Steric Effects in Fast Metal Complex Substitution Reactions. I[1]

Kenneth Kustin, Robert F. Pasternack,[2] and Elliot M. Weinstock

Contribution from the Department of Chemistry, Brandeis University, Waltham, Massachusetts 02154. Received May 2, 1966

Abstract: The temperature-jump method has been used to determine the complexation rate constants for the formation of α- and β-alanine complexes with nickel(II) and cobalt(II). With α-alanine, cobalt substitution is significantly faster than nickel substitution at 20°. The rate constants determined are consistent with a mechanism in which release of a water molecule from the inner coordination sphere of the metal ion is rate determining. With β-alanine, while the nickel substitution rate is approximately the same as before, cobalt substitution is significantly slower than with α-alanine at 20°. The results are consistent with a mechanism in which the rate of closure of the metal chelate ring is comparable to (nickel) or slower than (cobalt) water release. The complexation of manganese-(II) with α- and β-alanine has also been studied with the temperature-jump method at the same temperature. The rate constant determined for the β-alanine complexation is consistent with the rate-limiting ring closure mechanism.

The stabilities of complexes of a fixed geometrical configuration formed between a given metal ion and monodentate ligands increase with increased basicity of the ligand.[3] On the other hand, the stability of a complex formed between a metal ion and a chelate ligand depends to a large measure on the inherent stability of the metal chelate ring.[4] Kinetically, it has been observed that, for transition metal ions, the rate constant of ligand–metal association is invariant with change of ligand.[5] The relative stability of the complex is therefore governed by the magnitude of the ligand–metal dissociation rate constant.[6] To examine the influence of chelate structure on the kinetics of metal complex formation we have studied the formation of the α- and β-alanine complexes of nickel, cobalt, and manganese by the temperature-jump method.

Experimental Section

Fisher reagent grade nitrate salts of potassium, cobalt, and nickel were used. The manganese(II) used was obtained as the sulfate. Nutritional Biochemicals Corp. α- and β-alanine were likewise used without further purification. The indicators used were Baker phenolphthalein and Aldrich phenol red, both reagent grade.

The temperature-jump apparatus has been described elsewhere.[7] Solutions were made up with requisite amounts of metal ion added to dissolved ligand and indicator. The ionic strength was brought to 0.1 M with KNO_3, and the pH was adjusted by the dropwise addition of dilute NaOH and/or HNO_3. The temperature was 20 ± 1° for all studies.

Each relaxation time represents an average of at least three photographic determinations. The relative error for these measurements is ±10%. Test solutions of either metal ion or ligand in the absence of the other showed no discernible relaxation effects. These "blank" experiments were carried out at concentration levels of the free metal ion and ligand characteristic of solutions containing a mixture of the two. The pH range was restricted by precipitation at the upper end and diminishing effect amplitude at the lower. Representative oscillograms are shown in Figure 1.

Results

The reactions studied were of the type

$$ML_{n-1} + L \underset{k_{-n}}{\overset{k_n}{\rightleftharpoons}} ML_n \qquad (I)$$

where n can equal 1, 2, or 3. The symbol "L" refers to the form of the ligand complexing with the metal ion, which, in these systems, is the anionic form (charges have been neglected in writing this and all following reactions).[8] The equilibrium quotient at constant ionic strength is given by

$$K_n = \frac{k_n}{k_{-n}} = \frac{[ML_n]}{[ML_{n-1}][L]} \qquad (1)$$

We shall begin with the results for nickel(II) and cobalt(II), then follow with the less well-characterized manganese(II) systems.

(A) Nickel and Cobalt. The stability constants for these systems have been previously determined. They are well described for cobalt and nickel with α-alanine and for nickel with β-alanine. The equilibrium constants are less precisely known for cobalt with β-alanine (*cf.* Table I).

A general treatment for obtaining relaxation time expressions in metal–ligand systems represented by reaction I has already been given by Hammes and Steinfeld,[9] so that only the main equations for calculating the rate constants will be given here. The reciprocal relaxation time for a system containing an uncoupled reaction of type I is

$$\frac{1}{\tau_n} = k_{-n} + k_n\left(\frac{[ML_{n-1}]}{1+\alpha} + [L]\right) \qquad (2)$$

where

$$\alpha = \frac{[H]}{K_L + [L]\left(\dfrac{K_{In} + [H]}{K_{In} + [H] + [In]}\right)}$$

In α, the terms K_L and K_{In} refer to the acid dissociation constants of ligand and indicator, respectively (see Table I).

In those cases where a sequence of coupled complexation reactions prevails, more than one relaxation

(1) The authors gratefully acknowledge partial support from Public Health Service Research Grant GM-08893-04 from the National Institute of General Medical Sciences, Public Health Service. The authors wish to thank the National Science Foundation for College Faculty Summer Participation Grant GE-7569 to R. F. P.

