Acta Medica Scientia 02 [06] (2015)
www.asdpub.com/index.php/ams
E-ISSN: 2454-3594

Original Article

Synthesis, characterization and biological evaluation of sulfonamide based transition metal complexes

Hitesh R Patel and Asha D. Patel*

Department of Chemistry, M.N. College, Visnagar– 384315 India

***Corresponding Author**
Asha D. Patel
Department of Chemistry,
M.N. College, Visnagar –
384315 India
E-mail: dr.ashapatel123@gmail.com

Keywords:
Maleic anhydride,
Sulphanilamide,
Magnetic moment,
Spectroscopic study and Antifungal properties

Abstract

In the present study a noval 4-oxo-4-(4-sulfamoylphenylamino) but-2-enoic acid (OSPAB) was prepared by reaction of maleic anhydride with sulphanilamide. The prepared ligand was characterized by elemental analysis and spectral studies. The transition metal complexes viz. Cu^{2+}, Ni^{2+}, Co^{2+}, Mn^{2+} and Zn^{2+} of OSPAB were prepared and characterized by metal-ligand (M:L) ratio, IR, reflectance spectroscopies and magnetic properties. All the prepared metal complexes and ligand were studies as antimicrobial agent. Among all the metal complexes, Zn^{2+} and Cu^{2+} metal complexes have shown significant activity.

1. Introduction

In inorganic chemistry most active research area is coordination chemistry. Recently, numbers of coordination metal complexes have been synthesized and investigated, which exhibit various biological activities [1-5]. Sulpha drugs are largely in used as chemotherapeutic agents whose molecular structures contain a 4-aminobenzene sulfonamide moiety. The Sulpha drugs and their derivatives show diverse biological activities like antihypertensive agent bosentan [6], antibacterial [7], antiprotozoal [8], antifungal [9], anti-inflammatory [10], nonpeptidic vasopressin receptor antagonists [11] and translation initiation inhibitors [12]. The reaction of maleic anhydride derivatives with sulphanilamide has not been reported for metal complaxation so far. Hence, it was thought that maleic anhydride and sulphanilamide moieties can put into one molecule frame may afford good biological active compound. The present article discuss about synthesizes, characterization and biological studies of 4-oxo-4-(4-sulfamoylphenylamino) but-2-enoic acid (OSPAB). Also its metal complexes based on literature serve regarding importance of complexes, it was thought to synthesis transition metal complexes of prepared ligand in order to improve in biological activity.

2. Experimental

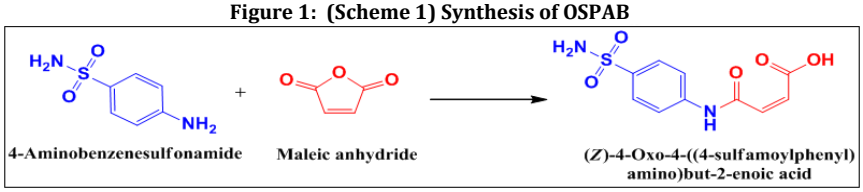
2.1. Materials and measurements

All the chemicals used were of laboratory grade received from Sigma–Aldrich. Sulphanilamide was prepared according to method reported in literature [13]. ^1H, ^{13}C and DEPT-135 NMR spectra were recorded in $CDCl_3$ at room temperature using a Bruker AVANCE III 500 MHz (AV 500) multi nuclei solution NMR Spectrometer, TMS was used as internal reference. IR spectra were recorded neat by ATR on a Thermo Nicolet iS50 FT–IR spectrometer and are reported in cm^{-1}. HR–MS data were obtained in methanol, with Thermo Scientific Orbitrap Elite Mass spectrometer. The elemental contents were determined by Thermo Finigen Flash1101 EA (Itally) the metals were determined volumetrically by Vogel's method [13]. To a 100 mg chelate sample, each 1 ml of HCl, H_2SO_4 and $HClO_4$ were added and then 1 g of $NaClO_4$ was added. The mixture was evaporated to dryness and the resulting salt was dissolved in double distilled water and diluted to the mark. From this solution the metal content was determined by titration with standard EDTA solution. Magnetic susceptibility measurements of the synthesized complexes were carried out on Gouy Balance at room temperature. Mercury tetrathiocynatocobalate (II) $Hg[Co(NCS)_4]$ was used as a calibrant. The electronic spectra of complexes in solid were recorded on at room temperature. MgO was used as reference. Melting point is measured by open capillary method using Sigma Melting Point Apparatus.

