



## ILJS-24-100 (SPECIAL EDITION)

**One-pot Synthesis and Characterization of 1,10-dimethylphenanthroline Sulphate Derivative****Baker M. T., Adeleye O. J., Fasola P. E., Oguntoye S. O.**

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**Abstract**

A new 1,10-dimethylphenanthroline sulphate ionic liquid synthesis was accomplished in a one-pot procedure in a three-neck flask using symmetrical 1,10-phenanthroline (PHEN) derivative. The synthesis involves the alkylation of PHEN, followed by sulphonation and acetylation to yield the desired product. Comprehensive characterization was carried out using techniques such as Thin Layer Chromatography (TLC), Fourier Infrared Spectroscopy (FTIR) and Nuclear Magnetic Resonance Spectroscopy (NMR), to confirm the purity, functional group and the structure of the compound. The infrared spectral studies using a FTIR spectroscopic technique revealed absorption bands 3534, 1644, and 1226  $\text{cm}^{-1}$  which correlates to quaternized nitrogen ( $\text{NR}_4^+$ ), a carbonyl ( $\text{R}-\text{C}=\text{O}$ ) and an asymmetric sulfone in the synthesized compound.  $^1\text{H}$ NMR analysis provided important signals at 4.39 ppm assigned to  $-\text{N}^+(\text{C})\text{C}$ , a three proton singlet peak at 2.16 ppm assigned to  $-\text{C}(=\text{O})\text{O}$  and another single proton doublet peak at 10.06 ppm assigned to  $-\text{S}(=\text{O})(=\text{O})-\text{R}$ . The  $^{13}\text{C}$  NMR spectra exhibited four distinct signals in addition to all expected signals for the carbons. These signals include; a triplet carbon at 144 ppm assigned to  $-\text{S}(=\text{O})(=\text{O})-\text{R}$ , a singlet carbon showing peak at 175.4 ppm indicating  $-\text{C}=\text{O}$  of an acetyl, singlet carbons showing peaks at 50.9 ppm and 19.3 ppm indicating two aliphatic carbons respectively which confirms the synthesis of a new compound. The synthesized phenanthroline derivatives opens new channels of research for the discovery of more important derivatives with novel functionalities and applications.

**Keyword:** 1, 10-phenanthroline; 1,10 Phenanthroline derivative; Ionic liquid; NMR; FTIR**1. Introduction**

There has been a resurgence of interest in ionic liquids, whose origins may be traced to the nineteenth century and the discovery of "red oil" during a Friedel-Craft reaction (Gebbie, 2021). The term "ionic liquids" usually describes liquids (or salts mostly composed of ions— anions and cations) that are in liquid form at room temperature and can remain liquid up to 100 °C. They are popular in industrial applications because they have many beneficial properties, including low volatility, non-flammability, reduced-toxicity, chemical stability, high solubility in polar solvents, and the ability to easily stick to metal surfaces (Kianfar *et al.*, 2021). Usually, they are either eutectic combinations of an organic and an inorganic salt or organic salts (Freemantle 2010). Ionic liquids minimize waste production and encourage sustainable chemical processes, making them perfect for usage in batteries, super-capacitors, and fuel cells. In material synthesis, ionic liquids are also employed to create customized characteristics and effective catalysis and separation procedures. 1,10-Phenanthroline (PHEN) is such an ionic liquid with a prominent bidentate chelating ligand for transition metal ions that has made significant contributions to coordination chemistry (Bencini *et al.*, 2010). It serves as a valuable precursor in organic, inorganic, and supramolecular chemistry. Scientists have found the study of the basic chemistry of PHEN and its metal complexes intriguing. This interest is fueled by their fascinating properties