(2) Department of Chemistry, Ithaca College, Ithaca, N. Y.

(3) F. Basolo and R. G. Pearson, "Mechanisms of Inorganic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1958, p 17.

(4) H. Irving, R. J. P. Williams, D. J. Ferrett, and A. E. Williams, *J. Chem. Soc.*, 3494 (1954).
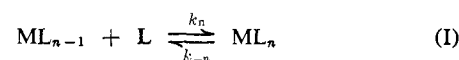
(5) L. C. M. DeMaeyer and K. Kustin, *Ann. Rev. Phys. Chem.*, 14, 5 (1963).

(6) G. A. Melson and R. G. Wilkins, *J. Chem. Soc.*, 4208 (1962).

(7) P. Hurwitz and K. Kustin, *Inorg. Chem.*, 3, 823 (1964).

(8) A. Albert, *Biochem. J.*, 47, 531 (1950).

(9) G. G. Hammes and J. I. Steinfeld, *J. Am. Chem. Soc.*, 84, 4639 (1962).

Table I.[a] Stoichiometric Equilibrium Constants at $\mu = 0.1\ M$ and $20°$

Ligand	Metal ion	K_L	K_1	K_2	K_3
α-Alanine	Co²⁺	1.35×10^{-10} [b]	1.86×10^{4} [c]	2.82×10^{3} [c]	56.2 [c]
α-Alanine	Ni²⁺	1.35×10^{-10} [b]	9.12×10^{5} [d]	5.02×10^{4} [d]	
β-Alanine	Co²⁺	5.50×10^{-11} [e]	1×10^{4} [e]	1×10^{3} [e]	
β-Alanine	Ni²⁺	5.50×10^{-11} [e]	4.26×10^{4} [e]	2.51×10^{3} [e]	

Indicator	K_{In}
Phenolphthalein	2.51×10^{-10} [f]
Phenol red	1.26×10^{-8} [g]

[a] $K_L = $ [H][L]/[HL]; $K_{In} = $ [H][In]/[HIn]. [b] D. P. Mellor and L. E. Maley, *Australian J. Sci. Res.*, **2**, 579 (1948). [c] C. Tanford and W. S. Shore, *J. Am. Chem. Soc.*, **75**, 816 (1953). [d] C. B. Monk, *Trans. Faraday Soc.*, **47**, 292, 297 (1951). [e] A. Albert, *Biochem. J.*, **47**, 531 (1950); H. Irving, R. J. P. Williams, D. J. Ferrett, and A. E. Williams, *J. Chem. Soc.*, 3494 (1954). [f] A. Thiel and G. Coch., *Z. Anorg. Allgem. Chem.*, **217**, 353 (1934). [g] I. M. Kolthoff, *J. Phys. Chem.*, **34**, 1466 (1930).

time may be observed. The only such systems of importance here are those for which two relaxation times are possible. The reciprocals of these two relaxation times are given by the expression

$$\frac{1}{\tau_{+,-}} =$$

$$\frac{1}{2}(a_{11} + a_{22} \pm \sqrt{(a_{11} + a_{22})^2 - 4(a_{11}a_{22} - a_{21}a_{12})}) \quad (3)$$

where

$$a_{11} = k_{-1} + k_1\left(\frac{[M]}{1 + \alpha} + [L]\right)$$

$$a_{12} = k_{-1} - k_1\left(\frac{[M]}{1 + \alpha}\right)$$

$$a_{21} = k_2\left([L] - \frac{[ML]}{1 + \alpha}\right)$$

$$a_{22} = k_{-2} + k_2\left(\frac{[ML]}{1 + \alpha} + [L]\right)$$

For this expression to be valid, it is necessary for the two relaxation times being considered to be resolvable, i.e., separated by at least one order of magnitude in time. In all cases, only one of the two relaxation processes could be seen, the magnitude of the other being very small. Usually the faster effect (positive root) was seen.[9]

The experimental conditions and a summary of all the pertinent relaxation data are given in Tables II and III. Equations 2 and 3 were used to calculate relaxation times from trial values of the rate constants for each system. The calculated relaxation times are shown for comparison.

