

Kinetics and mechanism of the interactions of imidazole and benzimidazole with *cis*-diaquo(nitrilotriacetato)cobalt(III)

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Abstract. The kinetics of the anation of *cis*-diaquo(nitrilotriacetato)cobalt(III) with imidazole (IMZ) and benzimidazole (BIMZ) have been studied in the pH range 6.10–7.10 and 5.60–6.85 respectively at $\mu = 0.1$ M and in the temperature range 40–60°C. Both reactions produce the bisubstituted product but the entry of the first ligand is rate determining in each case. The pH dependence of rate shows that the neutral ligand reacts with both the acid and the base forms of the complex, the reactivity of the base form being slightly higher in each case. The pseudo first-order rate constants show a non-linear dependency on the concentration of incoming ligand at a particular pH. A pure *D* (dissociative) mechanism rather than *I_a* (dissociative interchange) is operative which is supported by previously reported results of imidazole substitution reactions.

Keywords. Anation; *cis*-diaquo(nitrilotriacetato)cobalt(III); imidazole; benzimidazole; pure dissociative conjugate base mechanism.

1. Introduction

Much of the studies on substitution reactions at octahedral metal centres are confined to the substituted or unsubstituted cobalt(III) amine complexes (Wilkins 1974; Moore 1977). Complexes with ligands having fewer than four donor nitrogens are not well explored. In keeping with this, we have attempted to follow the reaction of *cis*-diaquo(nitrilotriacetato)cobalt(III) with imidazole and benzimidazole. Prior to this work Thacker and Higginson (1974) have made some investigations on the reaction of this complex with a few non-metallic substrates in aqueous solution, and Meloon and Harris (1977) have studied its formation from the acid catalysed hydrolysis of the binuclear di- μ -hydroxo-*bis*(nitrilotriacetato)cobalt(III) species. The choice of imidazole and benzimidazole as possible substituents is due to the fact that the imidazole as a histidine moiety functions as ligand toward transition metal ions in a variety of biologically important molecules (Martin 1974) while substituted benzimidazole is an integral part of the structure of vitamin B₁₂ (Preston 1974). Consequently, a massive effort is being expended currently on the reactivity of imidazole and benzimidazole with various transition metal ions and complexes (Randall and Alberty 1967; Shepherd and Taube 1973; Krishnamurthy 1978; Thompson and Krishnamurthy 1979).

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2. Materials

Imidazole and benzimidazole have been purchased from BDH and all other chemicals are of reagent grade. The mononuclear *cis*-[Co(NTA)(OH)₂]₂ (H₃NTA = nitrilotriacetic acid) is generated *in situ* by adding dilute nitric acid to K₂[Co₂(NTA)₂(OH)₂] following Meloon and Harris (1977). The molar extinction coefficients of the diaquo species are 208 M⁻¹ cm⁻¹ and 221 M⁻¹ cm⁻¹ at 398 and 554 nm respectively. These are exactly half of that shown in figure 2(I) of Meloon and Harris's (1977) report since the dissociation of one mole of the binuclear species results in two moles of the mononuclear complex. Fresh solutions of the diaquo species have been prepared each day as it decomposes by reduction on long storage.

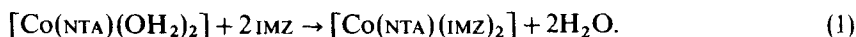
3. Methods

A Pye-Unicam SP8-150 spectrophotometer has been used for all absorption spectral studies. The kinetics are followed by measuring the change in absorbance of the reaction mixture at definite time intervals. For this a little of the mixed solution has to be quickly withdrawn from the reaction vessel (kept in a thermostatic bath) with the help of a jacketted pipette containing pieces of ice to quench the reaction. Initial pH adjustments are done by additions of a little 0.01 M NaOH or HNO₃, employing the self-buffering capacity of the excess imidazole or benzimidazole in the experimental pH range. The pH measurements have been carried out with a digital Beckman (Model 4500) pH-meter. Ionic strength is adjusted to 0.10 M by using recrystallized NaClO₄.

