

A STUDY ON AROMATIC HETEROCYCLIC ORGANIC COMPOUNDS

Abstract

The synthesis of newer and more novel molecules has always been a goal for research in organic chemistry. Heterocyclic compounds are those in which the fundamental compound structure contains an element other than carbon. These molecules may also be aromatic, which means they have a distinct odor. The composition of heterocyclic compounds will be discussed in depth in this study. The paper will also go through the synthesis and application methodologies. The pharmaceutical sector makes substantial use of these chemicals. It is largely employed in histamine and serotonin-related medications in that country. These chemicals are also used in the cosmetics and DNA vaccine industries, as well as in genetic research. Advancements in organic chemistry are allowing for a more thorough investigation of aromatic heterocyclic compounds in order to get a better knowledge of their structural and chemical compatibility with other molecules.

Keywords: Aromatic, Heterocyclic, innovation, pharmaceutical, histamine, serotonin

Introduction

In organic chemistry the heterocyclic compounds are defined as those organic, cyclic compounds which have a carbon atom of their basic framework structure being replaced by some other atom such as oxygen, nitrogen or sulphur. Some examples of these compounds include; furan (C₄H₄O), Pyridine (C₅H₅N), pyrrole (C₄H₅N), and thiophene (C₄H₄S).

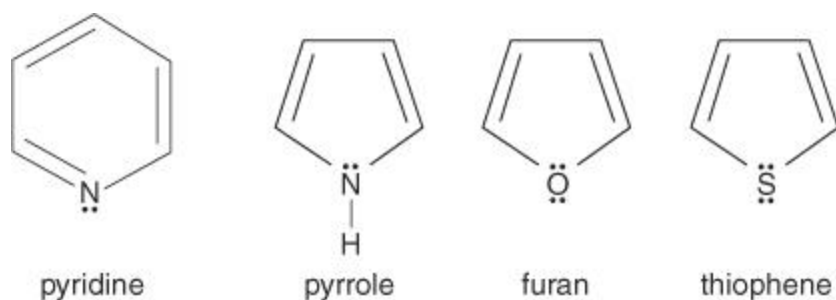


Fig. 1. heterocyclic compounds

The compounds that are monocyclic and aromatic generally follow the Hückel's Rule. The rule given by Huckle states that an organic compound that has cyclic and aromatic properties must have the $4n + 2\pi$ electrons [1-4]. Thus according to this rule it is propounded that the most of the aromatic compound must contain 6π electrons when n is taken equal to 1. The Huckle's rule also has some exceptions like furan, thiophene, and pyrrole. These compounds only have 4π electrons (2π bonds) instead of standard 6π electrons. In these compounds the aroma generating extra electron comes from the unshared electron pairs in sp^2 hybrid orbital around the non-carbon atom that can be oxygen, sulphur or nitrogen.

The term Aromatic comes from the root word 'Aroma' that means smell. The Aromatic compounds are a type hydrocarbon that possess the ability to impart a characteristic smell or aroma to any given mixture they are added in as they inherently has a molecular structure that imparts them this characteristic aroma. In organic chemistry it is established by many scientists that the aromatic compounds are highly stable in terms of reactivity and temperature treatments; way more than other hydrocarbons such as the unsaturated hydrocarbons. The classic example of an aromatic compound is Benzene which was founded by Michael Faraday in 1825. The aromatic compounds generally known and used are monocyclic i.e. having carbon only as the backbone. But there is another class of Aromatic compounds which are heterocyclic that means that the backbone structure has at least one non carbon atom that could be oxygen, nitrogen or sulphur. The heterocyclic compounds are widely studied nowadays for better understanding of these compounds and their usage in various fields such as petroleum, cosmetics or biochemical studies.

