# 91. Base Hydrolysis of Pentaaminecobalt(III) Complexes: The [CoX(dien)(dapo)]$^{n+}$ System

Part 3

## The Internal Conjugate Base Mechanism

by **Peter Comba**[a])*, **W. Gregory Jackson**[c])*, **Werner Marty**[b])[1]), and **Luc Zipper**[a])

[a]) Institut für Anorganische Chemie, Universität Basel, CH-4056 Basel
[b]) Institut de Chimie, Université de Neuchâtel, CH-2000 Neuchâtel
[c]) Chemistry Department, University College (N. S. W.), Australian Defence Force Academy, Campbell, A.C.T., Australia 2600

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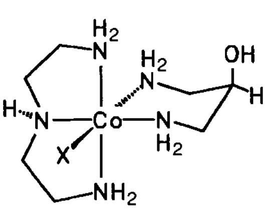
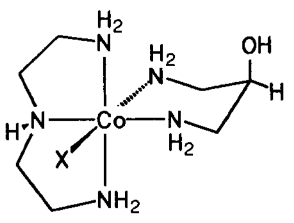
Azide anation and racemization of optically pure *mer-exo*(H)- and *mer-endo*(H)-[Co(OH)(dien)(dapo)]$^{2+}$ (**A** and **B** (X = OH), resp.; dien = *N*-(2-aminoethyl)ethane-1,2-diamine; dapo = 1,3-diaminopropan-2-ol) involve the same symmetrical pentacoordinate intermediate as the base hydrolyses of the corresponding *mer-exo*(H)- and *mer-endo*(H)-[CoX(dien)(dapo)]$^{2+}$ species **A** and **B**, respectively, where X = Cl, Br, or $N_3$. The kinetic parameters of the anation process are fully compatible with the independently measured competition ratio. The rate data reveal that substitution of $OH^-$ is unexpectedly fast, *viz.* it is not consistent with the usual sequence $Br^- > Cl^- > H_2O > N_3^- > OH^-$. This behavior is interpreted on the basis of an internal conjugate base mechanism which involves an amino-hydroxo/aminato-aqua tautomerism, *viz.* the reaction is actually an $OH^-$-catalyzed substitution of [CoH$_2$O(dien)(dapo)]$^{3+}$ where deprotonation occurs effectively at the secondary-amine site NH of dien.

**Introduction.** – Base hydrolysis of pentaaminecobalt(III) is an extensively studied example of an induced substitution process [1]. The widely accepted $S_N1CB$ mechanism incorporates the formation of a conjugate base in a fast pre-equilibrium and rate-determining loss of the leaving group[2]). We designed and investigated a pentaaminecobalt(III) system, *mer-exo*(H)- and *mer-endo*(H)-[CoX(dien)(dapo)]$^{n+}$ (**A** and **B**, resp.; X = Cl$^-$,



**A** *mer-exo*(H)



**B** *mer-endo*(H)

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[1]) Deceased on September 20th, 1986.

[2]) A recent study of kinetics of and competition during base hydrolysis of pentaaminecobalt(III) complexes was interpreted in terms of an $I_DCB$ mechanism [2] [3]. This is not fully compatible with our results, *viz.* an $I_DCB$ mechanism is only possible if the intermediate is allowed to relax stereochemically (see below and [4–6]).

$Br^-$, $N_3^-$, $OH^-$, and $H_2O$)[3]) and the corresponding *fac*-isomers. The two major features of this system are: *i*) The *mer*-isomers experience a large catalysis of hydrolysis in base (acceleration factor *ca.* $10^{10}$) and the intermediate of reduced coordination number is comparably selective. *ii*) The availability of two epimeric pairs of enantiomers allows the determination of the deprotonation site leading to the reactive conjugate base (secondary NH of dien) and of the structure of the pentacoordinate intermediate (trigonal bipyramidal); the stage of back-protonation is not known unambiguously but believed to occur after capture of nucleophiles. A preliminary report [4], synthetic, structural, and spectroscopic details of all geometric isomers [5] and a thorough study of kinetics and mechanism of the *fac*- and *mer*-isomers [6] were published.

