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Proton nuclear magnetic relaxation in aqueous copper(II) amine chelate solutions

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Abstract

Nuclear magnetic relaxation dispersion measurements are reported for aqueous solutions of copper(II) ion in solutions of ammonia, 1,2-diaminoethane and triethylenetetraamine. The water proton spin relaxation efficiency is increased dramatically over the hexaaquocopper(II) ion rate when square planar complexes are formed. The major factor contributing to this change is the development of a large hyperfine coupling between the coordinated amine protons and the copper(II) center that dominates low field relaxation rates. The relaxation is generally controlled by the rate of ligand exchange which is catalyzed by high ligand concentration. The triethylenetetraamine complex is substitutionally inert on the time scale of the nuclear spin relaxation and the water proton relaxation induced is dominated by the relative translational motion of the water and the metal center, i.e. outer sphere effects.

Introduction

Nuclear magnetic relaxation of water protons has become increasingly important with the development of magnetic imaging as an efficient medical diagnostic tool [1]. The spin relaxation is related to the contrast in the image because the image intensity is very largely controlled by the differences between spin–spin and spin–lattice relaxation rates in different regions of the sample studied [2]. Control of the spin relaxation rate may, therefore, control not only the image contrast, but also the image information content. A very promising method for controlling water proton spin relaxation times is though the introduction of paramagnetic metal ions in the sample that can dramatically alter the spin relaxation rates through both contact and dipolar electron–nuclear couplings [3–6].

Aqueous copper(II)–amine solutions provide a useful series of complexes that permit systematic study of geometric changes on the magnetic relaxation properties of an $S=1/2$ metal complex [7–13].

The hexaaquocopper(II) ion has an octahedral geometry while the tetraamminecopper(II) ion and related di, tri and tetraamine complexes are square planar [14, 15]. The hexaaquo complex is labile while the proton and ligand exchange rates of the amine complexes are much slower. In addition the relaxation efficiency of the complexes is generally a function of the electron spin relaxation rates, which may change in response to changes in the electronic structure of the metal center [16, 17]. We report here measurements of the water proton nuclear magnetic spin–lattice relaxation rate as a function of magnetic field strength, pH, temperature and ligand structure that lead to a fairly comprehensive picture of copper(II) ion induced water proton spin relaxation in these systems.

Experimental

Nuclear magnetic relaxation measurements were made on a field cycling spectrometer described elsewhere [18] that switches magnetic field strengths in real time from values limited by the earth's magnetic field to a proton Larmor frequency of 42 MHz. The relaxation rates were extracted from 16, 14 or 30 data points that were fitted to an exponential using a non-linear least-squares procedure. The statistical errors were typically about 1% though reproducibility more nearly 5%. Samples were contained in 10 mm Pyrex sample tubes sealed with rubber stoppers and a screw cap. Temperature in the measurement coil

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was maintained by a flow of liquid perchloroethylene that was thermostated in an external Neslab RTE-8 temperature controller which serviced the sample region using outboard Little Giant pumps.

Solutions were made in deionized water with reagent grade chemicals (Baker Analyzed). pH was measured using a combination glass electrode operating in conjunction with a Corning model 240 or 125 pH meter. UV–Vis spectra were recorded using an Hewlett-Packard model 8451A diode array spectrophotometer.

Results

The affinity of ammonia and amines for copper is high with the logarithm of the association constant in the range 10 or so [19]; however, hydrogen ion is a significant competitor making the effective association constants strong functions of pH in the regions of physiological interest. The pH dependence of the complexation reactions of copper(II) ion are represented in Fig. 1 based on tabulated association constants. In addition to these reactions, hydroxide ion may complex with copper at high pH values as well [19].