2.2. Synthesis of 4-oxo-4-(4-sulfamoylphenylamino) but-2-enoic acid (OSPAB)

The reaction mixture of maleic anhydride (0.01 mole) in ethanol and (0.01 mole) sulphanilamide in ethanol was refluxed for 2-3 hrs. The resulting solid was washed with water, dried and recrystallized from MeOH. Yield: 73.24 %, M.P. (193-194°C) was measurement with open capillary method and it is uncorrected. IR (cm^{-1}): 2950-2850 (Ar C-C), 3450-3360 (CONH, NH_2), 3430, 1680 (COOH), 1620-1680 (C=C); ^1H-NMR(δ ppm, 500 MHz, CDCl3): 11.80 (s, 1H, COOH), 8.32 (s, 1H, NH), 7.71-7.98 (m, 4H, Ar-H), 6.51-6.92 (d, 2H, CH=CH), 3.14 (s, 2H, NH_2). ^{13}C MNR (δ ppm, 125 MHz, CDCl3): 182.23, 172.62, 152.12, 148.07, 138.20, 129.38, 127.98. DEPT-135 (δ ppm, 125 MHz, CDCl3): 138.20, 129.38, 127.98.

Figure 1: (Scheme 1) Synthesis of OSPAB



2.3. Synthesis of metal complexes of 4-oxo-4-(4-sulfamoylphenylamino) but-2-enoic acid (OSPAB)

The metal complexes of OSPAB with Cu^{2+}, Co^{2+}, Zn^{2+}, Mn^{2+}, and Ni^{2+} metal ions were prepared in two steps. All the metal complexes were prepared in an identical procedure.

2.3.1 Preparation of OSPAB solution

The OSPAB (0.05 mol) was taken in 100 ml beaker and formic acid (85% v/v) was added up to slurry formation. To this slurry water was added till the complete dissolution of OSPAB. It was diluted to 20 ml.

2.3.2 Synthesis of OSPAB-metal-complexes

In a solution of metal acetate (0.025 mol) in acetone: water (50:50 v/v) mixture (40 ml) the 20 ml of above mentioned OSPAB solution (i.e. containing 0.05 M OSPAB) was added with vigorous stirring at room temperature. The appropriate pH was adjusted by addition of sodium acetate for complete precipitation of metal chelate. The precipitates were digested on a boiling water bath and filtered off, washed by water and air-dried.

Figure 2: (Scheme – 2) Synthesis of metal complexes of OSPAB

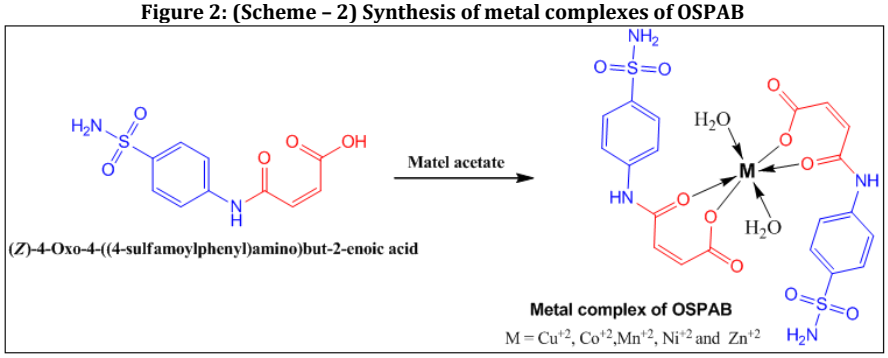


Table 1: Analysis of OSAPB ligand and its metal complexes

Empirical Formula	Yield (%)	Elemental Analysis									
		C%		H%		N%		S%		M%	
		Cald	Found	Cald	Found	Cald	Found	Cald	Found	Cald	Found
OSPAB	73	44.44	44.42	3.73	3.72	10.37	10.35	11.86	11.84	-	-
$(OSPAB)_2Cu^{2+}$	65	37.64	37.62	3.45	3.43	8.78	8.76	10.04	10.02	9.97	9.95
$(OSPAB)_2Co^{2+}$	62	37.92	37.91	3.48	3.45	8.85	8.83	10.11	10.10	9.31	9.30
$(OSPAB)_2Ni^{2+}$	63	37.93	37.92	3.48	3.46	8.85	8.82	10.12	10.11	9.28	9.27
$(OSPAB)_2Mn^{2+}$	66	38.16	38.14	3.50	3.48	8.90	8.88	10.18	10.17	8.74	8.72
$(OSPAB)_2Zn^{2+}$	62	37.54	37.51	3.44	3.42	8.76	8.74	10.01	10.00	10.23	10.21

