Inaccuracies also arise in the extrapolation to infinite dilution used[4] to obtain a value for the chemical shift of the HF molecule due to the steep slope of the curve in this region.

We have tried to interpret the experimental data given by Haque and Reeves[4] in terms of our derived chemical shifts values, δ_{HF} and $\delta_{HF_2^-}$. The equilibrium can be described by

$$\underset{(1-\alpha)}{HF_2^-} \rightleftharpoons \underset{\alpha}{HF} + \underset{\alpha}{F^-} \tag{9}$$

where α is the degree of dissociation. This quantity can be expressed in terms of the observed chemical shift, δ, and the shifts of the three fluorine-containing species as

$$\alpha = 2\frac{\delta_{HF_2^-} - \delta}{(2\delta_{HF_2^-} - \delta_{HF} - \delta_{F^-})} \tag{10}$$

By inserting our derived values for the chemical shifts δ_{F^-}, δ_{HF}, and $\delta_{HF_2^-}$ together with the experimental values for the resultant chemical shift obtained by Haque and Reeves[4] into eq 10, we find that the calculated values for the degree of dissociation, α, are greater than 1 at concentrations below 0.5 *M*. We have repeated the determination of the ^{19}F chemical shift for a number of KHF_2 solutions in the concentration range 0.5–2.0 *M*. Using our experimental technique we obtain values approximately 1 ppm to high field of those reported by Haque and Reeves.[4] A change of this magnitude reduces calculated values of the degree of dissociation, α, to less than 1.

A possible explanation for the discrepancy between our results and those of Haque and Reeves[4] might arise from their use of glass tubes. Both fluoride[16,24] and bifluoride solutions readily attack glass to produce complex fluoride ions including SiF_6^{2-}. The ^{19}F resonance of the SiF_6^{2-} ion occurs approximately 30 ppm to low field of that for HF_2^- in solution,[25] and, if significant amounts are present in the KHF_2 solutions, this will lower the value of the observed average signal below that expected solely from exchange between HF_2^-, HF, and F^-.

Acknowledgment. We wish to thank Dr. H. J. Bernstein for helpful comments concerning the original manuscript.

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(24) I. Solomon and N. Bloembergen, *J. Chem. Phys.*, **25**, 261 (1956).
(25) See ref 21, p 881.

Mechanism of the Metal-Ion-Catalyzed Hydrolysis of Ethyl Valinate- and Ethyl Leucinate-N,N-diacetic Acids

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Abstract: Ethyl valinate-N,N-diacetic acid (EVDA) was prepared by the reaction of iodoacetic acid and valine ethyl ester in basic solution and was identified by elemental analysis, nmr, and infrared spectra. Ethyl leucinate-N,N-diacetic acid (ELDA) was prepared analogously and identified by nmr. Formation constants were determined with the metal ions copper(II), cobalt(II), nickel(II), lead(II), and samarium(III) which indicate that EVDA coordinates strongly to these metal ions as a tridentate ligand; *i.e.*, the extent of ester carbonyl coordination to these metals is small. Hydroxo-complex, M(EVDA)(OH), formation constants were determined at several temperatures so that ΔH and ΔS could be calculated. The rate of ester hydrolysis in M(EVDA) and M(ELDA) in the pH range 7.0–9.0 which includes the range of hydroxo-complex formation was studied and found to obey the rate law: rate = $k[M(EVDA)][OH^-]$. Enthalpies and entropies of activation were also determined for the hydrolysis reaction of the copper(II) complex of ethyl glycinate-N,N-diacetic acid, Cu(EGDA). Nitrite ion, 4-picoline, pyridine, acetate ion, and phosphate dianion exhibited general nucleophilic catalysis with the order of nucleophilicity being roughly the same as observed for simple organic esters which undergo hydrolysis by external nucleophilic attack. The most probable mechanism for the ester hydrolysis of M(EVDA) and M(ELDA), which is consistent with all observations, involves external hydroxide ion attack on the carbonyl carbon of the ester which has coordinated to the metal ion in a rapid prior equilibrium.

A number of mechanisms have been proposed for the metal-ion-promoted hydrolysis of α-amino acid esters.[1–7] Most explain the promoted hydrolysis by assuming polarization of the carbonyl group by the metal ion. The most difficult problem has been to identify the nucleophile and particularly to distinguish between external hydroxide ion attack (mechanism A) and internal attack by a hydroxo group bound to the metal ion (mechanism B). Both mechanisms obey the same rate law.

