and hence less effective in stabilizing Ru^{II}. The reduced π-acidity of pyrazole-containing ligands relative to polypyridine ligands has been noted previously.[17-19] Therefore, it is interesting that the $[Ru(bpp)_2]^{3+/2+}$ and $[Ru(tpy)_2]^{3+/2+}$ couples differ by only 40 mV. The similarity in the $Ru^{III/II}$ redox potentials suggests that, in addition to being a weaker π-acceptor, bpp is also a weaker σ-donor than tpy. Pyrazole-containing ligands are expected to be weaker donors than the analogous pyridine-containing ligands, given the difference in ligand basicities for pyridine and pyrazole ring systems.[20,21] The dimethyl-substituted pyrazoles are more basic than pyrazole and hence are expected to be better donors. As such, Me_2-bpp and Me_4-bpp are better able to stabilize the Ru^{III} oxidation state, which is reflected in the $Ru^{III/II}$ couples of complexes containing these ligands.

In conclusion, the 2,6-bis(*N*-pyrazolyl)pyridine ligands described here are structural and redox analogues of 2,2′:6′,2″-terpyridine, with the added feature that the ligand superstructure can be conveniently varied, providing an opportunity for rational ligand design. The methyl-substituted ligands demonstrate the potential for gradually regulating the driving force for electron transfer over a relatively broad range (200 mV). The synthetic methodologies described here can be easily extended to prepare a wide array ligands with the possibility of optimizing both steric and electronic effects, which may be of great importance in the design of redox catalysts based on these ligands.

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Supplementary Material Available: Elemental analyses for the new ligands (Table I) and complexes (Table II) (1 page). Ordering information is given on any current masthead page.

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(21) The reduced donor ability of bpp relative to tpy may also be a result of the geometric constraints on the chelate bite of a planar tridentate ligand containing two five-membered heterocycles.[19]

(22) See paragraph at end of paper regarding supplementary material.

Articles

Contribution from the Institute for Inorganic Chemistry, University of Witten/Herdecke, Stockumer Strasse 10, 5810 Witten, FRG, and Institute for Inorganic Chemistry, University of Regensburg, 8400 Regensburg, FRG

Kinetics and Mechanism of the Anation of Aquocobalamin (Vitamin B_{12a}) by Cyanoferrates. Isolation and Identification of a Cyano-Bridged Product and Mechanistic Information from Pressure Effects

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Aquocobalamin and $Fe(CN)_6^{4-}$ react to produce the binuclear anion $[cobalamin-\mu-NC-Fe(CN)_5]^{3-}$, which could be isolated and identified as the zinc salt. The anation reactions of aquocobalamin by N_3^-, $Fe(CN)_5NO^{2-}$, $Fe(CN)_5H_2O^{2-}$ and $Fe(CN)_6^{4-}$ were studied as a function of ligand concentration, pH, temperature, and pressure. The observed second-order rate constants vary between 930 and 3600 $M^{-1}\ s^{-1}$ at pH ≈ 6 and 25 °C. The activation entropies and activation volumes are significantly positive and thus support the operation of a dissociative mechanism. Solvational effects caused by changes in electrostriction can account for the variation in the volume of activation with the charge on the anating ligand. The results are discussed in reference to earlier data reported in the literature.

Introduction

Recent reports in the literature dealing with the interaction of aquocobalamin with cyanide and cyanoferrate complexes[2-7] have stimulated our interest in the intimate mechanism of anation reactions of aquocobalamin (hereafter referred to as $B_{12}-H_2O^+$). Although $B_{12}-H_2O^+$ was originally recommended for use as an effective antidote for potential cyanide poisoning induced by the hypotensive agent nitroprusside, later studies revealed qualitatively that $B_{12}-H_2O^+$ reacts much faster with nitroprusside itself than with free cyanide.[5,8] This interaction was recently studied in detail by employing ^{13}C NMR,[6] from which it follows that nitroprusside forms 1:1 and 1:2 complexes with $B_{12}-H_2O^+$, containing Fe–C–N–Co fragments including the axial cyano ligand in the 1:1 complex and a trans pair of equatorial cyano ligands in the 1:2 complex. This interaction drastically affects the pharmacology of nitroprusside, such that $B_{12}-H_2O^+$ cannot be regarded as a satisfactory antidote.[5,9] Other cyanoferrate species produce similar

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complexes with B_{12}–H_2O^+, and the reactions are in general controlled by the availability of the latter species.[5,6] Similar complex formation reactions were reported for $Fe(CN)_6^{4-}$ in the literature[5,6] and were observed in this study for $Fe^{II}(CN)_5NO^{2-}$, $Fe^{III}(CN)_5H_2O^{2-}$, $Fe^{II}(CN)_5H_2O^{3-}$, and $Fe^{II}(CN)_5NH_3^{2-}$. Such reactions are in general controlled by the availability of B_{12}–H_2O^+.

