IJCRCPS

International Journal of Current Research in Chemistry and Pharmaceutical Sciences
www.ijcrcps.com Volume 1 Issue: 6 2014 Pages:101-107

(pISSN: 2348-5213; eISSN: 2348-5221)

RESEARCH ARTICLE

SYNTHESIS, CHARACTERRISATION AND ANTIMICROBIAL PROPERTIES OF SOME TRANSITION METAL COMPLEXES OF 4,4'-BIPYRIDINE

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Abstract

Co(II), Cu(II) and Zn(II) complexes with 4,4'-bipyridine as ligand have been synthesised and characterised by elemental analyses, FTIR and thermogravimetric analyses. The results obtained indicate that the ligand is coordinated to the metal ions. Antimicrobial studies revealed that the Co(II) complexes showed higher activities than the reference antibiotic against the five tested bacteria strains.
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Keywords: Bipyridine; Antimicrobial; Cobalt(II); Copper(II); Zinc(II)

Introduction

There has been considerable interest in the design and synthesis of coordination polymers because of their intriguing structural diversity and potential applications in gas storage (Ferey, 2008; Yaghi, 2005; Roswell & Yaghi, 2006), magnetism (Barthelet *et al*., 2002), non-linear optics (Evans & Lin, 1998; Lin *et al*., 1998), separations (Kitaura *et al*., 2002), catalysis (Seo *et al*., 2000) and drug delivery (Horcajada *et al*., 2006). Coordination polymers are obtained from transition metal ions and multidentate organic ligands through coordination-directed self-assembly (Moulton & Zaworotko, 2001; Kitagawa *et al*., 2004; Fang *et al*., 2004). The structures and properties of these coordination polymers can be tailored by a careful choice of the metal ion and organic linker (Imaz *et al*., 2011). Among various ligands, nitrogen heterocycles, such as the simple ligand 4,4'-bipyridne, has been extensively used as bridging ligands for the design and synthesis of functional materials because of their good bridging ability (Chen *et al*., 1992; Hagman *et al*., 1997; Fujita *et al*., 1994; Yaghi & Li, 1995; Yaghi & Li, 1996; Losier & Zaworotko, 1996; Lu *et al*., 1998; Zhang *et al*., 1999; Ma *et al*., 2001). The ligand 4,4'-bipyridine is an ideal connector between transition metal atoms for the propagation of coordination networks because: it has two potential binding sites which are arranged in a divergent (*exo*) fashion; has a rigid structure which will help in predicting the network geometries; the length of the ligand (~10 Å) is good enough to create the cavities of molecular dimensions upon the formation of networks with the metal atoms.

The complexes of, 4,4'-bipyridine have gained sustained interest because of their use as models in biological systems and biomimetic reactions (Chen *et al*., 2007). The application of this class of materials in diverse domains has been extensively studied but their antimicrobial properties have been rarely studied. Although effective antimicrobial therapy is available for most infections, the inappropriate use of antimicrobials has led to high levels of resistance, with the emergence of strains resistant to almost all antimicrobial agents (Petrus *et al*., 2011). Thus, it is imperative to seek alternative ways of fighting the problem of resistance.

It has been found that-bipyridine compounds present intense antibacterial containing and antifungal activities (Kumar & Rao, 2005). The antimicrobial activity of some pyridinium salts derived from 4,4'-bipyridine have been reported (Rotaru *et al*., 2004). Some of these compounds inhibit the growth of microorganisms (bacteria and fungi), with the substituent on the aromatic ring bonded to the nitrogen atom partially influencing activity and largely influencing selectivity (Rotaru *et al*., 2004).

The approach of using specific metal centres bound to organic molecules as antimicrobials provides an alternative method of mitigating the threat to public health posed by microbial resistance. The incorporation of metals or some metal-based systems into the molecules of antibacterial and antifungal molecules is expected not only to enhance the bactericidal or fungicidal properties, but also to improve the potential of the less active compounds.

Experimental

All the chemicals were of reagent grade and were used as such without further purification. All solvents used were dried and distilled according to standard methods.

