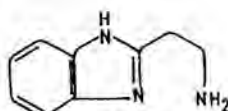## PAPERS

Complex formation of cobalt(II) with 2-(imidazoleazo)benzene and 2-(2-aminoethyl)benzimidazole: A kinetic and equilibrium study

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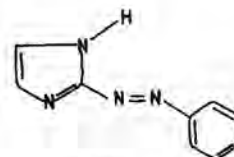Department of Chemistry, Utkal University, Bhubaneswar 751 004, India

The reversible complexation of cobalt(II) with 2-(imidazoleazo) benzene (IAB) and 2-(2-aminoethyl)benzimidazole (AEB) has been studied at I=0.3 mol dm^{-3}. At 25°C the values of log K_M (K_M is the stability constant), ΔH^o/kJ mol^{-1}, and ΔS^o/JK^{-1} mol^{-1} are 2.09±0.03, 14.4±2.4, 88±8 for Co(IAB)$^{2+}$ and 2.65±0.01, 20.0±7.2, 120±21 for Co(AEB)$^{2+}$ respectively. The rate constants of formation of CoL^{2+} chelate via the reaction: Co(OH$_2$)$_6$$^{2+}$+L Co(OH$_2$)$_4$L^{2+}, ($10^{-4}$ k_f^L/dm^3 mol^{-1} s^{-1}=11.7±0.4 (IAB), 1.01±0.03 (AEB) at 10°C) are at least 10 times smaller than the rate constant of water exchange from Co(OH$_2$)$_6$$^{2+}$. Data analysis further indicates that the chelate formation involves *Chelation Controlled Substitution* mechanism. The dissociation of Co(AEB)$^{2+}$ is strongly acid catalysed unlike that for Co(IAB)$^{2+}$.

The need of metal complexes for use in the clinical applications of medical technology[1,2] is increasing. In that context both the thermodynamic and kinetic stabilities of complexes are important. One of the salient features of a metal complex of a multidentate ligand is that it may have a high thermodynamic stability and thus can exist in solution at low *p*H for specific use. Study of complexes in solution also has several dimensions, of which (i) elucidation of structure and bonding, (ii) mechanism of reversible formation, (iii) metal ion mediated coordinated ligand reactions, and above all (iv) simulation of biological activities of enzymes comprise some of the important aspects. When a multidentate ligand is a proton donor as well as a proton acceptor with steric constraints due to bulky groups disposed around donor sites, intramolecular hydrogen bonding, steric effects and restriction to rotation might control the rates and equilibria of its complexation with a metal ion. We have been investigating this aspect using potentially bidentate and biologically important azole ligands[3,4]. In order to elucidate these aspects further, we report herein the kinetics and equilibria of cobalt (II) complexes of 2-(2-aminoethyl)benz-imidazole (AEB), and 2-(imidazoleazo) benzene (IAB).

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(AEB)

