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SYNTHESIS, CHARACTERIZATION, BIOLOGICAL AND CHELATING PROPERTIES OF NEW ANTIPYRINE DERIVED AZO DYES AND ITS TRANSITION METAL COMPLEXES

KHUSHBU K. MEHTA and ASHA D. PATEL*

Department of Chemistry, M. N. College, VISNAGAR (N. Guj.) INDIA

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ABSTRACT

4-((1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)diazenyl)-3-hydroxy-2-naphthoic acid (L) (D*p*AAPBA) has been synthesized from diazotized *p*-aminoantipyrine (D*p*AAP) and Bon acid (BA). Transition metal complexes of synthesized ligand with Cu(II), Ni(II), Co(II), Mn(II) and Zn(II) acetate were prepared. The structures of the ligand and its transition metal complexes are investigated by means of their metal-ligand (M:L) ratio, elemental, IR, NMR and mass spectral studies. Further, the structure of metal complexes was confirmed using magnetic measurement and reflectance spectral analysis, which suggest octahedral geometry for all complexes. Also, biological evaluation of all synthesized compound shows moderate to good activity against employed strains.

Key words: 4-Aminoantipyrine, Spectroscopic study, Bon acid, Structural study, Antimicrobial activity.

INTRODUCTION

A number of coordination compounds are explored for their applications in different field[1-3]. Antipyrine and its derivatives are well known for its pharmaceutical as well as medicinal applications[4-7]. The antipyrine compounds containing nitrogen especially 4-nitroantipyrine derivatives play a vital role in many biological processes like antibacterial, antifungal, antituberculosis, anticancer, cycotoxic, antitumor, antioxidant, anti-HIV, analgesic and anti-inflammatory activity[8-13]. Also coordination compounds containing antipyrine derivatives have been synthesized and studied recently for their numerous applications[14-18]. Several azo dyes compounds based on bon acid are reported for their dyeing, chelating, biological and ion exchange properties[19-21]. Interestingly, coordination chemistry of azo Schiff bases derived from Bon acid is not very well explored. Also the reaction of aminoantipyrine with Bon acid has not been reported so far. Based on these facts, it was thought that combined molecule of 4-aminoantipyrine and bon acid may explore good biological active compound. The present article comprises the synthesis, characterization and chelating properties of transition metal complexes containing aminoantipyrine azo dye as ligand. Also the antimicrobial activity of all synthesized compounds was evaluated against different antimicrobial strains.

EXPERIMENTAL

All chemicals used were purchased from local market and are of analytical grade. All reactions were monitored by thin-layer chromatography (alluminium plates coated with silica gel, E. Merck, Mumbai-India)

Available online at www.sadgurupublications.com
*Author for correspondence; E-mail: khushiikhushiihappy@yahoo.com

and detection of the components were measured under UV light, explored in Iodine chamber and other necessary reagents. C, H, N analysis was carried out by elemental analyzer PerkinElmer, USA 2400-II CHN analyzer. Metal content was determined by EDTA titration method. Infrared spectra of the synthesized compounds were recorded on Nicolet 400D FT-IR spectrometer by using KBr pallets method. NMR spectrum of D*p*AAPBA was recorded on Bruker-400 MHz NMR spectrophotometer. Mercury tetrathiocynatocobalate (II) $Hg[Co(NCS)_4]$ was used as a calibrant. The reflectance spectra of transition metal complexes in solid phase were recorded at room temperature. MgO was used as reference. Antimicrobial activity of all synthesized compounds was examined against various antimicrobial strains using method reported in literature[22]. Magnetic susceptibility measurement was carried out by using Gouy method.

Synthesis of 4-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)diazenyl)-3-hydroxy-2-naphthoic acid (L) (D*p*AAPBA)

p-Aminoantipyrine (*p*AAP) (0.01 mole) was dissolved in an 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 moles) was added to this solution. The synthesized diazonium salt solution of *p*AAP was filtered into a cooled solution of Bon acid (0.01mole) at 0-5°C. The final solid azo dye was washed with water, dried and recrystallized from methanol. Yield: 74%, m.p. 220-222°C (decompose) uncorrected. Anal. Calc. for $C_{22}H_{18}N_4O_4$ (402): C, 65.66; H, 4.55; N, 13.92. Found: C, 65.6; H, 4.5; N, 13.9. IR cm^{-1}: 3200-3600 (OH), 3010-3070 (C-H, of Ar.), 1635, 1572 (Azo group), 1678 (CO of COOH), 1727 (CO). ^{1}H NMR: 6.84-8.36 (m, 10H, Ar-H), 5.32 (s, 1H, OH), 11.41 (s, 1H, OH), 2.32 (s, 3H, CH_3), 3.05 (s, 3H, CH_3).

