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SYNTHESIS, CHARACTERIZATION AND DNA BINDING STUDIES OF A TUNGSTEN COMPLEX WITH SODIUM (N,N-DIMETHYL) DITHIOCARBAMATE

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ABSTRACT
Dithiocarbamates are versatile ligands with a wide range of chemistry. Coordinating this ligand with Tungsten metal produces complex with enhanced biological properties and this can be a basis for novel compounds. The Synthesized Tungsten complex was characterized by Infrared, Electronic and NMR spectroscopy. The interaction of the complex with calf Thymus DNA (CT-DNA) was studied by using Electronic absorption Titration Spectroscopy, Thermal denaturation and viscometry studies. The result suggest that the Tungsten complex intercalates into DNA base pairs Via the ligand dithiocarbamate.

KEYWORDS: Dithiocarbamate, Tungsten complex, DNA binding.

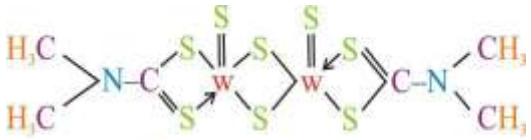
INTRODUCTION
Dithiocarbamates are a class of sulfur based metal chelating compounds with Various applications. The Chemistry of dithiocarbamates transition metal complexes has received considerable attention largely due to their catalytic and bioinorganic relevance. Such complexes are also important due to their potential biological activities such a. Antibacterial, Antifungal, Antimalerial and Antitumor activity. The Ligand which is strong complexing agent which forms Bridging complex with Tungsten. Studies on the interaction of transition metal complex with Nucleic acid have gained prominence[1-7] because of their relevance in the development of new reagents for biotechnology and medicine. FTIR and Electronic spectra were recorded on ThermoNicolet Avatar 370 with KBr discs and varian carry 5000 UV-VISIBLE-NIR spectrophotometer respectively.

NMR spectra was recorded on Bruker Avance 111,400 MHz spectrometer. The conductance measurement was carried out in a Toshniwal CL-01-06 conductivity Bridge using 1×10^{-3}M Dimethyl Formamide solution. C,H, N,S were analyzed on Elementar vario EL111 and the DNA concentration per nucleotide was determined by absosption spectroscopy using moalr absorption coefficient 6600 M^{-1} Cm^{-1} at 260 nm [8]. The Complex was dissolved in a solvent mixture of 1% DMSO and 99% Tris-HCl buffer (5mm Tris HCl; 50 mm NaCl, PH 7.1) viscosity measurements were carried out using a schott AVS 310 viscometer maintained at a constant temperature at 25.0 ± 0.1^0C in a Thermostatic bath. Thermal denaturation studies were carried out with an Elico Bio-spectrophotometer model BL 198, equipped with temperature controlling programmer (±0.1^0C).

The ligand N,N-dimethyl dithiocarbamate was synthesized by standared procedure.[9] The complex was prepared in high yield from a reaction of Ammonium tetrathiotungstate (0.340g, 1m-mol) in double distilled water (30ml) with sodium N,N-dimethyl dithiocarbamate ligand (0.140g, 1m-mol) under stirring and refluxing for 1 h at 70^0C. The light yellow precipitate obtained on cooling was filtered, washed with alcohol followed by ether, then dried in Vacuo over $CaCl_2$.yield: 0.047g (87%). IR (KBr disc): 1500 (C⁻⁻⁻N), 1039 (C⁻⁻⁻S), 494 $(W\text{-}S)_t$, 444 $(W\text{-}S)_b$ and 343 (W-S-W) Cm^{-1}. Elemental analysis: Calc: W, 50.0, C, 9.78, H, 1.63, N, 3.80, S, 34.78. Found: W, 49.42, C, 9.50, H, 1.56, N, 3.50, S, 34.40. That the conductance value is 25.4 Ω^{-1} Cm^2 mol^{-1} in DMF (N,N-dimethyl-formamide) implies that the complex has non electrolytic nature. ^{1}H NMR [400 MHz; Solvent $(CD_3)_2SO$)] of the complex contains a sharp singlet, corresponding to three protons, in the region 3.64 ppm, ascribed to methyl linked directly with N atom contained in dithiocarbamate. A down field by δ=0.4 ppm as compared to the chemical shift of dimethyl dithiocarbamate (observed in the region δ=3.26)[10] is observed. The difference could be due to the effect of the electronegativity of nitrogen atom compared to alkyl. Carbon.[11] It is shown that the coordinated dithiocarbamate group is more electronegative than in the case where there is no coordination.[12] ^{13}C NMR spectra of the complex exhibit weak singal in the region 198.6 ppm assign to NCS_2 carbon atom of the

dithiocarbamate moiety. Signal observed at 45.2 ppm for Tungsten complex corresponding to methyl carbon attached to the nitrogen atom on complexation, the electron density on -NH decreases, the processional frequency of proton bonded to Nitrogen increases, hence the signal was shifted to down field region.

