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A Polarographic Study of Cadmium(II)–Amino Acid Complexes[1]

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Complexes of cadmium(II) with several amino acid anions have been studied polarographically. The complexes investigated were those of glycine, α-alanine, β-alanine, phenylalanine, γ-aminobutyric acid, leucine, and valine. Cadmium(II) forms 1:1, 1:2, and 1:3 complexes with most of these amino acids. Evidence indicates that these complexes are chelates. The concentration dissociation constants of the complexes are reported, and the effects of ring size and steric factors are discussed.

Introduction

In spite of the intense interest in coördination complexes in recent years, it was found that little has been done with cadmium(II) complexes of amino acids. Albert[3] recently investigated glycinate complexes of cadmium(II) and reported 1:1 and 1:2 chelate complexes. A 1:3 complex with glycinate was found by Li, White, and Yoest,[4] who reported a formation constant and postulated a structure. Rebertus,[5] in a polarographic and potentiometric investigation, found evidence for a 1:3 complex of cadmium(II) valinate in addition to the lower complexes. Chelate complexes of cadmium(II) with cysteine and histidine were studied by Li and Manning.[6] These workers believe that they found evidence for tridentate behavior of the trifunctional substance, cysteine. Li and Chen[7] investigated complexes of several polypeptides and glycine derivatives with cadmium(II). Stable complexes were found for each of the polypeptides studied.

The objective of this work was to study the complexes of cadmium(II) with several of the simpler amino acids.

Experimental

A. Materials.—Reagent grade chemicals and Eastman white label amino acids were used without purification. Potentiometric titration of the amino acids indicated purity of 99.9% or higher in all cases. Solutions were refrigerated and used promptly, to minimize bacterial growth. Ionic strengths were adjusted with potassium nitrate, which evidently forms a weak nitrate complex with cadmium(II). A half-wave potential shift of 13 mv. was caused by increasing the nitrate concentration from 0.1 to 2.0 *M*. Though this is minor compared to the shift due to amino acids, its effect was minimized by maintaining a nearly constant nitrate ion concentration, at 2 *M*.

B. Apparatus.—Polarograms were obtained using a Sargent-Heyrovsky Model XII recording polarograph. A wave spreader was incorporated into the circuit to increase precision. A Leeds & Northrup potentiometer, Model K, was used to obtain voltage readings. A Beckman Model G *p*H meter was used to measure *p*H.

C. Techniques and Procedures.—Solutions for analysis contained 0.001 *M* cadmium nitrate, and varying concentrations of complexing agent. Sufficient potassium nitrate was added to maintain an ionic strength of 2.00. Solutions were prepared and analyzed at 25.0 ± 0.1°.

Reversibility of electrode reduction was verified by plotting $\log i/i_d - i$ *vs.* $E_{d.e.}$. The reaction was considered reversible since the slope of the plot was found to correspond to that observed in the reduction of simple cadmium(II).

Half-wave potentials were reproducible to ±0.002 volt. Corrections for iR drop were found to be negligible in all cases.

In the study of the higher complexes, ligand concentration was varied directly at constant *p*H. Low anionic concentrations were required to form the lower complexes; ligand concentration was controlled in this range by varying *p*H, at constant amino acid concentration. The concentration of ligand anion was calculated from the *p*H of the solutions, the dissociation constant of the amino acid, and the concentration of undissociated amino acid.

Results

Coördination numbers of cadmium(II) in the amino acid media studied were calculated from the slopes of plots of $\Delta E_{1/2}$ *vs.* log concentration of anion, according to the equation[7]

$$\Delta E_{1/2}/\log (X^{-b}) = -p\ 0.0591/n$$

(1) Presented at the 138th National Meeting of the American Chemical Society, New York, N. Y., September 12, 1960.

(2) Abstracted in part from: (a) Ph.D. thesis of A. M. Cruickshank, Univ. of Mass., 1954; (b) M.S. thesis of J. T. Donoghue, Univ. of Mass., 1960; and (c) Honors thesis of J. F. Pysz, Jr., Univ. of Mass., 1959.

(3) A. Albert, *Biochem. J.*, **46**, Proc. of Soc. XXXIX (1950).

(4) N. C. Li, J. M. White, and R. L. Yoest, *J. Am. Chem. Soc.*, **78**, 5218 (1956).

(5) R. L. Rebertus, Ph.D. thesis, Univ. of Ill., 1955.

(6) N. C. Li and R. A. Manning, *J. Am. Chem. Soc.*, **77**, 5225 (1955).

(7) N. C. Li and M. Chen, *ibid.*, **80**, 5678 (1958).

