ^{1}H NMR (400 MHz, DMSO-d^6) δ 2.60 (s, 3H), 4.35 (s, 2H), 7.19 (dt, J = 17.9, 7.9 Hz, 4H), 7.49-7.57 (m, 2H), 7.58-7.65 (m, 2H), 7.72 (d, J = 8.9 Hz, 1H), 9.17 (d, J = 6.8 Hz, 1H), 10.54 (s, 1H); ^{13}C NMR (101 MHz, DMSO-d^6) δ 15.64, 37.25, 107.13, 114.79, 115.82, 116.04, 117.01, 121.37, 127.68, 128.09, 135.57, 146.58, 148.31, 157.45, 159.36, 159.84, 161.68, 165.29; MS(*m/z*):384.3(m^+); Anal. Calcd. For $C_{18}H_{14}FN_5O_2S$: C, 56.39; H, 3.68; N, 18.27 ; found: C, 56.36; H, 3.66; N, 18.24.

_N_-(4-chlorophenyl)-2-((5-(2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)acetamide(6c):



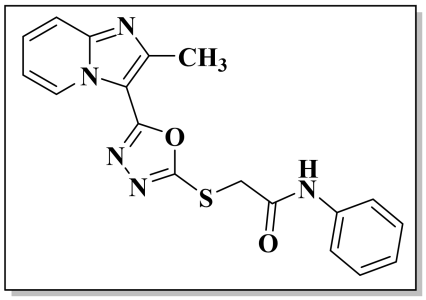
Oyster white; Yield:60%; M.P.:228-230°C; IR(KBr,υ_{max},cm^{1}): 3456.55, 3117.07, 2931.90, 1894.16, 1689.70, 1608.69, 1546.96, 1481.38, 829.42; ^{1}H NMR (400 MHz, DMSO-*d*^{6}) δ 2.59 (s, 3H), 4.35 (s, 2H), 7.17 – 7.25 (m, 1H), 7.38 (d, *J* = 8.8 Hz, 2H), 7.48 – 7.56 (m, 1H), 7.61 (d, *J* = 8.9 Hz, 2H), 7.71 (d, *J* = 9.0 Hz, 1H), 9.17 (d, *J* = 6.9 Hz, 1H), 10.58 (s, 1H); ^{13}C NMR (101 MHz, DMSO-*d*^{6}) δ 15.18, 36.86, 106.67, 114.34, 116.56, 120.71, 127.22, 127.25, 127.64, 128.81, 137.64, 146.13, 147.85, 158.91, 161.19, 165.09; MS(*m/z*):400.3(m^{+}); Anal. Calcd. For $C_{18}H_{14}ClN_5O_2S$: C, 54.07; H, 3.53; N, 17.52; found: C, 54.04; H, 3.51; N, 17.50.

_N_-(4-bromophenyl)-2-((5-(2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)acetamide(6d):



Oyster white; Yield:58%; M.P.:244-246°C; IR(KBr,υ_{max},cm^{-1}): 3498.99, 3109.35, 2935.76, 1890.30, 1689.70, 1604.83, 1543.10, 1485.24,829.42, ^{1}H NMR (400 MHz, DMSO-*d*^{6}) δ 2.58 (s, 3H), 4.35 (s, 2H), 7.19 (t, *J* = 6.7, 6.7 Hz, 1H), 7.48 – 7.58 (m, 5H), 7.70 (d, *J* = 8.9 Hz, 1H), 9.14 (d, *J* = 6.8 Hz, 1H), 10.58 (s, 1H); ^{13}C NMR (101 MHz, DMSO-*d*$_{6}$) δ 15.63, 37.37, 107.10, 114.76, 115.76, 116.99, 121.53, 127.65, 128.06, 132.16, 138.51, 146.57, 148.29, 159.34, 161.63, 165.56; MS(*m/z*) :446.3(m^{+}); Anal. Calcd. For $C_{18}H_{14}BrN_5O_2S$: C, 48.66; H, 3.18; N, 15.76; found: C, 48.64; H, 3.16; N, 15.75.

2-((5-(2-methylimidazo[1,2-*a*]pyridin-3-yl)-1,3,4-oxadiazol-2-yl)thio)-*N*-phenylacetamide(6e):



Oyster white; yield:81%; M.P.:207-209°C; IR(KBr,υ_{max},cm^{-1}): 3352.39, 3136.36, 2982.05, 1728.28, 1658.84, 1604.83, 1500.67, 1446.66, 856.42; MS(*m/z*): 366.3(M^+); Anal. Calcd. For $C_{18}H_{15}N_5O_2S$: C, 59.17; H, 4.14; N, 19.17; found: : C, 59.15; H, 4.12; N, 19.15.