Synthesis of transition metal complexes of ligand (DpAAPBA)

The metal complexes of D*p*AAPBA with Cu^{2+}, Ni^{2+}, Co^{2+}, Mn^{2+} and Zn^{2+} metal ions were prepared in two steps. The general procedure is as follows;

Preparation of DpAAPBA solution

Ligand D*p*AAPBA (0.05 mole) was taken in 500 mL beaker followed by the addition of formic acid (85% v/v) up to slurry formation. Complete dissolution of D*p*AAPBA was obtained by adding water to the above solution. Further, it was diluted upto 100 mL.

Synthesis of DpAAPBA-metal(II)-complexes

D*p*AAPBA solution (20 mL) (i.e. containing 0.01 M D*p*AAPBA) 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 appropriate 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

Simple coupling reaction between diazonium salt of *p*-aminoantipyrine (*p*AAP) and Bon acid (BA) resulted into the 4-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)diazenyl)-3-hydroxy-2-naphthoic acid (L) (DpAAPBA). The synthesized (*p*AAP) ligand and their metal complexes were in form of colored amorphous powder. The compounds were insoluble in water and most organic solvents but soluble in DMSO as well as found stable in air. The experimental C, H, N data of synthesized ligand (L) and their transition metal complexes (Table 1) were in very good agreement with predicted structure (**Scheme 1**). The metal contents of metal complexes of DpAAPBA (Table 1) are also consistent with the predicted structure. The results show that the metal: ligand (M:L) ratio for all divalent metal complex is 1:2.

Table 1: Analytical and elemental data of D*p*AAPBA ligand and their transition metal complexes