An intriguing feature of the base-hydrolysis reactivity of *mer*-$[CoX(dien)(dapo)]^{n+}$ (**A** and **B**) is the fact that the hydroxo complexes are substantially more reactive than expected on the basis of the usual reactivity sequence $Br^- > Cl^- > H_2O > N_3^- > OH^-$. Herein we present results supporting an internal conjugate base mechanism [7–10], based on the analysis of the kinetics and stereochemistry of the azide-ion anation and racemization of *mer-exo*(H)- and *mer-endo*(H)-$[Co(OH)(dien)(dapo)]^{2+}$ (**A** and **B**, X = OH).

**Experimental.** – *General.* See [5] [6].

*Azide-Anation Kinetics.* The anation of *mer-exo*(H)- and *mer-endo*(H)-$[Co(OH)(dien)(dapo)]^{2+}$ (**A** and **B**, X = OH) was followed spectrophotometrically ($\lambda$ = 300 or 350 nm) as a function of $[N_3^-]$ and pH. The $[N_3^-]$-dependent kinetics were followed at two ionic strengths ($I$ = 1.0 and 1.1M ($NaClO_4$) and at two pH's (pH 7.58 and 8.06, 2,2′,2″-nitrilotris(ethanol), $[base]_{tot}$ = 0.2M). In the first set of experiments, the azide concentration was adjusted by mixing stock solns. ($I$ = 1.0M each) of buffer and $NaN_3$ in appropriate ratios, and thus the total base concentration was not constant. In a second set of experiments, both the $NaClO_4$ and $NaN_3$ solns. were identically buffered ($I$ = 1.1M, 1.0M ($NaClO_4$ or $NaN_3$), 0.2M 2,2′,2″-nitrilotris(ethanol) 1/2-neutralized with $HClO_4$). To these solns., placed in a 1-cm quartz cell, thermostated to 25.0 ± 0.1°, was injected a thermostated soln. (25 µl) of *mer-exo*(H)- or *mer-endo*(H)-$[Co(H_2O)(dien)(dapo)]Cl_3 \cdot H_2O$ (**A** $Cl_3 \cdot H_2O$ or **B** $Cl_3 \cdot H_2O$, X = $H_2O$; pH *ca.* 2.5 ($HClO_4$), resulting complex concentration *ca.* $1 \cdot 10^{-4}$M), rapidly mixed, and the absorbance *vs.* time measurements started within *ca.* 5 s. The pH-dependent kinetics were done in a similar way but using $[N_3^-]$ = 1.0M and different buffers (pyridine, 2,2′,2″-nitrilotris(ethanol), 2,2′-iminobis(ethanol), azide alone).

*$pK_a$ Measurements.* Titrations were performed on solns. of pure *mer-exo*(H)- and *mer-endo*(H)-$[Co(H_2O)(dien)(dapo)]^{3+}$ (**A** and **B**, resp.; X = $H_2O$), prepared *in situ* by nitrosation of the corresponding azido complexes [5][4]). Blank experiments showed that neither of the added substrates had any significant influence on the measured pH values.

**Results and Interpretation.** – Azide anation of **A** and **B** (X = OH) and of the corresponding aqua complexes is a reversible process (*Eqn. 1*).

$$[Co{-}OH]^{2+} + N_3^- \underset{k_r}{\overset{k_f}{\rightleftharpoons}} [Co{-}N_3]^{2+} + OH^- \qquad (1)$$

Thus, to avoid the problem of reversibility in the study of the base hydrolysis of the azido isomers, we had to work at sufficiently low cobalt concentrations (and hence $[N_3^-]$) and

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[3]) Abbreviations: dien = *N*-(2-aminoethyl)ethane-1,2-diamine; dapo = 1,3-diaminopropan-2-ol.

[4]) In the timescale of the titration experiments, equilibration between epimers **A** and **B** (X = OH) would have occurred ($t_{1/2}$ *ca.* 10 s), and $pK_a$ is, therefore, a weighted (90 :10) average for the two forms; the two values are unlikely to be very different.

high [OH$^-$]. Conversely, to observe the anations reported herein, we had to work at sufficiently high [$N_3^-$] and low [OH$^-$] to avoid appreciable reversibility.