in catalysis, redox reactions, photochemistry, chemosensing and antimicrobial activities (Alreja *et al.*, 2016, Leverett *et al.*, 2012). PHENs are analogs of diazaphenanthrene and belong to a class of polycyclic aromatic hydrocarbons found in compounds like sterols, sex hormones, cardiac glycosides, bile acids, and morphine alkaloids (Bonacorso *et al.*, 2016). In comparison to the more commonly utilized 2,2'-bipyridine, PHEN classified as an ionic liquid, serves as the parent compound for a significant array of chelating agents. This compound exhibits several distinctive properties; its rigid, planar, hydrophobic structure is electron-deficient, with nitrogen atoms optimally arranged for cooperative cation binding. These structural traits enhance its coordination capabilities with metal ions, with the rigid core ensuring that the two nitrogen atoms remain closely aligned. Leveraging their structural characteristics such as planarity, rigidity, and hydrophobicity (Coulibaly *et al.*, 2021). PHEN derivatives and their metal complexes have been employed as intercalating or groove-binding agents for DNA and RNA. Certain metal complexes are also effective at cleaving the DNA backbone, with the complex  $[\text{Cu}(\text{phen})_2]^{2+}$  being widely used in molecular biology as a DNA-cleaving reagent (Bencini *et al.*, 2010). It is also one of the most frequently utilized ligands in the field of organic synthesis, playing a crucial role in facilitating a wide range of chemical reactions and processes (Sun *et al.*, 2019). Additionally, PHEN is utilized in the development of intercalating agents for polynucleotides and molecular chemo-sensors and recent studies have shown that PHEN and its derivatives are valued for their excellent coordination abilities with various metal ions, making them useful in numerous applications involving metal complexes. They serve multiple roles, such as ligands in catalysis or stabilizing agents in nanoparticle synthesis. PHEN derivatives are key heterocyclic ligands in many metal complexes that contribute significantly to technological and medicinal advancements. Notable applications include electroluminescent materials, organic light-emitting devices (OLEDs), organic semiconductors, and as chemical nucleases and therapeutic agents, owing to their capacity to bind with DNA (Helio *et al.*, 2016). However, challenges such as production costs, lack of standardization, and environmental concerns persist. Despite these issues, the unique properties of ionic liquids continue to render them an attractive area for research and application, particularly in the context of sustainable practices.

The objective of this work is to synthesize 1,10-dimethylphenanthroline sulphate derivative of PHEN, via a one-pot synthesis from a symmetrical PHEN derivative, and to characterize the synthesized ionic liquid. The unique combination of properties in this ionic liquid suggests potential use in catalysis, environmental applications, and biological research leveraging its excellent solvation properties, stability and excellent solubility for various metal complexes, making it a valuable solvent in different chemical processes. Further research is recommended to explore its environmental impact and scalability for real-world applications.

## 2. Materials and Methods

### 2.1 Materials

All chemicals used in the present work include; 1,10-phenanthroline (PHEN), Methyl Chloride (MeCl), Sulphuric acid ( $\text{H}_2\text{SO}_4$ ), Acetic acid ( $\text{CH}_3\text{COOH}$ ), Acetic anhydride ( $\text{AcO}_2$ ), and Acetonitrile. All reagents and solvents were of analytical grade and were used as received from commercial sources. All the reactions were monitored by TLC using 0.25mm silica gel plates and UV indicator.

### 2.2 Methodologies

1,10-dimethylphenanthroline sulphate ionic liquid was synthesized in one-pot protocol from symmetrical 1,10-phenanthroline following previously reported work with slight modifications (Cai *et al.*, 2010). The PHEN was alkylated/quaternized in the one-step synthesis process, which was followed by acetylation, and the addition of an organic acid. The required symmetric PHEN derivative was produced by the reaction.

### 2.3 Alkylation

In a three-necked round-bottom flask, MeCl (0.5 mL; 1.39mmol; 5:1v/wt of MeCl/PHEN) and then added in drops to PHEN (0.25g; 1.39mmol; 1:5wt/v of PHEN/MeCl) in acetonitrile from a dropping funnel to facilitate the alkylation. Then the reaction mixture was stirred continuously and refluxed at 30°C for 3 hours, the resulting mixture exhibited an orange coloration. The progress of the reaction was monitored by TLC.