The anation of B_{12}–H_2O^+ by HCN/CN^- was studied in detail by Reenstra and Jencks.[2] This system is complicated by the various acid–base equilibria, acid-catalyzed reactions, and isomerization steps. In addition, the B_{12}–CN species can undergo subsequent substitution to produce *trans*-NC–B_{12}–CN. The authors discuss their kinetic data in terms of an I_d substitution mechanism for the anation step.

We were able to isolate and identify the binuclear bridged species $Zn_3[cobalamin\text{-}\mu\text{-}NC\text{-}Fe(CN)_5]_2\cdot 2H_2O$, produced during the reaction of B_{12}–H_2O^+ and $Fe(CN)_6^{4-}$. We have also studied the kinetics of the anation of B_{12}–H_2O^+ by $Fe^{II}(CN)_5NO^{2-}$ (nitroprusside), $Fe^{III}(CN)_5H_2O^{2-}$, $Fe(CN)_6^{4-}$ and N_3^- as a function of concentration, pH, temperature, and pressure. The reported activation parameters enable us to comment in detail on the intimate nature of the anation process.

Experimental Section

Materials. Crystalline hydroxocobalamin hydrochloride (Sigma) was used as the source of aquocobalamin. The characteristic absorption at 350 nm was used to standardize the stock solution.[10] Solutions were prepared from doubly distilled water stored in the dark at ca. 5 °C. $Fe^{III}(CN)_5H_2O^{2-}$ was prepared in solution from $Fe^{III}(CN)_5NO_2^{3-}$ as described elsewhere.[11] All other chemicals were of analytical reagent grade.

Synthesis of $Zn_3[cobalamin\text{-}\mu\text{-}NC\text{-}Fe(CN)_5]_2\cdot 2H_2O$. To a solution of 0.41 g of hydroxocobalamin hydrochloride in 5 mL of water was added a solution of 0.145 g of $Na_4[Fe(CN)_6]\cdot 10H_2O$ (Fluka) in 1 mL of water. The color of the combined solution turned immediately to red-blue. After the solution was stirred for 5 min, 1 mL of a saturated aqueous solution of $Zn(ClO_4)_2\cdot 6H_2O$ was added. A red-blue powder precipitated. This material was collected by filtration, washed with a small amount of water, acetone, and finally ether, and dried under vacuum; yield 0.25 g (24%). Anal. Calcd for $C_{136}H_{184}Co_2Fe_2N_{38}O_{30}P_2Zn_3$: C, 48.74; H, 5.53; N, 15.88. Found: C, 48.45; H, 5.10; N, 15.77. UV/visible spectrum (in water): λ_{max} = 537 nm (ϵ = 10400), 508 nm (ϵ = 10100), 410 nm (ϵ = 4700), 356 nm (ϵ = 31350). IR spectrum in the region of the cyanide stretching vibrations (in KBr): ν_{max} = 2060 cm^{-1} (very strong); ν_{max} = 2100 cm^{-1} (shoulder).

Procedure and Instrumentation. A ligand solution of the desired pH and ionic strength (0.1 or 0.5 M adjusted with $NaClO_4$) was mixed with a B_{12}–H_2O^+ solution of the same pH and ionic strength. In all cases the ligand concentration after mixing was at least 50 times that of B_{12}–H_2O^+, which was kept at $(1-2) \times 10^{-4}$ M. The pH of the test solution was adjusted by addition of NaOH or $HClO_4$, and in a few cases Merck buffers were used: citrate–NaOH (pH 4, 5); citrate–HCl (pH 6); phosphate–NaOH (pH 7). pH measurements were performed on a Metrohm E250 pH meter. UV–vis absorption spectra were recorded on a Shimadzu UV–250 spectrophotometer. Kinetic measurements at ambient pressure were performed on a Durrum D110 stopped-flow spectrometer and at elevated pressure on a homemade high-pressure stopped-flow unit.[12] Absorbance time plots were analyzed with the aid of a data acquisition system,[13] and the corresponding pseudo-first-order plots were linear for at least 2–3 half-lives of the reaction. Both these instruments were thermostated to within ±0.1 °C. The anation reactions were monitored at 570 or 580 nm, i.e. where a large change in absorbance occurs during the reaction.

