

Synthesis, Spectral and Thermal Degradation Kinetics of Divalent Cadmium Complexes of Dothiepine and Diphenhydramine

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Cadmium(II) complexes with 3-(6H-dibenzo[b,e] thiepin-11-ylidene) propyl dimethyl amine chloride (dot) and 2-diphenyl methoxy-N,N-dimethylamine hydrochloride (dp) were synthesised and characterised by reflectance, IR, ^1H NMR, magnetic moments and conductivity measurements. The new complexes studied for kinetics of thermal degradation by thermogravimetric analyses (TGA) and derivative thermogravimetric studies (DTG) in a static nitrogen atmosphere at a heating rate of $10^\circ\text{C min}^{-1}$. The kinetic and thermodynamic parameters such as energy of activation (E_a), frequency factor ($\ln A$), enthalpy (ΔH), free energy (ΔG), and entropy (ΔS) evaluated. The energy of activation values for the degradation of (dot) and (dp) complexes were found to be in the range $22.3\text{--}125.4 \text{ kJ mol}^{-1}$.

Introduction

Antidepressant drugs such as 3-(6H-dibenzo[b,e] thiepin-11-ylidene) propyl dimethyl amine chloride (dot) and 2-diphenyl methoxy-N,N-dimethylamine hydrochloride (dp), commercially known as dothiepine hydrochloride, and diphenhydramine hydrochloride have a wide application as a pharmaceutical agent^{1–3} and hence are used in medicinal chemistry. Due to the presence of a tertiary nitrogen atom in their structure they form stable complexes with transition metals. The complexation ability of Co(II) ⁴ and Pd(II) ⁵ with (dot) has been reported earlier.

A survey of the literature reveals^{6–10} that the thermogravimetric studies, decomposition kinetics and thermodynamic parameters of transition metal complexes have been studied systematically and intensively. This paper reports the synthesis, structural elucidation and thermal degradation kinetics of Cd(II) complexes of (dot) and (dp) heterocyclic ligands employing TGA studies at a heating rate of $10^\circ\text{C min}^{-1}$.

Experimental

The chemicals and solvents used were of AR grade. The ligands dothiepine hydrochloride (dot) and diphenhydramine hydrochloride (dp) were received as gift samples from INTAS Pharmaceutical Limited and PARKE-DAVIS (India) Limited, Mumbai, respectively.

General procedure for the syntheses of complexes

An ethanolic solution of 4 m mol of (dot) was added to 2.5 m mol solution of $\text{CdX}_2\text{nH}_2\text{O}$ (where $\text{X} = \text{Cl}^-$, NO_3^- , or I^- and $n = 0, 1, 2, 3$.) with continuous stirring and was warmed in a water bath (75-80°C) for about 2 h. The solid complexes formed were filtered, washed with cold ethanol and then with ether and dried in a vacuum desiccator over fused CaCl_2 .

Cd(II) -chloro, nitrate complexes of (dp) were prepared by refluxing the mixture for 6 h. Cd(II) -iodide complex was synthesised in aqueous media. The colourless solid complexes formed were filtered, washed with cold ethanol and then with ether and dried in a vacuum desiccator over fused CaCl_2 .

Physical measurements and analytical methods

Equiptronics Conductivity meter model EQ-DCM-P was used for measuring molar conductance in 1×10^{-3} M solution at room temperature. The magnetic susceptibility measurements were performed with a Gouy balance using $[\text{Hg}(\text{Co}(\text{SCN})_4)]$ as calibrant at 305 K. IR spectra were recorded on a Hitachi model 297 spectrometer in the 4000-250 cm^{-1} region using KBr disks. The reflectance spectra were recorded on PYEUNICAM SP₈₋₁₀₀ UV-Vis spectrophotometer in the 200-800 cm^{-1} region using MgO as reflectance standard. Proton NMR spectra were recorded on a JEOL 60 MHz spectrometer using DMSO- d_6 as solvent and chemical shifts were relative to internal TMS at room temperature. The elemental analyses were carried out at the Dept. of Chemical Technology, University of Bombay, Mumbai. A DuPont 9900 computer/thermal analyser with a 951 TG module thermobalance was used for recording TG curves in the atmosphere of nitrogen at a heating rate of 10°C min^{-1} by taking 8-10 mg of the complexes. The metal content was determined by the EDTA method.