## 2.4 Sulphonation

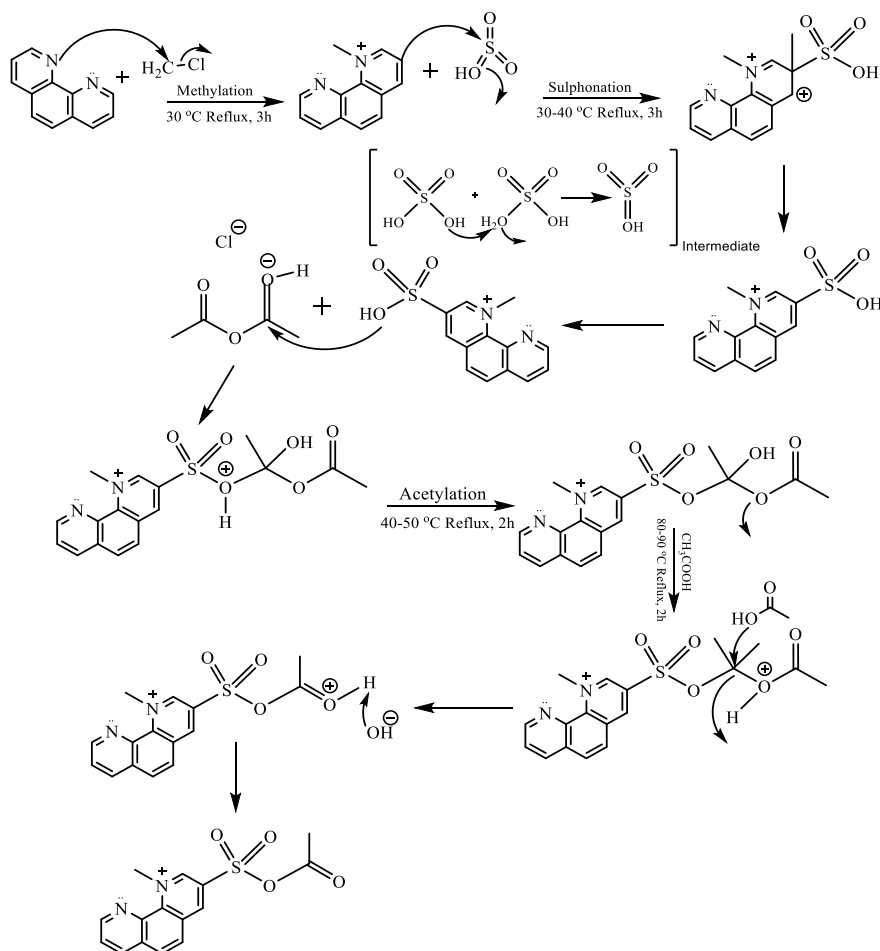
Following the alkylation procedure, in a three-necked round-bottom flask, H<sub>2</sub>SO<sub>4</sub> (0.5 mL; 4.8mmol; 1:1v/v of H<sub>2</sub>SO<sub>4</sub>/Alkyl-PHEN) was added to the alkylated phenanthroline (Alkyl-PHEN) (1 mL; 4.8mmol; 1:1 v/v of Alkyl-PHEN/H<sub>2</sub>SO<sub>4</sub>) in acetonitrile. The reaction mixture was stirred and refluxed at 35°C for 3 hours until the reaction was completed (monitored by TLC. In this instance, the reaction mixture coloring changed from violet to dark brown.

## 2.5 Acetylation

Following the sulphonation process in the three-necked flask, Ac<sub>2</sub>O (0.7 mL; 3.24mmol; 2:1:2v/v/v of Ac<sub>2</sub>O/SuP/CH<sub>3</sub>COOH) was introduced to the sulphonated product (SuP) (1 mL; 3.24mmol; 1:2:2v/v/v of SuP/Ac<sub>2</sub>O/CH<sub>3</sub>COOH) in acetonitrile. The mixture was refluxed and stirred at approximately 40-50°C. After 2 hours, CH<sub>3</sub>COOH (0.2 mL; 3.24mmol; 2:2:1v/v/v of CH<sub>3</sub>COOH/Ac<sub>2</sub>/SuP) was added dropwise from a dropping funnel to aid in acetylation and the mixture was stirred and refluxed as the temperature was raised to 85 °C for an additional 2 hours for the reaction to come into completion while monitoring the progress via TLC. An orange-colored solution resulted following the heating.