At the higher of the two pH's used (8.06), we determined spectrophotometrically, both directly and indirectly using ion-exchange chromatography to separate the azido and aqua (after acid quenching) complexes, that at 0.05M $N_3^-$, the anation proceeded to 93% completion. Thus, at lower pH and for higher [$N_3^-$], reversibility was not significant, but some allowance was required in the data analysis as described below.

*$N_3^-$ Anation of* mer-exo*(H)-[Co(OH)(dien)(dapo)]$^{2+}$* (**A**, X = OH). Excellent single exponential behavior was observed for all pH's and [$N_3^-$] for the large absorbance increases with time at 350 and 300 nm, and pseudo-first-order rate constants, calculated in the usual way, are averages of at least three determinations. Identical results were obtained at either wavelength. Significantly, results for the same [$N_3^-$] but different pH's, corresponding to a *ca.* 3-fold variation in [OH$^-$], were identical. Also, the data sets for varied [$N_3^-$] at a particular pH but different ionic strength ($I$ = 1.0 and 1.1M) were essentially the same (*Table 1*).

Table 1. *Observed Azide-Anation Rates* (corrected for reversability) *of* mer-exo*(H)- and* mer-endo*(H)-[Co(OH)(dien)(dapo)]$^{2+}$* (**A** and **B** (X = OH), resp.). Both data sets are identical within the error, see text; shown are averaged $k_{obs}$ as a function of [$N_3^-$] at pH 8.06, 298 K, and $I$ = 1.0M.

| [$N_3^-$] [M] | $k_{obs} \cdot 10^2$ [s$^{-1}$] | | [$N_3^-$] [M] | $k_{obs} \cdot 10^2$ [s$^{-1}$] | |
|---|---|---|---|---|---|
| | $I$ = 1.0M[a][c] | $I$ = 1.1M[b][c] | | $I$ = 1.0M[a][c] | $I$ = 1.1M[b][c] |
| 0.05 | 0.49 | 0.49 | 0.60 | 2.41 | 2.25 |
| 0.10 | 0.83 | 0.78 | 0.70 | – | 2.49 |
| 0.20 | 1.32 | 1.32 | 0.75 | 2.47 | – |
| 0.26 | 1.57 | – | 0.76 | 2.51 | – |
| 0.30 | 1.76 | 1.65 | 0.80 | – | 2.50 |
| 0.40 | 1.97 | 1.83 | 0.90 | 2.52 | 2.63 |
| 0.50 | 2.23, 2.22[d] | 2.20 | 1.0 | – | 2.65 |

[a] Data fit to *Eqn. 6* using a 0,0 point yields $k = (3.51 \pm 0.09) \cdot 10^{-2}$ s$^{-1}$, $K = 3.18 \pm 0.15$; data fit to *Eqn. 9* with $k_r = 3.9 \cdot 10^{-4}$ s$^{-1}$ yields $k = (3.61 \pm 0.10) \cdot 10^{-2}$ s$^{-1}$, $K = 2.91 \pm 0.15$.

[b] Data fit to *Eqn. 6* using a 0,0 point yields $k = (3.56 \pm 0.09) \cdot 10^{-2}$ s$^{-1}$, $K = 2.95 \pm 0.15$; data fit to *Eqn. 9* with $k_r = 3.9 \cdot 10^{-4}$ s$^{-1}$ yields $k = (3.67 \pm 0.09) \cdot 10^{-2}$ s$^{-1}$, $K = 2.69 \pm 0.13$.

[c] Results of all the data fitted to *Eqn. 9*: $k = (3.63 \pm 0.07) \cdot 10^{-2}$ s$^{-1}$, $K = 2.8 \pm 0.1$.

[d] *mer-endo*(H)-reactant **B** (X = OH); $k_{obs}$ for slower reaction phase.

