

## Syntheses and Spectroscopic Characterizations of Some Vanillin Schiff Bases as Potential Metal Chelators

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### ARTICLE INFO

#### Article history:

Received: 16 August 2022;

Received in revised form:

12 October 2022;

Accepted: 22 October 2022;

#### Keywords

Schiff bases,  
Vanillin,  
Anilines,  
Melting points,  
IR/UV Spectra.

### ABSTRACT

New vanillin Schiff bases (A<sub>1</sub>-A<sub>6</sub>) have been prepared. The Schiff bases were synthesized via condensation of vanillin with various substituted anilines. Compounds A<sub>1</sub>-A<sub>4</sub> came out as crystals of different colours while A<sub>5</sub>-A<sub>6</sub> were obtained as thick viscous liquid. The organic compounds were characterized by IR spectra, UV/Visible spectra and melting points measurements. Purity of the new compounds was revealed by their sharp melting points. The coordination feasibility of the compounds was tested using compound A<sub>1</sub> with Zn<sup>2+</sup>, Cu<sup>2+</sup>, Co<sup>2+</sup> and Ni<sup>2+</sup> salts.

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### Introduction

Schiff bases are important class of compounds, which are characterized by azomethine functional groups. They are usually formed from the reaction of primary amine and an active carbonyl compounds which may be aliphatic or aromatic. Schiff bases with aryl substituents are more stable and readily synthesized than those containing alkyl substituents which are relatively unstable and readily polymerizable [1]. The study of Schiff bases has been a subject of considerable interest especially in the field of coordination and supramolecular chemistry, biochemistry, pharmaceutical chemistry etc. due to their preparative accessibility, structural variety and versatile coordination ability with easily tunable steric and electronic effects [2-5]. For the past few decades, many Schiff bases and their metal(II) complexes have been prepared [6-9], vanillin Schiff bases in particular are of special interest because of their immense applications ranging through biological, agrochemical to optical as well as electroluminescence applications [10-13]. Their catalytic role in carbonylation, polymerization and carbon-carbon cross coupling reactions [14] (e. g. Suzuki-Miyaura) cannot be overemphasized.

Over the years, Schiff bases especially those derived from vanillin have gained importance due to their application in many pharmacological activities like antibacterial [1,15,16], antifungal [17], anti-proliferative [18], antitumor [19], and antipyretic properties.

Considering the increased occurrences of severe bacterial infections in immunological deficient patients coupled with the development of drug resistance among pathogenic organisms there is a great need to find new organic compounds that will be active against drug resistant bacteria. In view of the above and the current growing

interest in the development of bacteria resistant drug, we are motivated to synthesize, structurally characterize and study of antibacterial activity of vanillin Schiff bases derived from electronically and structurally diversified 4-((phenylimino)methyl)phenol (**scheme 1**). In this present work a novel series of six Vanillin Schiff bases were synthesized (A<sub>1</sub> to A<sub>6</sub>) and structurally characterized by spectroscopic studies.

### Experimental

All starting materials were of analytical grade and obtained commercially from Sigma-Aldrich and British Drug Houses (BDH) Chemicals Limited and were used without further purification. Preparation of the organic ligands and the metal complexes were achieved according to published procedure [13, 17]. IR spectra were recorded on Shimadzu 8740 FT-IR spectrometer as KBr discs in the range of 4000–400 cm<sup>-1</sup>. UV/Visible spectra were measured on Carry 500 UV/Visible Spectrophotometer. Melting points were recorded on Gallenkamp melting point apparatus and were uncorrected.

### Syntheses of the organic compounds

#### Synthesis of (E)-2-methoxy-4-((4-methoxyphenylimino)methyl)phenol (A<sub>1</sub>)

1.5215g(10 mmol) of vanillin dissolved in 10mL ethanol was added dropwise to a 15mL warm ethanolic solution of 1.2316g (10mmol) of p-Anisidine in a 200 mL round-bottomed flask while stirring. The mixture was heated at reflux for 20 minutes on a oil bath after which 30 mL of ethanol was added to the mixture. The resulting solution was then refluxed at 60 – 70 °C for 8 hrs. The colour of the mixture changed gradually from black to very dark green. The solution was then concentrated to about half of the original volume and then left for 2 days. The solid which

came out was filtered, washed with little ethanol and n-hexane. The product was then recrystallized from aqueous ethanol. Yield=1.574g, 61%, M.P.=104–106, Colour = dark green.

