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Properties of Metal Complexes in the Interphase of an Oil Continuous Microemulsion. 2. Interaction of Copper(II) with the Side Chains of Lysine, Glutamine, and Methionine[1]

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Complexes of Cu(II) and the side chains of N^{α}-dodecanoyl-L-lysinol, N^{α}-dodecanoyl-L-glutaminol, and *N*-dodecanoyl-L-methioninol were investigated in the interfacial domain of an oil continuous microemulsion. The microemulsion consisted of water solubilized in a hexane continuous phase by hexadecyltrimethylammonium perchlorate and 2-propanol. Potentiometry and/or absorption and electron paramagnetic resonance spectroscopy were used to determine the nature of the complexes. In the Cu(II)/N^{α}-dodecanoyl-L-lysinol system, the limit species is a CuL_4^{2+} complex in which four ϵ-amino groups are bound to Cu(II) in a square-planar geometry. The calculated formation constants are log K_1 = 6.13, log K_2 = 5.66, log K_3 = 4.97, and log K_4 = 3.93. The measured values for $g_{\parallel}$, $A_{\parallel}$, $g_{\perp}$, and $A_{\perp}$ are respectively 2.25, 170 G, 2.07, and 15 G. The side chains of glutamine and methionine contain functional groups which are very weak ligands for Cu(II). These two side chains were "forced" to interact with Cu(II) by significantly decreasing the amount of water in the microemulsion. In the Cu(II)/N^{α}-dodecanoyl-L-glutaminol system, the limit species is a CuL^{2+} complex (log K = 0.23), for which $g_{\parallel}$ = 2.36 and $A_{\parallel}$ = 140 G. The carbonyl oxygen of the amido group is believed to be the ligand site. CuL^{2+} and CuL_2^{2+} complexes were observed in the Cu(II)/*N*-dodecanoyl-L-methioninol system, but a limit species was not identified.

Introduction

The influence of surfactant systems on chemical phenomena has been a subject of considerable investigation in recent years. To date, surfactant solutions containing micelles[4] or inverse micelles[5] have been used most commonly for these studies. We recently initiated a project which employs a different kind of surfactant solution, namely, an oil continuous microemulsion.[6,7a] A primary objective of this research is to determine the effect, if any, of an interfacial environment on transition metal complexes. We are presently investigating the interaction of transition metals with the side chains of certain amino acids. Both the metal and the ligand are microencapsulated in the aqueous droplets of the dispersed phase. The ligand is introduced into the system as a surface-active derivative, an N^{α}-dodecanoyl amino alcohol, and, consequently, the side chains (and their metal complexes) are located within the interfacial domain of the droplet. This system is potentially suitable for characterizing complicated metal–ligand interactions, such as those which occur in metalloproteins and other complexes of biological interest.

Recently, a few investigators have studied systems in which metal complexes were incorporated into inverse micelles. Fendler and his co-workers have studied systems of this type.[5] In addition, Klein and Miller have investigated the tetrachlorocuprate(II) complex, and Kitahara et al., a Mn(II)-surfactant complex in such a system.[7b]

This paper describes the interaction of Cu(II) with N^{α}-dodecanoyl-L-lysinol, N^{α}-dodecanoyl-L-glutaminol, and N^{α}-dodecanoyl-L-methioninol. The host system is a hexane continuous microemulsion stabilized by hexadecyltrimethylammonium perchlorate and 2-propanol. Of particular interest is our observation that the metal can be "forced" to interact with very weak ligands by making certain adjustments in the composition of the microemulsion.

Experimental Section

Materials. All organic solvents were reagent grade. Amino acids were purchased from Sigma and the other chemicals from Aldrich. Water was twice-distilled with a Pyrex still. Hexadecyltrimethylammonium perchlorate and β-hydroxyethyl dodecanoate were prepared as previously described.[6] The N^{α}-dodecanoyl derivatives of L-lysinol, L-glutaminol, L-methioninol, and glycinol were synthesized following the general procedure previously outlined for the synthesis of N^{α}-dodecanoyl-L-histidinol.[6] Relevant modifications on the general procedure are described below for the pertinent derivatives.