The present investigation utilizes metal complexes of ethyl valinate-N,N-diacetic acid and ethyl leucinate-N,N-diacetic acid which undergo slow ester hydrolysis even at pH 7–9 in the region where hydroxo complexes

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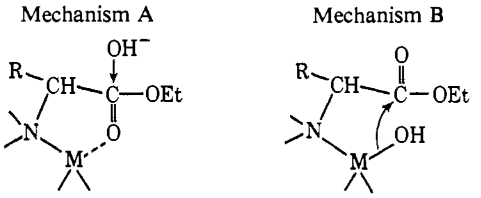
(1) R. J. Angelici and B. E. Leach, *J. Am. Chem. Soc.*, **89**, 4605 (1967).
(2) H. Kroll, *ibid.*, **74**, 2036 (1952).
(3) M. L. Bender and B. W. Turnquest, *ibid.*, **79**, 1889 (1957).
(4) H. L. Conley, Jr., and R. B. Martin, *J. Phys. Chem.*, **69**, 2914 (1965).
(5) W. A. Conner, M. M. Jones, and D. L. Tuleen, *Inorg. Chem.*, **4**, 1129 (1965).
(6) M. D. Alexander and D. H. Busch, *J. Am. Chem. Soc.*, **88**, 1130 (1966).
(7) R. W. Hay and P. J. Morris, *Chem. Commun.*, 23 (1967).



form. The slow rates of hydrolysis of these sterically hindered esters[8] have allowed the determination of formation constants and hydroxo formation constants without appreciable interference from the ester hydrolysis reaction. These slow rates have also enabled us to examine general nucleophilic catalysis by several nucleophiles.

Experimental Section

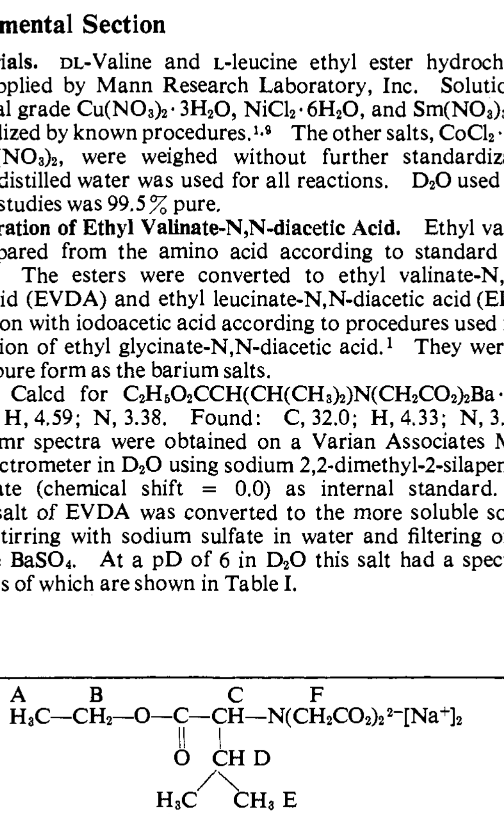
Materials. DL-Valine and L-leucine ethyl ester hydrochloride were supplied by Mann Research Laboratory, Inc. Solutions of analytical grade $Cu(NO_3)_2 \cdot 3H_2O$, $NiCl_2 \cdot 6H_2O$, and $Sm(NO_3)_3$ were standardized by known procedures.[1,9] The other salts, $CoCl_2 \cdot 6H_2O$ and $Pb(NO_3)_2$, were weighed without further standardization. Doubly distilled water was used for all reactions. D_2O used in the spectral studies was 99.5% pure.

Preparation of Ethyl Valinate-N,N-diacetic Acid. Ethyl valinate was prepared from the amino acid according to standard techniques.[10] The esters were converted to ethyl valinate-N,N-diacetic acid (EVDA) and ethyl leucinate-N,N-diacetic acid (ELDA) by reaction with iodoacetic acid according to procedures used in the preparation of ethyl glycinate-N,N-diacetic acid.[1] They were isolated in pure form as the barium salts.

