

# SYNTHESIS, CHARACTERIZATION AND ANTIOXIDANT STUDIES OF HETEROCYCLIC SCHIFF BASE DERIVATIVES

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## ABSTRACT

Due to diverse applications of schiff base derivatives is the significant subject of research. In view of this, we have synthesized and characterized Schiff base derivatives by condensation of appropriate amount of *p*-amino Phenol with respective aldehyde in glacial acetic acid. The structural investigation of the synthesized compounds was done by UV-Vis., IR, <sup>1</sup>H and <sup>13</sup>C NMR and elemental analysis. The synthesized compounds were evaluated for their antioxidant potential using 2,2-diphenyl-1-picrylhydrazyl (DPPH) as a scavenging agent. The test compounds exhibited remarkable antioxidant and DNA binding activities. The antioxidant activity of Schiff base derivatives also investigated by DPPH free radical and H<sub>2</sub>O<sub>2</sub> scavenging method.

## KEYWORDS

Heterocyclic; Schiff Base; Antioxidant; DPPH.

## INTRODUCTION

Normally, heterocyclic chemistry is useful in biosynthesis and in drug metabolism as well (Benramdanea 2015). A large number of synthetic heterocyclic compounds possess important applications and many are valuable arbitrates in synthesis (Nagesh 2015 and Kumar 2015). The chemistry involved in fused heterocyclic analogues has attained significant consideration over the past few decades owing to their synthetic and excellent biological importance (Ali 2007). Quinolines and their derivatives are considered as important scaffolds in medicinal chemistry because of their wide spectrum of biological activities (Lalehzari 2008). Annually, nearly 2000 tons of quinolines are produced from all over the world indicating its biological importance (Klein 2000). A Schiff base is a compound with a functional group of carbon- nitrogen double bond with an aryl or alkyl group and synthesized by the condensation reaction of aldehyde/ketone with primary amine in the presence of dil. acid. The formation of C=N double bond plays an important

role in organic synthesis, which may be achieved by the reaction of aldehydes and amines in acidic medium which leads to synthesis of imines (Schiff base). The presence of more electronegative nitrogen, oxygen or sulphur atoms on the ligand structure is established to enhance the coordinating possibilities of ligands. Hence, there has been a continuous quest over the many years for nitrogen or sulphur donor ligands, which possess a variety of coordination possibilities. Schiff base ligands are able to coordinate metals through imine nitrogen and another group, usually linked to the aldehyde or ketone. Schiff base ligands are able to coordinate many different metals and to stabilize them in various oxidation states. The reactivity of carbonyl functions of 1,3-diketones and metal 1,3-diketonates towards amino compounds has been utilized in the synthesis of a large number of multidentate and macrocyclic ligands (Saritha 2006). Schiff base often has the property of luminescence, especially, when its metal complexes have structure of rigidity plane and rich-electronic conjugation. Schiff base and its derivatives are important for the photometric and fluorescent analysis (Jun 2012). Increase in oxidative stress boosts the high glucose level in our human body which prompts cellular hypertrophy by excess production of ROS. Clinical analyses also show that high glucose increases the pathology of diabetes by enhancing the oxidative stress. In common, ROS are identified as a chief source of molecular damage during hyperglycemia which can be efficiently neutralized by antioxidants. The antioxidant activity of the synthesized compounds may be assessed by many methods and among them DPPH method is the most prevalent method which is discussed in this present work. DNA is one primary target for ROS but also for various drugs that may eventually affect its functioning thereby regulating cell activities and leading to the control of diseases (Hassan 2000).

These compounds are effective and stereo specific catalysts for oxidation, reduction hydrolysis and also for biological activity and other transformations of organic and inorganic chemistry. A large number of Schiff bases and their complexes have been studied for their interesting and important properties, e.g., their ability to reversibly bind oxygen, catalytic activity in hydrogenation of olefins and transfer of an amino group, photo chromic properties, and complexing ability towards some toxic metals. Synthesis of quinoline derivatives and its analogues has been an attractive goal for the synthetic organic chemists due to their pharmacological role as substructures in the wide variety of designer and natural products (Sies 1997).

