https://doi.org/10.65646/3rc20dmp2r0701

SYNTHESIS, CHARACTERISATION, AND ANTIBACTERIAL POTENTIAL OF A Pt(II) COMPLEX WITH A NOVEL LINEAR SULFONAMIDE LIGAND TERMINATED BY BENZIMIDAZOLYL MOIETIES

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Platinum complexes have been extensively studied for their antibacterial and anticancer properties, primarily due to their ability to bind to DNA and proteins. In recent years, there has been growing interest in the development of novel N-donor ligands to enhance these biological activities. This study aimed to synthesise and characterise a novel *N,N′,N″*-donor linear sulfonamide ligand terminated with benzimidazolyl rings, along with its corresponding platinum (II) complex, to investigate their potential biological applications. The compounds were characterised using ^{1}H and ^{1}H–^{1}H ROESY NMR, FTIR, UV–Visible, and fluorescence spectroscopy. The ^{1}H and ROESY NMR spectra reveal that the methylene protons, which appear as singlets in the free ligand (L), split into two doublets in the platinum complex, indicating bidentate coordination to the Pt(II) centre, forming a symmetrical complex. This coordination restricts the free rotation of the methylene group, leading to the observed spectral changes. Tridentate binding is considered unlikely, as literature evidence suggests that similar *N,N′,N″*-donor linear sulfonamide ligands do not coordinate to Pt(II) in a tridentate fashion due to electronic and steric restrictions. The resulting yellow solid of the platinum complex is soluble in chloroform but insoluble in polar solvents such as water. Spectroscopic and literature data collectively support the formation of a Pt(L)Cl_2-type complex, featuring an eight-membered chelate ring. Notably, complexation results in significant fluorescence quenching compared to the free ligand. The potential antibacterial activity of both the ligand (L) and the complex (C) was evaluated against gram-positive, *Staphylococcus aureus* ATCC25923, and gram-negative, *Escherichia coli* ATCC25922, using the agar well diffusion method. Both compounds exhibited minimal to no antibacterial activity even at 4000 ppm, suggesting limited interaction with bacterial cellular components. Nevertheless, further cytotoxicity studies on mammalian cell lines are warranted to assess their potential as anticancer agents.

Keywords: N-donor sulfonamide ligands, Benzimidazole, antibacterial.

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1. Introduction

Metallodrugs have garnered considerable interest in bioinorganic chemistry due to their wide-ranging biological effects and promising medical applications. Sulfonamides (SN) are a key group of synthetic antimicrobial agents widely employed in healthcare to combat bacterial infections. Benzimidazole derivatives are known for their diverse biological activities and have emerged as promising partners in sulfonamide chemistry, contributing to the development of hybrid molecules with enhanced pharmacological profiles (Arshaf *et al*., 2016). This study focuses on the synthesis and characterisation of novel *N,N′,N″*-donor linear sulfonamide ligands terminated with benzimidazole rings and their corresponding platinum complex to explore the potential biological applicability of them. Specifically, it has been investigated that when bis[(1-methylbenzimidazol-2-yl)methyl]amine ($\mathbf{L_{pre}}$) binds with 5-(dimethylamino)naphthalene-1-sulfonyl chloride to form *N,N*-bis-(1-methylbenzoimidazol-2-yl)methyl)-5-(dimethylamino)-naphthalene-1-sulfonamide (**L**)

2. Materials and methods

Synthesis and Characterisation of $\mathbf{L_{pre}}$, **L,** and **C**

N-methyl-1,2-phenylenediamine, Iminodiacetic acid (97%), Acetone, Distilled water, acetonitrile, Sodium sulphate (99.5%), and K_2PtCl_2 (47%) were obtained commercially. Synthesis bis[(1-methylbenzimidazol-2-yl)methyl]amine ($\mathbf{L_{pre}}$) was carried out with iminodiacetic acid and *N*-methyl-1,2-phenylenediamine by modifying a known procedure (Wei *et al*., 2006). $\mathbf{L_{pre}}$ was combined with 5-(dimethylamino)naphthalene-1-sulfonyl chloride, stirred in dioxane to prepare *N,N*-bis-(1-methylbenzoimidazol-2-yl)methyl)-5-(dimethylamino)-naphthalene-1-sulfonamide (**L**) and **L** was combined with $Pt(DMSO)_2Cl_2$, refluxed in acetonitrile, to prepare its platinum complex (**C**).