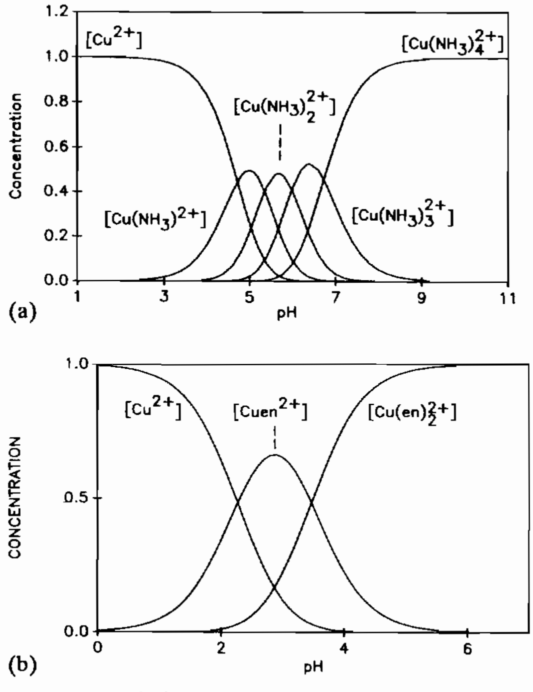

Fig. 1. The relative concentrations of the several copper(II) complexes as a function of pH. (a) The copper(II)–ammonia system with the total ammonia concentration of 1.8 M and the copper concentration of 1.0 mM. (b) The copper(II)–ethylenediamine system with the total copper concentration of 2.5 mM and the ethylenediamine concentration of 5.0 mM. Stability constants were taken from ref. 27.

The paramagnetic contribution to the water proton relaxation rate induced by copper(II) complexes is a function of the copper coordination geometry, pH and temperature. The hexaaquocopper(II) ion is labile [20], but its efficiency as a water proton relaxation agent is low because the magnetic moment is small ($S=1/2$) and the electron–proton hyperfine coupling is weak. The dispersion observed in the range between 5 and 10 MHz is caused by the rotational motion of the complex modulating the electron–proton dipole–dipole coupling which disperses in part when the electron Larmor frequency matches the rotational correlation time.

The addition of ammonia to an aqueous copper(II) ion solution produces the square planar complex with the familiar intense blue color often used as a diagnostic for copper(II) ion [21]. The relaxation profile changes drastically with this change in geometry to yield much greater efficiency in the low field region. The effect is caused by the electron–proton hyperfine coupling constant becoming large in the square planar complex with the electron relaxation time remaining long. The inflection point in the profile provides an estimate of the electron relaxation time which is taken as 4 ns. The relaxation equation for the first coordination sphere relaxation of the ligand protons by the metal center has been developed by Solomon [22], Bloembergen [23] and, Bloembergen and Morgan [24] and is presented in detail elsewhere [25]. For the present case, it is crucial to appreciate that the relaxation efficiency of the metal center is limited in part by the rate of the proton and or ligand exchange between the relaxation site and the bulk water population. That is,

$$1/T_1 = P_m(T_{1m} + \tau_m) + 1/T_{1o} \qquad (1)$$

where the subscript m stands for the metal first coordination sphere sites and τ_m is the mean residence time of the proton in the first coordination sphere, and P_m is the probability that a proton is located in the first coordination sphere [26]. In the case where the lifetime becomes in the order of or longer than the relaxation time, T_{1m}, the amplitude of the relaxation dispersion decreases and the inflection shifts to higher frequency. Thus, the observed inflection point in Fig. 2 represents an underestimate of the electron relaxation time. The amplitude of the relaxation dispersion profile is attenuated by τ_m when it become large compared with T_{1m}. Thus, estimates of the proton–copper(II) hyperfine coupling requires knowledge of the proton residence time in

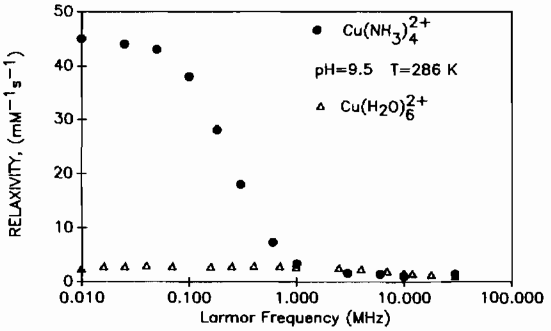

Fig. 2. The water proton relaxation spin–lattice relaxation rate as a function of magnetic field strength plotted as the proton Larmor frequency for hexaaquocopper(II) ion and tetraamminecopper(II) ion at pH 9.5 at 286 K.