The two pH's employed for the varied [$N_3^-$] studies are both well above the p$K_a$ of **A** and **B** (X = $H_2O$; p$K_a \approx 5.5$), and hence the rate data are appropriate to the [Co(OH)(dien)(dapo)]$^{2+}$ species which clearly is fully formed. The pH independences of the specific rates, therefore, exclude significant *external* base-catalysis for the loss of OH$^-$ from the hydroxo complex, at least up to pH 8.5.

The dependence of $k_{obs}$ on [$N_3^-$] clearly is nonlinear (see *Fig. 1*), and the data were fitted to the two rate laws of *Eqns. 2* and *3*.

$$k_{obs} = \frac{a \cdot [N_3^-]}{1 + b \cdot [N_3^-]} \tag{2}$$

$$k_{obs} = \frac{a' + a \cdot [N_3^-]}{1 + b \cdot [N_3^-]} \tag{3}$$

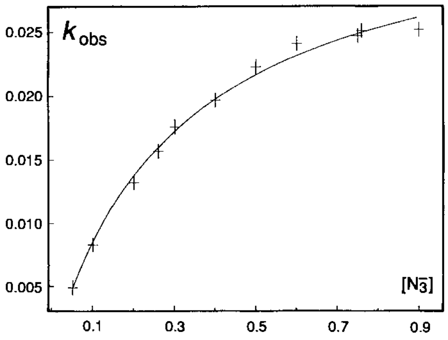


Fig. 1. *Observed specific azide-anation rates of* mer-exo*(H)-[Co(OH)(dien)(dapo)]*$^{2+}$ (A, X = OH) *as a function of* *[*$N_3^-$*]*. At pH 8.06, 298 K, and $I$ = 1.0M; fitted to the rate law $k_{\mathrm{obs}} = (k_r + kK\,[N_3^-])/(1 + K[N_3^-])$ using $k_r = 3.9 \cdot 10^{-4}$ s$^{-1}$ (fixed) and with values for the parameters $k = (3.6 \pm 0.09) \cdot 10^{-2}$ s$^{-1}$ and $K = 2.8 \pm 0.3$M$^{-1}$ (solid line).

The rate law of *Eqn. 3* is more highly parameterized, and we argue (see below) that *a*' should be effectively zero (in the fit of the data to this model, it comes out close to zero). Thus the simpler model is used for the moment.

At least two chemically reasonable mechanisms can accomodate this rate law. For the ion-pair mechanism of *Eqn. 4*, the rate law is given in *Eqn. 5*.

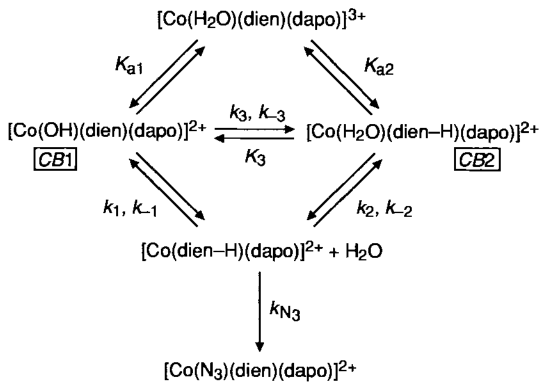
$$[\mathrm{Co(OH)}]^{2+} + \mathrm{N}_3^- \underset{\text{fast}}{\overset{K}{\rightleftharpoons}} [\mathrm{Co(OH)}]^{2+}, \mathrm{N}_3^- \underset{\text{slow}}{\overset{k}{\rightarrow}} [\mathrm{Co(N)}]_3^{2+} \tag{4}$$

$$k_{\mathrm{obs}} \frac{k \cdot K \cdot [\mathrm{N}_3^-]}{1 + K \cdot [\mathrm{N}_3^-]} \tag{5}$$

For the ion-pair model, $K$ = 3.1 (or 2.8, see below) is far too large for a 2+/1− ion pair interaction at $I$ = 1.0M [11]. Also, if no internal conjugate base process is involved, the value of $k$ ($3.6 \cdot 10^{-2}$ s$^{-1}$) is far too large for simple substitution of OH$^-$ by another nucleophile, *viz.* the model does not accommodate the enormous reactivity of the hydroxo complex towards Co—OH bond cleavage.

