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Thermodynamic and NMR studies of mixed-ligand complex formation of cadmium ethylenediaminetetraacetate with diamines in an aqueous solution

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Abstract The mixed-ligand complex formation in the systems Cd2 + Edta4–$(CH_2)_n(NH_2)_2$, $n = 2$ (En), 6 (L) has been NMR and calorimetrically studied in aqueous solution at 298.15 K and the ionic strength of $I = 0.5$ (KNO_3). The thermodynamic parameters of formation of the $CdEdtaL^{2-}$, $CdEdtaHL^{-}$, $(CdEdta)_2L^{4-}$, and $(CdEdta)_2En^{4-}$ complexes have been determined. The most probable coordination mode for the complexone and the diamine ligand in the mixed-ligand complexes was discussed.

Keywords Thermodynamic parameters · Mixed-ligand complex · Cadmium ethylenediaminetetraacetate · Hexamethylenediamine · Ethylenediamine · Denticity

Introduction

Recently [1] the seven-coordinated EDTA complex of Cd has been obtained and structurally characterized. There were some other articles in which the coordination number of Cd2+ being more than 6 was shown. Therefore, the $CdEdta^{2-}$ complex is coordinately unsaturated, resulting in mixed complex formation of the type CdEdtaL. Earlier, the thermodynamic studies of CdEdtaEn formation have been carried out [2]. The author proposed the possible monodentate character of En in mixed complex. To verify this suggestion, the systems mentioned above should be studied not only thermochemically but also by means of NMR spectroscopy. The unusual monodentate character of these diamine ligands, particularly En that can be coordinated only by one NH_2 group, has been shown in previous articles [3, 4]. Unfortunately, data on any mixed complex formation of CdEdta are practically absent in literature.

The behavior of CdEdta in the presence of amine and amino carboxylate ligands is sufficiently interesting because of application of EDTA in chelating therapy. EDTA forms stable complex under physiological pH value that is used to remove toxic Cd ions from human organism. However, its coordinately unsaturated character permits it to coordinate N- and S-donor atoms of amino acids. The recent articles [5, 6] demonstrate the binding mechanism of Cd and Hg in living cell by S-containing amino acids and peptides. Taking into account of such mixed complex formation is necessary to make chelating therapy more efficient. There are some other fields of technique and analytical chemistry, which need an effective method of Cd binding and masking, for example, the treatment of semiconductor surface.

Experimental

Sodium salt of cadmium(II) ethylenediaminetetraacetate $Na_2CdEdta\cdot 4H_2O$ used in this study was purified by recrystallization from an aqueous-DMFA solution. A solution of the complexonate was prepared from En exact weight of the reagent. Solutions of the ethylenediamine (freshly distilled) and hexamethylenediamine (high purity grade) were prepared by dissolving the reagents in CO_2-free distilled water. The concentration of diamines in solution was potentiometrically determined. Analytical grade KNO_3 used for adjusting the solution ionic strength was doubly recrystallized from distilled water.

The mathematical simulation of the equilibrium compositions of solutions containing $CdEdta^{2-}$–L(En)–H^{+} in a

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wide pH range at various $CdEdta^{2-}$ to L(En) ratios has been carried out using the RRSU program [7]. The possibility of occurrence of the following reactions has been taken into account:

$$H_2O = H^+ + OH^- \quad (1)$$

$$L + iH^+ = H_iL^{i+}, i = 1, 2 \quad (2)$$

$$CdEdta^{2-} + H^+ = CdHEdta^- \quad (3)$$

$$CdEdta^{2-} + OH^- = CdEdtaOH^{3-} \quad (4)$$

$$CdEdta^{2-} + L = CdEdtaL^{2-} \quad (5)$$

$$CdEdta^{2-} + HL^+ = CdEdtaHL^- \quad (6)$$

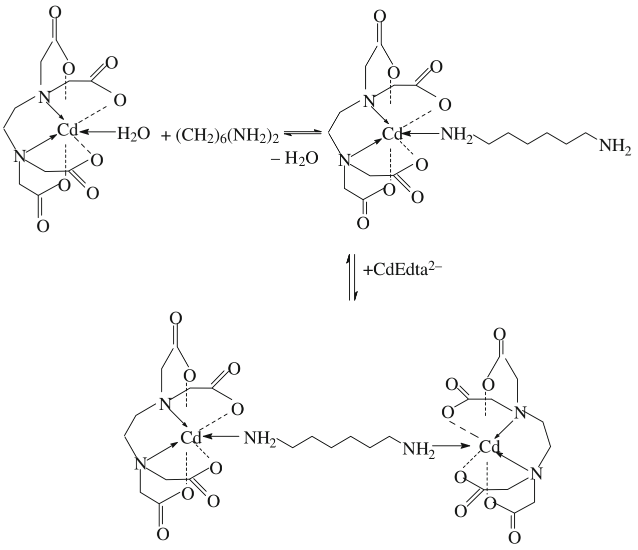
The results of simulation revealed the most informative range of concentrations and permitted us to choose the method of calorimetric measurements. We used practically the same approach as in the previous research [4].