Results and Discussion

Aquocobalamin chloride (hydroxocobalamin hydrochloride) reacted with $Na_4[Fe(CN)_6]\cdot 10H_2O$ in water according to

$$[cobalamin\text{-}H_2O]^+ + [Fe(CN)_6]^{4-} \rightarrow [cobalamin\text{-}\mu\text{-}NC\text{-}Fe(CN)_5]^{3-} + H_2O$$

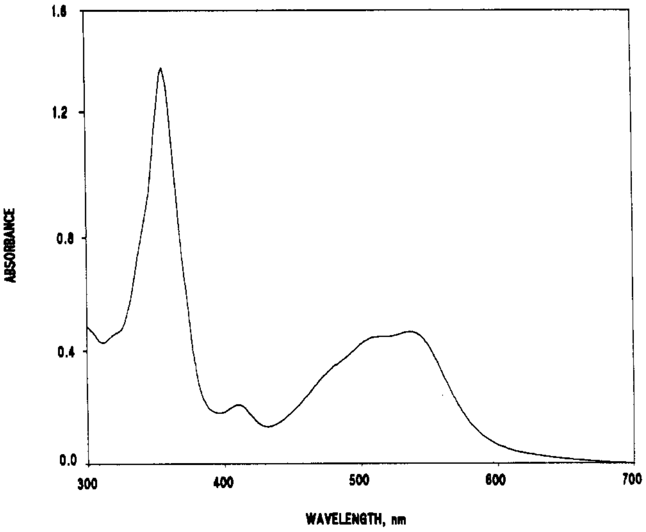

Figure 1. Visible absorption spectrum of [cobalamine-μ-NC–Fe(CN)$_5$]$^{3-}$. [binuclear complex] = 4.42×10^{-5} M; optical path length = 1 cm.

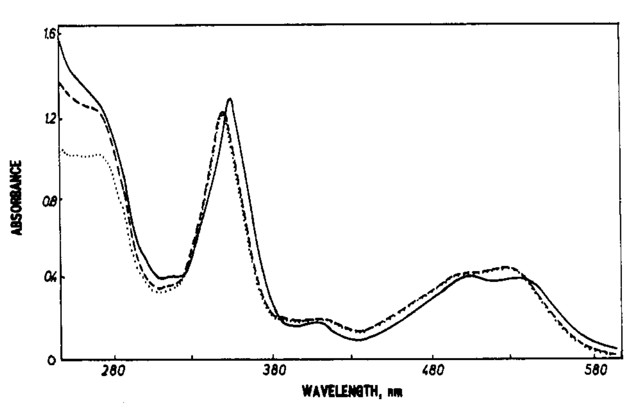

Figure 2. Spectral changes observed during the reaction of 1×10^{-4} M aquocobalamin with 1×10^{-3} M $Fe(CN)_5NO^{2-}$: (···) B_{12}–H_2O^+; (--) B_{12}–H_2O^+/$Fe(CN)_5NO^{2-}$; (—) [B_{12}-μ-NC–Fe(CN)$_4$NO]$^-$. Optical path length = 0.88 cm.

The binuclear anion formed in this reaction was precipitated as the zinc salt, which is sparingly soluble in water and insoluble in organic solvents such as ethanol and acetone. For the synthesis the sodium instead of the potassium salt of $[Fe(CN)_6]^{4-}$ was used in order to avoid the precipitation of $KClO_4$ upon addition of $Zn(ClO_4)_2$.

The electronic absorption spectrum (Figure 1) of [cobalamin-μ-NC–Fe(CN)$_5$]$^{3-}$ is dominated by the intense intraligand bands of the corrin ligand.[14] The maxima of the characteristic α, β, and γ bands appear at 537, 508, and 356 nm. Any other bands of different origin (e.g. ligand field bands) are not apparent and may be obscured by or hidden under the intraligand bands.

While the IR spectrum of [cobalamin-μ-NC–Fe(CN)$_5$]$^{3-}$ shows two distinct absorptions at 2060 and 2100 cm^{-1} in the region of the cyanide stretching vibrations, $[Fe(CN)_6]^{4-}$ displays only one at 2050 cm^{-1}. The lower frequency band of [cobalamin-μ-NC–Fe(CN)$_5$]$^{3-}$ is then assigned to the terminal cyanide of the Fe(CN)$_5$ moiety while the absorption at 2100 cm^{-1} is indicative of bridging cyanide.[15-18] In the binuclear complex [(NC)$_5$Co-μ-NC–Fe(CN)$_5$]$^{6-}$ the cyanide bridge absorbs at 2090 cm^{-1}.[15,16]

The complex formation reactions between B_{12}–H_2O^+ and various cyanoferrate species are accompanied by characteristic

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Table I. Rate Data for the Anation of Aquocobalamin by Azide and Cyanoferrates:[a] $B_{12}-H_2O^+ + L \rightarrow B_{12}-L^+ + H_2O$