An alternative mechanism, involving an internal conjugate base process leading to a reduced coordination number intermediate is shown in *Scheme 1*. If the steady-state

*Scheme 1*



approximation is applied to $[Co(H_2O)(dien - H)(dapo)]^{2+}$ and $[Co(dien - H)(dapo)]^{2+}$, *Eqn. 6* is obtained.

$$k_{obs} = \frac{\cdot \dfrac{k_2}{k_{-3}} \cdot \dfrac{k_{N3}}{k_{-3}} \cdot k_3 \cdot [N_3^-]}{1 + \left(\dfrac{k_2}{k_{-3}} + 1\right) \cdot \dfrac{k_{N3}}{k_{-2}} \cdot [N_3^-]} \tag{6}$$

$k_{N3}/k_{-2} = R = 1.4 M^{-1}$ (competition ratio) is known independently [6], and it follows that $k_2/k_{-3} = 1.0$ and $k_3 = 0.026\ s^{-1}$. Since $K_3 = k_3/k_{-3} \approx 10^{-9}$, $k_{-3} \approx 10^7$–$10^8\ s^{-1}$ and $k_2 \approx 10^7$–$10^8\ s^{-1}$, similar to the corresponding bromo complex ($k_{OH} = k_2 \cdot K_b$, $K_b \cdot 0.01$–$0.1 M^{-1}$), is estimated.

An (aqua)(amine)metal-ion complex has two kinds of proton acidities, *viz.* deprotonation of the coordinated $H_2O$ molecule leading to the conjugate base *CB*1 ($pK_{a1} \approx 6$, see below) and deprotonation of a coordinated amine leading to the conjugate base *CB*2 ($pK_{a2} \approx 15$ [12]5); $pK_{a2} \approx 15$ and $pK_{a2} \approx 16.5$ for 3+ (aqua) and 2+ (hydroxo, chloro, bromo, and azido) complexes, respectively, seem to be reasonable assumptions). The equilibrium constant governing the formation of the internal conjugate base $K_3$ (*Scheme 1*) may, therefore, be estimated (*Eqn. 7*).

$$K_3 = \frac{[[H_2N{-}Co{-}OH_2]^{2+}]}{[[H_3N{-}Co{-}OH]^{2+}]} = \frac{K_{a2}}{K_{a1}} \approx 10^{-9} \tag{7}$$

The metal ion, overall charge, amine substituents, and the presence of other ligands all affect individual $pK_a$ values. However, to some extent, they are not critical variables for $K_3$ because these are common factors. From *Scheme 1* and *Eqn. 8* it follows that with $K_3 \approx 10^{-9}$, appreciable reaction (e.g. $\geqslant 50\%$) *via CB*2 requires $k_2/k_1 > 10^9$.

$$\%\ \text{reaction}\ \textit{via CB}2 = \frac{10^2 \cdot (k_2/k_1) \cdot K_3}{1 + (k_2/k_1) \cdot K_3} \tag{8}$$

The rate law for the reaction of the hydroxo complexes, based on *Scheme 1*, has the form of $k_{obs} = k_1 + k_2 \cdot K_3$, where the $k_1$ term corresponds to the usual slow substitution reaction of the hydroxo(pentaamine)cobalt(III) complex ($k_1 \leqslant 10^{-6} s^{-1}$ [5] [6]), while the $k_2 \cdot K_3$ term corresponds to the reaction of the (aminato)(aqua) tautomer, low in abundance ($K_3 \approx 10^9$), but extremely reactive ($k_2 \approx 10^6\ s^{-1}$)6)). Thus the $k_2 \cdot K_3$ term (*ca.* $10^{-3}\ s^{-1}$) dominates over the $k_1$ term (*ca.* $10^{-6}\ s^{-1}$), and the internal conjugate base path is thus viable. This analysis is consistent with the magnitude of the observed limiting anation rate ($3.6 \cdot 10^{-2}\ s^{-1}$).

