

Thermodynamics of Ion Association. XXI. Mixed Complexes of Transition Metal Ions with Aminopolycarboxylate and Amine Ligands¹

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The association of the divalent metal ions manganese, cobalt, nickel, zinc, and cadmium with ethylenediaminediacetic acid (EDDA) and ethylenediaminedipropionic acid has been studied potentiometrically at 25° and a constant ionic strength of 0.10 *M*. A sensitive calorimeter has been used to measure the enthalpy changes. The further association, with ethylenediamine, of these 1:1 complexes together with CuEDDA to form 1:1:1 mixed complexes has also been studied by the same methods. The thermodynamic functions are discussed in terms of the important factors involved in the association reactions, and the temperature-dependent and -independent components of ΔH have been calculated.

Introduction

In recent years there has been considerable interest in the formation of metal complexes in which the metal ion is simultaneously bound to two or more different ligand molecules. Writing K_A and K_B , respectively, for the stability constants of the separate complexes MA and MB involving ligands A and B and K_{AB} for the stability constant of the mixed complex MAB, we can distinguish between two types of mixed complex formation. In the first, K_A and K_B have similar values so that each of the ligand molecules is capable of displacing the other when their relative concentrations are changed by a small amount. In the second type, $K_A \gg K_B$ or $K_B \gg K_A$ and one of the complexes MA or MB is considerably more stable than the other. In such systems, the stable metal complex, in which the metal ion is not fully coordinated to the ligand molecule, is allowed to react with a second ligand which is then forced to bond to the metal sites not already occupied. In such cases, there is the possibility of characterizing the higher coordination sites of the metal ion. In addition, in biological systems, there is a special interest in the possibility that the coordination of a metal ion to a first ligand may cause discrimination for a second ligand.

Previous mixed complex studies have been confined to stability measurements and in some instances the mixed complexes have been found to be more stable than predicted on statistical grounds. Metal mixed complexes formed by competing ligands have been investigated by a number of workers. Thus copper(II) readily forms mixed complexes with various nitrogen- and oxygen-coordinating ligands but is reluctant to bind more than two bidentate ligands.³⁻⁷ Similar studies have also been made with nickel(II)⁸⁻¹¹ and a number

of methods for the calculation of K_{AB} values have been described.^{5,7-9}

Potentiometric studies, in which a stable metal chelate is allowed to react with a second ligand ($K_A \gg K_B$), have heretofore been mainly confined to multicharged metal ions such as Th⁴⁺, Zr⁴⁺, and La³⁺.¹²⁻¹⁴ In the present work, a potentiometric and calorimetric study has been made of the formation of the ethylenediaminediacetate (EDDA) and ethylenediaminedipropionate (EDDP) complexes of the divalent metal ions Mn²⁺, Co²⁺, Ni²⁺, Cu²⁺, Zn²⁺, and Cd²⁺ and the subsequent formation of mixed complexes of these stable chelates with ethylenediamine (en).

Experimental Section

Materials.—Grade A glassware and reagent grade chemicals were used, and solutions were prepared with doubly distilled water; carbon dioxide was excluded by bubbling with nitrogen. The metal nitrate solutions were analyzed by titration with standard EDTA and also by exchanging the cations for hydrogen ions on a Dowex 50 ion-exchange resin column and titrating the liberated nitric acid with standard potassium hydroxide solution. Ethylenediamine dihydrochloride was prepared from ethylenediamine (Fisher Scientific Corp.) and concentrated hydrochloric acid in ethanol and recrystallized three times from water-ethanol mixtures. Ethylenediaminediacetic acid (K & K Laboratories) was purified by two recrystallizations from hot water. Ethylenediaminedipropionic acid was prepared according to a modified method of Martell and Chaberek.¹⁵ To 129 g (0.8 mol) of rapidly stirred dicyanoethylethylenediamine, 400 ml of concentrated HCl was added dropwise over a period of 1.5 hr. The reaction flask was cooled down to 0-5° and stirring was continued at room temperature for 2 hr. The yellow solution was then refluxed for 6 hr during which time gaseous HCl was bubbled through the reaction mixture. After standing overnight the solution was evaporated to dryness under vacuum, and the residue was dissolved in hot water, mixed with strong aqueous sodium hydroxide solution, and refluxed in a stream of air to remove the ammonia. Ethylenediaminedipropionic acid dihydrochloride was isolated after concentrating and acidifying with concentrated HCl, by extraction with ethanol. It was recrystal-