4. Results and discussion

4.1 Reaction of *cis*-[Co(NTA)(OH)₂]₂ with imidazole

During the course of the reaction of the complex with excess imidazole (2×10^{-4} – 2×10^{-3} M), the absorption maximum characteristics of the diaquo species at 554 nm decreases in intensity and that at 526 nm increases in intensity resulting in the appearance of two maxima at 526 nm (log ϵ , 2.25) and 368 nm (log ϵ , 2.29). These changes are accompanied by a clear set of isosbestic points at 536, 444 and 372 nm (figure 1). Results of the spectrophotometric titration of imidazole show definite break at 1:2 stoichiometry for the diaquo(nitrilotriacetato)cobalt(III): imidazole (figure 2). Thus the overall reaction is represented as



Under the conditions of kinetic study to be delineated later, the reaction goes to completion as revealed from the constancy of A_∞ values at a particular cobalt(III) complex concentration but with varying amounts of the heterocyclic base.

In this reaction system there was the possibility of observing two consecutive reactions. However, a detailed examination of the log($A_t - A_\infty$) vs t kinetic plots (where A_t and A_∞ denote the absorbances at time t and infinity respectively) indicates only one observable reaction which might be either the first or second imidazole reacting. The actual reaction studied is the entry of the first imidazole because (i) for a consecutive

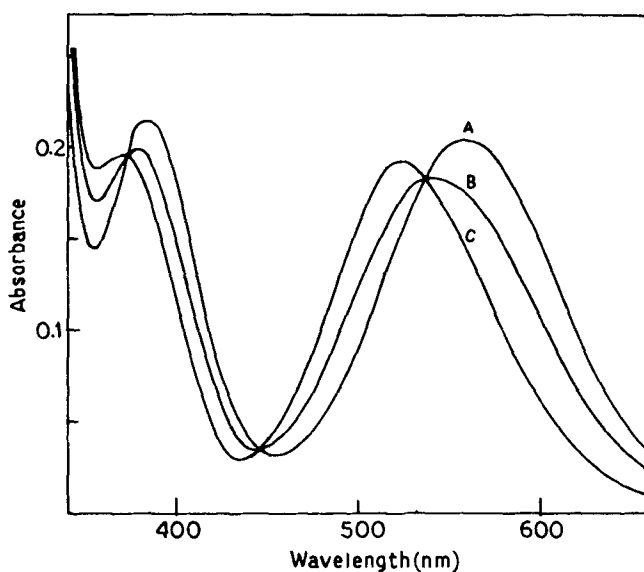


Figure 1. Absorbance spectral change for the system $\text{cis-}[\text{Co}(\text{NTA})(\text{OH}_2)_2]/\text{imidazole}$ at 50°C $\text{pH} = 6.50$, $\mu = 0.1 \text{ M}$, $[\text{Complex}]_T = 1 \times 10^{-3} \text{ M}$, $[\text{IMZ}]_T = 0.1 \text{ M}$, A—spectrum of $\text{cis-}[\text{Co}(\text{NTA})(\text{OH}_2)_2]$, C—spectrum recorded after keeping the mixture for 24 hr.

