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Studies on Chelating Properties of Antipyrine Based Azo Ligands and Its Coordination Compounds

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ABSTRACT

Diazotized p-aminoantipyrine (DpAAP) and salicylic acid upon coupling reaction in the presence of solution of sodium nitrite (aqueous) yields 5-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)diazenyl)-2-hydroxy benzoic acid (DpAAPSA) (L), which upon further reacting with solution of metal acetates (Viz. Cu^{2+}, Ni^{2+}, Co^{2+}, Mn^{2+} and Zn^{2+}) gave different coordination compounds. The novel azo ligand based on aminoantipyrine was further characterized by elemental analysis, mass, Infrared (IR) and Nuclear Magnetic Resonance (NMR) spectral studies. While the coordination compounds of newly prepared azo ligand were characterized on the basis of metal-ligand stoichiometry (M:L), IR and reflectance spectroscopy and magnetic properties. The antimicrobial activity of DpAAPSA and its coordination compounds was screened against various bacterial and fungal strains. The results show that all these coordinated compounds are good antimicrobial agents.

Keywords: Aminoantipyrine, Reflectance studies, Salicylic acid, Magnetic measurement, Antimicrobial activity

INTRODUCTION

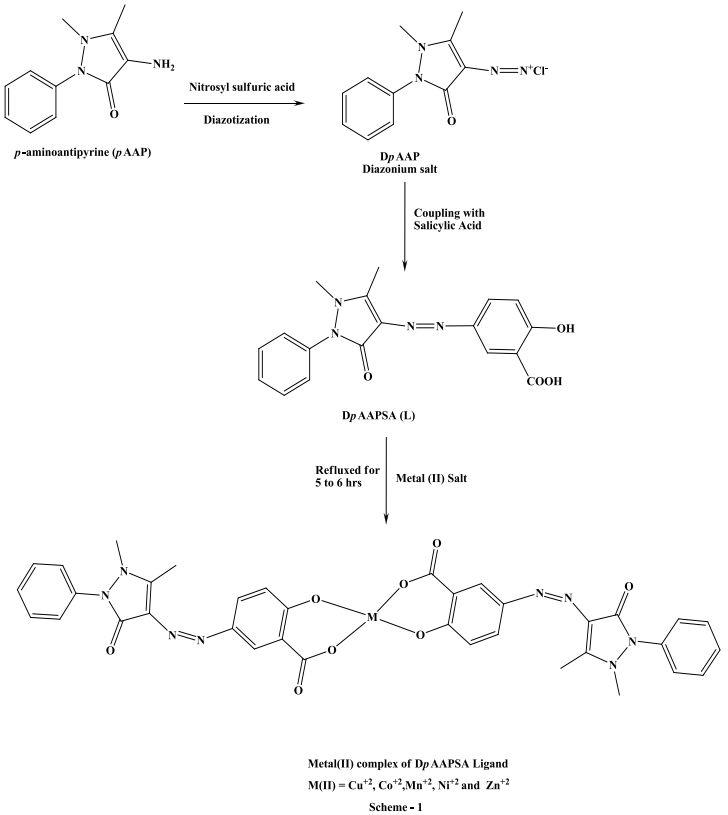
Metal complexes synthesized from different ligands are developing importance into different fields since its first discovery [1-4]. Also the novel ligands are continuously investigated for possible applications in fields such as analytical, pharmacological and other industrial fields. Salicylic acid and its substituted derivatives are one of such ligands which also well known as complexing agent [5-8]. From a recent years no of metal complexes of salicylic acid and derivatives have been synthesized and studied for their biological activities such as antibacterial, antifungal, antitumor, anticancer, cycotoxic, antioxidant, antimalarial and anti-inflammatory activity [9-14]. The antipyrine and its derivatives show distinct biological activities like antituberculosis, anti-inflammatory, analgesic, antibacterial and antifungal activity [15-17]. Also coordination compounds containing antipyrine derivatives can be synthesized and studied recently for their various applications [18-21]. The reaction of antipyrine derivatives with salicylic acid has not been reported largely. Hence, it was thought that antipyrine and Salicylic acid into same molecule may provide good biologically active compound. So in continuation of our previous work [22] the present article discuss about studies on chelating properties of antipyrine based azo ligands and its coordination compounds (Scheme 1).