1.10.4 Representative Spectra:

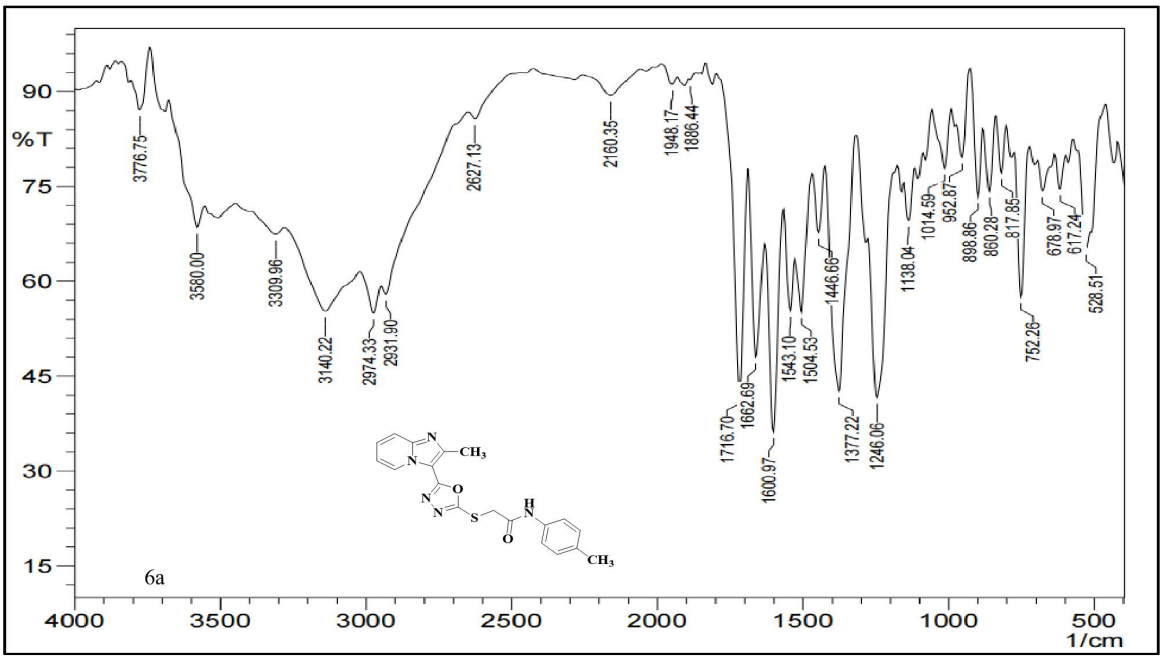


Fig.1.5: Representative IR spectrum of compound 6a

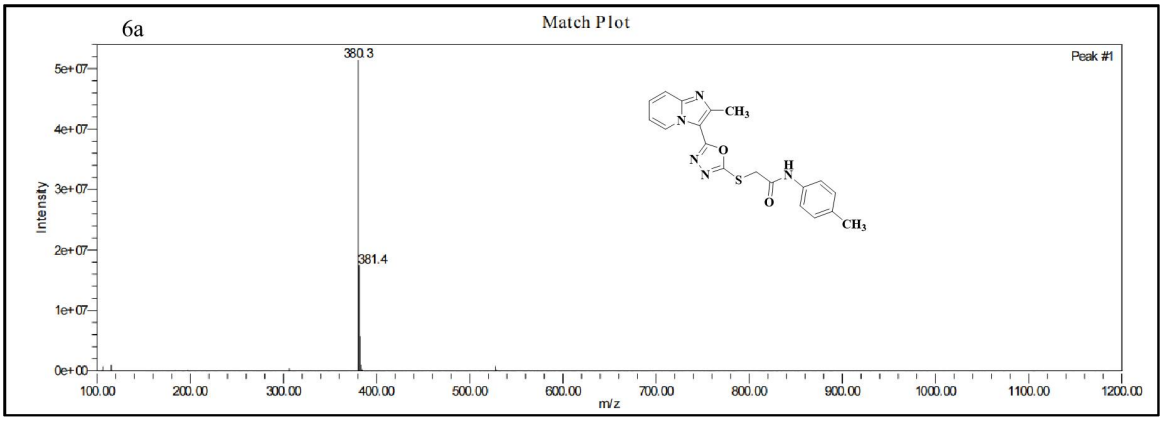


Fig.1.6: Representative mass spectrum of compound 6a

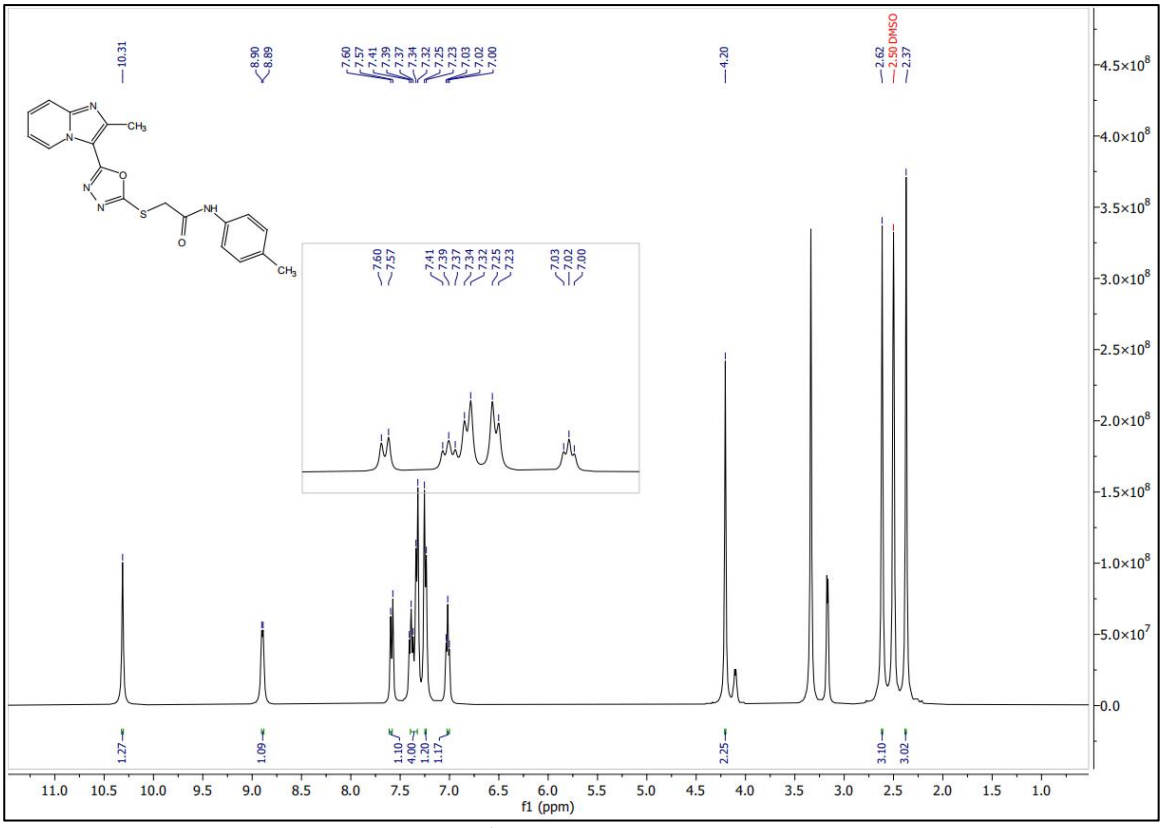