The heterocyclic compounds are not just synthetically made in laboratories rather they actually exist in the natural settings as well. These compounds are found in some of the most crucial and basic systems of living organisms; both plants and animals. In human beings these compounds are found in the most crucial biological entity that is human DNA. In human beings the nucleic acid bases which are the building block of the DNA are composed of the heterocyclic compound. These nucleic acids are derived from purine, which makes 2 bases which are adenine and guanine. The second one is pyrimidine which makes other two bases which are thymine and cytosine. All 4 of these are very important for replication of the genetic material. Taking this as inspiration a vaccine named Puromycin is created [5-8]. Another example of heterocyclic compound in natural system is found in Chlorophyll which is the most crucial element of plants that help in photosynthesis and heme protein present in the molecule of chlorophyll is also heterocyclic. It is also found that many vitamins that are crucial for human body such as vitamin B1 (thiamine), vitamin B2 (riboflavin), vitamin B3 (nicotinamide), vitamin B6 (Pyridoxin), and ascorbic acid (vitamin C) are all structurally heterocyclic in nature.

Usage of Aromatic Heterocyclic Compounds:

- **Biologically active aromatic compounds (BACs):** The biologically active aromatic compounds are primarily used in many pharmaceutical drugs that are effectively used against diseases like leukemia and in irradiation of tumors. The BACs are also used in making the anti-biotic medicines like ofloxacin, ofloxacin etc. which are widely used broad spectrum antibiotics. Another usage of the BACs is found in the aromatic vitamins such as riboflavin, nicotinamide, etc. are used as antioxidants in chemotherapy. A compound named methylxanthines is very potent in biological activity in the body which is essential at keeping the body healthy is also present in many food items and this itself is a biologically active aromatic compound.
- **Aromatic heterocyclic Pyridine and Pyrrole:** Both pyridine and pyrrole are nitrogen containing heterocyclic aromatic compounds that are not only chemically synthesized but are also found in nature in trace form. When manufactured chemically these compounds are generally made through chemical reactions that produce them in oily consistency. These compounds are mainly used in pharmaceutical sector for making medicines and certain cosmetics like dyes. Pyridine is also used as a solvent in many chemical

syntheses. It is also used for waterproofing and as an additive in rubber making. It also finds usage as an alcohol denaturant and an additive in dyes.

- **Heterocyclic Furan and Thiophene:** In organic chemistry Furan is an oxygen-containing heterocyclic aromatic compound while Thiophene is Sulphur containing heterocyclic aromatic compound. Furan is mainly used in conversion reactions to make it into pyrrole. A close compound to furan called as furfural is an intermediate in nylon synthesis reaction. Thiophene which is sulfur containing has resemblance with a monocyclic benzene in terms of chemical and physical properties. Thiophene contaminates benzene in natural form this is where the existence of thiophene has been discovered while the process of purification of benzene. Thiophene is used primarily in various conversion reactions. The heterocyclic compounds are not just made in labs but are also naturally occurring and are crucial to metabolic activities in the living cells. Heterocyclic compounds have a wide range of application but prominently they are used in pharmaceutical industries.
- **Use in agrochemicals industry and in veterinary products:** The heterocyclic aromatic compounds are used in agriculture industry as well as the veterinary field widely. It is used to make animal medicines, sanitizers and various other ointments. In field of agriculture they find usage in agro products like corrosion inhibitors, as copolymers and some form of polyfibres. These compounds are also used in making certain types of insecticides and pesticides. The heterocyclic compounds are widely used because they have very malleable structures which mean their structure can be molded in a subtle way to produce required compounds. The range of heterocyclic compounds can be acidic, basic or even neutral. Depending on the requirement of pH in a particular compound the appropriate compound is used. The structural changes can happen either when one hetero atom is changed to another or the position of the hetero atom is changed within the ring.

Large numbers of the drugs and the vast majority of the other heterocyclic mixtures with viable applications are not separated from natural sources however are chemically synthesized. The starting points of natural science really do anyway lie in the investigation of naturally occurring material. These have framed the reason for the plan of a significant number of the useful compounds grew consequently. The example of this inspiration from

nature to making compounds in labs can be seen in manufacturing of vat dyes which are based on the structure of naturally occurring indigo. Another such example is the continuing invention of new antibacterial agents based on the β -lactam structure of penicillin.