#### Synthesis of (E)-2-methoxy-4-((ptolylimino)methyl)phenol (A<sub>2</sub>)

1.0716(10 mmol) of p-Toluidine dissolved in 10mL ethanol was added to a stirring 10 mL warm ethanolic solution of 1.5215g(10 mmol) of vanillin in a 200 mL round-bottomed flask. The mixture was heated at reflux for 20 minutes on a oil bath after which 30 mL of ethanol was added to the mixture. The resulting solution was then refluxed at 60 – 70 °C for 8hrs. The colour of the mixture changed gradually from light brown red. The solution was then concentrated to about one-third of the original volume and then cooled and poured into crushed ice. The solid which came out was filtered, washed with little ethanol and n-hexane and then recrystallized from aqueous ethanol. Yield = 0.682g, 30%, M.P. = 85 – 88. Colour = yellow.

#### Synthesis of (E)-2-methoxy-4-((4- nitrophenylimino)methyl)phenol (A<sub>3</sub>)

1.3813g(10 mmol) of p-nitroaniline and 1.5215g (10mmol) of vanillin dissolved in 50 mL ethanol were reacted in a 200 mL round-bottomed flask while stirring. The mixture was heated at reflux for 6 hrs at 60 – 70 °C. The colour of the mixture changed gradually from light yellow to orange red. The solution was then concentrated to about half of the original volume and then left for 4 days. The crystals that came out of the solution was filtered, washed with diethylether. Yield = 1.077 g, 40%, M.P. =118 – 120, Colour = yellow.

#### Synthesis of (E)-2-methoxy-4-((3- nitrophenylimino)methyl)phenol (A<sub>4</sub>)

1.3813 g (10 mmol) of m-nitroaniline was added to 1.5215 g (10mmol) of vanillin dissolved in 25mL of warm ethanol in a 200 mL round-bottomed flask while stirring. The mixture was heated at reflux for 7 hrs on a oil bath. The colour of the mixture changed gradually from light yellow to orange red. The solution was then concentrated to about half of the original volume and then left for 5days to crystallize out. The crystals which came out of the solution was filtered, washed with diethylether and ethanol. Yield = 0.723 g, 27 %, M.P. = 68 – 70, Colour = yellow.

#### Synthesis of (E)-4-((3-chlorophenylimino)methyl)-2-methoxyphenol (A<sub>5</sub>)

2.098 g (20 mmol) of m-chloroaniline dissolved in 10mL ethanol was added to a stirring 10 mL warm ethanolic solution of 3.0430 g (20 mmol) vanillin in a 200 mL round-bottomed flask. The mixture was heated at reflux for 20 minutes on a oil bath after which 40 mL of ethanol was added to the mixture. The resulting solution was then refluxed at 70 °C for 8 hrs. The colour of the mixture changed gradually from light yellow to brown. The solution was then concentrated to about one-third of the original volume, cooled and then left to crystallize. After the evaporation of the solvent, a very thick, viscous brown liquid was obtained. Colour = brown. Yield = 2.6 g, 51%.

#### Synthesis of (E)-2-methoxy-4-((m- tolylimino)methyl)phenol (A<sub>6</sub>)

m-Toluidine 2.17 mL(20 mmol) dissolved in 20 mL ethanol was added to a stirring solution of 30 mL ethanolic solution of 3.0430 g (20 mmol) vanillin in a 200 mL round-bottomed flask. The mixture was heated at reflux for 8 hrs on

a oil bath. The colour of the mixture changed gradually from light yellow to brown. The solution was then concentrated to about one-third of the original volume, cooled and then left to crystallize. After the evaporation of the solvent, a very thick, viscous brown liquid was obtained. Colour = brown. Yield = 3.6 g, 68%.

## Results and Discussions

### Syntheses of the compounds

The reaction of vanillin with the different anilines is schematically represented in **Scheme 1** below. All the reactions were heated at reflux between 60 – 70 °C for atleast 6 hours to obtain the product. The products were obtained either as solid crystalline compound (A<sub>1</sub> – A<sub>4</sub>) or as liquid syrup (A<sub>5</sub> – A<sub>6</sub>). The compounds exhibit different colours ranging from dark green to yellow. All the solid products melted sharply with the lowest melting point observed for A<sub>4</sub> while the highest melting point was recorded for A<sub>3</sub>. The sharp melting point indicates high purity of the synthesized compounds.

### Infrared spectra

In the IR spectrum of vanillin, very prominent, notable and important IR bands observed are;  $\nu$ OH of phenol was observed as a broad band at 3178 cm<sup>-1</sup>, the  $\nu$ C=O carbonyl functional group at 1666 cm<sup>-1</sup>. The  $\nu$ C-H(aromatics) has been obscured by the broad band of phenolic  $\nu$ O-H. The  $\nu$ C=C of benzene ring was seen at 1589 cm<sup>-1</sup>, 1510 cm<sup>-1</sup>. Other notable IR bands are 1300 cm<sup>-1</sup> and 1267 cm<sup>-1</sup> which are assigned to phenolic/methoxy  $\nu$ C-O.