Fig.1.7: Representative ^{1}H NMR spectrum of compound 6a

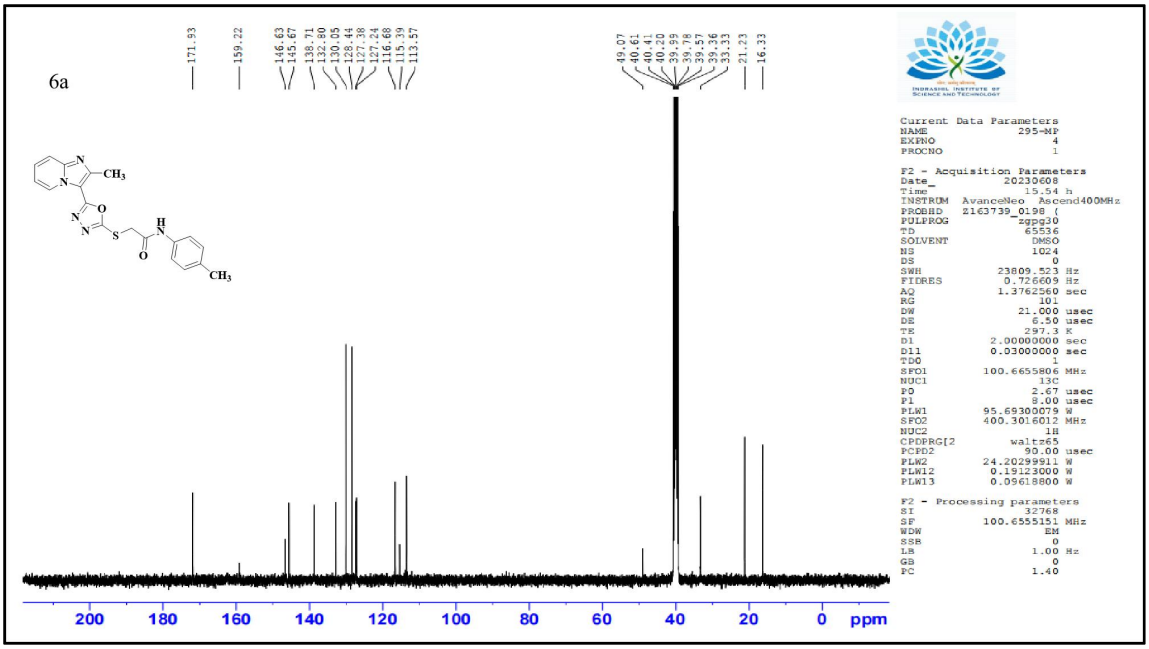


Fig.1.8: Representative ^{13}C CMR spectrum of compound 6a

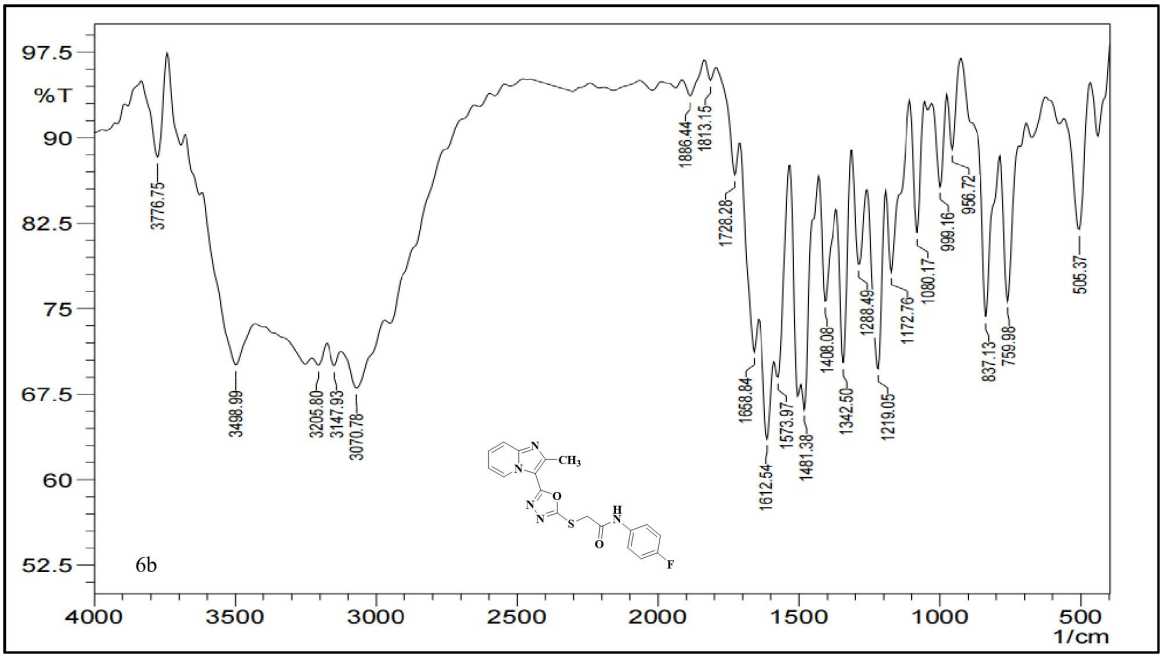


Fig.1.9: Representative IR spectrum of compound 6b

