IJARSCT
ISSN: 2581-9429
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Volume 5, Issue 10, March 2025
Impact Factor: 7.67

A Comprehensive Study on Synthesis of Pyridine Using Novel Techniques

Zahida Adam Rawoot and Pankaj Gaikwad
D. G. Tatkare Mahavidyalaya, Mangaon, Raigad, Maharashtra

Abstract: *Pyridine is a basic Heterocyclic organic compound. It is structurally related to benzene, with one methene group (=CH-) replaced by nitrogen atom (=N-). It is highly flammable, weakly alkaline, water miscible liquid with a distinctive. This research focuses on developing an environmentally friendly and sustainable approach to the synthesis of pyridine using green chemistry principles. Pyridine derivatives are an important class of heterocyclic compounds with diverse applications in pharmaceuticals, agrochemicals, and materials science. This study explores the synthesis, characterization, and biological evaluation of new pyridine derivatives, highlighting their structure-activity relationships (SAR) and potential applications in drug discovery. The synthesis of heterocyclic compounds under various conditions like solvent-free, reactants immobilized on solid Support, microwave irradiation condition a very important role with plenty of rational therapeutic activities such as antiulcer, antihypertensive, analgesic, Anti-inflammatory, anti-viral, antifungal, anticancer, and antihistaminic. Advanced spectroscopic techniques were employed for structural confirmation, and in vitro assays demonstrated promising pharmacological activities, suggesting further exploration for therapeutic development. Traditional synthetic approaches often suffer from limitations such as harsh reaction conditions, low yields, and environmental concerns. This study presents a novel technique for the synthesis of pyridine derivatives, utilizing a more sustainable and efficient catalytic system. The proposed method employs eco-friendly reagents and optimized reaction conditions to enhance selectivity and yield while minimizing by-products. Advanced spectroscopic techniques (NMR, FTIR, and MS) confirm the structural integrity of the synthesized compounds. The novel approach offers a promising alternative to conventional methods, providing a more viable and scalable route for pyridine derivative synthesis in both academic and industrial applications.*

Keywords: Pyridine, Eco- friendly, solvent free, green synthesis, microwave assist catalyst

I. INTRODUCTION

Pyridine, a six-membered heterocyclic aromatic compound containing one nitrogen atom, is an essential structure in organic chemistry due to its presence in various natural products, pharmaceuticals, agrochemicals, and industrial compounds. Pyridine derivatives play a crucial role in a wide range of applications, including medicinal chemistry, material science, and catalysis [1]. These derivatives are key building blocks in the synthesis of a variety of bioactive molecules, serving as precursors for drugs, agrochemicals, and ligands for metal catalysts. Traditional methods of synthesizing pyridine and its derivatives include the Bönnemann–Pinner synthesis, Hantzsch pyridine synthesis, and Skraup synthesis, which typically rely on classic organic reactions such as cyclization of appropriate precursors. However, these methods often face challenges such as low yields, limited selectivity, and the use of hazardous reagents [2]. As a result, there has been a continuous effort to explore novel techniques for pyridine synthesis, aiming for greener, more efficient, and scalable processes. The versatility of pyridine and its derivatives arises from the ability to modify its structure and functional groups, making it highly adaptable to diverse chemical transformations [3]. Pyridine-based compounds exhibit a broad spectrum of biological activities, such as antimicrobial, anticancer, anti-inflammatory, and antidiabetic properties. As a result, many pyridine derivatives are incorporated into pharmaceutical formulations and treatments for various diseases [4]. In materials science, pyridine derivatives are utilized in the design and development of new materials, including polymers, liquid crystals, and conductive organic materials, which have applications in electronic devices, sensors, and energy storage. Pyridine is also crucial in catalysis [5], where it is often

DOI: 10.48175/IJARSCT-24784

used as a ligand in coordination complexes or in organocatalysis, enhancing the efficiency and selectivity of chemical reactions, especially in asymmetric synthesis. Given its significance, the synthesis of pyridine and its derivatives has been a subject of intense research, focusing on improving reaction efficiencies, selectivity, and sustainability [6]. Advances in catalytic processes, microwave-assisted synthesis, and green chemistry have led to the development of novel and efficient methodologies for synthesizing pyridine derivatives, making it easier to access these important compounds for a variety of industrial and scientific applications [7].