In treating these data, reaction pathways via hydrolytic species of the type MOH^+ and/or protonated ligands have been omitted. Reactants of this type lead to additional terms in eq 1 and 2. These terms would be, respectively, inversely and directly dependent on hydrogen ion concentration, which in the course of the experiments has been varied by a factor of about 17 (*cf.* Tables II–IV.) Nevertheless, the same set of rate constants yielded uniformly good agreement between τ_{exptl} and τ_{calcd} without the inclusion of additional hydrogen ion dependent terms. We may therefore conclude that, within experimental error, the major contribution to the relaxation expression involves only terms arising from reaction I. Should the other terms be present to some extent, however, the

conclusions to be drawn with respect to substitution of α-alanine *vs.* β-alanine would remain essentially unchanged.
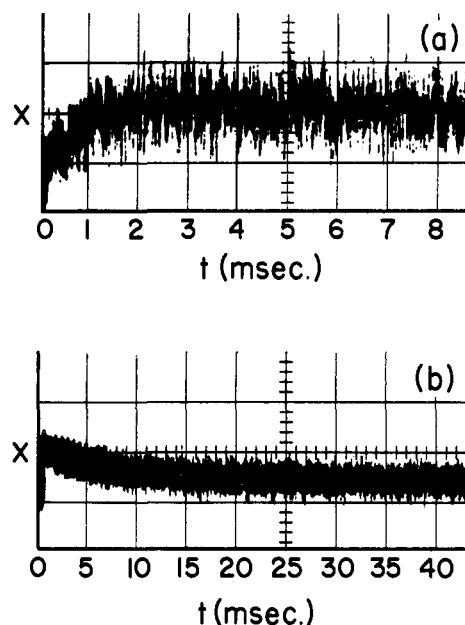

Figure 1. Sample temperature-jump relaxation spectra. The vertical and horizontal axes represent absorbancy (in arbitrary units) and time, respectively. Both traces show results obtained with cobalt, but the ligand in a is α-alanine, whereas in b it is β-alanine. The sums of the concentrations of the reacting species are within a factor of two of each other, yet the β-alanine relaxation requires some 25 msec to go to completion, while the α-alanine relaxation is essentially complete in about 2.5 msec. The compositions and relaxation times of the solutions for which these results were obtained are: (a) $[Co^{2+}]_0 = 6.00 \times 10^{-4}\ M$, $[\alpha\text{-alanine}]_0 = 1.20 \times 10^{-2}\ M$, $[\text{phenolphthalein}]_0 = 3 \times 10^{-5}\ M$, pH 9, temperature $20°$, $\tau = 0.7$ msec; (b) $[Co^{2+}]_0 = 1.10 \times 10^{-3}\ M$, $[\beta\text{-alanine}]_0 = 2.19 \times 10^{-3}\ M$, $[\text{phenol red}]_0 = 1 \times 10^{-5}\ M$, pH 8.5, temperature $20°$, $\tau = 7.7$ msec. In both solutions $\mu = 0.1\ M$.

(B) Manganese. Complexation reactions of manganese, which are known to be among the most rapid of this type,[10] have not been frequently investigated by means of the temperature-jump method, other relaxation techniques having been preferred. The reason is, principally, that the reactions are so fast that very low concentrations have to be employed in order to keep the effects within the compass of this relaxation technique. At such concentration levels, the magnitude of the effect is usually too small to produce a detectable

(10) G. F. Atkinson and S. K. Kor, *J. Phys. Chem.*, **69**, 128 (1965).

Table II.[a]   Relaxation Spectra of Cobalt(II)–α-Alanine and Nickel(II)–α-Alanine Solutions

$[\alpha\text{-Alanine}]_0$, M	$[Co^{2+}]_0$, M	$[H^+]$, M	τ_{exptl}, sec	τ_{calcd}, sec
1.50×10^{-3}	6.00×10^{-4}	3.16×10^{-10}	1.2×10^{-3}	1.4×10^{-3}
5.00×10^{-4}	7.00×10^{-4}	1.00×10^{-9}	6.4×10^{-3}	6.1×10^{-3}
1.20×10^{-2}	6.00×10^{-4}	1.00×10^{-9}	7.0×10^{-4}	6.5×10^{-4}
1.50×10^{-2}	6.00×10^{-4}	1.00×10^{-9}	5.3×10^{-4}	5.9×10^{-4}
1.80×10^{-2}	6.00×10^{-4}	1.00×10^{-9}	5.7×10^{-4}	5.8×10^{-4}
	$[Ni^{2+}]_0$, M			
5.00×10^{-4}	7.17×10^{-4}	1.00×10^{-9}	0.20	0.22
2.11×10^{-3}	1.11×10^{-3}	1.00×10^{-9}	0.066	0.061
1.22×10^{-3}	8.00×10^{-4}	1.00×10^{-9}	0.099	0.098
5.00×10^{-3}	1.01×10^{-3}	3.16×10^{-10}	0.043	0.048

[a] The subscript zero refers to the total stoichiometric concentration.   The total stoichiometric concentration of phenolphthalein was 3.0×10^{-5} M in each experiment.

