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Green Synthetic Methods for a Schiff Base from 2-Aminopyridine and 4-Ethoxybenzaldehyde

[1]OGBONDA-CHUKWU, E; [2]ABAYEH, OJ; *[2]ACHUGASIM, O

[1]Department of Chemistry, Rivers State University, Rivers State Nigeria
*[*2]Department of Pure and Industrial Chemistry, University of Port Harcourt, Choba, Rivers State, Nigeria*

**Corresponding Author Email: ozioma.achugasim@uniport.edu.ng*
Co-Authors Email: umofiae@gmail.com; oviabayeh@gmail.com

ABSTRACT: The novel Schiff base was acquired from the reaction between 2-aminopyridine and 4-ethoxybenzaldehyde using three (3) techniques; refluxing in ethanol for 2 hours, stirring in ethanol and an ethanol-water (1:1) mixture at room temperature for an hour. The synthesis of the 2-aminopyridine-4-ethoxybenzaldehyde Schiff base produced dark yellow crystals with melting point range of 95-97^{o}C. The reaction in ethanol under reflux produced the highest yield of 88.2% while the reaction in ethanol and ethanol-water (1:1 v/v) mixture at room temperature gave 69.2% and 43.5% yield of the compound respectively. The IR spectrum showed the following bands; 1681cm^{-1} (C=N), 1595cm^{-1} (aromatic C=C stretch), 2981cm^{-1} (aromatic C-H stretch), 1509cm^{-1} (aromatic C=N stretch), 1155cm^{-1} (aliphatic C-C stretch), 1036 (aromatic C-O stretch), 2825 (aliphatic C-H stretch). The ^{13}C NMR spectrum showed the following chemical shifts (δppm); 158.48 (C=N, imino), 154.98 and 150.18 (C-N of aromatic pyridine moiety), 121.44 – 137.53 (aromatic carbons), 158.68 (aromatic C-O), 63.88 (aliphatic C-O), 15.22 (aliphatic C). The ^{1}H NMR spectral data (δppm) for the compound gave the following results; 7.06-7.91, m (8H) (Ar-H), 9.71, s (1H) (HC=N-), 4.10, q (2H) and 1.32, t (3H) (OCH_2CH_3). The spectral data was in agreement to the predicted structure of the Schiff base.

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The family of organic compounds comprised of the imino functional group (HC=N-) are known imines. Schiff bases are a subclass of imines, hence, also possess the imino group (Ibrahim *et al*., 2006). The synthesis of Schiff bases have been successfully achieved using different methods like stirring under reflux temperature (Jamuna *et al*., 2011; Uddin *et al.*, 2014) stirring at room temperature (Shipra *et al*., 2019; Khashi *et al*., 2018), microwave irradiation [Shntaif and Rashid, 2016; Bhagat *et al*., 2013) ,sonication (Li *et al*, 2001, Bendale *et al.*, 2011), and grinding (Abood, 2014). The classical method for Schiff base synthesis is by stirring the reactants under reflux for a certain time duration in the presence of a catalyst (acid or base) (Qin *et al*., 2013). In addition, different solvents have also been utilized for the synthesis of these compounds, however, a large number of the solvents used are considered to be toxic to the environment. Such toxic solvents include dichloromethane (Mishra *et al*., 2012), methanol (Essa *et al*., 2012), benzene, N,N-dimethyl formamide (Tomma *et al*., 2014), etc. Moreover, the green solvents that have been used include water (Sachdeva *et al*., 2014), ethanol (Endale and Desalegn, 2018) and an ethanol-water mixture (Umofia *et al*., 2018, Ogbonda-Chukwu *et al.*, 2021). Schiff bases have a variety of uses including the manufacture of pharmaceuticals (Saini *et al*., 2011), dyes (Kumar *et*

**Corresponding Author Email: ozioma.achugasim@uniport.edu.ng* *al*., 2009), agrochemicals (Zhu *et al*., 2003), corrosion inhibitors (Ashassi-Sorkhabi *et al*., 2006), etc. This paper concentrates on the use of three different green routes for the synthesis of a new Schiff base derived from 2-aminopyridine and 4-ethoxybenzaldehyde with the goal of ascertaining the best method(s) for the synthesis with focus on yield obtained.

