

Synthesis and Characterization of Metal Complexes with 4-Methyl-*N*-(*p*-methylphenylsulphonyl)-*N*-(pyridin-2-yl)benzene Sulphonamide

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Abstract: 4-methyl-*N*-(*p*-methylphenylsulphonyl)-*N*-(pyridin-2-yl)benzene sulphonamide is an important sulphonamide derivative that houses multiple essential moieties like pyridine nucleus, benzene core and sulphonamide. The research is aimed at the synthesis of 4-methyl-*N*-(*p*-methylphenylsulphonyl)-*N*-(pyridin-2-yl)benzene sulphonamide *via* the ditosylation of 2-aminopyridine. The ditosylated 2-aminopyridine was complexed with Zinc (II) ion and Copper (II) ion. The structural elucidations were achieved through UV-Vis, FTIR, ¹HNMR, ¹³CNMR, ESI-MS and Micro-analysis. The data of the elemental analysis agrees with the molecular masses of ESI-MS. The molar conductance revealed that all the complexes are non-electrolyte in nature. The UV-VIS electronic band of 375–362 nm was assigned to n → π* electronic transition of ligand metal charge transfer (LMCT) of zinc (II) complex while 490–358nm and 690nm were assigned to n → π* electronic transition of ligand metal charge transfer (LMCT) and d → d to electronic transition of copper (II) complex respectively. The infrared (IR) spectra studies indicated the bond between the ligand and the transition metals. The spectra of the complexes showed an absorption shift, with the free ligand of azomethine having the absorption band of 1689.70 cm⁻¹ while that of the complexes, Zn (II) and Cu(II) have the absorption bands of 1674.27cm⁻¹ and 1651.12cm⁻¹ respectively. The complexation of 4-methyl-*N*-(*p*-methylphenylsulphonyl)-*N*-(pyridin-2-yl)benzene sulphonamide may hopefully increase the biological and catalytic potential of the ligand in the pharmaceutical and chemical industries.

Keywords: 2-Aminopyridine, Complexation, Ditosylation, 4-methyl-*N*-(*p*-methylphenylsulphonyl)-*N*-(pyridin-2-yl)benzene Sulphonamide, Synthesis

1. Introduction

The coordination chemistry of organic compounds has undergone noticeable development in recent years due to the interesting properties in medicinal chemistry. Research has proved that the physical properties and the antimicrobial activities of an organic compound are enhanced upon complexation. Thus, the variety of exciting and valuable drugs that are already in the market has made metal-ligand based drugs to become a vibrant and growing aspect of research among organic chemists over the last few decades

[1-4].

Metal complexes can present different chemical, physicochemical and biochemical properties than the constituents (central metal and ligands). The biological effectiveness does not depend solely on the release of metal ion or the active ligand, but it is associated rather strongly on the nature and structure of the new compound to which the metal ion is bound. The size, charge distribution, shape and redox potentials of complexes are essential properties related to the mechanism of action [5-8].

Research on the physical properties and bioactivity of

copper and zinc complexes and their ligands depict that the complexes possess better physical properties (molar conductivity, magnetism) and biological activity than their ligands. This essential attribute could be associated with the corrosive nature of the metals in their free state [9, 10]. In addition, many compounds with zinc and copper have been prepared and their applications, physicochemical and biological activity probes have been investigated [11-13].

Sulphonamides are functional moieties found in many biologically important compounds. This is as a result of the various uses to which they have been employed. The modification and variation of the structures have opened up newer areas of opportunities for many other uses. Sulphonamides have been used as antiprotozoal, antifungal and anti-inflammatory agents [14-16]. They have also been employed in the treatment of urinary, intestinal and ophthalmic infections. Only recently they have found uses as anticancer, antiviral, HIV protease inhibitor and in the treatment of Alzheimer disease [17, 18].