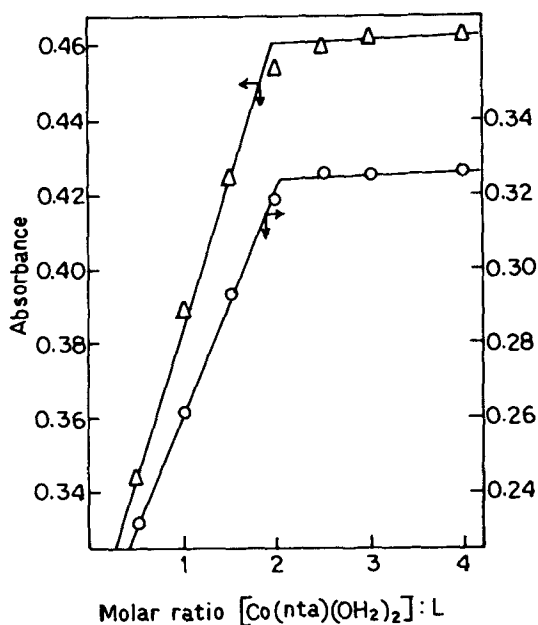


Figure 2. Spectrophotometric determination of the stoichiometry of the complexes of imidazole (O) and benzimidazole (Δ) with $[\text{Co}(\text{NTA})(\text{OH}_2)_2]$ determined at 500 and 380 nm respectively.

reaction $A \rightarrow B \rightarrow C$, the presence of isosbestic points as described earlier (figure 1) throughout the reaction is indicative that the first stage $A \rightarrow B$ is rate determining with no measurable build-up of species B and (iii) the plots of k_{obs} vs $[\text{IMZ}]_T$ which are highly curved in nature show zero intercepts (vide supra). It is tempting to speculate that the first imidazole increases the affinity of the metal ion for the second imidazole molecule, i.e., a *cis*-labilising effect caused by the apparent electron density around nitrogen of the imidazole ring is operative.

The kinetics of the reaction have been studied at 580 nm with various concentrations of cobalt(III) (4×10^{-5} – 1×10^{-4} M), imidazole (2×10^{-4} – 4×10^{-3} M) and hydrogen ions (7.94×10^{-8} – 7.94×10^{-7} M) and the results are shown in table 1. It should be mentioned here that for the runs in which imidazole is not in greater than five-fold excess with respect to complex concentration, the values of k_{obs} are deduced from the initial portions of the rate data where reasonable first-order kinetics prevail. Except in those runs the plots of $\log(A_t - A_\infty)$ vs time t are linear for more than three half-lives of the reaction. The first acid dissociation constant of $[\text{Co}(\text{NTA})(\text{OH}_2)_2]$ has been found by Thacker and Higginson (1974) to be 1.95×10^{-7} M ($pK_1 = 6.71 \pm 0.01$) at 25°C and we have found this pK_1 to be nearly temperature independent. The reported pK_a values (Sillen and Martell 1971) of imidazole are 6.70, 6.49 and 6.35 at 40, 50 and 60°C respectively. So the acid dependency of the rate is analysed as the occurrence of (2)–(7).

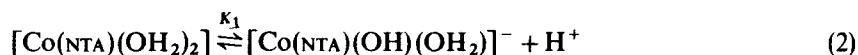
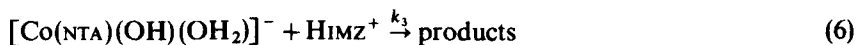


Table 1. Kinetic data for the reaction of *cis*- $[\text{Co}(\text{NTA})(\text{OH}_2)_2]$ with imidazole.

Temperature ($^\circ\text{C}$)	$[\text{IMZ}]_T$ ($\times 10^4$ M)	k_{obs} ($\times 10^5 \text{ sec}^{-1}$)	k_a ($\times 10^5 \text{ sec}^{-1}$)	k_b/k_c ($\times 10^5$)
40	2	1.69	2.70	2.24
	3	1.96		
	4	2.23		
	5	2.30		
	8	2.30		
	12	2.38		
	20	2.53		
50	2	4.16	8.25	5.29
	3	5.44		
	4	5.76		
	5	6.08		
	8	6.65		
	10	6.65		
60	2	11.00	17.85	4.64
	3	12.22		
	4	13.70		
	5	14.21		
	8	15.28		
	12	16.09		
	20	16.88		

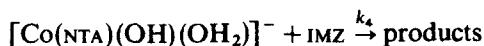
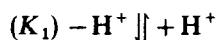
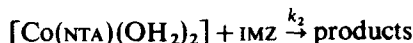
pH = 6.10 ± 0.04 , ionic strength $\mu = 0.1$ M (NaClO_4), $[\text{complex}]_T = (4\text{--}10) \times 10^{-5}$ M.