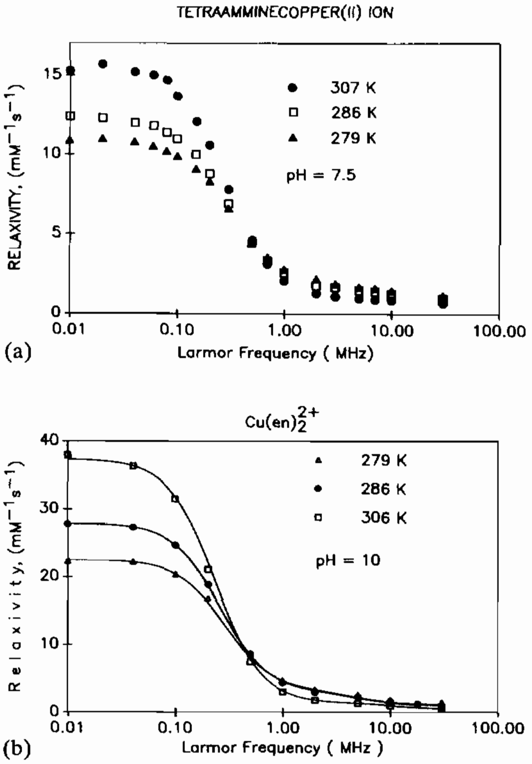

Fig. 3. (a) The water proton spin–lattice relaxation rate per mM of copper complex as a function of magnetic field strength plotted as the proton Larmor frequency for several temperatures at pH 7.5. (b) The water proton spin–lattice relaxation rate per mM of bis(ethylenediamine)copper(II) ion at several temperatures as a function of magnetic field strength plotted as the proton Larmor frequency. The pH was 10.

the complex that may depend on pH, ligand concentration and temperature.

Representative temperature dependencies of the nuclear magnetic relaxation dispersion profiles are summarized in Fig. 3 for the ethylenediamine complexes and the tetraamminecopper(II) complexes. The data for the tetraamminecopper(II) ion were taken at pH 7.5; reference to Fig. 1 indicates that at this pH, the solution contains a mixture of complexes. Nevertheless, the low field relaxation rate increases clearly with increasing temperature, which is anticipated in the case where the mean residence time, τ_m, limits the relaxation rate. Similar data is shown for the bis(ethylenediamine)copper(II) ion in Fig. 3 at pH 10 where the proton is not an effective competitor for the metal behaving as a Lewis acid. These data are similar to the ammonia solution and demonstrate clearly the contribution of the chemical exchange rate in limiting the low frequency water proton relaxation rate. In both cases the relaxation profiles cross; that is, the high frequency data for the high temperatures lies below that of the low temperature data, while at low frequencies the opposite is true. This observation results from the fact that the high frequency contribution to the relaxation rate is dominated by the dipole–dipole term in the relaxation equation which is modulated by the rotational correlation time of the complexes. The correlation time for rotation decreases with increasing temperature, thus, the high field temperature dependence is opposite to that for the low field relaxation rates. The pH may affect the effective proton exchange rate in two distinct ways: (i) the exchange rate of the amine protons is a base catalyzed process, and increasing pH increases this rate, which is generally slow compared with the ligand exchange rate [27]; (ii) the pH controls the effective ligand concentration, [L], through the proton equilibrium involving the protonated ligand, $[LH^+]$. For the square planar complexes, the ligand exchange rate may depend on the total ligand concentration for associative pathways for ligand exchange [28]. These effects are demonstrated clearly in Fig. 4 for the ethylenediamine and triethyletetraamine complexes.

The data for the ethylenediamine complexes were collected at pH values above 9.6 where the proton equilibrium makes a minor contribution to the effective ligand concentration. Thus, the bis(ethylenediamine)copper(II) ion is the dominant copper species throughout the range of ligand concentrations shown. The temperature is constant, but the low field relaxation rate increases dramatically and the low field inflection shifts to lower frequency with increasing ligand concentration. Both of these observations are consistent with the exchange rate determining the effective relaxation rate. That the exchange rate is a function of ligand concentration supports the view that the ligand exchange not the proton exchange is the faster process.

