Binuclear Copper(II) Chelates with a 24-Membered Amide-Based Macrocycle

Michiko B. Inoue,*,†,‡ Enrique F. Velazquez,‡
Adriana Ruiz-Lucero,‡ Motomichi Inoue,‡
Arnold Raitsimring,† and Quintus Fernando†

Department of Chemistry, University of Arizona, Tucson,
Arizona 85721-0041, and CIPM, Universidad de Sonora,
Apartado Postal 130, Hermosillo, Sonora 83000, Mexico

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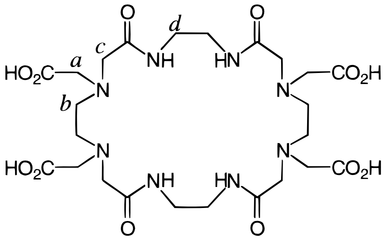
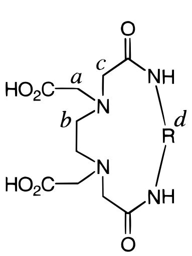
Introduction

A 24-membered tetraoxooctaaza macrocycle **1**, abbreviated as (24edtaen)H_4, in which two ethylenediaminetetraacetate (edta) and two ethylenediamine units are linked by amide bonds, is expected to form a neutral binuclear Cu^{2+} chelate with coordination mode **I** (Chart 1), which has been established by X-ray studies of the Mn^{2+} and Co^{2+} complexes of the ligand.[1,2] In some Cu^{2+} complexes with amide-based ligands, amide oxygen atoms coordinate the central metal ion in acidic media, and in basic media, deprotonated amide nitrogen atoms coordinate the metal ion.[3−11] This type of structural conversion occurs in the Cu^{2+} complex of a 13-membered dioxotetraaza macrocycle **2b**, (13edtapn)H_2, but does not occur in the Cu^{2+} complex of a smaller ring macrocycle **2a**, (12edtaen)H_2.[12] The binuclear Cu^{2+} complex of (24edtaen)H_4 is expected to form a variety of chelate species in solution when the amide groups alter their coordination mode with pH, and the resulting binuclear species may exhibit characteristic spectral and magnetic properties that reflect the coordination mode. In this work, we have identified species formed between Cu^{2+} and (24edtaen)H_4 in aqueous media by potentiometric titrations and characterized them by EPR and electronic absorption spectroscopy.



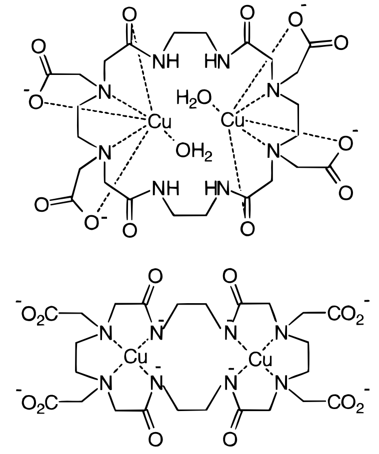
1 (24edtaen)H_4



2a (12edtaen)H_2
R = CH_2CH_2

2b (13edtapn)H_2
R = $CH_2CH_2CH_2$

Chart 1



I

II

Experimental Section

The 24-membered macrocycle (**1**) was synthesized by the method reported previously;[1] separation from the 12-membered isomer (**2a**) was performed by recrystallization from hot water and confirmed by ^1H NMR. The binuclear Cu^{2+} complex was synthesized by a reaction between the ligand and a slight excess of Cu^{2+} carbonate at ≈40 °C. The resulting solution was mixed with an equal amount of ethanol, and a royal blue solid was formed in a few days. Anal. Calc for $Cu_2(C_{24}H_{36}N_8O_{12})\cdot 5H_2O$: C, 34.08; H, 5.48; N, 13.25. Found: C, 34.03; H, 5.56; N, 12.65. Mass spectrum (ESI, NH_3/methanol): m/z ($^{63}Cu-{}^{63}Cu$) = 753.1 (100) $[Cu_2L - H]^-$; 376.0 (13) $[Cu_2L - 2H]^{2-}$.