Anal. Calcd for $C_2H_5O_2CCH(CH(CH_3)_2)N(CH_2CO_2)_2Ba \cdot H_2O$: C, 31.9; H, 4.59; N, 3.38. Found: C, 32.0; H, 4.33; N, 3.69.

The nmr spectra were obtained on a Varian Associates Model A-60 spectrometer in D_2O using sodium 2,2-dimethyl-2-silapentane-5-sulfonate (chemical shift = 0.0) as internal standard. The barium salt of EVDA was converted to the more soluble sodium salt by stirring with sodium sulfate in water and filtering off the insoluble $BaSO_4$. At a pD of 6 in D_2O this salt had a spectrum, the values of which are shown in Table I.

Table I

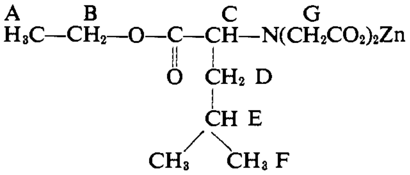


δ, ppm	Rel intensity	Multiplicity	Assignment
1.27	3	Triplet	A
4.19	2	Quartet	B
3.2	1	Multiplet	C
2.0	1	Multiplet	D
0.94	6	Doublet	E
3.2	4	Singlet	F

To improve the solubility of the barium salt of ELDA it was dissolved in D_2O containing Zn^{2+}. This solution had an nmr spectrum, the values of which are shown in Table II. The infrared spectrum of the barium salt of EVDA in KBr showed characteristic absorptions at 3390 (H_2O), 2900 (C–H), 1725 (ester C=O), 1560 and 1405 (salt of a carboxylic acid), and 1200 and 1142 cm⁻¹ (ester).

Determination of the pK_a. The pK_a of the NH^+ proton of ethyl valinate-N,N-diacetic acid was determined by titration of samples of the ester with HNO_3 and NaOH. The pH at the midpoint of the titration was determined for six successive runs, and the average value (6.75) was taken as the pK_a ($K = 1.78 \times 10^{-7}$).

Table II



δ, ppm	Rel intensity	Multiplicity	Assignment
1.23	3	Triplet	A
4.28	2	Quartet	B
~3.5	1	Multiplet	C
~3.3	2	Multiplet	D
~1.6	1	Multiplet	E
0.88	6	Doublet	F
3.64	4	Singlet	G

Determination of Formation Constants. Formation constants for ethyl valinate-N,N-diacetate ($EVDA^{2-}$) with metal ions (eq 1) were determined by measuring the pH of partially neutralized ester-metal ion solutions ranging in concentration from metal:ester of 1:1 to 1:8. The concentration of metal ion used was 0.002 *M*. The total volume of the sample solutions was 10.0 ml, and the ionic strength was maintained at 0.05 *M* by the addition of KNO_3. Estimates of the first and second formation constants were determined by conventional computer techniques.[11] Estimates of the first constant have an uncertainty of 10% whereas the second formation constants have an uncertainty of about 25%.

$$\begin{gathered} M^{2+} + EVDA^{2-} \overset{K_1}{\rightleftarrows} M(EVDA) \\ M(EVDA) + EVDA^{2-} \overset{K_2}{\rightleftarrows} M(EVDA)_2^{2-} \end{gathered} \quad (1)$$

Determination of Hydroxo Complex Formation Constants. Formation constants for hydroxo complex formation (eq 2) were evaluated using the following procedure. A 1:1 metal-ester solution (10 ml; $[M] = 6 \times 10^{-4}$ *M*) was titrated with 0.216 *N* NaOH. The ionic strength was maintained at 0.05 *M* using KNO_3 as the supporting electrolyte, and the temperature was constant to within ±0.05°. From the pH at the half-reaction, values of K_{fOH} were determined. Since the hydroxide activities, a_{OH^-}, were converted to concentrations, $[OH^-]$, by estimation of the activity coefficients by the Guggenheim equation,[12] the K_{fOH} values are expressed in units of molarity. Values of ΔH and ΔS were determined graphically from determinations at 25, 35, and 45°.