EXPERIMENTAL

All chemicals used in the work were purchased from local market and of analytical grade. All reactions were monitored by Thin Layer Chromatography (TLC) (aluminium plates coated with silica gel, E. Merck, Mumbai-India). The detection of the components were measured under UV light, explore in Iodine chamber and other necessary reagents. C, H, N elemental analysis was carried out by elemental analyzer PerkinElmer, USA 2400-II CHN analyzer. The metal content was determined by Ethylenediaminetetraacetic Acid (EDTA) titration method. IR spectra of the synthesized compounds were recorded on Nicolet 400D Fourier Transform Infrared (FT-IR) spectrometer by using KBr pallets method. Nuclear Magnetic Resonance (NMR) spectrum of D*p*AAPSA was recorded on Bruker-400 MHz NMR spectrophotometer. Mercury Tetrathiocyanatecobaltate (II) ($Hg[Co(NCS)_4]$) was used as a celebrant. The reflectance spectra of coordination compounds in solid phase were recorded at room temperature. In which MgO was used as reference. Antimicrobial activity of all synthesized compounds was examined against various antimicrobial strains using method reported in literature [23]. Magnetic susceptibility measurement was done by using Gouy's method.

Synthesis of 5-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)diazenyl)-2-hydroxybenzoic acid (D*p*AAPSA)

p-Aminoantipyrine (*p*AAP) (0.01 mole) was dissolved in a equimolar mixture of H_2SO_4 and water. Further the reaction mixture allows cooling at 0-5°C in ice bath. A cold aqueous solution of sodium nitrite (0.04 mol) was added to this solution. The synthesized diazonium salt solution of *p*AAP was filtered into a cooled solution of salicylic acid (0.01 mol) at 0-5°C. The final solid azo dye was washed with water, dried and recrystallized from methanol. Yield was 72%. Molecular weight 352 g/mol, its' m.p. was 198-199°C (uncorrected).



Scheme 1: Metal(II) complex of D*p*AAPSA ligand M(II)=Cu^{+2}, Co^{+2}, Mn^{+2}, Ni^{+2}, and Zn^{+2}

Analysis

C%, H%, N%: Elemental analysis calculated: 61.36 4.58 15.90. $C_{18}H_{16}N_4O_4$ Found: 61.3 4.5 15.8. IR cm^{-1}: 3200-3600 (OH), 3010-3070 (C-H, of Ar.), 1642, 1565 (Azo group), 1680 (CO of COOH), 1739 (CO). ^{1}H-NMR: 6.82-8.42 (m, 8H, Ar-H), 5.27 (s, 1H, OH), 11.26 (s, 1H, OH), 2.25 (s, 3H, CH_3), 3.10 (s, 3H, CH_3).

Synthesis of coordination compounds of ligand (D*p*AAPSA)

The coordination compounds of D*p*AAPSA with Cu^{2+}, Ni^{2+}, Co^{2+}, Mn^{2+} and Zn^{2+} metal acetates were prepared in following two steps. The general procedure is as follows.

Preparation of D*p*AAPSA solution

Ligand D*p*AAPSA (0.05 mol) was taken in 500 ml beaker. The addition of formic acid (85% v/v) up to slurry formation was carried out in to the ligand. Complete dissolution of D*p*AAPSA achieved by adding water to the above solution. Further the solution was diluted up to 100 ml.

Synthesis of coordination compounds

D*p*AAPSA solution (20 ml) (i.e., containing 0.01 M D*p*AAPSA) was taken. It was added to a solution of metal acetate (0.005 mol) in Acetone: Water (50:50 v/v) mixture (40 ml) with vigorous stirring at room temperature. The suitable pH was adjusted by addition of sodium acetate for complete precipitation of metal complex. The precipitates were digested on a boiling water bath. The precipitates of complex were filtered off, washed by water and air-dried.