The formation constants of the metal complexes were determined by potentiometric titrations in an aqueous KCl medium with an ionic strength of 0.1 at 25 °C; the experimental details are given in Supporting Information. All related calculations were performed by the program BEST.[13] The electronic absorption spectra were obtained by a Perkin-Elmer Lambda 2 UV−vis spectrophotometer. The sample solutions were prepared from stock solutions of $CuCl_2\cdot 2H_2O$ and the ligand in an appropriate ratio. The EPR spectra were obtained by a Bruker ESP-300 X-band spectrometer at liquid nitrogen temperature for 50% methanol glass matrixes in a concentration of 8−10 mM per Cu^{2+} ion. The pH values of the sample solutions were adjusted to desired values before the addition of methanol.

Results and Discussion

Formation Constants. The protonation constants of $(24edtaen)^{4-}$ were determined (with standard deviations in parentheses) as log $K_1 = 7.78(0.02)$, log $K_2 = 7.26(0.04)$, log

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[†] University of Arizona.
[‡] Universidad de Sonora.
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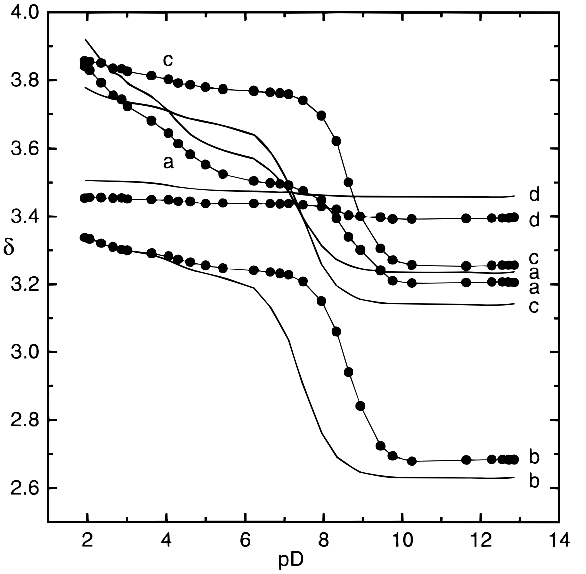

Figure 1. ^1H NMR shifts δ (referenced to sodium 2,2-dimethyl-2-silapentane-5-sulfonate, DSS) of $(24edtaen)H_4$ as functions of pD at a probe temperature of $\approx$23 °C. The solid lines show the shifts of $(12edtaen)H_2$ for comparison. The labels of the protons are given in structures **1** and **2**. The pD values were obtained by the relation pD = $pH_{meas} + 0.44$, where pH_{meas} was determined by a pH electrode calibrated with aqueous standard buffers.

$K_3 = 4.18(0.02)$, and log $K_4 = 3.30(0.01)$. As shown in Figure 1, the ^1H NMR signals of three CH_2 groups bonded to amino nitrogen atoms are shifted simultaneously in the pD range corresponding to the first and the second protonation processes, which are deduced to occur at the amino nitrogen atoms. The pD value at which the slope is a maximum in the buffer region is about 8.6, which corresponds to the "protonation" constant in D_2O media. This value is consistent with the log K_1 and log K_2 values when the difference between the pK_w values of H_2O and D_2O and the difference between acid dissociation constants in H_2O and D_2O media are taken into account.[14] The pD value of the maximum slope of $(24edtaen)^{4-}$ is approximately 1.1 higher than that of $(12edtaen)^{2-}$. This is consistent with the difference in their protonation constants: log $K_1 = 6.50$ for $(12edtaen)^{2-}$ (log $K_2 = 3.54$).[15] In the pD range where amino nitrogen atoms were being protonated, the ^1H NMR signals were broadened, except for the *d* proton (in structure **1**), and were broadest around the pD of maximum slope; the full width at half-maximum (fwhm) of the *b* proton was, for example, 3.9 Hz at pD $\leq$ 7.48, 17 Hz at pD = 7.96, 42 Hz at pD = 8.65−8.93, 15 Hz at pD = 9.46, and 3.9 Hz at pD $\geq$ 10.25. This line-broadening indicates that the rate at which equilibrium between the protonated and deprotonated species is attained is comparable to the NMR frequency. Such a slow equilibrium was not observed for $(12edtaen)^{2-}$; the fwhm of the *b* proton signal was 9 Hz (maximum) at pD = 7.50 and 2.7 Hz at pD $\leq$ 5.04 and $\geq$ 9.4. These observations suggest that intramolecular hydrogen bonds formed by protonated amino nitrogen atoms in $[(24edtaen)H_2]^{2-}$ are more stable than in $[(12edtaen)H]^-$. This higher stability of the protonated state leads to a higher basicity of the larger ring macrocycle.