## **EXPERIMENTAL WORK**

### Chemicals

p-hydroxy benzaldehyde, p-amino Phenol, Phenyl hydrazine, glacial acetic acid, Methanol were used. All solvents were of AR and LR grade which were used without further purification. Precoated aluminium sheets (silica gel 60 F<sub>254</sub>, Merck Germany) were used for thin layer chromatography (TLC) and spots were visualized under UV light.

### Instruments/Equipment

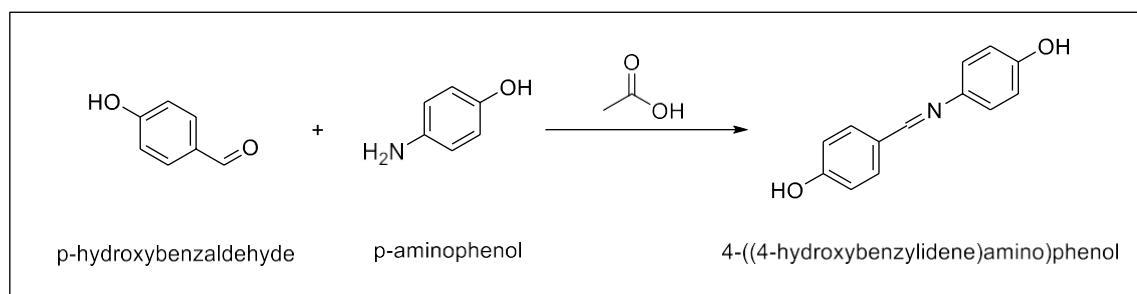
UV-Visible (Perkin Elmer Lambda 40), Infra red (Agilent technologies) and NMR spectrophotometer (Bruker DPX-300 NMR), UV light cabinet and Melting point apparatus (Veego Technology).

### Synthesis of Schiff Base Ligand (L<sub>1</sub>)

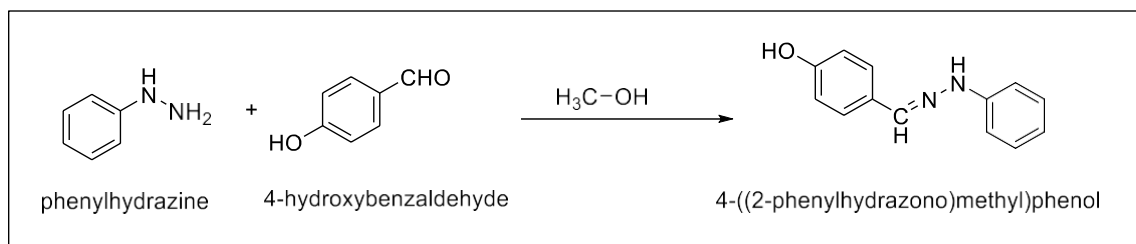
An ethanolic solution of p-hydroxy benzaldehyde (0.61 g, 5 mmol) was slowly added to the acetic acid solution of p-amino Phenol (0.54 g, 5 mmol) in 250 mL round bottom flask. The dark purple colored solution was refluxed for 2 h with constant stirring and poured into cold water. The completion of the reaction was monitored by using TLC (ethyl acetate: hexane, 1:1). The blackish precipitate that obtained was filtered, washed with distilled water and ethyl acetate and finally dried under vacuum on fused CaCl<sub>2</sub> and recrystallized in ethanol. Yield 83%. The synthesis of Schiff base ligand is represented in **Scheme I**.

### Synthesis of Schiff base ligand (L<sub>2</sub>)

To the solution of phenylhydrazine (5 mmol) in 10-20 ml of methanol, p-hydroxy benzaldehyde (5 mmol) dissolved in 10-20 ml of methanol was added. The mixture was stirred for 15 minutes and kept overnight. The yellow precipitate was filtered, washed with ethyl acetate and dried in vacuum desiccator. Yield is 81%. The synthesis of Schiff base ligand is represented in **Scheme II**.