$$M(EVDA) + OH^- \overset{K_{fOH}}{\rightleftarrows} [M(EVDA)(OH)]^- \quad (2)$$

Kinetic Measurements. The rates of ester hydrolysis according to eq 3 were determined with a Radiometer titrator and titrigraph using previously described[1] pH-Stat techniques. During a kinetic run, the pH was maintained at the desired value by addition of 0.0187 *N* NaOH. Nitrogen was bubbled into the reaction solution (10-ml volume) to exclude air. Details of the treatment of the kinetic data have been given previously.[1] Standard first-order plots of ln ([initial ester] − [hydrolyzed ester]) *vs.* time yielded slopes which were the pseudo-first-order rate constants, k_{obsd}. The amount of NaOH consumed during the reaction was identical with that calculated from eq 3. The pH, $-\log a_{H^+}$, values maintained by the pH-Stat were converted to concentration units by dividing a_{H^+} by activity coefficients calculated from the Guggenheim equation,[12] $\log \gamma_\pm = -[A]|Z_1Z_2|I^{1/2}/(1 + I^{1/2})] + BI$, where $A = 0.507$ and $B = 0.1$. The hydroxide ion concentrations were calculated from the expression $\log [OH^-] = \log K_w + pH - \log \gamma_\pm$. The method of measurement of the rate of hydrolysis in the presence of other nucleophiles was the same. The rate constant, k_e, for the

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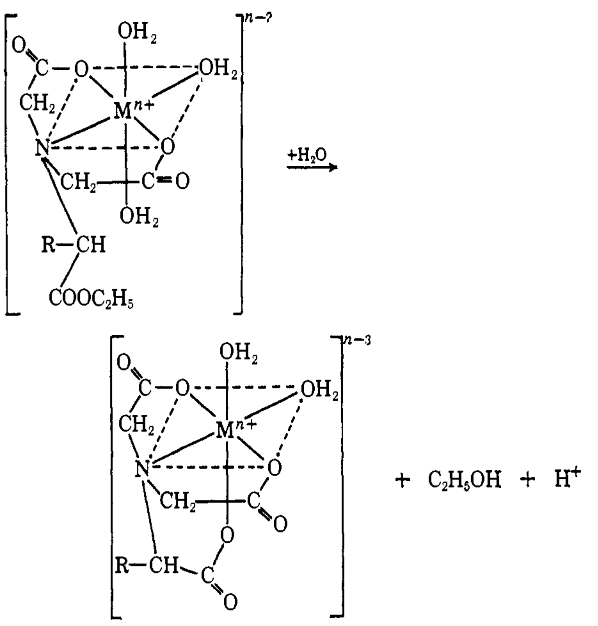
[8] M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p 206.

[9] J. S. Fritz, J. E. Abbink, and M. A. Payne, *Anal. Chem.*, **33**, 1381 (1961).

[10] J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1961.

[11] J. C. Sullivan, J. Rydberg, and W. F. Miller, *Acta Chem. Scand.*, **13**, 2023 (1959) (adapted by Rowlands and Powell). We thank Dr. Powell for helpful discussions in adapting the method and program to the current problem.

[12] E. A. Guggenheim, *Phil. Mag.*, **22**, 322 (1936).



(3)

other nucleophiles was obtained by subtracting the k_{obsd} obtained in the absence of added nucleophiles from the over-all k_{obsd} determined in the presence of added nucleophiles.

Results and Discussion

The slow rate of hydrolysis of EVDA in metal complexes at neutral pH values has permitted the measurement of complex formation constants, K_1 and K_2, and hydroxo-complex formation constants, K_{fOH}, without appreciable ester hydrolysis. The calculated values of the stepwise formation constants, K_1 and K_2 (eq 1), of EVDA with several metal ions are given in Table III. The very high values of K_1 and significantly lower values of K_2 ensure that solutions of 1:1 metal:EVDA contain only the complexes, M(EVDA) and [M(EVDA)(OH)]$^-$, in the pH region (5–9) under kinetic examination.

Table III. Formation Constants,[a] K_1 and K_2, for the Reaction of EVDA with Metal Ions According to Eq 1

Metal ion	$10^{-6}K_1$	$10^{-3}K_2$	K_1/K_2
Cu(II)	10.9 ± 0.8	1.23 ± 0.36	8800
Pb(II)	2.2 ± 0.18	35.5 ± 10.0	62
Ni(II)	0.45 ± 0.05	6.2 ± 0.4	72
Sm(III)	0.14 ± 0.01	7.2 ± 0.6	18
Co(II)	0.0825 ± 0.0025	3.5 ± 0.12	24

[a] At 25° and 0.05 *M* ionic strength.