4-methyl-*N*-(*p*-methylphenylsulphonyl)-*N*-(pyridin-2-yl)benzene sulphonamide is an organic compound obtained with ditosylation of 2-aminopyridine. It holds pyridine ring, benzene core and sulphonamide as functional moieties. It has been established that this sulphonamide is sensitive to some microorganisms, like *Escherichia coli*, *Staphylococcus aureus*, *B. subtilis*, *B. licheniformis*, *B. linens*, *K. pneumonia*, *Streptococcus pyogenes*, *Aspergillus niger* and *Candida albicans*. [19]

In the light of this interest, we here describe the synthesis and characterization of the metal complexation of 4-methyl-*N*-(*p*-methylphenylsulphonyl)-*N*-(pyridin-2-yl)benzene sulphonamide using 2-aminopyridine and tosyl chloride as the precursors. The two metals used in the complexation were Zn (II) and Cu (II) ions. The detailed spectroscopic (UV-Vis, FTIR, NMR and ESI-MS) and the micro-elemental analysis of the ligand, zinc (II) and copper(II) complexes are also discussed in this article.

2. Materials and Methods

2.1. Equipment Used in This Study

The chemicals 2-aminopyridine, tosyl chloride ethanol, acetic acid, acetone, sodium trioxocarbonate (IV) and others were of analytical grade and were used without purification. TLC analysis was carried out using pre-coated silica gel plate (10x10 cm); the R_f value was obtained using a solvent mixture of acetic acid and ethanol in a ratio of 1:2. The chromatogram was visualized using an ultraviolet lamp at 256nm. The melting point was recorded with Digital Melting Point Electrothermal IA9300X1. The IR spectra were obtained from the FTIR-8400S Fourier Transform Infrared spectrophotometer at NARICT Zaria using an ATR disc. It was used to identify the functional groups, Liquid Chromatography/Mass Spectrometer was used for molecular formula/mass identification, and Proton Nuclear Magnetic Resonance (¹HNMR) and Carbon-13 Nuclear Magnetic

Resonance (¹³CNMR) were recorded on a JEOLA-LA-400 MHz-NMR Spectrophotometer at the University of Strathclyde, United Kingdom.

2.2. Experimental Methods

2.2.1. Ditosylation of 2-Aminopyridine

The method adopted for the tosylation of 2-aminopyridine was by Orié *et al.*, [4] and Abdul-Qadir *et al.*, [20] with minor modification. Aminopyridine (0.053mol) and sodium trioxocarbonate (IV) (1M, 20ml) were placed in distilled water (25ml) and stirred vigorously for 15 minutes. Thereafter, tosyl chloride (0.106 mol) was gradually added to the mixture and stirred vigorously at room temperature for 4 hours. After completion of the reaction monitored by pH change and TLC analysis, few drops of concentrated HCl were added to adjust the pH of the solution. This thus led to the precipitation of the product which was washed severally with distilled water and recrystallized with a mixed solvent system of ethanol and water at a ratio of 1:5. The resulting crystal was collected via filtration, washed with distilled water and dried.

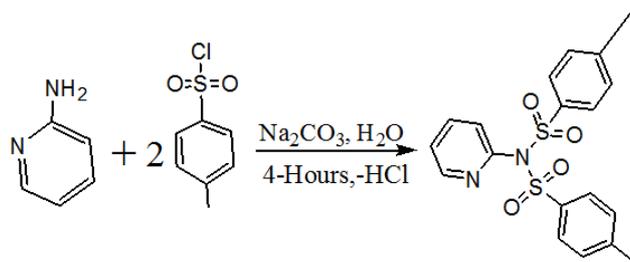
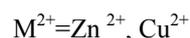
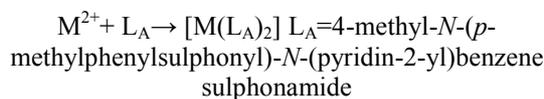


Figure 1. Ditosylation of 2-aminopyridine.