In the synthesis of N^{α}-dodecanoyl-L-glutaminol the reaction times for the acylation and reduction steps were relatively short (~60 min). This procedure avoided the formation of significant amounts of undesirable side products, but the overall yield (8%) was significantly decreased.

The synthesis of N^{α}-dodecanoyl-L-lysinol was quite tedious, since the ϵ amino group had to be blocked while the α amino group was acylated.[8] The Cu(II) complex of 25 g (0.137 mol) of L-lysine monohydrochloride was prepared by the procedure of Kjaer and Larsen.[9] Subsequently, 12.9 g (0.137 mol) of freshly distilled benzaldehyde and 11 g (0.27 mol) of NaOH were added to the reaction mixture, which was then stirred vigorously for 30 min at 0 °C.[10] The ϵ Schiff base formed as a pale blue precipitate. The precipitate was dispersed in water, and thioacetamide (10.3 g, 0.137 mol) was added, the mixture was heated to boiling, and CuS was removed by filtration. The solution of N^{ϵ}-benzylidene-L-lysine was treated with dodecanoyl

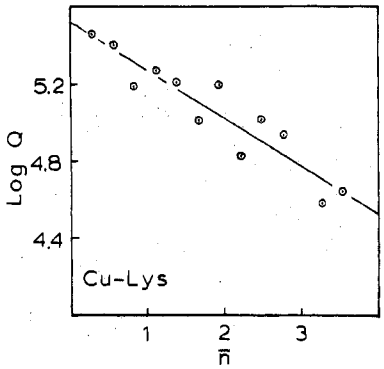

Figure 1. A Scatchard plot for the titration of microemulsified N^{α}-dodecanoyl-L-lysinol and Cu(II). To ensure that the composition of the microemulsion remained constant throughout the experiment, a separate microemulsion was prepared for each point on the titration curve. The volume of water plus the volume of 0.05 M NaOH was 2.0 ml in each microemulsion. The Scatchard plot was constructed as described in ref 12. See the Experimental Section and Results for other details.

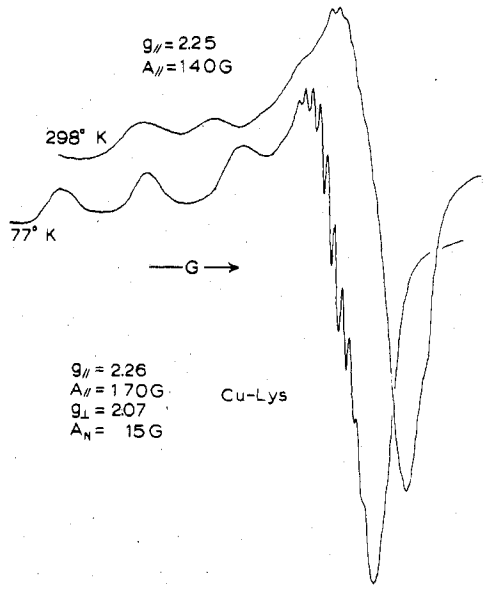

Figure 2. Electron paramagnetic resonance spectra of Cu(II) in microemulsions containing N^{α}-dodecanoyl-L-lysinol. The top spectrum was obtained at room temperature; the bottom spectrum, at liquid nitrogen temperature. A 10:1 mole ratio of ligand to metal was present in each case. The appropriate parameters are tabulated on the figure.

chloride as previously described.[6] The blocking group was removed from the ε amino group by boiling the Schiff base in HCl (pH 2) for 15 min. The ε-(ammonium perchlorate) salt of N^{α}-dodecanoyl-L-lysinol was formed by neutralizing 2-propanol solutions of the free base with a solution of anhydrous $HClO_4$ in 2-propanol.