## 3. Result and Discussion

The synthesis of PHEN was performed via alkylation/quaternization, sulphonation, and acetylation sequentially in a one-pot system (Scheme 1). The PHEN was quaternized with methyl chloride to produce the equivalent Alkyl-PHEN. Sulphonation was then performed by adding sulfuric acid, and acetylation was carried out using acetic anhydride and acetic acid. This was an easy process to follow; the compounds that were synthesized were soluble in acetonitrile, and the TLC result revealed a single spot with R<sub>f</sub> value (0.5) using DCM/MeOH (1:1), indicating that the products were pure. The FTIR and NMR examine of the novel product confirmed the production of a new molecule, as its spectra differed from the PHEN spectra and were consistent with the expected structure.



**Scheme 1:** Synthesis of 1,10-dimethylphenanthroline sulphate ionic liquid

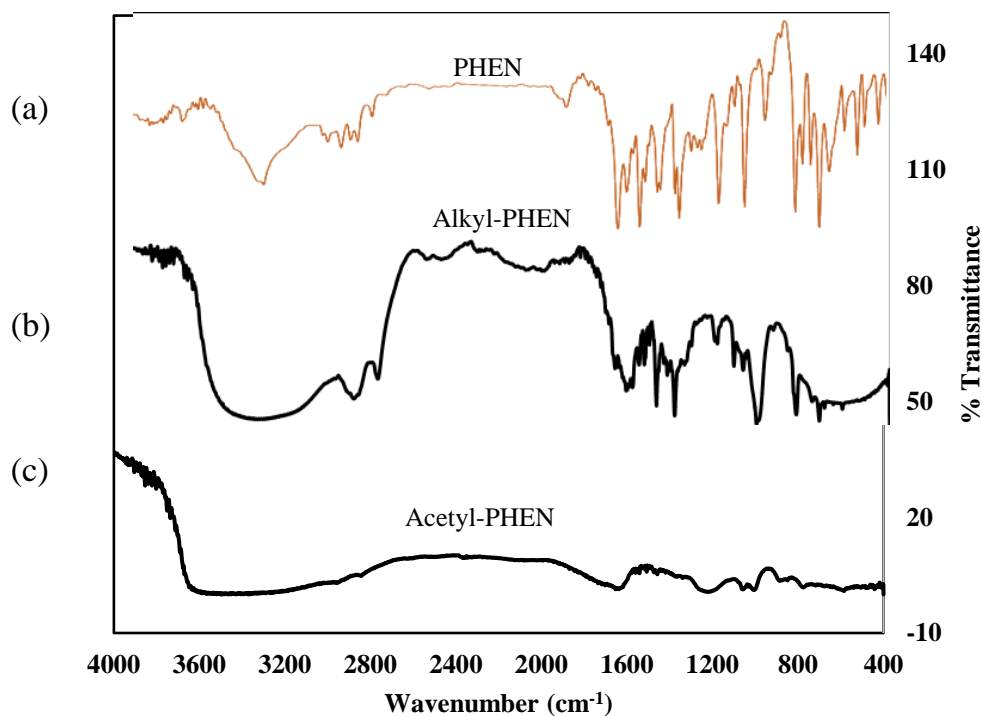
### 3.1 Fourier Transform Infrared Analysis

#### 3.1.1 Alkyl-PHEN

The superimposed FTIR spectra of PHEN and the Alkyl-PHEN (Fig.1) revealed the phenanthroline absorption bands at  $3077$  and  $1418\text{ cm}^{-1}$  assigned to C-H and  $\text{CH}_2$  stretching and bending vibrations respectively (Parada *et al.*, 2014). Compared with the spectra of the Alkyl-PHEN, the stretching vibrations have shifted thus: C-H at  $2948\text{ cm}^{-1}$  and  $\text{CH}_2$   $1425\text{ cm}^{-1}$ . A single resonance is shown at  $3404\text{ cm}^{-1}$  for the Alkyl-PHEN, indicating the presence of a protonated secondary amine further affirming the formation of the intended complex.

