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Copper(II) Complexes of 2-Thiocytosine and 2,4-Dithiouracil

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The interventions of metal ions like copper(II) with nucleic acid bases and their derivatives has attracted attention in recent years [1]. As part of our efforts to systematically elucidate the chemical properties of copper(II) complexes of nucleic acid constituents in the solid state [2], we recently reported the synthesis, IR spectra, and chelation of some copper(II) coordination compounds with 5X-uracil and 6X, 2-thiouracil [3]. Since 2-thiouracil is known to have chemotherapeutic activity, by virtue of its ready incorporation into nucleic acids [4], we decided to extend our investigation to other sulfur containing pyrimidine bases analogous to 2-thiouracil. In this paper we wish to report the synthesis, and electronic and magnetic properties of three novel copper(II) complexes with 2-thiocytosine and 2,4-dithiouracil (Fig. 1).

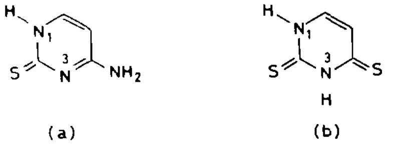

Fig. 1. Structures and numbering schemes for (a) 2-thiocytosine and (b) 2,4-dithiouracil.

Experimental

Measurements

All materials and methods used in the collection of physical data were the same as those described previously [2]. Complete tabulations of the IR, electronic, EPR, and magnetic susceptibility data as well as a listing of the FORTRAN IV program LIGFIT used in fitting stoichiometries to analytical data can be found elsewhere [5].

Synthesis of Cu(2-thiocytosine)Cl$_2$

Dropwise addition of 4 ml of a methanol solution containing 0.0229 g (0.134 mmol) of $CuCl_2 \cdot 2H_2O$ to 20 ml of a methanol solution containing 0.0175 g (0.138 mmol) of 2-thiocytosine at 63 °C yielded a fluffy, light yellow mixture that was heated for 5 minutes, cooled to room temperature, filtered, washed with methanol, and oven-dried at 90 °C to a green-brown powder. *Anal.* Calcd for $CuC_4H_5N_3S_1Cl_2$: C, 18.36; H, 1.93, N, 16.07. Found: C, 17.94; H, 2.12; N, 16.75%.

Synthesis of Cu(2-thiocytosine)$_4$Cl$_2$·4H$_2$O

An acidic solution of 2-thiocytosine, prepared by addition of 0.3138 g (2.5 mmol) of ligand to 20 ml of distilled water at 65 °C containing 25 drops of 10% HCl solution, was added in small increments with constant stirring to 5 ml of a 0.25 *M* $Cu(Ac)_2 \cdot H_2O$ solution (1.25 mmol). The resulting yellow-green, viscous mixture, which developed from an initial black colored solution, was allowed to heat 15 minutes. After cooling in an ice-bath, the orange-yellow, gel-like mixture was filtered, washed with water, and oven-dried. The color changed from orange to brown after 2 days storage over P_2O_5. *Anal.* Calcd for $CuC_{16}H_{28}N_{12}O_4S_4Cl_2$: C, 26.88; H, 3.95; N, 23.52. Found: C, 26.47; H, 3.06; N, 23.78%.

Synthesis of Cu(2,4-dithiouracil)(OH)·H$_2$O

A solution of 1 mmol of $Cu(NO_3)_2 \cdot 3H_2O$ in 4 ml of distilled water was added quickly with stirring to a basic, saturated solution of 2,4-dithiouracil, prepared from a mixture of 0.1635 g (1 mmol) of ligand in 80 ml of water at 65 °C containing 20 drops of 10% NaOH solution. An immediate green-brown mixture developed that was heated for 15 minutes. During this time the mixture turned yellow-brown and then to its final orange color at which time it was filtered, washed with copious amounts of water, and oven-dried at 85 °C. *Anal.* Calcd for $CuC_6H_4N_2O_2S_2$: C, 19.88; H, 2.50; N, 11.60. Found: C, 19.22; H, 1.56; N, 11.84%.