L	[L], M	k_{obs},[b] s^{-1}	k_1,[c] $M^{-1}\ s^{-1}$	remarks
$Fe^{II}(CN)_5NO^{2-}$	2.5×10^{-3}	9.7 ± 0.8	3560 ± 79	
	6.25×10^{-3}	23.7 ± 0.9		
	1.25×10^{-2}	47.0 ± 1.2		
	2.0×10^{-2}	71.0 ± 1.1		
$Fe^{II}(CN)_6^{4-}$	1.25×10^{-3}	1.84 ± 0.05	1750 ± 92	
	2.5×10^{-3}	3.59 ± 0.15		
	6.25×10^{-3}	10.8 ± 0.4		
$Fe^{III}(CN)_5H_2O^{2-}$	5×10^{-4}	1.57 ± 0.08	3010 ± 65	*d*
	1×10^{-3}	3.29 ± 0.15		
	2×10^{-3}	6.44 ± 0.20		
	4×10^{-3}	12.0 ± 0.4		
N_3^-	9.5×10^{-3}	8.80 ± 0.25	927 ± 40	*e*

[a] $[B_{12}-H_2O^+] = 2 \times 10^{-4}$ M; temp = 25 °C; ionic strength = 0.1 M; pH ≈ 6 (no buffer was added). [b] Mean value of at least four kinetic runs. [c] Calculated from the slope of k_{obs} versus [L] by using one zero point. [d] $[B_{12}-H_2O^+] = 1 \times 10^{-4}$ M. [e] Ionic strength = 0.5 M.

Table II. Rate Data for the Anation of Aquocobalamin by $Fe^{II}(CN)_5NO^{2-}$ as a Function of pH and Ionic Strength[a]

pH	ionic strength, M	$[Fe^{II}(CN)_5NO^{2-}]$, M	k_{obs},[b] s^{-1}	k_1,[c] $M^{-1}\ s^{-1}$
4	0.13	2.5×10^{-3}	5.7 ± 0.3	2680 ± 67
		6.25×10^{-3}	15.8 ± 0.9	
		1.25×10^{-2}	33.3 ± 1.1	
5	0.3	2.5×10^{-3}	5.6 ± 0.3	2910 ± 110
		6.25×10^{-3}	16.5 ± 0.5	
		1.25×10^{-2}	35.9 ± 1.8	
6	0.3	2.5×10^{-3}	7.2 ± 0.1	2870 ± 55
		6.25×10^{-3}	17.1 ± 0.2	
		1.25×10^{-2}	36.0 ± 1.1	
7	0.15	2.5×10^{-3}	7.6 ± 0.2	2700 ± 50
		6.25×10^{-3}	17.3 ± 0.6	
		1.25×10^{-2}	34.0 ± 2.1	
6.7–7.2[d]	0.1	2.5×10^{-3}	9.7 ± 0.8	3560 ± 79
		6.25×10^{-3}	23.7 ± 0.9	
		1.25×10^{-2}	47.0 ± 1.2	
		2.0×10^{-2}	71.0 ± 1.1	
6.7–7.2[d]	0.5	2.5×10^{-3}	3.6 ± 0.1	1520 ± 40
		6.25×10^{-3}	9.4 ± 0.4	
		1.25×10^{-2}	17.6 ± 0.2	

[a] $[B_{12}-H_2O^+] = 2 \times 10^{-4}$ M; temp = 25 °C. [b] Mean value of at least four kinetic runs. [c] Calculated from the slope of k_{obs} versus [L] by using one zero point. [d] Unbuffered solution.

UV–vis spectral changes as demonstrated in Figure 2 for 1:1 mixtures of the reactants. Similar spectra are obtained on increasing the cyanoferrate concentration to ratios larger than 1:1. A number of important observations allow us to assign the observed bands unequivocally. First, cyanocobalamin (B_{12}–CN) does not react with the cyanoferrate species, which indicates that a labile site on the Co center is required for the complex formation step. The complexes $Fe^{II}(CN)_5NO^{2-}$, $Fe^{III}(CN)_5H_2O^{2-}$, and $Fe^{II}(CN)_6^{4-}$ all produce the same type of spectrum, indicating that CN^- is an essential reaction component. The shape of the spectra and the characteristic γ band for cobalamins are in close agreement with the data for $B_{12}-NH_3^+$, but differ significantly from the data for B_{12}–CN.[14,19] All these observations indicate that the cyanoferrates bind to the Co center through the N atom of the CN^- bridging ligand. This is in agreement with the ^{13}C NMR observations metioned before.[6] Bonding through the carbon atom of the CN^- ligand only occurs in the case of the nonlabile B_{12}–CN species.[2,20]

