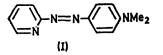
## Kinetics of Ternary Complex Formation Involving Cobalt(11): an Enzyme Model System

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Summary The rate constants for the formation and dissociation of ternary complexes of  $Co^{II}$  with pyridine-2-azo-*p*-dimethylaniline in water follow closely the trends observed for comparable  $Zn^{II}$  complexes.

COBALT(II) can frequently be exchanged in metalloenzymes for the natural co-factor zinc and it has been shown in some cases<sup>1</sup> and suggested in others<sup>2</sup> that the metal acts as a bridge between the enzyme and the substrate and/or product. This mechanism necessitates complex formation



between a ligand and a metal ion which is already complexed. The reason why zinc can often be replaced by  $Co^{II}$  but not by certain other bivalent metal ions, such as  $Ni^{II}$ , is not known, though it has been suggested<sup>3</sup> that one important factor is the ability of the co-ordinating ligands readily to assume different geometries around the central metal ion if the latter is  $Zn^{II}$  or  $Co^{II}$ . To help towards an understanding of the effect of such bound ligands on the reactivity of metal ions we are studying reactions of type (1),

$$L_1M + L_2 \stackrel{k_f}{\approx} L_1ML_2 \quad \dots \quad \dots \quad (1)$$

where  $L_1$  is a firmly bound multidentate ligand, and M = metal.

Very little systematic work of this type has been published. The effect of  $L_1$  on the reactivity of  $Mg^{2+}$  is comparatively minor,<sup>4</sup> even with large, highly charged ligands L. With  $Mn^{2+}$ , which is also electronically symmetrical, the effect also seems to be small in many cases.<sup>5</sup> For Ni<sup>2+</sup>, Margerum *et al.* have shown<sup>6</sup> that  $k_f$  and  $k_d$  both increase markedly as the water molecules in the inner co-ordination sphere of the metal ion are replaced by groups which bind through nitrogen, and that the rate constants seem to be proportional to the number of nitrogen atoms bound. Charge, as such, has comparatively little effect.

We have used the temperature-jump relaxation method to study the kinetics of formation and dissociation of complexes between  $Co^{II}$  species and the bidentate ligand pyridine-2-azo-*p*-dimethylaniline, (I). This study forms an extension of a similar one with  $Zn^{II}$  species<sup>7</sup> and we have chosen the ligands  $L_1$  so that a direct comparison is possible between the two systems. Our results are summarized in the Figure, together with those of Margerum *et al.* on the reaction of Ni<sup>II</sup> species with NH<sub>3</sub>. In all cases the conditions could be chosen such that a simple relaxation effect was observed, and the variation of relaxation time with concentration agreed very closely with that predicted for reaction (1). Preliminary temperature-variation studies with several systems confirmed that the reactions followed this scheme cleanly. The values of  $k_f$  given in the Figure have been adjusted<sup>4,5,7</sup> for the reduced number of water molecules available for substitution in ML<sub>1</sub> as compared with M<sup>2+</sup>. [It was only possible to obtain lower limits for

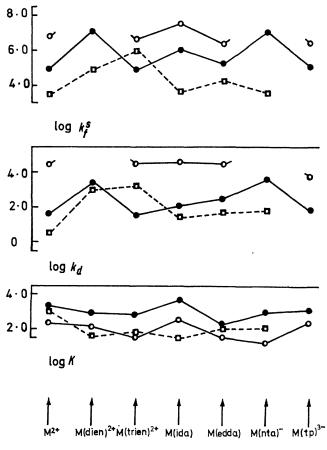


FIGURE. Rate and equilibrium data for ternary complexes of  $Co^{II}$ ,  $Zn^{II}$ , and  $Ni^{II}$ . Equilibrium (K) and rate constants for formation ( $k_1^8$ ) and dissociation ( $k_d$ ) of ternary complexes of  $Co^{I+}$  ( $\odot$ ) and  $Zn^{2+}$  ( $\bigcirc$ ) with (I) and of  $Ni^{2+}$  ( $\square$ ) with  $NH_a$  at 25°. Units of  $k_1^8$  are l mole<sup>-1</sup> s<sup>-1</sup> and of  $k_d$ , s<sup>-1</sup>. The firmly bound ligands are diethylenetriamine (dien), triethylenetetramine (trien), iminodiacetate (ida), NN'-ethylenediaminetetra-acetate (edda), nitrilotriacetate (nta), and polytriphosphate (tp). Data for zinc are taken from ref. 7 and for nickel from ref. 6 (with suitable adjustments for differences in temperature, where necessary).

the rate constants for the  $Zn(dien)^{2+}$  (dien = diethylenetriamine) and  $Zn(nta)^-$  (nta = nitrilotriacetate) systems.]

The pattern of 1:1 complex formation involving labile metal ions has become well-established in recent years.<sup>8</sup>  $k_f$  depends primarily on the nature of the metal and, in particular, reactions between a given metal and most ligands of the same charge type have approximately the same value of  $k_f$ ; the variation in equilibrium constant is usually reflected in differences in  $k_d$ . There is evidence

that NH<sub>3</sub> and (I) are "normal" ligands,<sup>7-9</sup> so the values of  $k_{f}$ , at least for the L<sub>1</sub>M species which contain two or more replaceable cis-water molecules, may reasonably be compared; the  $k_d$  and K values for Co<sup>II</sup> and Zn<sup>II</sup> reflect the chelating nature of (I), however.

There is a remarkable similarity between the patterns for Co<sup>II</sup> and Zn<sup>II</sup>, and the contrast between these patterns and the one for Ni<sup>II</sup>. The rate constants show a greater variation than the equilibrium constants for all three metals. As for Mg<sup>II</sup>, Mn<sup>II</sup>, and Ni<sup>II</sup>, charge does not appear to be the dominant factor affecting the rates. It is also unlikely that crystal field effects are important for  $Co^{II}$  since they would be absent for  $Zn^{II}$ . It is possible that the relative positions of the non-replaceable groups around the metal ion are important in these reactions with (I), and we have further evidence<sup>10</sup> that the rearrangement of the nonreplaceable groups necessary to accommodate the incoming bidentate ligand can considerably reduce  $k_f$ . Activation parameters are being measured for these and similar systems in the hope that they will reflect such factors.

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