Physical Measurements

Elemental analysis for carbon, nitrogen, and hydrogen were carried out using a Flash 2000 CHNSO Thermoscientific Analyser. The melting point/decomposition temperatures of the complexes were obtained using the Mel-Temp II Lab Device. The infrared spectra of the ligand and complexes were recorded using Perkin Elmer (FT-IR spectrum 100) spectrophotometer in the spectral range 4000 - 400 cm^{-1} with resolution of 4 cm^{-1}. Thermal analyses were carried out with a TGA Perkin Elmer Thermogravimetric analyser TGA 4000 in the temperature range 30 –900 °C at a standardised heating rate of 10 $°C min^{-1}$ under the flow of nitrogen gas.

Synthesis of the Complexes

Generally, the complexes were prepared by reaction of the respective metal salts with 4,4'-bipyridine using 1:1 mole ratio, i.e. one mole of metal salt to one mole of 4,4'-bipyridine.

For example, $Cu(Bpy)(NO_3)_2{\cdot}6.5H_2O$ was synthesised by adding $Cu(NO_3)_2{\cdot}2.5H_2O$ (0.465 g; 2 mmol) in 30 mL of an ethanol/water solution (1:1 v/v) and the solution was heated to 60 °C while stirring. A solution of 4,4'-bipyridine (0.312 g; 2 mmol) in 10 mL of ethanol was added drop-wise to the hot solution. The mixture was refluxed for two hours at 60 °C and the resulting pale-blue precipitate was filtered and washed with diethylether and dried in vacuo over silica gel. The other complexes were similarly prepared.

Anti-Microbial Tests

The in-vitro antimicrobial activities of the complexes were done at the Department of Pharmacy and Pharmacology, University of the Witwatersrand, Medical School, South Africa. These tests were carried out following a published method (Muriana *et al*., 2009) with slight modifications. Five species of bacteria namely: *Staphylococcus aureus*, *Bacillus cereus* (Gram-positive bacteria), *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumonaie* (Gram-negative) were used for this study.

Using a starting concentration of 10 mg/ml, dilutions of each of the metal complexes were made in 100 ml of enriched pleuropneumonia-like organism basal (PPLO) medium in a sterile microtitre plate. Thereafter, 100 ml of 1:10 dilution of 48 hours actively growing bacteria broth culture was added to each well. One percent glucose and phenol red as an indicator was added to an aliquot of the enriched PPLO. The antibiotic ciprofloxacin at concentration of 1.28 mg/ml was also serially diluted and used as drug positive control while half strength acetone was used as negative control. One well on each plate also had a positive growth control containing no metal complex extract or ciprofloxacin. The microtitre plates were covered with thin aluminium foil and incubated at 37 °C for 24-36 hours before the results were read. After 24 hours of incubation, 40 mL of freshly prepared 0.2 mg/mL INT (p -

iodonitrotetrazolium) was added to each well of the plate that had the medium that did not contain glucose and phenol red. It was incubated for a further 4-5 hours before being read. In this case, a change of the medium to pinkish-red indicated that the bacteria were metabolically active. The MIC was taken as the last well where no change of colour (i.e. no bacterial growth) was observed for both methods.

Results and Discussion

Physical and Analytical Measurements

Metal complexes of 4,4'-bipyridine were prepared by refluxing the starting materials at 60 °C for two hours. The physical and analytical data for the complexes are presented in Table 1. The complexes formed are crystalline solids that are air stable and non-hygroscopic as opposed to the starting salts. They are less intense in colour than the respective metal salts from which they were derived (except the Zn complexes). The yields range from 71 to 85 %. Most of the complexes are stable up to 360 °C.

FTIR Spectral Analysis

The FTIR data of ligand and complexes are listed in Table 2, the main IR bands are assignedaccording to the literature (Xiu-Min *et al*., 2010).

The ν(OH) band 3500atcm 3428for compound scm **1** and **2**, respectively, indicates the coordination of water molecules (Agwara *et al*., 2011). Coordination of the 4, -bipyridine4‟ molecule to the metal ions leads to new M –N coordination bonds is formed. Consequently, changes in the vibrational frequencies of the C –N, C = C, C –C and C –H bonds occur in the complexes. The ν(C band= C)forthe ligand at 1589 cm^{-1} is blue shifted in all the complexes and found in the range 1601 to 1614 cm^{-1}. In all the complexes, the strong ligand band at 807 cm^{-1} for γ(C–H) has been blue shifted in the complexes and fall in the range 810 to 820 cm^{-1}. The bands of the ligand at 1219 and 1076 cm^{-1} and those for the complexes (**1**-**5**) at 1229 and 1102 cm^{-1}; 1226 and 1099 cm^{-1}; 1219 and 1084 cm^{-1}; 1221 and 1080 cm^{-1}; and 1221 and 1078 cm^{-1}, respectively, are attributed to in-plane C –H bending vibration in the bipyridine ring. The –ν(CH)ofpyridine ring bands in the ligand appeared at 3025 cm^{-1}, but appeared at 3083, 3060, 3085, 3061 and 3054 cm^{-1} in the complexes.