The kinetics of the complex formation reactions were studied as a function of ligand concentration, pH, temperature, and pressure. The overall reaction can be formulated as in (1). The

$$B_{12}-H_2O^+ + L \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B_{12}-L^+ + H_2O \qquad (1)$$

observed pseudo-first-order rate constants increase linearly with increasing concentration of L (Table I). Plots of k_{obs} versus [L] exhibit no significant intercepts, indicating that $k_1[L] \gg k_{-1}$ and K_1 $(=k_1/k_{-1})$ is large. As a comparison a formation constant of $1.2 \times 10^{14}\ M^{-1}$ was reported for the anation of $B_{12}-H_2O^+$ by CN^-.[3] The rate law for reaction 1 can thus be simplified as shown in (2), and k_1 can be calculated from k_{obs} as a function of [L] in the usual way.

$$k_{obs} = k_{-1} + k_1[L] \approx k_1[L] \qquad (2)$$

The values of k_1 in Table I clearly demonstrate that we are dealing with relatively fast reactions, which are ca. 10 times faster than the anation of $B_{12}-H_2O^+$ by CN^- for which a typical k_1 value is 250 $M^{-1}\ s^{-1}$ at 25 °C,[2] although values as high as 1500 $M^{-1}\ s^{-1}$ were reported elsewhere.[21,22] Throughout the remainder of this study, k_1 was determined from the dependence of k_{obs} on [L] as a function of the kinetic variable under investigation.

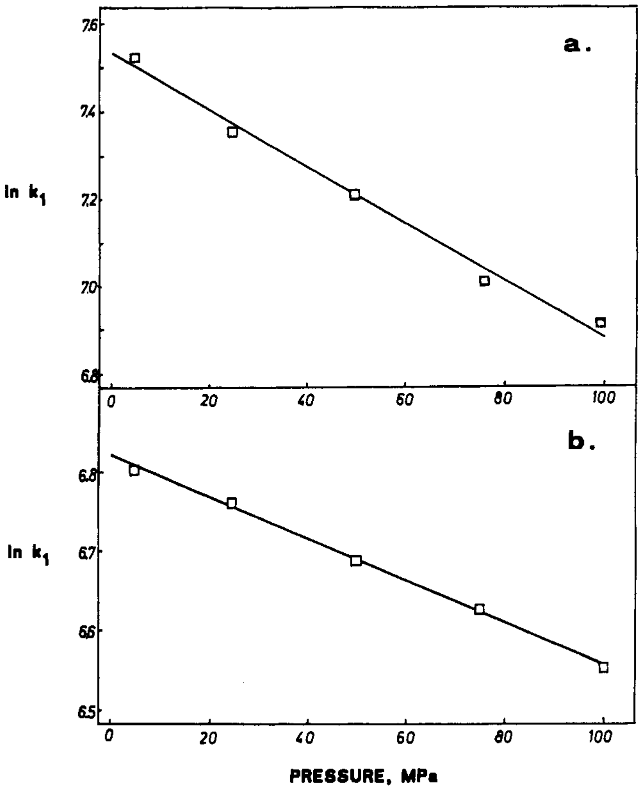

Figure 3. Pressure dependence of k_1 for the anation of aquocobalamin by $Fe(CN)_6^{4-}$ (a) and N_3^- (b). For experimental conditions see Table III.

The anation reaction is expected to be significantly pH dependent since $B_{12}-H_2O^+$ can deprotonate to hydroxocobalamin B_{12}–OH, which was reported to be substitution inert.[2,22] Acid dissociation constants reported in the literature for $B_{12}-H_2O^+$ vary between (pK_a) 7.6 and 7.9 depending on the ionic strength of the medium.[21,23] A more recent value of 8.1, determined in 1.0 M KCl, was corrected for the binding of chloride ion to $B_{12}-H_2O^+$ and reduced to 7.7.[2] In an effort to avoid this complication, a possibly suitable pH range of 4–7 was selected to check the pH dependence of k_1. The results in Table II demonstrate that k_1 does not exhibit a significant pH dependence in this range. The lower values found in the buffered compared to the unbuffered solution can be explained in terms of the higher ionic strength. When the ionic strength of the unbuffered solution is changed from 0.1 to 0.5 M, k_1 decreases from 3560 ± 80 to 1520 ± 40 $M^{-1}\ s^{-1}$ at 25 °C. The observed trend accounts for the apparent discrepancy in Table II and is in line with the expected decrease in k_1 with increasing ionic strength for a reaction involving a cationic $B_{12}-H_2O^+$ species and an anionic ligand.