Of particular importance for the catalysis of these ester hydrolysis reactions is whether the ester carbonyl group is coordinated to the metal ion or not. Nmr and ir studies were inconclusive in determining this for ethyl glycinate-N,N-diacetic acid.[1] Schwarzenbach[13] has determined formation constants of metal ions with a number of substituted iminodiacetic acids, RN$(CH_2COOH)_2$, containing various functional groups in the R moiety. By comparing K_1 and K_2 values (eq 1) he was able to determine whether R was coordinated to metal ions or not. The K_1/K_2 ratio was much higher for tetradentate ligands than for tridentates. Using R groups which could not possibly coordinate with the metal ion and R groups that almost certainly did, it was established that R was coordinated to the metal when the K_1/K_2 ratio was (a) at least 10^6 for Cu(II), (b) at least 10^5 for Pb(II), and (c) at least 1000 for Co(II) and Ni(II). That the ratios for EVDA are much lower than these values suggests that the ester group is not or only slightly coordinated to Cu(II), Pb(II), Ni(II), or Co(II). Although Schwarzenbach did not investigate Sm^{3+}, one can compare K_1/K_2 ratios for known tri- and tetradentates. This ratio is 290 for $N(CH_2COOH)_3$[14] and 25 for $HN(CH_2COOH)_2$.[15] The low ratio (18) for EVDA suggests that this ligand is only tridentate and that the ester group is not coordinated to Sm^{3+}.

Schwarzenbach[13] has used another method to determine whether the R group in $RN(CH_2COOH)_2$ was coordinated to a metal ion or not. He found, for a given metal ion, a linear correlation between log K_1 and the pK_a for the $^+$NH proton of $[R{}^+NH(CH_2COO)_2]^-$ when R was a noncoordinating group. Thus the more basic the nitrogen atom in the ligand, the more stable its metal complex. Ligands which contained coordinating R groups were considerably more stable than predicted from the correlation. Using the pK_a of 6.75 for EVDA and the K_1 values listed in Table I, it is clear that EVDA follows the relationship for tridentate ligands very well for Cu(II), Pb(II), Ni(II), and Co(II). This evidence supports the other data and suggests that the ester group is largely uncoordinated to these metal ions, as shown in eq 3.

These complexes, M(EVDA), increasingly form the hydroxo complexes [M(EVDA)(OH)]$^-$, according to eq 2 as the pH is raised. Values of this equilibrium constant, K_{fOH}, for several metal complexes are given in Table IV. These values show that at a pH of 6.5 at 25° less than 10% of the metal–EVDA complex is present in the hydroxo form, [M(EVDA)(OH)]$^-$. At pH 7.5, roughly half of the complex Cu(EVDA) is in the hydroxo form. Most of the kinetic studies were conducted at these higher pH values where appreciable amounts of both Cu(EVDA) and [Cu(EVDA)(OH)]$^-$ were present in solution. Although hydroxo-complex constants for [Cu(ELDA)(OH)]$^-$ and [Sm(ELDA)(OH)]^0 were not determined, they were assumed to be the same as for the EVDA complexes. Values of ΔH and ΔS for hydroxo complex formation for [Cu(EVDA)(OH)]$^-$ and [Sm(EVDA)(OH)]^0 are also given in Table IV.

Table IV. Hydroxo Complex, [M(EVDA)(OH)]$^-$, Formation Constants,[a] K_{fOH}, According to Eq 2

Complex	Temp, °C	K_{fOH}
Ni(EVDA)	25.0	$\sim 3.0 \times 10^2$
Co(EVDA)	25.0	$\sim 6.0 \times 10^2$
Pb(EVDA)	25.0	$\sim 6.0 \times 10^2$
Cu(EVDA)[b]	25.0	1.31×10^6
	35.0	7.86×10^5
	45.0	4.80×10^5
[Sm(EVDA)]$^+$ [c]	25.0	2.31×10^6
	35.0	2.16×10^6
	45.0	2.04×10^6

[a] In 0.05 *M* ionic strength. [b] ΔH = 9.6 kcal/mole, ΔS = 4.2 eu. [c] ΔH = −1.2 kcal/mole, ΔS = 23.6 eu.

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(13) G. Schwarzenbach, G. Anderegg, W. Schneider, and H. Senn, *Helv. Chim. Acta*, 38, 1147 (1955).