The azido complexes mutarotate far too slowly to account for the observed inversion in the products of the azide anation [6]. The inversion arises *during* substitution, thus

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5) However, cage hexaaminecobalt(III) complexes have $pK_a \approx 10$, and the conjugate bases are stable and well characterized [12]. The $pK_a$ values of $[Co(en)_3]^{3+}$ (14.9) and $[Co(NO_2)(NH_3)_5]^{2+}$ (16.8) were determined spectrophotometrically in $DMSO/H_2O$ mixtures ($1 \rightarrow 0$) [13]. Recently, experimentally determined $pK_a$ values of hexaaminecobalt(III) ($pK_a \approx 13.8$) were obtained [14].

6) A value of $k_2$ can be estimated from $k_{OH}$ for the corresponding chloro complexes $k_{OH} = k_2 \cdot K_a / K_W \approx 10^5 M^{-1} s^{-1}$; $K_a \approx 10^{-15}$; $K_W = 10^{-14}$; $k_2 \approx 10^6\ s^{-1}$.

establishing the important result that N-deprotonation is a mechanistic requirement, and also identifying the site of deprotonation [6]. We note, however, that epimerization for the reactants **A** and **B** (X = OH) is quite rapid (see below), and it was conceivable that N-inversion occurred *prior* to azide substitution. The observed specific rate of epimerization is 0.13 $s^{-1}$, and the equilibrium is 90% of **A** (X = OH) and 10% of **B** (X = OH) [6]. Thus the specific rate for **A** → **B** (X = OH) is 0.013 $s^{-1}$, comparable but not faster than the rate of azide anation. The immediate appearance of both products **A** ($X = N_3$) and **B** ($X = N_3$), in a fixed isomeric ratio, therefore, precludes N-inversion by the route **A** (X = OH)→ **B** (X = OH)→ **B** ($X = N_3$). In fact, we show below that epimerization and anation proceed in parallel, through a common intermediate. $H_2O$ entry leads to epimerization (or regenerated reactant), while $N_3^-$ entry leads to anation with retention and inversion at the N-atom of dien. Thus, the observation of inversion at the N-atom during substitution coupled with the anomalously high azide-anation rates are consistent with an internal conjugate base process.

It is pertinent to note that $k_{obs}$ as determined is a measure of the forward plus reverse rates, and in the context of the azide anation kinetics, it is important to examine the magnitude of the reverse term, especially at low $[N_3^-]$ where it could assume significance (*Eqn. 9*, see also *Eqns. 2* and *3* and pertinent discussion).

$$k_{obs} = k_r + k_f = \frac{k_{OH} \cdot [OH^-] + k \cdot K \cdot [N_3^-]}{1 + K \cdot [N_3^-]} = \frac{k_r + k \cdot K \cdot [N_3^-]}{1 + K \cdot [N_3^-]} \text{ at a specific pH} \qquad (9)$$