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Table III. Rate Data as a Function of Temperature and Pressure for $B_{12}–H_2O^+ + L \rightarrow B_{12}–L^+ + H_2O$[a]

L	temp, °C	press., MPa	[L], M	k_{obs},[b] s^{-1}	k_1,[c] $M^{-1}\ s^{-1}$	remarks
$Fe^{II}(CN)_5NO^{2-}$	20	0.1	1.25×10^{-3}	3.0 ± 0.1	2520 ± 120	
			2.5×10^{-3}	6.0 ± 0.2		
			6.25×10^{-3}	17.9 ± 0.9		
			1.25×10^{-2}	30.9 ± 1.1		
	25		2.5×10^{-3}	9.7 ± 0.5	3560 ± 79	
			6.25×10^{-3}	23.7 ± 1.1		
			1.25×10^{-2}	47.0 ± 1.2		
			2.0×10^{-2}	71.0 ± 2.0		
	32		1.25×10^{-3}	12.1 ± 0.4	6060 ± 460	
			6.25×10^{-3}	46.0 ± 1.0		
			1.25×10^{-2}	76.6 ± 2.5		
	37		1.25×10^{-3}	14.2 ± 0.3	9360 ± 154	
			2.5×10^{-3}	28.5 ± 0.5		
			6.25×10^{-3}	63.0 ± 2.0		
			1.25×10^{-2}	120 ± 4		
	25	5			4010 ± 180	
		25			3840 ± 150	
		50			3530 ± 180	
		75			3160 ± 150	
		100			2870 ± 140	
$Fe(CN)_6^{4-}$	20	0.1	1.25×10^{-3}	1.02 ± 0.05	1080 ± 79	
			2.5×10^{-3}	2.0 ± 0.1		
			6.25×10^{-3}	6.6 ± 0.2		
	25		1.25×10^{-3}	1.84 ± 0.05	1750 ± 92	
			2.5×10^{-3}	3.59 ± 0.15		
			6.25×10^{-3}	10.8 ± 0.4		
	37		1.25×10^{-3}	5.6 ± 0.1	7400 ± 600	
			2.5×10^{-3}	12.1 ± 0.3		
			6.25×10^{-3}	33.2 ± 1.5		
			1.25×10^{-2}	92.2 ± 3.0		
	25	5			1850 ± 25	*d*
		25			1560 ± 30	
		50			1350 ± 40	
		75			1090 ± 40	
		100			1005 ± 80	
$Fe^{III}(CN)_5H_2O^{2-}$	25	0.1	5×10^{-4}	1.57 ± 0.08	3010 ± 65	
			1×10^{-3}	3.3 ± 0.1		
			1.5×10^{-3}	4.5 ± 0.1		
			2×10^{-3}	6.4 ± 0.2		
			4×10^{-3}	12.0 ± 0.4		
	32		2×10^{-3}	18.0 ± 1.2	9000 ± 100	
	40		2×10^{-3}	35.2 ± 2.0	17600 ± 400	
	25	5			2980 ± 80	
		25			2800 ± 120	
		50			2650 ± 100	
		75			2450 ± 80	
		100			2140 ± 70	
N_3^-	20	0.1	9.5×10^{-3}	5.7 ± 0.1	604 ± 30	*e*
	25		9.5×10^{-3}	8.8 ± 0.2	927 ± 40	
	37		9.5×10^{-3}	26.0 ± 0.8	2740 ± 100	
	25	5			898 ± 40	*e*
		25			863 ± 30	
		50			802 ± 30	
		75			753 ± 20	
		100			700 ± 25	

[a] $[B_{12}–H_2O^+] = (1–2) \times 10^{-4}$ M; ionic strength = 0.1 M; pH ≈ 6. [b] Mean value of at least four kinetic runs. [c] Calculated from the slope of k_{obs} versus [L] by using one zero point. [d] pH = 6.0; ionic strength = 0.125 M. [e] pH = 6.4; ionic strength = 0.5 M.

Data for the temperature and pressure dependence of k_1 are summarized in Table III. The temperature parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were estimated in the usual way, whereas the pressure parameter $\Delta V^{\ddagger}$ was calculated from the slope ($=-\Delta V^{\ddagger}/RT$) of a ln k_1 versus pressure plot. The latter plots were linear within the experimental error limits (see Figure 3) and a summary of the rate and activation parameters for the studied anation reactions of $B_{12}–H_2O^+$ is given in Table IV. Data for the anation by N_3^- are also included in these tables, since by way of comparison N_3^- is also a N-donor ligand but with a single negative charge. This reaction was studied in the pH range 6.0–6.7 where the principal reactive species are $B_{12}–H_2O^+$ and N_3^-. At lower or higher pH, protonation or deprotonation interferes, respectively, with the anation process.[21,24] The activation parameters were studied at pH 6.4, and k_1 was determined in the way described above.