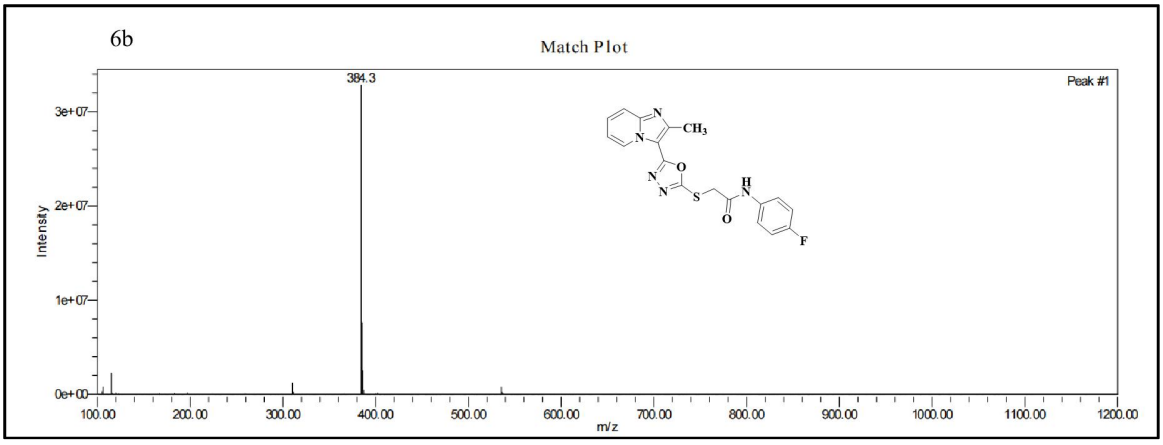


Fig.1.10: Representative mass spectrum of compound 6b

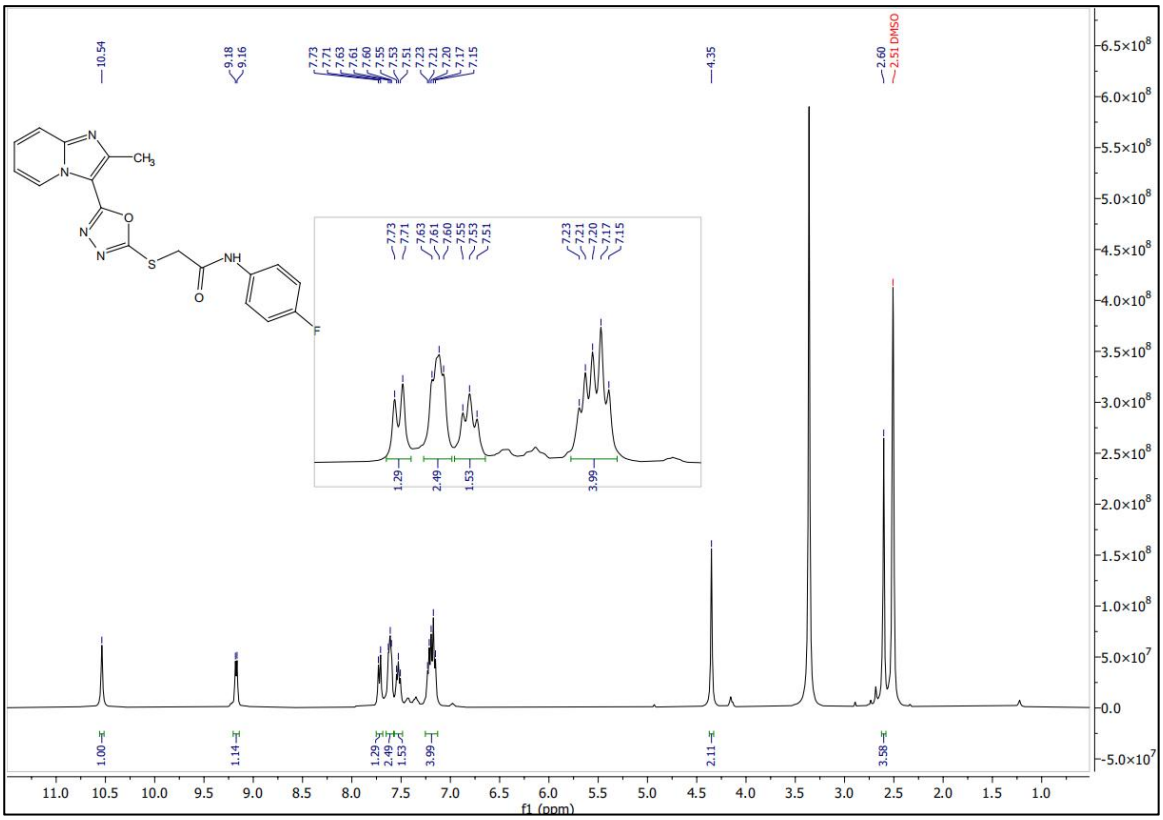


Fig.1.11: Representative ^{1}H NMR spectrum of compound 6b

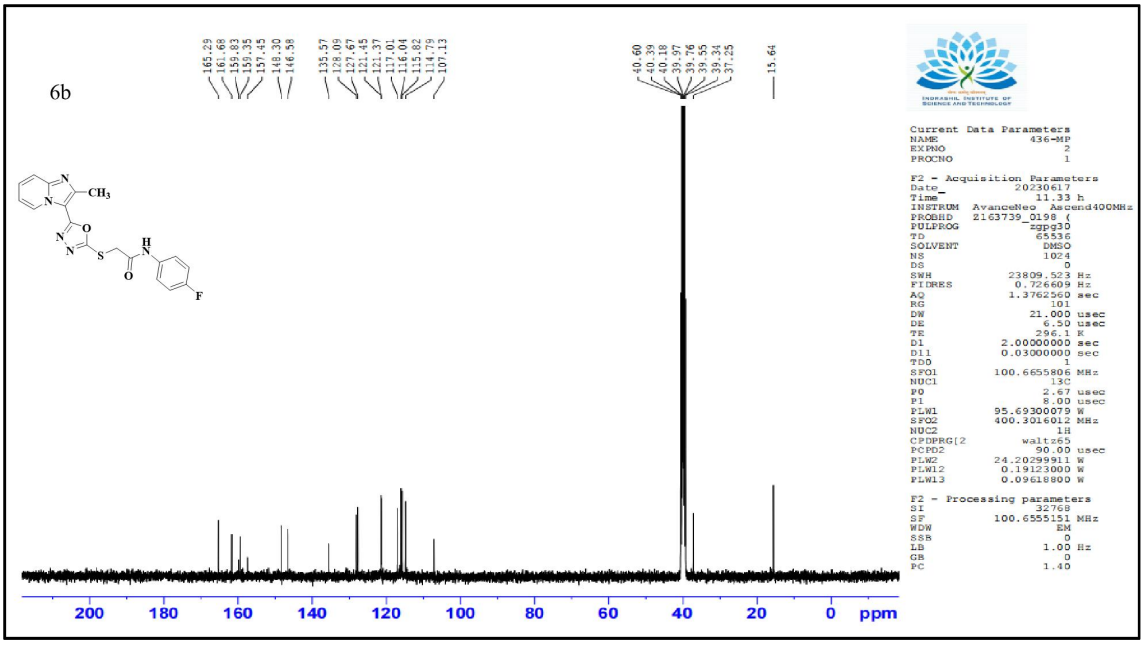


Fig.1.12: Representative ^{13}C CMR spectrum of compound 6b