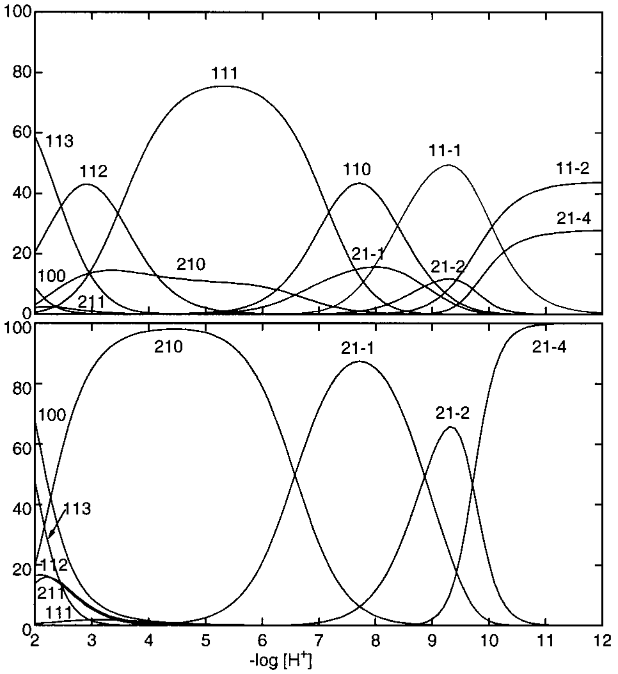

Figure 2. Distributions (%) of $Cu_pL_qH_r$ species (labeled by *pqr*) for [Cu]/[24edtaen] = 1 (top) and 2 (bottom): the formation constants are given in the text; L denotes $(24edtaen)^{4-}$, [24edtaen] = 1.0 mM, μ = 0.1 (KCl), *T* = 25 °C. Uncoordinated ligand species are not shown for clarity.

In potentiometric titrations for [Cu]/[L] = 1 and 2, six $CuLH_r$ species and five Cu_2LH_r species were detected; L denotes $(24edtaen)^{4-}$. Their logarithmic overall formation constants, log $\beta(Cu_pLH_r)$, were determined (with estimated uncertainties in parentheses) as follows: for $CuLH_3$, 25.37 (0.10); $CuLH_2$, 22.91 (0.04); CuLH, 19.45 (0.08); CuL, 12.28 (0.15); $CuLH_{-1}$, 3.9 (0.2); $CuLH_{-2}$, −6.2 (0.7); Cu_2LH, 24.0 (0.7); Cu_2L, 22.15 (0.04); Cu_2LH_{-1}, 15.57 (0.10); Cu_2LH_{-2}, 6.71 (0.13); Cu_2LH_{-4}, −12.72 (0.14). The species distributions are shown in Figure 2: in the [Cu]/[L] = 2 system, the concentrations of $CuLH_r$ species are negligibly low at pH > 4; in the [Cu]/[L] = 1 system, considerable concentrations of the Cu_2LH_r species are present. The logarithmic stability constant of CuL is slightly higher than the value, log [ML]/[M][L] = 11.34, reported for $(12edtaen)^{2-}$ [12] and is consistent with the higher basicity of the amino nitrogen of $(24edtaen)^{4-}$. $CuLH_{-1}$, Cu_2LH_{-1}, and Cu_2LH_{-2} species are hydroxy complexes which have the general formula $[Cu_mL(OH)_n]^{2m-4-n}$. In $CuLH_{-2}$ and Cu_2LH_{-4}, deprotonation occurs on amide nitrogen atoms as described below; the coordination mode in Cu_2LH_{-4} is schematically shown by **II**.