MATERIALS AND METHODS

Materials: The chemicals used for this research were synthesis grade chemicals purchased from Sigma-Aldrich. The melting point was determined with a melting point apparatus and was uncorrected. Thin Layer Chromatography (TLC) was carried out using a Merck pre-coated silica gel plate (10 x 10 cm), the Rf value obtained using ethyl acetate as the mobile phase and the spot located and visualized using an ultraviolet lamp at 256 nm. The IR spectrum of the sample was recorded on a Fourier Transform Infrared spectrometer, Carry 630 Agilent Technologies in the range of 650-4000 cm^{-1}. ^{1}H NMR and ^{13}C NMR spectrum of the sample was recorded on a JEOL Eclipse 400 NMR spectrophotometer by JEOL (Pleasanton, USA) using DMSO-d_6.

Synthesis in ethanol at reflux temperature: 2-aminopyridine (0.01 mol, 0.94 g) and 4-ethoxybenzaldehyde (0.01 mol, 1.50 g, 1.39 ml) were dissolved separately in 20 ml ethanol in a 50 ml beaker. The amine was poured into a 150 ml flat bottom flask followed by the aldehyde. The reaction mixture was stirred under reflux at 80 ^{0}C for 1 hr followed by the addition of a few drops of concentrated hydrochloric acid (HCl). The reaction mixture was then stirred for one more hour. The reaction was monitored to completion using thin layer chromatography (TLC) with ethyl acetate as the mobile phase. The dark yellow mixture was extracted using water and dichloromethane and this gave dark yellow crystals after standing overnight. The solid product was recrystallized using ethanol and hexane filtered and air-dried.

Rf: 0.53, m.p: 95-97^{o}C, yield: 88.2%. IR (KBr): 1681cm^{-1} (C=N), 1595cm^{-1} (aromatic C=C stretch), 2981cm^{-1} (aromatic C-H stretch), 1509cm^{-1} (aromatic C=N stretch), 1155cm^{-1} (aliphatic C-C stretch), 1036 (aromatic C-O stretch), 2825 (aliphatic C-H stretch). ^{13}C NMR (δppm); 158.48 ($\underline{C}$=N, imino), 154.98 and 150.18 ($\underline{C}$-N of aromatic pyridine moiety), 121.44 – 137.53 (aromatic carbons), 158.68 (aromatic C-O), 63.88 (aliphatic C-O), 15.22 (aliphatic C). ^{1}H (δppm) 7.06-7.91, m (8H) (Ar-H), 9.71, s (1H) ($\underline{H}$C=N-), 4.10, q (2H) and 1.32, t (3H) ($OC\underline{H}_2C\underline{H}_3$).

Synthesis in ethanol at room temperature: 2-aminopyridine (0.01 mol, 0.94 g) and 4-ethoxybenzaldehyde (0.01 mol, 1.50 g, 1.39 ml) were dissolved separately in 20 ml ethanol in a 50 ml beaker and poured into a 150 ml flat bottom flask. The reaction mixture was stirred at room temperature for 30 min. A few drops of concentrated hydrochloric acid (HCl) was added to the mixture with further stirring for another 30 min. The reaction was monitored to completion using thin layer chromatography (TLC) with ethyl acetate as the mobile phase. The dark yellow mixture was extracted using water and dichloromethane and this gave dark yellow crystals after standing overnight. The solid product was recrystallized using ethanol and hexane filtered and air-dried.

