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SCHIFF BASE AS A LEADING MOLECULE TO SYNTHESIZED HETEROCYCLIC COMPOUNDS AND ITS APPLICAION

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ABSTRACT

Schiff bases are substances with a carbon-nitrogen double bond in their structure that are created when aldehydes or ketones react nucleophilically with primary amines under certain circumstances. Because of their simple synthesis, these molecules—which are created by condensation of primary amines with carbonyl compounds like aldehydes or ketones—are regarded as preferred ligands. Ketones need more complicated circumstances to generate Schiff bases than aldehydes, which react with primary amines to form Schiff bases more easily. This entails selecting catalysts with care, preserving a suitable pH range, selecting a solvent that can combine with the water created during the reaction to form an azeotropic combination, and making sure the reaction temperature is right. In Schiff bases, the carbon-nitrogen double bond that results from aldehyde reactions is referred to as Schiff bases.

KEYWORDS: Schiffbases, Nucleophilic addition reaction, Aldehydes, Ketones, Privileged ligands, Imine, Ketimine.

INTRODUCTION

Schiff bases are compounds characterized by the presence of a carbon-nitrogen double bond in their structure, formed when aldehydes or ketones undergo nucleophilic addition reactions with primary amines under specific conditions.

Schiff base ligands are considered as privileged ligands as they are simply synthesized by condensation of primary amines and carbonyl compounds, aldehydes or ketones.

Aldehydes react very easily with primary amines to form Schiff bases, but this process is not so easy for ketones. In order to obtain Schiff bases from ketones, it is necessary to pay attention to factors, such as the choice of catalyst, the appropriate pH range, the selection of a solvent that can form an azeotrope mixture with the water to be formed in the reaction, and the appropriate reaction temperature. The carbonnitrogen double bond in Schiff bases formed as a result of the reaction of primaryamines with aldehydes is called azomethine or aldimine, while the bond formed as a result of reaction with ketone is called imine or ketimine Schiff bases are named for Hugo Schiff, a German chemist, Nobel Prize winner, who discovered them in 1864 1

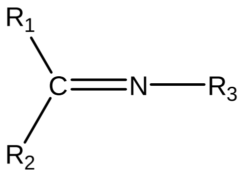


Fig. 1: General representation of Schiff base.

Due to their pharmacological properties they show broad applications in medicine. The C¼N in azomethine derivatives is essential for biological activity. Hence, several azomethines were reported to possess antimicrobial (antibacterial, antifungal), anticancer and diuretic activities.[2] Schiff base ligands have been extensively studied mainly because of their simple syntheses, availability and electronic properties. Recently due to significant roles in analytical chemistry, organic synthesis, refining of metals, electroplating, metallurgy, and photography, Schiff base coordination chemistry has attracted much attention.[3] Schiff bases play vital roles in modern coordination chemistry as well as in the improvement of bioinorganic chemistry. There are wide applications of Schiff bases in food and dye industry, analytical chemistry, catalysis, fungicidal and agrochemical activities.[5] The importance of Schiff base complexes in supramolecular chemistry, catalysis and material science, separation and encapsulation processes, biomedical applications and formation of compounds with unusual properties and structures has been well recognized and reviewed.[6] In biological systems, azomethine nitrogen of Schiff bases provides a binding site for metal ions to be attached with various bio-molecules like proteins and amino acids for anti-germ activities. Schiff bases generated by our body catalyze many metabolic reactions in the form of enzymes that show activities against various microbes. Biofunctions of Schiff bases and their metal complexes have been improved by various researches. They have antibacterial, antifungal, antiviral, antiulcer and anticancer activities depending upon the transition metal ions present in Schiff bases.[7] Over the past few decades, there have been many reports on applications, especially in biology including antibacterial, antifungal, anticancer, antioxidant, anti-inflammatory, antimalarial and antiviral activities and hence a review highlighting the uses of Schiff base ligands and their complexes is needed. Versatile applications of Schiff base metal complexes have been reported in review articles.[8–14]

PHYSICAL PROPERTIES OF SCHIFF BASE

Schiff bases are usually colored and transparent solids. They are used in the determination of metal amounts and in the identification of carbonyl compounds due to their precise melting points. Schiff bases exhibit a higher rotational flexibility in the carbon-nitrogen double bond compared to the carbon-carbon double bond, facilitating interconversion between stereoisomers. Schiff bases exhibit a higher rotational flexibility in the carbon-nitrogen double bond compared to the carbon-carbon double bond, facilitating interconversion between stereoisomers. The reason for this: polarization occurs in the azomethine bond due to the fact that nitrogen is more electronegative than carbon.

The stereoisomers of Schiff bases cannot be isolated with a few exceptions due to the very small energy difference between them. If only an electronegative group is attached to the nitrogen atom, stereoisomers become isolated, since this group reduces the ease of rotation around the azomethine bond. Since the electronegative group attached to the nitrogen atom in the azomethine group will push the negative charges of the nitrogen atom toward the carbon, this will cause a decrease in polarization and an increase in the character of the covalent double bond.

