CHAPTER I

INTRODUCTION
Chapter I

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1. INTRODUCTION

1.1. BRIEF HISTORY AND IMPORTANCE OF HETERO CYCLIC CHEMISTRY

Heterocycles (Katritzky 1996, Katritzky 2008, Martins 2004, Druzhinin 2007 and Martins 2008) make up an exceedingly important class of compounds. In fact more than half of all known organic compounds are heterocycles. Many natural drugs such as quinine, papaverine, emetine, theophylline, atropine, procaine, codeine, morphine and reserpine are heterocycles. Almost all the compounds we know as synthetic drugs such as diazepam, chlorpromazine, isoniazid, metronidazole, azidothymidine, barbiturates, antipyrine, captopril and methotrexate are also heterocycles. Some dyes (mauveine), luminophores, (acridine orange), pesticides (diazinon) and herbicides (paraquat) are also heterocyclic in nature.

All these natural and synthetic heterocyclic compounds can and do participate in chemical reactions in the human body. Furthermore, all biological processes are chemical in nature. Such fundamental manifestations of life as the provision of energy, transmission of nerve impulses, sight, metabolism and the transfer of hereditary information are all based on chemical reactions involving the participation of many heterocyclic compounds, such as vitamins, enzymes, coenzymes, ATP, DNA, RNA and serotonin.

The maximum of pharmaceutical products are like natural products with biological activity are heterocycles. Therefore, researchers are on a continuous pursuit to design and produce better pharmaceuticals, pesticides, insecticides, rodenticides, and weed killers by following natural models. Heterocycles play a major part in biochemical processes and are also side groups of the most typical and essential constituents of living cells. Other important practical applications of these compounds can also be cited, for instance, their use as additives and modifiers in a wide variety of industries including cosmetics, reprography, information storage, plastics, solvents, antioxidants, and vulcanization accelerators. Finally, as an applied science, heterocyclic chemistry is an inexhaustible resource of novel compounds. A vast number of combinations of carbon,
hydrogen, and heteroatom's can be designed, providing compounds with the most diverse physical, chemical, and biological properties (Balaban 2004 and Wilson 1991). Among the approximately 20 million chemical compounds identified by the end of the second millennium, more than two-thirds are fully or partially aromatic, and approximately one-half are heteroaromatic. It is, therefore, easy to understand why both the development of new methods and the strategic deployment of known methods for the synthesis of complex heterocyclic compounds continue to drive the field of synthetic organic chemistry.

Organic chemists have been engaged in extensive efforts to produce these heterocyclic compounds by developing new and efficient synthetic transformations. The cyclic condensation reactions are of the most efficient method for synthesizing heterocyclic compounds. If some references are more recent, they correspond to results that became available to us during the elaboration of this thesis. We have arranged the large volume of data in terms of the type of heterocycles formed, starting with six membered rings, in the order of an increasing number of heteroatom, i.e., first with one heteroatom, two heteroatom, three heteroatom; and the heteroatom order of N > S.
1.2. CHEMISTRY OF QUINAZOLINE

The quinazoline is made up of two fused six-membered aromatic and heterocyclic rings system, that is benzene ring and a pyrimidine ring, C₈H₆N₂ is its chemical formula and it is yellow crystalline nature. Any derivative of benzene fused with pyrimidine nucleus may be described as quinazoline derivatives. Medicinally it's used to treat malaria and cancer.

In organic chemistry worldwide research, heterocyclic chemistry and its compounds are doing major role. In particular, heterocyclic structures form the basis of many pharmaceutical products. Quinazolines (Fig 1) are classes of fused heterocycles that are of considerable interest because of the diverse range of their biological properties.

Quinazoline² (German chinazolin) is universally used today to denote the 1,3 – benzodiazine ring system (I). The name quinazoline (Fig 2) was first proposed at the University of Leipzig in 1887 by Widdige on observing that his compounds were isomeric with the than known cinnoline (II) and quinoxaline (III) derivatives.
In 1869, Peter Griess was the first to report a compound containing the quinazoline (Fig 3) nucleus, denoted his compound by the term bicyanoamidobenzoyl (IV) now known as 2-cyano-4-quinazolone. The Bischler and co-workers at the University of Zurich named their compounds as derivatives of phenmiazin and Lellman and Stickel at the University of Tubingen used the term benzyleneamidine.

The numbering was proposed by Paal and Busch in year of 1889 (I), and its suggested by L. Knorr of the University of Berlin, who was the first to designate individual atoms of a ring with numbers. Before this time the positions were designated variously as follows.

On the basis of their physical and chemical properties, preparation of quinazoline nucleus falls into three distinct classes.

1. In quinazoline, substituents in the benzene ring are called benzene substituted quinazoline and not in the heterocyclic substituted quinazoline (Fig 4).

\[
\text{K}_3\text{Fe(CN)}_6 \overset{\text{aq. KOH}}{\longrightarrow} 70\% 
\]
Chapter I Chemistry of Quinazoline

2. Quinazoline nucleus (Fig 5) which have a keto group in the 2\textsuperscript{nd} position is called as 2(1)-Quinazolone, 4\textsuperscript{th} position of keto groups are known as 4, (3)-Quinazolone and 2\textsuperscript{nd}, 4\textsuperscript{th} positions of keto group in quinazoline ring is called benzoyleneurea.

![Chemistry of Quinazoline](image.png)

1. Hydrogenated quinazoline (Fig 6).
   Quinazoline nucleus when under goes mild reduction and oxidation it leads hydrogenated quinazoline

![Chemistry of Quinazoline](image.png)
2. REFERENCES