Rf: 0.53, m.p: 95-97^{o}C, yield: 69.2%. IR (KBr): 1681cm^{-1} (C=N), 1595cm^{-1} (aromatic C=C stretch), 2981cm^{-1} (aromatic C-H stretch), 1509cm^{-1} (aromatic C=N stretch), 1155cm^{-1} (aliphatic C-C stretch), 1036 (aromatic C-O stretch), 2825 (aliphatic C-H stretch). ^{13}C NMR (δppm); 158.48 ($\underline{C}$=N, imino), 154.98 and 150.18 ($\underline{C}$-N of aromatic pyridine moiety), 121.44 – 137.53 (aromatic carbons), 158.68 (aromatic C-O), 63.88 (aliphatic C-O), 15.22 (aliphatic C). ^{1}H (δppm) 7.06-7.91, m (8H) (Ar-H), 9.71, s (1H) ($\underline{H}$C=N-), 4.10, q (2H) and 1.32, t (3H) ($OC\underline{H}_2C\underline{H}_3$).

Synthesis in ethanol-water (1:1 v/v) at room temperature: 2-aminopyridine (0.01 mol, 0.94 g) and 4-ethoxybenzaldehyde (0.01 mol, 1.50 g, 1.39 ml) were dissolved separately in 20 ml ethanol-water (1:1 v/v) in a 50 ml beaker and poured into a 150 ml flat bottom flask. The reaction mixture was stirred at room temperature for 30 min followed by the addition of a few drops of concentrated hydrochloric acid (HCl). The mixture was further stirred for another 30 min. The progress of the reaction was monitored to completion using thin layer chromatography (TLC) with ethyl acetate as the mobile phase. The dark yellow mixture was extracted using water and dichloromethane and this gave dark yellow crystals after standing overnight. The solid product was recrystallized using ethanol and hexane filtered and air-dried.

Rf: 0.53, m.p: 95-97^{o}C, yield: 43.5%. IR (KBr): 1681cm^{-1} (C=N), 1595cm^{-1} (aromatic C=C stretch), 2981cm^{-1} (aromatic C-H stretch), 1509cm^{-1} (aromatic C=N stretch), 1155cm^{-1} (aliphatic C-C stretch), 1036 (aromatic C-O stretch), 2825 (aliphatic C-H stretch). ^{13}C NMR (δppm); 158.48 ($\underline{C}$=N, imino), 154.98 and 150.18 ($\underline{C}$-N of aromatic pyridine moiety), 121.44 – 137.53 (aromatic carbons), 158.68 (aromatic C-O), 63.88 (aliphatic C-O), 15.22 (aliphatic C). ^{1}H (δppm)

7.06-7.91, m (8H) (Ar-H), 9.71, s (1H) (<u>H</u>C=N-), 4.10, q (2H) and 1.32, t (3H) (OC$\underline{H}_2$C$\underline{H}_3$).

The general reaction equation for the synthesis of a Schiff base derived from 2-aminopyridine and 4-ethoxybenzaldehyde is illustrated in figure 1.

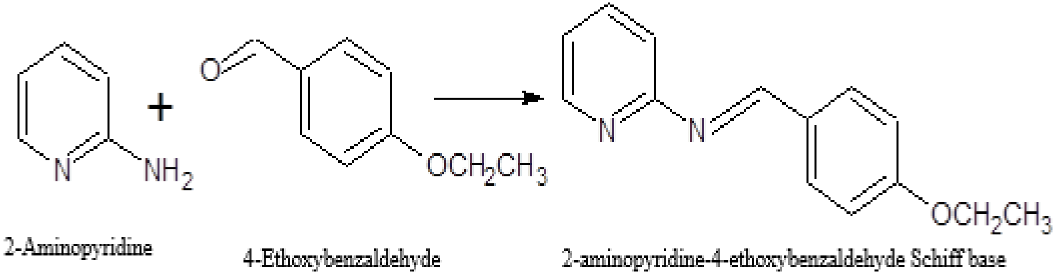

Fig. 1. Reaction equation for the synthesis of 2-aminopyridine-4-ethoxybenzaldehyde Schiff base

RESULTS AND DISCUSSION

The synthesis of the novel 2-aminopyridine-4-ethoxybenzaldehyde Schiff base was carried out using three (3) different methods; the conventional method (stirring in ethanol under reflux for 2 hours) and two (2) new methods (stirring in ethanol at room temperature for an hour and in an ethanol-water (1:1 v/v) mixture at room temperature for an hour).