The complex is soluble in DMF and DMSO (dimethyl-Sulphoxide) but insoluble in water. The water soluble ligand dithiocarbamate shows two bands one in the UV region 40000 cm^{-1} which is associated with polarization of nitrogen conjugation and the other slightly more intense at about 34482 cm^{-1} is associated with sulfur conjugation. These bands are assigned to the intramolecular intra ligand transitions corresponding to π-π* of the N-C=S System, π-π* of the S-C=S group. The intra ligand π-π* Transition of the S-C=S group generally appears as a shoulder band associated with non equivalence of the C=S band of the ligand. This band tends to disappear in the case of Tungsten complex showing thereby that the dithiocarbamate ligand S-S bonded to metal ion. The complex displayed two bands associated with ligand molecule. The strong band at 23000 cm^{-1} is assigned to charge transfer transition of sulfur to Tungsten (S→W). The complex displayed d-d transition bands in the region 14780 cm^{-1} and 12475 cm^{-1} respectively. These bands are attributed to $3_E \rightarrow {}_1A^1$ and $1_E \rightarrow 1A^1$ transition which indicate the presence of dithiocarbamate bound to tungsten (V).



Tungsten Complex

Electronic absorption spectroscopy serves as the most common means to study the interaction between metal complex and DNA.[13] A complex binds to DNA hypochromism and bathochromism, due to intercalation mode involving a strong stacking interaction between the electronic state of the intercalating chromophore and the base pairs of DNA. It is evident after careful analysis of literature reports that a large bathochromic shift (15-20 nm) and a high percentage of hypochromicity of the UV/VIS soret band is an indication of ligand interclalation with DNA. The extent of hypochromicity is directly proportional to the strength of ligand intercalation which also emphasizes its strong intercalative mode of interaction with DNA. The absorption spectra of complex in the absence and presence of CT DNA are depicted in Fig.1 The binding constant was determined using $(DNA)/(\varepsilon_A-\varepsilon_F) = (DNA)/(\varepsilon_B-\varepsilon_F) + 1/K_b$ ($\varepsilon_A-\varepsilon_F$) where

(DNA) is the total concentration of base pairs. ε_A, ε_F, and ε_B correspond to the extinction coefficients for the absolutely bound Tungsten complex, free Tungsten complex and the actually bound Tungsten complex, respectively. A plot of (DNA)/($\varepsilon_A-\varepsilon_F$) Vs. (DNA), give K_b as the ratio of the slope to the intercept. From the plot of (DNA)/($\varepsilon_A-\varepsilon_F$) Vs. (DNA), the intrinsic binding constant of the complex $W_2(C_6H_{12}N_2S_8)$ with DNA was calculated to be $4.01\times10^4 M^{-1}$. The binding constant indicate that Tungsten complex binds DNA more strongly.

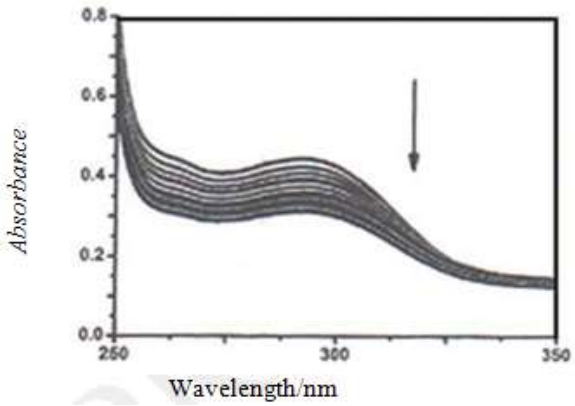


Fig. 1 Absorption spectra of tungsten complex in the absence or presence of increasing amounts of CT-DNA. Arrow indicates the change in absorbance upon increasing the concentration of CT-DNA.

For further establishment of the interaction between the complex and DNA, Viscosity measurement was carried out. The hydrodynamic measurements that are sensitive to length change (Viscosity and sedimentation) are regarded as the least ambiguous and the most critical test of binding in solution in the absence of crystallographic structural data. A classical intercalation model demands that the DNA helix must lengthen as base pairs are separated to accommodate the binding ligand which leading to the increase of DNA viscosity. The effects of W(V) complex on the viscosity of DNA are depicted in Fig.2. The relative viscosity of DNA increase with increasing in the concentration of the W(V) complex which suggests that the complex can bind to DNA by the classical intercalation.