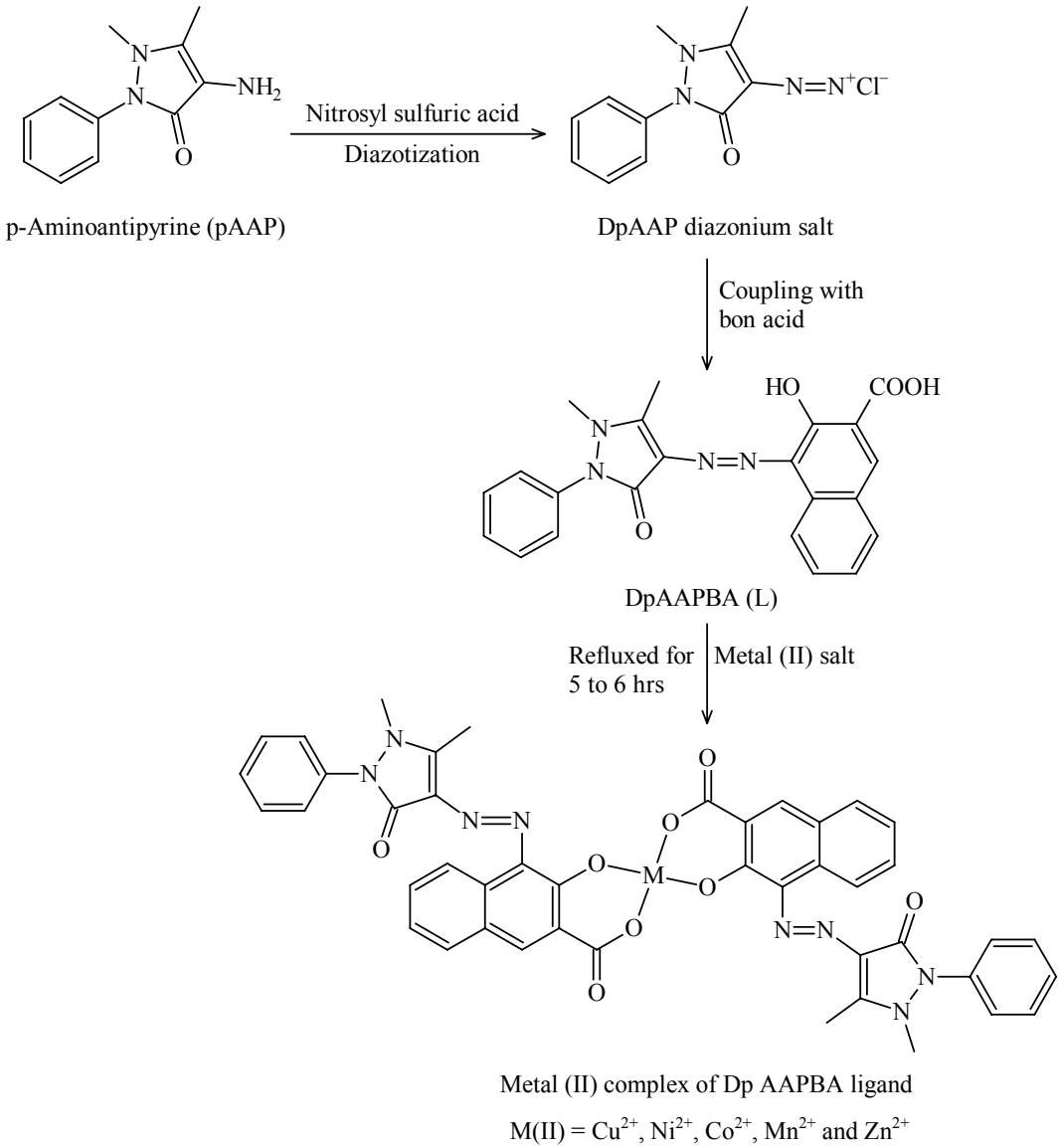
Compound/Mol. formula	Mol wt.	Yield (%)	Elemental analysis							
			C%		H%		N%		M%	
			Cal.	Found	Cal.	Found	Cal.	Found	Cal.	Found
D*p*AAPBA	402	74	65.66	65.6	4.55	4.5	13.92	13.9	-	-
$(DpAAPBA)_2Cu^{2+}$ / $C_{44}H_{32}CuN_8O_8$	864	70	61.14	61.1	3.73	3.7	12.96	12.9	7.35	7.3
$(DpAAPBA)_2Ni^{2+}$ / $C_{44}H_{32}N_8NiO_8$	859	67	61.49	61.4	3.75	3.7	13.04	13.0	6.83	6.8
$(DpAAPBA)_2Co^{2+}$ / $C_{44}H_{32}CoN_8O_8$	859	69	61.47	61.4	3.75	3.7	13.03	13.0	6.86	6.8
$(DpAAPBA)_2Mn^{2+}$ / $C_{44}H_{32}MnN_8O_8$	855	67	61.76	61.7	3.77	3.7	13.09	13.0	6.42	6.4
$(DpAAPBA)_2Zn^{2+}$ / $C_{44}H_{32}N_8O_8Zn$	866	65	61.01	60.9	3.72	3.7	12.94	12.9	7.55	7.5

The IR spectral data of ligand (L) and its metal complexes are summarized as follow; The IR spectrum of the (DpAAPBA) ligand shows band in between 3200 and 3600 cm^{-1} due to stretching vibration of OH group. The IR spectrum of DpAAPBA comprises two important bands due to azo group at 1635 and 1572 cm^{-1}. The IR spectrum shows ν (C=O) stretching vibration band in free ligand at 1678 cm^{-1} due to CO group of COOH. Another keto stretching band was found at 1727 cm^{-1} for pyrazolone ring CO. Also bands for aromatic carbon were found at their respective positions. The analysis of the FT-IR spectra of transition metal complexes gives information on the coordination mode between the ligand and the metal ion. All the complexes have found identical bands as its parent ligand, the only difference was found that with the formation of all the metal complexes, band characteristic for free –OH group was having absenct, which confirms coordination of metal at OH group of Bon acid. In all the synthesized complexes, a new band is seen in respective region for particular metal, which is probably supports the formation of the weak bond for the respective metal-ligand bonding.

NMR spectrum of ligand shows two important singlets at 5.32 ppm and 11.41 ppm for –OH and –COOH, respectively, while rest of the aromatic protons appeared as multiplets at δ 6.84-8.36 ppm. Also the NMR spectrum shows peaks for CH_3 at 2.35 and 3.05 ppm. Thus, the structure of D*p*AAPBA is confirmed as shown in **Scheme 1**.