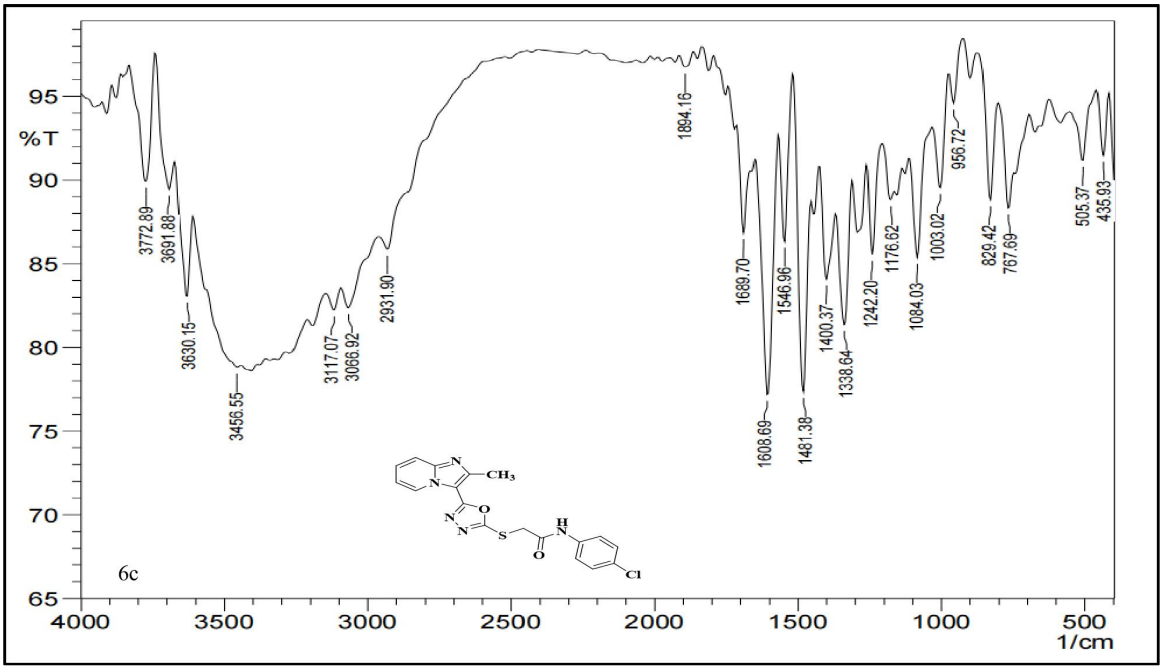


Fig.1.13: Representative IR spectrum of compound 6c

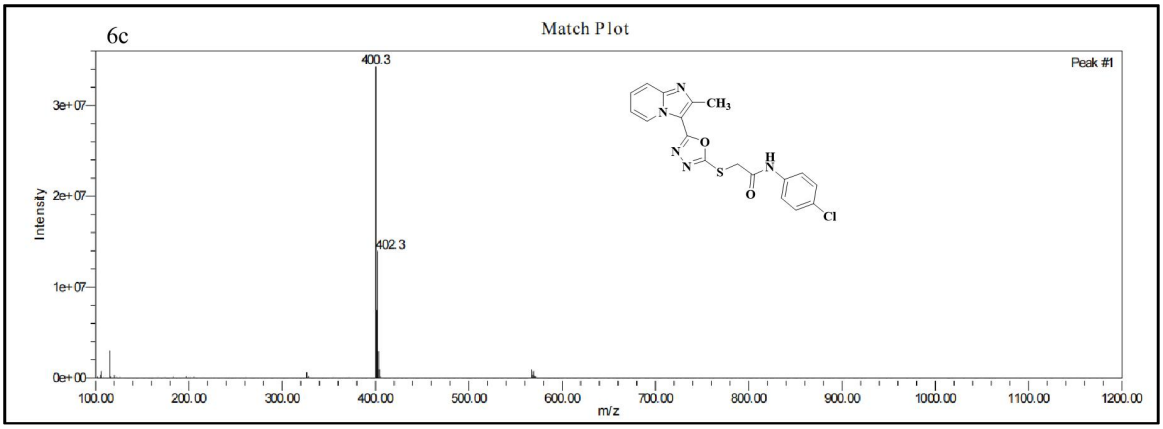


Fig.1.14: Representative mass spectrum of compound 6c

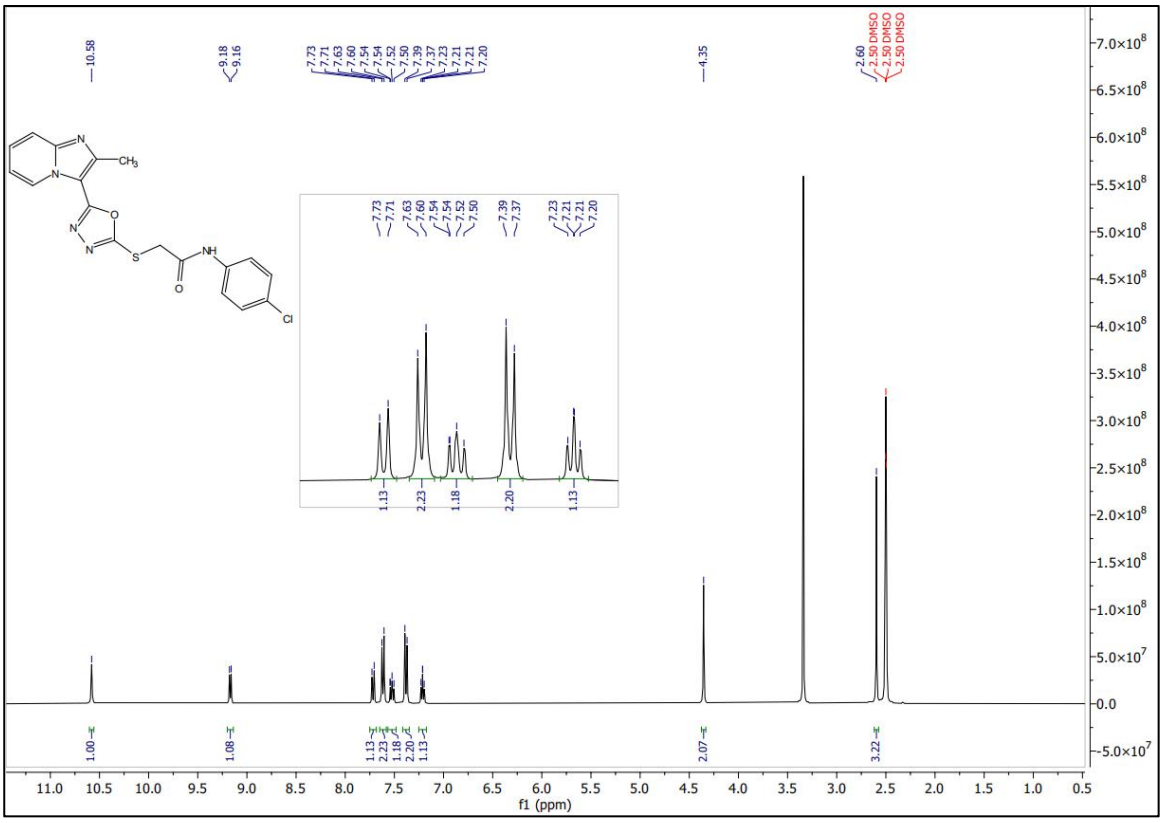