The purification of the N-acylated amino alcohols was accomplished by extraction of fatty acids with petroleum ether and precipitation of the residue from aqueous solutions. The approximate pH of minimum solubility in water was determined for each N-acylated amino alcohol: lysinol derivative, 10.0; glutaminol derivative, 2.0–3.0; glycinol derivative, 2.0–3.0; methioninol derivative, 2.0–3.0. At other pH's tested, the molecules formed gels which were virtually impossible to filter, or they were relatively soluble. The purity of the various products was confirmed by thin-layer chromatography on silica gel G. The R_f's of the compounds on plates developed with chloroform–methanol (9:1 v/v) are as follows: lysinol derivative, 0.80; glutaminol derivative, 0.91; glycinol derivative, 0.94; methioninol derivative, 0.88. The identity of the products was confirmed by IR and NMR spectroscopy.

Methods. Hexane continuous microemulsions were prepared as previously described.[6] The compositions of the different microemulsions used in the present studies are given in the relevant portions of the Results. These compositions were shown to be microemulsions by an ultracentrifugation procedure.[11]

The equipment and procedures used for obtaining potentiometric measurements, electron paramagnetic resonance spectra, and optical spectra were previously described.[6]

Results

A. The Cu(II)/N^{α}-Dodecanoyl-L-lysinol System. The interaction of Cu(II) and N^{α}-dodecanoyl-L-lysinol was studied in a microemulsion composed of 10 ml of hexane, 2 ml of water, 100 mg of hexadecyltrimethylammonium perchlorate, and 10.4 ml of 2-propanol.

Potentiometry. An apparent pK_a of 9.3 was measured for the ε amino group of N^{α}-dodecanoyl-L-lysinol in the microemulsion by titration of the ε ammonium salt (8.0×10^{-5} mol) with NaOH. For determination of formation constants by the method of Edsall et al.,[12] 8.0×10^{-6} mol of $Cu(ClO_4)_2 \cdot 6H_2O$ was added to a microemulsion containing 8.0×10^{-5} mol of the ε ammonium salt. The system was again titrated with NaOH. The average number of amino groups bound to each Cu(II) atom was found to be 4 from a plot of the formation function described by Bjerrum.[13] Thus, the limit complex appears to be the CuL_4^{2+} species. Values for the formation constants were determined with the aid of a Scatchard plot (Figure 1). The calculated values are $\log K_1 = 6.13$, $\log K_2 = 5.66$, $\log K_3 = 4.97$, and $\log K_4 = 3.93$.

Electron Paramagnetic Resonance. In EPR studies at 77 K, a limiting line shape was not obtained until the mole ratio of N^{α}-dodecanoyl-L-lysinol to Cu(II) was 10:1. The limit spectrum is shown in Figure 2. The Cu(II) nuclear hyperfine signal at liquid nitrogen temperature (the 77 K spectrum in Figure 2) indicates that only one species is present, $g_{\parallel} = 2.25$ and $A_{\parallel} = 170$ G. Also, this spectrum exhibits a clearly defined superhyperfine splitting of nine lines on the perpendicular signal. This pattern can be attributed to a complex with four nitrogen atoms tightly bound to Cu(II).[14] It is possible to calculate a $g_{\perp}$ value of 2.07 for this complex and a superhyperfine splitting of 15 G.[15,16] These results are not only in agreement with the stoichiometric results of the potentiometric measurements but are also indicative of square-planar geometry for the complex.

The spectrum at room temperature for a microemulsion containing a 10:1 mole ratio of ligand to metal is also shown in Figure 2. Both the hyperfine and superhyperfine patterns are evident in this spectrum. In comparison, the superhyperfine features were not evident in room-temperature spectra of complexes present in pure alcohols, e.g., 2-propanol, although hyperfine features were evident.