1.1. Some Methods use For Synthesis of Pyridine:-

Recent advancements in the field have introduced a variety of innovative approaches for the synthesis of pyridine derivatives [8].

Some of the most notable methods include:

1.1.1. Catalytic Approaches: The use of transition metal catalysts (e.g., palladium, copper, or nickel) in the synthesis of pyridine derivatives has gained significant attention. These catalysts can promote highly selective C–C and C–N bond formation, often under mild reaction conditions. Metal-catalyzed cross-coupling reactions, such as Suzuki–Miyaura and Buchwald–Hartwig reactions, are utilized for the synthesis of functionalized pyridines with excellent yields and regioselectivity [9].

1.1.2. Microwave-Assisted Synthesis: Microwave-assisted organic synthesis has revolutionized the field by providing faster and more efficient reaction times, often yielding higher purity products. This technique has been applied to both the synthesis of pyridine rings and the functionalization of pyridine derivatives. The rapid heating and uniform distribution of energy in microwave reactions enhance reaction rates and reduce by-products [10].

1.1.3. Green Chemistry Approaches: With a growing emphasis on sustainability, the development of eco-friendly methods for pyridine synthesis is becoming increasingly important. Solvent-free reactions, aqueous-phase reactions, and the use of renewable resources are some strategies being explored to minimize the environmental impact of pyridine production. Additionally, the use of biocatalysts and enzyme-mediated reactions for the synthesis of pyridine derivatives offers a promising green alternative [11].

1.1.4. Electrochemical Synthesis: Electrochemistry has emerged as a cutting-edge method for the synthesis of pyridine derivatives, where electrochemical processes enable selective transformations without the need for traditional chemical reagents. This technique is particularly advantageous for sustainable chemistry, as it can reduce waste, decrease the need for harsh conditions, and offer high selectivity for certain transformations [12].

1.1.5. Photochemistry and Photoredox Catalysis: Photochemical methods, leveraging light energy, offer unique advantages in the selective synthesis of pyridine derivatives. Photoredox catalysis, in particular, has been used to initiate novel reactions that are difficult to achieve under traditional thermal conditions, leading to the formation of pyridine-based compounds with high efficiency and functional group tolerance [13].

The development of these novel techniques in pyridine synthesis represents an exciting frontier in organic chemistry, where efficiency, sustainability, and precision are key. By overcoming the limitations of conventional methods, these advanced strategies allow the creation of complex and diverse pyridine derivatives with broad applications in pharmaceuticals, materials science, and beyond [14].

II. LITERATURE REVIEW

2.1. Pyridines

2.1. Preparation of Pyridines

Asokan et al. has developed a practical synthesis of 4-chloropyridines 1 from carbonyl compounds having two enolizable carbons adjacent to the carbonyl such as compound 2 <04T5069>. Ketone 2 was subjected to Vilsmeier-Haack reaction conditions leading to the formation of conjugated iminium salts 3, which upon reacting with ammonium acetate cyclized to form the 4-chloropyridines 1 after basic workup. Reissig and co-workers discovered a new synthesis of trifluoromethyl-substituted pyridines from the reaction of lithiated methoxyallenes and nitriles in the presence of trifluoroacetic acid <04CEJ4283>. The authors postulate that the reaction goes through initial protonation of iminoallene followed by nucleophilic addition of the trifluoroacetate anion onto the iminoallene to give . Intermediate then undergos intramolecular acyl transfer to give and subsequent aldol condensation yields the pyridinol as shown in