Table III.[a]   Relaxation Spectra of Cobalt(II)–β-Alanine and Nickel(II)–β-Alanine Solutions

$[\beta\text{-Alanine}]_0$, M	$[Co^{2+}]_0$, M	$[H^+]$, M	τ_{exptl}, sec	τ_{calcd}, sec
1.05×10^{-3}	2.11×10^{-3}	3.17×10^{-9}	6.1×10^{-3}	5.9×10^{-3}
1.92×10^{-3}	3.01×10^{-3}	4.08×10^{-9}	4.6×10^{-3}	4.3×10^{-3}
1.48×10^{-3}	3.03×10^{-3}	3.46×10^{-9}	4.2×10^{-3}	4.3×10^{-3}
2.19×10^{-3}	1.10×10^{-3}	3.17×10^{-9}	7.7×10^{-3}	7.7×10^{-3}
3.98×10^{-3}	1.05×10^{-3}	3.17×10^{-9}	7.1×10^{-3}	7.2×10^{-3}
	$[Ni^{2+}]_0$, M			
1.66×10^{-3}	1.05×10^{-3}	3.98×10^{-9}	0.093	0.10
9.65×10^{-4}	2.01×10^{-3}	4.47×10^{-9}	0.069	0.067
1.44×10^{-3}	3.17×10^{-3}	4.47×10^{-9}	0.050	0.043
1.02×10^{-3}	1.03×10^{-3}	3.98×10^{-9}	0.10	0.11
2.40×10^{-3}	1.01×10^{-3}	5.01×10^{-9}	0.10	0.11

[a] The subscript zero refers to the total stoichiometric concentration.   The total stoichiometric concentration of phenol red was 1.0×10^{-5} M in each experiment.

signal. To improve the sensitivity, the temperature-jump apparatus used in the previously described experiments was modified by replacing the tungsten filament lamp with a mercury arc lamp. This modification improved the signal-to-noise ratio by a factor of about
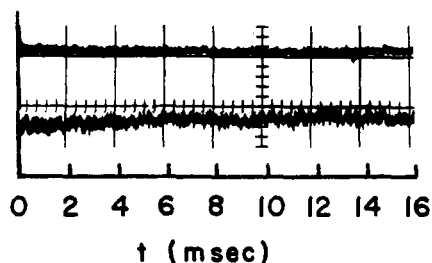

Figure 2. An oscillograph of the temperature-jump relaxation experiment for manganese with β-alanine. The data for this system are given in the third row of Table IV. The straight-line effect is for manganese and indicator in the absence of ligand. It is shown for comparison to demonstrate the absence of an effect. The rising curve shows the presence of the effect with β-alanine.

three. An oscillogram of the effect observed with β-alanine is shown in Figure 2; no discernible effect was found with α-alanine. The results are listed in Table IV.

For the reasons given in the first paragraph of (B) it cannot be unequivocally claimed that negative evidence for the α-alanine system constitutes definitive proof of the fact that complexation here follows the expected pattern of highly rapid substitution. Previous studies[10–12] of this metal ion, however, do strongly

Table IV.   Relaxation Spectra of Manganese(II) Complexes at 20°

$[Mn^{2+}]_0$, M	$[\alpha\text{-Alanine}]_0$,[a] M	$[\beta\text{-Alanine}]_0$,[b] M	pH	τ_{obsd}, sec
0.050×10^{-2}	0.10×10^{-2}		9.0	No discernible effect
0.50×10^{-2}	0.40×10^{-2}		9.0	No discernible effect
0.970×10^{-2}		2.02×10^{-2}	8.4	2×10^{-3}
2.03×10^{-2}		1.65×10^{-2}	8.4	1×10^{-3}

[a] $[\text{Phenolphthalein}]_0 = 3 \times 10^{-5}$ M.   [b] $[\text{Phenol red}]_0 = 2 \times 10^{-5}$ M.

suggest that the negative results may be construed to mean that the reaction is too fast to be detected by this method. In any event, it is clear that this type of complexation kinetics is not being displayed by the β-alanine system.

A complete kinetic analysis, similar to those performed in (A), could not be made for manganese(II) with β-alanine because all of the necessary thermodynamic data are not available. Regardless of this fact, it is possible to gain a meaningful estimate of k_1 since the manganous ion is present in an excess over the concentration of the anionic form of the ligand; therefore $1/\tau \sim k_1[Mn^{2+}]$ and $k_1 \leq 5 \times 10^4$ M^{-1} sec^{-1}.
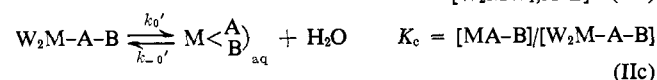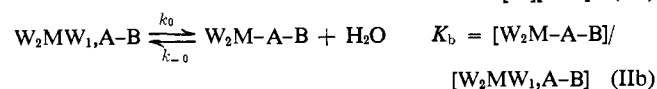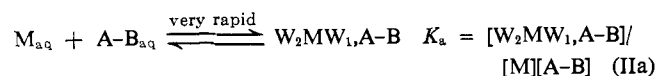
Mechanism of Substitution

Previous investigations of fast transition metal ion complexation reactions have shown that substitution

