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One Pot Synthesis and Biological Activities of Schiff Base

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A B S T R A C T

In the present study an intermolecular reductive Schiff base formation from nitroarene and benzaldehyde to yield diarylimine is carried out in the presence of iron powder and ammonium chloride. In the present study new Schiff base compound derived from 2- nitro 4, 6-dimethylpyridine with Indole-3-carboxaldehyde. The ligand and metal complexes have been screened for their microbiological activity. The experimental results suggest that Schiff base and metal complex ligands are more potent in anti-bacterial activities

Keywords: Tandem reaction, intermolecular reduction, green chemistry, Antibacterial activity, Antifungal activity

A R T I C L E I N F O

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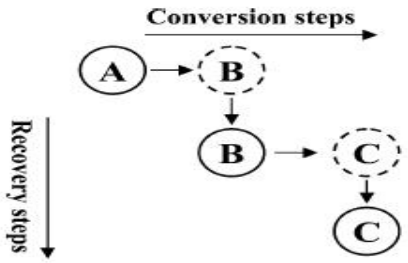
1. Introduction

Tandem reactions have several advantages over a series of individual reactions. First, they allow construction of complex structures in as few steps as possible.

However, organic synthesis, i.e., chemistry by mankind, still uses often a simple step-by-step approach to convert

a starting material **A** into a final product C, in which intermediate products B is isolated and purified for next conversion step.



Multistep synthesis of specialty chemicals normally requires stoichiometrically excess reagents, leading to high effluent loads. Hence, search is now on for clean, non-hazardous and 'green' chemical transformations, which will have negligible bi-products and high selectivity. The chemistry of biological science has produced a number of compounds that are now employed as antibacterial agents. Such type of compounds revealed great promise in this area is the Schiff bases. Schiff bases are well known in the pharmaceutical industry and have been shown to possess a broad spectrum of biological activities. In light of these significances, a variety of synthetic strategies have been developed for the preparation of Schiff base, despite the progress, the synthesis of these compounds remains less than ideal. Thus, the development of environmentally friendly benign, high-yielding and clean approaches for the synthesis of Schiff base is still remains a highly desired goal in organic synthesis. [1] The reported Schiff bases exhibits antibacterial [2-5], antifungal [6] and antitumor activity [7]. This has led to concentrate deep research on this class of compounds [8]. Similarly, the presence of hetero-atoms in the Schiff bases enhances activity [9].

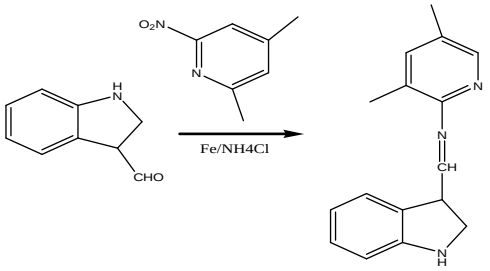
During the past two decades, considerable attention has been paid to the chemistry of the metal complexes of Schiff bases containing nitrogen and other donor atoms. Therefore, their synthesis has been the focus of much interest for organic and medicinal researchers. These promising results are encouraging further research in this field for future applications. Traditional formation of Schiff bases from nitroarene starting materials requires a two-step process in which the nitroarene is first reduced to the aniline, then isolated, and subsequently condensed with the desired carbonyl [10,11]. In view of these facts we can clear about that Schiff base are important not only in medical chemistry, but also in organic synthetic chemistry. Schiff base perhaps are synthesized in various method. Recently, catalytic Schiff base formation from nitroarenes and carbonyls has been reported [12,13]. Herein we wish to report our findings of a tandem iron reduction of nitroarenes and subsequent condensation of aldehydes under mild reaction conditions.

2. Materials and Methods

All chemicals and solvents were of AR grade. The percentage compositions of the elements (CHNO) of the compounds were determined using an Elementar Vario Micro Superuser (CHNS) analyzer. The Infrared spectra were recorded as potassium bromide (KBr) discs using 8400S FTIR Perkin Elmer Spectrophotometer.

Synthesis of ligand: N-(indolin-3-ylmethylene)-3, 5-dimethylpyridin-2-amine

15 gm Iron powder added to 2nitro 4,6 dimethyl pyridine (1 mole) ammonium chloride (4.5mole) heated to 85-95 ^{O} C and maintained to 90 to 120 minutes. Cool to 40^{O}C indole 3 carboxaldehyde (1 mole) added and maintained at 65-75 ^{O} for 6 hours. On cooling the reaction mixture, sharp Brown Crystal separated out (yield 50%, m.p.173 -178^{O}C). The synthesized Schiff base stable to air at room temperature, soluble in DMSO, DMF and THF.