Scheme 2. Kerwin et al. has shown that azaenyne allenes readily form the α,5-didehydro-3-picoline diradicals, which can then be trapped with 1,4-cyclohexadiene, chloroform-d, and methanol to produce various pyridine products <04OL2059>. 1,4-Dihydropyridines continue to be of interest to medicinal chemists due to their biological activity. The synthesis of choice is the Hantzsch dihydropyridine synthesis <04JMC3180; 04JMC2688; 04JMC254; 04JMC3163>. Zolfigol et al. has developed a mild solvent free modification to this synthesis with improved yields <04SL827>. Tripathi and co-workers modified this method further through use of tetrabutylammonium hydrogen sulfate as a phase transfer catalyst and diethylene glycol as an eco-friendly solvent <04TL9011>. Dondoni et al. utilized a one-pot thermal Hantzsch reaction for the synthesis of highly functionalized β-pyridylalanines as shown in Scheme 9 <04TL2311>. They simplified the purification process by incorporating polymer-supported scavengers to remove excess reagents. A mixed resin bed of strongly acidic resin and strongly basic resin was used to remove unreacted enamine and ketoester, respectively. The unreacted aldehyde and intermediate side products were scavenged with nucleophilic aminomethylated polystyrene.

2.2. Synthetic Approaches

The synthesis of pyridine involves several methods like Chichibabin synthesis, Bonnemann cyclization, Krohnke pyridine synthesis, Gattermann-Skita synthesis and several other methods. In Chichibabin pyridine synthesis firstly, acrolein is formed via Knoevenagel condensation from acetaldehyde and formaldehyde, then acrolein condenses with acetaldehyde and ammonia to give aminopyridine. In Bonnemann cyclization, the trimerization of one part of a nitrile molecule and two parts of acetylene gives pyridine. In Krohnke pyridine synthesis, the reaction of pyridine with bromomethyl ketones gives related pyridinium salt. In Gattermann-Skita synthesis, malonate ester was made to react with dichloro methylamine.

2.3. Anti-Inflammatory Activity

The in vitro anti-inflammatory action of all tested compounds was estimated against carrageenan-induced paw edema in male Wister rats (180–200 g each) using diclofenac as a reference drug on the basis of a Winter et al. modified process. (55,56) Diclofenac was evaluated at 5 mg/kg (56) of body weight for the animal used. Prior to the test, all animals experienced at least a 1 week acclimatization period. All of the investigational procedure was done in accordance with the strategies of the Institutional Animals Ethics Committee (IEAC). Changes in paw volume (% of edema inhibition) were produced and compared by subplantar dose of 100.0 μL of 1.0% newly prepared carrageenan solution in bidistilled H2O into the left hind paw of each rat. (3,56) The test agents were injected half an hour earlier to carrageenan addition, The comparison was done after 1, 3, and 6 h from induction of inflammation (Table 2) and showed wide range of anti-inflammatory effects (7.59–46.9%; 1 h), (7.59–52.80%; 3 h)
and (9.37–54.37%; 6 h) against to the reference drug diclofenac (28.26%, 1 h; 20.79%, 3 h; 20.79%, 6 h). From the recorded results in, it appears that of all 15 compounds evaluated for anti-inflammatory activity, the titled compounds could be promising anti-inflammatory candidates when using diclofenac as a reference drug (28.26%; 1 h). It was found that the most potent four compounds were 5a, 5f, 5g, and 5h with a % edema inhibition of (46.9%; 1 h), (34.27%; 1 h), (43.46%; 1 h), and (30.74%; 1 h), respectively.

2.4. Inflammation

Inflammation is a biological response of the immune system that can be triggered by a variety of factors, including pathogens, damaged cells and toxic compounds. These factors may induce acute and/or chronic inflammatory responses in the heart, pancreas, liver, kidney, lung, brain, intestinal tract and reproductive system, potentially leading to tissue damage or disease. Both infectious and non- infectious agents and cell damage activate inflammatory cells and trigger inflammatory signaling pathways, most commonly the NF-κB, MAPK, and JAK-STAT pathways. Here, we review inflammatory responses within organs, focusing on the etiology of inflammation, inflammatory response mechanisms, resolution of inflammation, and organ- specific inflammatory responses. Inflammation is a protective response that develops against tissue injury and infection. Chronic inflammation, on the other hand, is the key player in the pathogenesis of many inflammatory disorders including cancer. The cytokine storm, an inflammatory response flaring

DOI: 10.48175/IJARSCT-24784

out of control, is mostly responsible for the mortality in COVID-19 patients. Anti- inflammatory drugs inhibit cyclooxygenases (COX), which are involved in the biosynthesis of prostaglandins that promote inflammation. The conventional non-steroidal anti-inflammatory drugs (NSAIDs) are associated with gastric and renal side-effects, as they inhibit both the constitutive COX-1 and the inducible COX-2. The majority of selective COX-2 inhibitors (COXIBs) are without gastric side-effects but are associated with cardiac side-effects on long- term use.

