1. INTRODUCTION

Heterocyclic chemistry has now become a separate field of chemistry with long history, present society and future prospects. The earliest compounds known to mankind were of heterocyclic origin. Life, like ours, is totally dependent on the heterocyclic compounds, it takes birth with purine / pyrimidine bases, nourishes on carbohydrates and in case of disease, is cured from medicines, many of which are heterocyclic in nature. Today, the heterocyclic chemistry delivers reagents and synthetic methods of its own traditional activity in synthesis of drugs, pesticides and detergents as well as into the related fields such as biochemistry, polymers and material sciences.

2. CHEMISTRY OF 1, 2, 4-TRIAZOLE

The presence of three nitrogen hetero-atoms in five-membered ring systems defines an interesting class of compounds, the triazole. This may be of two types, the 1,2,3-triazoles and the 1,2,4-triazoles. The name triazole was first given to the carbon nitrogen ring system C2N3H3 by Bladin who described its derivatives in early 1885, although the structures reported slightly incorrect1-2. An alternative name, pyrrodiazole was given by Andreocci in 1889 regarding it as a member of a class of compounds analogous to pyrrole.

A little interest emerged in this field from about 1925 to 1946. The successors of Andreocci carried out most intensive investigations of the chemistry of 1,2,4-triazoles. The chemical industry got renewed attention in the synthesis of both simple and fused triazole systems after the discovery that certain triazoles capable of inhibiting fog formation in photographic emulsions and some others being useful herbicides and convulsants3. All triazoles are of synthetic origin and there is no triazole ring system detected as yet in nature.

2.1 Aromaticity and Stability

The stability of 1,2,4-triazole nucleus is an inherent property of its aromatic nature. An aromatic sextet is formed by contribution of one π electron from each atom joined by double bonds and the remaining two electrons from a nitrogen atom. Such a system is stabilized by resonance and though the triazole nucleus may be represented by tautomeric forms, each tautomer is capable of extended resonance and its structure is more correctly represented as a hybrid to which the following canonical forms contribute3.

![1.2,4-triazole canonical forms](image)

It is also necessary to consider the tautomeric form where the imino hydrogen atom is at the 4-position. The canonical forms that contribute to this resonance hybrid are given below3.
This representation makes the assumption that the triazole nucleus actually consists of two hybrid structures, each representing an individual tautomeric form. In modern theories such a view is incorrect. A more suitable expression is to regard 1,2,4-triazoles as a true aromatic system, stabilized by resonance and represented below.

![Triazole Structures](image)

It is not intended to represent the charges on a nitrogen atom and on the hydrogen atom as separate, complete charges but merely as a slight, overall negative charge on the ring, balanced by a corresponding positive charge on the hydrogen atom.

2.2 Amphoteric Nature

1, 2, 4-Triazoles are amphoteric in nature, forming salts with acids as well as bases.

2.3 Tautomerism in Triazoles

Tautomerism is possible in both the structural isomers of triazoles.

a. Tautomerism in 1, 2, 3-triazoles

1,2,3-Triazoles have two tautomeric forms, \(1H\)-1,2,3-triazole (1) and \(2H\)-1,2,3-triazole (2).

![Tautomerism in 1,2,3-triazoles](image)

b. Tautomerism in 1,2,4-triazoles

1,2,4-Triazoles exhibit two tautomeric forms namely \([4H]\)-1,2,4-triazoles (3) and \([1H]\)-1,2,4-triazoles (4).

![Tautomerism in 1,2,4-triazoles](image)

The higher stability for tautomer (4) is indicated by temperature coalescence studies, x-rays studies, basicity measurements, dipole moment studies, NMR-spectra and theoretical methods.

c. Tautomerism in substituted-1,2,4-triazoles

Among the substituted 1,2,4-triazoles, 3-mercapto-1,2,4-triazoles exist in two tautomeric forms, because the labile hydrogen may be attached either to the nitrogen or the sulfur atom. It exhibits thione-thiol tautomerism forms shown below. This compound exists predominantly in thione (5) form.

![Tautomerism in substituted-1,2,4-triazoles](image)
Chloro-1,2,4-triazoles exist as 3-chloro-1H-1,2,4-triazole (7a), 3-chloro-4H-1,2,4-triazole (7b) and 5-chloro-1H-1,2,4-triazole (7c). These tautomers have the stability order: 7a > 7c > 7b according to physical and theoretical calculations. In case of bromo-1,2,4 triazoles, the possible tautomeric forms are, 3- bromo-1H-1,2,4-triazole (8a), 3-bromo-4H-1,2,4-triazole (8b) and 5-bromo-1H-1,2,4-triazole (8c). According to physical and theoretical calculations, the tautomer (8a) and (8c) are of similar energy and the most stable tautomer is (8c). These calculations agree with the results of Flammang et al.