**Scheme I.** Synthesis of Schiff base ligand (L<sub>1</sub>).



**Scheme II.** Synthesis of Schiff base ligand (**L<sub>2</sub>**).

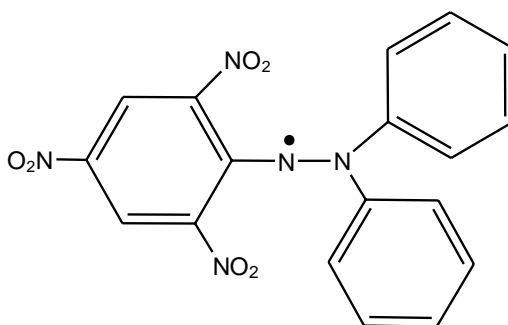
## ANTIOXIDANT STUDIES

### *DPPH Radicals Scavenging Activity*

Scavenging activity of antioxidants compounds was measured by the DPPH (2,2-diphenyl-1-picryl-hydrazyl) (**Figure 1**) free radical assay which was the best method based on electron-transfer. DPPH free radical scavenging activity of the compound was measured by the method (Bakar 2011). Test compound (1ml) in methanol and in each solution 0.5 ml 0.1 mM DPPH free radical in methanol was added. All test compounds were incubated at 60°C for 2 h and the decrease in absorbance was noted at 511 nm using UV-Vis. spectrophotometer. Absorbance of DPPH without compound was recorded at 513 nm as a control. For each of the test compound experiment was done in triplicate and antioxidant property of the compounds was measured by using the equation:

$$\% \text{ Inhibition} = \frac{A_{\text{Control}} - A_{\text{Sample}}}{A_{\text{Control}}} \times 100$$

Where  $A_{\text{control}}$  = absorbance of DPPH free radical in methanol without an antioxidant and  $A_{\text{sample}}$  = absorbance of DPPH free radical in the presence of an antioxidant.



**Figure 1.** 2,2-diphenyl-picryl-hydrazyl (Free radical).

**Hydrogen Peroxide Scavenging Activity**

The scavenging ability of the compound to hydrogen peroxide was determined by using standard method (Patel 2005). Hydrogen peroxide solution (2mM) was prepared in phosphate buffer (50mM, pH 7.4). 3 ml of test compounds, 1.8 ml of H<sub>2</sub>O<sub>2</sub> solution was added and absorbance was recorded after incubating 10 minutes against phosphate buffer as a blank by UV-Vis spectrophotometer. The absorbance of test samples was noted at 240 nm and compared with hydrogen peroxide concentration which was taken as a control. The scavenging ability of hydrogen peroxide was calculated using following equation:

$$\% \text{ Inhibition} = \frac{A_B - A_T}{A_B} \times 100$$

Where A<sub>B</sub> was the absorbance of blank (without compounds) and A<sub>T</sub> was the absorbance of tested samples.

**RESULTS AND DISCUSSION**

All the synthesized compounds are stable in air. The ligand and its complexes are soluble in ethanol, methanol and DMSO. The solubility of the ligand and metal complexes in different solvents is given in **Table 1**. The reaction was monitored by thin layer chromatography (TLC) in solvent system in ethyl acetate: hexane(1:1) for ligand. The molecular weight, analytical data, molar conductance, colour, % yield and melting point are presented in **Table 2**.

**Table 1.** Solubility of the ligands

Solvents	Ligand, (L <sub>1</sub> )	Ligand, (L <sub>2</sub> )
Methanol	√	√
Water	X	X
DCM	√	√
Ethyl acetate	√	√
Petroleum Ether	X	√
Chloroform	√	√

Hexane	X	√
Acetic acid	√	√

Compounds (Mol. Wt.)	Yield (%)	Colour	M.P. (°C)	Analytical data % Calcd.			
				C	H	N	O
[C <sub>13</sub> H <sub>10</sub> NO <sub>2</sub> ], (L <sub>1</sub> ) (212)	83	Blackish Purple		73.58	4.71	6.6	15.09
[C <sub>13</sub> H <sub>10</sub> N <sub>2</sub> O], (L <sub>2</sub> ) (210)	81	Yellow		74.28	4.76	13.33	7.61