Absorption Spectroscopy. Microemulsions of the type examined by EPR were also investigated by optical spectroscopy. In these studies a microemulsion without metal or ligand was used as a reference. The difference spectra in Figure 3 show the characteristic d–d transition of Cu(II) complexes. The curve marked "Cu" in this figure is the spectrum of aquated Cu(II). As the mole ratio of ligand to metal is raised, the field strength and the intensity both increase. The limit spectrum is obtained at a mole ratio of 8:1.

B. The Cu(II)/N^{α}-Dodecanoyl-L-glutaminol System. The amido group in N^{α}-dodecanoyl-L-glutaminol is a much weaker ligand for Cu(II) than the amino group of lysine or the imidazole group of histidine. Therefore, the interaction of Cu(II) with the glutamine derivative was investigated in microemulsions which contained a substantially reduced volume of water. Decreasing the amount of water altered the physical nature of the microemulsion in a manner which was beneficial for studying the interaction of Cu(II) with weak ligands.[7a] In the first place, the volume of interphase in the system was significantly reduced. Since the amount of ligand added to the system was not changed, the effective concentration of ligand in the interphase was considerably increased. Second,

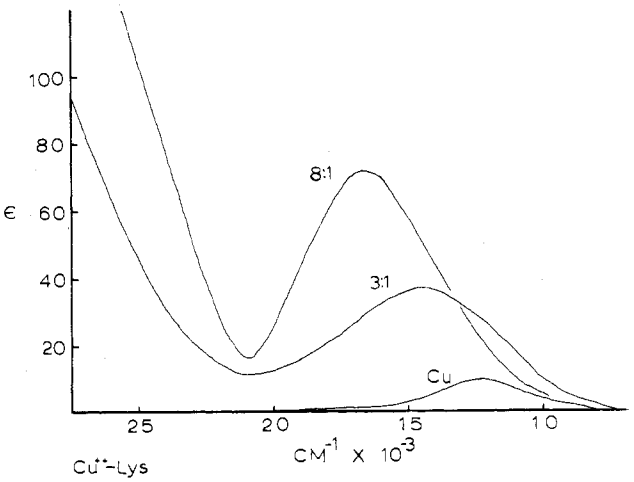

Figure 3. Absorption spectra showing the d–d transition of Cu(II) in microemulsions with and without N^{α}-dodecanoyl-L-lysinol. Compositions of the respective microemulsions: Cu, 77 μmol of $Cu(ClO_4)_2 \cdot 6H_2O$; 3:1, plus 230 μmol of N^{α}-dodecanoyl-L-lysinol; 8:1, plus 620 μmol of N^{α}-dodecanoyl-L-lysinol. Molar absorptivities are based on the concentration of Cu(II), 3.45×10^{-3} M.

the ratio of the interphase volume to the core volume (i.e., "bulk" water volume) in a dispersed water-rich droplet was significantly increased. Or, in other words, the ratio of surface area to volume of a droplet was increased. Consequently, modifying the composition of the microemulsion had the effect of forcing Cu(II) to interact with weak ligands present in the interphase portion of the droplets.

The microemulsion used to investigate the interaction of N^{α}-dodecanoyl-L-glutaminol with Cu(II) was composed of 10 ml of hexane, 0.3 ml of water, 30 mg of hexadecyltrimethylammonium perchlorate, and 3.6 ml of 2-propanol.

Electron Paramagnetic Resonance Spectroscopy and Potentiometry. The EPR spectra of Cu(II) complexes in the modified microemulsion are shown in Figure 4. The bottom spectrum, labeled "Cu", was obtained at 77 K for a microemulsion containing Cu(II) but no N^{α}-dodecanoyl-L-glutaminol. The signal indicated by pattern a is from aquated Cu(II), while the signal marked by pattern b is attributed to a complex of Cu(II) with 2-propanol (for which $g_{\parallel} = 2.41$, $A_{\parallel} = 125$ G). Once ligand is added to the microemulsion, pattern b disappears.