Two new bands each, which appear at 1064 and 975 cm^{-1} for **1**, 1054 and 979 cm^{-1} for **2** are absent in the free ligand and the chloride complexes (**3**-**5**). These new bands are attributed to S = O and S – O vibrations of the SO_4^{2-} counter ion [28]. The absence of vibrational bands in the 2400 cm^{-1} region where N –H stretching is expected, indicates that - Bpy4,4‟isnot protonated (Soleimannejada *et al*., 2010).

Thermogravimetric Analysis

Thermogravimetric analysis (TGA) performed on one of the complexes (**3**), **$Cu(Bpy)Cl_2·1/4H_2O$**, shows that it undergoes mass loss in two steps from about 200 –900 ºC (Fig. 1). The TGA curve shows a decomposition pattern which corresponds to the loss of ca. 48.11% and 25.60 % mass consistent with the departure of one 4,4‟-bipyridine molecule at 400 ºC and two chloride ions per molecule in the temperature range 410 –890 ºC, respectively.

Antibacterial Tests

The sensitivity of the bacterial strains to the reference antibiotic (*ciprofloxacin*) and the complexes were judged by measuring the Minimum Inhibitory Concentration (MIC), and the results obtained are presented in Table 3.

The results indicate that the metal complexes showed selective activity on the tested pathogens, with activity increasing in the order $Cu(Bpy)Cl_2·1/4H_2O$ < $Zn(Bpy)Cl_2·3H_2O$< $Cu(Bpy)_{1/2}SO_4·2.5H_2O$ < $Co(Bpy)_{1/2}SO_4·5H_2O$ < $Co(Bpy)_{1.5}Cl_2·3.3H_2O$ (**3**<**5**<**1**<**2**<**4**). All the complexes (**1-5**) were found to be less active than the reference antibiotic against *P. aeroginosa*. Complexes **2**, **3** and **4** were more active than the reference antibiotic against *S. aureus*, with complex **4** having the greatest the activity. Complex **5** was significantly more active than the reference antibiotic against *B. cereus*. The complexes **1**, **2** and **4** showed higher activity than that of the reference antibiotic against *E. coli*, with the activity of complex **2** being the highest. The complexes **2** and **4** were significantly more active than the reference against *K. pneumoniae*. The cobalt complexes (**2** and **4**) are thus the most active among the tested compounds while the copper and zinc complexes were the least active.

Table 1: Physical and Analytical Data of the Complexes

Complexes	Molecular Weight	Colour	Yield (%)	Melting Point (°C)	Elemental Analysis %Found (%Calculated)			
					%C	%H	%N	%S
$Cu(Bpy)_{1/2}SO_4·2.5H_2O$ **1**	282.73	Pale Blue	85	>360	21.24 (21.35)	3.21 (2.85)	4.95 (4.96)	11.34 (11.23)
$Co(Bpy)_{1/2}SO_4·5H_2O$ **2**	323.16	Violet	81	>360	18.58 (18.47)	4.37 (2.78)	4.33 (4.14)	9.92 (10.16)
$Cu(Bpy)Cl_2·1/4H_2O$ **3**	290.15	Green	71	>360	40.70 (40.85)	2.90 (3.19)	9.49 (9.19)	
$Co(Bpy)_{1.5}Cl_2·3.3H_2O$ **4**	423.57	Violet	73	>360	42.54 (42.43)	4.43 (3.01)	9.92 (9.57)	
$Zn(Bpy)Cl_2·3H_2O$ **5**	346.97	White	71	>360	34.66 (34.89)	4.07 (2.87)	8.08 (7.97)	