At relatively low pH (< 5) repetitive spectral scanning indicates no usual substitution (at $\approx 60^\circ\text{C}$), rather slow reduction to Co^{2+} is noticed by the gradual diminution of absorption intensities. This observation precludes any reaction path arising from the k_1 term and (8) can be derived.

$$k_{\text{obs}} = \frac{(k_2 + k_3 K_1 K_a^{-1})[\text{H}^+]^{-1} + k_4 K_1 [\text{H}^+]^{-2}}{(1 + K_1 [\text{H}^+]^{-1})(1 + [\text{H}^+] K_a^{-1})[\text{H}^+]^{-1}} \quad (8)$$

Plots of $k_{\text{obs}} (1 + K_1 [\text{H}^+]^{-1})(1 + [\text{H}^+] K_a^{-1})$ vs $[\text{H}^+]^{-1}$ at imidazole concentrations $(5-10) \times 10^{-4}$ M yield curves rather than straight lines which indicate the invalidity of the composite scheme (Tsukahara *et al* 1982). Earlier workers (Krishnamurthy 1978; Randall and Alberty 1967) have shown that the species HIMZ^+ is not at all reactive in the substitution reactions of imidazole with tetra-*p*-sulphophenylporphinato-chromium(III) and also with aquocobalamin. Participation of neutral imidazole with the acidic and basic forms of the complex, as shown below, seems the possible pathway.



As will be discussed later, the reaction attains a limiting rate at $[\text{IMZ}]_T > 5 \times 10^{-4}$ M, i.e., the reaction becomes independent of imidazole concentrations at such conditions and therefore behaves as an aprotic substituent. The observed rate is given by

$$k_{\text{obs}} = \frac{k_2 [\text{H}^+] + k_4 K_1}{K_1 + [\text{H}^+]}. \quad (9)$$

At $[\text{IMZ}]_T = 1 \times 10^{-3}$ M, $\mu = 0.1$ M and temperature 50°C , plot of $k_{\text{obs}} (K_1 + [\text{H}^+])$ vs $[\text{H}^+]$ gives very good linear fits (figure 3). The ratio k_4/k_2 is 3.00 ± 0.09 which indicates that the hydroxoquo species is only slightly more reactive than its diaquo analogue.

The pseudo first-order rate constants show non-linear dependency on the total concentrations of imidazole at a particular $[\text{H}^+]$. The observed rate law is

$$-\frac{d[\text{Co(III)}]_T}{dt} = \frac{a[\text{IMZ}]_T}{b + [\text{IMZ}]_T} [\text{Co(III)}]_T \quad (10)$$

where $[\text{Co(III)}]_T$ and $[\text{IMZ}]_T$ denote the total concentration of the diaquocobalt(III)

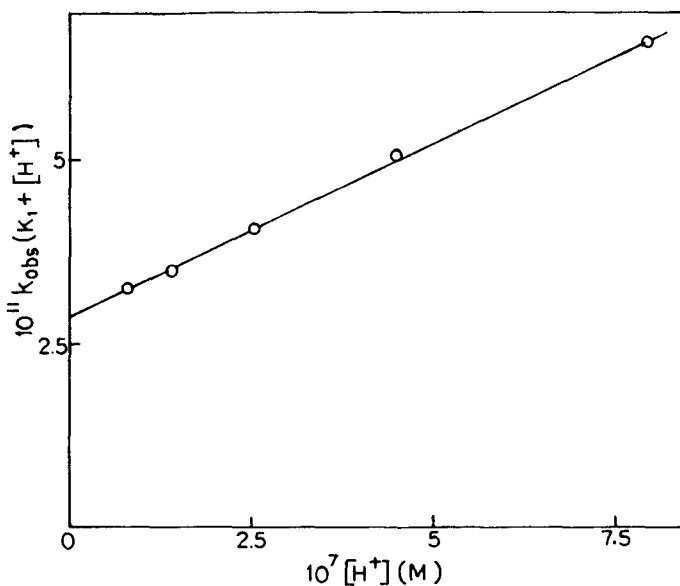
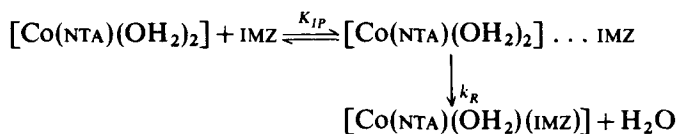