The heats of reactions were measured on an isothermal-jacket ampoule flow-mixing calorimeter equipped with a thermistor temperature gage and automated recording of temperature–time curves. The calorimeter was verified against the heat of solution of KCl in water at 298.15 K. Earlier, elaborative methods of calorimetric measurements for Cu(II) complexes had been used. A series of calorimetric data for mixing of a solution of L or En with solutions containing excess of Cd (II) complexonate showed that the values of $\Delta_{mix}H$ calculated to obtain the required amount of diamine ligand are significantly more than those of the heats of reactions (5) and (6). This can be explained by binuclear complex formation (7) only (Scheme 1).

$$2CdEdta^{2-} + (CH_2)_n(NH_2)_2 = (CdEdta)_2(CH_2)_n(NH_2)_2^{4-}, n = 2, 6 \quad (7)$$

The above analogical situation has been observed earlier [4]. Parts of experimental data are given in Tables 1 and 2. The simultaneous treatment of lg*K* and Δ_rH of reaction (7) for L and En taking into account the contributions of processes (1) and (2) and (4)–(6) permitted us to evaluate its full thermodynamic characteristics. The heats of the reactions computed using the HEAT program [7] and other thermodynamic parameters are listed in Table 3. The heats of water ionization ($\Delta_rH_1 = -56.90$ kJ/mol [8]), ligand protonation ($\Delta_rH_3 = -51.60$ and $\Delta_rH_4 = -95.20$ [9] for En and $\Delta_rH_3 = -63.31$ and $\Delta_rH_4 = -114.06$ kJ/mol [3] for hexamethylenediamine), and the formation of $CdEdtaOH^{2-}$ ($\Delta_rH_5 = -8.25$ kJ/mol [2]) were accepted according to published data.

To verify the structure model of complexes mentioned above which was proposed on the basis of thermodynamic data, the NMR measurements have been carried out. ^1H and ^{13}C spectra were collected at resonance frequencies, 500.17 and 125.76 MHz, respectively, using a Bruker AVANCE III-500 spectrometer at 273 ± 0.1 K. Chemical shifts were measured relative to an external standard, cyclohexanol ($\delta_{exp} = 1.93$ ppm for ^1H and $\delta_{exp} = 27.93$ ppm for ^{13}C). In the case of ^1H spectra of solutions containing hexamethylenediamine, the 3-(Trimethylsilyl)propionic acid-d_4 sodium salt was used as internal standard ($\delta_{exp} = 0.00$ ppm). The NMR samples with different ratios $CdEdta^{2-}$:L(En) were prepared by dissolving the exact amounts of crystalline $Na_2CdEdta$ and L (En, 10 mol/kg of solution) in D_2O. In order to compare, the ^1H and ^{13}C spectra of



Scheme 1 The addition of hexamethylenediamine to the cadmium(II) ethylenediaminetetraacetate

Table 1 Heats of mixing of a solution of $Na_2CdEdta$ (0.5056 mol/kg of solution) with solutions of hexamethylenediamine at 298.15 K, and *I* = 0.5 (KNO_3)

No.	Weighed sample of $Na_2CdEdta$ solution/g	Concentration of $Na_2CdEdta$ after mixing/mol/l	$\Delta_{mix}H$/ kJ/mol	$\Delta_{mix}H - \Delta_{dil}H$/ kJ/mol
$C_L = 0.01852$ mol/l				
1	0.52060	0.00525	−11.08	−10.71
2	0.54035	0.00545	−11.08	−10.70
3	0.43545	0.00439	−12.61	−12.23
4	0.39935	0.00403	−12.83	−12.45
$C_L = 0.03704$ mol/l				
5	0.48700	0.00491	−14.26	−13.89
6	0.45035	0.00454	−15.10	−14.73
$C_L = 0.05552$ mol/l				
7	0.42460	0.00428	−16.89	−16.51
8	0.65000	0.00656	−16.72	−16.34