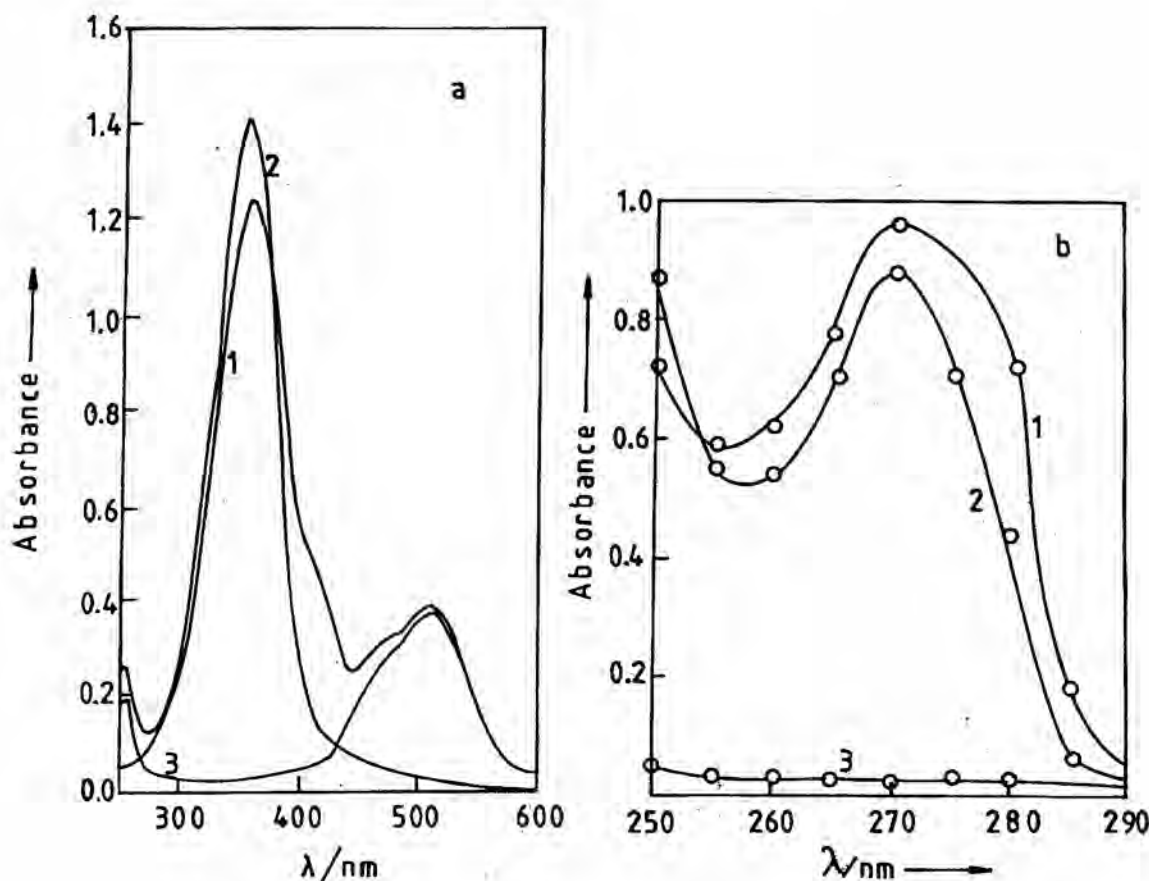(IAB)

Materials and Methods

2-(2-Aminoethyl)benzimidazole dihydrochloride (AEB, 2HCl) and 2-(imidazoleazo)benzene (IAB) were received from our earlier works[3,4]. Other reagents used were of Analar grade. NaClO$_4$ was used for ionic strength adjustment. The buffer MES (4-morpholinoethanesulphonic acid) was used for *p*H adjustment in the *p*H range 6-7. A Jasco model 7800 spectrophotometer was used to record UV-visible spectra. The cell compartment was thermostatted by circulating water from a constant temperature bath. Matched quartz cells (10 mm) were used for absorbance measurements. The *p*H measurements were done with an Elico digital *p*H meter model LI 120 equipped with a glass-Ag/AgCl, Cl$^-$ (2 mol dm^{-3} NaCl) electrode CL 51.

Kinetics

The kinetics of complex formation between cobalt(II) and the ligands (AEB, IAB) and the acid catalysed decomposition of Co(AEB)$^{2+}$ and Co(IAB)$^{2+}$ were studied under pseudo-first order conditions using a HITECH (UK) stopped flow spectrophotometer SF 51 as described earlier[4]. For

Fig. 1— Spectral evidence for the interaction of Co(II) with IAB and AEB at $[H^+]=0.003$ mol dm^{-3} and $pH=7.42$ ($I=0.3$ mol dm^{-3}) respectively: (a) Co^{II} (0.08 mol dm^{-3})+IAB (6.03×10^{-5} mol dm^{-3}) (1), IAB (6.03×10^{-5} mol dm^{-3}) (2), Co^{II} (0.08 mol dm^{-3}) (3); (b) AEB (1.52×10^{-4} mol dm^{-3}) (1), Co^{II} (0.01 mol dm^{-3})+AEB (1.52×10^{-4} mol dm^{-3}) (2), Co^{II} (0.010 mol dm^{-3}) (3).

the acid catalysed aquation, the preformed complexes ($CoAEB^{2+}$ or $CoIAB^{2+}$) were rapidly acidified by mixing the complex solution with $HClO_4$ in the flow module of the equipment. The working wavelengths were 280 and 400nm for AEB and IAB respectively. The absorbance-time curves fitted excellently to single exponential characteristic of first order kinetics. The rate constants reported are average of seven replicate measurements and the errors quoted are standard deviations.