The work-up procedure for the extraction of the product from the reaction solvent was tiresome and time-consuming for the 3 methods but this was necessary to ensure that the compound was pure. Although the syntheses at room temperature were preferred due to their shorter reaction time, a higher yield of the 2-aminopyridine-4-ethoxybenzaldehyde Schiff base was obtained using the conventional method for Schiff base preparation (88.2%). However, one of the new methods which involved stirring in ethanol at ambient temperature gave a relatively high yield of 69.2%. The physicochemical and spectral studies proved that the three methods gave the same Schiff base.

The results acquired from the spectral studies ascertained that the structure of the compound was as predicted. The presence of a peak at 1681cm^{-1}, portraying the presence of the imino group (C=N) and the absence of the amino and carbonyl group peaks at 3400-3250cm^{-1} and 1740-1720cm^{-1} respectively, substantiated the formation of the new 2-aminopyridine-4-ethoxybenzaldehyde Schiff base. This is in line with the works of Endale and Desalegn (2018)

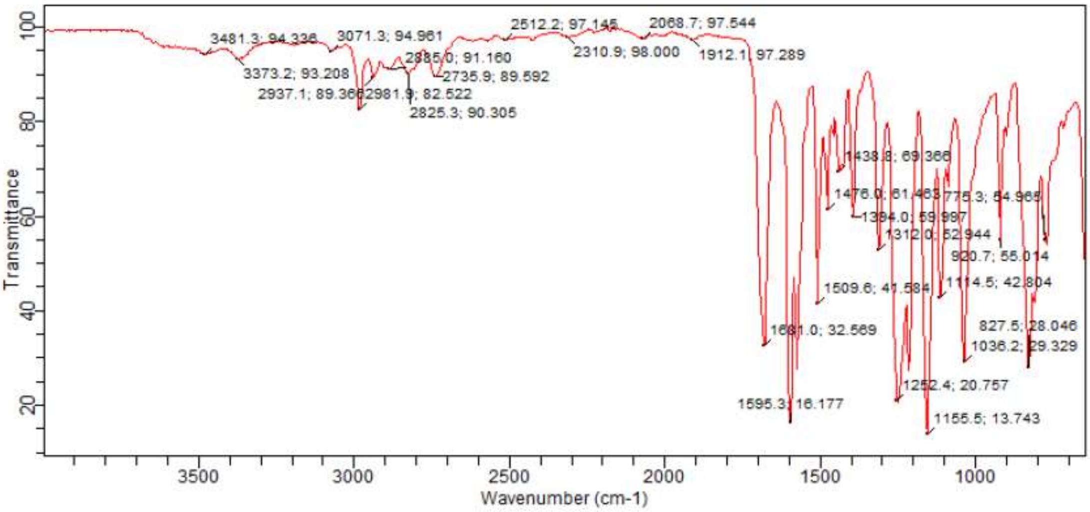

Fig 2: IR Spectrum of 2-aminopyridine-4-ethoxybenzaldehyde Schiff base

Furthermore, the ^{1}H NMR result revealed the presence of the imino proton, with a single peak at 9.71 ppm and the ^{13}C NMR showed the imino (C=N) peak at 158.48 ppm as a result of the deshielding effect of the nitrogen atom doubly bonded to the carbon atom. Imino hydrogens of Schiff bases have been found to lurk around this region (Abod 2014; Bhagat et al 2013)