Results and Discussion

All synthesised divalent cadmium complexes of (dot) and (dp) were colourless, amorphous and non-hygroscopic towards air and moisture. The results obtained from microanalytical measurements and metal determination data (Table 1) suggest a monomeric 2:1 ratio for ligand to cadmium(II) chloride, nitrate and iodido complexes. These elemental analysis data are in good agreement with the chemical formula of the complexes. The molar conductance values in the range 13.45-16.49 $\text{mhos cm}^2 \text{mol}^{-1}$ at room temperature confirmed the covalent nature of the complexes and that anions are present within the coordination sphere¹⁰.

Infrared spectra

In the IR spectrum of free ligands (dot) and (dp) a characteristic band appeared at 2550-2400 cm^{-1} due to the tertiary nitrogen atom attached to the alkyl group combined with halogen^{5,11}. This band disappeared in the spectra of all the complexes showing that the side chain nitrogen atom is a site of coordination. In the

free ligand (dot) the band appeared at 760 cm^{-1} for $\nu(\text{C-S-C})$ and in (dp) at 1060 cm^{-1} for $\nu(\text{C-O-C})$ ^{8,11}, respectively. This band appeared in almost the same region in the corresponding metal complexes, thus indicating that the sulphur and oxygen atoms of the ligands were not involved in bonding. Furthermore, the presence of new bands in the complexes around $425\text{-}445\text{ cm}^{-1}$ is an indication of $\nu(\text{M-N})$ bonds.

Table 1. Elemental analyses, molar conductance and magnetic moments of the complexes.

Complex	Yield %	C Found (Calcd.)%	H Found (Calcd.)%	N Found (Calcd.)%	M Found (Calcd.)%	$\Omega\text{ M}$ mhos $\text{cm}^2\text{ mol}^{-1}$	μ^{eff} (B. M)
[Cd(C ₁₉ H ₂₁ NS) ₂ Cl ₂]	64	58.85 (58.96)	4.92 (5.47)	3.01 (3.62)	13.94 (14.52)	16.48	Diamg
[Cd(C ₁₉ H ₂₁ NS) ₂ (NO ₃) ₂]	72	54.26 (55.17)	4.89 (5.12)	6.13 (6.77)	12.87 (13.58)	13.57	Diamg
[Cd(C ₁₉ H ₂₁ NS) ₂ I ₂]	46	46.86 (47.69)	4.08 (4.42)	2.72 (2.93)	10.67 (11.74)	14.65	Diamg
[Cd(C ₁₇ H ₂₁ NO) ₂ Cl ₂]	72	60.43 (61.5)	4.99 (5.7)	3.06 (3.76)	14.85 (15.14)	16.25	Diamg
[Cd(C ₁₇ H ₂₁ NO) ₂ (NO ₃) ₂]	59	56.97 (57.4)	4.43 (5.32)	6.85 (7.04)	14.01 (14.13)	16.49	Diamg
[Cd(C ₁₇ H ₂₁ NO) ₂ I ₂]	58	48.56 (49.34)	3.98 (4.58)	2.97 (3.03)	12.03 (12.15)	13.45	Diamg

The Far-IR spectra of Cd(II)-chloride and iodide complexes of (dot) and (dp) registered a medium band in the region $345\text{-}365\text{ cm}^{-1}$, which are assigned to $\nu\text{M-Cl}$ and $\nu\text{M-I}$, respectively. The Cd(II)-nitrate complexes exhibited three bands at ca. 1460 , 1365 and 1046 cm^{-1} , which are attributed to ν_4 , ν_1 and ν_2 of coordinated nitrate ions, which are not observed in the spectra of the ligand. Since the separation between ν_4 and ν_1 ions is $\sim 110\text{ cm}^{-1}$ it is presumed that the nitrate ions are coordinated unidentately to the cadmium(II) ion^{12,13}. The non-electrolytic nature of the complexes in the DMF further supports this observation.