A competition between a ligand–Cu(II) species (pattern c) and aquated Cu(II) is evident in the EPR spectra of Figure 4, as the mole ratio of ligand to metal is increased. The limit spectrum is achieved at a mole ratio of 20:1. For this species the value of $g_{\parallel}$ is 2.36, and $A_{\parallel} = 140$ G. Evidently, the CuL^{2+} complex is the limit species in this system.

A complex potentiometric experiment was performed to determine a formation constant for the CuL^{2+} species. A competing reaction procedure[17] was employed, wherein N^{α}-dodecanoyl-L-histidinol was the competing ligand for which the formation constants were known.[6] The value calculated for the formation constant was $\log K_1 = 0.23$.

Absorption Spectroscopy. Optical spectra for microemulsions containing aquated Cu(II) and a 20:1 mole ratio of N^{α}-dodecanoyl-L-glutaminol to Cu(II) are shown in Figure 5. The complex with the glutamine side chain exhibits an increase in Dq of about 300 cm^{-1} over that of aquated Cu(II). Also shown in Figure 5 are spectra for microemulsions in which the ligand was N-dodecanoylglycinol or β-hydroxyethyl dodecanoate. A 40:1 mole ratio of ligand to Cu(II) was used in these latter studies.

C. The Cu(II)/N^{α}-Dodecanoyl-L-methioninol System. Since the thioether group in the side chain of methionine is a very weak ligand for Cu(II), a microemulsion containing a reduced amount of water was also used in studies with this system. The composition of the microemulsion was given under part B, above.

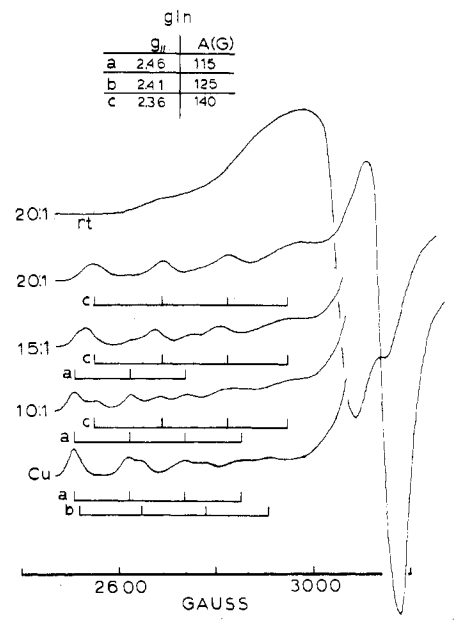

Figure 4. Electron paramagnetic resonance spectra of Cu(II) in microemulsions containing N^{α}-dodecanoyl-L-glutaminol. Each system contained 77 μmol of $Cu(ClO_4)_2 \cdot 6H_2O$. The microemulsion represented by the bottom spectrum contained only Cu(II); the others contained N^{α}-dodecanoyl-L-glutaminol as depicted by the ratio of ligand to metal. The bottom four spectra were obtained at liquid nitrogen temperature, and the top spectrum was obtained at room temperature.

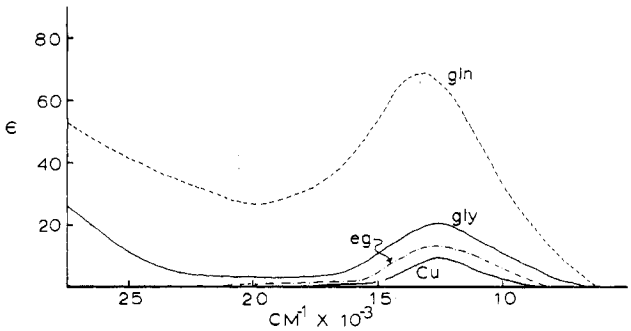

Figure 5. Absorption spectra showing the d–d transition of Cu(II) in microemulsions containing N^{α}-dodecanoyl-L-glutaminol or control ligands. Each system contained 77 μmol of $Cu(ClO_4)_2 \cdot 6H_2O$. The spectra marked "eg" and "gly" are for microemulsions containing 40:1 mole ratios of ligand—β-hydroxyethyl dodecanoate and N-dodecanoylglycinol, respectively—to metal. The spectrum marked "gln" was obtained with a system containing a 20:1 mole ratio of N^{α}-dodecanoyl-L-glutaminol to Cu(II). Molar absorbtivities are based on the concentration of Cu(II), 5.55×10^{-3} M.

