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Synthesis, Spectral, Thermal Studies and Antimicrobial Activity of Cobalt(II) Complexes of Propantheline Bromide

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The synthesis, spectral characterization, magnetic susceptibility and molar, conductance studies of a new series of cobalt(II) complexes of propantheline bromide (PPB) with general stoichiometry $[Co(PPB)_2(H_2O)_2X_2]$ are reported, where $X = Cl^-, Br^-, ClO_4^-$ and CH_3COO^-. In all the complexes PPB behaves as a unidentate ligand. Thermal studies (TG/DTA) have been used to evaluate kinetic parameters such as order of the thermal reaction (n) and activation energy (E_a). These new complexes were found to be more potent as antimicrobial agents than the free ligand.

INTRODUCTION

The cobalt(II) complexes have aroused great interest because they could be used as starting materials to synthesise many other compounds[1, 2] with asymmetrical properties and at the same time could be active as potential biominic[3] and biocidal agents[4]. Propantheline bromide (2-hydroxy ethyl) diisopropyl methyl ammonium bromide xanthene-9-carboxylate, is found to exhibit anticholinergic, parasympatholytic and spasmolytic action[5] and hence used in medicinal chemistry. At the same time due to the presence of tertiary nitrogen it acts as donor especially suitable for coordination of biometals. Literature survey reveals that very less work has been done on its coordination properties. There is no literature available for the study of complexing ability of this compound (PPB), We consider it worthwhile to study the reactions of PPB with cobalt(II). The coordination chemistry of biologically active molecules has been of great interest since the complexation is found to alter the activity of the organic compounds considerably[6, 7]. The cobalt(II) complexes have already shown that their fungal activity at least partially can be related to bonding of these biotics and change in their homeostasis[8]. The motivation for the present study is dedicated to the complexation of Co(II) with PPB and the identification of the complexes by its structure and properties. The next step of the investigation will be to study the physiological activity of the Co(II) complexes in comparison with the pure, non-complexed legating agent.

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EXPERIMENTAL

All materials used throughout the work were of AnalaR grade. Solvents were used after distillation. The ligand propantheline bromide used in the preparation of complexes was received as gift sample from Searle Ltd., and used as supplied.

The carbon and hydrogen micro-analysis were done on a Carlo Erba 1108 Heraeus. The electronic spectra of the complexes was recorded on Jasco UVIDEC-610 double beam spectrophotometer. The ^{1}H NMR spectra were obtained with AMX-400 FT NMR spectrometer using TMS as the internal standard. The IR spectra were recorded in KBr pellets/Nujol on Perkin-Elmer 580 spectrophotometer. The magnetic susceptibility of the complexes were measured with Guoy balance using $Hg[Co(SCN)_4]$ as calibrant. DuPont 9900 computer/thermal analyser with 951 TGA module thermobalance was used for recording TG curves. The molar conductance of the new complexes in DMSO (1.0×10^{-4} M) were measured at 303 K using Systronics conductivity meter 304. The analysis of cobalt content, chloride and bromide were carried out by literature methods[9] Nitrogen content of the complexes were estimated by Kjeldahl's method[10].

Preparation of the Complexes

All the complexes were prepared according to the following general method. 50 mL of 0.02 M ethanolic solution of the ligand was slowly added to 50 mL of 0.01 M ethanolic solution of the Co(II) salt separately. The reaction mixture was magnetically stirred for 2 h by Remi 2 MLH magnetic stirrer at 60–70°C. The blue-coloured precipitate obtained on cooling in each case were filtered, washed several times with absolute alcohol, finally with ether and dried in *vacuo*.

RESULTS AND DISCUSSION

All the complexes are insoluble in ether, benzene, carbon tetrachloride and cold ethanol but soluble in chloroform, acetonitrile, DMF and DMSO. The analytical, physical and molar conductance data are summarised in Table-1. The elemental analysis of the metal chelates indicate 1:2 stoichiometry for all the complexes. Molar conductance values (25.2–15.8 $ohm^{-1}\ cm^2\ mole^{-1}$) suggest their non-electrolytic behaviour in solution.