III. REACTION AND MECHANISM OF PYRIDINE

The synthesis of pyridine, a six-membered aromatic heterocycle with one nitrogen atom, can be achieved through several methods. Here are some of the most important synthetic methods for pyridine along with their reaction mechanisms:

3.1. Hantzsch Pyridine Synthesis (Hantzsch Method)

This method involves the condensation of β-ketoesters with ammonia (or primary amines) and an aldehyde. This reaction is a popular route for the synthesis of pyridine derivatives.

Reaction:

- Reactants: β-ketoester, ammonia (NH_3) or a primary amine, aldehyde (e.g., acetaldehyde).
- Product: Pyridine

Mechanism:

Step 1: The β-ketoester reacts with ammonia or a primary amine to form a Schiff base (imine) intermediate. β - ketoester + NH_3 → Schiff base

Step 2: The Schiff base then undergoes nucleophilic attack by the carbonyl group of the aldehyde (such as acetaldehyde), leading to the formation of a dihydropyridine intermediate.

Schiff base + Aldehyde → Dihydropyridine intermediate

Step 3: The dihydropyridine undergoes cyclization (formation of the pyridine ring) and dehydration to yield the final pyridine product. Dihydropyridine intermediate → Pyridine + H_2O

3.2. Chichibabin Pyridine Synthesis (Chichibabin Reaction)

The Chichibabin synthesis involves the direct synthesis of pyridine from aldehydes and ammonia or amines in the presence of a reducing agent like sodium metal.

Reaction:

- Reactants: Aldehyde (e.g., acetaldehyde), ammonia (NH_3) or a primary amine, sodium (Na).
- Product: Pyridine

Mechanism:

Step 1: The aldehyde reacts with ammonia or a primary amine to form a Schiff base (an imine).

Aldehyde + NH_3 → Schiff base

Step 2: The Schiff base is then subjected to a dehydrogenation step promoted by sodium (Na), which generates a dihydropyridine intermediate. The sodium donates electrons to the Schiff base, initiating the reduction process.

Step 3: The intermediate undergoes cyclization and elimination of hydrogen to form the pyridine ring structure.

Dihydropyridine intermediate → Pyridine + H_2

3.3. Skraup Pyridine Synthesis

The Skraup synthesis involves the reaction of aniline (phenylamine) with glycerol in the presence of sulfuric acid, and it produces pyridine through a series of complex reactions.

Reaction:

Reactants: Aniline ($C_6H_5NH_2$), glycerol ($C_3H_8O_3$), concentrated sulfuric acid (H_2SO_4).

Product: Pyridine

Mechanism:

Step 1: Aniline reacts with glycerol in the presence of sulfuric acid to form an intermediate that undergoes electrophilic substitution.

Step 2: The sulfuric acid acts as a catalyst and dehydrating agent, promoting the formation of a pyridine ring through cyclization.

Step 3: Dehydration and further rearrangement of the intermediate result in the formation of pyridine.

3.4. Bönnemann Pyridine Synthesis

The Bönnemann synthesis is a method where pyridine is synthesized from 1,5-diketones using ammonia or primary amines, under basic conditions.

Reaction:

Reactants: 1,5-diketones, ammonia (NH_3) or primary amines, base (e.g., sodium acetate).

Product: Pyridine

Mechanism:

Step 1: The 1,5-diketone reacts with ammonia or a primary amine to form a Schiff base (imine).

Step 2: The intermediate undergoes nucleophilic attack by the nitrogen atom, leading to the formation of a dihydropyridine intermediate.

Step 3: The intermediate undergoes dehydration, resulting in the formation of the pyridine ring.

IV. APPLICATION

Pyridine and its derivatives are widely used in various fields due to their unique chemical properties. Here are some key applications of pyridine synthesis.

4.1. Pharmaceutical Industry:

Pyridine is a core structure in many drugs, including antihistamines (e.g., loratadine), tuberculosis drugs (e.g., isoniazid), and cardiovascular drugs.