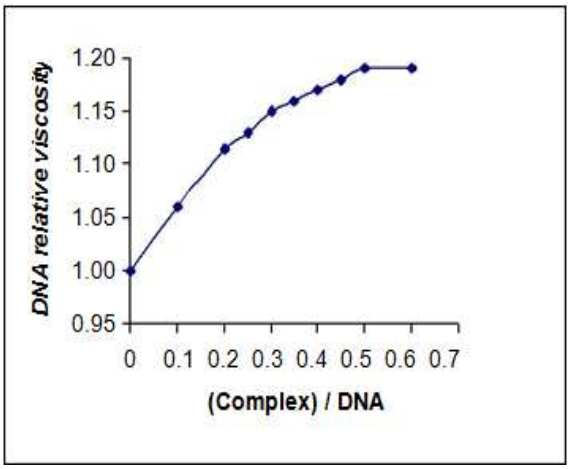


Fig. 2 The effect of the complex on the relative viscosity of DNA

Other strong evidence in support of the about interaction comes from thermal denaturation measurement. Interaction of small molecules into nucleic base pairs can stabilize the double helix, increasing the melting point of DNA [15]. The increase in the melting temperature lends strong support for the intercalation of Tungsten complex into the helix.

The present complex and CT DNA alone were incubated with CT DNA, their temperatures raised from 25 to 95^0C and the absorbance of the solution at 260 nm was monitored the melting curve of CT DNA alone and that of CT DNA in the presence of complex are depicted in Fig. 3 The intercalation of small molecules into the double helix is known to significantly increase the helix melting temperature at which the double helix denatures into single stranded DNA. The extinction coefficient of DNA bases at 260 nm in the double helical form is much less than that in the single stranded form hence the melting of the helix leads to an increase in the absorption at this wavelength. Thus the helical to coil transition temperature can be determined by monitoring the absobance of DNA bases at 260 nm as a function of temperature (T_m) However the T_m will increase slightly when interaction of small molecules with DNA through non specific electrostatic interactions with the phosphate backbone of DNA occurs. CT DNA was seen to melt at 65^0C in the absence of complex. Whereas in the presence of complex the melting temp (T_m) was found to be 70^0C. This observed behaviour in that expected for an intercalative binding mode.

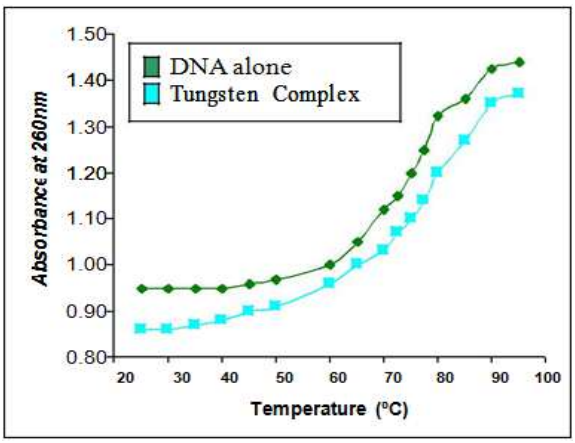


Fig. 3 The melting curves of CT-DNA at 260 nm in the absence and presence of Tungsten complex.

REFERENCES

1. J. Patole, S. Dutta, S. Padhye, E. Sinn, Inorg. Chim, Acta, 2001; 318: 207.
2. M.B. Hursthouse, M.A. Malik, M. Motevalli, Polyhedron, 1992; 11: 45-48.
3. J. Stary, K. Kratzer, J. Radioanal. Nucl. Chem. Lett, 1992; 165: 137-143.
4. A.R. Cowly, J.R. Dilworth, P.S. Donnely, E. Labisbal, A. Sousa, J. Am. Chem. Soc., 2002; 124: 1713.
5. E.M. Jouad, X.D. Thanh, G. Bouet, S. Bonneau, M.A. Khan, Anticancer Res, 2002; 22: 1713.
6. V.G. Vaidyanathan, U.N. Balachandran, J. Inorg. Biochem, 2002; 91; 405-412.
7. J.G. Liv, B.H. Ye, H.Li, Q.X. Zhen, L.N.Ji, Y.H. Fu, J. Inorg. Biochem, 1999; 76: 265-271.
8. M.F. Reichmann, S.A. Rice, C.A. Thomas, P. Doty, J. Am. Chem. Soc, 1954; 76: 3047.
9. M. Delepine, Bull. Soc. Chem. France, 1908; 3: 643.
10. P.C. Riveros, I.C. Perilla, A. Poveda, H.J. Keller, H. Pritzkow, Polyhedron, 2000; 19: 2327-2335
11. B.A. Prakasam, K. Ramalingam, G. Bocelli, A. Cantoni, Polyhedron, 2007; 26: 4489-4493.
12. H.D. Yin, J. Zhai, Y.Y. Sun, D.Q. Wang, Polyhedron, 2008; 27: 663-670.
13. T.M. Kelly, A.B. Tussi, D.J. Mccuonell, T.C. Strekas, Nucleic Acid Res., 1985; 13: 6017.
14. Wolfe, G.H. Shimer, T. Meehan, Biochemistry, 1987; 26: 6392-6396.
15. D.J. Patel, Acc. Chem. Res, 1979; 12: 118.