Electron Paramagnetic Resonance and Absorption Spectroscopy. The EPR spectrum at 77 K of a microemulsion containing an 80:1 mole ratio of N^{α}-dodecanoyl-L-methioninol to Cu(II) is shown in Figure 6. Signals from three species are evident in this spectrum. Aquated Cu(II) is designated by pattern a. Patterns b ($g_{\parallel} = 2.36$, $A_{\parallel} = 120$ G) and c ($g_{\parallel} = 2.32$, $A_{\parallel} = 135$ G) presumably designate the CuL^{2+} and CuL_2^{2+} complexes, respectively. Due to solubility problems, it was not practical to study mole ratios in excess of 80:1. Thus, we do not know whether the CuL_2^{2+} species is the limit complex in this system.

The optical spectrum of a microemulsion containing an 80:1 mole ratio of ligand to Cu(II) is shown in Figure 7. It must

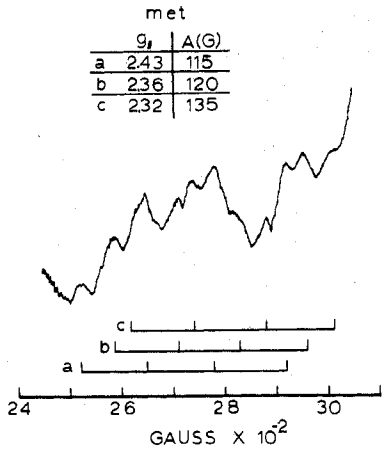

Figure 6. EPR spectrum of Cu(II) in a microemulsion containing *N*-dodecanoyl-L-methioninol. The spectrum was obtained at liquid nitrogen temperature. A mole ratio of ligand to metal of 80:1 was employed. See Figure 4 and the text for other details.

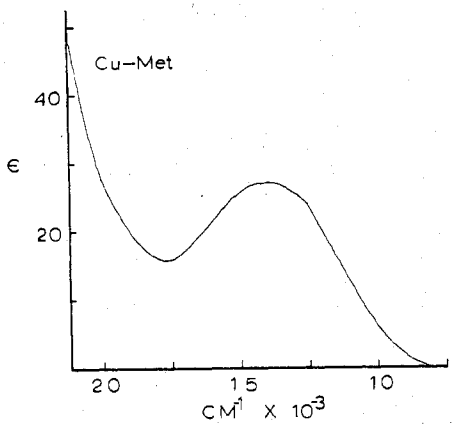

Figure 7. Absorption spectrum of Cu(II) in a microemulsion containing an 80:1 mole ratio of *N*-dodecanoyl-L-methioninol to metal. See Figure 5 for other details. Note that this is *not* the spectrum of a limit species.

be emphasized that this is not the spectrum of a limit complex. However, the spectrum does illustrate the trends in energy and intensity of the d–d transition as Cu(II) interacts with the thioether group.

Discussion

The studies of the interaction of Cu(II) with N^{α}-dodecanoyl-L-lysinol show that the limit species which forms in the interphase of the microemulsion is the CuL_4^{2+} complex. The essential structural feature of this complex is the coordination of four ϵ amino groups in a square-planar geometry. The hydrocarbon moieties extend out of the interphase into the hexane-rich phase.

The ϵ amino group of lysine is a strong ligand for Cu(II), as indicated by the relatively large formation constants calculated for this system ($\log K_1 = 6.13$, $\log K_2 = 5.66$, $\log K_3 = 4.97$, $\log K_4 = 3.93$). These formation constants are somewhat larger than those measured for the interaction of Cu(II) with aminoethanol in aqueous solution.[18] However, as pointed out previously,[6] there is a small degree of uncertainty introduced into the measurement of formation constants in the microemulsion because the volume of the aqueous phase is not precisely known.

