Synthesis and Applications of Heterocyclic Compounds: A Short Review

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Abstract:

In everyday in the life, heterocyclic compounds are used and they are highly fascinating. Heteroatoms can be found in one or more heterocyclic compounds' structural elements. They could have a cyclical or non-cyclic structure. Chemicals classified as heterocyclic have one or more rings containing atoms other than carbon. Neon, oxygen, sulfur, and other elements are examples of these heteroatoms. Medicinal chemistry, materials science, and many other disciplines place great emphasis on the synthesis and uses of heterocyclic molecules. Heterocyclic compounds can be incorporated into polymers to impart specific properties, such as improved conductivity, thermal stability, and mechanical strength. Certain heterocyclic compounds are key components in the development of agrochemicals, helping control pests and enhance crop yields. The development of new synthetic techniques and the emergence of novel applications in a variety of sectors are continuous research endeavors in the dynamic field of heterocyclic compound synthesis and applications. The current review paper is present the recent synthesis techniques and different applications of heterocyclic compounds on the basis of previous work carried out by the researchers.

Keywords: *Heterocyclic compounds, cyclic structure, biochemistry, stability, crop yields.*

1. INTRODUCTION:

Heterocyclic compounds have a cyclic structure with at least one heteroatom in the ring. It can be classified based on the number of heteroatoms and the size of the ring [1]. Common examples include pyridines, furans, thiophenes, and imidazoles. Any of a significant family of organic chemical compounds that are distinguished by having at least one atom of an element other than carbon connected to all or some of the atoms in their molecules in rings. The largest and most varied family of organic chemicals is called heterocyclic compounds [2, 3]. Among these, aromatic heterocyclic compounds are patterns of structure prevalent in many synthetic and organic substances, agricultural chemicals, and pharmaceuticals that are physiologically relevant. Furthermore, aromatic heterocyclic compounds are widely used in the synthesis of significant polymeric materials and colors [4, 5]. Numerous papers discuss the usage of aromatic heterocyclic molecules as intermediary in organic synthesis [6]. While several extremely effective methods have been previously reported for the synthesis of aromatic heterocyclic molecules and derivatives of them, there is always a need for the development of novel techniques. Few techniques are available for the photochemical synthesis of heterocycles, given the significant relevance of these molecules [6, 7]. Nonetheless, photochemical processes are frequently straightforward, uncontaminated, and safe for the ecosystem. Cyclization of linear compounds, [x+y] cyclization, and ring closure are the main techniques used to construct heterocycles. Comparatively speaking, there has been a major surge in research in this area to elucidate the reaction processes and find novel approaches [8, 9]. Heterocyclic compounds are widely used in many branches of biology and medicine, and they are important components of biological systems.

Heterocyclic compounds are important and efficient in the development of molecules for certain biological activities because of their various structural characteristics [9, 10]. Heterocyclic compounds are diverse and can be classified based on various criteria, such as the number of heteroatoms, the size of the ring, and the nature of heteroatoms involved. Based on ring size the heterocyclic compounds are divided into five ways such as epoxides (three-membered ring), Oxetanes and Aziridines (four-membered ring), Furans, Thiophenes, Pyrroles, and Imidazoles (five-membered ring), Pyridines, Pyrans, Thiazines, and Pyrimidines (six-membered ring) and larger rings containing seven or more than seven rings examples like an azepines, diazepines, etc [9-11]. The many varieties of heterocyclic compounds, each with unique characteristics and uses in many scientific domains, including drug development and medical chemistry.
The current research work focus on the review of different synthesis techniques and applications of heterocyclic compounds.