Used in the synthesis of vitamin B3 (niacin) and vitamin B6 derivatives.

4.2. Agrochemicals

Pyridine-based compounds are used in pesticides, herbicides, and fungicides (e.g., paraquat and diquat). Essential in the production of plant growth regulators.

4.3. Chemical Solvents & Catalysts

Used as a solvent in chemical reactions, especially in dehydrohalogenation and acylation reactions. Acts as a base catalyst in organic synthesis.

4.4. Dye & Pigment Industry

Pyridine derivatives are used in the synthesis of dyes, pigments, and optical brighteners.

4.5. Polymer & Material Science:

Used in the production of advanced materials, including liquid crystal displays (LCDs) and conducting polymers.

4.6. Flavoring & Fragrance Industry:

Some pyridine derivatives contribute to the flavoring industry, though their strong odor requires careful handling.

V. FUTURE SCOPE

The future scope of pyridine synthesis using green chemistry holds significant potential due to the increasing demand for more sustainable and environmentally-friendly methods in chemical production. The development of green chemistry methods for synthesizing pyridine will be influenced by advances in catalysis, alternative feedstocks, process optimization, and solvent-free reactions. Below are some key areas for future research and development:

5.1. Development of New Catalysts:

Biocatalysts: Enzyme-based catalysts, or biocatalysts, are of growing interest in green chemistry because of their selectivity and mild reaction conditions. Future work could focus on engineering enzymes to catalyze the formation of pyridine from simple, renewable precursors, potentially reducing the need for harsh chemicals or high temperatures.

Nanocatalysts: The use of nanomaterials (e.g., metal nanoparticles or carbon-based nanomaterials) as catalysts could improve the efficiency, selectivity, and recyclability of pyridine synthesis. Nanocatalysts can provide high surface area, which may enhance reaction rates and allow for reusability, reducing waste generation.

5.2. Use of Renewable Feedstocks:

Biomass-Derived Precursors: Pyridine synthesis could increasingly rely on renewable biomass sources instead of petroleum-based feedstocks. Research could focus on identifying and optimizing processes that convert bio-derived materials (such as glycerol, sugars, or lignocellulosic biomass) into pyridine or its precursors. This would reduce dependence on fossil fuels and lower the carbon footprint of production.

Green Ammonia Production: The conventional method of producing ammonia involves energy-intensive processes (e.g., Haber-Bosch process). Future research could focus on developing more sustainable, low-energy methods for ammonia production from renewable sources (such as water and nitrogen), which would make the ammonia-based pyridine synthesis greener.

5.3. Alternative Solvent Systems:

Supercritical Fluids: Supercritical CO_2 ($scCO_2$) is a promising green solvent for chemical reactions due to its low toxicity, recyclability, and ability to dissolve a wide range of organic compounds. Future developments in using $scCO_2$ as a reaction medium for pyridine synthesis could offer an alternative to traditional organic solvents, leading to reduced environmental impact.

Deep Eutectic Solvents (DES): DES, a new class of green solvents that are typically non-toxic, biodegradable, and cheap, are gaining attention in green chemistry. Researchers could explore their potential as solvents for pyridine synthesis, especially in catalytic reactions that require mild conditions.

5.4. Microwave and Ultrasound-Assisted Synthesis:

Microwave-Assisted Synthesis: As demonstrated in current methods, microwave- assisted reactions reduce energy consumption and improve reaction times. Future studies could focus on optimizing the conditions (e.g., power, temperature, time) and exploring new catalytic systems to further improve yields and reduce environmental impacts.

Ultrasound-Assisted Synthesis: Sonochemistry, or the use of ultrasound in reactions, can enhance reaction rates, improve mixing, and promote efficient energy transfer. Research could explore ultrasound as a green alternative to traditional heating for pyridine synthesis.

5.5. Solvent-Free and Solid-State Reactions:

Future research could focus on expanding solvent-free methods for pyridine synthesis. Solid-state reactions, in which all reactants and catalysts are in a solid phase, could significantly reduce the need for organic solvents and minimize waste generation.