Equilibrium constant measurements

The acid dissociation constants of the ligands ($LH_2^{2+}=LH^++H^+$, K_1; $LH^+=L+H^+$, K_2) have been reported earlier[3,4]. The ligand AEB undergoes two-step protonation[3] (one at the primary amine site and

the other at the benzimidazolyl tertiary N-site; $pK_1=4.60$, $pK_2=7.49$ at 25°C; $I=0.3$ mol dm^{-3}) while IAB is protonated[4] only at the tertiary N-site of the imidazole moiety ($pK_2=4.00$ at 25°C, $I=0.3$ mol dm^{-3}). The UV-visible spectra of the ligands at constant pH were strongly affected by cobalt(II) indicating complex formation (see Fig. 1). The equilibrium constants (Eq. 1),

$$Co^{2+}+L \overset{K_M}{\Longleftrightarrow} CoL^{2+}$$

... (1)

were determined spectrophotometrically (ë=280 and 400nm for AEB and IAB respectively) as described earlier[4] and the pK values of the ligands and the associated enthalpy and entropy data reported previously[3,4] were used wherever necessary. The

Table 1—Values of the stability constants (log K_M) and associated thermodynamic parameters for the complexation of cobalt(II) withAEB and IAB[a]

Temp., °C	Log K_M	
(±0.1°C)	AEB	IAB
25.0	2.65±0.01	2.09±0.03
30.0	2.72±0.02	2.13±0.01
35.0	2.75±0.03	2.15±0.03
40.0	2.83±0.03	2.22±0.03[b]
ΔH^0, kJ mol^{-1}	20.6±7.2	14.4±2.4
ΔS^0, JK[-1] mol^{-1}	120±21	88±8

[a]I=0.3 mol dm^{-3}, values of K_1 and K_2 were taken from ref. (3, 4); [$\epsilon_L, \epsilon_{LH}+, \epsilon_{CoL}^{2+}$], dm[3] mol^{-1} cm^{-1} (L, λ nm): [3.331, 2.11, 19.36]×10[3] (IAB, 400); [4.845, 4.845, 1.753] × 10[3] (AEB, 280); note that the values of the extinction coefficient of AEBH$_2$[2+] and AEBH[+] quoted in the foot note of Table 1 in ref. (3) are to be interchanged and $\epsilon_L = \epsilon_{LH}+$ for AEB. The equilibrium constant measurements

calculated values of K_M and the associated enthalpy and entropy data are collected in Table 1.

Results and Discussion

Kinetics of formation/dissociation of CoL²⁺

The ligand AEB exists as LH$_2$[2+], LH[+] and L, the latter two species being predominant, under the experimental pH. The free (L) and monoprotonated (LH[+]) forms of this ligand were assumed to be the reactive species. Accordingly, k_{obs} is given by Eq. (2) (see Scheme 1).

$$L + Co^{2+} \underset{k_r^L}{\overset{k_f^L}{\Longleftrightarrow}} CoL^{2+}$$

$$K_2(\text{-H}^+) \quad \Updownarrow$$

$$LH^+ + Co^{2+} \underset{k_r^H}{\overset{k_f^{HL}}{\Longleftrightarrow}} CoL^{2+} + H^+$$
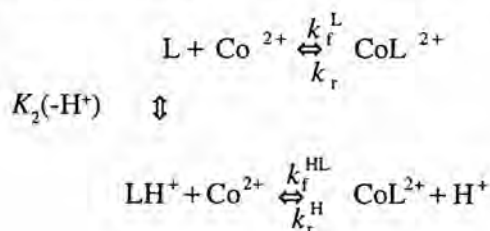
Scheme-1

$$k_{obs} = k_f^{app}[Co^{2+}] + k_d \quad \ldots (2)$$

where

$$k_f^{app} = (k_f^L + k_f^{HL}[H^+]/K_2)/(1+[H^+]/K_2 \quad \ldots (3)$$
$$+ [H^+]^2/K_1 K_2)$$

$$k_d = k_r + k_r^H[H^+] \quad \ldots (4)$$

and k_f^L and k_f^{HL} denote the formation rate constants for the free and monoprotonated ligand respectively, k_r and k_r^H are the spontaneous and H^{+}-assisted dissociation rate constants for CoL[2+], and K_1, K_2 are the first and second acid dissociation constants of AEBH$_2$[2+] respectively.