3. Results and Discussion

Infrared Spectral Analysis

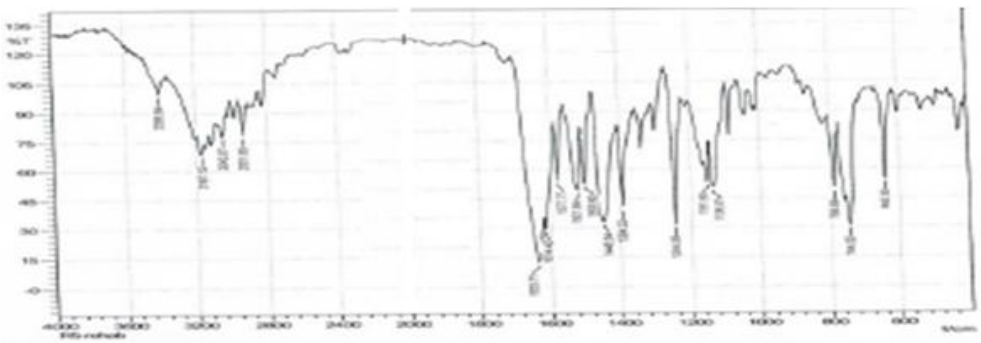


Figure 1: IR spectrum of N-(indolin-3-ylmethylene)-3,5-dimethylpyridin-2-amine

The synthesized Schiff base showed a sharp band at 1604-1633 cm*P*-1*P* assigned to the azomethine group (-C=N), thus clearly gave an evidence of intramolecular condensation between an aldehydes and nitro derivative. A sharp band at 3147-3167 cm*P*-1*P* assigned to N-H of indole moiety.

^{1}H NMR

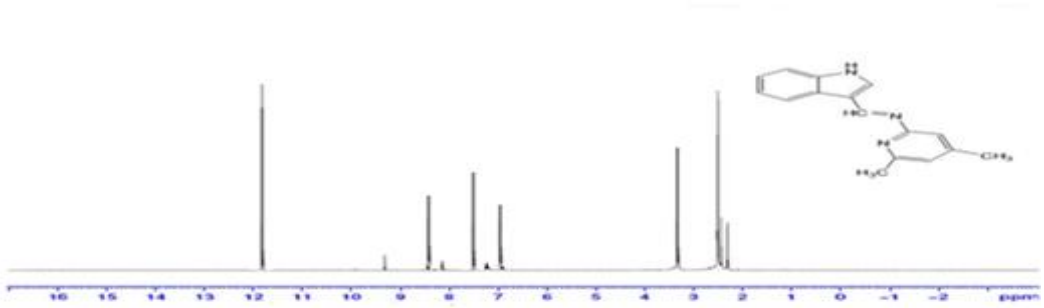


Figure 2: NMR spectrum of N-(indolin-3-ylmethylene)-3,5-dimethylpyridin-2-amine

^{1}H NMR spectrum of in DMSO-d6. A signal The azomethine proton signal appears at 8.29 and the aromatic protons at the region 7.2-8.29 ppm . 1H NMR spectrum of R4 showed a signal of indole N-H at 12.3 as a broad band, the azomethine proton at 9.9 ppm. The other aromatic protons in expected region. Indole N-H at 11.86, and the azomethine

Biological activity

Antimicrobial Activity:

The antibacterial activity of the synthesized compound was screened against the Gram positive bacteria such as Bacillus subtilis and Staphylococcus aureus and the Gram-negative bacteria, that is, Pseudomonas aeruginosa and Escherichia coli using nutrient agar medium. The antifungal activity of the compounds was tested against Aspergillus niger using Potato dextrose agar (PDA) medium. The minimum inhibitory concentration (MIC) was carried out using micro dilution susceptibility method. Ciprofloxacin was used as a standard antibacterial drug, and Fluconazole was used as a standard antifungal drug. The observed data on the antimicrobial activity of compounds and control drugs are given in Table 1. The MIC values were determined as the lowest concentration that completely inhibited visible growth of the microorganisms. The investigation of antibacterial screening (Table 1) revealed that some of the newly synthesized compound showed moderate to-good inhibition at 25–100 ҂g/mL in DMSO. The investigation of antifungal screening (Table 1) revealed that some of the newly synthesized compound showed moderate-to-good inhibition at 25–100 ҂g/mL in DMSO.

Table 1: Minimum inhibitory concentration (MIC) of the synthesized Schiff base

Compound	**Gram positive Bacteria**		**Gram negative bacteria**		**fungi**
	B subtilis	**S aureus**	**P aeuroginosa**	**E coli**	**A niger**
Schiff base	**375**	**400**	**175**	**375**	**175**

4. Conclusion

We developed the new route for Schiff bases in which we maintained the green chemistry parameter. At the same time yield of product is also increased by maintaining purity of products. This type reaction is economically attractive method for synthesis of Schiff base compounds and their derivatives. This methodology uses only Fe powder in ammonium chloride as a reducing agent for nitro derivatives which upon reduction spontaneously condense with an aldehyde in situ. The synthesized Schiff base compound therefore, present a new scaffold that can be used to yield potent antimicrobial compounds. It can be concluded that these compounds certainly holds great promise towards good active leads in medicinal chemistry.

5. Acknowledgements

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