#### 3.1.2 Acetyl-PHEN

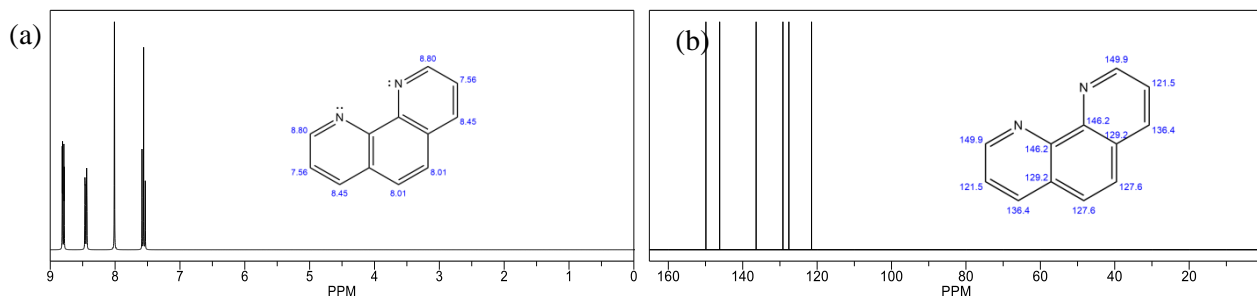
In comparison to the FTIR spectra of PHEN (Fig.1a) and the FTIR spectra of the methylated product (Fig 1b), the FTIR spectra of the acetylated product shows three new absorption bands: the vibration peaks of a quaternized nitrogen ( $-\text{N}^+-\text{CH}_3$ ), C=O bonds and an  $\text{sp}^2$  asymmetric O=S=O stretching appeared at  $3534\text{ cm}^{-1}$ ,  $1644\text{ cm}^{-1}$  and  $1226\text{ cm}^{-1}$  bending respectively (Fig 1c) providing additional evidence that the complex proposed was obtained.



**Fig 1:** FTIR Spectrum of (a) phenanthroline monohydrate (PHEN) (b) the alkylated phenanthroline (Alkyl-PHEN) and, (c) the final product (an acetoxy-sulfonyl derivative of phenanthroline) (Acetyl-PHEN)

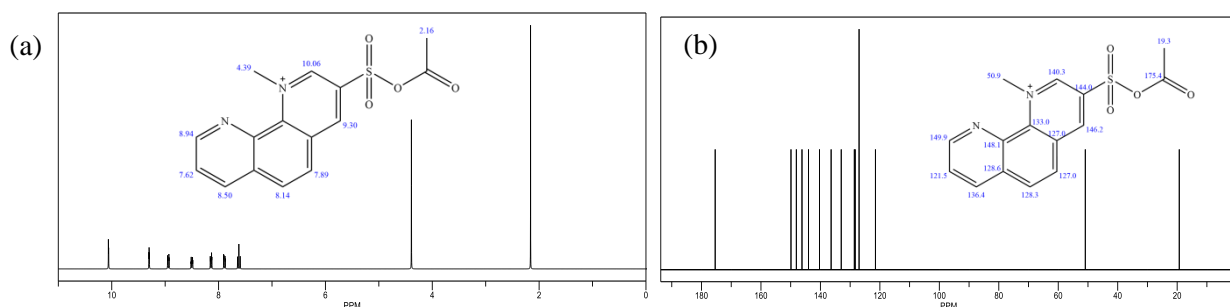
### 3.2 Nuclear Magnetic Resonance (NMR) Spectra Analysis

The proton ( $^1\text{H}$ ) NMR spectra of PHEN molecule contains four pairs of equivalent protons which resonate within the range of 7.6 - 9.2 ppm, (Fig 2a) and the  $^{13}\text{C}$  NMR spectra showed all expected signals for the compound (Fig 2b).