**Table 2:** Molecular weight, analytical data, molar conductance, colour, % yield and melting point

### <sup>1</sup>H NMR Spectra

The <sup>1</sup>H NMR spectra of ligand was exhibited resolved signals. <sup>1</sup>H NMR spectrum showed a signal at 10.64 ppm and 12.03 ppm as a singlet due to two phenolic protons for the heterocyclic ligand 1 and 2, respectively (**Fig. 2**). The signal appears at 12.83 ppm assigned to N-H proton (2° amine) of heterocyclic ligand 2. The signal appears at 8.71 and 8.91 ppm as singlet may be attributed to proton of azomethine group for the heterocyclic compounds 1 and 2, respectively. The signals as multiplet for the ligand appear at 7.31–8.51 ppm due to protons of aromatic rings.

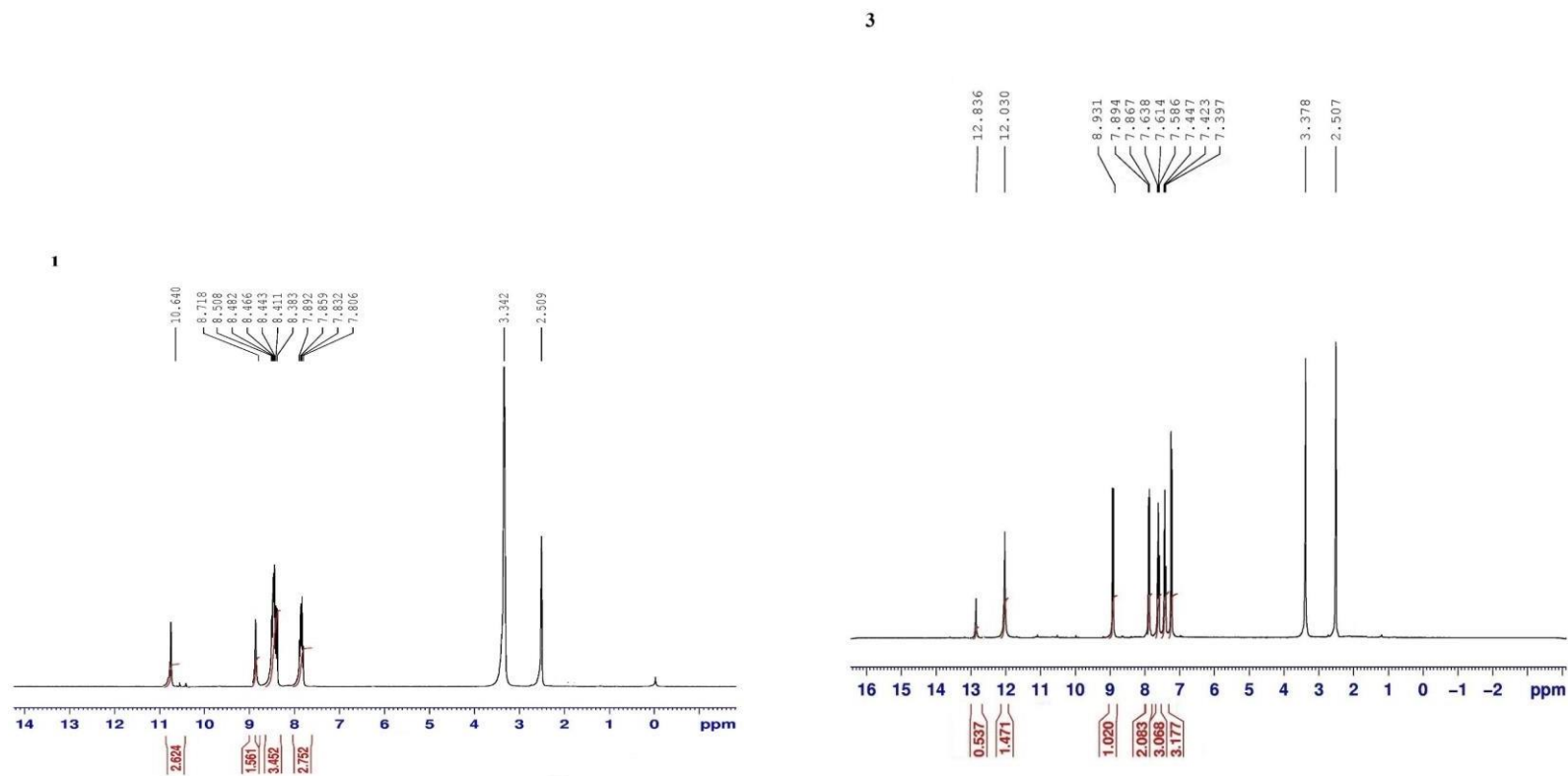
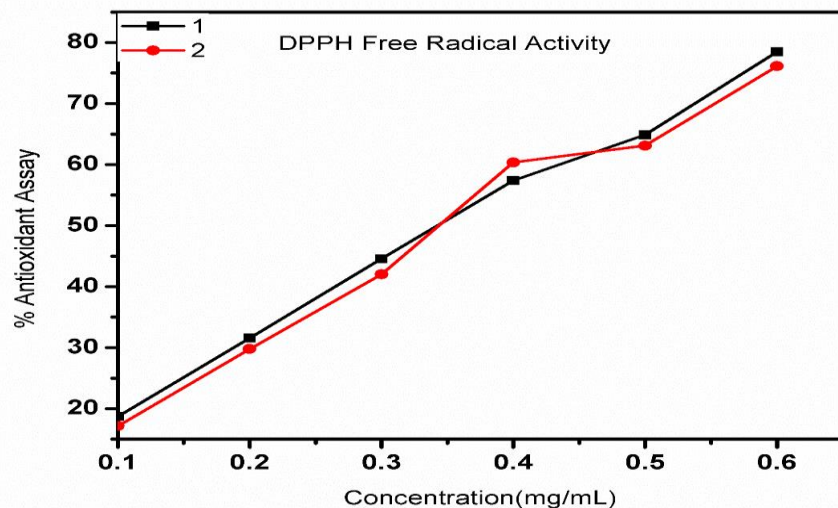