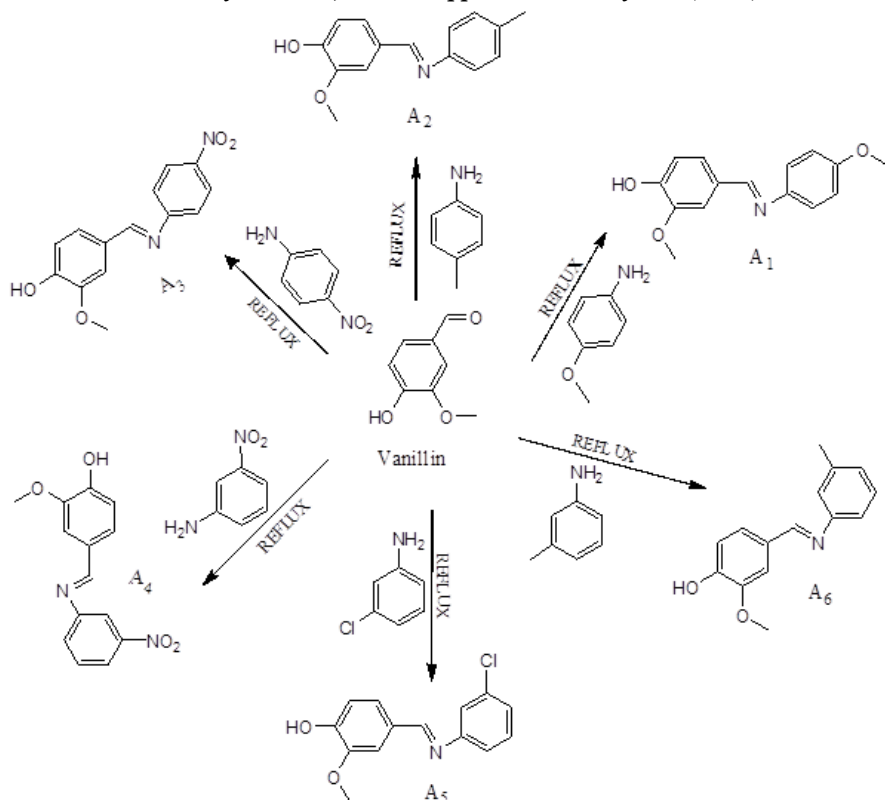
However, in the spectra of the synthesized compounds, (**Scheme 2**) the band observed at 1666 cm<sup>-1</sup> which is due to  $\nu$ C=O of vanillin is completely absent or disappeared. This confirms that the C=O, carbonyl functional group has been replaced by the azomethine, C=N group designated by a newly emerged band found at 1631 cm<sup>-1</sup> to 1624 cm<sup>-1</sup> for all the synthesized compounds. This confirms the formation of the Schiff bases. Other notable bands experienced different bathochromic/hypsochromic shift in the synthesized compounds. Bands observed in the range 3402 cm<sup>-1</sup> to 3086 cm<sup>-1</sup> are due to phenolic  $\nu$ OH. At the same time the phenolic  $\nu$ C-O band for the Schiff bases were seen in the range 1300 – 1267 cm<sup>-1</sup> while the  $\nu$ C-H(aromatics/imine) was observed at 3107 – 3010 cm<sup>-1</sup>.

### Ultraviolet spectra

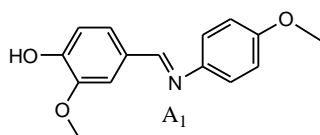
In the UV spectra of aromatic Schiff bases, notable transitions which normally occur within the molecules are  $\pi - \pi^*$  transition associated with benzene ring at 48000 – 43000 cm<sup>-1</sup>,  $\pi - \pi^*$  transition of the azomethine group at 38000 – 34000 cm<sup>-1</sup> while the  $n - \pi^*$  transition of the azomethine chromophore usually found around 32000 – 25000 cm<sup>-1</sup> [13]. In the UV spectra of the synthesized compounds (**Scheme 2**), all these transitions were observed. The  $\pi - \pi^*$  transition of the benzene ring was observed in the range 47929 – 40728 cm<sup>-1</sup>. Bands observed at 36852 – 32546 cm<sup>-1</sup> are assigned to  $\pi - \pi^*$  transition of the azomethine group. While the  $n - \pi^*$  transition of the azomethine chromophore were observed at 30939 – 28640 cm<sup>-1</sup>.