Reflectance spectra and magnetic measurements

The solid state electronic spectra of all these Cd(II) complexes exhibited the weakest absorption band in the region ca. 19600 cm^{-1} due to metal-ligand charge transfer processes. These bands are ascribed to a charge transfer from d-orbital of the Cd(II) to the π^* system of the ligands. These complexes also exhibited a maximum intense band around at ca. 37000 cm^{-1} corresponding to an intramolecular charge transfer transition within the ligand, which is assigned to $n \rightarrow \pi^*$ transitions. The absence of d-d bands in these complexes at longer wavelength is quite reasonable since the metal ion filled d-subshells where d-d transitions are highly forbidden. All these complexes exhibited diamagnetism as expected for d^{10} configuration.

Proton NMR studies

The free ligands (dot) and (dp) in DMSO- d_6 (δ , ppm) showed the following proton NMR signals: $\delta 2.45\text{-}2.55\text{ ppm}$ for $-\text{N}-(\text{CH}_3)_2$ (6H); $\delta 2.2\text{-}2.4\text{ ppm}$ for 2CH_2 (4H); $\delta 5.7\text{-}6.1\text{ ppm}$ for CH, (H); and $\delta 7.0\text{-}7.5\text{ ppm}$ for aromatic H, (10H). In the spectra of complexes all the NMR signals of ligands appeared in their appropriate position except for $-\text{N}-(\text{CH}_3)_2$ protons, which showed a sharp signal at $\delta 2.6\text{-}2.75\text{ ppm}$ indicating the bonding

of metal ion to the nitrogen of the side chain. Thus proton NMR data support the conclusion drawn on the basis of IR data regarding the involvement of the side chain nitrogen atom in bonding with the Cd(II) ion.

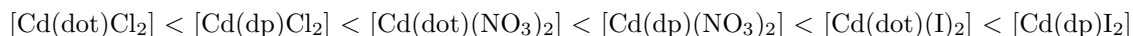
Thermogravimetric studies

Thermal studies of Cd(II) complexes of (dot) and (dp) were carried out to observe the thermal behaviour in order to determine the degradation mechanism at a heating rate of 10 °C min⁻¹. The thermograms obtained under dynamic TGA scans were analysed to give percentage weight loss as a function of temperature. In order to determine the thermal stability trends the temperature characteristic values were evaluated. The temperature characteristics such as T₀ (temperature onset of decomposition), T₁₀ (temperature for 10% weight loss), T₂₀ (temperature for 20% weight loss), and T_{max} (temperature of maximum rate of degradation) and integral procedure decomposition temperature (IPDT) of the degradation process were calculated and are presented in Table 2.

Table 2. Data obtained from TGA analysis. Temperature characteristics and integral procedure decomposition temperature

Compound	T ₀ (°C)	T ₁₀ (°C)	T ₂₀ (°C)	T _{max} (°C)	IPDT(°C)
[Cd(dot) ₂ Cl ₂]	216	265	300	695	410
[Cd(dot) ₂ (NO ₃) ₂]	234	295	315	725	420
[Cd(dot) ₂ I ₂]	237	275	320	735	420
[Cd(dp) ₂ Cl ₂]	208	270	340	690	385
[Cd(dp) ₂ (NO ₃) ₂]	220	290	315	715	395
[Cd(dp) ₂ I ₂]	224	305	390	710	395