Table IV. Rate and Activation Parameters for $B_{12}–H_2O^+ + L \rightarrow B_{12}–L^+ + H_2O$[a]

L	k_1(25 °C), $M^{-1}\ s^{-1}$	$\Delta H^{\ddagger}$, kJ mol^{-1}	$\Delta S^{\ddagger}$ J $K^{-1}\ mol^{-1}$	$\Delta V^{\ddagger}$, $cm^3\ mol^{-1}$
$Fe^{II}(CN)_5NO^{2-}$	3560 ± 79	56 ± 2	10 ± 8	+8.9 ± 0.5
$Fe(CN)_6^{4-}$	1750 ± 92	84 ± 5	101 ± 16	+16.2 ± 1.2
$Fe^{III}(CN)_5H_2O^{2-}$	3010 ± 65	88 ± 15	119 ± 49	+8.2 ± 0.8
N_3^-	927 ± 40	65 ± 2	30 ± 5	+6.9 ± 0.2

[a] For experimental conditions and experimental data see Table III.

A comparison of the rate and activation parameters indicates that the anation reaction is rather independent of the nature of the anating ligand, an observation that has been reported before.[21] Furthermore, the reported values of $\Delta S^{\ddagger}$ and $\Delta V^{\ddagger}$ are significantly positive, which also underline the operation of a dissociative

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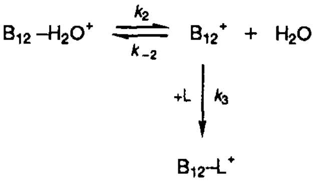
substitution mode. Lengthy discussions in the literature[2,25] have, on the basis of kinetic data at ambient temperature and pressure, favored a dissociative interchange substitution mechanism. We will in our discussion mainly focus on the interpretation of the now available activation parameters, especially $\Delta V^\ddagger$, which is now generally accepted as a strong mechanistic discrimination parameter.[26,27] The data can be interpreted in terms of either a limiting D or an I_d mechansim, and both possibilities will be treated.



(3)

In terms of a limiting D mechanism, the reaction scheme outlined in (3), in the presence of excess L and with the steady-state approximation applied to the five-coordinate intermediate, results in the rate expression (4). It is safe to assume on the basis

$$k_{obs} = k_2k_3[L]/(k_{-2} + k_3[L]) \qquad (4)$$

of the linear dependence of k_{obs} on [L] that $k_{-2} \gg k_3[L]$, such that eq 4 simplifies to (5). Comparison of eq 2 and 5 introduces

$$k_{obs} \approx k_2k_3[L]/k_{-2} = k_1[L] \qquad (5)$$

the final equality, from which it follows that $k_1 = k_2k_3/k_{-2}$. The pressure dependence of k_1 will then result in $\Delta V^\ddagger(k_1) = \Delta V^\ddagger(k_2) + \Delta V^\ddagger(k_3) - \Delta V^\ddagger(k_{-2})$. The studied reactions are such that $\Delta V^\ddagger(k_2)$ and $\Delta V^\ddagger(k_{-2})$ should be common for all L and independent of L. We expect that $\Delta V^\ddagger(k_2) - \Delta V^\ddagger(k_{-2})$, i.e. the reaction volume for the formation of the five-coordinate intermediate, should be positive since a water molecule is being released from the coordination sphere, with a maximum value of 18 cm^3 mol^{-1}, the partial molar volume of water. Theoretical calculations,[28] however, demonstrate that this number can only be as large as +13 for an octahedral complex ion. The entrance of L into the B_{12} coordination sphere should be accompanied by an intrinsic volume decrease due to bond formation and a solvational volume increase due to charge neutralization and a decrease in electrostriction during this reaction. The magnitude of the intrinsic component should depend on the size, i.e. partial molar volume, of the entering ligand, whereas the solvational contribution should mainly be determined by the charge on the entering ligand L. A closer inspection of the $\Delta V^\ddagger$ data in Table IV demonstrates that these expected trends clearly show up. The gradual increase in $\Delta V^\ddagger(k_1)$ with increasing charge on the entering ligand demonstrates the important role of charge neutralization that will offset the volume decrease associated with the bond formation step. This effect will depend on the square of the charge on the reactant and transition state species, which accounts for the substantial increase in $\Delta V^\ddagger(k_1)$ observed for the reaction with $Fe(CN)_6^{4-}$, i.e. where the decrease in electrostriction in going from a 1+ and 4− species to a 3− species will be the largest. It follows from the above discussion that the smallest $\Delta V^\ddagger(k_1)$ value will be expected for the reaction with a neutral entering ligand since then $\Delta V^\ddagger(k_3)$ will be significantly negative due to the intrinsic bond formation component and will offset the positive $\Delta\bar{V}(K_2)$ contribution. In this respect it is interesting to note that a recent thesis reported $\Delta V^\ddagger(k_1)$ values of +3.6 ± 0.5 and +6.0 ± 0.6 cm^3 mol^{-1} for the anation of $B_{12}-H_2O^+$ by thiourea and $S_2O_3^{2-}$, respectively.[29] In addition, Hasinoff[30] reported a value of +5.5 ± 0.8 cm^3 mol^{-1} for the anation by iodide. These values seem to be in good agreement with the results in Table IV, especially when the size of the entering ligand is also taken into account. Important seems to be the significantly smaller value found for the reaction with the neutral thiourea as expected on the basis of the above given arguments.

