

Synthesis and Spectroscopic Studies of the Complexes of Tumor Cell Differentiating Agent Hexamethylene Bisacetamide with Manganese and Cobalt Halides

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Summary: The syntheses of the complexes of tumor cell differentiating agent hexamethylene bisacetamide (HMBA) with manganese (II) and cobalt(II) halides which include $M_2(HMBA)_3X_4$ (M= Mn and Co; X=Cl or Br) have been reported. The complexes have been characterized by elemental analysis and their structures have been established on the basis of their electronic spectra, e.s.r. spectra and magnetic susceptibilities. All these complexes have been assigned the mixed octahedral-tetrahedral structures and similar to the corresponding nickel complexes [1], can correctly be formulated as $[M(HMBA)_3][MX_4]$.

Introduction

During recent years, much work has been devoted to test the numerous chemical compounds, which induce the differentiation of several types of malignant tumor cells [2,3]. Among these compounds, HMBA has a number of characteristics, which render it one of the most potent differentiating agent of transformed cell lines [4-6]. In vitro studies with HMBA provide a basis for the application of this compound to clinical therapy as human cancers [7] and it has been entered in phase I clinical trials, for the treatment of human cancers [8]. Recently, HMBA has also been reported to affect phenotypic modulation and inhibits the proliferation of human and rat vascular smooth-muscle cells [9,10].

Present interest in this kind of complexes arises due to the opportunity to study the complexing ability of the clinically significant compound, HMBA (Fig. 1),

with divalent metal halides such as those of manganese and cobalt. Previously, little attention has been devoted to study the complexes of HMBA with divalent metals and only those of nickel(II) halides have been reported [1]. Here, we report the synthesis of the complexes of HMBA with manganese (II) and cobalt(II) halides, which include $M_2(HMBA)_3X_4$ (M= Mn and Co; X = Cl or Br). These complexes have been characterized by elemental analysis and their structures studied by their electronic spectra, e.s.r. spectra and magnetic susceptibilities.

Results and Discussion

The characteristic bands in the reflectance spectra ($4000-30000\text{ cm}^{-1}$) of the complexes $M_2(HMBA)_3Cl_4$ (M= Mn and Co; X=Cl or Br) are listed in Table-1 and their magnetic susceptibilities are collected in Table-2.

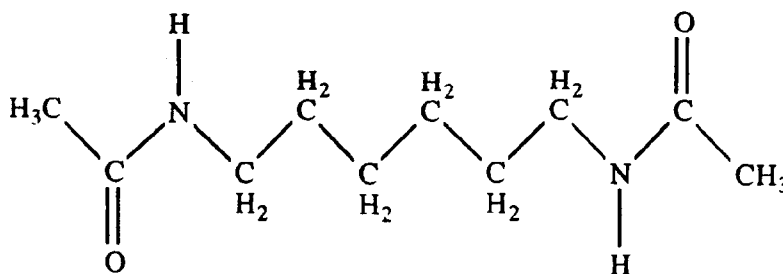


Fig. 1: Structure of the HMBA.

Table-1: Reflectance spectra of complexes of HMBA with manganese (II) and cobalt (II) halides

Complex	Absorption maxima (cm ⁻¹)
[Mn(HMBA) ₃][MnCl ₄]	26400S, 23200 Sh, 22500 M.
[Mn(HMBA) ₃][MnBr ₄]	26300 VS, 23000 Sh, 22300 S, 21500 Sh.
[Co(HMBA) ₃][CoCl ₄]	25000 W, 22700 W, 19100 M, 16300 Sh, 15800 Sh, 14950 S, 14400 VS, 6190 M, 5585 M, 4950 M.
[Co(HMBA) ₃][CoBr ₄]	25300 W, 23500 VW, 21650 W, 15600 Sh, 14925 Sh, 14500 VS, 13900 Sh, 7400 Sh, 5600 M.
	Broad Absorption 5000-4000.