2. Literature survey

Beginning in the 1800s, heterocyclic chemistry developed concurrently with the advancement of organic chemistry [9]. Additionally, the usage of heterocyclic compounds as an intermediate step in organic synthesis is growing [12]. This occurs frequently due to a ring structure that is generally stable might undergo several synthetic stages before being fractured at the necessary point to reveal additional functional groups [12, 13]. The potency and enthusiasm of this field of organic chemistry is demonstrated to by the rate at which heterocyclic compounds are still being developed [14]. The difficulties in finding new heterocyclic structures and analyzing their characteristics additionally motivate the research community in this field ongoing [14, 15].
Abu-Melha, S., and team et. al [16] synthesized a novel sequence of thiazole-based heterocycles using vinylpyridine as an environmentally acceptable biopolymeric basic catalyst in 1, 3-dipolar cycloaddition processes. Spectroscopic and elemental studied and provided an illustration of the synthetic compounds' molecular structure. The newly synthesized compounds were used for their possible anticancer, antibacterial, and hepatoprotective properties using a variety of in vitro biological experiments. Authors reported that all of the compounds showed anticancer activity when tested against human hepatocellular carcinoma, colonic carcinoma, and breast cancer cell lines. The most effective compounds were those that included chlorine, specifically 11c and 6g. Regarding the employed gram positive and gram negative bacterial species, most of the investigated thiazole derivatives shown adequate antibacterial activity. Furthermore, a large number of derivatives have marginal hepatoprotective action against hepatotoxicity caused by CCl4.
El-Salam, A., et al [17] synthesized a hetrocylic compounds like dropyridazino [6,1-b]quinazolin-10-ones,1,2,4-benzotriazinopyrid-azinethione,imidazo[1,2-b]pyridazinethione, 1,2,4-triazolo[4,3-b] pyridazinethione, and disulfide. Based on elemental analysis and spectral data, Author studied the structure of every new synthesized molecules. Several of these substances exhibit strong antibacterial and antifungal properties against both gram-positive and gram-negative bacteria.
Al-Majid, et al [18] describes an effective and useful process for the synthesis of 2,6-diaryl-4-oxo-N,N′-di(pyridin-2-yl)cyclohexane-1,1-dicarboxamide. This reaction takes place via a double Michael addition reaction between diamide and different dibenzalacetones. Dichloromethane (DCM) was used as the reaction medium, and 1, 8-diazabicyclo[5.4.0]undec-7-ene (DBU) was present. The chemical compounds that were created were assessed for their anticancer properties using multiple cancer cell lines, such as MCF-7, MDA-MB-231, SAS, PC-3, HCT-116, HuH-7, and HepG2 cells.
Khandazhinskaya, A., et al [19] synthesised new flexible analogues of 8-aza-7-deazapurine nucleosides as potential antibacterial agents. The 8-aza-7-deazahypoxanthine fleximer scaffolds were used as the basis for

the design, synthesis, and antibacterial activity screening of a number of ribo-, 2′-deoxyribo-, and 5′-norcarbocyclic derivatives. For the synthesis of the 8-aza-7-deazainosine fleximers, chemical and chemoenzymatic approaches were contrasted. Side products were formed during the transglycosylation reaction of the 8-aza-7-deazahypoxanthine fleximer. Only one product was formed during the selective reaction involving the protected fleximer base 1-(4-benzyloxypyrimidin-5-yl)pyrazole.

3. Synthesis approach of heterocyclic compounds

The variety and adaptability of techniques available for the synthesis of heterocyclic molecules are demonstrated by these synthetic methodologies.