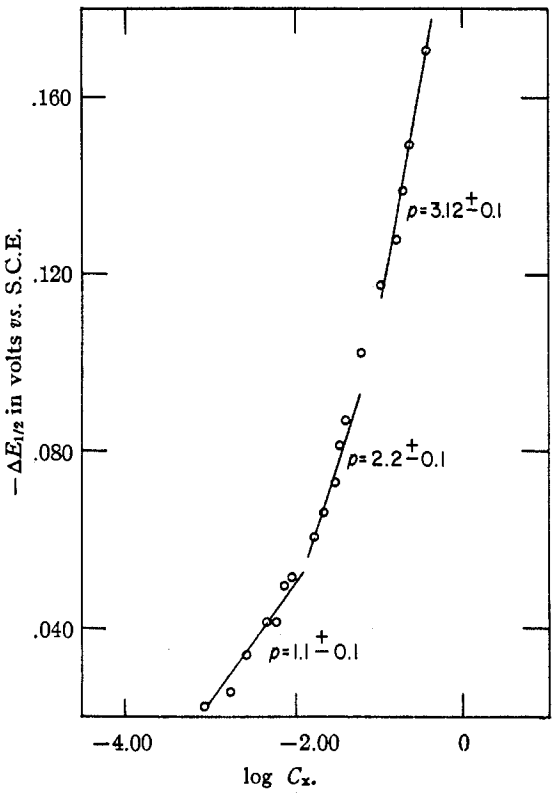


Fig. 1.—Cadmium(II) β-alaninate complexes.

where $\Delta E_{1/2}$ is the shift of half-wave potential and p is the number of ligands bound.

The over-all concentration dissociation constants of the complexes studied were determined by application of the equation[8]

$$\Delta E_{1/2} = (E_{1/2})_c - (E_{1/2})_s = (0.0591/n) \log (K_c f_c k_s / f_s k_c) - p\ 0.0591/n \log (X^{-b})$$

where f is the activity coefficient, k is a constant proportional to the square root of the diffusion coefficient of the ion, and n is the number of electrons transferred in the reduction. The subscripts s and c refer to simple cadmium ions and the complex, respectively. The ratio, $f_c k_s / f_s k_c$, was assumed to be unity.

The p values and dissociation constants were evaluated for each of the amino acid complexes. The cadmium(II) β-alaninate results are typical of those obtained for all systems, and are presented in detail in Fig. 1 and Table I. The pK values, similarly obtained for the other systems, are summarized in Table II.

The values for p, given in Fig. 1 and Table II, were obtained from a least squares treatment of the polarographic data. The precision indicated in the figure is a measure of the agreement between the conventional point slope formula values and the slopes obtained from least squares treatment.

(8) I. M. Kolthoff and J. J. Lingane, "Polarography," Interscience Publishers, New York, N. Y., 1952, Vol. I, p. 214.

TABLE I

HALF-WAVE POTENTIAL OF CADMIUM(II) β-ALANINATE COMPLEXES AS A FUNCTION OF THE pH OF SOLUTIONS CONTAINING 0.001 M CADMIUM(II) AND VARYING CONCENTRATION OF LIGAND

Solutions of ionic strength 2.00

pH	Nominal concn. of β-alanine	Molarity of alaninate (calcd.)	$-E_{1/2}$ vs. S.C.E.	pK diss.
...	0.100	0.00	0.588	...
8.13	.100	8.60×10^{-4}	.611	3.72
8.42	.100	1.67×10^{-3}	.614	3.65
8.64	.100	2.74×10^{-3}	.623	3.82
8.89	.100	4.78×10^{-3}	.630	3.65
9.00	.100	6.06×10^{-3}	.630	3.72
9.20	.100	9.30×10^{-3}	.639	3.65
9.28	.100	1.10×10^{-2}	.641	3.75
			Av. pK_1 =	3.71 ± 0.1
9.52	.100	1.76×10^{-2}	.649	5.54
9.65	.100	2.16×10^{-2}	.655	5.63
9.82	.100	2.98×10^{-2}	.661	5.61
9.95	.100	3.65×10^{-2}	.669	5.58
10.11	.100	4.55×10^{-2}	.676	5.60
10.41	.100	6.26×10^{-2}	.691	
			Av. pK_2 =	5.59 ± 0.0
10.50	.110	0.110	.706	6.83
10.82	.150	.150	.716	6.83
10.86	.200	.200	.727	6.86
10.61	.260	.260	.738	6.83
10.61	.400	.400	.759	7.03
			Av. pK_3 =	6.88 ± 0.1

Discussion

All of the amino acid complexes of cadmium(II) studied in this investigation were found to dissociate reversibly at the dropping electrode. All of the amino acid anions except leucinate and γ-aminobutyrate were found to form 1:1, 1:2, and 1:3 complexes. For leucinate, neither a 1:1 nor 1:2 complex was found, due to precipitation effects which occurred in the concentration range in which these quite unstable complexes probably exist. For similar reasons, it was impossible to characterize a 1:2 complex of cadmium(II) and γ-aminobutyrate.