Figure 3. Plot of $k_{\text{obs}}(K_1 + [\text{H}^+])$ vs $[\text{H}^+]$ at 50°C , $[\text{complex}]_T = 5 \times 10^{-5} \text{ M}$, $[\text{IMZ}]_T = 1 \times 10^{-3} \text{ M}$, $\mu = 0.1 \text{ M}$, for the reaction of $[\text{Co}(\text{NTA})(\text{OH}_2)_2]$ with imidazole.

complex and imidazole respectively. As revealed from pH variation studies neutral imidazole species, denoted by $[\text{IMZ}] = K_a[\text{IMZ}]_T / (K_a + [\text{H}^+])$, takes part in the reaction. Hence under pseudo first-order conditions, the above equation reduces to

$$k_{\text{obs}} = \frac{a[\text{IMZ}]}{b + [\text{IMZ}]} \quad (11)$$

Two possible mechanisms which fit the above experimental rate law are I_d and D . For an I_d mechanism the following sequence of reactions may be envisioned to occur.

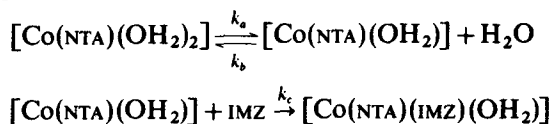


with

$$k_{\text{obs}} = \frac{k_R[\text{IMZ}]}{(1/K_{IP}) + [\text{IMZ}]} \quad (12)$$

The above parameters in (12) also take into account the contributions from the hydroxoquo species. The values of k_R correspond to a and those of $1/K_{IP}$ to b . Values of K_{IP} (ion pair formation constant) obtained from the plots of k_{obs}^{-1} vs $[\text{IMZ}]^{-1}$ are 44647, 18886 and 21550 at 40, 50 and 60°C respectively at pH 6–10. These values of K_{IP} are very large if one considers a 0, 0 or $-1, 0$ interaction. The large values of K_{IP} seem unreasonable for justifying an I_d path.

If a *D* mechanism is operative, the following reaction sequence is applicable for the diaquo species



with

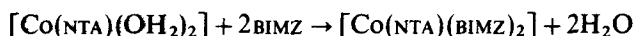
$$k_{\text{obs}} = \frac{k_a[\text{IMZ}]}{(k_b/k_c) + [\text{IMZ}]} \quad (13)$$

The k_a and k_b/k_c values have been extracted from the respective intercepts and slopes of the plots of k_{obs}^{-1} vs $[\text{IMZ}]^{-1}$ and are listed in table 1. The values of k_a correspond to *a* and those of k_b/k_c to *b*. It is to be mentioned here that these kinetic parameters should be treated as composite, since contribution from the hydroxo-aquo species is also present. From a temperature dependent study of k_a at pH 6-10, $\Delta H^\ddagger = 80 \pm 9 \text{ kJ mol}^{-1}$ and $\Delta S^\ddagger = -80 \pm 21 \text{ JK}^{-1} \text{ mol}^{-1}$ have been evaluated.