(11) M. Eigen, *Z. Elektrochem.*, **64**, 115 (1960).
(12) T. J. Swift and R. E. Connick, *J. Chem. Phys.*, **37**, 307 (1962).

requires at least two steps.[13] First, there is the diffusion-limited ion-pair formation between the aquated metal ion and the reactant ligand. Second, and rate determining, is the substitution of the reactant ligand into the inner coordination shell. This process is normally controlled by the rate of release of a water molecule from the inner coordination sphere and is, therefore, a characteristic of the metal ion. Mainly monodentate ligands and multidentate ligands such as EDTA[14] have been used in establishing this mechanism; in contrast, this study concerns bidentate ligands only. Let the two water molecules in the inner coordination sphere which must eventually be replaced by the incoming ligand be represented by W_1 and W_2; the ligand and its two binding sites are represented by the symbol A–B. Then, the mechanism of substitution may be written as

$$M_{aq} + A-B_{aq} \xrightleftharpoons{\text{very rapid}} W_2MW_1,A-B \quad K_a = [W_2MW_1,A-B]/$$
$$[M][A-B] \quad \text{(IIa)}$$

$$W_2MW_1,A-B \underset{k_{-0}}{\overset{k_0}{\rightleftharpoons}} W_2M-A-B + H_2O \quad K_b = [W_2M-A-B]/$$
$$[W_2MW_1,A-B] \quad \text{(IIb)}$$

$$W_2M-A-B \underset{k_{-0'}}{\overset{k_0'}{\rightleftharpoons}} M{<}^A_B\Big)_{aq} + H_2O \quad K_c = [MA-B]/[W_2M-A-B]$$
$$\text{(IIc)}$$

where $W_2MW_1,A-B$ represents an ion pair, and W_2M-A-B represents the monosubstituted intermediate. A similar set of reactions may be written to describe the substitution of the second and third bidentate ligand molecules.

If we now restrict our attention to the first substitution, we may obtain the experimentally determined rate constants k_1 and k_{-1} in terms of reaction mechanism II. The two assumptions made are: (1) that step IIa is very rapid with respect to b and c and (2) that $d[W_2M-A-B]/dt = 0$. The result[9] is

$$k_1 = k_0K_a\left(\frac{k_0'}{k_{-0} + k_0'}\right) \quad (4a)$$

$$k_{-1} = k_{-0}\left(\frac{k_{-0'}}{k_{-0} + k_0'}\right) \quad (4b)$$

To facilitate the remainder of this discussion, the rate constants have been collected together in Table V, to which all further references will be made.

Table V. Rate Constants of Metal Complexation at 20° and $\mu = 0.1\ M$

Metal	n	k_n, M^{-1} sec^{-1}	
		α-Alanine	β-Alanine
Co^{2+}	1	6.0×10^5	7.5×10^4
	2	8.0×10^5	8.6×10^4
	3	9.0×10^4	...
Ni^{2+}	1	2.0×10^4	1.0×10^4
	2	4.0×10^4	6.9×10^3
Mn^{2+}	1	...	5×10^4
		k_{-n}, sec^{-1}	
Co^{2+}	1	32	7.5
	2	280	86
	3	1.6×10^3	...
Ni^{2+}	1	0.022	0.23
	2	0.80	2.7

(13) M. Eigen, *Ber. Bunsenges. Physik. Chem.*, **67**, 753 (1963).
(14) M. Eigen, *Pure Appl. Chem.*, **6**, 97 (1963).

α-**Alanine.** The rate constants for this ligand show two main features. First, nickel substitution is slower than cobalt. Second, for both nickel and cobalt, the rate constant increases when n increases from 1 to 2 (*vide infra* for $n = 3$). In terms of the magnitude of these rate constants, the results are in good agreement with other studies of ligands of this charge type.[5] The increased rate in the substitution of the second (and third) ligand is interpreted on the basis of a loosening in the binding between the metal ion and the remaining coordinated waters. This effect results from the withdrawal of charge into the metal-ligand bond. Consideration of mechanism II shows that a further comparison is possible.

If the rate-limiting step is expulsion of a water molecule from the inner coordination sphere, then, in terms of eq 4, in the extreme where $k_0' \gg k_{-0}$ it follows that $k_1 = k_0K_a$. The contributions of Connick and co-workers[12] have established that oxygen-17 line-broadening measurements can be employed to yield a direct determination of k_0. To effect the comparison, it is necessary to know K_a. Experimental determinations of this quantity are infrequent and resort is usually made to a theoretically derived estimation.[9,15,16] Although the calculation is surely approximate, we compute for the first substitution $K_a = 2\ M^{-1}$ which results in k_0 values of 1×10^4 and 3×10^5 sec^{-1} for nickel and cobalt, respectively, in good agreement with other such studies.[13]

Similarly, the first-order substitution rate constants for $n = 2$ and $n = 3$ for cobalt are 1.2×10^6 and 1×10^6 sec^{-1}, respectively. The last value is less accurately known than the previous two, due to the relatively smaller effect involved. With $n = 2$ for nickel, the first-order rate constant would be 6×10^4 sec^{-1}.