Table 2 Heats of mixing of solution of ethylenediamine (1.164 mol/kg of solution) with solutions of $Na_2CdEdta$ at 298.15 K, and $I = 0.5$ (KNO_3)

Weighed sample of $(CH_2)_2(NH_2)_2$ solution/g	Concentration after mixing/mol/l		$\Delta_{mix}H$/kJ/mol	$\Delta_{mix}H - \Delta_{dil}H$/kJ/mol
	$CdEdta^{2-}$	$(CH_2)_2(NH_2)_2$		
0.31315	0.1001	0.007278	−26.07	−25.55
0.24015	0.1001	0.005581	−26.65	−26.13
0.19330	0.1001	0.004492	−26.18	−25.66
0.19780	0.1001	0.004597	−26.38	−25.86
0.16850	0.2002	0.003916	−29.59	−29.07
0.19395	0.2002	0.004507	−29.79	−29.27
0.26320	0.2002	0.006117	−28.98	−28.46
0.37175	0.2002	0.008640	−29.04	−28.51
0.31430	0.2002	0.007305	−29.51	−28.99
0.19729	0.3007	0.004585	−30.98	−30.46

Table 3 The thermodynamic parameters of mixed-ligand complex formation in the systems $CdEdta^{2-} - L$, En at 298.15 K, and $I = 0.5$ (KNO_3)

Process	lg*K*	$-\Delta_rG^0$/kJ/mol	Δ_rH/kJ/mol	Δ_rS/J/mol/K
$CdEdta^{2-} + NH_3 \leftrightarrow CdEdtaNH_3^{2-}$	1.77 ± 0.05	10.10 ± 0.29	−20.5 ± 0.8	−34.9 ± 2.9
$CdEdta^{2-} + Gly^- \leftrightarrow CdEdtaGly^{3-}$	1.2 ± 0.10	6.85 ± 0.57	−18.6 ± 0.80	−39.4 ± 3.3
$CdEdta^{2-} + En \leftrightarrow CdEdtaEn^{2-}$	1.88 ± 0.03	10.73 ± 0.17	−22.6 ± 1.0	−39.8 ± 3.4
$CdEdta^{2-} + L \leftrightarrow CdEdtaL^{2-}$	2.03 ± 0.06	11.59 ± 0.34	−19.58 ± 0.66	−26.8 ± 1.0
$CdEdta^{2-} + HL^+ \leftrightarrow CdEdtaHL^-$	1.89 ± 0.06	10.79 ± 0.34	−16.7 ± 1.7	−19.9 ± 5.7
$CdEdta^{2-} + H^+ + L \leftrightarrow CdEdtaHL^-$	11.94 ± 0.03	68.15 ± 0.17	−80.02 ± 0.46	−39.8 ± 1.6
$2CdEdta^{2-} + L \leftrightarrow (CdEdta)_2L^{4-}$	2.92 ± 0.03	16.68 ± 0.17	−51.36 ± 0.88	−116.3 ± 3.0
$CdEdtaL^{2-} + CdEdta^{2-} \leftrightarrow (CdEdta)_2L^{4-}$	0.89 ± 0.07	5.08 ± 0.40	−31.8 ± 1.1	−89.6 ± 3.9
$2CdEdta^{2-} + En \leftrightarrow (CdEdta)_2En^{4-}$	3.08 ± 0.05	17.58 ± 0.28	−32.96 ± 0.33	−51.6 ± 1.5
$CdEdtaEn^{2-} + CdEdta^{2-} \leftrightarrow (CdEdta)_2En^{4-}$	1.20 ± 0.04	6.85 ± 0.22	−10.4 ± 0.79	−11.8 ± 2.5

Table 4 ^1H NMR chemical shifts for $CdEdta^{2-} - L$, En systems

Solution composition	Edta		$(CH_2)_6(NH_2)_2$			En
	$(CH_2)_{En}$	$(CH_2)_{ac}$	$(CH_2)_2$	$(CH_2)_2$	CH_2–N	CH_2
$(CH_2)_6(NH_2)_2$, En	–		1.38	1.50	2.66	2.74
$CdEdta^{2-}$	2.72	3.06–3.28	–			–
$CdEdta^{2-}$:L = 1:3	2.59	2.98–3.18	1.26	1.39	2.57	–
$CdEdta^{2-}$:L = 10:1	2.57	2.92–3.14	1.25	1.46	2.75	
$CdEdta^{2-}$:En = 1:5	2.69	3.06–3.27	–			2.69
$CdEdta^{2-}$:En = 4:1	2.70	3.07–3.28				2.92
$HgEdta^{2-}$	2.84	3.24–3.39	–			–
$HgEdta^{2-}$:L = 2:1	2.83	3.27–3.38	1.38	1.61	3.00	–
$HgEdta^{2-}$:En = 2:1	2.68	3.12–3.23				3.11

solutions containing the mercury(II) complexes of the same type were collected. Some NMR spectra are given in Figs. 1 and 2. The chemical shift values of functional groups of EDTA and amines are summarized in Tables 4 and 5.