RESULTS AND DISCUSSION

Reaction between diazonium salt of *p*-aminoantipyrine (*p*AAP) and Salicylic acid gave diazotized azo ligand i.e. 5-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)diazenyl)-2-hydroxybenzoic acid (DpAAPSA). The synthesized ligand and their coordination compounds were appeared in the form of colored amorphous powder. The obtained compounds were insoluble in water and most organic solvents but soluble in DMSO as well as found stable in air. The C, H, N analysis data along with metal content of synthesized coordination compounds are presented in Table 1 and are well coordinated with predicted structure as per Scheme 1. The results confirm the metal (1): (2) ligand ratio for all divalent coordinated compounds is 1:2.

The IR spectral data of ligand and its coordinated compounds are discussed as follow; The IR spectrum of the (DpAAPSA) ligand shows band in between 3200 and 3600 cm^{-1} region due to stretching vibration of OH group. The IR spectrum of DpAAPSA consists of two important bands at 1642 and 1565 cm^{-1} due to azo group. The IR spectrum shows ν (C=O) stretching vibration band found in free ligand at 1680 cm^{-1} because of CO group of COOH. Another keto stretching band found at 1739 cm^{-1} due to pyrazolone ring CO. Bands for aromatic carbon was found at their respective positions. The analysis of the FT-IR spectra of coordination compounds provides information on the coordination mode between the ligand and the metal ion. All the coordination compounds are found identical bands as its parent ligand. The only difference found that formation of all the coordination compounds having absence of band characteristic for free –OH group which confirms coordination of metal at OH group of salicylic acid. In all the synthesized coordination compounds, a new band is seen in respective region for particular metal, which supports the formation of the weak band for the respective metal-ligand bonding.

Table 1: Characterization data of D*p*AAPSA and their coordinated compounds

Compound	Molecular Weight	Yield (%)	Elemental analysis							
			C%		H%		N%		M%	
			Cal.	Found	Cal.	Found	Cal.	Found	Cal.	Found
D*p*AAPSA	352	72	61.36	61.3	4.58	4.5	15.90	15.8	-	-
$(D\textit{p}AAPSA)_2\,Cu^{2+}$	764	70	56.58	56.5	3.69	3.6	14.66	14.6	8.32	8.3
$(D\textit{p}AAPSA)_2\,Ni^{2+}$	759	65	56.94	56.9	3.72	3.7	14.76	14.7	7.73	7.7
$(D\textit{p}AAPSA)_2\,Co^{2+}$	759	67	56.92	56.8	3.72	3.6	14.75	14.7	7.76	7.7
$(D\textit{p}AAPSA)_2\,Mn^{2+}$	755	69	57.22	57.2	3.74	3.7	14.83	14.8	7.27	7.2
$(D\textit{p}AAPSA)_2\,Zn^{2+}$	766	62	56.44	56.4	3.68	3.6	14.63	14.6	8.54	8.5

NMR spectrum of ligand shows two identical singlets at δ=5.27 ppm and 11.26 ppm for –OH and –COOH respectively. The other aromatic protons are appeared in multiplicity at δ=6.82-8.42 ppm. The NMR spectrum shows peaks at 2.25 and 3.10 ppm for CH_3 also. So, that the structure of D*p*AAPSA is confirmed as shown in Scheme 1.

