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Cascade 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. New Schiff base ligand synthesized from 4 nitro toluene with 2-hydroxy-3-methoxy benzaldehyde. 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, metal complexes, green chemistry biological properties.

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].

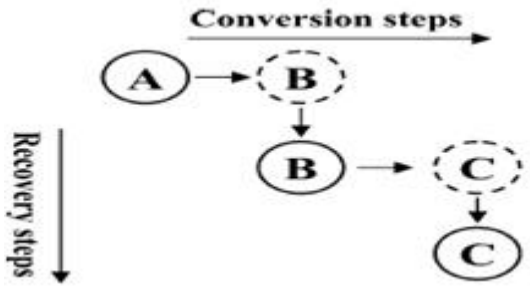


Figure 1

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: 2-methoxy-6-((p-tolylimino) methyl) phenol: 15 gm Iron powder added to 4-nitro toluene (1 mole) ammonium chloride (4.5mole) heated to 85-95^{O}C and maintained to 90 to 120 minutes. Cool to 40^{O}C 2 hydroxy 3-methoxysalicylaldehyde (1 mole) added and maintained at 65-75 ^{O} for 6 hours. On cooling the reaction mixture, sharp orange crystals separated out (yield 80%, m.p.98 -99^{O}C). The synthesized Schiff base stable to air at room temperature, soluble in DMSO, DMF and THF.

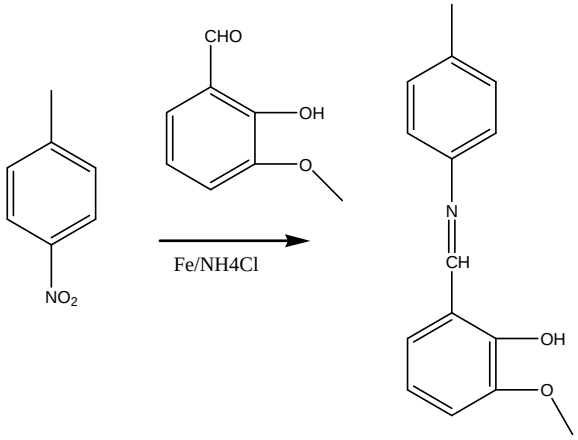


Figure 2

3. Results and Discussion

Infrared Spectral Analysis

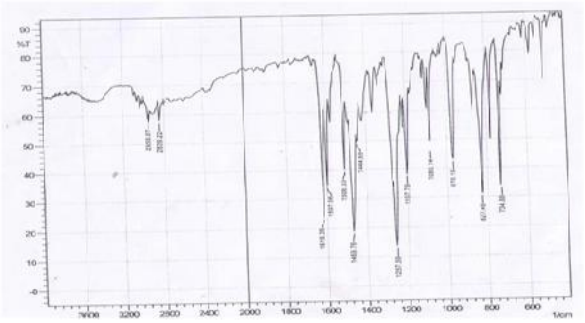


Figure 1: IR spectrum of 2-methoxy-6-((p-tolylimino) methyl) phenol

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.

1 H NMR

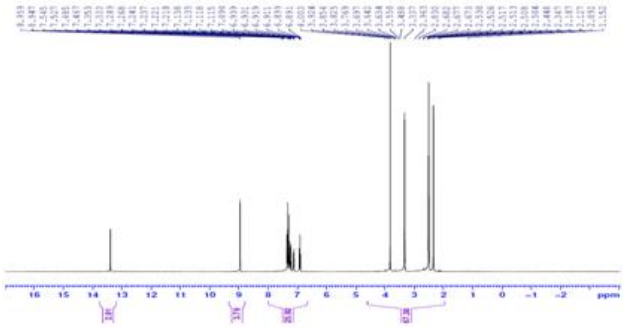


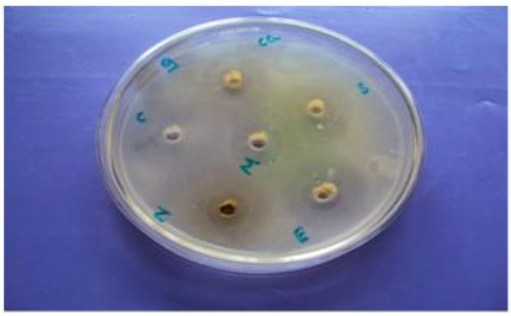
Figure 2: NMR spectrum of methoxy-6-((p-tolylimino) methyl) phenol

^{1}H NMR spectrum of 2-methoxy-6-((p-tolylimino) methyl) phenol in DMSO-d6 showed a signal at13.39 ppm attributed to hydroxyl proton while a signal at 8.95 ppm asigned to azomethine proton. The aromatic protons appear in the region 6.9-7.35 ppm as a multiple signal. The signal of OCH3 protons appear at 3.82 ppm and the signal of CH3 proton at 2.34 ppm

Biological activity

Antibacterial

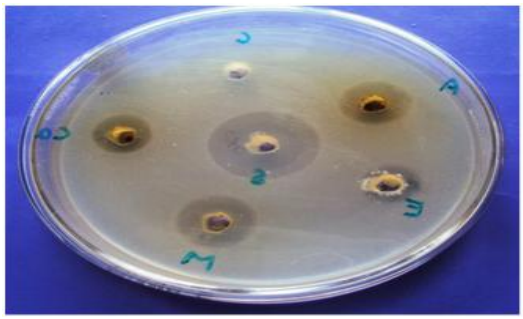
The Schiff base 2-methoxy-6-(p-tolylimino) methyl phenols screened for in vitro biological screening effects against the bacteria Bacillus subtilis. Paper discs of Whatman filter paper no. 1 were cut and sterilized in an autoclave. The paper discs were saturated with 10 µl of the compounds dissolved in DMSO solution or DMSO as negative control and was placed aseptically in the Petri dishes containing Nutrient agar media inoculated with the above mentioned two bacteria separately. The petridishes were incubated at 37^{0}C and the inhibition zones were recorded after 24 h of incubation. Antibiotic disc of amoxycillin100 µg/disc) was used as positive control, while DMSO used as negative control.



Ca: standard drug amoxycillin C: control S: 60mg in DMSO M: 40mg in DMSO E: 20mg in DMSO N: 10mg in DMSO

Antifungal

The Schiff base 2-methoxy-6-((p-tolylimino) methyl)phenol screened for their antifungal activity against fungi viz. candida. Filter paper discs of 5 mm in size, prepared by using Whatman filter paper no. 1 (sterilized in an autoclave) was saturated with 10 µl of the compounds dissolved in DMSO solution. The fungal culture plates were inoculated and incubated at 25± 2^{0}C for 48 h. Antibiotic discs of and fluconazole (100 µg/disc) was used as positive control, while DMSO used as negative control. The plates were then observed and the diameters of the inhibition zones (in mm) were measured and tabulated.



Ca: standard drug fluconazole C:control S: 60mg in DMSO M:40mg in DMSO E: 20mg in DMSO A: 10mg in DMSO

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, presents 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.

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6. References

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