Electronic spectra and magnetic moments.

The electronic spectra of the new Co(II) complexes in DMSO (Fig. 1, Table-2) exhibit three bands at *ca.* 14400 cm^{-1}, *ca.* 15600 cm^{-1} and *ca.*16500 cm^{-1}. These bands can be assigned to $^4T_{1g} \rightarrow {}^44T_{2g}$, $^44A_{2g}(F)$ and $^44T_{1g}(P)$ transitions respectively. These bands characterise octahedral ligand field around Co(II) ion[11]. The more intense band beyond *ca.* 36700 cm^{-1} are charge transfer bands. The magnetic moment values of these diaquo Co(II) complexes (Table-2) are in the range 4.61-5.07 B.M. and suggest high spin octahedral geometry around Co(II) ion[11]. The crystal field splitting energies (10 Dq) calculated for cobalt(II) complexes (Table-3) are in agreement with the values obtained for known octahedral complexes[12].

TABLE-1
ANALYTICAL, PHYSICAL AND MOLAR CONDUCTANCE DATA

Complex Colour m.p. (°C)	% Found (Calcd.)					λ_M	
	C	H	N	Cl/Br	Co	Yield %	ohm^{-1} cm^2 mole^{-1}
[Co(PPB)$_2$(H$_2$O)$_2$Cl$_2$] (Blue) (170–172)	60.18 (60.48)	66.66 (66.64)	3.23 (3.20)	8.20 (8.13)	6.71 6.75	76	22.4
[Co(PPB)$_2$(H$_2$O)$_2$Br$_2$] (Blue) (190–192)	54.57 (54.90)	6.01 (6.03)	2.90 (2.92)	16.68 (16.60)	6.08 (6.12)	67	25.2
[Co(PPB)$_2$(H$_2$O)$_2$(ClO$_4$)$_2$] (Blue) (195–197)	44.13 (44.00)	4.80 (4.83)	2.30 (2.34)	5.96 (5.92)	4.94 (4.91)	59	20.5
[Co(PPB)$_2$(H$_2$O)$_2$(CH$_3$COO)$_2$] (Blue) (200–202)	55.60 (55.50)	6.20 (6.17)	2.73 (2.70)	–	5.70 (5.67)	62	15.8