The kinetics of the reversible complexation of AEB with Co^{2+} was studied at 0.01 [Co^{2+}]$_T$/ mol dm^{-3} 0.06, [AEB]$_T$=6.0×10^{-4} mol dm^{-3}, pH=6.44-6.99 (10.0°C, I=0.3 mol dm^{-3}). The k_{obs} versus [Co^{2+}]$_T$ plot at constant pH (=6.79±0.02) was linear and yielded virtually a zero intercept on the rate axis indicating that the dissociation of CoAEB[2+] was not significant under this condition. This was also supported by the calculated value of [CoAEB[2+]] at equilibrium using the known values of K_1, K_2 and K_M (ca. 90% of total AEB was complexed with Co^{2+} at the lowest pH and lowest [Co^{2+}]$_T$ used). Further, k_{obs} increased with increasing pH at constant [Co^{2+}] thus supporting the view that both LH[+] and L were the reactive species, the latter being more reactive than the former. Accordingly, k_d in Eq. (2) was dispensed with and data analysed to get k_f^L and k_f^{HL} from k_f^{app} (see Table 2).

The dissociation of Co(AEB)[2+] was H^{+}-catalysed in the range 0.005 [H^{+}]/mol dm^{-3} 0.15 (10°C, I=0.3 mol dm^{-3}). The k_{obs} versus [H^{+}] plot is an excellent straight line (see Fig. 2, corr. coeff.=0.999) with positive gradient and intercept consistent with Eq. (5).

$$K_{obs} = k_d = k_r + k_r^H[H^+] \quad \ldots (5)$$

Values of k_r and k_r^H were found to be 95.4±1.1 s^{-1} and 1122±22 dm[3] mol^{-1} s^{-1} (10°C, I=0.3 mol dm^{-3}) respectively.

The formation of Co(IAB)[2+] was studied at [H^{+}]=0.003 mol dm^{-3} with 0.01 [Co^{2+}]$_T$/mol dm^{-3} 0.080 (10°C, I=0.3 mol dm^{-3}). The k_{obs} versus [Co^{2+}]$_T$ plot was linear with positive gradient and positive intercept on the rate axis. Earlier in the Ni(II) complexation reaction, it was shown that the free ligand (IAB) was the only reactive species.

Table 2—Rate constants for the formation of [Co(AEB)$^{2+}$ at 10.0°C^a

10^2 [Co^{2+}]$_T$ mol dm^{-3}	pH	K_{obs}, s^{-1}	10^2 [Co^{2+}]$_T$ mol dm^{-3}	pH	K_{obs}, s^{-1}
1.0	6.79	14.1±0.5	3.0	6.44	24.2±0.2
2.0	6.80	25.6±1.2	3.0	6.54	29.1±1.2
3.0	6.85	43.6±1.7	3.0	6.60	30.9±1.2
4.0	6.78	55.4±2.2	3.0	6.65	33.2±1.4
5.0	6.79	69.4±3.1	3.0	6.99	53.0±3.2
6.0	6.80	82.3±3.6			
10^{-5} k_f^L dm^3 mol^{-1} s^{-1}		1.01±0.03^b			
k_f^{HL}, dm^3 mol^{-1} s^{-1}		348±20^b			

^{a}I=0.3, [AEB]$_T$=6.0×10^{-4} mol dm^{-3}, λ=280 nm
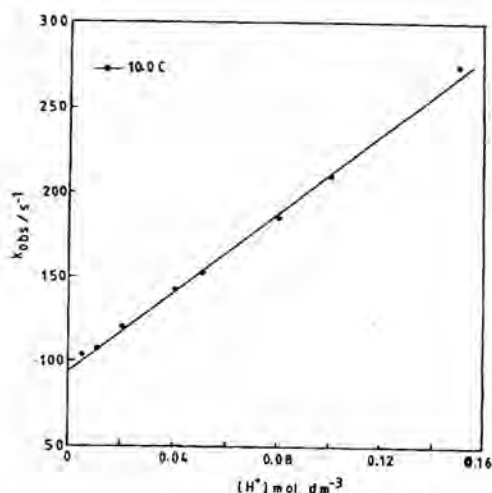
Fig. 2— k_{obs}/s^{-1} versus [H$^+$]/mol dm^{-3} plot for the acid catalysed dissociation of Co(AEB)$^{2+}$ at 10°C; λ=280 nm, the initial pH of the preformed complex with [AEB]$_T$=1.5×10^{-3} and [Co^{2+}]$_T$=0.03, I=0.3 mol dm^{-3} was adjusted to 6.79.

Accordingly in this case, Eqs (2-4) take the form,

$$K_{obs}=k_f^L/(1+[H^+]/K_2)+k_r \qquad \ldots (6)$$

where K_2 denotes the acid dissociation constant of IABH$^+$. The calculated values of the formation (k_f^L) and dissociation (k_r) rate constants for CoIAB^{2+} are collected in Table 3. The dissociation of Co(IAB)$^{2+}$ was studied at 0.0055 [H$^+$]/mol dm^{-3} 0.10, I=0.3 mol dm^{-3}. The rate constant (k_{obs}) was independent of [H$^+$] yielding k_r=160±10 s^{-1} (10.0°C) in satisfactory

agreement with its value obtained from the formation study.