Fig.1.15: Representative ^{1}H NMR spectrum of compound 6c

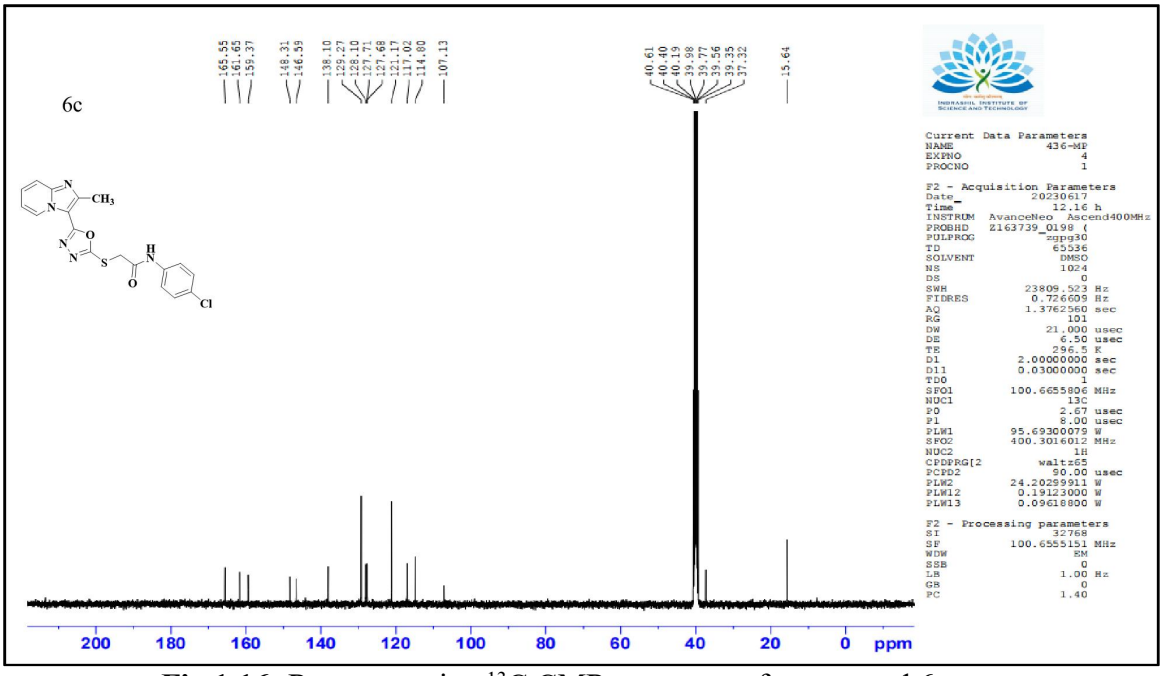


Fig.1.16: Representative ^{13}C CMR spectrum of compound 6c

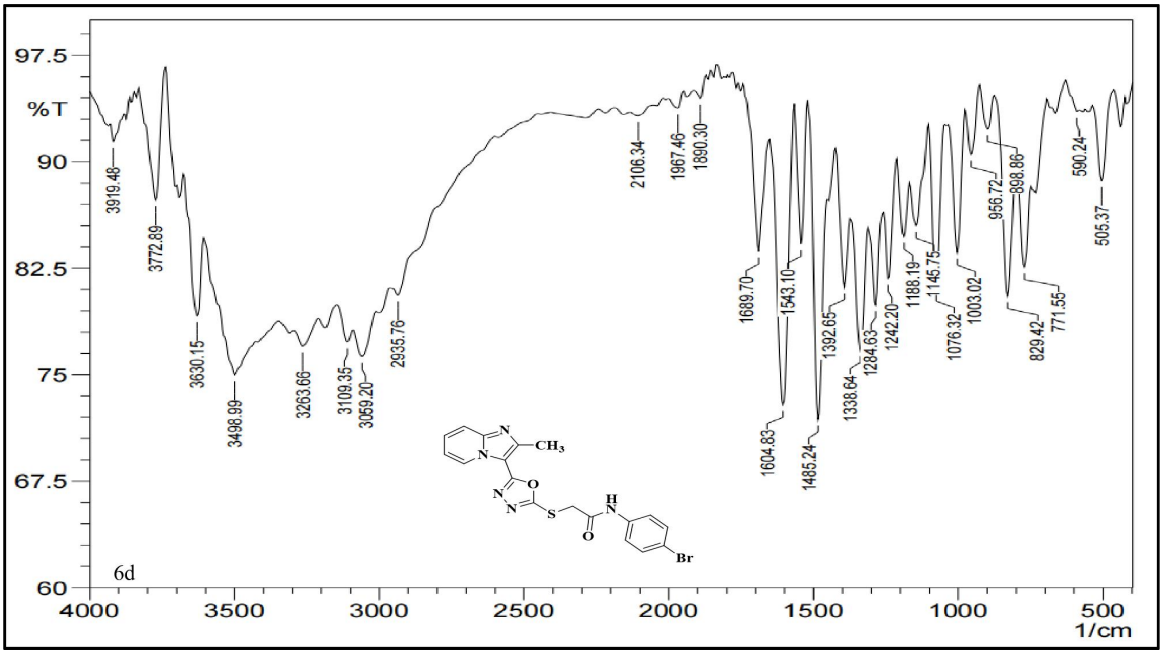


Fig.1.17: Representative IR spectrum of compound 6d