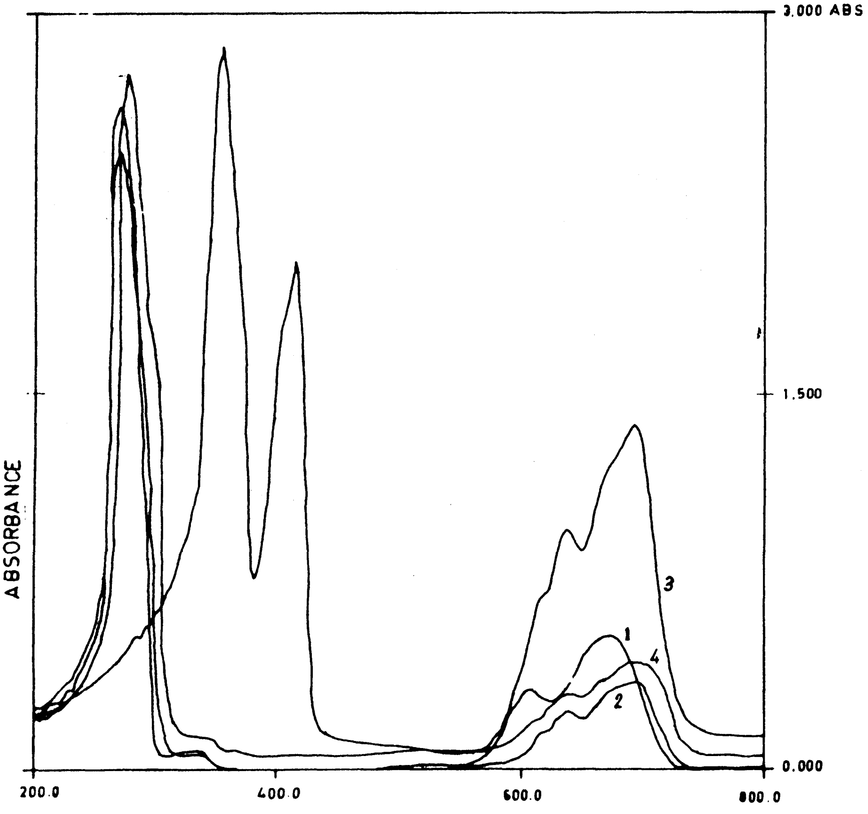


Fig. 1. Electronic spectra of
1. [Co(PPB)$_2$Cl$_2$(H$_2$O)$_2$],
2. [Co(PPB)$_2$Br$_2$(H$_2$O)$_2$]
3. [Co(PPB)$_2$(ClO$_4$)$_2$(H$_2$O)$_2$],
4. [Co(PPB)$_2$(CH$_3$COO)$_2$(H$_2$O)$_2$]

TABLE-2
ELECTRONIC SPECTRAL DATA AND MAGNETIC MOMENTS

Complex	Energies of Band Maxima nm (cm^{-1})	μeff B.M	10 Dq KJ mole^{-1}
$[Co(PPB)_2(H_2O)_2Cl_2]$	674 (14859) 604 (16556) 272 (36765)	4.93	198.04
$[Co(PPB)_2(H_2O)_2Br_2]$	694 (14409) 637 (15699) 616 (16234) 271 (36873)	4.61	194.19
$[Co(PPB)_2(H_2O)_2(ClO_4)_2]$	694 (14409) 639 (15649) 615 (16255) 272 (36765)	4.87	194.44
$[Co(PPB)_2(H_2O)_2(CH_3COO)_2]$	670 (14925) 610 (16393) 271 (36900)	5.07	196.09

IR Spectra

The IR spectral data are presented in Table-3. The strong and broad band in the region 3000-2900 cm^{-1} can be attributed to the tertiary nitrogen atom attached to alkyl group combined with bromide ion[13]. The sharp peaks occurring at 1150 cm^{-1} and 1725 cm^{-1} respectively in the ligand PPB are due to $\nu_{C—O—C}$ of the heterocyclic ring and ν_{COO} vibrations of the side chain.

In the spectra of the corresponding Co(II) complexes, the broad band around 3000–2900 cm^{-1} has completely disappeared thereby indicating that the tertiary nitrogen of the ligand is the site of coordination. The other bands for $\nu_{C—O—C}$ of the heterocyclic ring and ν_{COO} of the side chain remain at the same positions in the IR spectra of the respective Co(II) complexes suggesting that heterocyclic oxygen atom and the oxygen atom of the ester group were not involved in the bonding with Co(II) ions. In addition to this a very strong band appearing around 3400 cm^{-1} for the Co(II) complexes and the additional peak at 750 cm^{-1} can be assigned to $\nu_{O—H}$, thus showing the presence of coordinated water[15]. The presence of coordinated water is also checked from the TG studies. The IR data suggest that the ligand PPB acts as unidentate ligand.

When a ligand of high symmetry coordinates to a metal its symmetry is lowered and the marked changes in the spectra are expected because of changes in selection rule. This principle has been used extensively to determine whether acid anion (Cl^- and Br^-) coordinates to the metal as unidentate, chelating bidentate or bridging bidentate ligand[16]. The (Co—Cl), (Co—Br) stretching bands are observed around 320–310 cm^{-1} in the IR spectra of both the Co(II) complexes and the band around 425–410 cm^{-1} is assigned to $\nu_{(Co—N)}$. The non-conducting behaviour of these complexes further suggests that Cl^- and Br^- are present within the coordination sphere. The perchlorate group is shown to be coordinated in the