Results and discussion

The thermodynamic characteristics of addition of L and HL^+ to Cd(II) complexonate are shown in Table 3. The

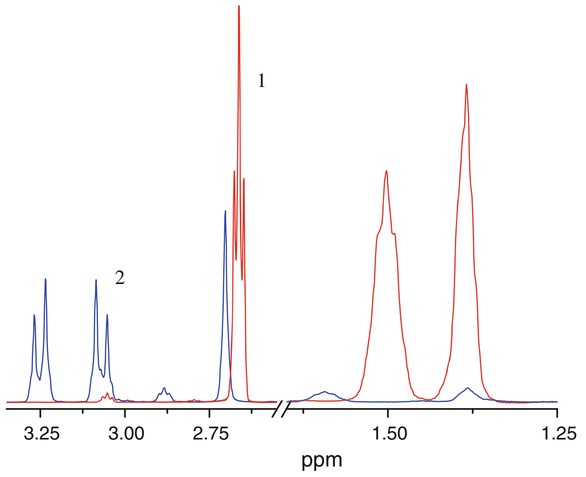


Fig. 1 ^{1}H NMR spectra of solutions: *1* 0.87 mol/kg D_2O $(CH_2)_6(NH_2)_2$, *2* 0.25 mol/kg $Na_2CdEdta$ + 0.034 mol/kg $(CH_2)_6(NH_2)_2$ ($CdEdta^{2-}$:L = 10:1)

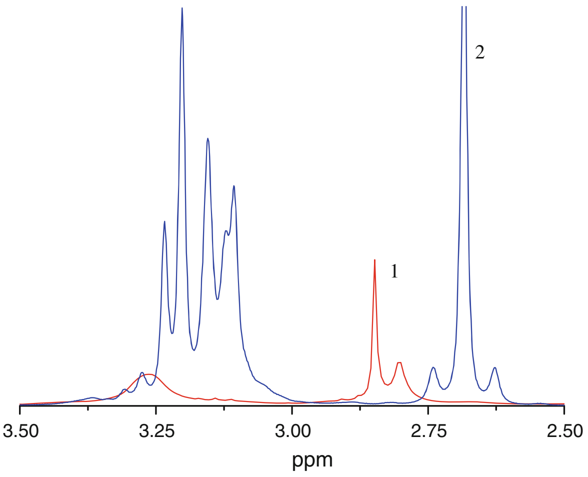


Fig. 2 ^{1}H NMR spectra of solutions: *1* 0.25 mol/kg D_2O $HgEdtaEn^{2-}$, *2* 0.25 mol/kg $(HgEdta)_2En$

uncertainties of indirect treated values are obtained taking into account the rule of error sum. Data for CdEdtaEn complex (Table 4) have been calorimetrically obtained at 298.15 K and $I = 1.5$ (KNO_3) [2].

The addition of L and HL^+ to $CdEdta^{2-}$ is accompanied by negative changes in the enthalpy and entropy (see Table 3), which is characteristic of mixed-ligand complex formation involving the coordinately saturated copper(II), nickel(II), zinc(II), and cadmium(II) complexonates and occurring with a decrease in the EDTA denticity because of the opening of one or two glycinate chelate rings. The factors that cause such thermodynamic characteristics are comprehensively described in [2, 10]. Also, for the En, the heat effects of reactions (5), (6) are close to the heats of addition of the ammonia and glycinate ion to the cadmium(II) complexonate (Table 4). As the formation of the nine-membered chelate ring in the case of hexamethylenediamine is energetically unfavorable because of the loss of configurational entropy of the ligand (especially under opposition with the donor atoms of EDTA), it can be assumed that hexamethylenediamine is coordinated through one donor nitrogen atom. The close values of the heats of addition of NH_3, Gly^-, L, HL^+, and En to the $CdEdta^{2-}$ indicate not only the monodentate character of hexamethylenediamine but also the probable monodentate character of ethylenediamine (Scheme 1).