3. SPECTROSCOPY OF 1,2,4-TRIAZOLE

Ultraviolet, infrared and nuclear magnetic resonance spectroscopic studies are very informative about the structure of 1,2,4-triazoles and their derivatives.

3.1 Ultraviolet spectroscopy

The unsubstituted 1,2,4-triazole (9) shows a very weak absorption at 205 nm in the ultraviolet absorption spectrum. Bathochromic shift occurs in N-acetyl-1,2,4-triazole (10), with the absorption band being located at 221.5 nm. A similar shift in the absorption maximum of 3,5-dimethyl-1,2,4-triazole (11) appears on conversion into N-acetyl-3,5-dimethyl-1,2,4-triazole (12).

Cyclopentadiene has an absorption maximum at 238.5 nm and by replacing carbon-carbon unsaturation with carbon-nitrogen unsaturation, known hypsochromic shift occurs, therefore, the lower value obtained for 1,2,4-triazoles is understandable.

A large hyperchromic effect occurs on the acetylation of triazole and its derivatives which may be compared qualitatively to the similar effect observed in passing from benzene to acetophenone. In case of 5-substituted-3-mercapto-1,2,4-triazoles, the thione-thiol tautomeric forms can also be differentiated by UV spectroscopy. The ultraviolet spectra of an ethanolic solution of 5 show two absorption maxima at 252 and 238.5 nm, with the lower value obtained for 1,2,4-triazoles.

3.2 Infrared spectroscopy

The infrared spectroscopy is also very useful in characterization of triazole ring. The absorptions in the region of 1570-1550 cm\(^{-1}\) due to N=N and in the region of 1640-1650 cm\(^{-1}\) due to C=N functions are the diagnostic features. 4-Amino-1,2,4-triazoles show the characteristic strong N–H stretching of a primary amine at 3400-3200 cm\(^{-1}\). In 5-substituted-3-mercapto-1,2,4-triazoles, the thione-thiol tautomeric forms can also be differentiated in the IR spectra by the presence of C=S absorption band at about 1325-1300 cm\(^{-1}\) for thione and by characteristic SH absorption band at about 2600-2550 cm\(^{-1}\) for thiol forms. The N–H stretching vibrations at 3165 cm\(^{-1}\) and 3450 cm\(^{-1}\) have also been found supportive of thione-thiol equilibrium. 4-Amino-1,2,4-triazoles have been characterized by the appearance of N–H bands in the regions of 3200-3100 cm\(^{-1}\). For NH\(_2\) group, the absorption bands appear at about 3400-3300 cm\(^{-1}\).

3.3 NMR and mass spectrometry

\(^{13}\)C NMR is a powerful tool to characterize 1,2,4-triazol-3-ones. In the spectrum of 1,2,4-triazol-3-ones two values for chemical shifts are obtained, one at about 164-173 ppm for imine (C=N) and the other at 150-160 ppm for carbonyl (C=O) carbon. In EIMS of 1,2,4-triazoles, a strong molecular ion peak is always observed and the cleavage of bonds between N1–N2 and N4–C5 has been observed usually. The triazole ring also undergoes N1–N2 and C3–N4 cleavage.
4. APPLICATIONS AND BIOLOGICAL ACTIVITIES

1,2,4-Triazole and its derivatives are an important class of compounds which possess diverse agricultural, industrial and biological activities, including anti-microbial, sedative, anticonvulsant, anticancer, anti-inflammatory, diuretic, antibacterial, hypoglycemic, antitubercular, antifungal, and antimicrobial activities. In recent years, the synthesis of these heterocyclic compounds has received considerable attention. This wide range of applications has been covered by more than sixty papers in the literature, many in the form of patents.