TABLE-3

SELECTED IR DATA (cm^{-1}) OF THE LIGAND AND ITS Co(II) COMPLEXES

Compound	$\nu_{N—CH_3}$	$\nu_{C—O—C}$	ν_{COO^-}	$\nu_{O—H}$	ν_{Cl}	ν_{Br}	ν_{ClO_4}	ν_{CH_3COO}	$\nu_{Co—N}$	$\nu_{Co—X}$
$C_{23}H_{30}NO_3Br$(PPB)	3000–2900	1150	1725	–	–	–	–	–	–	–
$[Co(PPB)_2(H_2O)_2Cl_2]$		1170	1725	3450 755	1250	–	–	–	410	310
$[Co(PPB)_2(H_2O)_2Br_2]$	–	1180	1720	3420 750	–	1275	–	–	425	320
$[Co(PPB)_2(H_2O)_2(ClO_4)_2]$	–	1180	1715	3405 750	–	–	1100	–	415	317
$[Co(PPB)_2(H_2O)_2(CH_3COO)_2]$	–	1170	1725	3410 750	–	–	–	1320	413	316

TABLE-4

^1H NMR DATA (δ) OF THE LIGAND AND ITS Co(II) COMPLEXES

Compound	Ar—H	C—H	—O—CH_2	—N—CH_2	—N—CH_3	—N—$(CH)_2$	—C—$(CH_3)_4$
$C_{23}H_{30}NO_3Br$(PPB)	7.1 to 7.4	5.32	4.38	3.45	3.30	3.71–3.81	1.14–1.34
$[Co(PPB)_2(H_2O)_2Cl_2]$	7.1 to 7.4	5.30	4.38	3.50	–	3.71–3.76	1.10–1.32
$[Co(PPB)_2(H_2O)_2Br_2]$	7.1 to 7.4	5.31	4.36	3.50	–	3.71–3.76	1.12–1.36
$[Co(PPB)_2(H_2O)_2(ClO_4)_2]$	7.1 to 7.4	5.32	4.35	3.50	–	3.71–3.76	1.12–1.34
$[Co(PPB)_2(H_2O)_2(CH_3COO)_2]$	7.1 to 7.4	5.32	4.38	3.50	–	3.71–3.76	1.12–1.34

Ar—aromatic

TABLE-5
STEPS OF THERMAL DEGRADATION, THEIR COMPOSITION AND ACTIVATION ENERGIES

Complex	Transitions	Temperature range in K	Leaving group	Weight calculated (%)	Weight experimental (%)	Residue			Order of reaction (n)	Activation energy E_a KJ mole^{-1}
						Nature	Calculated (%)	Exptl (%)		
[Co2L$(H_2O)_2Cl_2$]	I	440–563	$2H_2O$	4.12	4.15	CoO	8.58	8.54	1	09.5
	II	567–693	2Cl	8.13	8.08				1	10.7
	III	696–865	2L	79.99	75.23				1	13.0
[Co2L$(H_2O)_2Br_2$]	I	465–574	$2H_2O$	3.74	3.77	CoO	7.79	7.81	1	10.4
	II	577–657	2Br	16.63	16.10				1	15.3
	III	663–850	2L	73.51	72.32				1	41.2
[Co2L$(H_2O)_2(ClO_4)_2$]	I	458–493	$2H_2O$	3.0	3.06	CoO	6.24	6.48	1	05.8
	II	508–693	$2ClO_4$	33.71	33.01				1	08.6
	III	698–863	2L	58.92	57.45				1	12.6
[Co2L$(H_2O)_2(CH_3COO)_2$]	I	463–498	$2H_2O$	3.47	3.51	CoO	7.22	7.22	1	12.8
	II	498–698	$2CH_3COO$	22.76	22.78				1	17.5
	III	723–998	2L	68.12	66.46				1	61.5

L = PPB

complex, since the broad band (ν_3) at about 1100 cm^{-1} due to ionic (T_d) perchlorate is absent. The band splits into a doublet at 1120 cm^{-1} (overlapping with the ligand peak) and 1090 cm^{-1} and a sharp at *ca.* 620 cm^{-1} in Co(II) perchlorate complex. Thus monodentate (C_{3V}) is indicated in the complex[18]