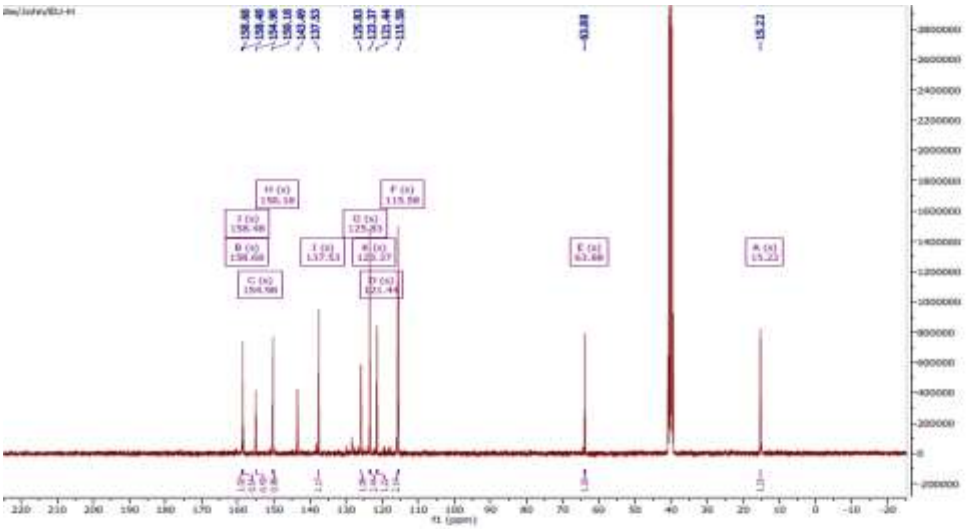

Fig 3: ^{13}C NMR Spectrum of 2-aminopyridine-4-ethoxybenzaldehyde Schiff base

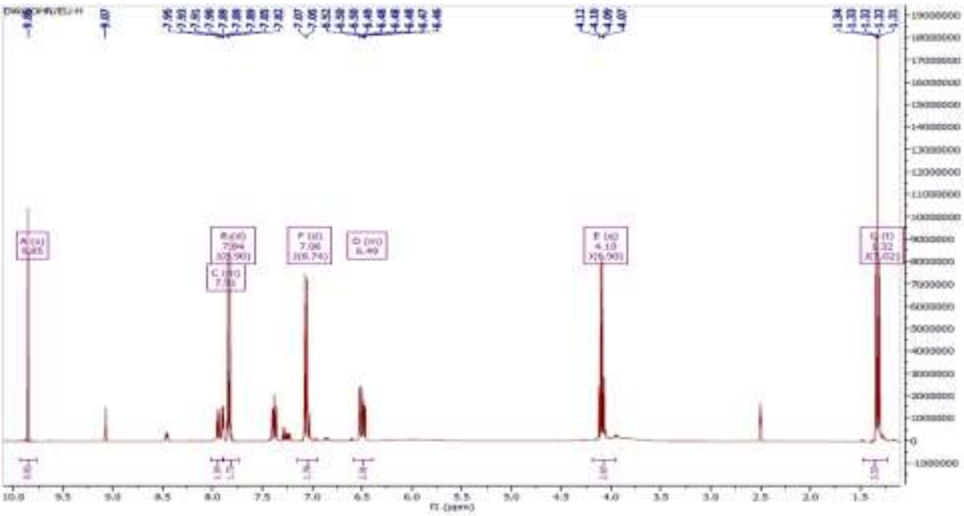

Fig 4: ^{1}H NMR Spectrum of 2-aminopyridine-4-ethoxybenzaldehyde Schiff base

*Conclusion***:** The results from this investigation prove that the novel Schiff base of 2-aminopyridine and 4-ethoxybenzaldehyde can be synthesized through the use of eco-friendly solvents and methods. In addition, this research has found that this title compound can be obtained at a very high yield using ethanol at reflux temperature.

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