All compounds containing an azomethine group show basic properties due to the unshared electron pairs on the nitrogen atom and the electron donating feature of the double bond. Schiff bases show weaker basic properties compared to their corresponding amines. The reason for this is that while the nitrogen atom in amines undergoes sp3 hybridization, this hybridization turns into sp2 hybridization when the imine structure is formed. Since the s character will increase in hybridization, the basicity will decrease greatly.

The C double bond N system is a weak chromophore that shows absorption in theultraviolet field. Conjugation with phenyl groups shifts absorption to the visibleregion. In the presence of a deactivating substituent like a halogen on the aromatic ring, the absorption wavelength decreases, typically positioning aryl alkyl ketimines between the absorption values of dialkyl and diaryl ketimines.[5] The IR stretch bands of the Cdouble bond N system are generally observed at 1610–1635 cm_1 and that of Cdouble bond N+ at 1665–1690 cm.

CHEMICAL PROPERTIES

Schiff bases have many properties that vary according to the substituents attached to the azomethine group. The stability of the azomethine compound increases when there is an electronegative group attached to the nitrogen atom. The Schiff base formation reaction is reversible. As a result of the reaction, one mole of water is formed and the water in the environment shifts the direction of the reaction to the left. Therefore, the reaction is usually carried out in solvents where water can be removed from the environment by distillation, forming an azeotrope. If the reaction is carried out using amines containing an electronegative atom with unpaired electrons in the nitrogen atom, the reaction is completed and since hydrolysis will not occur, Schiff bases can be isolated with high efficiency. The structures of Schiff bases are determined by the tautomeric transformations that occur depending on the polarity of the solvent and the hydrogen bonds that occur in the molecule. The preferred conformation in terms of the stability of Schiff bases is the nonplanar structure seen in following figure.

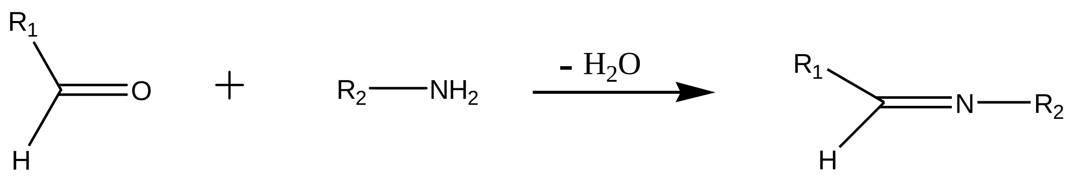


Figure 2.

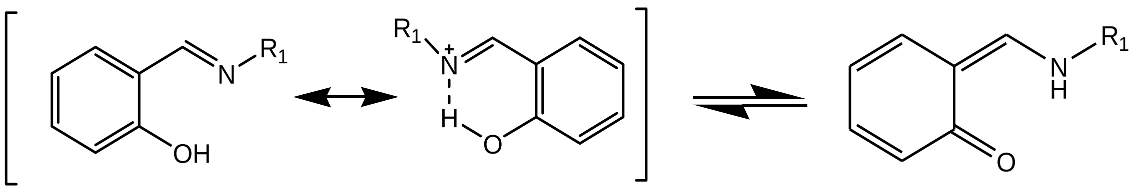
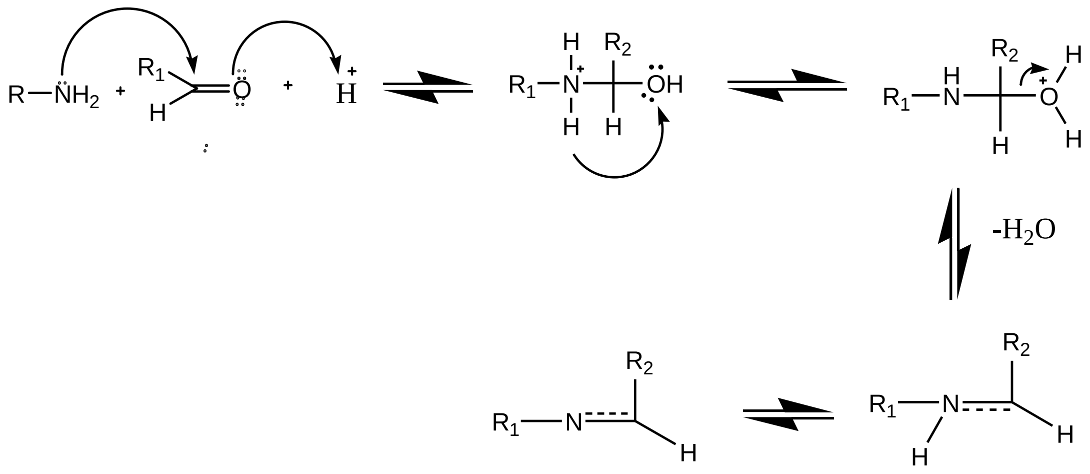


Figure 3.