TABLE-6

ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY INHIBITION ZONE IN mm

Compound	Disk potency	*S. aureus*	*E. Coli*	*Pseudomonas*	*Candida**	*A. niger**
$C_{23}H_{30}NO_3Br$(PPB)	25 μg	15	08	08	15	16
$[Co(PPB)_2(H_2O)_2Cl_2]$	25 μg	20	12	15	20	22
$[Co(PPB)_2(H_2O)_2Br_2]$	25 μg	18	10	10	18	20
$[Co(PPB)_2(H_2O)_2(ClO_4)_2]$	25 μg	25	12	14	23	25
$[Co(PPB)_2(H_2O)_2(CH_3COO)_2]$	25 μg	20	11	10	21	22
Gentamycin	10 μg	30	16	23	21	22
Griseofulvin	40 μg				20	22

*Fungal growth .

Diameter of the disk : 6.5 mm. DMSO (Solvent) : No inhibition.

^{1}H NMR

The ^{1}H NMR spectra of the ligand and its complexes have been recorded in DMSO-d_6 using TMS as an internal standard. The relevant data and assignments are presented in Table-4. The ligand PPB exhibits a triplet at δ 1.16 ppm which is assigned to C—$(CH_3)_4$. The sharp signal (singlet) at δ 3.30 ppm is due to the tertiary nitrogen attached to the alkyl group, *i.e.* —N—CH_3. The multiplet centred at δ 3.7 ppm is attributed to —NCH_2. The other multiplet δ 7.1–7.4 ppm is due to aromatic protons.

In the spectrum of Co(II) complexes all these resonance signals are retained except a sharp signal at δ 3.30 ppm *i.e.*, N—CH_3 has completely disappeared indicating the bonding of the Co(II) ion to the tertiary nitrogen atom of the ligand. Thus ^{1}H NMR supports the conclusion drawn on the basis of IR data regarding the involvement of tertiary nitrogen atom in bonding with Co(II) ion.

Thermogravimetric analysis

The decomposition temperatures of the complexes obtained from their thermograms are recorded in Fig. 2. The TG curves were analysed to give percentage weight loss as a function of temperature. TGA and DTA of the complexes show three decompostion steps accompanied by three exothermic peaks. The first decomposition step occurs in the temperature range 440–493 K and the weight loss corresponds to the loss of two molecules of water. The expulsion of water from the complexes in the above temperature range suggests the water molecules in the coordination sphere[19] The second decomposition step occurring in the