Table I shows the 1:1 complex of cadmium(II) β-alaninate to be the predominant species in the ligand concentration range 10^{-4} to 10^{-2} M. The 1:2 complex predominates from 0.01 to 0.06 M. The highest order complex found, the 1:3, is stable above 0.1 M. Similar statements can be made regarding the other complexes; the more stable the complexes the lower the concentration for the various ranges.

TABLE II

CONCENTRATION DISSOCIATION CONSTANTS OF CADMIUM(II)–AMINO ACID COMPLEXES

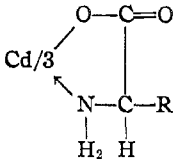
Ionic strength 2.0

Amino acid	1:1 Complex		1:2 Complex		1:3 Complex	
	Exptl. p	pK_1	Exptl. p	pK_2	Exptl. p	pK_3
Glycine	1.0 ± 0.1	5.68 ± 0.1	1.9 ± 0.1	8.45 ± 0.1	2.95 ± 0.1	11.0 ± 0.1
α-Alanine	1.1 ± 0.1	5.13 ± 0.0	2.1 ± 0.1	7.82 ± 0.1	2.95 ± 0.1	9.16 ± 0.5
β-Alanine	1.1 ± 0.1	3.71 ± 0.1	2.2 ± 0.1	5.59 ± 0.0	3.12 ± 0.1	6.88 ± 0.1
Phenylalanine	0.9 ± 0.1	4.06 ± 0.1	2.0 ± 0.1	6.92 ± 0.0	3.00 ± 0.1	7.77 ± 0.1
γ-Aminobutyric acid	$.9 \pm 0.1$	3.39 ± 0.1	...	...	2.9 ± 0.1	5.71 ± 0.2
Leucine	...	...	...	...	3.06 ± 0.1	8.47 ± 0.2
Valine	$.9 \pm 0.1$	4.58 ± 0.1	...	...	3.05 ± 0.1	7.85 ± 0.2

The results obtained (see Table II) can be correlated in terms of two factors: (1) ring size, assuming the complexes to be chelates; and (2) steric effects.

The most stable complexes are those involving ligands capable of forming five-membered chelate rings; these are glycinate, α-alaninate, leucinate, valinate, and phenylalaninate. Stability decreases in the order listed. The β-alaninate complex, a six-membered ring chelate, is less stable than those involving the five-membered ring, as is generally observed. The γ-aminobutyrate, capable of forming only a seven-membered ring—if chelation does occur—forms the least stable complex, as one would predict.

With ring size constant, one can see the influence of steric factors. For the five-membered ring series, which can be visualized as



where R = H, CH_3, $CH_2CH(CH_3)_2$, $CH(CH_3)_2$, or $CH_2C_6H_5$, stability is found to decrease in the order listed. This order parallels an increase in steric bulk of the substituent group. It is evident that interposing the methylene group between the ring and the isopropyl group decreases steric strain, with the result that the isobutyl complex is more stable than the isopropyl.

Chelated structures are clearly indicated for the cadmium(II)–amino acid complexes. If monodentate linkage were involved, one might expect the cadmium(II) to attach more strongly to the nitrogen than the oxygen of the carboxyl group. For example, the γ-aminobutyrate complex then might be expected to be more stable than the valinate complex, since the aminobutyrate is the stronger base[9] and less steric strain would be expected in the γ-aminobutyrate than in the valinate complex. Just the reverse is found as shown in the data of Table II. The valinate complex is far more stable than the γ-aminobutyrate. This is interpreted as evidence that chelation is involved, at least in the case of the valinate, which is capable of forming a stable five-membered chelate. The seven-membered γ-aminobutyrate is far less stable, if it forms at all. In other words, the ring size factor, due to chelation, outweighs the other considerations. It is concluded by similar reasoning that the other complexes are chelates, with the possible exception of the γ-aminobutyrate.

Comparisons with the results of other workers are possible in only a few cases, and these show fairly good agreement. Albert[3] obtained a pK value of 8.1 for the 1:2 complex of cadmium(II) glycinate, as compared with 8.45 in this investigation. The pK_3 of 9.94 at ionic strength 0.15 reported by Li, White, and Yoest[4] differs considerably from the 11.0 value at ionic strength of 2.0 found in this study. Such a large difference may indicate interaction of cadmium(II) with nitrate ion, as well as ionic strength effects. For cadmium(II) valinate, Rebertus[5] reported pK 1:2 = 7.49, which is in good agreement with the value of 7.35 obtained in this study.

(9) J. S. Fruton and S. Simmonds, "General Biochemistry," J. Wiley and Sons, Inc., New York, N. Y., 1953, p. 90.