Figure 2: <sup>1</sup>H NMR Spectrs of Heterocyclic Schiff Base Ligand (L<sub>1</sub> & L<sub>2</sub>)

## ANTIOXIDANT STUDIES

### *DPPH Radicals Scavenging Activity*

The DPPH Free radical assay is a very significant and appropriate method which provided an easy and rapid way for the estimation of the antioxidant activity of the test compounds. It is a stable free radical that can accept hydrogen ion or electron on reaction with antioxidant compound and become reduced. The change in colour after the reaction and decrease in absorbance at 512 nm reveals that scavenging activity heterocyclic Schiff base Ligand (**L<sub>2</sub>**) is greater than heterocyclic Schiff base Ligand (**L<sub>1</sub>**) **Figure 3**).

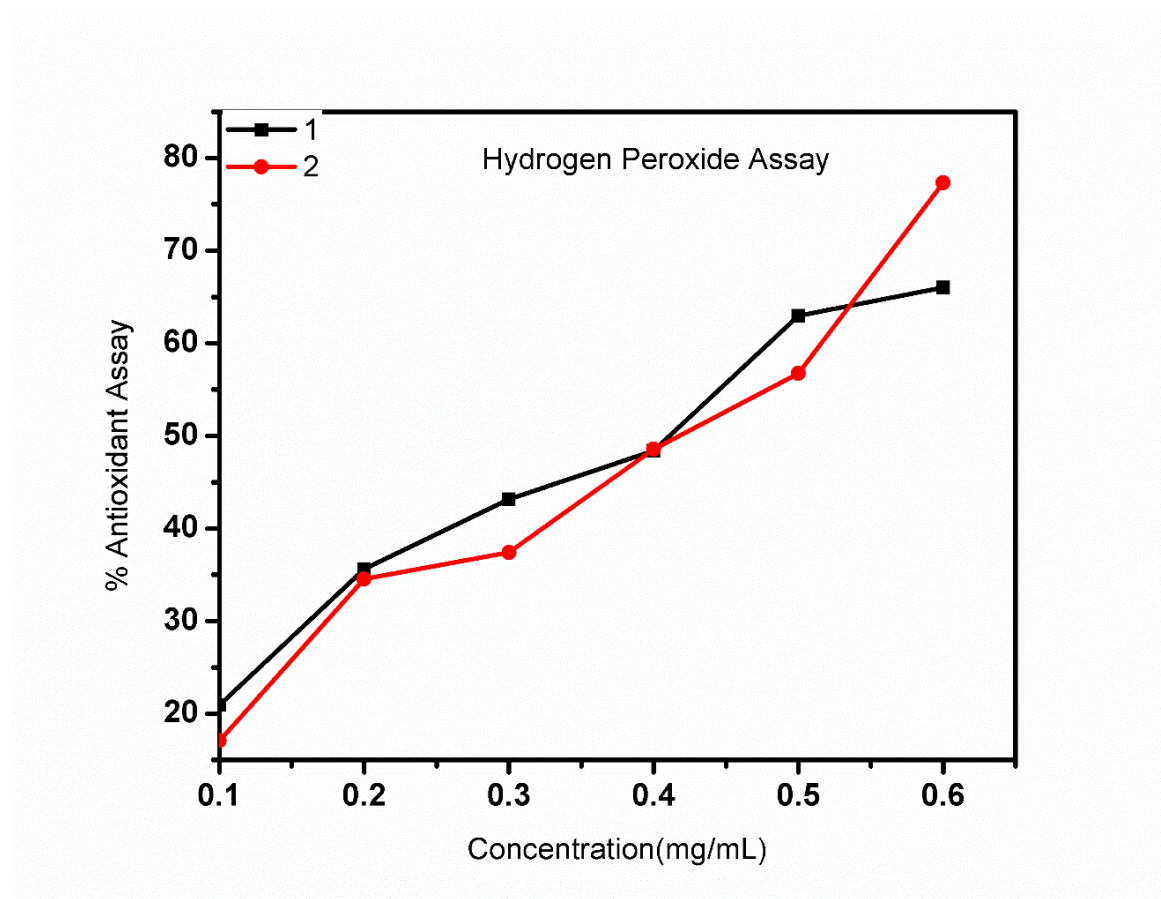


**Figure 3: DPPH Free Radical Scavenging Activity of Heterocyclic Schiff base Derivatives (L<sub>1</sub> & L<sub>2</sub>)**



### Hydrogen Peroxide Scavenging Activity

Hydrogen peroxide radical is very reactive species among all the oxygen containing compound used for the estimation of antioxidant activity of compounds. .Therefore, the antioxidant activity of our compounds also estimated by hydrogen peroxide radical. The capabilities of target compounds to scavenge the hydrogen peroxide radicals were monitored using UV-vis. Spectrophotometer (**Figure 4**). The investigation of antioxidant assay demonstrates that Heterocyclic Schiff Base Ligand (**L<sub>2</sub>**) showed the greater rate of H<sub>2</sub>O<sub>2</sub> scavenging activity and the results are accordance with the results obtained by DPPH free radical method.



**Figure 4. Hydrogen Peroxide Scavenging Activity of the Heterocyclic Schiff base Derivatives (L<sub>1</sub> & L<sub>2</sub>).**

### CONCLUSIONS

In this project report, heterocyclic Schiff base derivatives were synthesized and structurally characterized by UV-Vis., IR and  $^1\text{H}$  NMR spectral analysis and Antioxidant properties. All synthesized compounds are stable in air. Heterocyclic Schiff Base derivatives are known to have a wide spectrum of applications in the design and development of drugs for the treatment of various diseases caused by different microorganisms like bacterial, fungal, amoebal, viral and several other pathogenic diseases.

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