2.2.2. Complexation of 4-methyl-*N*-(*p*-methylphenylsulphonyl)-*N*-(pyridin-2-yl)benzene sulphonamide

A hot ethanolic solution of C₁₉H₁₈N₂O₄S₂ (4Mmol) was placed in a boiled ethanolic solution of Cu(NO₃)₂·6H₂O / ZnCl₂ (4Mmol.). The mixture was stirred for 2hours allowed to stand for 2 hours undisturbed. The precipitate formed was filtered and washed severally with ethanol. The products were recrystallized with a mixed solvent of DMSO and ethanol (1:6). It was allowed to dry at ambient temperature.



3. Results and Discussion

3.1. Solubility Analysis of Ligand and Complexes

The solubility of the ligand and the complexes were investigated in eight different solvents (see table 1). The ligand was soluble in ethanol, acetic acid, Dimethylformamide and Dimethyl sulphoxide but insoluble in water, *n*-hexane, acetone and ethyl acetate while complexes are soluble in acetic acid, DMF and DMSO but insoluble in water, *n*-hexane, acetone, ethanol and ethyl acetate [9, 10].

Table 1. Solubility analysis of Ligand and Complexes.

Serial No	Ligand/ Complexes	Hex	EtOH	Ace	EA	AA	DMF	DMSO	H ₂ O
1	C ₁₂ H ₁₂ N ₂ O ₂ S	X	S	X	X	S	S	S	X
2	[Zn(C ₁₂ H ₁₂ N ₂ O ₂ S) ₂]	X	X	X	X	S	S	S	X
3	[Cu(C ₁₂ H ₁₂ N ₂ O ₂ S) ₂]	X	X	X	X	S	S	S	X

S=Soluble, X=Insoluble, EA=Ethyl acetate, AA=Acetic acid, Ace=Acetone, Hex=Hexane, EtOH=Ethanol, DMF=Dimethylformamide, DMSO=Dimethyl sulphoxide

3.2. NMR Analysis the Ligand, 4-methyl-N-(p-methylphenylsulphonyl)-N-(pyridin-2-yl)benzene Sulphonamide

The ¹HNMR analysis of the ligand, 4-methyl-N-(p-methylphenylsulphonyl)-N-(pyridin-2-yl)benzene sulphonamide is shown in table 2. The table contains the experimental ¹HNMR data, estimated Chemdraw ¹HNMR and

¹HNMR data from the literature. The presence of the chemical shift value from 7.12-8.13 ppm is assigned to the aromatic zone, which confirms the presence of both benzene and pyridine rings of the ligand [7]. The chemical shift value of 2.22ppm is assigned to the methyl group of the tosyl moieties. Both the Chemdraw estimation and literature [4, 19, 20] agrees with the experimental information in table 2.

Table 2. Proton Nuclear Magnetic Resonance.

Position	Experimental	Chemdraw analysis	Literature (ref)
	¹ HNMR (500 MHz, DMSO), (δppm)	Chem. NMR H-1 Estimation	¹ HNMR(500MHz, MeOD), ¹ H (δ ppm)
	δ=8.13 (m, 1H)	δ=8.11 (d, 1H, CH)	δ=8.19 (s, H, CH),
	δ=7.92, (m, 1H, CH),	δ=6.60 (m, 1H, CH)	δ=8.02 (d, J=8.09Hz, 1H, CH),
	δ=7.53 (d, J=7.84Hz, 1H, CH),	δ=7.44 (dd, 1H, CH)	δ=7.87 (t, J=8.41Hz, 1H, CH),
1	δ=7.70 (d, J=8.00 Hz, 1H, CH),	δ=6.70 (d, 1H, CH)	δ=7.68 (d, J=8.11Hz, 1H, CH),
	δ=7.12 (d,d J=7.93, 2.42, H, CH)	δ=7.81 (d, 4H, CH)	δ=7.61 (d, J=8.37Hz, 1H, CH),
	δ=2.22 (m, 3H, CH ₃)	δ=7.34 (d, 4H, CH)	δ=7.55 (d, J=7.27Hz, 1H, CH),
		δ=2.35 (s, 3H, CH ₃)	δ=2.46 (s, 3H, CH ₃)

The carbon-13 NMR chemical shift value of 111.62-154.63 ppm was assigned to the aromatic zone, thus, confirming both the presence of pyridine and benzene ring. The chemical shift value of 21.21ppm confirms the presence of the methyl group. This observation was in line with both the Chemdraw estimation and literature [19, 21].