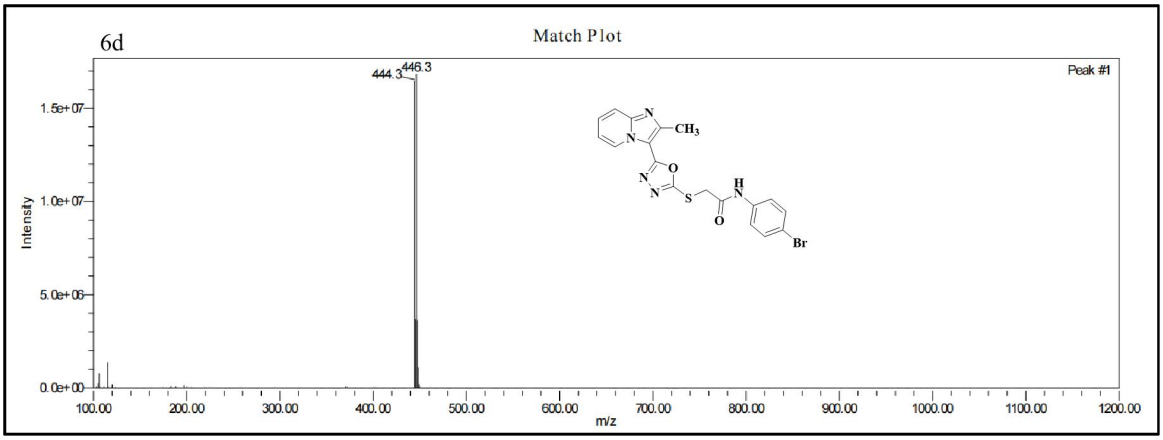


Fig.1.18: Representative mass spectrum of compound 6d

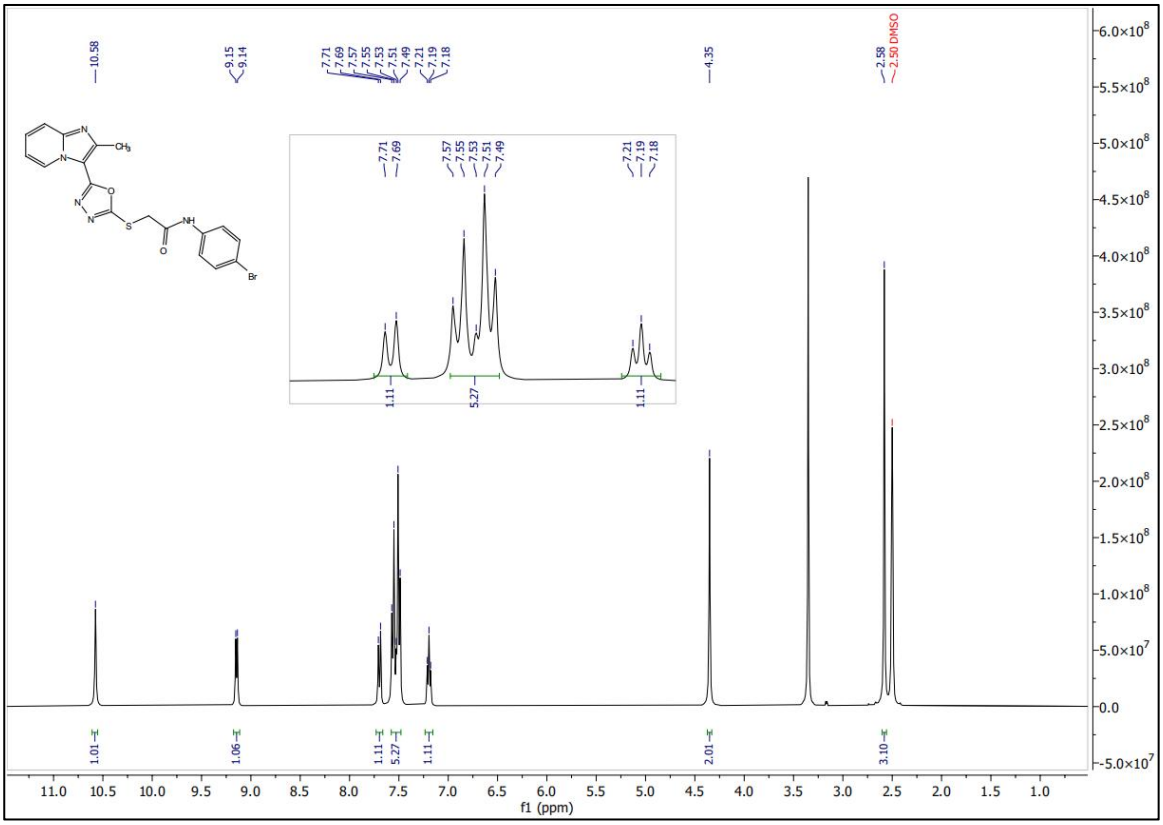


Fig.1.19: Representative ^{1}H NMR spectrum of compound 6d

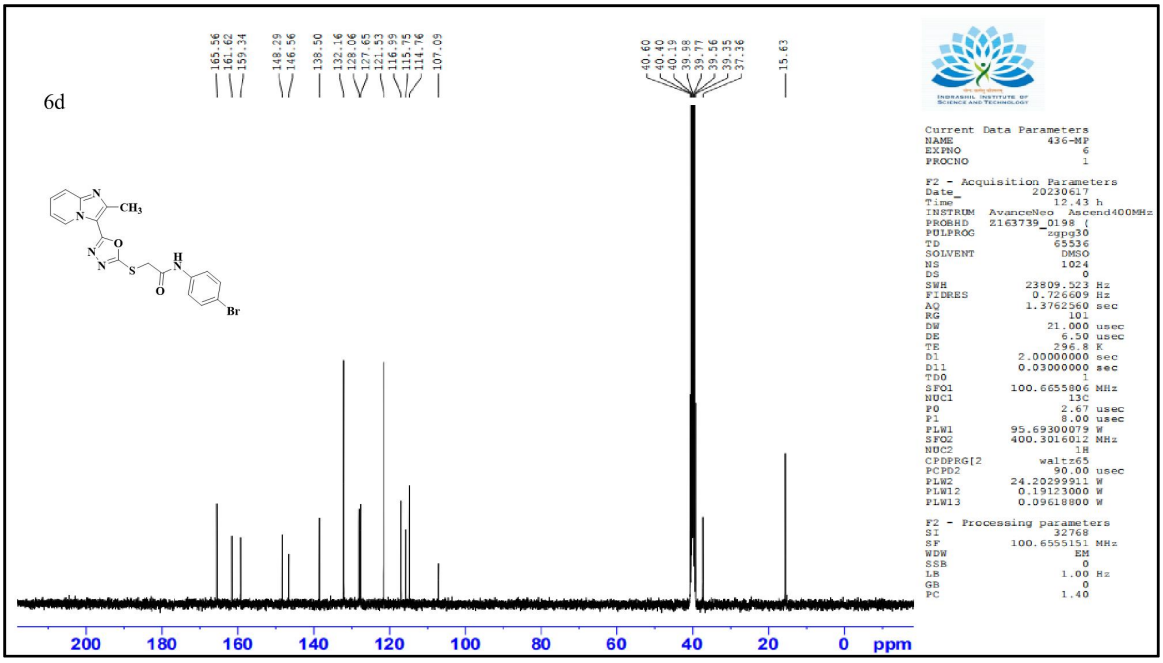