In these the T₀, T₁₀, T₂₀, and T_{max} are the main criteria indicating the thermal stability of complexes and they are also the sole features of TG curves. The higher the value of T₀, T₁₀, T₂₀, and T_{max} the higher will be the thermal stability¹⁴. The thermal processes specific for each complex are due to the organic and inorganic ligands. It is often eliminated stepwise, either as a free base or as decomposition products over a wide temperature range. Its influence on the common thermal processes depends on its structure and basic character (involving the metal-ligand bond strength, electronic effects etc.), melting point, reactivity and stability against heat. In these new complexes the higher thermal stability was found in Cd(II)-iodide [T₀(237-224°C and T_{max}(735-710°C)] complexes. The lowest stability was observed for Cd(II)-chloride complex, which may be ascribed to the purely high electronegative nature of the chloride ion. This low stability was confirmed by observing the least value temperature characteristics of Cd(II)-chloride complexes. The trend of thermal degradation stability is in the order



To obtain a quantitative assessment of the relative stability, IPDT values can be regarded as having significant importance because this represents the overall nature of the TGA curves¹⁵.

TG curves of all Cd(II) complexes of (dot) and (dp) show two significant temperature transitions of weight loss with common and specific stages, termed as two stages of thermal degradation. The thermal decomposition of the complexes under study takes place according to mechanisms involving the decomposition process of organic ligand followed by anions that support the formations of the complexes and affords some consideration on the thermal degradation mechanisms. The temperature decomposition percentage

weight loss of ligands and the percentage of residue are presented in Table 3. The TG curve and DTG peak temperature of all these complexes indicate that the decomposition of the complexes takes place in two identical stages. The TG plateau of the complexes shows that these complexes start decomposition after 205°C. This observation suggests that neither ligand complex has water molecules either inside or outside the coordination sphere. The weight loss in the range 205-423°C in TG curves of complexes is termed the first stage of thermal degradation. In this case, the present weight loss is in the range 56.98-72.15%, which may be attributed to the decomposition of less thermally, stable organic moiety. The onset of second step decomposition occurs in the range 405-723°C, which gave the loss of inorganic ligand bonding with the metal ion. The experimental values were in full agreement with the percent weight calculated on the basis of stoichiometry proposed for the complexes. The terminal solid residue was cadmium oxide in all cases in conformity with the percentage losses of mass obtained from TG curves.

Table 3. Thermogravimetric characteristics of the complexes under study

Complex	Process	Temp. Range (° C)	Product	Weight Found (calcd.)%	No. of moles	Residue Found (calcd.)%	Nature
[Cd(dot) ₂ Cl ₂]	Decomposition of Coordination sphere (L,Cl)	216-405 410-672	L Cl	72.15 (74.77) 09.32 (08.97)	2 2	14.96 (16.25)	CdO
[Cd(dot) ₂ (NO ₃) ₂]	Decomposition of Coordination sphere (L, NO ₃)	231-423 423-675	L NO ₃	69.54 (70.04) 12.90 (14.10)	2 2	17.56 (15.22)	CdO
[Cd(dot) ₂ I ₂]	Decomposition of Coordination sphere (L, I)	231-423 433-698	L I	61.38 (60.72) 25.78 (26.05)	2 2	12.84 (13.19)	CdO
[Cd(dp) ₂ Cl ₂]	Decomposition of Coordination sphere (L, Cl)	205-395 405-655	L Cl	70.81 (71.92) 08.95 (09.98)	2 2	19.24 (18.08)	CdO
[Cd(dp) ₂ (NO ₃) ₂]	Decomposition of Coordination sphere (L, NO ₃)	218-420 421-678	L NO ₃	66.03 (66.92) 15.23 (16.24)	2 2	17.04 (16.82)	CdO
[Cd(dp) ₂ I ₂]	Decomposition of Coordination sphere (L,I)	222-423 425-688	L I	56.98 (57.19) 28.99 (28.42)	2 2	14.03 (14.38)	CdO

Thermal degradation kinetic and thermodynamic parameters

The graph of $[\ln(\ln 1/y) \text{ Vs } 1/T]$ (where y is the fraction not yet decomposed) for the first and second stages of thermal degradation was plotted by treating the TGA data in terms of Broido's method¹⁶, and is presented in Figs. 1 and 2. From the slope of the graph the kinetic parameters such as activation energy E_a and pre-exponential factor $\ln A$ were evaluated and are given in Table 4. The activation energies are low in first stage transition (17.58-32.10 kJ mol⁻¹) and the activation energies are high in second stage transition (91.48-125.5 kJ mol⁻¹). The lowest value for first step due to this low energy is utilised to remove the coordinate organic ligand. The abnormal values of $\ln A$ indicate that the decomposition reaction of the complex can be classified as a slow reaction¹⁷.