3.3. Physical Characteristics and Analytical Data of Ligand/Complexes

The ligand was synthesized in aqueous basic media by a simple reaction of 2-aminopyridine and tosyl chloride in a mole ratio of 1:4. The complexes, [Zn(C₁₉H₁₈N₂O₄S₂)₂] and [Cu(C₁₉H₁₈N₂O₄S₂)₂] were synthesized hot alcoholic

solution. The percentage yield of the ligand was 60%, while that of Zn (II) and Cu (II) complexes were 75% and 88% which indicates that the compound synthesized was in good yield. The melting point range for both the ligand and complexes as shown in table 3 has the difference of two, which at this point indicates the purity of the compounds. The molar conductance of the complexes was determined in DMSO. It was found to be 12.3, 13.6 and 14.2 Ω⁻¹cm²mol⁻¹ for the ligand, Zn and Cu complexes respectively. The obtained values also imply that no anions are present outside the coordination sphere in all the complexes. These values suggested their non-electrolytic nature [4, 22, 23].

Table 3. Physical Properties of Ligand and Complexes.

Compound	Colour	Mol. weight	Melting point, °C	% Yield	Molar conductivity Ω ⁻¹ cm ² mol ⁻¹	TLC Analysis	
						R _F Value	Solvent mixture/ ratio
C ₁₉ H ₁₈ N ₂ O ₄ S ₂	Offwhite	403.12	160-162	70	12.3	0.79	AA: ETOH: H ₂ O (2:1:1)
[Zn(C ₁₉ H ₁₈ N ₂ O ₄ S ₂) ₂]	white	871.24	220-222	75	13.6	0.72	DMF: ACE (2:1)
[Cu(C ₁₉ H ₁₈ N ₂ O ₄ S ₂) ₂]	Ligh blue	869.74	210-212	88	14.2	0.69	DMF: ACE (2:1)

Elemental Analysis of the Ligand and its Complexes

The elemental analyses of 4-methyl-N-(p-methylphenylsulphonyl)-N-(pyridin-2-yl)benzene sulphonamide and its complexes are in Table 4. This

analytical data were in good agreement with the ESI-MS estimation and the proposed empirical formula of the complexes [19, 23].

Table 4. Elemental Analysis of the Ligand and Complexes.

compounds	Mol. weight	Analysis Found (calculated)%					
		M	C	H	N	O	S
C ₁₉ H ₁₈ N ₂ O ₄ S ₂	403.12	-	56.12 (56.58)	4.044 (4.47)	7.00 (6.95)	16.00 (15.88)	16.89 (15.88)
[Zn(C ₁₉ H ₁₈ N ₂ O ₄ S ₂) ₂]	871.24	7.60 (7.50)	52.13 (52.34)	4.43 (4.13)	6.54 (6.43)	14.65 (14.69)	14.65 (14.69)
[Cu(C ₁₉ H ₁₈ N ₂ O ₄ S ₂) ₂]	869.74	7.55 (7.58)	52.37 (52.43)	4.31 (4.14)	6.39 (6.44)	14.69 (14.75)	14.69 (14.75)

3.4. Electronic Spectral Data of Ligands and Complexes

The electronic transition the pure sulphonamide, Zn(II) and Cu(II) ion were measured in DMSO solution between 200–1100 nm at room temperature. The absorption below 250 nm was obscured in the DMSO spectra due to solvent absorption. The band at 225–203 nm corresponds to the $\pi \rightarrow \pi^*$ transition of the benzene rings, while the absorptions at 289–256 nm and 334–289 nm were assigned, respectively, to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions of the azomethine group, HC=N of 2-aminopyridine. The electronic absorption band of