(14) T. Moeller and R. Ferrus, *Inorg. Chem.*, 1, 49 (1962).

(15) L. C. Thompson, *ibid.*, 1, 490 (1962).

The previously reported[1] rate study of the ester hydrolysis of Cu(II) and Sm(III) complexes of ethyl glycinate-N,N-diacetic acid (EGDA) was conducted in the pH range 5.5–7.0 where only small amounts of the hydroxo complexes, *e.g.*, $[Cu(EGDA)(OH)]^-$, were present. In these cases, the observed rate law was

$$\text{rate} = k[M(EGDA)][OH^-]$$

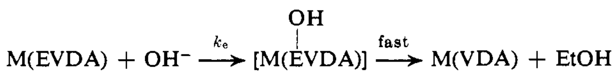
and the predominating complex present in solution was M(EGDA). In the present study, a higher pH was required for studying the slower rate of hydrolysis of EVDA and ELDA in their metal complexes. At these higher pH values appreciable amounts of both, *e.g.*, M(EVDA) and $[M(EVDA)(OH)]^-$, were present in solution. The observed rate of hydrolysis is experimentally determined to be rate = $k_{obsd}[M(EVDA)]_t$, where $[M(EVDA)]_t$ is the total concentration of both M(EVDA) and $[M(EVDA)(OH)]^-$, and k_{obsd} depends upon the pH of the solution. At low pH, $k_{obsd} = k[OH^-]$, but at high pH it becomes independent of pH (Table V). Dividing k_{obsd} by $[OH^-]$ gives the second-order rate constant, k, which is constant at low pH but decreases at higher pH (Table V).

Table V. Rates[a] of Hydrolysis of Cu(EVDA), $[Sm(EVDA)]^+$, Cu(ELDA), and $[Sm(ELDA)]^+$ According to Eq 3

pH	f_{OH}	10^4k_{obsd}, sec^{-1}	10^4k_i, sec^{-1}	k, M^{-1} sec^{-1}	k_e, M^{-1} sec^{-1}
		Cu(EVDA)			
7.1	0.14	0.280	2.00	182	212
7.5	0.29	0.551	1.90	143	202
7.8	0.45	0.854	1.90	111	200
8.1	0.62	1.18	1.90	77.2	203
8.5	0.80	1.75	2.18	45.2	226
9.0	0.91	1.70	1.87	13.9	155
		$[Sm(EVDA)]^+$			
7.5	0.42	0.753	1.79	195	465
		Cu(ELDA)			
7.0	0.115	2.52	21.9	2060	2320
7.3	0.206	4.33	21.0	1770	2230
7.5	0.29	5.37	18.6	1390	1960
7.9	0.51	11.5	22.6	1180	2320
8.2	0.67	15.5	23.2	800	2400
		$[Sm(ELDA)]^+$			
7.1	0.225	2.84	12.7	1850	2400
7.3	0.315	4.61	14.6	1890	2760

[a] At 25.0° and 0.050 M KNO_3.

Two mechanisms can be postulated to account for this rate behavior. Mechanism A assumes a nucleophilic attack of OH^- on the carbonyl carbon atom of the ester group in M(EVDA) and that the hydroxo complex, $[M(EVDA)(OH)]^-$, does not react.



$$M(EVDA) + OH^- \xrightarrow{k_e} [M(\overset{\overset{\text{OH}}{|}}{E}VDA)] \xrightarrow{\text{fast}} M(VDA) + EtOH$$

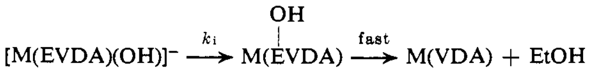
The end products are ethanol and the metal complex of valine-N,N-diacetic acid (VDA). This mechanism yields a rate law, rate = $k_e[M(EVDA)][OH^-]$, in which [M(EVDA)] is the actual concentration of the nonhydroxo complex. From K_{fOH}, the fraction, f_{OH}, of the total complex concentration, $[M(EVDA)]_t$, which is in the hydroxo form, $[M(EVDA)(OH)]^-$, can be calculated. Then $(1 - f_{OH})$ is the fraction of $[M(EVDA)]_t$ which is present as M(EVDA). The rate law in terms of these known parameters is

$$\text{rate} = k_e(1 - f_{OH})[M(EDVA)]_t[OH^-]$$

Division of k by $(1 - f_{OH})$ gives the k_e values shown in Table V. The constancy of these values indicates that mechanism A is consistent with the rate data.