The values for the **g** tensors and the hyperfine splitting constant obtained for the CuL_4^{2+} complex (vide supra) are quite comparable to those measured for the $Cu(NH_3)_4^{2+}$ complex and the tissue copper proteins.[19,20] However, the hyperfine splitting constant (A = 170 G) obtained for the CuL_4^{2+} complex is considerably larger than that measured for copper enzymes.

In the absorption spectra for the Cu(II)/N^{α}-dodecanoyl-L-lysinol system, the value of Dq for the limit complex is 1690 cm^{-1}. This value is quite consistent with literature values for tetraamine complexes of Cu(II).[22] Also, a value of 1690 cm^{-1} for Dq is indicative of a square-planar geometry for the limit complex.[23]

The ϵ amino group of lysine is one of the strongest donor groups in the side chains of amino acids, yet this group is seldom implicated as a ligand in metalloproteins.[24a] It is clear that most lysyl ϵ amino groups would be protonated at physiological pH and thus unable to interact with a metal. However, for a number of enzymes, the proposed bioorganic mechanism includes the participation of an unprotonated ϵ amino group. A thoroughly documented example of such a mechanism is that proposed for acetoacetate decarboxylase by Westheimer and co-workers.[24b] With acetoacetate decarboxylase, the measured pK_a of the ϵ amino group at the active site is 5.9, which indicates that this lysyl side chain is essentially unprotonated at physiological pH. In light of these results, it is highly conceivable that the ϵ amino group can serve as a ligand in a metalloprotein. As more information on metal complexing in metalloproteins becomes available, the ϵ amino group presumably will be more frequently implicated as a ligand site.

We propose that Cu(II) binds N^{α}-dodecanoyl-L-glutaminol through the carbonyl oxygen of the γ amide. This proposal is supported by the following observations: (a) In numerous titrations between pH 2 and 12 in microemulsions, we have never observed the release of protons attributable to the ionization of a peptide (or amide) nitrogen. (b) The optical spectra shown in Figure 5 indicate that Cu(II) interacts with each of the three ligands—N^{α}-dodecanoyl-L-glutaminol, *N*-dodecanoylglycinol, and β-hydroxyethyl dodecanoate. A carbonyl oxygen is the only ligand site common to these three molecules.[25] (c) In addition, EPR spectra of frozen microemulsions containing 20:1 mole ratios of *N*-dodecanoylglycinol, or β-hydroxyethyl dodecanoate, to Cu(II) manifested a species with a $g_{\parallel}$ value of 2.36 and an $A_{\parallel}$ value of 140 G. In other words, the ligands in these control experiments form a species with EPR parameters which are identical with those of the CuL^{2+} complex in Figure 4.

The formation constant for the Cu(II)–N^{α}-dodecanoyl-L-glutaminol interaction was measured by a rather complicated experiment. Nonetheless, the value obtained ($\log K = 0.23$) is comparable to the formation constant for $Cu(urea)^{2+}$ ($\log K$ = 0.5–0.7).[26]

The interaction of N^{α}-dodecanoyl-L-methioninol and Cu(II) was very weak and a limit complex could not be determined even at an 80:1 ligand to metal mole ratio. The interfacial area in the microemulsions used for these studies would not dissolve more ligand, and attempts to use less metal or a larger dispersed volume resulted in excessive dilution of the weakly formed complexes. There is, consequently, some doubt about the bonding interactions in the complexes which produce the EPR signals represented by patterns b and c of Figure 6. However, the EPR and optical parameters of these complexes are different from those of the other systems we have studied. Therefore, it is reasonable to suggest coordination to the thioether sulfur atoms.