MECHANISM OF SCHIFF BASED SYTHESIS

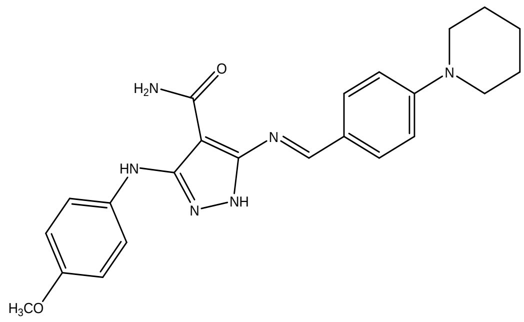


Schiff bases synthesized by reaction between the aldehyde or ketone and primary amine they formed the reaction intermediate which upon hydrolysis will give stable product. These reaction takes place in two steps. In the first steps carbonalamine formed from reaction between primary amine and carbonyl carbon. In the second steps dehydration occurs to formed Schiff base.[9-12]

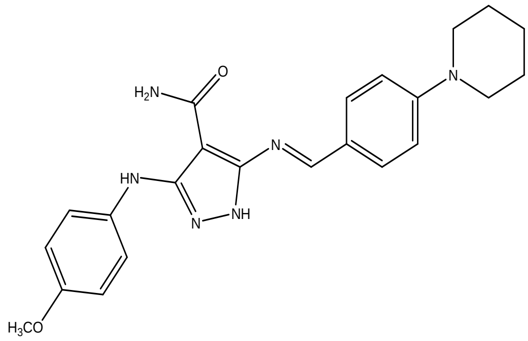
PYRAZOL CONTAING SCHIFF BASE AS ANTICANCER

Some of the Schiff bases are further derivated which are converted into different heterocyclic molecules, such derivatization result into different biological activity like antimicrobial, anticancer, antioxidant, antifungal, etc.

According to some research work it was found that pyarazol containg Schiff base shows anticancer activity A new series of mono and bispyrazol derivative was synthesized and their biological activity was evaluated as antimicrobial activity. From these study it was found that six Schiff bases exhibit best antiprolifarative activity against two cell lines HepG-2 and MCF-7, immunomodulatory, drug resistance and antiproliferative activity against healthy non-cancer vero cells that exhibit IC_{50} more than (120 micrometer), referemce drug used (tetracycline and amphotericin B)Among the all two mono pyrazol shows better activity. These derivative checked against dihydrofolate reductase (DHFR) and DNA gyrase exhibite IC_{50} more than reference drug trimethoprim and ciprofloxacin.[12-15]



COMPOUND A



COMPOUND B

1,4 BENZODIAZEPAM CONTAING SCHIFF BASE AS ANTICONVUSANT ACTIVITY

There are the different types 1,4 benzodiazepam derivative are available with there their significant biological activity. here the some derivatives were synthesized which contained the Schiff bases and they have anticonvulsant activity, which were improved as compared to standard drug.

Here 4 different types of 1,4 benzodiazepam containg Schiff bases were synthesized. they have checked activity on PTZ-induced acute clonic model. They have compared anticonvulsant activity with standared as a diazepam. They were found most significant action as compared to standared.

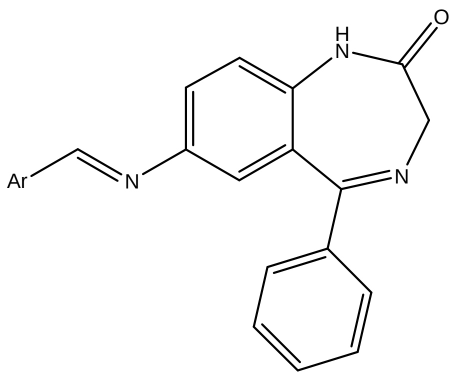
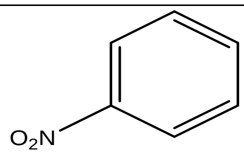
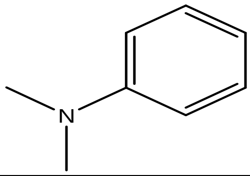
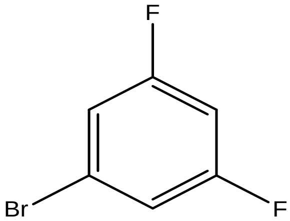
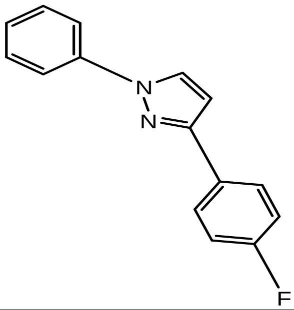


Fig. Substituted benzodiazepam containg Schiff bases.

Compound	Ar	Anticonvulsant activity (%)
A		57.73

B		74.4
C		52.68
D		57.63

CONCLUSION

Schiff bases, which are created by combining aldehydes or ketones with primary amines, are adaptable compounds having a carbon-nitrogen double bond. Because of their ease of production and customizability, they are useful in chemistry. Ketones are more difficult to create Schiff bases from than aldehydes. The proper catalysts, pH regulation, water-removal solvent, and temperature control are necessary for their effective manufacture. A result of their special qualities, schiff bases are used in chemistry, synthesis, materials science, and catalysis, among other areas.

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