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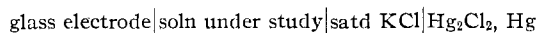
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lized from ethanol. After a potentiometric titration with standard potassium hydroxide, some impurities were still present and so the chloride was converted to the sulfate with silver sulfate. The hot solution was then made strongly acidic with sulfuric acid and cooled. The resulting colorless blades of $\text{EDDP} \cdot \text{H}_2\text{SO}_4 \cdot \text{H}_2\text{O}$ were recrystallized three times from hot 0.5 *N* H_2SO_4 .

Potentiometric Experiments.—Emf measurements were made at $25 \pm 0.02^\circ$ with cells of the type



using Beckman Type 39099-E3 glass electrodes, a Leeds and Northrup Type K3 potentiometer, and a Victoreen picometer (Model 474) as null detector; the emf reproducibility was ± 0.1 mV. Each cell incorporated a pair of glass electrodes so that any irregularity in the behavior of one of them was immediately apparent. The electrode systems were standardized before and after each experiment with NBS standard buffer solutions as previously described^{16,17} pH ($= -\log a_{\text{H}^+}$) values were converted to hydrogen ion concentration by using an f_{H^+} activity coefficient value (0.7815) calculated from the Davies equation.¹⁸

Calorimetric Experiments.—The calorimeter and experimental technique previously described¹⁶ were modified slightly for this work. A single calorimeter vessel with a working volume of 150 ml was used and temperatures were measured with a 10^5 -ohm thermistor (Type A189, Victory Engineering Co.) incorporated in a dc Wheatstone bridge. The bridge was energized by a 1.35-V mercury cell and the other arms of the bridge consisted of a 10^5 -ohm standard resistor contained in a constant-temperature bath and a 10^6 -ohm "Helipot" potential divider connected in series with a similar 100-ohm potentiometer to provide for both coarse and fine balancing of the bridge. The out-of-balance signal, amplified by means of a dc null detector (Leeds and Northrup, Model 9834) was fed to a strip chart recorder (Sargent, Model SR). The electrical calibration of the calorimeter and the cooling of its contents were done as described previously.¹⁶ A double titrator consisting of two motor-driven burets (Dosimat automatic buret, Metrohm Herisau, Switzerland) was used in place of the single titrator so that controlled additions of acid as well as base could be made to the calorimeter. The advantage of not having to equilibrate metal ion and ligand solutions at high pH for lengthy periods was especially noticeable in the case of Co(II). The possibility of oxidation to Co(III) during the preequilibrium stage was eliminated. In addition, calorimetric titrations could be conducted in both directions along the titration curves.

The enthalpies of formation of the EDDA and EDDP complexes of the metal ions were obtained from calorimetric titrations of 1:1 mixtures of ligand and metal nitrate solutions ($(5-10) \times 10^{-3}$ *M*) with potassium nitrate added to maintain an ionic strength of 0.10 *M*. After equilibration overnight at $25 \pm 0.002^\circ$, a small volume of 0.1 *M* potassium hydroxide solution was added, and the titration was performed by adding 1.0–1.5-ml portions of 0.1 *M* nitric acid also at $25 \pm 0.002^\circ$. After each addition, the temperature of the calorimeter contents was brought back to 25° with a cooler consisting of a small glass bulb through which water and nitrogen gas could be passed. Parallel experiments were made of the heat of mixing of the nitric acid solution with 0.10 *M* potassium nitrate and the corrections were found to be negligible. In typical mixed complex experiments, 1:1:1 mixtures of metal nitrate, ethylenediamine dihydrochloride, and EDDA ($(5-10) \times 10^{-3}$ *M* with sufficient potassium nitrate to give an ionic strength of 0.10 *M*) were placed in the calorimeter. After temperature equilibrium, base was added until 95% of the mixed complex was formed, and the titration with nitric acid was carried out as described.