2.4. Antibacterial activity

The synthesized compounds were screened for their antibacterial activities against *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Staphylococcus aureus*, and

Pseudomonas aeruginosa at a concentration of 200 µg ml^{-1} in dimethylsulphoxide by agar diffusion method using streptomycin as standard. The minimum inhibitory concentrations (MIC) were detected by serial dilution method. The lowest concentration (µg ml^{-1}) of the compound, which inhibits the growth of bacteria maximum after 24 h inhibition at 37 ºC, was taken as MIC. The stock solution (10^{-2} M) was prepared by dissolving the complex in dimethylsulphoxide and the solutions were diluted to different concentrations in the same solvent in order to find the MIC values.

3. Results and Discussion

The synthesis of 4-oxo-4-(4-sulfamoylphenylamino) but-2-enoic acid (OSPAB) was performed by a simple reaction of maleic anhydride and Sulphanilamide. The resulted OSPAB ligand was an amorphous brown powder. The C, H, N contents of OSPAB (Table-1) are consistent with the structure predicted (**Scheme-1**). The IR spectrum of OSPAB comprises the important bands of structure.

Table 2: Spectral features and magnetic moment of OSPAB metal complexes

Metal Complexes	μ_{eff} (BM)	Electronic spectral data (cm^{-1})	Transition
$OSPAB\text{-}Cu^{2+}$	2.52	23443 13205	Charge transfer $^2B_{1g} \rightarrow {}^2A_{1g}$
$OSPAB\text{-}Ni^{2+}$	3.68	22588 15362	$^3A_{1g} \rightarrow {}^3T_{1g}(P)$ $^3A_{1g} \rightarrow {}^3T_{1g}(F)$
$OSPAB\text{-}Co^{2+}$	4.74	23725 19094 8916	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$
$OSPAB\text{-}Mn^{2+}$	5.56	23223 19025 16837	$^6A_{1g} \rightarrow {}^6A_{2g}\ {}^4E_g$ $^6A_{1g} \rightarrow {}^4T_{2g}$ (4G) $^6A_{1g} \rightarrow {}^4T_{1g}$(PG)
$OSPAB\text{-}Zn^{2+}$	Diamag.	--------	---------

The broad band due to –OH group appeared at 3430 cm^{-1}. In this band the inflections are observed at 2970, 2930 and 2850cm^{-1}. The NMR spectrum of OSPAB in DMSO indicates that the singlet of 1H at 11.8 δ ppm due to –COOH group. The aromatic protons are appeared in multiplicity at 7.7-7.9 δ. Thus the structure of OSPAB is confirmed as shown in **Scheme - 1**.

The metal and C, H, N contents of metal complexes of OSPAB (Table - 1) are also consistent with the predicted structure. The results show that the metal: ligand (M:L) ratio for all divalent metal chelate is 1:2.

Table 3: Antibacterial activity of OSPAB ligand and its metal complexes

Sample	Zone of inhibition at 1000 ppm (%)			
	Escherichia coli	*Klebsiella pneumoniae*	*Proteus vulgaris*	*Staphylococcus aureus*
OSPAB	52	57	46	55
$OSPAB\text{-}Cu^{2+}$	71	72	68	70
$OSPAB\text{-}Co^{2+}$	64	71	68	64
$OSPAB\text{-}Ni^{2+}$	59	68	66	67
$OSPAB\text{-}Mn^{2+}$	68	58	62	63
$OSPAB\text{-}Zn^{2+}$	72	71	57	73
Ampicillin	82	90	78	86

The infrared spectra of all the complexes are identical and suggest the formation of the entire metalocyclic compound by the absence of band characteristic of free –OH group of parent OSPAB. The other bands are almost at their respectable positions as appeared in the spectrum of parent-OSPAB ligand. However, the band due to (M-O) band could not be detected as it may appear below the range of instrument used. The important IR Spectral data are shown in Table - 2.