Fig.1.20: Representative ^{13}C CMR spectrum of compound 6d

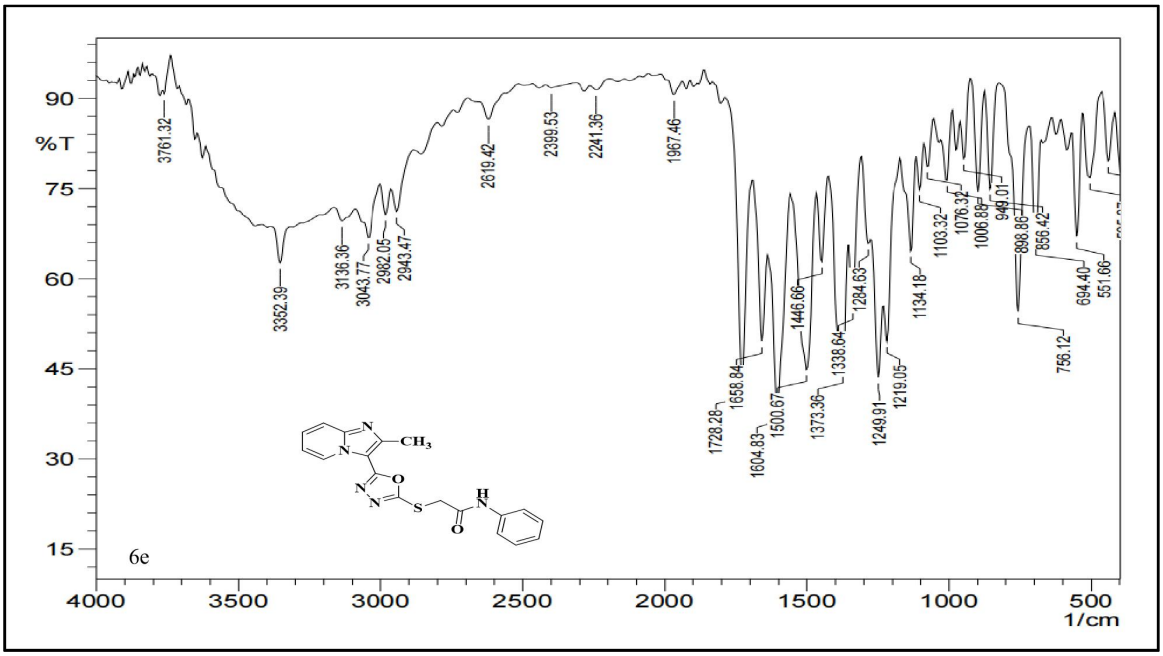
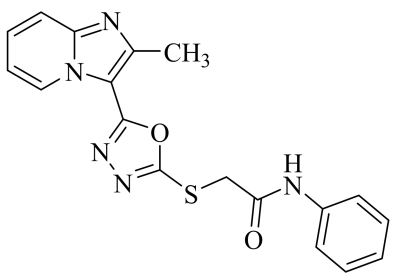


Fig.1.21: Representative IR spectrum of compound 6e



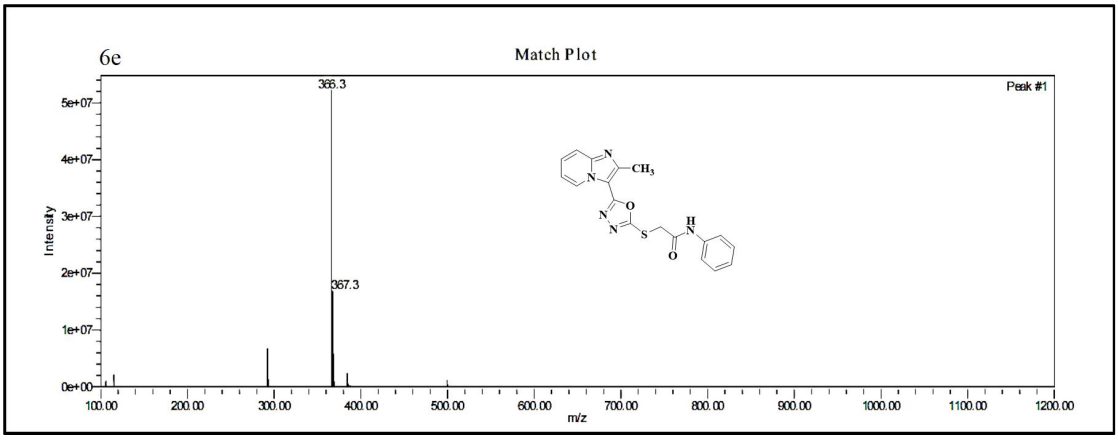


Fig.1.22: Representative mass spectrum of compound 6e