375–362 nm was attributed to $n \rightarrow \pi^*$ internal ligand metal charger transfer (LMCT) of zinc complex, while the electronic transitions of 490–358nm and 690 nm were attributed to $n \rightarrow \pi^*$ internal ligand metal charger transfer (LMCT) and d–d electronic transition of the copper complex [17, 24]. However, the electronic spectrum of the zinc (II) complex does not show any band that corresponds to the central metal ion and the bands observed are mainly due to the ligands and metal-to-ligand interactions. This could be attributed to the filled d orbital in the zinc(II) atom [25, 26].

Table 5. Selected UV-VIS Absorption Bands for Ligand and Complexes.

compound	Adsorption nm	Band assignment
C ₁₉ H ₁₈ N ₂ O ₄ S ₂	225–203, 289–256, 334–289	$\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$
[Zn(C ₁₉ H ₁₈ N ₂ O ₄ S ₂) ₂]	375–362	$\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$
[Cu(C ₁₉ H ₁₈ N ₂ O ₄ S ₂) ₂]	490–358, 690	$\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$, d → d

$\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$: Electronic transition from highest occupy molecular orbital(HOMO) to lowest unoccupy molecular orbital(LUMO)

Major FTIR Spectral Data of Ligands and Complexes

The IR vibration frequency of the ligand and its metal complexes are given in Table 6. The ligand contains three potential donor sites: the heterocyclic azomethine nitrogen, the sulfonamide oxygen and the sulphonamide nitrogen. The vibration frequency band of 1010.02 cm^{-1} was assigned to sulphonamide nitrogen, the band at 1519.96 cm^{-1} was assigned to the carbon to carbon double bond in aromatic and

the band at 1689.98 cm^{-1} was assigned to the heterocyclic azomethine nitrogen [27, 28]. The evidence of the imine nitrogen coordinated to zinc (II) ion was depicted with a frequency band of 1674.24 cm^{-1} and that of the copper (II) was indicated with the vibration frequency band of 1651.12.30 cm^{-1} . This observation is in line with the azomethine (C=N) frequency range of 1643.41–1575 cm^{-1} observed by Al-Noor [25].

Table 6. Selected FT IR Absorption Bands for and complexes.

S/no	Ligand/complex	V _{C-H}	V _{C=N}	V _{C=C}	V _{-N-S=O}
1	C ₁₉ H ₁₈ N ₂ O ₄ S ₂	2916.47	1689.70	1519.92	1003.02-1134.18
2	[Zn(C ₁₉ H ₁₈ N ₂ O ₄ S ₂) ₂]	2908.75	1674.27	1527.67	1010.73-1134.18
3	[Cu(C ₁₉ H ₁₈ N ₂ O ₄ S ₂) ₂]	2931.90	1651.12	1519.96	1010.02-1134.18

4. Conclusion

The compound 4-methyl-*N*-(*p*-methylphenylsulphonyl)-*N*-(pyridin-2-yl)benzene sulphonamide is coordinated with zinc (II) ion and Cu (II) ion through the imine of 2-aminopyridine. This inference was on the basis that there was a shift in the vibration frequency band of the imine in both the free ligand and the complexes. The decrease in the vibration frequency band of the ligand to the frequency band of the complexes proved that there was a transfer of electrons from the ligand to the metal complexes. Further estimation was on the platform that the ESI-MS mass of the ligand and complexes was in agreement with the micro-elemental analysis of the ligand and the complexes. The UV-VIS transition band implied the formation of ligand metal charger transfer (LMCT) in both zinc (II) ion and Cu (II), and a d–d electronic transition of the

copper complex. The metal complexes with the synthesized ligand were new and could be potential anti-microbial agents in the pharmaceutical industries.

Conflicts of Interest

All the authors do not have any possible conflicts of interest.

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