Table 2: Characteristic Bands in the FTIR Spectra of the Complexes

Ligand	**1**	**2**	**3**	**4**	**5**	**Assignment**
-	3428	3500				ν(O-H)
3025m	3083m	3062w	3085w	3061m	3054m	ν(C-H)
1589s	1614s	1608s	1609m	1606s	1601s	ν(C–N)
1531m	1539w	1538m	1536m	1534m	1535m	ν(C-C)
1486w	1498w	1491w	1494m	1492m	1493m	δ(C-N)
1405s	1421m	1414m	1415s	1413vs	1415vs	Ring breathing
1219m	1229s	1226s	1219s	1221s	1221s	δ(C–H)
1076w	1102br	1099br	1084m	1080w	1078m	δ(C–H)
	1064m	1054m				$ν(SO_4^{2-})$
	975	979				ν(S–O)
1038w	1044m	990s	1048s	1049m	1045m	Ring breathing
850w	872w	875m	850w	857w	858w	γ(C–H)
807vs	817s	820vs	811vs	810vs	819vs	γ(C–H)
735w	728m	728m	728m	729m	729m	Ring breathing

Fig. 1: TGA curve for $Cu(bpy)Cl_2 \cdot 0.25H_2O$ (**3**)

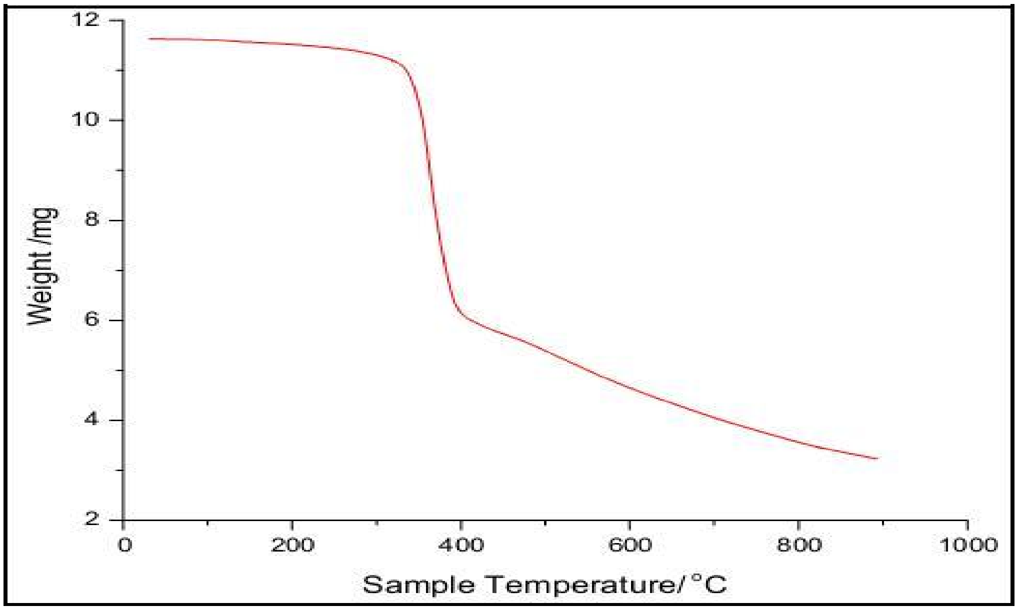

Table 3: Antibacterial Activities of the Complexes and the Reference Antibiotic Evaluated by Minimum Inhibitory Concentration (MIC: µg/mL)

Complexes	Bacteria				
	P. aeroginosa	*S. aureus*	*B. cereus*	*E. coli*	*K. pneumonaie*
1	0.625	0.625	1.25	0.625	0.625
2	0.625	0.3125	0.3125	0.3125	0.156
3	>5	0.3125	>5	>5	>5
4	0.625	0.156	0.3125	0.625	0.156
5	0.625	>5	0.019	>5	>5
Ciprofloxacin	0.039	0.625	0.039	1.25	0.313

Conclusion

Metal complexes of Co(II), Cu(II) and Zn(II) with 4,4'-bipyridine as ligand have been synthesized and characterized by elemental analyses, infrared spectroscopy and thermal analysis. Antibacterial studies on the complexes revealed that they showed selective activity against the tested pathogens.

The cobalt(II) complexes (**2** and **4**) were found to be the most active compounds against some of the tested bacteria strains. The considerably higher activity of the cobalt(II) complexes reveals the effect of chelation on the biological activity of the ligand.

Acknowledgement

Professor Sandy van Vuuren, Department of Pharmacy and Pharmacology, University of the Witwatersrand, Medical School Faculty of Health Sciences, 7 York Road, Parktown, 2193 South Africa for the biological tests

Conflict of Interests

"The authors declare that there is no conflict.

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