Magnetic moments of metal complexes are given in Table - 2. The diffuse electronic spectrum of Cu^{2+} complexes shows two broad bands around 13205 and 23443 cm^{-1}. The first band may be due to a $^2B_{1g} \rightarrow {}^1A_{1g}$ transition. While the second band may be due to charge transfer. The first band shows structures suggesting a distorted octahedral structure for the Cu^{2+} metal complexes.

The higher value of the magnetic moment of the Cu^{2+} chelate supports the same. The Co^{2+} metal chelate gives rise to two absorption bands at 23725 and 19094 cm^{-1}, which can be assigned $^4T_{1g} \rightarrow {}^2T_{2g}$, $^4T_{1g} \rightarrow {}^4T_{1g}$(P)transitions, respectively. These absorption bands and the μeff value indicate an octahedral configuration of the Co^{2+} metal chelate [15]. The spectrum of Mn^{2+} polymeric chelate comprised two bands at 19025cm^{-1} and 23223cm^{-1}. The latter does not have a very long tail. These bands may be assigned to $^6 A_{1g} \rightarrow {}^4T_{2g(G)}$ and $^6 A_{1g} \rightarrow {}^4A_{2g(G)}$ transitions, respectively. The high intensity of the bands suggests that they may have some charge transfer character. The magnetic moment is found to be lower than normal range. In the absence of low temperature measurement of magnetic moment it is difficult to attach any significance to this. The observed μeff values in the range 2.52-5.56 B.M are consistent with the above moiety [15].

The examination of antibacterial activity of ligand and its all complexes (Table - 3) reveals that the ligand is moderately toxic against bacteria, while all the complexes are more toxic than ligand. Among all the complexes the Cu^{2+} chelate is more toxic against tested bacteria.

References

[1] G.Y. Nagesh, K. Mahendra Raj, B.H.M. Mruthyunjayaswamy, *J Mol Stru*, 2015, 1079, 423-432.

[2] J.P. Philips, *Chem. Review*, 1984, 56, 271.

[3] D. K. Patel, and A. Singh, *E-journal of chemistry*, 2009, 6(4), 1017.

[4] J.C. Patel, H.R. Dholariya, K.S. Patel, K.D. Patel, Appli. *Organomett. Chem*.2012, 26,604.

[5] J.R. Anaconaa, N. Noriegaa, J. Camusb, *Spec Chemica* Part-A, 2015, 137, 16-22.

[6] Kanda Y., Kawanishi Y., Oda K., Sakata T., Mihara S., Asakura K., Kanemasa T., Ninomiya M., Fujimoto M., Kanoike T. *Bioorg. & Med. Chem*. 2001, 9, 897.

[7] Stokes S. S., Albert R., Buurman Ed T., Andrews B., Shapiro A. B., Green O. M., McKenzie A. R., Otterbein L. R., *Bioorg. & Med. Chem. Lett*. 2012, 22, 7019.

[8] Chibale K., Haupt H., Kendrick H., Yardley V., Saravanamuthu A., Fairlamb A. H., Croft S. L., *Bioorg. & Med. Chem. Lett*. 2001, 11, 2655.

[9] Rahavi Ezabadi I., Camoutsis C., Zoumpoulakis P., Geronikaki A., Soković M., Glamočilija J., Čirič A., *Bioorg*. *& Med. Chem*. 2008, 16, 1150.

[10] Kennedy J. F., Thorley M.: Pharmaceutical Substances, 3rd ed., Kleeman A. Engel J., Kutscher B., Reichert D.: Thieme: Stuttgart, 1999.

[11] Serradeil-Le Gal C., *Cardiovascular Drug Rev*. 2001, 19, 201.

[12] Natarajan A., Guo Y., Harbinski F., Fan Y.-H., Chen H., Luus L., Diercks J. Aktas H., Chorev M., Halperin J. A., *J. Med. Chem*. 2004, 47, 4979.

[13] Vogel, A.I., 1996. A Text Book of Practical Organic Chemistry. 5th ed., 883.

[14] W.R. Baily and E.G. Scott, *Diagnostic Microbiology*, The C. V. Moshy Co. St. Lovis, 1966, 257.

[15] B.R. Patil, *Oriental J. Chem.,* 2006, 18, 547.