The value of K_M for Co(IAB)$^{2+}$ calculated from the kinetic data (log K_M=log (k_f^L/k_r)=2.8±0.04 at 10°C) compares with that obtained from the equilibrium measurements (log K_M=2.1±0.03 at 25°C). It is, however, striking to note that the complexes, M(IAB)$^{2+}$ [M=Ni^{II}, Co^{II}; log K_M=2.85 for M=Ni^{II} at 25°C, I=0.3 mol dm^{-3} (ref. 4)] are thermodynamically less stable compared to their imidazole analogues, M(im)$^{2+}$ (log K_M=2.4±0.07, 3.02±0.02, 25°C, I=0.1 mol dm^{-3} for Co(im)$^{2+}$ and Ni(im)$^{2+}$ respectively[5]) despite the fact that IAB, unlike imidazole, is a chelating agent. However, this unexpected stability sequence arises partly due to considerable pK perturbation by the azophenyl substituent in the imidazole moiety of IAB 7.3±0.03 at 25°C, I=0.16 mol dm^{-3} (ref. 5), 3.9 at 25°C, I=0.3 mol dm^{-3})^4 and also steric effect and presumably intramolecular hydrogen bonding of IAB (between the ring -NH and the exocyclic azo function) which are lacking in imidazole. The formation of M(IAB)$^{2+}$ involves relatively more endothermic heat change but large positive entropy change as compared to those for M(im)$^{2+}$ (ref. 5). The large positive entropy change points to the release of water molecules from the coordination sphere of Co(II) and thus supports the chelate structure of the complex. The comparison also reflects the effects of steric constraints and basicity of the ligands on the thermodynamic stabilities of the complexes [Co(AEB)$^{2+}$>Co(IAB)$^{2+}$].
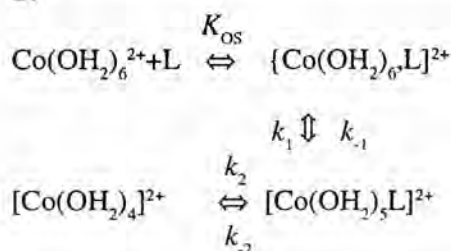
Table 3—Rate constants for the formation/dissociation of CoIAB^{2+} at 10.0°C^a

$10^2 [Co^{2+}]_T$ mol dm^{-3}	K_{obs}, s^{-1}	$10^2 [Co^{2+}]_T$ mol dm^{-3}	K_{obs}, s^{-1}
1.0	162±3	5.0	251±10
2.0	175±4	6.0	262±11
3.0	205±9	7.0	294±12
4.0	225±9	8.0	314±15
$10^{-5} k_f^L$ dm^3 mol^{-1} s^{-1}		1.17±0.04^b	
k_r, s^{-1}		138±3	

$^a I$=0.3, [IAB]$_T$=2.0×10^{-4}, [C$^+$]$_T$=0.003 mol dm^{-3}, λ=400 nm.

Mechanism of formation of CoL^{2+}

The complex formation between Co^{2+} and L on a microscopic basis may be delineated^6 as in Scheme 2:

$$Co(OH_2)_6^{2+}+L \overset{K_{OS}}{\Leftrightarrow} \{Co(OH_2)_6,L\}^{2+}$$

$$k_1 \Updownarrow k_{-1}$$

$$[Co(OH_2)_4]^{2+} \underset{k_{-2}}{\overset{k_2}{\Leftrightarrow}} [Co(OH_2)_5,L]^{2+}$$

Scheme 2: L=AEB, IAB

which in relation to Eqs (2) and (3) corresponds to Eqs (7) and (8) respectively,

$$k_f^L=K_{OS}k_1k_2/(k_{-1}+k_2) \qquad ...(7)$$
$$k_r=k_{-1}k_{-2}/k_{-1}+k_2) \qquad ...(8)$$

where $k_{\pm i}$'s are as denoted in Scheme 2 and K_{OS} is the outer-sphere association constant. This is based on the assumption that the diffusion controlled outer-sphere association between Co(OH$_2$)$_6^{2+}$ and L does not proceed to any significant extent and the steady state approximation is valid for the monobonded intermediates. The value of k_f^{IAB} (1.17×10^5 dm^3 mol^{-1} s^{-1} at 10°C) may be compared with that for Co(II)-bipyridyl (k_f=0.63×10^5 dm^3 mol^{-1} s^{-1} at 25°C)^7, Co(II)-terpyridyl (k_f=0.24×10^5 dm^3 mol^{-1} s^{-1} at 25°C)^7, Co(II)-imidazole (k_f=0.13×10^5 dm^3 mol^{-1} s^{-1} at 25°C)^{8,9} and Co(II)-NH$_3$ (k_f=1.1×10^5 dm^3 mol^{-1} s^{-1} at