The conclusive piece of information supporting this *D* mechanism is obtainable from the invariance of k_a as the entering ligand is changed i.e., k_a should be independent of the entering ligand and would be unique to $[\text{Co}(\text{NTA})(\text{OH}_2)_2]$ in a particular solvent system. Till now no other ligand has been studied that reacts with $[\text{Co}(\text{NTA})(\text{OH}_2)_2]$ to give a rate law similar to (13). Hence we have attempted the reaction of *cis*- $[\text{Co}(\text{NTA})(\text{OH}_2)_2]$ with benzimidazole (vide supra). It is worthwhile to mention here that in the redox studies with this cobalt(III) species, Thacker and Higginson (1974) have noted that (i) the hydroxo-aquo species is more reactive than its conjugate acid, and (ii) the rate limiting step is a ligand substitution, involving replacement of the ligand water by the reducing substrates. Finally the reactions have been designated as dissociative by observing the close similarity of rate constants for all the reductants studied.

4.2 Reaction of *cis*- $[\text{Co}(\text{NTA})(\text{OH}_2)_2]$ with benzimidazole

The rate studies have been carried out at ionic strength 0.1 M (NaClO_4) having $[\text{Co}(\text{III})]_T = 5 \times 10^{-5} \text{ M}$ and $[\text{BIMZ}]_T = 2 \times 10^{-4} - 2 \times 10^{-3} \text{ M}$ at pH 5.60-6.85 and the results are summarized in table 2. The complexation occurs in one step with excellent retention of isosbestic points at 536, 444 and 390 nm for the entire course of the reaction. Absorbance changes are recorded with time at 580 nm where the change during the reaction is greatest. The stoichiometry of the reaction as studied by spectrophotometric titration (figure 2) is



The same arguments, as have been presented in imidazole substitution, can be drawn here to establish that the observed reaction is the entry of first benzimidazole. The plots of $\log(A_t - A_\infty)$ vs t are linear for more than three half-lives of the reaction. At pH 5.60 there is the possibility of the following two reactions occurring

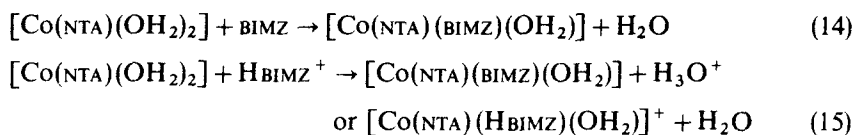


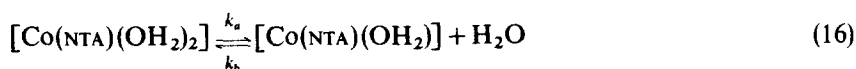
Table 2. Kinetic data for the reaction of *cis*-[Co(NTA)(OH)₂]_T with benzimidazole.

Temperature (°C)	pH	[BIMZ] _T (× 10 ⁴ M)	<i>k</i> _{obs} (× 10 ⁵ sec ⁻¹)	<i>k</i> _a (× 10 ⁵ sec ⁻¹)	<i>k</i> _b / <i>k</i> _c (× 10 ⁴)	
40	5.60	2	0.93	3.70	3.55	
		3	1.31			
		4	1.60			
		5	1.71			
		6	1.95			
		8	2.11			
		10	2.18			
50	5.60	2	2.38	8.12	3.08	
		3	3.17			
		4	3.63			
		5	4.12			
		6	4.67			
		8	5.12			
		10	5.31			
60	5.60	2	5.87	17.58	2.51	
		3	7.98			
		4	9.37			
		5	10.21			
		6	11.52			
		8	12.67			
		10	12.86			
		20	13.24			
		5.85	10			17.08
		6.10	10			25.33
		6.50	10			28.02
6.85	10	32.63				

$\mu = 0.1$ M (NaClO₄), [complex]_T = 5 × 10⁻⁵ M.

But no usual substitution, rather a slow reduction from Co³⁺ to Co²⁺ is observed at [H⁺] > 1 × 10⁻⁴ M. We have determined the acid dissociation constant (*K*_b) of benzimidazole by the pH-titration method (figure 4). The data give *pK*_b = 5.47, 5.44, 5.39, 5.34 and 5.29 at 25, 30, 40, 50 and 60°C respectively at $\mu = 0.1$ M (NaClO₄). So this observation excludes the possibility of (15) occurring.