The naturally existing Aromatic heterocyclic compounds containing pharmaceuticals are synthesized and extracted using primarily 3 techniques which are discussed below:

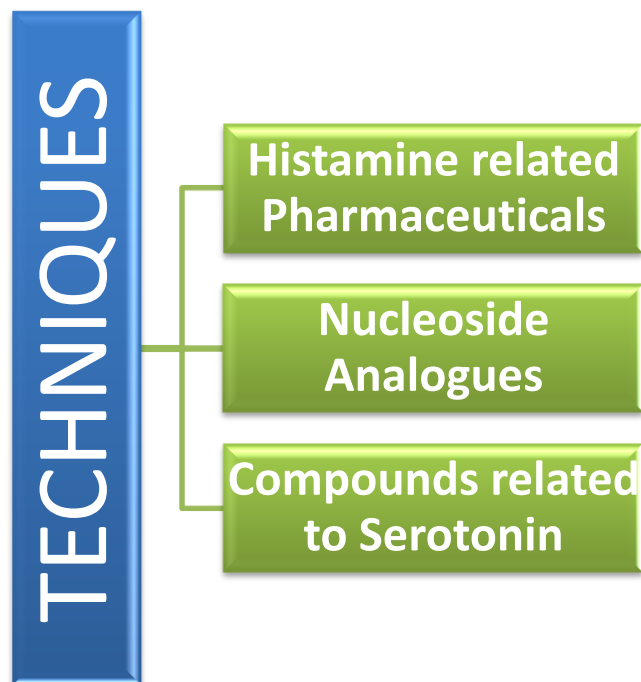


Figure 2 : List of Techniques

1. **Histamine related Pharmaceuticals:** Histamine is extracted from an amino acid named histidine in laboratory conditions using a decarboxylation reaction in presence of the enzyme histidine decarboxylase. Histamine is a mono substituted imidazole. It is a biologically produced amine that has a role to play in local immune responses. Histamine also acts as neurotransmitter. It is engaged with unfavorably susceptible responses and is secreted from skin cells on injury and furthermore it also plays a key role in regulation of the gastric secretions. Hence the pharmaceutical sector uses this to produce acidity regulator medicines like ranitidine and zantac that interfere with the receptors of histamine present in the lining of the stomach wall.

2. **Nucleoside Analogues:** To find the possible cure for ailments like cancer and other highly communicable viral diseases the most potent drugs are the ones that affect the DNA structure of the virus. The use of nucleoside analogues is the most efficient approach that has been intensively explored for making drugs of high potency. The analogues are produced from the fragments of nucleic acids that contain heterocyclic nitrogenous base that is called purine and pyrimidine that is linked to a sugar called 2'-deoxythymidine. When the nucleoside analogues are synthesized then the structure is modified by either modifying the heterocyclic nitrogenous base is modified, or the structure of sugars is modified, or both can be modified. Compound made in such a way interferes in the replicative cycle of a virus like Zidovudine/azidothymidine (AZT) (also called ZDV) and can prevent its replication in the human system. The mentioned modified medicine is used in potential cure of AIDS.
3. **Compounds related to Serotonin:** Serotonin is a naturally occurring product but it is produced in small quantity in nature which makes it very difficult to extract. To make serotonin available in mass form the scientists devised a chemical reaction to produce serotonin. Naturally serotonin is derived from the amino acid tryptophan. This can be artificially obtained by chemically reacting two enzymes, tryptophan hydroxylase and amino acid decarboxylase. The neurotransmitter serotonin has impact on both physical and mental health of human beings. In physiology serotonin plays a crucial role in aggregation of blood platelets and also acts as constrictor of arteries in the brain leading to migraine. Changes in serotonin concentration in the brain also alter mood and appetite. Therefore serotonin is used in production of anti-depressant drugs because in many researches it is found that decrease in level of naturally occurring serotonin in human brain can result in depressive episodes and ailments [8-10].