25°C)^{10} complexes. The k_f values compare within a factor of 10 despite the fact that the first three complexes are chelates while the last two are monobonded species. Thus, the insensitiveness on the rate on the nature of the ligands is consistent with the rate limiting Co-OH$_2$ bond breaking in the species, [Co(OH$_2$)$_6$,L]$^{2+}$. By contrast, the water exchange rate constant of Co(OH$_2$)$_6^{2+}$, k_{ex}(H$_2$O), is greater than k_f [10^{-6} k_{ex}(H$_2$O)/s^{-1}=2.2; ÄH_{ex} =43.1 kJ mol^{-1} at 25°C]^{11}.

The value of K_{OS} cannot be experimentally determined. Fuoss theory^{12} predicts a value of K_{OS}=0.13 mol dm^{-3} taking the distance of closest approach between Co(OH$_2$)$_6^{2+}$ and L as 500 ppm. Setting k_1=f.k_{ex}(H$_2$O) with f=0.75 (f is a statistical factor suggested by Neely and Connick)^{13} and k_{ex}(H$_2$O)=8.7×10^5 s^{-1} at 10°C (extrapolated value)^{11}, we calculate k_{-1}/k_2=0.67±0.01. Thus the ring closure is only marginally faster than the dissociation of the monobonded species, [Co(OH$_2$)$_5$,IAB]$^{2+}$ (k_2=1.5 k_{-1}). This suggests that the formation of the chelate is only entirely governed by the rate limiting formation of the first metal-ligand bond via the limiting water dissociation mechanism. If IAB first enters the primary coordination sphere of Co^{2+} via the ring tertiary N of imidazole moiety, which is of course most likely, it is then reasonable to expect that intramolecular hydrogen bonding in the ligand, the steric effect and restriction to rotation around the exocyclic N=N moiety will be the impediments to the normal substitution mechanism (i.e., $k_2 \gg k_{-1}$). The value of k_{-1}/k_2 combined with the value of k_r yields k_{-2}=343±8 s^{-1} for the ring opening rate constant of CoIAB^{2+} at 10°C (see Eq. 8). The calculated value of k_{-2} is not appreciably different from the value of the dissociation rate constant of Co(II)-imidazole complex (k_{-1}=507 s^{-1} at 25°C)^8. Thus the chelate ring in Co(IAB)$^{2+}$ appears to be considerably strained.

The monoprotonated ligand AEBH$^+$ reacts with Co(II) at least ~29 times slower than its neutral form (k_c^L/k_f^{HL}=29 at 10°C). This is the usual reactivity trend observed in the complexation of AEB with Ni(II) (k_f^L /k_f^{HL}=70 at 25°C)^3. Using the value of k_f^L, and with the same argument as mentioned above, we calculated the value of k_{-1}/k_2 to be ca. 18.4±0.1. Thus, it is evident that the rate of intramolecular chelation in the species [Co(OH$_2$)$_5$,AEB]$^{2+}$ is significantly slower than the dissociation of the monobonded species to the reactants. A similar observation was made in the Ni(II) complexation of AEB.

Furthermore, the result $k_2 < k_{-1}$, points to the fact that the chelation process is substantially controlled by the chelated ring size as expected for the *Chelation Controlled Substitution Mechanism*[14].

The dissociation of $[Co(AEB)^{2+}$ is susceptible to H^+-catalysis. However, our results do not indicate the formation of a protonated species, $[Co(AEB)^{3+}$, to any detectable extent. The protonation of available N-site in $[Co(AEB)^{2+}$ may occur and the dissociation of Co^{2+} from the protonated species, $[Co(AEBH)^{2+}$, is likely to be enhanced due to the electrostatic repulsion between the like charge centres. The contrasting behaviour of $[Co(IAB)^{2+}$ is possibly attributable to the very poor affinity of the azo function towards protonation.

Acknowledgement

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