All calculations were performed with the aid of CDC 6400 computer.

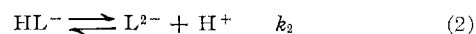
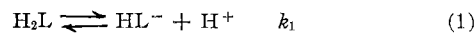
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Results and Discussion

It was first necessary to determine the thermodynamic functions for the successive proton dissociations of EDDA written as L in the equations



Potentiometric measurements of hydrogen ion activities were made on the addition of sodium hydroxide to $(5-10) \times 10^{-3}$ *M* EDDA at an ionic strength maintained within 2% of 0.10 *M* by the addition of potassium nitrate. Concentrations of ionic species were calculated in the usual manner from mass balance and electroneutrality expressions,¹⁹ and the values of the dissociation constants at 25° given as the mean of at least 25 independent points are $\text{pk}_1 = 6.550 \pm 0.005$ and $\text{pk}_2 = 9.62 \pm 0.01$. These may be compared with two sets of values available in the literature: $\text{pk}_1 = 6.48$ and $\text{pk}_2 = 9.57$ at 25° at $I = 0.1$ *M* KNO_3 ;²⁰ $\text{pk}_1 = 6.42$ and $\text{pk}_2 = 9.46$ at 30° in 0.1 *M* KCl .²¹ The results of at least 15 independent calorimetric measurements of the enthalpies of deprotonation gave $\Delta H_1 = 7.31 \pm 0.08$ kcal mol⁻¹ and $\Delta H_2 = 7.45 \pm 0.08$ kcal mol⁻¹ for reactions 1 and 2, respectively.

In the presence of the metal ions with a 1:1 metal:ligand ratio, the additional complex formation equilibrium may be formulated



The calculation of *K* values from the experimental data was performed as previously described²⁰ and the values included in Table I are the means of at least 20 inde-

TABLE I
THERMODYNAMIC FUNCTIONS FOR THE ASSOCIATION OF
TRANSITION METAL IONS WITH ETHYLENEDIAMINEDIACETIC
ACID ($I = 0.1$ *M* (KNO_3))

Reaction	Log <i>K</i>	$-\Delta G$, kcal mol ⁻¹	$-\Delta H$, kcal mol ⁻¹	ΔS , cal deg ⁻¹ mol ⁻¹
$\text{Mn}^{2+} + \text{EDDA}^{2-}$	7.05 ± 0.02	9.62	0.85 ± 0.1	29.4
$\text{Mn}^{2+} + \text{en}$		3.75	2.80	3.0
$\text{Co}^{2+} + \text{EDDA}^{2-}$	11.25 ± 0.02	15.35	5.76 ± 0.1	32.2
$\text{Co}^{2+} + \text{en}$		8.10	6.90	4.0
$\text{Co}^{2+} + 2\text{IMDA}^{2-}$		16.5	6.0	35.8
$\text{Ni}^{2+} + \text{EDDA}^{2-}$	13.65 ± 0.02	18.62	10.0 ± 0.2	28.9
$\text{Ni}^{2+} + \text{en}$		10.25	9.05	4.0
$\text{Ni}^{2+} + 2\text{IMDA}^{2-}$		19.2	9.5	33.1
$\text{Zn}^{2+} + \text{EDDA}^{2-}$	11.22 ± 0.01	15.31	6.1 ± 0.1	31.0
$\text{Zn}^{2+} + \text{en}$		8.05	7.0	3.5
$\text{Zn}^{2+} + 2\text{IMDA}^{2-}$		16.9	5.9	37.5
$\text{Cd}^{2+} + \text{EDDA}^{2-}$	9.40 ± 0.02	12.82	5.38 ± 0.1	25.0
$\text{Cd}^{2+} + 2\text{IMDA}^{2-}$		13.7	5.5	27.9

pendent measured values for each metal ion. The experiments at 30° of Chaberek and Martell²⁰ yielded *K* values (log *K*: for NiEDDA, 13.5; CoEDDA, 11.2; ZnEDDA, 11.1; CdEDDA, 8.8) which are in good agreement with those in Table I. Enthalpy