### Chelation feasibility of the organic compounds

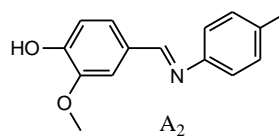
The coordination ability of the organic ligands were tested by mixing different metal (Zn<sup>2+</sup>, Cu<sup>2+</sup>, Co<sup>2+</sup> and Ni<sup>2+</sup>) salt and A<sub>1</sub> in ethanol solution. Evidence of coordination was recorded from the colour changes and precipitates observed after the reaction. This is an indication that the organic ligands will be good metal chelators.



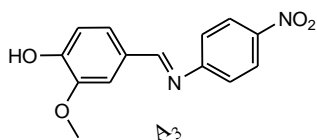
Scheme 1. synthetic scheme for the compounds



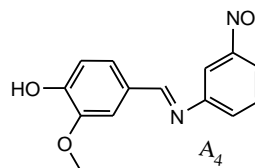
Dark green crystalline solid, Yield = 61%,  
M.P. = 104-106 °C, IR( $\text{cm}^{-1}$ ):  $\nu_{\text{Ph/C-H}}$  = 3010  
 $\nu(\text{C=N}) + \nu(\text{C=C})$  = 1624, 1593,  
 $\nu_{\text{Ph/C-O}}$  = 1290, UV( $\text{cm}^{-1}$ ) = 47929 30228, 28640



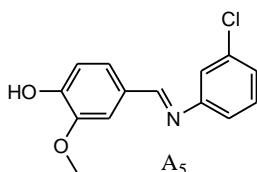
Yellow crystalline solid, Yield = 30%,  
M.P. = 85-88 °C, IR( $\text{cm}^{-1}$ ):  $\nu_{\text{OH}}$  = 3086,  
 $\nu(\text{C=N}) + \nu(\text{C=C})$  = 1624, 1589, 1514,  
 $\nu_{\text{Ph/C-O}}$  = 1280,  $\nu_{\text{Ph/C-H}}$  = 3012  
UV( $\text{cm}^{-1}$ ) = 47223, 43478, 36339, 30745



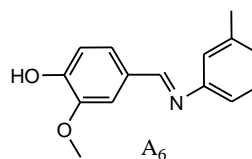
Yellow crystalline solid, Yield = 40%,  
M.P. = 118-120 °C, IR( $\text{cm}^{-1}$ ):  $\nu_{\text{OH}}$  = 3362,  
 $\nu(\text{C=N}) + \nu(\text{C=C})$  = 1631, 1587, 1506,  
 $\nu_{\text{Ph/C-O}}$  = 1300,  $\nu_{\text{Ph/C-H}}$  = 3107  
UV( $\text{cm}^{-1}$ ) = 47256, 43704, 36852, 32546, 30328



Yellow crystalline solid, Yield = 27%,  
M.P. = 68-70 °C, IR( $\text{cm}^{-1}$ ):  $\nu_{\text{OH}}$  = 3335,  
 $\nu(\text{C=N}) + \nu(\text{C=C})$  = 1631, 1589, 1525,  
 $\nu_{\text{Ph/C-O}}$  = 1288,  $\nu_{\text{Ph/C-H}}$  = 3076  
UV( $\text{cm}^{-1}$ ) = 40909, 30,936



Brown viscous thick liquid,  
IR( $\text{cm}^{-1}$ ):  $\nu_{\text{OH}}$  = 3387,  $\nu_{\text{Ph/C-H}}$  = 3066  
 $\nu(\text{C=N}) + \nu(\text{C=C})$  = 1626, 1577,  
 $\nu_{\text{Ph/C-O}}$  = 1288, UV( $\text{cm}^{-1}$ ) = 45390, 42295  
36220, 32826, 30954, 29,634



Brown viscous thick liquid,  
IR( $\text{cm}^{-1}$ ):  $\nu_{\text{OH}}$  = 3402,  $\nu_{\text{Ph/C-H}}$  = 3016  
 $\nu(\text{C=N}) + \nu(\text{C=C})$  = 1626, 1514,  
 $\nu_{\text{Ph/C-O}}$  = 1267, UV( $\text{cm}^{-1}$ ) = 47118,  
42226, 40728, 35119, 33190, 30855

Scheme 2. Result in schematic representation

### Conclusions

Six new vanillin Schiff bases (A<sub>1</sub> - A<sub>6</sub>) were successfully synthesized. The Schiff bases were synthesized via condensation of vanillin with various substituted anilines. Compounds A<sub>1</sub> - A<sub>4</sub> came out as crystals of different colours while A<sub>5</sub>-A<sub>6</sub> were obtained as thick viscous liquid. The organic compounds were characterized by IR spectra, UV/Visible spectra and melting points measurements. Purity of the new compounds was revealed by their sharp melting points. This research presents further motivation for the preparation of metal complexes of the compounds for possible biological properties.

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