If we consider the possibility of an I_d mechanism as outlined in (6), the expression for the observed rate constant is given in (7), which simplifies as shown under the conditions of this in-

$$B_{12}-H_2O^+ + L \xrightleftharpoons{K_4} B_{12}-H_2O^+\cdot L \xrightarrow{k_5} B_{12}-L^+ + H_2O \qquad (6)$$

$$k_{obs} = k_5K_4[L]/(1 + K_4[L]) \approx k_5K_4[L] = k_1[L] \qquad (7)$$

vestigation, i.e. linear dependence of k_{obs} on [L] and $1 + K_4[L] \approx 1$. In this case the pressure dependence of k_1 will result in $\Delta V^\ddagger(k_1) = \Delta V^\ddagger(k_5) + \Delta\bar{V}(K_4)$, where the latter term represents the reaction volume for the formation of the intermediate ion-pair complex. It is expected that $\Delta\bar{V}(K_4)$ will strongly depend on the charge on L, since that will determine the change in electrostriction and the associated volume increase. Again $\Delta V^\ddagger(k_5)$ for a dissociatively activated interchange process should be fairly independent of the nature of L. In the case of a neutral entering ligand, $\Delta\bar{V}(K_4)$ will be close to zero, and the value of +3.3 ± 0.5 cm^3 mol^{-1} reported for the reaction with thiourea should mainly represent $\Delta V^\ddagger(k_5)$. This is indeed a very realistic value for an I_d type of mechanism based on the magnitude of such values reported for anation and solvent-exchange processes.[31,32] Furthermore, the contribution of $\Delta V^\ddagger(k_5)$ should be independent of the nature of the entering group, such that $\Delta V^\ddagger(k_1) - \Delta V^\ddagger(k_5)$ should represent $\Delta\bar{V}(K_4)$, which should increase with increasing charge on the entering ligand. The values in Table IV suggest that this component increases from approximately 3 cm^3 mol^{-1} for the anation by N_3^- to approximately 5 cm^3 mol^{-1} for the anation by $Fe^{II}(CN)_5NO^{2-}$ and $Fe^{III}(CN)_5H_2O^{2-}$, up to approximately 12 cm^3 mol^{-1} for the anation by $Fe^{II}(CN)_6^{4-}$. Theoretical calculations using the Fuoss equation and the outlined procedure reported before[33] reveal that for an ionic strength of 0.1 M and a distance of closest approach of 0.5 nm, $\Delta\bar{V}(K_4)$ has values of 2.2, 3.3, and 5.5 cm^3 mol^{-1} for $Z_+Z_- = -1, -2$, and -4, respectively. It follows that the observed effects are significantly larger especially for $Z_+Z_- = -4$, from which we conclude that the variation in the $\Delta V^\ddagger(k_1)$ data in Table IV cannot be ascribed to the contribution from ion-pair formation in terms of an I_d mechanism.

We conclude from the above treatment that it is more appropriate to assign the observed pressure effects to the operation of a D mechanism. This is also in good agreement with the enhanced substitution reactivity reported for cobalt(III) porphyrin complexes, for which the positive volumes of activation were also interpreted in terms of a D mechanism.[34,35] Labilization of the Co(III) center in $B_{12}-H_2O^+$ follows a similar trend as for porphyrin complexes and induces the operation of a D mechanism.

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Registry No. $Zn_3[cobalamin-\mu-NC-Fe(CN)_5]_2$, 123148-17-4; $Na_4[Fe(CN)_6]$, 13601-19-9; $Fe(CN)_5NO^{2-}$, 15078-28-1; $Fe(CN)_5H_2O^{2-}$, 19413-97-9; N_3^-, 14343-69-2; hydroxocobalamin hydrochloride, 59461-30-2.

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