The magnetic measurement of synthesized coordination compounds was carried out by utilizing Gouy's method and summarized in Table 2. The Cu(II), Ni(II), Co(II) and Mn(II) complexes show magnetic moments of 1.78. 3.15, 3.85 and 5.82 B.M. respectively which is characteristic values for Cu(II) (d^9), Ni(II) (d^8), Co(II) (d^7) and Mn(II) (d^5) octahedral complexes [24]. The reflectance spectral data of the coordination compounds was carried out in Dimethylformamide (DMF) solution. Reflectance spectral data and magnetic susceptibility measurements gave evidence to determine the geometry of coordination compounds. The Cu(II) complexes showed two prominent bands. Low intensity broad band in the region 15185 cm^{-1} was assigned as 10 Dq band corresponding to $^2B_{1g} \rightarrow {}^1A_{1g}$ transition. Another band was a high intensity band at 24204 cm^{-1} due to symmetry forbidden ligand → metal charge transfer transition. Therefore distorted octahedral geometry around Cu(II) ion was assumed on the basis of reflectance spectra and magnetic moment [25]. The reflectance spectrum of the Ni(II) complex found two bands at 14721 and 22,456 cm^{-1}, attributable to $^3A_1g \rightarrow {}^3T_1g$ (P) and $^3A_1g \rightarrow {}^3T_1g$ (F) transitions, respectively, which proved an octahedral geometry for Nickel (II) complex [26]. The reflectance spectrum of the Cobalt (II) complex shows two bands at 18,694 and 22,411 cm^{-1} which are assigned to $^4T_{1g} \rightarrow {}^2T_{2g}$ and $^4T_{1g} \rightarrow {}^4T_{1g}$(P) transitions, respectively, as achieved for an octahedral Co(II) complex. Mn(II) complexes show two bands at 19565 cm^{-1} and a weak band at 23,640 cm^{-1} assigned to $^6A_{1g} \rightarrow {}^4T_{2g(G)}$ and $^6A_{1g} \rightarrow {}^4A_{2g(G)}$ transitions, respectively for octahedral geometry. The high intensity of the bands supports that they may have some charge transfer character. The observed magnetic moment value 5.82 is consist with expected spin only value for Mn^{+2} complex [27]. Zn(II) metal complex is diamagnetic in nature and its reflectance spectra do not furnish any characteristic d-d transitions.

The synthesized ligand and corresponding coordination compounds were screened for their antimicrobial activity against two Gram-positive strains, two Gram-negative strains and three antifungal strains using the agar dilution method [23]. The ampicillin (S_1) and griseofulvin (S_2) used as standard drugs for comparison. The zone of inhibition was measured (in mm) around the disc was measured and the results are shown in Table 3. The examination of antimicrobial activity of D*p*AAPSA ligand and its coordination compounds (Table 3) reveals that all synthesized compound shows good activity compare to standard drug. While all the coordination compounds are show good activity than its parent ligand. Among all the coordination compounds the Cu^{2+} complex shows good against all employed strains.

Table 2: Structural data of D*p*AAPSA and their coordinated compounds

Compound	μ_{eff} (BM)	Reflectance spectral data (cm^{-1})	Transition
$(D\textit{p}AAPSA)_2\,Cu^{2+}$	1.78	24204 15185	Charge transfer $^2B_{1g} \rightarrow {}^1A_{1g}$
$(D\textit{p}AAPSA)_2\,Ni^{2+}$	3.15	22456 14721	$^3A_{1g} \rightarrow {}^3T_{1g}$(P) $^3A_{1g} \rightarrow {}^3T_{1g}$(F)
$(D\textit{p}AAPSA)_2\,Co^{2+}$	3.85	22411 18694	$^4T_{1g}$(F) $\rightarrow {}^2T_{2g}$ $^4T_{1g} \rightarrow {}^4T_{1g}$(P)
$(D\textit{p}AAPSA)_2\,Mn^{2+}$	5.82	23640 19565	$^6A_{1g} \rightarrow {}^4T_{2g}$ (G) $^6A_{1g} \rightarrow {}^4T_{1g}$(G)
$(D\textit{p}AAPSA)_2\,Zn^{2+}$	Diamagnetic	-	-

Table 3: Antimicrobial activity of D*p*AAPSA and their coordinated compounds

Compound	Diameter of zone of inhibition (In mm)						
	Bacillus subtilis	***Staphylococcus aureus***	***Escherichia coli***	***Pseudomonas aeruginosa***	***Candida albicans***	***Aspergillus niger***	***Nigrospora* sp.,**
L	11	14	15	08	09	11	07
$(L)_2Cu^{2+}$	19	20	21	16	19	20	12
$(L)_2Ni^{2+}$	11	15	19	13	14	17	09
$(L)_2Co^{2+}$	10	13	19	11	12	15	10
$(L)_2Mn^{2+}$	15	14	18	12	15	18	07
$(L)_2Zn^{2+}$	14	17	16	11	14	17	11
S_1	19	22	24	18	-	-	-
S_2	-	-	-	-	20	21	16

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