Conclusion

The field of organic chemistry is renovating intensely with newer aromatic heterocyclic compounds being synthesized for various medicinal and commercial purposes. The ever changing field of research and manufacturing of the organic compounds have paved way for more innovation and now the researcher not only make the traditional type of chemicals but are also ready to explore new dimensions of the heterocyclic compounds that are aromatic in nature.

Through this paper it can be concluded that pharmaceutical products having heterocyclic compounds can be manufactured using primarily three methods which are; first being the histamine related methods which is primarily used in pharmaceutical industry. Second is the nucleoside analogues method through which cancer combating medicines can be produced. The third method is through the serotonin related methods using which mental ailment related drugs can be produced. The aromatic heterocyclic compounds find usage in many fields such as isolation and study of genetic material, cosmetic industry and most widely in the pharmaceutical industry. Even though a lot of accomplishments have been achieved by the researchers yet to better understand the usage and synthesis of these compounds more extensive research is needed.

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References

1. Alami, Anouar. (2016). Heterocyclic Compounds: Synthesis, Characterization and Electrochemical Study. *Study and Prediction of Biological Activity*. Pg 12-21
2. Alexandru T. Balaban Daniela C. Oniciu and Alan R. Katritzky. (2004). Aromaticity as a Cornerstone of Heterocyclic Chemistry. *Chem. Rev.* 2004, 104, 5, 2777–2812
3. Das, Ratnesh & ROY, Atish & BAHE, Anil & CHANDERIYA, Aayushi & Dangi, Hemlata & MISHRA, Pratibha & MISHRA, Arunesh. (2021). Synthesis of nitrogen and oxygen containing heterocyclic compounds using nano catalyst: A review. *Journal of the Turkish Chemical Society Section A: Chemistry*. 8. 851-862. 10.18596/jotcsa.904246.
4. Deepak Behera, Subramanian Thiyagarajan, Puthannur K. Anjalikrishna, Cherumuttathu H. Suresh, Chidambaram Gunanathan. Ruthenium(II)-Catalyzed Regioselective 1,2-Hydrosilylation of N-Heteroarenes and Tetrel Bonding Mechanism. *ACS Catalysis* 2021, 11 (10) , 5885-5893.

5. Kaddouri, Yassine et. al. (2020). New Heterocyclic Compounds: Synthesis, Antioxidant Activity and Computational Insights of Nano-Antioxidant as Ascorbate Peroxidase Inhibitor by Various Cyclodextrins as Drug Delivery Systems. *Current Drug Delivery*.
6. Manuel Goubet, Marie-Aline Martin-Drumel, Florent Réal, Valérie Vallet, Olivier Pirali. Conformational Landscape of Oxygen-Containing Naphthalene Derivatives. *The Journal of Physical Chemistry A* **2020**, *124* (22), 4484-4495.
7. Karami, Bahador & Eskandari, Khalil & Khodabakhshi, Saeed. (2012). One-pot, three component approach to synthesis of multipart fused heterocyclic compounds: Synthesis of fused pyran-2-ones. *ARKIVOC: archive for organic chemistry*. (ix). 76-84.
8. Martí Gimferrer, Abdulrahman Aldossary, Pedro Salvador, Martin Head-Gordon. Oxidation State Localized Orbitals: A Method for Assigning Oxidation States Using Optimally Fragment-Localized Orbitals and a Fragment Orbital Localization Index. *Journal of Chemical Theory and Computation* **2022**, *18* (1)309-322
9. Steven J. Peters, Krutil Patel. Electron Distribution in 1,2,3-Benzotriazole and 1,2,3-Triazole Anion Radical Isomers: An EPR and DFT Study. *The Journal of Organic Chemistry* **2021**, *86* (21).
10. Tarun Kumar Roy, Kuntal Chatterjee, Jai Khatri, Gerhard Schwaab, Martina Havenith. Stepwise Microhydration of Isoxazole: Infrared Spectroscopy of Isoxazole Clusters in Helium Nanodroplets. *The Journal of Physical Chemistry A* **2021**, *125* (22).