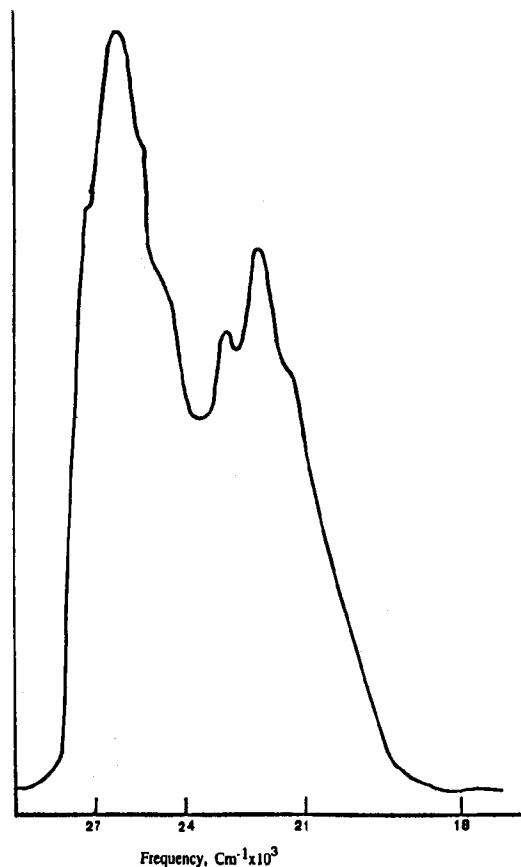
VS = Very Strong, S = Strong, M = Medium, Sh = Shoulder, Br = Broad. W = Weak

Table-2: Magnetic properties of complexes of HMBA with manganese (II) and cobalt (II) halides

Complex	T (°K)	X _m (per metal ion) m ³ mol ⁻¹ x 10 ⁻¹¹	μ _{eff} (per metal ion) (B.M.)
[Mn(HMBA) ₃][MnCl ₄]	297	18444	5.90
[Mn(HMBA) ₃][MnBr ₄]	295	19012	5.96
[Co(HMBA) ₃][CoCl ₄]	297	11930	4.74
[Co(HMBA) ₃][CoBr ₄]	297	12416	4.84

In the reflectance spectra of manganese complexes, Mn₂(HMBA)₃Cl₄ and Mn₂(HMBA)₃Br₄, the strong multiple transitions in the regions 21000 - 24000 cm⁻¹ and 25000-28000 cm⁻¹ (Fig. 2), can easily be assigned to the ν₁ band, caused by transition to the states originating from the ⁴G term and ν₂ band, originating from ⁴D and ⁴P terms of Mn(II) ion in tetrahedral environment, respectively. The observed electronic band energies for both of these complexes are very similar to those of corresponding [MnX₄]²⁻ anions (X = Cl or Br) reported previously [11]. Further, observed magnetic moments of about 5.9 B.M. (Table-2) for both of these complexes confirm the presence of high spin d₅ configuration of Mn(II) ions. The observed electronic and magnetic properties for manganese (II) halide complexes lead to the conclusion that both of these complexes contain the tetrahedral [MnX₄]²⁻ chromophores (X = Cl or Br) and, like corresponding nickel complexes [1], can correctly be formulated as [Mn(HMBA)₃][MnX₄] (X=Cl or Br).

The e.s.r. spectra of manganese complexes consist of a broad band centered at g_{eff}=2 region, suggesting either considerable magnetic interactions between neighboring metal ions or very regular cubic symmetry. This result is again consistent with the formulation [Mn(HMBA)₃][MnX₄] in which both

Fig. 2: Reflectance spectrum of [Mn(HMBA)₃][MnBr₄].

manganese ions are in fairly regular cubic environments.