Since it was not possible to identify a limit species in the system containing N^{α}-dodecanoyl-L-methioninol, the interaction between the ligand and Cu(II) is not clearly defined. Two different types of interaction are plausible. A chelate structure could form in which Cu(II) binds the ligand through the thioether sulfur and the peptide carbonyl oxygen. This

type of chelation would feature an eight-member ring. (An analogous complex has been proposed for Cu(N^{α}-dodecanoyl-L-histidinol)$_2^{2+}$ [6]). On the other hand, Cu(II) may bind the ligand only at the thioether sulfur. We favor the former possibility because, where sterically feasible, chelation is a favored process on the basis of entropy considerations.

Jones et al. have reported molar extinction coefficients of $\sim 1 \times 10^3$ for the d–d transition of Cu(II) bound to cyclic thioethers.[27] We have calculated a rough estimate for the extinction coefficient of the d–d transition in the Cu(II)/*N*-dodecanoyl-L-methioninol system. The EPR spectrum in Figure 6 permits one to partition the available Cu(II) into three species, each present in more or less equal amounts. Thus, about two-thirds of the Cu(II) is bound to the ligand, yet the measured extinction for this system is less than 30 (Figure 7). Therefore, in our system the extinction coefficient for 1 mol of Cu(II)–thioether interactions would not exceed 60.[28]

The side chains of both glutamine and methionine contain functional groups which are very weak ligands for Cu(II). Apparently, these two side chains would provide a ligand site for a metal only in an environment essentially free of competing ligands, even bulk water. Such an environment is feasible within the metal binding site of a metalloprotein. The initial, "trapping" interaction between the protein and the metal presumably would involve side chains with strong donor groups, however.

Finally, the present studies demonstrate both the utility and the versatility of an oil continuous microemulsion for studying metal–ligand complexes. By substantially reducing the water content of the microemulsion, an interaction between Cu(II) and the side chains of both glutamine and methionine was forced to occur. To date, published studies on the interaction of metals with these two side chains are rare.

Registry No. Cu^{II}(N^{α}-dodecanoyl-L-lysinol)$_4$, 61278-46-4; Cu^{II}(N^{α}-dodecanoyl-L-glutaminol), 61278-47-5; N^{α}-dodecanoyl-L-methioninol, 61259-54-9; Cu, 7440-50-8.

References and Notes

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Anisotropic Exchange in Heterocyclic Amine–Copper(II) Complexes

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The purpose of this paper is to report high-temperature magnetic susceptibility and EPR data for three systems, bis-(1,2,4-triazolato)copper(II) [Cu(tr)$_2$], dichloro(phenazene)copper(II) [CuCl$_2$(pnz)], and chloro(1,2,4-triazolato)copper(II) dihydrate [CuCl(tr)·2H$_2$O], and to relate these data to the anisotropic exchange which may be experimentally observed when the isotropic exchange is fairly large. The strength of the isotropic exchange term is related to the high-temperature Curie–Weiss constant and is −49 K for CuCl$_2$(pnz) and −97 K for Cu(tr)$_2$. A larger isotropic exchange field is believed to be present in CuCl(tr)·2H$_2$O. The anisotropic exchange is related to the EPR line width and is expected to be proportional to the isotropic exchange with a constant proportionally of about 10^{-4}. This simple model is consistent with the data for Cu(tr)$_2$ and CuCl$_2$(pnz). Possible alternative mechanisms for the data on CuCl(tr)·2H$_2$O are considered as the simple model seems inadequate.

Introduction

Recent studies of spin-exchange interactions ($\overline{S_1}$:$\mathbf{J}$:$\overline{S_2}$) in clusters, semidilute systems, and concentrated paramagnetic systems have considerably extended our knowledge in this area.[2-6] While the dominant interaction in systems with little orbital magnetism appears to be an isotropic coupling ($J\overline{S_1}\cdot\overline{S_2}$) between spins, there is increasing interest in the temperature dependence[5,7-9] of J and in anisotropic exchange (ae) between