A second mechanism which is consistent with the kinetic results is the internal attack of OH^- which is bound to the metal (mechanism B)

$$M(EVDA) + OH^- \overset{K_{fOH}}{\rightleftharpoons} [M(EVDA)(OH)]^-$$



$$[M(EVDA)(OH)]^- \xrightarrow{k_i} M(\overset{\overset{\text{OH}}{|}}{E}VDA) \xrightarrow{\text{fast}} M(VDA) + EtOH$$

The rate law is

$$\text{rate} = k_i[[M(EVDA)(OH)]^-]$$

or in terms of f_{OH} and $[M(EVDA)]_t$

$$\text{rate} = k_if_{OH}[M(EVDA)]_t$$

In this case $k_{obsd} = f_{OH}k_i$. Dividing k_{obsd} by the f_{OH} values calculated from K_{fOH} gives the k_i values listed in Table V. The constancy of these values suggests that mechanism B as well as mechanism A is in agreement with the equilibrium and kinetic results.

Since K_{fOH} was not measured for Cu(ELDA) and $[Sm(ELDA)]^+$, f_{OH} values were calculated by assuming that the K_{fOH} constants were the same as for Cu(EVDA) and $[Sm(EVDA)]^+$. The constancy of k_e and k_i in Table V supports this assumption.

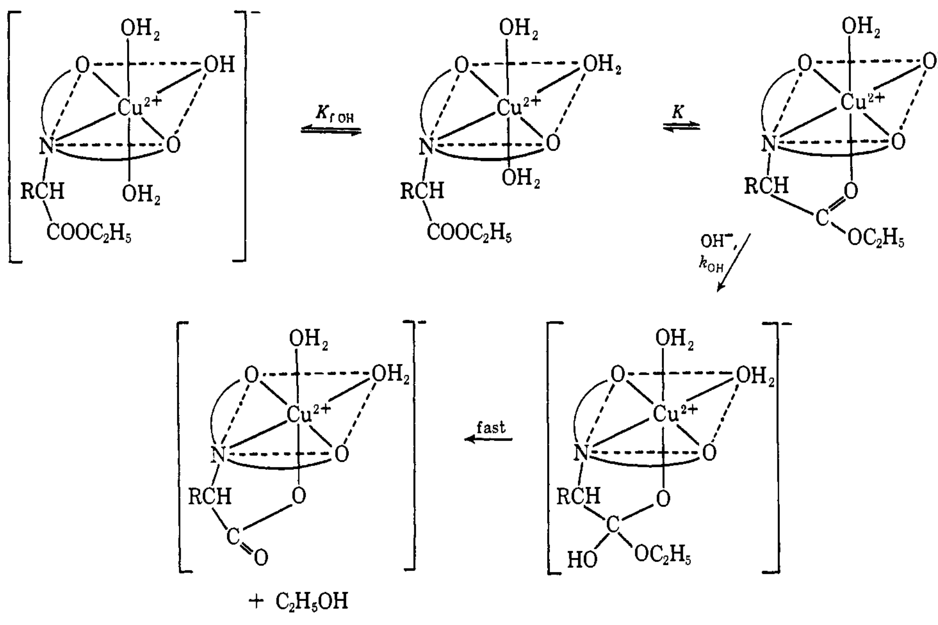
To determine whether mechanism A or B was correct, the rates were examined for general nucleophilic catalysis. These studies were conducted at pH values near 7.8 where appreciable amounts of Cu(EVDA) and $[Cu(EVDA)(OH)]^-$ were present in solution. The observed but small catalytic effects of the nucleophiles listed in Table VI clearly eliminate a third possible mechanism of H_2O attack on $[Cu(EVDA)(OH)]^-$. If this were the mechanism, rate constants should have been far greater for these other nucleophiles than for H_2O, as observed in simple organic systems (Table VI).