Noncoordinated NH_2 group in the complexes CdEdtaL and CdEdtaEn can result in binuclear complex formation with bridging function of diamine ligand. Such effect has been studied previously [3, 4] in the case of Hg(II) and Cu(II) complexonates. Thermochemical data using the latter method show the effect. Also, the close values of the thermodynamic parameters of reaction:

$$\begin{aligned}&CdEdta(CH_2)_n(NH_2)_2^{2-} + CdEdta^{2-}\\&\quad = (CdEdta)_2(CH_2)_n(NH_2)_2^{4-},\\&\quad n = 2, 6\end{aligned} \tag{8}$$

Table 3 confirm the monodentate character of diamines in the complexes being studied. It should be noted that the entropy change in reaction (8) involving the hexamethylenediamine is sufficiently less than the same involving En due to the loss of configurational entropy of the ligand with long aliphatic chain.

The received NMR data obtained allowed us to reveal some structure details of complexes being studied. CdEdta complex has comprehensively been studied previously by NMR on different nuclear [11–13]. This further complicated spectrum of $CdEdta^{2-}$ is attributed to cadmium isotopes content and natural abundance. CdEdta complex has an AB quartet pattern for the acetate protons and a singlet for the ethylenic protons, which implies long N → Hg and short O–Hg bond lifetimes. First of all, the presence of AB pattern in spectra being considered demonstrates the hexadentate character of EDTA in mixed complexes, and the loss of its denticity does not takes place. The ^{1}H and ^{13}C chemical shift values of diamines in the case of mercury complexes (see Tables 4, 5) demonstrate well not only the coordinated character of L or En, but also of the remainder of initial chelate structure of metal complexonates. Therefore, in the spectrum of solution containing $(HgEdta)_2En$ complex (HgEdta:En = 2:1), the characteristic AB pattern of the acetate protons takes place, but at the ratio 1:1 where the complex HgEdtaEn is the predominant complex species, the AB pattern gives a width singlet (Fig. 2) that can be a consequence of the weakening of the bonds N → Hg (it becomes more labile) or decreasing of EDTA denticity.

Table 5 ^{13}C NMR chemical shifts for $CdEdta^{2-}$ − L, En systems

Solution composition	Edta			$(CH_2)_6(NH_2)_2$			En
	$(CH_2)_{En}$	$(CH_2)_{ac}$	COO^-	$(CH_2)_2$	$(CH_2)_2$	CH_2–N	CH_2
$(CH_2)_6(NH_2)_2$, En	–			26.73	32.44	41.32	43.58
$CdEdta^{2-}$	52.13	58.90	178.81	–			–
$CdEdta^{2-}$:L = 1:3	51.17	58.16	177.62	25.96	31.63	40.84	–
$CdEdta^{2-}$:L = 10:1	52.12	58.92	178.76	25.98	–	41.40	
$CdEdta^{2-}$:En = 1:5	51.44	58.87	178.29	–			43.18
$CdEdta^{2-}$:En = 4:1	51.93	58.79	178.62				43.27
$HgEdta^{2-}$	51.36	58.59	177.03	–			–
$HgEdta^{2-}$:L = 2:1	51.68	58.88	176.77	26.02	30.78	44.64	–
$HgEdta^{2-}$:En = 2:1	51.56	58.76	178.86	–			45.92

Thermodynamic data obtained do not exclude the existence of the complex $CdEdtaEn^{2-}$ with bidentate character of the En due to opening of glycinate chelate [2]. The equilibrium among the different forms of $CdEdtaEn^{2-}$ complex in which the ethylenediamine is bi- and monodentate apparently is shifted to the complex with monodentate character of the En. The reaction (8) is less exothermic in the case of En. This can be due to the opening of ethylenediamine chelate ring or participation of the noncoordinated NH_2 group of En in a weak interaction with the acetate groups of the complexone through hydrogen bonding in CdEdtaEn.

Conclusions

All these facts allow us to consider that under saturation of coordination sphere and opposition between donor atoms of two ligands, the coordination of the En can take place without chelate structure arising. The coordination of ancillary amine ligand brings about the substitution of inner sphere water molecule in $MEdta(H_2O)^{2-}$ (M = Cd, Hg) (Scheme 1). The ethylenediamine can be monodentate in the mononuclear mixed complex or bidentate with the bridging function in the binuclear complex. Such coordination mode is sufficiently unusual for En.

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