Antibacterial Potential of **L** and **C**

The organisms tested were gram-positive, *Staphylococcus aureus* (ATCC25923), and gram-negative, *Escherichia coli* (ATCC25922).

MHA (Muller-Hinton Agar) plates were prepared and inoculated with the above standard bacterial suspensions. The calibration was done against a 0.5 McFarland solution (2 mL), and the suspension was spread on the surface of the media. Five wells were cut in the MHA plate using a sterile cork borer. Hot sterilised MHA (one drop) was added to each well and allowed to set. 4 mg of each sample was dissolved in 1 mL (4000 ppm) of 85 % DMSO (Dimethyl sulfoxide). Each solution (50 µL) was added to wells in triplicate. 85 % DMSO, and Ciprofloxacin were used as the negative control and positive control, respectively. The plates were then incubated in an upright position at 37 °C for 24 hours. After incubation, the inhibition zone diameter was measured along three different axes and averaged (Devillers *et al*., 1989).

3. Results and Discussion

The ligand (**L**) was synthesised and purified by column chromatography, yielding a dark maroon solid. The metal complex (**C**) was subsequently prepared and isolated as a grey-yellow precipitate after chloroform washing. ^{1}H NMR analysis revealed distinct shifts in the methylene proton signals: while the ligand displayed a singlet, the complex exhibited two doublets, confirming successful coordination. This indicates that the ligand is bound to the metal bidentately. If the ligands were bound bidentately or tridentately, the free rotation of the methylene protons would be restricted, producing complicated NMR signals (Ranasinghe *et al*., 2018). The bulkiness near the coordination sphere created due to the benzimidazole moieties allows bidentate coordination of the ligands to the Pt(II) ion. Further, the tertiary sulfonamide *N,N′,N″*-donor linear sulfonamide ligand is geometrically positioned to form an eight-membered chelate ring with Pt(II) ions.
^{1}H NMR signals (ppm) of **L** in $CDCl_3$ (400 MHz, $CDCl_3$) δ 8.39 (dd, J = 17.8, 8.6 Hz, 2H), 8.09 (dd, J = 7.4, 1.2 Hz, 1H), 7.58 – 7.43 (m, 3H), 7.17 – 7.01 (m, 8H), 4.98 (s, 4H), 3.64 (s, 6H), 2.81 (s, 6H) FTIR (cm^{-1}) 781 (S–N), 1142 $(S=O)^{(as)}$, 1328 $(S=O)^{(s)}$, 621 (C–S), 1674 (C=N).

^{1}H NMR signals (ppm) of **C** in $CDCl_3$ (400 MHz, $CDCl_3$) δ 8.73 (d, J = 8.5 Hz, 1H), 8.57 (d, J = 8.2 Hz, 2H), 8.46 (d, J = 8.6 Hz, 1H), 8.09 (d, J = 7.4 Hz, 1H), 7.68 (t, J = 8.1 Hz, 1H), 7.61 (t, J = 7.9 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.39 – 7.29 (m, 4H), 5.84 (d, J = 15.6 Hz, 2H), 5.41 (d, J = 15.6 Hz, 2H), 4.02 (s, 1H), 2.98 (s, 1H) FTIR (cm^{-1}) 525 (Pt–Cl), 652 (S–C), 788 (S–N), 1142 $(S=O)^{(as)}$ 1328 $(S=O)^{(s)}$