A kinetically slower situation is represented by the data for triethylenetetraaminecopper(II) ion also shown in Fig. 4. The complex is clearly formed at

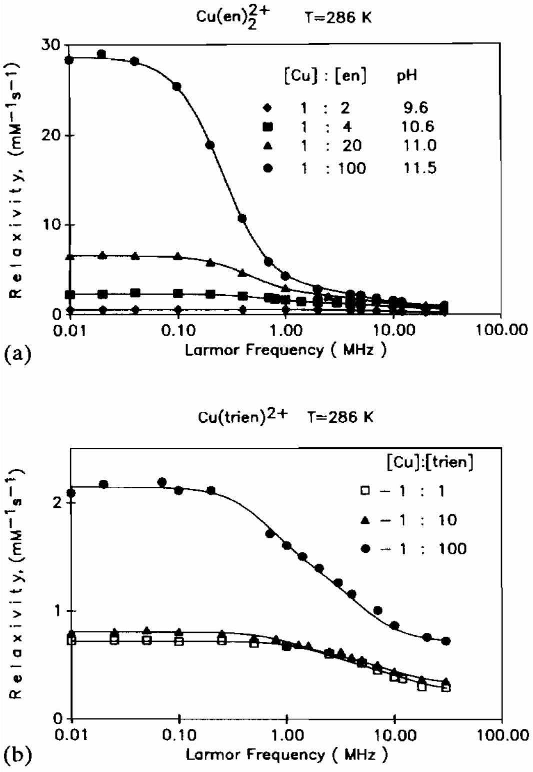

Fig. 4. (a) The water proton spin–lattice relaxation rate per mM of bis(ethylenediamine)copper(II) ion as a function of magnetic field strength at several concentrations of ligand at 286 K and pH values between 9.6 and 11.5. (b) The water proton spin–lattice relaxation rate per mM of triethylenetetraaminecopper(II) ion as a function of magnetic field strength for several concentrations of ligand at pH 9.5 and 286 K.

very low ligand concentrations, but the exchange rate is slow such that the relaxation profile is dominated by the translational mobility of water in the vicinity of the complex or outer sphere effects and the relaxation is inefficient. Increasing the ligand concentration drastically, however, changes the shape of the relaxation curve and increases the low field rate. This increase could arise from changes in the ligand exchange rates or from changes in the microdynamic viscosity. If the ligand exchange rate increases very dramatically with increasing ligand concentration, the low field relaxation rate should increase with temperature as it does in Fig. 4. Representative data are shown for the triethylenetetraaminecopper(II) complex in Fig. 5. Several points are apparent: (i) the rates are low; (ii) the temperature dependence is minimal; (iii) the relaxation profiles are not clearly dominated by outer sphere effects alone.

The low rate is expected for the tetraamine complex if outer sphere effects dominate. The outer sphere rate is estimated by earlier work to contribute a relaxivity of approximately 0.2 to 0.3 (mM s)$^{-1}$ [29]. The observed rates are somewhat larger than this, particularly in the solution with high concentrations of excess ligand. Thus, some exchange processes make a measurable contribution to the relaxation dispersion. This conclusion is supported by the observation that the shapes of the profiles shown in Fig. 5 do not match those expected for outersphere effects. In summary, the water proton relaxation induced by copper(II) ion complexes is complex. The change to square planar complexes causes large scalar or hyperfine couplings to dominate low field relaxation rates and make the copper(II) ion an efficient relaxation agent. This class of complexes, thus, provides a means for readily changing the water proton transverse relaxation rate without significantly affecting the longitudinal relaxation rate which samples the high field spectral densities. The relative inertness of the amine protons combined with the tendency of copper(II) to make square planar complexes makes the amines, which are often used to build macrocyclic ligand systems, an inefficient approach to high water proton relaxation rates in copper complexes. However, the series of complexes provides an easy approach to the study of what affects the electron spin relaxation rate at the copper center.

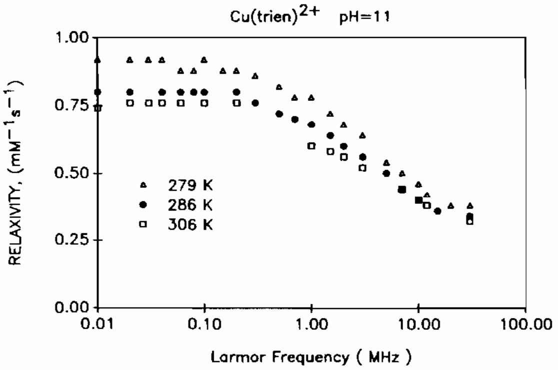

Fig. 5. The water proton nuclear magnetic relaxation rate per mM of triethylenetetraaminecopper(II) ion as a function of magnetic field strength at pH 11 for several temperatures.

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