As shown in figure 5 the dependence of the pseudo first-order specific rate on [BIMZ] shows rate saturation behaviour. Individual points shown in figure 5 have been determined experimentally, while the curve is calculated by substituting appropriate values of the rate constants into (13). The form of the curve implies that the rate-determining step involves rupture of the Co-OH₂ bond. By use of the mechanism represented in (16) and (17) and the steady-state approximation for the penta-coordinated species, [Co(NTA)(OH)₂], *k*_{obs} for the anation process is described by (18).



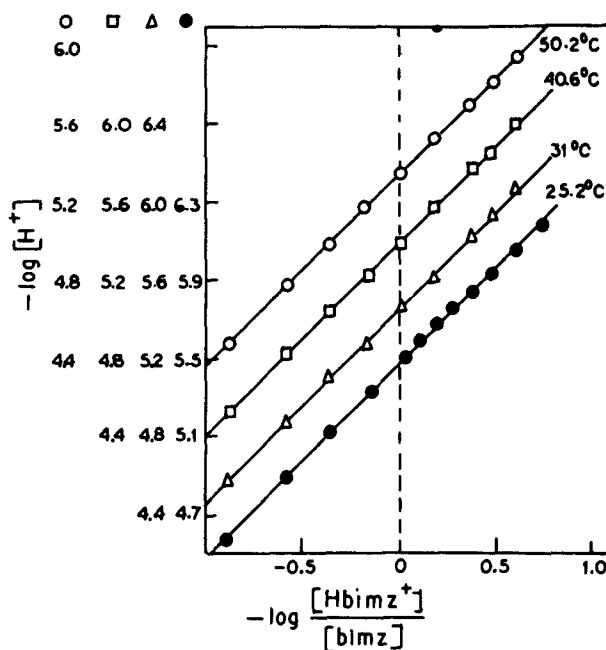


Figure 4. Graphical evaluation of the protonation constant (K_b) of benzimidazole at various temperatures. $[BIMZ]_T = 2 \times 10^{-3}$ M, $\mu = 0.1$ M ($NaClO_4$).

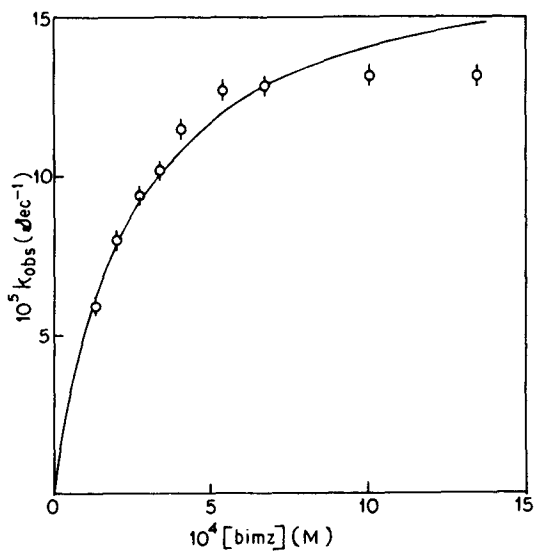
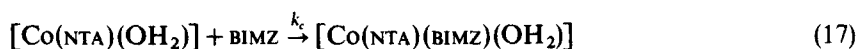


Figure 5. Plot of k_{obs} vs $[BIMZ]$ at 60°C , $\text{pH} = 5.60$, $\mu = 0.1$ M, $[\text{complex}]_T = 5 \times 10^{-5}$ M for the reaction of $[\text{Co}(\text{NTA})(\text{OH}_2)_2]$ with benzimidazole.