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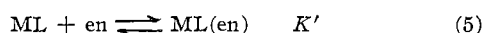
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titrations were made by the addition of nitric acid to solutions containing metal nitrate ($(5-10) \times 10^{-3} M$), EDDA ($(5-10) \times 10^{-3} M$), and sodium hydroxide together with sufficient potassium nitrate to maintain the ionic strength within 2% of 0.10 *M*. The measured heat changes, Q_{expt} , may be expressed in terms of the heats of formation in solution of the species represented by the subscripts in the equation

$$Q_{\text{expt}} = Q_{\text{H}_2\text{O}} + Q_{\text{HL}^-} + Q_{\text{H}_2\text{L}} + Q_{\text{ML}} \quad (4)$$

The changes in the concentration of ionic species from point to point in the enthalpy titrations may be used to calculate the corresponding Q values from the expressions $Q_{\text{H}_2\text{O}} = \Delta H_{\text{H}_2\text{O}}(-\Delta[\text{OH}^-])$ in which the heat of formation of water is $\Delta H_{\text{H}_2\text{O}} = -13.49 \text{ kcal mol}^{-1}$ and $Q_{\text{HL}} = \Delta H_{\text{HL}}(\Delta[\text{HL}] + \Delta[\text{H}_2\text{L}])$, $Q_{\text{H}_2\text{L}} = \Delta H_{\text{H}_2\text{L}}(\Delta[\text{H}_2\text{L}])$, and $Q_{\text{ML}} = \Delta H_{\text{ML}}(\Delta[\text{M}])$. Approximately 15 independent points were used for the determination of ΔH and the thermodynamic functions are given in Table I together with the corresponding functions of ethylenediamine (en)²² and diiminodiacetate (IMDA).²³ Since the pH of the calorimeter contents was also measured during an enthalpy titration, values of K for reaction 3 could also be calculated from the titration data. The resulting $\log K$ values were always within $\pm 0.08 \log K$ unit of those obtained from the separate potentiometric experiments. It was not possible to obtain thermodynamic data for the formation of the copper mono-EDDA complex on account of the exceptionally high stability. Data for mixed complex formation, however, could be obtained by assuming stoichiometric formation of the CuEDDA species; subsequent addition of ethylenediamine and titration with nitric acid enabled the calculation of thermodynamic data for the formation of the mixed complex by the reaction



The results of typical potentiometric and calorimetric experiments on the nickel mixed complex and of a calorimetric experiment for copper are summarized in Table II. Thermodynamic functions are collected in Table III together with the values for the stepwise formation of the $\text{M}(\text{en})_2^{2+}$ complexes.²²

It is seen in Table I that, with the exception of manganese, the mono-EDDA complexes are formed with exothermic enthalpies similar to those of the $\text{M}(\text{en})_2$ complexes. It is clear that the greatest contribution to ΔH is made by the coordination of N to the metal ion. Interactions with carboxylate groups, of a more electrostatic character, would be expected to have only a small and probably endothermic effect.¹⁹ Thus in the case of manganese, the metal ion of greatest A character,²⁴ the $-\Delta H$ value is considerably smaller as compared with the other metal ions. Interactions to form the bis-IMDA complexes, involving two dinegative anions, also take place with similar enthalpy

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TABLE II^a
DETERMINATION OF THERMODYNAMIC FUNCTIONS FOR MIXED
COMPLEX FORMATION (25°, $I = 0.10 M$ (KNO₃))

10 ³ [HNO ₃], <i>M</i>	pH	10 ³ [en], <i>M</i>	10 ³ [ML], <i>M</i>	10 ³ [ML- en], <i>M</i>	Log <i>K'</i>	$-\Delta H$, kcal mol ⁻¹
Expt 1						
0.200	6.85	3.43	1.76	2.76	6.63	13.3
0.300	6.73	2.47	2.11	2.38	6.64	13.4
0.500	6.51	1.27	2.80	1.63	6.65	13.2
0.600	6.41	0.87	3.12	1.28	6.66	13.3
0.700	6.30	0.59	3.43	0.94	6.67	13.4
						Av 13.3 ± 0.1
Expt 2						
0.200	7.49	35.12	3.41	1.11	5.53	9.4
0.300	7.36	26.87	3.60	0.90	5.52	9.5
0.400	7.23	19.94	3.77	0.70	5.52	9.6
0.500	7.11	14.53	3.91	0.53	5.52	9.4
0.600	6.99	10.08	4.04	0.37	5.53	9.4
						Av 9.46 ± 0.1