Solution Electronic Spectra. The solution spectra of Cu_n−$(24edtaen)H_4$ (*n* = 1 or 2) showed a pH dependence consistent with the species distribution, as summarized in Table 1. The d−d band showed a blue shift and an enhancement in the molar absorptivity with increasing pH. This spectral change resembles that of the $(13edtapn)H_2$ complex in which the coordination mode of the amide groups is changed with pH[12] and suggests that $[Cu_2L(H_2O)_2]^0$ with structure **I** is formed in acidic solutions, while $[Cu_2(LH_{-4})]^{4-}$ with structure **II** in highly basic solutions. The latter species was detected in the mass spectrum of an ammoniacal solution of $Cu_2(24edtaen)\cdot 5H_2O$; $[(Cu_2L) - nH]^{n-}$ species detected are described by $[\mathbf{II} + m\mathrm{H}]^{m-4}$, because the amide groups are the only potential deprotonation sites in $[Cu_2L]^0$. At pH where **II** was formed, a well-defined absorption band was observed at 270 nm. This band is attributable to a charge transfer from a metal d orbital to a π^* orbital of the $N^-{-}C{=}O$ system, in which the N−C bond has a partial double-bond character, as reported for $[Cu(13edtapnH_{-2})]^{2-}$ and some

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Table 1. Electronic and EPR Spectra of Cu^{2+} Complexes with $(24edtaen)H_4$ and Related Macrocycles

pH	major species	CT band λ/nm (ϵ^a)	d−d band λ/nm (ϵ^a)	EPR parameters[b]		
				$g_{\parallel}$	$10^4 A_{\parallel}$/cm^{-1}	$g_{\perp}$
		Cu−(24edtaen)$^{4-}$				
5.6	$[CuLH]^-$	250 (3100)	735 (75)	2.303	160	2.064
11.9	$[Cu(LH_{-2})]^{4-}$	268 (4300)	660 (190)	2.23^c	176^c	2.06^c
		Cu_2−(24edtaen)$^{4-}$				
4.6	$[Cu_2L]^0$	245 (3300)	730 (80)	2.328	152	2.075
7.6	$[Cu_2L(OH)]^-$	260 (3200)	675 (90)	*d*		
11.5	$[Cu_2(LH_{-4})]^{4-}$	270 (4400)^e	660 (150)	2.27	*f*	
		Cu−(12edtaen)$^{2-}$				
5.5	$[CuL]^0$	*g*	745 (45)^h	2.287	160	2.065
11.7	$[CuL(OH)_2]^{2-}$	*g*	670 (50)^h	2.245	180	2.052
		Cu−(13edtapn)$^{2-}$				
4.0	$[CuL]^0$	*g*	700 (70)^h	2.335	155	2.080, 2.060
10.3	$[Cu(LH_{-2})]^{2-}$	256 (5000)	570 (215)^h	2.194	188	2.045

[a] The molar absorptivities $\epsilon/M^{-1}cm^{-1}$ of Cu_2−(24edtaen)$^{4-}$ are given for each Cu unit for purpose of comparison with the other Cu chelates. [b] Hyperfine structure from $A_{\perp}$ was not observed for all complexes studied. [c] Only an approximate value was determinable owing to the coexistence of $[Cu_2(LH_{-4})]^{4-}$ as a secondary species. [d] The EPR spectrum could be explained by superposition of two simple spectra with almost equal intensities. This spectral pattern was unchanged with a pH variation of 0.6. However, no further experimental data could be obtained for supporting that the spectrum was intrinsically that of $[Cu_2L(OH)]^-$ which formed in a narrow pH range. [e] For a highly basic solution of $Cu_2(24edtaen)\cdot5H_2O$, the corresponding charge-transfer band was observed at 285 nm (ϵ = 4300 per Cu) on the envelope of a strong band at 245 nm (7000 per Cu); the spectrum in the UV region was slightly different from that of the solution prepared by dissolving $CuCl_2\cdot2H_2O$ and the ligand, although the absorption bands in the d−d region and the EPR spectra were identical. [f] The hyperfine structure in the $g_{\parallel}$ region consists of at least eight lines at slightly irregular intervals, suggesting the presence of magnetic interaction between two copper atoms. [g] Ill-defined shoulder at 240−250 nm. [h] Reference 12.