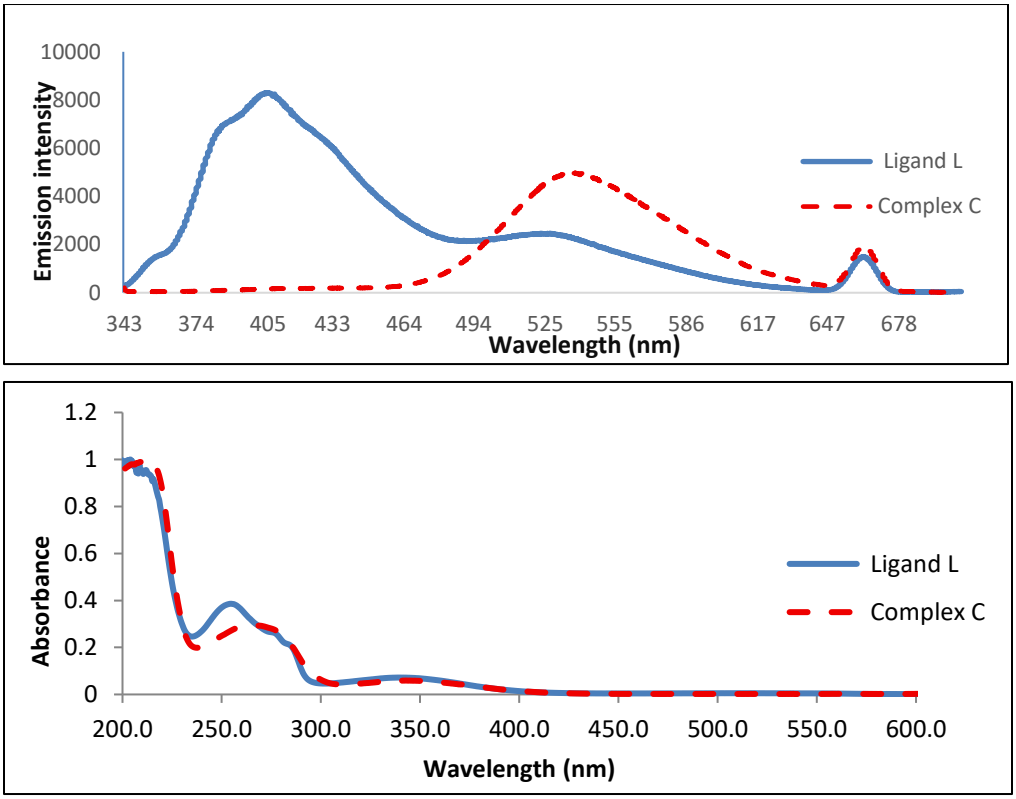

Figure 1- UV/Vis and Fluorescence spectra of Ligand **L** and complex **C**

Fluorescence spectral data (Figure 1) showed a decrease in fluorescence properties compared to ligands after complexation with the platinum metal, due to the anisotropic properties of platinum (II) metal complexes
Antibacterial Potential of Ligand (**L**) and complex (**C**) is being evaluated via the well diffusion method for their potential antimicrobial activity against gram-positive and gram-negative bacterial growth. Based on the results, at 4000 ppm, none of the tested compounds exhibited antibacterial activity.

4. Conclusion

A novel *N,N',N''*–donor sulfonamide ligand, *N,N*-bis-(1-methylbenzoimidazol-2-yl)methyl)-5-(dimethylamino)-naphthalene-1-sulfonamide (**L**) and its platinum complex Pt(**L**)Cl_2 (**C**) were successfully synthesised. Both compounds have been revealed through detailed spectroscopic characterisation, and their structural intricacies have been elucidated, which was conducted by ^{1}H NMR, FTIR, UV/V, and Fluorescence spectroscopies. Based on antibacterial studies, it is evident that at low concentrations, the tested compounds revealed no significant antibacterial activity.

References

A. Ashraf, W. Ahmad Siddiqui, J. Akbar, G. Mustafa, H. Krautscheid, N. Ullah, B. Mirza, F. Sher, M. Hanif, C.G. Hartinger, Metal complexes of benzimidazole derived sulfonamide: Synthesis, molecular structures and antimicrobial activity, Inorganica Chimica Acta (2016), doi: http://dx.doi.org/10.1016/j.ica. 2015.12.03

Wei, L., Babich, J. W., Ouellette, W., & Zubieta, J. (2006). Developing the $\{M(CO)_3\}^+$ core for fluorescence applications: rhenium tricarbonyl core complexes with benzimidazole, quinoline, and tryptophan derivatives. *Inorganic chemistry*, *45*(7), 3057-3066, doi: https://doi.org/10.1021/ic0517319

Devillers, J.; Steiman, R.; Seigle-Murandi, F. The Usefulness of the Agar-Well Diffusion Method for Assessing Chemical Toxicity to Bacteria and Fungi. *Chemosphere* 1989, *19* (10–11),1693–1700. doi: https://doi.org/10.1016/0045-6535(89)90512-2.

Ranasinghe, K.; Marzilli, P. A.; Pakhomova, S.; Marzilli, L. G. Linear Bidentate Ligands (L) with Two Terminal Pyridyl N-Donor Groups Forming $Pt(II)LCl_2$ Complexes with Rare Eight-Membered Chelate Rings. *Inorg Chem* 2018, *57* (20), 12756–12768. doi: https://doi.org/10.1021/acs.inorgchem.8b01943.