The reflectance spectra of cobalt complexes, Co₂(HMBA)₃Cl₄ and Co₂(HMBA)₃Br₄, are indicative of basically tetrahedral structures, although there are several shoulders which also suggest the presence of an octahedral chromophore. It seems likely that, similar to nickel and manganese analogues, both the complexes of cobalt also contain the tetrahedral [CoX₄]²⁻ anions, with [Co(HMBA)₃]²⁺ cations as the octahedral species and can correctly be formulated as [Co(HMBA)₃][CoX₄] (X=Cl or Br).

For both of these cobalt complexes the observed, very intense, electronic spectral bands in the regions 4500-6500 cm⁻¹ and 13500-16500 cm⁻¹ are assigned to the ν₂ transition (⁴T₁(F)-⁴A₂) and ν₃

transition (${}^4T_1(P) \rightarrow {}^4A_2$) of Co(II) in T_d symmetry, respectively. The electronic band energies observed for these complexes, are very close to those of the $[CoX_4]^{2-}$ anions, reported previously [12].

In the reflectance spectra of $[Co(HMBA)_3][CoBr_4]$, a band appears around 7500 cm^{-1} , which can easily be assigned to the ν_1 transition (${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$) of an octahedral $[Co(HMBA)_3]^{2+}$ chromophore. The ν_3 transition (${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$), in octahedral cobalt(II) complexes appears around 20000 cm^{-1} . In the chloride complex this band appears at 19100 cm^{-1} , but in the bromide complex it is difficult to assign the exact position of this band, due to the admixture of spin forbidden transitions to doublet states.

Like their electronic spectra, the observed values of magnetic moments for the complexes $[Co(HMBA)_3][CoCl_4]$ and $[Co(HMBA)_3][CoBr_4]$ (Table-2), also support the same conclusion i.e. the mixed octahedral-tetrahedral structures for both of these complexes. These values are nearly equal to the root-mean-square of the magnetic moments expected for the individual species.

Experimental

Preparation of complexes

All the chemicals were of the reagent grade and were used without further purification.

Hexamethylene bisacetamide (HMBA)

This compound was prepared by the method used previously [1]. Found %; C, 59.53; H, 10.45; N, 14.23. Calculated for HMBA %: C, 60.00; H, 10.00; N, 14.00.

$[M(HMBA)_3][MX_4]$ ($M=Mn$ and Co ; $X=Cl$ or Br)

All these complexes were synthesized by dehydrating the corresponding metal(II) halide (1 m. mole) in a mixture of ethanol (6 cm^3) and 2,2-dimethoxy propane (4 cm^3) and adding into it a warm solution of HMBA (3 m. mole) in ethylacetate (30 cm^3). The precipitates thus formed were filtered off, washed with ethylacetate and dried in vacuo. Found %:- C, 42.26; H, 7.02; N, 9.79. Calculated for $[Mn(HMBA)_3][MnCl_4]$ %:- C, 42.26; H, 7.04; N, 9.86. Found %:- C, 35.25; H, 5.88; N, 8.22.

Calculated for $[Mn(HMBA)_3][MnBr_4]$ %:- C, 34.96; H, 5.83; N, 8.16. Found %:- C, 41.69; H, 6.97; N, 9.66. Calculated for $[Co(HMBA)_3][CoCl_4]$ %:- C, 41.87; H, 6.98; N, 9.77. Found %:- C, 35.17; H, 5.96; N, 8.13. Calculated for $[Co(HMBA)_3][CoBr_4]$ %:- C, 34.69; H, 5.78; N, 8.09.

Analytical results were obtained by Imperial College Microanalytical Laboratory

Diffuse reflectance spectra of the powder samples, over the range $4000\text{--}18500\text{ cm}^{-1}$, were obtained on Beckman DK 2 spectrometer and for the range $12000\text{--}30000\text{ cm}^{-1}$ on a Pye Unicam SP8-100 spectrometer.

Magnetic susceptibilities of the powder samples were measured at room temperature using the Evans Balance and were then corrected for diamagnetism to provide fully corrected molar susceptibilities χ_M .

E.s.r. spectra were obtained as described previously [13], using polycrystalline samples at room temperatures.

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