unsaturated tetraazamacrocycles.[16−19] The charge-transfer band of the $(24edtaen)H_4$ complex shifted to a shorter wavelength with decreasing pH in close correlation with the red shift of the d−d band, indicating that charge transfer in Cu−O═C−N of structure **I** is weaker than in $Cu-N^--C=O$ of structure **II**.

EPR Spectra. The EPR spectra were obtained for the Cu^{2+} chelates in glass matrixes, in which Cu_pLH_r species formed in solutions were frozen without interchanging with any other species. Since the pH of the aqueous methanol solution does not exactly correspond to the pH of the aqueous solution, the EPR spectra were studied only for the species formed in a wide pH range. For the [Cu]/[L] = 1 system at pH values at which $[CuLH]^-$ (pH = 5.6) and $[CuLH_{-2}]^{4-}$ (pH = 11.9) were formed, a simple spectrum of axial symmetry was observed, together with a set of weak signals attributed to binuclear species that coexisted as secondary species at the same pH. Well-defined hyperfine peaks were observed in the $g_{\parallel}$ region, but no hyperfine lines were detected in the $g_{\perp}$ region. Table 1 shows the g factors and the hyperfine coupling constant $A_{\parallel}$ determined by computer simulation assuming axial symmetry.[20]

The binuclear chelate system exhibited quite distinctive spectra, as shown in Figure 3, at pH values at which Cu_2L (spectrum A) and Cu_2LH_{-4} (spectrum B) are formed. In spectrum B, at least eight lines were located in the $g_{\parallel}$ region at slightly irregular intervals which are approximately half of the regular interval in spectrum A and in the spectra of the mononuclear species. The spectral pattern of B is characteristic of a spin-paired system with an interaction energy comparable to the hyperfine coupling constant $A_{\parallel}$.[21,22] The observed spin concentration of the sample solution agreed with the Cu concentration within EPR accuracy, indicating that spectrum B is intrinsically that of $[Cu_2(LH_{-4})]^{4-}$, and the spin interaction energy is much smaller than the thermal energy kT at liquid nitrogen temperature, if the interaction is antiferromagnetic. The pattern of spectrum A observed for Cu_2L species is identical with that of the mononuclear species; a magnetic interaction that may be operative between two Cu^{2+} ions does not affect the hyperfine structure. This binuclear species probably has structure **I** resembling that of $[M_2(24edtaen)(H_2O)_2]^0$ (M = Mn or Co), in which the metal−metal distance is 7.575(1)−7.693(2) Å.[1,2] A Cu−Cu distance of 7.7 Å assumed for $[Cu_2L(H_2O)_2]^0$ yields a dipolar interaction corresponding to the field of $(1.9\ \mu_B)/r^3 \approx 39$ G. For structure **II**, the Cu−Cu distance is estimated to be around 6.4 Å in its most probable conformation (with D_2 molecular symmetry) generated by SYBYL molecular mechanics.[23] This Cu−Cu distance provides a dipolar interaction of ≈60 G, which is significantly greater than that in structure **I**. This dipolar interaction is expected to result in a half-field (or “forbidden”) transition, and the intensity ratio of the forbidden transition to the allowed transition is estimated to be on the order of magnitude of 10^{-4}.[22,24] Contrary to this expectation, no half-field transition could be observed. The transition probability of the half-field transition is strongly dependent on the relative orientations of the internuclear axis and the g axes of paired copper atoms.[22] Probably their orientations in structure **II** are not favorable for the observation of a half-field transition. The EPR spectra A and B are well correlated with structural conversion with pH, and the dipolar interaction is one of the factors that yield the difference in the spectra.