^a Initial total concentrations: expt 1, $[\text{Cu}^{2+}]_t = [\text{EDDA}]_t = [\text{en}]_t = 4.57 \times 10^{-3} M$; expt 2, $[\text{Ni}^{2+}]_t = [\text{EDDP}]_t = [\text{en}]_t = 4.60 \times 10^{-3} M$.

TABLE III
THERMODYNAMIC FUNCTIONS FOR THE FORMATION OF 1:1:1
MIXED COMPLEXES (25°, $I = 0.10 M$ (KNO₃))

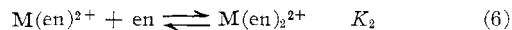
Reaction	Log <i>K</i>	$-\Delta G$, kcal mol ⁻¹	$-\Delta H$, kcal mol ⁻¹	ΔS , cal deg ⁻¹ mol ⁻¹
MnEDDA + en	2.1 ± 0.2	2.9
Mn(en) ²⁺ + en	2.1	2.9	3.20	-1.0
CoEDDA + en	4.36 ± 0.01	5.95	8.1 ± 0.2	-7.2
CoEDDP + en	3.95 ± 0.04 ^a	5.39
Co(en) ²⁺ + en	4.73	6.45	7.05	-2.0
NiEDDA + en	6.31 ± 0.01	8.61	9.86 ± 0.1	-4.2
NiEDDP + en	5.51 ± 0.02 ^a	7.52	9.46 ± 0.1	-6.5
Ni(en) ²⁺ + en	6.30	8.65	8.85	-0.7
CuEDDA + en	6.66 ± 0.02	9.09	13.3 ± 0.1	-14.1
Cu(en) ²⁺ + en	9.31	12.68	12.4	0.9
ZnEDDA + en	4.44 ± 0.01	6.06	7.1 ± 0.1	-3.5
ZnEDDP + en	4.03 ± 0.06 ^a	5.5	6.6 ± 0.2	-3.7
Zn(en) ²⁺ + en	5.15	7.05	4.90	7.2
CdEDDA + en	4.33 ± 0.01	5.91	7.1 ± 0.1	-4.0
CdEDDP + en	4.15 ± 0.08 ^a	5.66
Cd(en) ²⁺ + en	4.59	6.2

^a Mr. E. Burke performed these potentiometric titrations.

changes even though four charged carboxylate groups are presented to the metal ion. It is interesting to note that the enthalpies of formation of the EDDA complexes are more exothermic than the extremely stable EDTA complexes in the cases of cobalt, nickel, and zinc [$\Delta H(\text{CoEDTA}^{2-}) = -4.20 \text{ kcal mol}^{-1}$, $\Delta H(\text{NiEDTA}^{2-}) = -7.55 \text{ kcal mol}^{-1}$, and $\Delta H(\text{ZnEDTA}^{2-}) = -4.85 \text{ kcal mol}^{-1}$].¹⁹

This reflects the greater strain in MEDTA²⁻ complexes as compared with MEDDA; the greater stability of the former results from the much more positive entropy changes accompanying their formation. The latter is attributed to the release of solvated water molecules from the tetranegative anion during complex formation and concomitant charge neutralization. Electrostatic contributions to the bonding energy for highly charged anions will also be expected to contribute to the relative endothermicity for the formation of MEDTA²⁻ as compared with MEDDA.