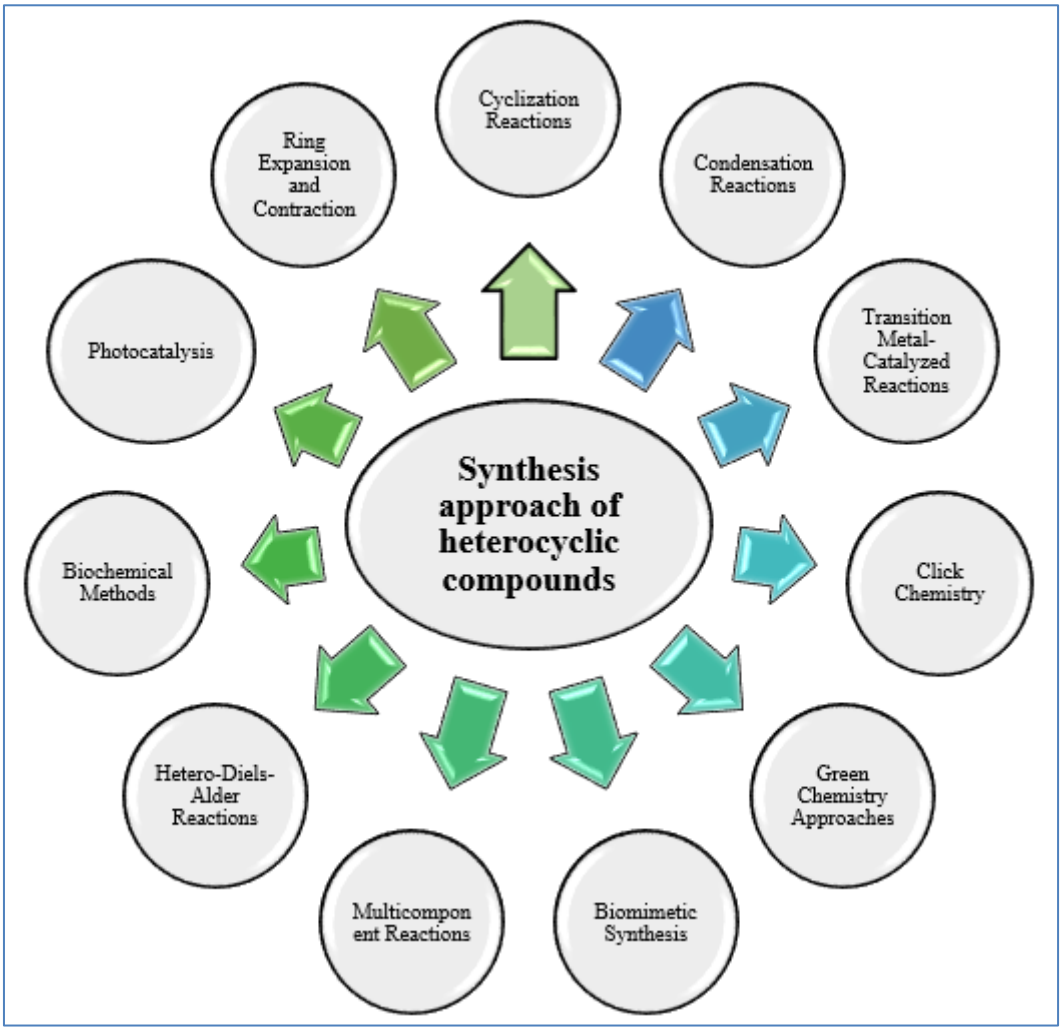

Figure 1: Different synthesis of heterocyclic compounds

The type of heterocycle, the accessibility of raw materials, the required stereochemistry, and the functional groups in the finished product all influence the technique selection. Scholars frequently utilize a blend of these techniques to accomplish intricate and effective synthesizes of various heterocyclic structures. The synthesis of heterocyclic compounds involves various strategies and methods to construct the ring structures containing atoms other than carbon [18-20]. The choice of synthetic approach depends on the specific heterocycle targeted and the desired functional groups. Some common approaches to the synthesis of heterocyclic compounds are shown in Figure 1.

1. Cyclization Reactions:

- Intramolecular Cyclization: Formation of heterocyclic rings within a single molecule. This can involve nucleophilic attacks on electrophilic centers, such as in the synthesis of oxiranes (epoxides) and aziridines.
- Ring-Closing Metathesis (RCM): A powerful method for the construction of cyclic structures using olefin metathesis reactions.