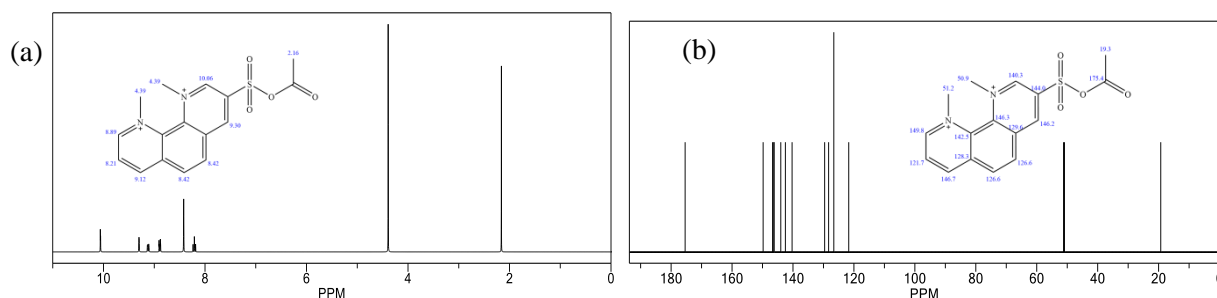
**Fig 2:** (a)  $^1\text{H}$  NMR Spectrum (b)  $^{13}\text{C}$  NMR spectrum of 1,10 phenanthroline

The  $^1\text{H}$  NMR spectra of the complex, in addition to the hydrogen signals of the PHEN, it exhibits three new signals attributed to the alkyl protons downfield. These signals include a three proton singlet peak at 4.39 ppm assigned to  $-\text{N}^+(\text{C})\text{C}$ , a three proton singlet peak at 2.16 ppm assigned to  $-\text{C}(=\text{O})\text{O}$  and another single proton doublet peak at 10.06 ppm assigned to  $-\text{S}(=\text{O})(=\text{O})-\text{R}$  (Fig 3a). The  $^{13}\text{C}$  NMR spectra exhibit, four distinct signals in addition to all expected signals for the carbons. These signals include a triplet carbon at 144 ppm assigned to  $-\text{S}(=\text{O})(=\text{O})-\text{R}$ , a singlet carbon showing peak at 175.4 ppm indicating  $-\text{C}=\text{O}$  of an acetyl, singlet carbons showing peaks at 50.9 ppm and 19.3 ppm indicating two aliphatic carbons respectively (Fig 5b). This adds credence in validation of the expected structure.



**Fig. 3:** (a) <sup>1</sup>H NMR (b) <sup>13</sup>C NMR spectrum of the final product (an acetoxy-sulfonyl derivative of phenanthroline)

The <sup>1</sup>H NMR spectra of the complex, in addition to the hydrogen signals of the PHEN, it exhibits three new signals attributed to the alkyl protons. These signals include a three proton singlet peak at 4.39 ppm assigned to two  $-N^+(C)C$ , a three proton singlet peak at 2.16 ppm assigned to  $-C(=O)O$  and another single proton doublet peak at 10.06 ppm assigned to  $-S(=O)(=O)-R$  from benzene ring A (Fig 4a). The <sup>13</sup>C NMR spectra exhibit, four distinct signals in addition to all expected signals for the carbons. These signals include a triplet carbon with peak at 144 ppm assigned to  $-S(=O)(=O)-R$ , a singlet carbon at 175.4 ppm indicating 1-Carboxyl group, singlet carbons at 50.9 ppm, 51.2 ppm and 19.3 ppm indicating three aliphatic carbons respectively (Fig 4b).



**Fig 4:** (a) <sup>1</sup>H NMR (b) <sup>13</sup>C NMR spectrum of the final product (an acetoxy-sulfonyl derivative of phenanthroline)

#### 4. Conclusion

The application of aromatic compounds with reduced cytotoxicity is a major challenge in the drug development. Due to their reported bioactivities and reduced cytotoxicity, phenanthrolines, a have drawn more attention in recent times. This study reports the one-pot synthesis of a new phenanthroline derivative, an ionic liquid which holds promise in drug synthesis and preparation of other important compounds. The structure of the phenanthroline, a polycyclic compound with an aceto-sulphonated group was confirmed without unequivocally using FTIR and NMR data. As a new aceto-sulphone phenanthroline, the skeleton may contribute to cancer researches due to the presence of electron-donating and electron-withdrawing groups. The biological application would be explored in future researches.

#### CONFLICT OF INTEREST

Authors declare no conflict of interest

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