We conclude, therefore, that complex formation with α-alanine is "normal." That is, the release of a water molecule from the inner coordination sphere of the metal ion is rate limiting. This case can be summed up in the following way (for the first substitution): limiting case (A): normal substitution, $k_0' \gg k_{-0}$; $k_1 = k_0K_a$ (M^{-1} sec^{-1}) and $k_{-1} = k_{-0}/K_c$ (sec^{-1}).

β-**Alanine.** The most striking feature of the substitution reactions for this ligand concerns cobalt and manganese. For now it is evident that there is a departure from the established kinetic pattern, since the rate constants for cobalt with β-alanine are almost one order of magnitude less than those of cobalt with α-alanine. Moreover, since the k_0 value for Mn(II) determined by nmr is 10^7 sec^{-1}, the expected bimolecular substitution rate constant for a ligand of the charge type of β-alanine would be about $2 \times 10^7\ M^{-1}$ sec^{-1}. Clearly, a much lower value is observed with β-alanine.

By virtue of these facts, k_0 cannot be obtained from the experimentally determined k_1 as has previously been done. Nor, by the same reasoning, can we compare k_1 to k_2 in the same way as before to find the presence or absence of a loosening effect. This situation does not necessarily imply a change in mechanism, however. It means, simply, that we are observing a different slow step in the over-all transformation.

Thus, if step c is rate determining, then $k_{-0} \geq k_0'$ and, under these circumstances, k_1 is smaller than it would

(15) R. Fuoss, *J. Am. Chem. Soc.*, **80**, 5059 (1958).
(16) M. Eigen, *Z. Physik. Chem.* (Frankfurt), **1**, 176 (1954).

otherwise have been, being reduced by the factor $1/(1 + k_{-0}/k_0')$. The effect is very pronounced for manganese and for cobalt, but not as much for nickel; although even in the latter case the k_2 value suggests that step c is making its presence felt during the second substitution. Complex formation with β-alanine does not show the behavior exhibited by the ligands previously studied. Since the most essential variation in going from α- to β-alanine is a change in ligand structure, this difference is due to a steric effect. Summarizing as before, for the first substitution: limiting case (B): sterically controlled substitution, $k_{-0} \gg k_0'$; $k_1 = k_0' K_a K_b$ and $k_{-1} = k_{-0}'$.

Sterically Controlled Substitution

Physically, limiting case A means that before the vacant site in the intermediate M–A–B can be reoccupied by a water molecule, ring closure occurs. In limiting case B, the repossession of the vacant site by a water molecule is a faster process than ring closure. Since the rate-limiting step in the forward direction of normal substitution occurs in reaction IIb, microscopic reversibility requires that the rate-limiting step for the reverse process take place in the same reaction, as is borne out by the expression for k_{-1}. When the shift to steric control occurs, and reaction c is rate determining, there is a corresponding change in the limiting expressions for the observed rate constants. Namely, the rate of association is now proportional to the equilibrium quotients for the rapid reactions IIa and IIb and the rate constant for the forward direction of IIc, k_0'. The reverse process is simply given by k_{-0}'.

Apparently, reaction IIb is slow enough for nickel, so that the effect does not entirely manifest itself. Most of the published studies on fast metal complex substitution reactions have been concerned with nickel(II).[17] Therefore, the effect has not been previously identified, although some nickel substitution rate constants have fallen somewhat short of the normal value. The discrepancy has been interpreted as resulting from the uncertainty in obtaining accurate values for K_a.[18] Thus, k_1 for the nickel–β-alanine system falls within the range of normal substitution rate constants. For cobalt, on the other hand, the transition from water release to steric control has been made, although judging by the k_2 rate constant, the limiting case has not been reached. Instead, it seems clear that $k_{-0} \approx k_0'$. Therefore, although k_0 can be obtained for cobalt and nickel with α-alanine, a further resolution of the composite rate constants into their elemental components cannot be made for β-alanine without some further assumptions. The limiting case seems to have been reached for the manganese–β-alanine system.