Results and Discussion

Cu(2,4-dithiouracil)(OH)·H$_2$O

The change in the IR spectrum upon going from free to complexed ligand is dramatic upon coordination. Thioamide bands III and IV at 1126 and 791 cm^{-1}, respectively, which contain major contributions from the C(2)=S and C(4)=S stretches [6], change position and intensity and suggest simultaneous involvement of C(2)S and C(4)S. The N(3)H bend at 1412 cm^{-1} disappears and points to N(3) deprotonation with concomitant coordination. The

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utilization of three ring sites might be anticipated for a polymeric complex and both the magnetic properties (*vide infra*) as well as the limited solubility properties in common inorganic and organic solvents support this contention.

The d–d transition maximum at 11.4 kK (1 kK = 1000 cm^{-1}) for the complex suggests a geometry of approximate C_{2v} microsymmetry around the copper(II) ion which is distinctly different from that found in a series of Cu(II)–5X-uracil complexes [7] where a tetragonally distorted octahedral microsymmetry predominates. Presumably, the large size of the sulfur atoms induces a symmetry low enough to allow d–d transitions from the $^2A_1$ ground state to either the $^2B_1$ or $^2B_2$ excited states [8]. Indeed, the electronic absorption is very broad and may consist of two overlapping semi-degenerate transitions which might be resolved only at temperatures below 20 K. Also, although the low energy d–d maximum is consistent with changes in site symmetry about copper(II) approaching tetrahedral or trigonal bipyramidal microsymmetries [8], EPR data preclude these geometries [9] as $g_z > g_{xy}$ (*i.e.*, 2.21 *vs.* 2.07, respectively).

The variable temperature bulk magnetic susceptibility data were fitted to the Ising model for antiferromagnetically coupled straight chain polymers [10] yielding theoretical best fit values for g_{av} and $-2J$, the exchange parameter, of 2.02 and 700 cm^{-1}, respectively. The 9% monomer correction used in the fitting procedure implies an average chain length of 22 metal ions (molecular formulas) [7] and indicates a more extensively polymerized and spin-coupled system when contrasted to the Cu(II)–5X-uracil complexes [7].

The EPR data for the complex support the magnetic interactions previously discussed as a weak half-field (H_{MIN}) transition at 1580 G and weak full-field transitions at 1700 and 5100 G originating in spin-coupled species [2, 7] are observed. No evidence for additional resonances was found at 77 K. These data, together with the results of the electronic, IR, and variable temperature magnetic susceptibility measurements, suggest a structure as shown in Fig. 2.

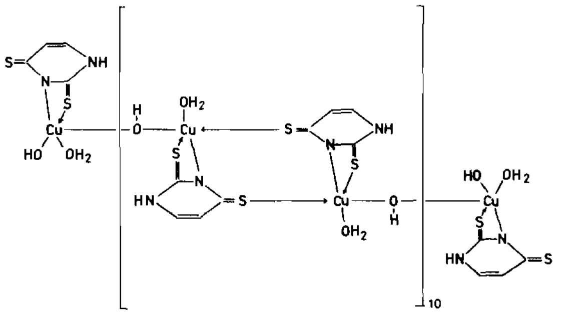

Fig. 2. Proposed structure for Cu(2,4-dithiouracil)(OH)·H_2O.

Cu(2-thiocytosine)Cl_2 and Cu(2-thiocytosine)$_4Cl_2$·4H_2O

The 2-thiocytosine ligand coordinates similarly in both complexes. The severe reduction in thioamide bands I and II [5] at approximately 1230 and 800 cm^{-1}, respectively, points to C(2)S coordination; simultaneous ring coordination at N(3) is also consistent with these data. Involvement of N(1) or C(4)NH_2 in coordination is ruled out in both complexes by the presence of the weak N(1)H bend at approximately 1543 cm^{-1}, and the presence of the NH_2 bend and NH_2 stretch (out-of-plane) at 1650 and 3333 cm^{-1}, respectively, of the C(4)NH_2 group.