It is seen in Table III that the K values for reaction 5 are, with the exception of copper, similar to the K_2 values for the reaction



The coordinated charged carboxyl groups of EDDA and EDDP therefore appear to have little influence on an association constant in which the only coordination taking place is that of two nitrogen atoms. This is in spite of a less favorable statistical term for reaction 3 in which fewer possible coordination sites are available than in reaction 5. The differences between these systems are manifested in the ΔH and ΔS values. In the case of copper, it is seen that K for the mixed complex is considerably less than K_2 , reflecting the special stability of $Cu(en)_2^{2+}$ in which the nitrogen atoms are favorably oriented for the formation of short Cu-N bonds in the plane of coordination. The difference between these copper complex formation constants results entirely from the large negative ΔS value for reaction 5 as compared with that for reaction 6 (Table III). This suggests that in the mixed complex $CuEDDAen$ the carboxylate groups may not be bound to the copper ion. The resultant charge separation and retention of some solvent ordering would account for the observed negative ΔS value.

It is convenient to divide the thermodynamic functions into two parts:²⁵ (1) ΔG_e and ΔH_e representing long-range electrostatic forces depending upon environment and increasing with temperature and (2) ΔG_c and ΔH_c reflecting both the covalent interactions and the structural changes. The experimental free energy change may be written¹

$$\Delta G = RT \ln 55.5 + \Delta G_e + \Delta G_c \quad (7)$$

where the first term on the right-hand side of eq 7 represents the cratic part of the free energy, 55.5 being the number of moles contained in 1000 g of water. For purely electrostatic interactions, the free energy will be inversely proportional to the dielectric constant, and the contributions to ΔG and ΔH may be calculated from the equations¹

$$\Delta G_e = \nu(\Delta S + R \ln 55.5) \quad (8)$$

$$\Delta H_e = (T - \nu)(\Delta S + R \ln 55.5) \quad (9)$$

in which ν is a temperature characteristic of the solvent (219°K for water). The temperature-independent

part of the enthalpy, ΔH_c , is given by the difference $\Delta H - \Delta H_e$ and values calculated for the systems in Table III are given in Table IV.

The similarity of the ΔH_c values in Table IV in-

TABLE IV
- ΔH_c VALUES FOR THE REACTION $ML + en \rightleftharpoons MLen$

Metal ion	L = en	L = EDDA	L = EDDP
Co ²⁺	8.0	8.2	...
Ni ²⁺	9.4	10.1	9.6
Cu ²⁺	13.1	12.8	...
Zn ²⁺	6.1	7.4	6.9
Cd ²⁺	...	7.4	...

icates that all four N atoms are coordinated in each case. For copper, the removal of the electrostatic components results in ΔH_c values for L = EDDA and L = en which agree to within experimental uncertainty in contrast to the larger differences in ΔH in Table III. The considerable ΔS difference of 15 cal deg⁻¹ mol⁻¹ in Table III between $CuEDDA + en$ and $Cu(en)_2^{2+} + en$ may indicate a degree of charge separation with the release of coordinated carboxyl groups of $CuEDDA$ in the formation of the mixed complex.

Similar comparison of data in Table IV may be made in the case of the zinc complexes in which the ΔH difference between reactions 5 and 6 is almost entirely accounted for by the electrostatic component, ΔH_e . In their interactions with nitrogen and oxygen coordinating ligands, it is well known that ions such as Co²⁺ and Ni²⁺ usually form octahedral complexes whereas Cd²⁺ and Zn²⁺ prefer tetrahedral coordination. It is of interest to examine the values of ΔH_c in the light of such coordination preferences. There is a significant change in ΔH_c as we go from Zn(en)²⁺ ($\Delta H_c = -8.0$ kcal mol⁻¹) to Zn(en)₂²⁺ ($\Delta H_c = -6.1$ kcal mol⁻¹) accompanying the change from an octahedral to a tetrahedral structure. This is in contrast to the almost constant corresponding ΔH_c values for Co²⁺ and Ni²⁺ which maintain an octahedral coordination. In the case of ZnEDDA ($\Delta H_c = -9.2$ kcal mole⁻¹) and ZnEDDAen ($\Delta H_c = -7.4$ kcal mol⁻¹) a large difference in ΔH_c is observed and this points to a tetrahedral coordination for the mixed complex ZnEDDAen. It occurs in spite of the necessity for breaking the already coordinated metal-carboxylate oxygen bonds in ZnEDDA. In a previous paper¹ it was pointed out, however, that the contribution of such metal-carboxylate bonds to the total ΔH_c values is rather small.

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