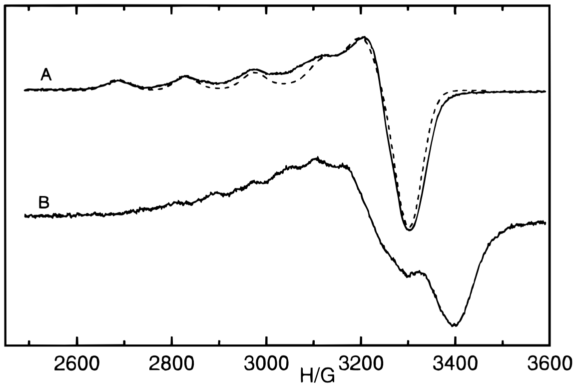

Figure 3. EPR spectra of [Cu]/[24edtaen] = 2 system at different pH: (A) $[Cu_2L(H_2O)_2]^0$ at pH = 4.5 and (B) $[Cu_2(LH_{-4})]^{4-}$ at pH = 11.5. Resonance frequency is 9.45 GHz; matrix, 50% methanol; T, 78 K. The broken line in A is obtained by simulation with $g_{\parallel}$, $g_{\perp}$, and $A_{\parallel}$ values shown in Table 1 and $A_{\perp} = 16 \times 10^{-4}$ cm^{-1}. The hyperfine structure in spectrum B consists of at least eight peaks, indicating the presence of spin coupling between two Cu^{2+} ions.

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Features of $[Cu_2(LH_{-4})]^{4-}$. The logarithmic equilibrium constant, log $[CuLH_{-2}][H]^2/[Cu][L] = -6.2$, of the first metalation accompanied by amide deprotonation is almost the same as the constant of the successive metalation, log $[Cu_2LH_{-4}][H]^2/[Cu][CuLH_{-2}] = -6.5$. The formation of a planar $CuN_2(N^-)_2$ geometry in one coordination center in $[Cu(LH_{-2})]^{4-}$ leads to preorganization of the second vacant center toward a metal ion, and amide hydrogen atoms in the uncoordinated cavity of the preorganized $[Cu(LH_{-2})]^{4-}$ have a strong mutual electrostatic repulsion and can be readily replaced by a Cu^{2+} ion. These effects compensate an instability due to electrostatic repulsion between two coordinated Cu^{2+} ions in the resulting $[Cu_2(LH_{-4})]^{4-}$. The formation of the stable $Cu^{2+}-N^-$ bonds is responsible for the strong charge-transfer band observed for this species and can cause spin delocalization from a copper atom to coordinating ligand atoms.[25] This spin delocalization leads to spin polarization in the σ bonds of the $Cu-N-CH_2-CH_2-N-Cu$ system. An example of spin polarization in a σ electron system has been reported for anhydrous copper(II) formate,[26] in which spin polarization in the σ bonds of *syn*−*anti* Cu−O−C−O−Cu linkages results in an indirect (or superexchange) interaction[27,28] between the Cu atoms with an energy of $\approx 10^{-22}$ J.[26] Spin polarization in a σ electron system is attenuated rapidly, but can still result in a magnetic interaction that contributes to the hyperfine coupling ($\approx 3 \times 10^{-25}$ J) in the $Cu-N-CH_2-CH_2-N-Cu$ linkage. A combined effect of this indirect magnetic interaction and the dipolar interaction gives the EPR hyperfine structure observed for $[Cu_2(LH_{-4})]^{4-}$. Since the charge-transfer interaction in the Cu−O═C−N system of structure **I** is weaker than in $Cu-N^--C{=}O$ of structure **II**, as indicated by the absorption spectra, the spin delocalization in the former occurs to a lesser extent than in the latter. In addition, the spin polarization is attenuated and is ineffective while propagating on 10 diamagnetic atoms between the two Cu ions. The absorption and EPR spectra characteristic of $[Cu_2(24edtaenH_{-4})]^{4-}$ are consistently explained by the binuclear structure **II**, which involves the coordination of amide nitrogen.

Supporting Information Available: Experimental details of potentiometric titrations, examples of titration curves, and pH variation of the charge-transfer band of a [Cu]/[L] = 2 solution. This material is available free of charge via the Internet at http://pubs.acs.org.

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