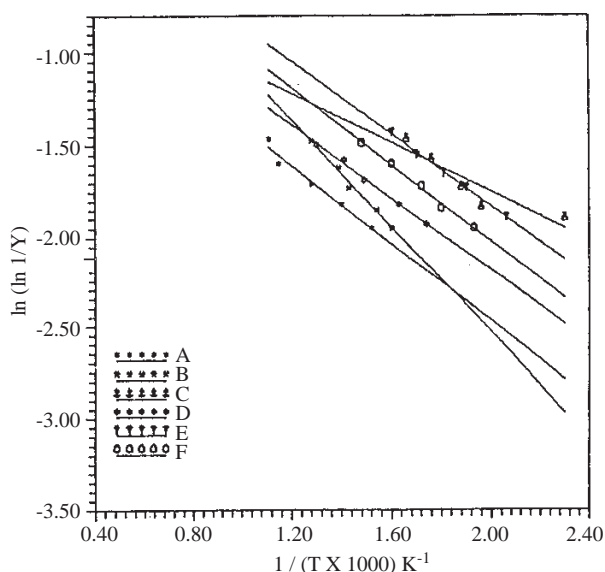


Figure 1. Graph of $[\ln(\ln 1/y) \text{ vs } 1/T]$ for first stage of thermal degradation of

- A.** $[\text{Cd}(\text{dot})_2\text{Cl}_2]$ **B.** $[\text{Cd}(\text{dot})_2(\text{NO}_3)_2]$ **C.** $[\text{Cd}(\text{dot})_2(\text{I})_2]$
D. $[\text{Cd}(\text{dp})_2\text{Cl}_2]$ **E.** $[\text{Cd}(\text{dp})_2(\text{NO}_3)_2]$ **F.** $[\text{Cd}(\text{dp})_2(\text{I})_2]$

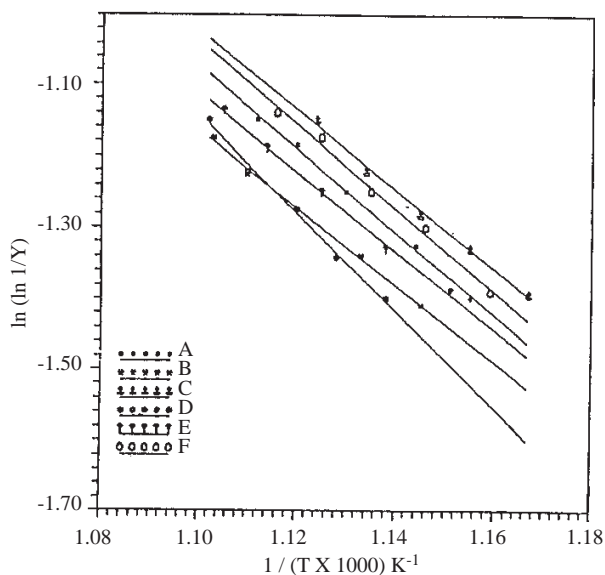


Figure 2. Graph of $[\ln(\ln 1/y) \text{ vs } 1/T]$ for second stage of thermal degradation of

- A.** $[\text{Cd}(\text{dot})_2\text{Cl}_2]$ **B.** $[\text{Cd}(\text{dot})_2(\text{NO}_3)_2]$ **C.** $[\text{Cd}(\text{dot})_2(\text{I})_2]$
D. $[\text{Cd}(\text{dp})_2\text{Cl}_2]$ **E.** $[\text{Cd}(\text{dp})_2(\text{NO}_3)_2]$ **F.** $[\text{Cd}(\text{dp})_2(\text{I})_2]$