The underlying cause for the slowness of reaction IIc is, as has already been pointed out, the difficulty in forming a six-membered ring with an aminocarboxylic acid ligand. The structures of α- and β-alanine are such that once attachment at the first site occurs, more energy would be required for β- than for α-alanine to produce attachment at the second site. The effect would therefore involve substantially larger contribu-

(17) M. Eigen and R. G. Wilkins, "Mechanisms of Inorganic Reactions," R. F. Gould, Ed., Advances in Chemistry Series, No. 49, American Chemical Society, Washington, D. C., 1965.
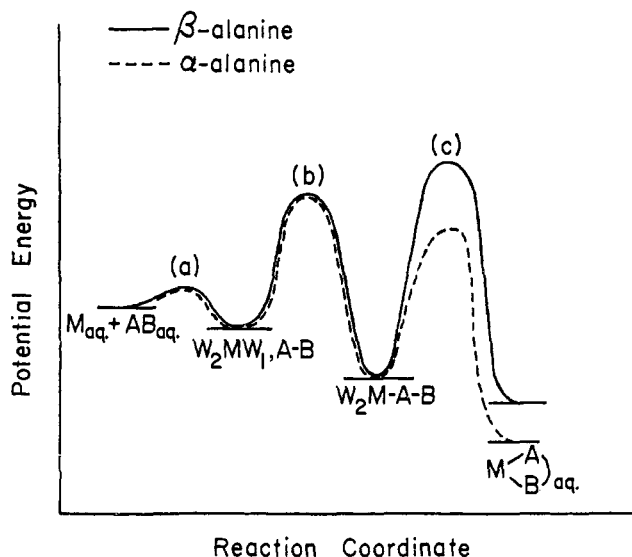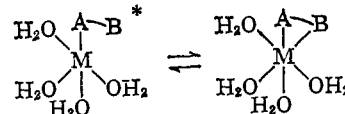(18) J. I. Steinfeld and G. G. Hammes, *J. Phys. Chem.*, **67**, 528 (1963).

Figure 3. Superimposed potential energy diagram.

tions to the energy of activation than the entropic "chelate effect" would indicate.

Activation Parameters for Metal Ion Substitution

Two contributions are responsible for making the energy barrier for ring closure of β-alanine appreciably higher than that for α-alanine. One is the result of ring strain and the other the additional entropy loss when forming a six-membered chelate ring as compared to a five-membered ring. A thermodynamic study[4] has demonstrated that, when chelate ring size increases beyond five members, the stability of the complex formed decreases. Although part of this effect could be accounted for on the basis of a chelate entropy effect,[19] the loss of entropy when closing a six-membered ring is no more than about 1.5 cal deg^{-1} mole^{-1} greater than when closing a five-membered ring. The magnitude of the destabilization is considerably larger than the value calculated from entropy considerations alone.

The last segment of the terminal step of the mechanism may be roughly pictured in the following way. The activated complex contains the atoms of the ring in the correct configuration for ring closure and all that remains to be done is the formation of a bond between the pentacoordinated metal and binding site B. Then the free energy of activation for the process

$$\left[\begin{matrix} H_2O & A{\sim}B \\ & \diagdown | \diagup \\ & M \\ & \diagup | \diagdown \\ H_2O & | & OH_2 \\ & H_2O & \end{matrix} \right]^* \rightleftharpoons \begin{matrix} H_2O & A{\sim}B \\ & \diagdown | \diagup \\ & M \\ & \diagup | \diagdown \\ H_2O & | & OH_2 \\ & H_2O & \end{matrix}$$

contains a contribution for the ring strain (ΔH^*) and one for entropy loss (ΔS^*). Although this picture is obviously an oversimplification, it does show how the ring strain and entropy terms enter into the kinetic argument.

A temperature dependence study was undertaken to obtain values for ΔH^* and ΔS^* in a sterically controlled substitution reaction. However, solutions of cobalt(II) with α-alanine and with β-alanine contain not only $Co(H_2O)_4(A-B)^+$, but higher complexes as well. The

(19) G. Schwarzenbach, *Helv. Chim. Acta*, **35**, 2344 (1952).

values of K_1 and K_2 in these systems (cf. Table I) are sufficiently close so that it is not possible to prepare a solution which contains almost exclusively $Co(H_2O)_4$-$(A-B)^+$ and which also shows a temperature-jump effect. Therefore, precise values of ΔH^* and ΔS^* could not be obtained.

The consequence of the treatment discussed in this section is that if the potential energy curves for both normal and sterically controlled substitution, as exemplified by cobalt(II) with α- and β-alanine, respectively,

are superimposed on the same diagram, the result would be Figure 3. The maximum (a) for both ligands is essentially the same and represents the small activation for the diffusion-controlled formation of the ion pair. The peak labeled (b) represents the barrier for dissociation of a water molecule (W_1) from the inner coordination sphere. Thus, the curves would almost exactly coincide until the energy barrier at (c), which is higher for β-alanine than for α-alanine by a small though detectable amount.