4.1 Agricultural applications

In the plant protection technology, the research has been promoted to discover more efficient pesticides to tackle new challenging problems. In order to selectively control the growth of weeds, a whole range of azole herbicides has been developed exhibiting high levels of activity, application flexibility, crop tolerance and low levels of toxicity to mammals. Triazoles play an important role among this class of heterocycles. A series of 1,2,4-triazole derivatives have been patented and extensively employed. One example of a herbicidal and pesticidal 1,2,4-triazole is given below.

\[ \text{(13)} \]

\[ \text{(14)} \]

4.2 Pharmacological applications

Over the last few decades, the biological and pharmaceutical properties of 1,2,4-triazoles have created considerable interest in their synthesis and characterization. 1,2,4-Triazole and its derivatives possess widely differing activities, e.g., bacteriostatic, antifungal, sedative, anticonvulsant, anticancer, anti-inflammatory, diuretic, and antiviral. Muscle relaxant and antihuman immunodeficiency virus (HIV). The pathogenic fungi cause life threatening infections that have become increasingly common during the past two decades. Fungal infections are common in individuals with immunocompromised hosts, such as patients undergoing anticancer chemotherapy or organ transplants and patients with AIDS. Three major fungal infections in immuno-compromised individuals are candidosis, aspergillosis and cryptococcosis. Whereas the most widespread human superficial and cutaneous fungal infections are dermatomycoses such as, tinea and onychomycosis. The common antifungal agents currently used in clinic are azoles (such as fluconazole, ketoconazole, and itraconazole), polyenes (such as amphotericin B) and echinocandins (such as caspofungin and micafungin) and allylamines (such as naftifine and terbinafine). In antifungal chemotherapy, azoles having fungistatic and broad-spectrum activities are used widely against most yeast and filamentous fungi. Fluconazole is preferred as first line antifungal chemotherapy with relatively low toxicity but is not effective against anavasiveaspergillosis and has suffered severe drug resistance. An improvement of fluconazole is itraconazole, having a broader antifungal spectrum and better tolerance but its variable oral absorption and low bioavailability has hampered its use. The second generation of azoles such as voriconazole, posaconazole, and ravuconazole, have been developed with improved profiles. They are noted for their broad antifungal spectrum, low toxicity, and improved pharmacodynamic profiles. Glycosylated triazole derivatives like 1-β-D-ribofuranosyl-[1H]-1,2,4-triazole-3-carboxamide (Virazol) belong to the highly potent drugs against DNA- and RNA-viruses. Moreover, this compound shows antitumor activity just as the anemeric 1-(2,3,4,6-tetra-O-acetyl-D-glucopyranosyl)-5-nitro-[1H]-1,2,4-triazole. The therapeutic use of non-steroidal anti-inflammatory drugs (NSAIDs) which are used in treatment of a number of arthritic diseases such as rheumatoid arthritis and osteoarthritis is limited because of their side effects, such as, gastrointestinal haemorrhage and ulceration. So, new drugs having potent anti-inflammatory activity with minimum side effects have been developed.

4.3 Industrial applications

Industrial applications of triazoles are given as follows.

- a. Chemical Industry
- b. Cotton industry
- c. Textile industry
a. Chemical Industry

Some selected triazole systems have been used as light emitting diodes (Electroluminescent devices)⁶⁶-⁶⁷. Some triazole systems have extensive use in the separation of silver from other metal cations in liquid membrane systems⁹⁰. In addition, these compounds are used as synthetic dyes and bleaching agents⁶⁸. Moreover, the inks having smooth writing properties also contain triazole derivatives e.g, 3-amino-5-mercapto-1,2,4-triazole⁹⁹. These compounds have also been reported as inhibitors of corrosion of copper, brass, aluminium and steel in marine environment and inhibit fog formation in photographic emulsions⁹⁶, plant growth inhibitors and herbicides.

b. Cotton industry

In the cotton industry, 3-amino-1,2,4-triazole under its trade name Amizol, has been used as a commercial defoliant for a number of years⁷².

c. Textile industry

The triazole derivatives have many applications in textile industry e.g, sodium salt of a sulphonatedtriazole derivative possesses good detergent action and N-benzylatedaminotriazoles have useful properties in inhibiting the acid fading of dyestuff⁷³.

5. CONCLUSION

Heterocyclic chemistry has now become a separate field of chemistry with long history, present society and future prospects. The earliest compounds known to mankind were of heterocyclic origin. Aromaticity and stability and Amphoteric nature are described Tautomerism in triazoles. Spectroscopy of 1,2,4-triazole are known by the Ultraviolet spectroscopy, Infrared spectroscopy, NMR and mass spectrometry. Applications and biological activities are like as described as Agricultural applications Industrial applications and Pharmacological applications.

REFERENCE