The thermodynamic parameters such as enthalpy of reaction (ΔH), entropy (ΔS) and free energy (ΔG) for all the complexes evaluated with the help of thermal degradation data, and the values are presented in Table 4. The enthalpy values observed for all the steps of complexes compared with those of T_0 show that with a decrease in the value of enthalpy, the decomposition temperature also decreases. The enthalpy value approximately characterises the band strength, together with the values of the activation energies. In both stages the free energy value is positive. The low entropy value is observed for first step degradation and high for second step degradation. The entropy value is negative $[(-)11.52 - (-)36.99 \text{ Jk}^{-1}]$ for the first step

degradation and positive [53.04-78.71 Jk⁻¹] for second step degradation. However, the negative values of entropies of activation are compensated for by the value of enthalpies of activation, leading to almost the same values (12.73-115.4 kJ mol⁻¹) for the free energies of activation^{18,19}. The data clearly indicates that the basic steps are similar in the thermal degradation of the complexes.

Table 4. Kinetic and thermodynamic parameters for the degradation process of complexes

Complex	Process ess	Ea±2 kJ mol ⁻¹	LnA±2 (min ⁻¹)	Δ H kJ mol ⁻¹	Δ S (kJ ⁻¹)	Δ G (kJ mol ⁻¹)
[Cd(dot) ₂ Cl ₂]	I	32.1	16.27	27.19	-11.52	33.99
	II	125.5	27.99	115.4	78.71	47.77
[Cd(dot) ₂ (NO ₃) ₂]	I	27.59	15.04	22.51	-21.08	35.37
	II	115.9	37.27	109	76.49	45.92
[Cd(dot) ₂ I ₂]	I	22.3	14.03	17.53	-27.98	33.71
	II	104.7	25.6	97.54	59.91	47.13
[Cd(dp) ₂ Cl ₂]	I	24.53	14.21	19.35	-27.28	36.34
	II	106.5	26.13	99.54	63.98	46.24
[Cd(dp) ₂ (NO ₃) ₂]	I	19.63	13.23	14.72	-33.24	34.33
	II	99.85	24.78	92.75	53.04	47.5
[Cd(dp) ₂ I ₂]	I	17.58	12.74	12.73	-40.25	25.69
	II	91.48	25.06	85.16	56.74	43.62

Based on the above evidence, the proposed probable structure of Cd(II)-dot complexes is presented in Figure 3.

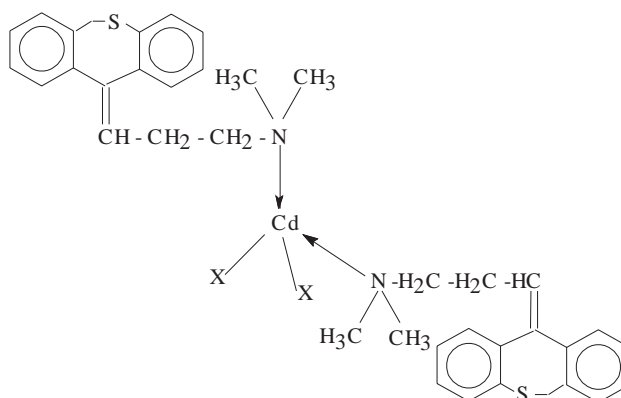
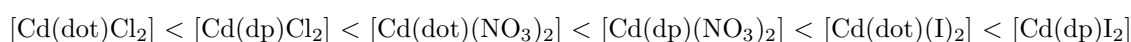


Figure 3. Probable structure of [Cd(dot)₂X₂] complexes

Where X = Cl⁻, NO₃⁻, or I⁻

Conclusion

The new synthesised Cd(II) complexes with (dot) and (dp) were characterised by the elemental analyses and spectral studies. The temperature characteristics, such as T₀, T₁₀T₂₀ and T_{max}, indicate that the relative thermal stability is in the order



The enthalpy values lies in the range 12.73-115.4 kJ mol⁻¹. The entropy value is negative for the first steps and positive for the next stage of degradation.

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