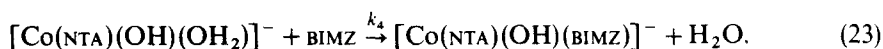
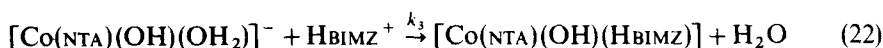
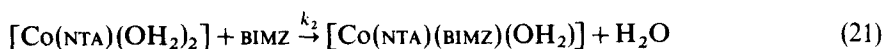


$$k_{\text{obs}} = \frac{k_a[\text{BIMZ}]}{(k_b/k_c) + [\text{BIMZ}]} \quad (18)$$

$$\frac{1}{k_{\text{obs}}} = \frac{k_b}{k_a k_c} \cdot \frac{1}{[\text{BIMZ}]} + \frac{1}{k_a} \quad (19)$$

At high $[\text{BIMZ}]$, $k_{\text{obs}} = k_a$ and the specific rate of the bond breaking step can be determined from the limiting rate in figure 5. At 60°C , $\text{pH} = 5.60$, $\mu = 0.1 \text{ M}$, this value is $(1.54 \pm 0.22) \times 10^{-4} \text{ sec}^{-1}$. The values of k_a and k_b/k_c obtained from the intercepts and slopes of the respective least-squares plots of k_{obs}^{-1} vs $[\text{BIMZ}]^{-1}$ are listed in table 2. The thermodynamic parameters obtained by using the k_a values at different temperatures are $\Delta H^\ddagger = 65 \pm 3 \text{ kJ mol}^{-1}$ and $\Delta S^\ddagger = -124 \pm 11 \text{ JK}^{-1} \text{ mol}^{-1}$.

pH variation studies have been performed at 60°C and at high benzimidazole concentration ($1 \times 10^{-3} \text{ M}$). The rate of the reaction increases slightly with the increase in pH. At higher pH values four reaction paths are possible:



The k_1 path has already been cancelled out by performing some experiments at $\text{pH} < 4$. The contribution of the k_3 path is also neglected by using treatment similar to that in the case of imidazole substitution. Invoking the remaining two paths, i.e., the reaction of diaquo and hydroxoquo complex with neutral benzimidazole, the rate law is

$$k_{\text{obs}} = \frac{k_2[\text{H}^+] + k_4 K_1}{K_1 + [\text{H}^+]}$$

A unique plot of $k_{\text{obs}}(K_1 + [\text{H}^+])$ vs $[\text{H}^+]$ at $[\text{BIMZ}]_T = 1 \times 10^{-3} \text{ M}$ and at 60°C gives the value of k_2 and k_4 which indicate that the hydroxoquo complex is a little (≈ 1.25 times) more reactive than the diaquo form.

5. Conclusion

The specific rates for the formations of the monoimidazole and monobenzimidazole complexes are almost similar. The results are consistent with the view that the substitution processes are primarily dissociative, in which the loss of a coordinated water molecule from the inner coordination sphere of cobalt(III) is rate-determining. It is to be mentioned here that Krishnamurthy (1978) has also found D mechanism to operate in the imidazole substitution reaction of tetra-*p*-sulphophenylporphinato-

chromium(III). The water exchange rate (k_{ex}) of *cis*-[Co(NTA)(OH₂)₂] is not presently available. However it is not likely to be widely different from that of the *cis*-[Co(en)₂(OH₂)₂]³⁺ (en = ethylenediamine) having $k_{\text{ex}} = 7.7 \times 10^{-5} \text{ sec}^{-1}$ at 40°C (Krause and Taube 1961) or that of aquopentaaminecobalt(III) ion having $k_{\text{ex}} = 1 \times 10^{-4} \text{ sec}^{-1}$ at 45°C and at $\mu = 0.6 \text{ M}$ (Hunt and Taube 1958). A critical test of the dissociative mechanism lies in the fact that k_a should equal the rate constant for the water exchange reaction. The present results support this generalisation at least in a modest way. Tobe (1968) has argued that for a reaction proceeding through the *D* path, square-pyramidal intermediates are feasible. This would lead to a retention of configuration and negative ΔS^\ddagger values are expected. Moreover the ΔH^\ddagger values for the formation of both imidazole and benzimidazole complexes are highly positive while the corresponding ΔS^\ddagger values are highly negative. These parameters implicate a largely dissociative transition state in which the Co^{III}-OH₂ bond is strongly weakened.

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