Oxidation of Some Chelating Agents and Complexes with Alkaline Ferricyanide[1]

Don G. Lambert and Mark M. Jones[2]

Contribution from the Department of Chemistry, Vanderbilt University,
Nashville, Tennessee 37203. Received May 5, 1966

Abstract: The rates of oxidation of a number of chelating agents by alkaline ferricyanide were determined in order to furnish a basis for determining the effect of chelation to a metal on such reaction rates. Examination of the rate of the oxidation of ethylenediaminetetraacetic acid (H_4Y) by ferricyanide in alkaline solution shows that the rate law is $-d[Fe(CN)_6{}^{3-}]/dt = k_2[Y^{4-}][Fe(CN)_6{}^{3-}]$. The reaction rate is not retarded by added ferrocyanide, cyanide, or fluoride but is strongly dependent on the cation in the "inert" electrolyte used to maintain constant ionic strength. Rate constants obtained for the magnesium and calcium complexes of (Y^{4-}) were 100-fold less than rate constants for the uncoordinated ligand. A linear relationship between the entropy of activation and heat of activation was found for the oxidation of a large number of chelating agents having charges from -1 to -5; no relation between the activation entropy and the charge was observed. Possible mechanisms for the oxidations are discussed.

Ferricyanide usually reacts with organic compounds by one-electron abstraction,[3] and, as might be anticipated, electron-rich compounds are reactive.[4] Kinetic studies show that radicals are produced from anions in the oxidation of mercaptans[5] and phenols,[6] though oxidation of aldehydes, ketones, and nitroparaffins with alkaline ferricyanide does not involve the production of radicals.[7]

Recent work from this laboratory[8] indicates that complexing with borate masks the ferricyanide oxidation of sugars. As part of a survey of the effect of coordination on ligand oxidation, the study of the ferricyanide oxidation of some chelating agents was undertaken. In particular, the oxidation of ethylenediaminetetraacetic acid (indicated as H_4Y henceforth) and a few of its complexes was investigated in some detail. The goal of the present work was to establish

some of the features of the rate behavior of ligand oxidations to facilitate work on their complexes.

Experimental Section

Materials. Potassium ferricyanide, disodium ethylenedinitrilotetraacetate dihydrate ($Na_2H_2Y\cdot2H_2O$), and the inorganic salts used were reagent grade. Chelating agents were the best commercially available grades. In each case the purity was checked by titration with standardized sodium hydroxide. Both the chromium(III)[9] and cobalt(III)[10] complexes, [Cr(Y)]$^-$ and [Co(Y)]$^-$, were prepared by standard methods. All solutions were prepared from deionized water.

Determination of Stoichiometry. The extinction coefficient for $K_3Fe(CN)_6$ in aqueous solution determined at 420 mμ with a Beckman Model B spectrophotometer was 0.972×10^3 (lit.[11] 1.00×10^3). A known excess of potassium ferricyanide was added to a known quantity of Na_2H_2Y containing sodium hydroxide and potassium nitrate. The ratio of moles of ferricyanide consumed per mole of Y^{4-} calculated from the absorbance at 420 mμ was 4.0 after six half-lives and increased slowly thereafter. From infinite time volumes of sodium hydroxide in kinetic studies using the Fischer titrimeter the moles of sodium hydroxide consumed per mole of Y^{4-} were determined to be 4.0 ± 0.3. That potassium ferrocyanide is the inorganic reaction product was confirmed by comparison of the infrared spectrum of the product with that of an authentic specimen.

Spectrophotometric Experiments. Approximate quantities of chelating agent, sodium hydroxide, and "inert" electrolyte were placed in a 100-ml volumetric flask in a constant temperature bath. After 30 min, potassium ferricyanide solution at the bath tem-

(1) Grateful acknowledgment is made of the support of this work by the U. S. Air Force Office of Scientific Research under Grant No. AF-AFOSR-630-64.

(2) To whom inquiries should be addressed.

(3) For reviews see (a) R. Stewart, "Oxidation Mechanisms," W. A Benjamin, Inc., New York, N. Y., 1964; (b) W. A. Waters, "Mechanisms of Oxidation of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1964; (c) T. A. Turney, "Oxidation Mechanisms," Butterworth, Inc,, Washington, D. C., 1965.

(4) B. S. Thyagarajan, Chem. Rev., 58, 439 (1958).

(5) (a) E. J. Meehan, I. M. Kolthoff, and H. Kakiuchi, J. Phys. Chem., 66, 1238 (1962); (b) I. M. Kolthoff, E. J. Meehan, M. S. Tsao, and Q. W. Choi, ibid., 66, 1233 (1962).

(6) C. G. Haynes, A. H. Turner, and W. A. Waters, J. Chem. Soc., 2823 (1956).

(7) P. T. Speakman and W. A. Waters, ibid., 40 (1955).

(8) M. M. Jones, D. O. Johnston, and C. J. Barnett, to be published.

(9) R. E. Hamm, J. Am. Chem. Soc., 75, 5670 (1953).

(10) F. P. Dwyer, E. C. Gyarfas, and D. P. Mellor, J. Phys. Chem., 59, 296 (1955).

(11) S. Minakemi, R. L. Ringler, and T. P. Singer, J. Biol. Chem., 237, 569 (1962).