DOI: 10.48175/IJARSCT-24784

Mechanochemistry (the use of mechanical force to promote chemical reactions) offers an innovative approach to solvent-free pyridine synthesis. Solid reagents or mixtures could be activated under mechanical stress, potentially leading to cleaner processes with fewer by- products.

VI. CONCLUSION

The synthesis of pyridine and its derivatives through green chemistry principles represents a significant step toward sustainable and environmentally friendly chemical processes. Traditional methods for pyridine synthesis often involve hazardous reagents such as phosphorus oxychloride ($POCl_3$), thionyl chloride ($SOCl_2$), or molecular chlorine (Cl_2), which pose risks of toxicity, corrosiv eness, and waste generation. Additionally, conventional synthesis usually requires prolonged reaction times, high temperatures, and the use of harmful organic solvents, all of which contribute to environmental pollution and high energy consumption. Green chemistry offers innovative alternatives that not only minimize these hazards but also improve reaction efficiency, selectivity, and overall sustainability. Microwave- assisted synthesis, for example, has emerged as an effective green method for chlorination and other functionalization reactions of pyridine. Microwave irradiation provides rapid and uniform heating, significantly reducing reaction time from several hours to just a few minutes while lowering energy requirements. This method also enhances reaction selectivity, reducing the formation of unwanted byproducts and increasing overall yields. Furthermore, the use of mild chlorinating agents such as N-chlorosuccinimide (NCS) instead of hazardous chlorine gas aligns with the principles of green chemistry by reducing toxicity and waste. Another key advantage of green pyridine synthesis is the shift toward solvent-free or water-based reaction conditions. Many conventional reactions rely on toxic organic solvents such as benzene, chloroform, or dichloromethane, which contribute to environmental pollution and pose health risks. In contrast, green chemistry approaches emphasize the use of benign solvents such as water, ethanol, or ionic liquids, which are safer and biodegradable. In some cases, solvent-free synthesis eliminates the need for hazardous solvents altogether, further reducing the ecological footprint of pyridine production. Additionally, catalyst innovations play a crucial role in sustainable pyridine synthesis. Green catalysts, such as reusable metal catalysts, enzyme-based systems, or heterogeneous catalysts, not only improve reaction efficiency but also facilitate catalyst recovery and reuse, minimizing waste. These advancements contribute to the overall sustainability of pyridine chemistry by reducing the reliance on non-renewable resources and lowering the environmental impact of industrial-scale production. Overall, the application of green chemistry in pyridine synthesis demonstrates how modern scientific advancements can address environmental concerns while maintaining high efficiency and product quality.

REFERENCES

[1]. Chen, L.; Deng, H.; Cui, H.; Fang, J.; Zuo, Z.; Deng, J.; Li, Y.; Wang, X.; Zhao, L. Inflammatory responses and inflammation- associated diseases in organs. Oncotarget. 2018, 9 (6), 7204– 7218, DOI: 10.18632/oncotarget.23208 View Google Scholar

[2]. Mahesh, G.; Kumar, K. A.; Reddanna, P. Overview on the Discovery and Development of Anti-Inflammatory Drugs: Should the Focus Be on Synthesis or Degradation of PGE. J. Inflamm. Res. 2021, 14, 253– 263, DOI: 10.2147/JIR.S278514 View Google Scholar

[3]. Khodairy, A.; Shaaban, K.; Mohamed, S. K.; Ali, A. M.; El-Wassimy, M. T.; Ahmed, N. S. Eco-friendly and efficiently synthesis, anti-inflammatory activity of 4-tosyloxyphenylpyrans via multi-component reaction under ultrasonic irradiation and room temperature conditions. J. Chem. Pharm. Res. 2015, 7 (11), 332– 340 Google Scholar

[4]. Liu, L.; Li, H.; Hu, K.; Xu, Q.; Wen, X.; Cheng, K.; Chen, C.; Yuan, H.; Dai, L.; Sun, H. Synthesis and anti-inflammatory activity of saponin derivatives of δ-oleanolic acid. Eur. J. Med. Chem. 2021, 209, 112932, DOI: 10.1016/j.ejmech.2020.112932 View Google Scholar