The magnetic measurement of synthesized complexes was carried out using Gouy's method. The Cu(II), Ni(II), Co(II), and Mn(II) complexes show magnetic moments of 1.82. 3.18, 3.81 and 5.89 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. The reflectance spectral data of the complexes were recorded in DMF solution. Reflectance spectral data and magnetic susceptibility measurements gave adequate support to determine the geometry of metal complexes. The Cu(II) complexes display two prominent bands. Low intensity broad band in the region 15122 cm^{-1} was assigned as 10 Dq band corresponding to $^2B_{1g} \rightarrow {}^1A_{1g}$ transition. The second band was a high intensity band at 24152 cm^{-1} due to symmetry forbidden ligand → metal charge transfer transition. Therefore, distorted octahedral geometry around Cu(II) ion was suggested on the basis of reflectance spectra and magnetic moment[23]. The reflectance spectrum of the Ni(II) complex exhibits two bands at 14785 and 22,452 cm^{-1}, attributable to $^3A_1g \rightarrow {}^3T_1g$ (P) and $^3A_1g \rightarrow {}^3T_1g$ (F) transitions,

respectively, which supports an octahedral geometry for Ni(II) complex[24]. The reflectance spectrum of the Co(II) complex shows two bands at 18,726 and 22,457 cm^{-1}, which are assigned to $^4T_{1g} \rightarrow {}^2T_{2g}$ and $^4T_{1g} \rightarrow {}^4T_{1g}(P)$ transitions, respectively, as expected for an octahedral Co(II) complex. Mn(II) complexes show two bands at 19521 cm^{-1} and a weak band at 23,635 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 suggests that they may have some charge transfer character. The observed magnetic moment value 5.89 is consistent with expected spin only value for Mn^{+2} complex[25]. Zn^{+2} metal complex is diamagnetic in nature and its reflectance spectra do not furnish any characteristic d-d transitions.



Scheme 1

The synthesized ligand and corresponding transition metal complexes were screened for their *in vitro* antimicrobial activity against two Gram (+ve) strain, *Bacillus subtilis, Streptococcus aureus* and two Gram (−ve) strain, *Escherichia coli*, *Pseudomonas aeruginosa*, and three antifungal strain, *Candida albicans, Nigrospora Sp., Aspergillus niger* using the Agar dilution method[22]. The standard drugs Ampicillin and Griseofulvin were used as standard drugs for comparison. The zone of inhibition was measured (in mm) around the disc and the results are represented in Table 2. The examination of antimicrobial activity of

D*p*AAPBA ligand and its metal complexes (Table 2) reveals that all synthesized compound show moderate to good activity compared to standard drug and all the complexes show good activity than its parent ligand. Among all the complexes, the Cu^{2+} complex shows good activity against all employed strains.

Table 2: Antimicrobial activity of D*p*AAPBA ligand and their transition metal complexes

Compound	Diameter of zone of inhibition (in mm)						
	B. S.	**S. A.**	**E. C.**	**P. A.**	**C. A.**	**A. N.**	**N. Sp.**
D*p*AAPBA	09	11	13	07	10	12	05
$(DpAAPBA)_2Cu^{2+}$	17	21	22	15	18	20	13
$(DpAAPBA)_2Ni^{2+}$	10	13	15	08	12	14	07
$(DpAAPBA)_2Co^{2+}$	09	12	13	08	10	12	07
$(DpAAPBA)_2Mn^{2+}$	11	12	14	07	12	15	08
$(DpAAPBA)_2Zn^{2+}$	13	15	17	11	13	16	10
Ampicillin	19	22	24	18	-	-	-
Griseofulvin	-	-	-	-	20	21	16

CONCLUSION

The complexes were obtained as colored powdered compounds and further characterized using elemental, IR, NMR analysis. The compounds were insoluble in water and most organic solvent but soluble in DMF and DMSO. The elemental analyses along with metal content were in good agreement with the predicted structure. Also the reflectance spectra along with magnetic measument confirm the octahedral geometry for all synthesized metal complexes. The antimicrobial activity data reveal that complexes possess higher activity compared to parent ligand. The increase in antimicrobial activity of the metal complexes may be due to the coordination with metal ion. Cu(II) is most active among all the synthesized transition metal complexes.

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