Table VI. Rates of Hydrolysis of Cu(EVDA), *p*-Nitrophenyl Acetate, and Ethyl Chloroformate as Catalyzed by Several Nucleophiles

		k_e, M^{-1} sec^{-1}		
Nucleophile	pK_a	Cu(EVDA)[d]	*p*-Nitrophenyl acetate[a]	Ethyl chloroformate[c]
H_2O		...	6×10^{-7}	...
Acetate	4.8	0.0002	0.0005	...
HPO_4^{2-}	6.9	0.02	0.007	...
Pyridine	5.4	0.01	0.1	...
4-Picoline	6.2	0.1	0.5[b]	...
Nitrite	3.4	0.38	0.001	32.2
Hydroxide	14	209	890	169

[a] W. P. Jencks and J. Carriuolo, *J. Am. Chem. Soc.*, **82**, 1778 (1960). [b] T. C. Bruice and G. L. Schmir, *ibid.*, **79**, 1663 (1957). [c] M. Green and R. F. Hudson, *Proc. Chem. Soc.*, 149 (1959). [d] At 25.0 and ionic strength 0.05 M or larger.

Because of the high nucleophilicity of OH^-, relatively high concentrations of other nucleophiles were required to obtain a measurable catalysis. Below concentra-



(4)

tions of 1 M acetate ion, no rate enhancement was observed, but above this a slight increase was noted. Subtracting off the OH^- rate gave the rate constant, k_e, for external attack by acetate ion. The margin of error for acetate ion is large. Because of the buffering action of HPO_4^{2-}, these rates were studied at pH values of 7.0–8.6 and at concentrations of roughly 0.005 to 0.1 M HPO_4^{2-} which were actual ionic concentrations in solution. For pyridine and 4-methylpyridine, concentrations of the nucleophile at pH 7.5 were less than 0.005 and 0.001 M, respectively. Above these concentrations, k_e decreases, probably because of complex formation as noted visibly by a change in the solution color. The most clear-cut example of general nucleophilic catalysis is that using nitrite ion, NO_2^-. At pH 7.5, k_e was constant over a nitrite concentration range of 0.0025–0.020 M. Values of k_e for these nucleophiles are given in Table VI along with those for *p*-nitrophenyl acetate and ethyl chloroformate.

The relative nucleophilicities, as measured by k_e, of these nucleophiles, including OH^-, are roughly the same for Cu(EVDA) and for the organic esters. This suggests that ester hydrolysis of Cu(EVDA) proceeds by general nucleophilic catalysis and not by internal OH^- attack (mechanism B). General nucleophilic catalysis of an amino acid ester complex of Co(III) by CH_3COO^- and $ClCH_2COO^-$ has also been reported.[6] That general base catalysis is probably not involved is suggested by the absence of a correlation between the pK_a of the nucleophile and the rate of hydrolysis.[16] Assuming that the hydrolysis of all of the ester–metal complexes proceeds by mechanism A, the k_e rate constants (M^{-1} sec^{-1}) for OH^- attack are as follows: Cu(EVDA), 209; [Sm(EVDA)]$^+$, 465; Cu(ELDA), 2250; [Sm(ELDA)]$^+$, 2580. These values compare with k_e for OH^- catalysis of the nonmetal-promoted hydrolysis of ethyl valinate (0.011 M^{-1} sec^{-1}) and ethyl leucinate (0.187 M^{-1} sec^{-1}).[17] Thus when ethyl valinate is tied into a metal complex, its rate of hydrolysis is 1.9×10^4 times faster with Cu(II) and 4.2×10^4 times faster with Sm(III). For ethyl leucinate, the rate is increased by a factor of 1.2×10^4 with Cu(II) and by 1.4×10^4 with Sm(III). It should be emphasized that Cu(EVDA) and Cu(ELDA) are neutral molecules, and the large rate enhancement brought about by the metal is probably a result of the coordination of the ester carbonyl oxygen atom to the metal. Although such coordination was precluded in a study of the ester hydrolysis of $[Co(en)_2(Cl)NH_2CH_2COOC_2H_5]^{2+}$, the rate of hydrolysis of ethyl glycinate was increased only by a factor of 100 despite the 2+ charge on the complex.[18] Ester carbonyl coordination was observed in a similar Co(III) reaction[6] and found to be important in increasing the rate of ester hydrolysis.

The results in this paper support the mechanism of eq 4. The value K is unknown but must be quite small. The over-all rate law becomes

$$\text{rate} = Kk_{OH}[\text{Cu(EVDA)}][OH^-]$$

where $Kk_{OH} = k_e$. It is probable that metal complexes of ELDA and EGDA[1] react by the same mechanism.

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