2. Condensation Reactions:

- Formation of Amidines: Condensation reactions between amines and carbonyl compounds, leading to the formation of amidines, which can subsequently cyclize to form heterocyclic rings.
- Ugi Reaction: Multicomponent reaction involving an amine, isocyanide, and carbonyl compound, leading to the formation of heterocyclic products.

3. Transition Metal-Catalyzed Reactions:

- Palladium-Catalyzed Cross-Coupling: Formation of C-C or C-N bonds under the catalysis of palladium. Useful for the synthesis of various heterocycles.
- Heck Reaction: Palladium-catalyzed reaction between an olefin and an aryl or vinyl halide, useful in heterocyclic synthesis.

4. Click Chemistry:

- Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC): Click chemistry reactions, such as CuAAC, allow for the selective and high-yielding synthesis of triazole-containing heterocycles.

5. Green Chemistry Approaches:

- Microwave-Assisted Synthesis: Accelerates reactions by using microwave irradiation, reducing reaction times and improving yields.
- Solvent-Free Reactions**:** Green and environmentally friendly methods that eliminate or reduce the use of solvents.

6. Biomimetic Synthesis:

- Bioinspired Approaches: Taking inspiration from biosynthetic pathways in nature to design and synthesize heterocyclic compounds.

7. Multicomponent Reactions (MCRs):

- Passerini Reaction: A three-component reaction involving an isocyanide, carboxylic acid, and an aldehyde, leading to the formation of α-acyloxy amides.

8. Hetero-Diels-Alder Reactions:

- Diels-Alder Cycloaddition with Heteroatoms: Involving the reaction between a conjugated diene and a dienophile, where one or more of the components contain heteroatoms.

9. Photocatalysis:

- Photochemical Synthesis: Utilizing light as a driving force for chemical reactions, particularly for the construction of complex heterocyclic structures.

10. Biochemical Methods:

- Enzymatic Synthesis: Employing enzymes for the selective formation of heterocyclic compounds.

11. Ring Expansion and Contraction:

- Ring Expansion Reactions: Transforming smaller rings into larger ones, often involving the insertion of new heteroatoms.
- Ring Contraction Reactions: Reducing the size of a ring, often resulting in the removal of heteroatoms.

4. Applications of heterocyclic compounds

The applications for heterocyclic compounds are diverse; they are primarily utilized in medicines, agricultural products, and veterinary medicines. They are also used as polymer chains, pigments, sanitizers, designers, anti-oxidants, and anti-corrosion agents. They serve as catalysts for the production of many organic substances [9-11]. The heterocyclic compounds are useful in a variety of domains, such as biology and pharmaceutical chemistry. Heterocyclic compounds are mostly used in veterinary products, agricultural pesticides, and medicines. A new phase of potential antifungal, anti-inflammatory, anti-bacterial, antiviral, antioxidant, anticonvulsant, anthelmintic, anti-histamine, herbicidal, anticancer, antihypertensive, and anti-leprosy therapeutics [21-25]. Numerous heterocyclic substances, such as analogues of triazine, have been used as antibacterial, urinary antiseptic, and therapeutic agents in the treatment of a wide range of diseases.

CONCLUSIONS:

The synthesis and applications of heterocyclic compounds are dynamic fields that contribute significantly to scientific advancements and technological innovations. Due to their many important biological and medicinal applications, heterocyclic compounds have attracted a lot of research. The vast synthetic investigation and functional value of heterocyclic compounds have led to a significant increase in scientific curiosity in these molecules. The ongoing exploration of these compounds holds promise for addressing diverse challenges and creating novel solutions in various scientific and industrial domains.

ACKNOWLEDGEMENT:

Author is very much thankful to Principal, MGV's, Arts, Commerce and Science College, Surgana, Tal-Surgana, Dist. Nashik, Maharashtra, India for his constant guidance and extensive support to encourage present research work.

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