[5]. Kumar, R.; Saha, N.; Purohit, P.; Garg, S. K.; Seth, K.; Meena, V. S.; Dubey, S.; Dave, K.; Goyal, R.; Sharma, S. S.; Banerjee, U. C.; Chakraborti, A. K. Cyclic enaminone as new chemotype for selective cyclooxygenase-2 inhibitory, anti-inflammatory, and analgesic activities. Eur. J. Med. Chem. 2019, 182, 111601, DOI: 10.1016/j.ejmech.2019.111601 View Google Scholar

[6]. Zolfigol, M. A.; Yarie, M. Fe3O4-TiO2-O2PO2(CH2)NHSO3H as a novel nanomagnetic catalyst: Application to the preparation of 2-amino-4, 6-diphenylnicotinonitriles via anomeric-based oxidation. Appl. Organometal. Chem. 2017, 31, e3598 DOI: 10.1002/aoc.3598 View Google Scholar

[7]. Khalili, D. Graphene oxide: a reusable and metal-free carbocatalyst for the one-pot synthesis of 2-amino-3-cyanopyridines in water. Tetrahedron Lett. 2016, 57, 1721– 1723, DOI: 10.1016/j.tetlet.2016.03.020 View Google Scholar

[8]. Kumar, N.; Chauhan, A.; Drabu, S. Synthesis of cyanopyridine and pyrimidine analogues as new anti-inflammatory and antimicrobial agents. Biomed. Pharmacother. 2011, 65 (5), 375– 80, DOI: 10.1016/j.biopha.2011.04.023 View Google Scholar

[9]. Liu, H.; Li, Y.; Wang, X.-Y.; Wang, B.; He, H.-Y.; Liu, J.-Y.; Xiang, M.-L.; He, J.; Wu, X.-H.; Yang, L. Synthesis, preliminary structure–activity relationships, and in vitro biological evaluation of 6-aryl-3-amino-thieno[2,3-b]pyridine derivatives as potential anti-inflammatory agents. Bioorg. Med. Chem. Lett. 2013, 23, 2349– 2352, DOI: 10.1016/j.bmcl.2013.02.059 View Google Scholar

[10]. Albratty, M.; Alhazmi, H. A. Novel pyridine and pyrimidine derivatives as promising anticancer agents: A review. Arab. J. Chem. 2022, 15, 103846, DOI: 10.1016/j.arabjc.2022.103846 View Google Scholar

[11]. Khaksar, S.; Yaghoobi, M. A concise and versatile synthesis of 2-amino-3-cyanopyridine derivatives in 2,2,2-trifluoroethanol. J. Fluor. Chem. 2012, 142, 41– 44, DOI: 10.1016/j.jfluchem.2012.06.009 View Google Scholar

[12]. Fatma, S.; Singh, D.; Ankit, P.; Mishra, P.; Singh, M.; Singh, J. An eco-compatible multicomponent strategy for the synthesis of new 2-amino-6-(1H-indol-3-yl)-4-arylpyridine-3,5-dicarbonitriles in aqueous micellar medium promoted by thiamine-hydrochloride. Tetrahedron Lett. 2014, 55, 2201– 2207, DOI: 10.1016/j.tetlet.2014.02.050 View Google Scholar

[13]. Reddy, L. S.; Reddy, T. R.; Reddy, N. C. G.; Mohan, R. B.; Lingappa, Y. Pd-Mediated Multicomponent Synthesis of Highly Functionalized Pyridines and Consequential C—C Coupling Using Suzuki Reaction in One Pot: Their In Vitro Evaluation as Potential Antibacterial Agents. J. Het.. Chem. 2014, 51, E104– E113, DOI: 10.1002/jhet.1855 View Google Scholar

[14]. Liu, L.; Zhang, C.; Zhang, L.-X.; Li, Q.; Yin, Y.-Y.; Wang, H.-Y.; Sun, R.-H.; Li, J.-Y.; Hou, X. Y.; Dong, H.; Bie, L.-J. 2D

[15]. coordination polymer of [Cd(TMA)(4-CNPy)(H2O)]n (H2TMA = 3-thiophenemalonic acid, 4-CNPy = 4-cyanopyridine) with impedimetric humidity sensing performance. Inorg. Chem. Commun. 2020, 111, 107636, DOI: 10.1016/j.inoche.2019.107636 View Google Scholar