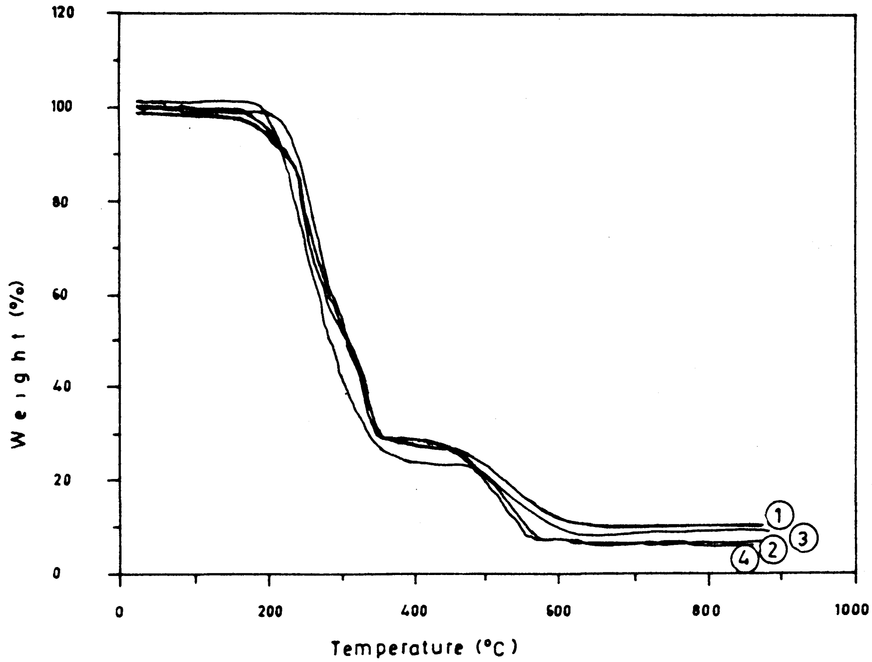


Fig. 2. TGA curves of
1. $[Co(PPB)_2Cl_2(H_2O)_2]$,
2. $[Co(PPB)_2Br_2(H_2O)_2]$
3. $[Co(PPB)_2(ClO_4)_2(H_2O)_2]$,
4. $[Co(PPB)_2(CH_3COO)_2(H_2O)_2]$

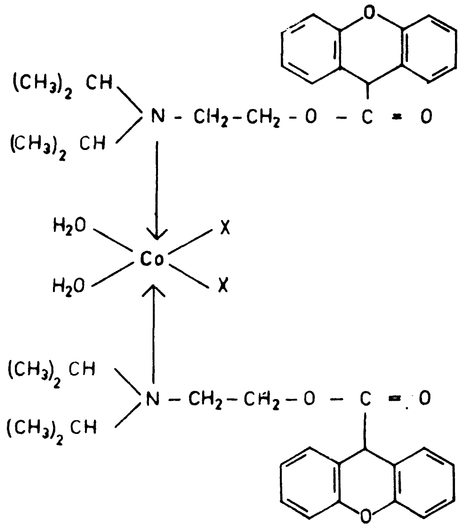
temperature range 508–657 K corresponds to the expulsion of coordinated Cl^-, Br^-, ClO_4^- and CH_3COO^- groups. The third decomposition step occurs in the temperature range 663–998 K corresponds to the loss of ligand moiety. The final product of the decomposition product at above 998 K in all the complexes corresponds to Co(II) oxide which was in confirmity with the observed and calculated weights of pyrolysis products (Table-4).

The Broido method[20] was applied to the TG data to determine the energy of activation (E_a) and the order of the thermal reaction (n). In order to estimate the kinetic parameters of the thermal degradation during the analysis of thermograms, it was assumed that the reaction follows the first order kinetics. In the present study the plots of $-\ln(\ln 1/Y)$ *vs* .$1/T \times 10^3$ are linear over the conversion range 0.1 to 0.9 supporting the assumption of first order reaction kinetics.

The bond strength between the same central atom and the ligand in different types of coordination polyhedra (octahedral, square planar, tetrahedral etc.) must be different, as the bonding possibilities of the central atom for different coordination polyhedra vary. Therefore only complexes of the same stoichiometric type and identical geometrical configuration may be compared with each other. The energy of activation data of different thermal decompostion processes are presented in Table-4. The highest thermal stability is noticed for $Co(CH_3COO)_2$ salt complex and the lowest for $Co(ClO_4)_2$ salt complex. The decreasing order of thermal stability is observed in the following order:

$$[CoL(H_2O)_2(CH_3COO)_2] > [CoL(H_2O)Br_2] > [CoL(H_2O)_2Cl_2] > [CoL(H_2O)_2(ClO_4)_2]$$

On the basis of chemical analysis and various physicochemical studies, we tentatively propose the following octahedral structure for the new Co(II) complexes.



[X = Cl, Br, ClO$_4$ and CH$_3$COO]

Antimicrobial activity

The new Co(II) complexes were subjected to antibacterial and antifungal activities. Gram positive *Staphylococcus aureus* and gram negative *Escherichia coli* and *Pseudomonas aeruginosa* were used for antibacterial activity. Two fungal cultures *Candida albicans* and *Aspergillus niger* were used for antifungal activity. For these two tests disk diffusion method[21, 22] was followed. The activities of the compounds were compared with those of standards, Gentamycin for antibacterial and Griseofulvin for antifungal activity.

The inhibition zones were measured to the nearest millimetre and the results are represented in Table-5. The results reveal that the new complexes exhibit promising activity against all tested organisms than the free ligand.

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