The electronic spectra of the two complexes exhibit broad structureless absorptions (kK) at 16.4 (Cu(L)Cl_2) and 15.2 (Cu(L)$_4Cl_2$·4H_2O), where L = 2-thiocytosine. The absorption maxima are consistent with tetragonally distorted octahedral geometries about copper(II) of approximate D_{4h} microsymmetry [8] and can be assigned to the transition from the $^2B_{1g}$ ground state to the ^2E_g excited state. The lower d–d maximum of the Cu(L)$_4Cl_2$·4H_2O complex as compared to the Cu(L)Cl_2 complex suggests that imposing four bulky 2-thiocytosine ligands about the copper(II) ion induces distortions away from a D_{4h} towards a C_{2v} microsymmetry with a concomitant lowering in energy of the d–d band maximum [8].

The effective magnetic moments for both complexes were low at room temperature (*ca.* 0.6 BM). Consequently, variable temperature magnetic susceptibility measurements were not performed below room temperature since these data would not yield useful information. In both cases, only magnetic susceptibility data above room temperature were collected. Little change in molar susceptibility over a large temperature range was noted for both complexes indicative of very strong antiferromagnetic coupling between copper(II) centers with effective magnetic moments due almost entirely to small amounts of monomeric impurities that are always present and difficult to remove. A theoretical best fit of the experimental data to various magnetic models (dimer, trimer, polymer, *etc.*) was difficult because small changes in g-values and/or percent monomer impurity corrections led to drastic changes in the molar susceptibilities. In addition, since the absolute values of the molar susceptibilities were small a high degree of accuracy in the fitting procedures was difficult to obtain. Our calculations, therefore, were restricted to determining lower limits of the exchange interaction parameter, $-2J$, in both complexes. Theoretical best fits to the antiferromagnetically exchanged-coupled dimer expression [11] gave values for $-2J$ and g_{av} of 1400 ± 200 cm^{-1} and 2.05, and 1400 ± 200 cm^{-1} and 2.06 for the Cu(L)Cl_2 and Cu(L)$_4Cl_2$·4H_2O complexes, respectively.

The EPR data for the 2-thiocytosine complexes are in harmony with the variable temperature magnetic susceptibility data previously discussed and support magnetic interactions originating in spin-coupled species as weak, half-field H_{MIN} (spin forbidden) [2, 7] transitions at 1500 and 1475 G as well as full-field transitions at 1600 and 5100 G, and 5060 G for the $Cu(L)Cl_2$ and $Cu(L)_4Cl_2 \cdot H_2O$ complexes, respectively, are observed. Broad structureless monomer absorptions appear in both complexes having identical g-values of 2.11. No additional absorptions were noted at 77 K. Attempts to grow single crystals of each of the three complexes suitable for X-ray study proved unsuccessful.

Summary

The principal conclusions that can be drawn from this work are: (*1*) The formation of highly strained four-membered chelate rings involving adjacent sulfur and nitrogen atoms on the pyrimidine moiety is preferred over monodentate coordination. These conclusions are supported by the recent structural work of Goodgame *et al.* on a number of metal complexes containing dimethyl- and trimethylsubstituted pyrimidine-2-thione [12, 13]. Similar bonding modes involving four-membered chelate rings were found in a series of copper(II) complexes of 5X-uracil (X = H, NO_2, and I) [3]. (*2*) Although the replacement of oxygen by sulfur at C(2) in uracil is associated with a change in the chelation sites from N(1)/C(2)O to N(3)/C(2)S in their respective copper(II) complexes [3], the data presented here suggest no such change in the chelation sites of cytosine when oxygen is replaced by sulfur in their respective complexes [14, 15]. (*3*) Replacement of oxygen at C(2) in cytosine induces the complexed copper(II) centers to: (a) undergo strong spin–spin coupling of an antiferromagnetic nature with $-2J \geqslant 1400 \pm 200\ cm^{-1}$ which represents the largest value of spin exchange of its kind reported to date in copper(II) complexes, and (b) distort from approximate pseudo-octahedral geometries towards C_{2v} or T_d microsymmetries.

Acknowledgement

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