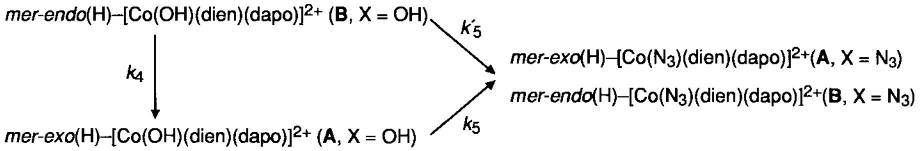
In the limit of $[N_3^-] = 0$, the 'reverse rate' is the specific hydrolysis rate $k_r$ at the pH in question, and this rate is known. The data were not of high-enough quality to directly evaluated this small correction term $k_r$ which diminishes with decreasing pH. Since the rate is known, $k_r$ was confined to its known value rather than used as an additional parameter which introduces larger uncertainties in the more important quantities $k$ and $K$. This strategy, however, is not straightforward. The azide anation gives both products **A** and **B**, and the reverse reaction is in fact a composite term of the hydrolysis of both epimers which have quite different rates [6]. The anation scheme can be kept simple if a reasonable approximation to the reverse rate can be made, and $k_r$ in the rate law (*Eqn. 9*) is small compared to $k$. An obvious approximation is given by the weighted average of the hydrolysis constants for the forms **A** and **B**, according to their relative abundances (70:30 [6]). Using the base-hydrolysis rates of the azido complexes (159 and 289$M^{-1}s^{-1}$ for **A** ($X = N_3$) and **B** ($X = N_3$), resp. [6]), the observed rates at pH 8.06 (25.0°, $I = 1.0$M) are $3.1 \cdot 10^{-4}$ and $5.9 \cdot 10^{-4} s^{-1}$, respectively. Thus $k_r$ is *ca.* $3.9 \cdot 10^{-4} s^{-1}$. The observed specific anation rate $k_f + k_r$ is $4.9 \cdot 10^{-3} s^{-1}$ at the lowest $[N_3^-]$ studied (0.05M), and thus $k_f > k_r$ by about a factor of 10 (at higher pH and lower $[N_3^-]$ the difference between forward and reverse rates diminishes). This analysis is consistent with spectral measurements of the hydroxo/azido pseudoequilibrium distribution which reveal 93% of azido and 7% of hydroxo complex ($[N_3^-] = 0.05$M, $I = 1.0$M, pH 8.06), giving a 13:1 ratio for the forward and reverse rates. The effect of *not* ignoring the small reverse term is that $k$ is hardly affected, but the value of $K$ is reduced from 3.1 to 2.8 (see *Table 1*).

*$N_3^-$ Anation of* mer-endo*(H)-[Co(OH)(dien)(dapo)]$^{2+}$* (**B**, X = OH). At 350 and 300 nm where the kinetics were examined, **A** and **B** ($X = H_2O$) (and presumably their hydroxo

forms) differ little in absorption. Similarly, the spectra of the products **A** and **B** ($X = N_3$) differ little from each other and are substantially more intense than the corresponding hydroxo ions. Thus, it was unexpected that the absorbance changes for the azide anations commencing with isomer **B** were considerably smaller than in the case of isomer **A**, especially as the product distributions were found to be identical. Also curious was the observation that the observed rates for the reactions from **A** and **B** were identical (within 5%). Similar but not identical rates might have been expected, based on the different hydrolysis rates for **A** and **B** ($X = N_3$).

Ion **B** (X = OH) is known to epimerize to **A** (X = OH) with a pH-independent specific rate of $0.13\ s^{-1}$ around pH 8 (25°, $I = 1.0$M, $NaClO_4$) [6]. This rate is *ca.* 5 times the azide-anation rate measured for the reactant **A** (X = OH) in 1M $N_3^-$, and, therefore, it is conceivable that we were actually measuring the rate starting from **A** (X = OH) when starting with **B** (X = OH) because the latter pre-isomerized. For the reaction shown in *Scheme 2*, the appropriate rate law is given in *Eqn. 10*. From simulated plots of $\ln(A - A_\infty)$, we could show for various relative magnitudes of the specific rates $k_5$ and $k_5'$ that it would indeed be difficult if not impossible to detect the very early curvature indicative of these consecutive reactions.

*Scheme 2*



$$[\text{azido complex}] = a \cdot \exp(-k_5 t) + b \cdot \exp((k_4 + k_5')t) \tag{10}$$

As discussed previously [6], **B** (X = OH) can epimerize to **A** (X = OH) by two pathways. In the first, N-inversion occurs in a 6-coordinate intermediate. In the second, the epimerization occurs by $H_2O$ exchange, involving a five-coordinate intermediate. An important difference between these two possibilities is that azide anation must occur *after* the epimerization in the first mechanism, and the resulting absorbance changes would be essentially the same as observed starting directly with isomer **A** (X = OH). This is in contrast to the facts. Also, if epimerization occurs *via* the $H_2O$ exchange route, $H_2O$ dissociation must be at least as fast as epimerization. It follows that azide capture, especially at higher concentrations, would also be fast because azide competes well with $H_2O$ in this system, and this is consistent with the facts. Finally, which mechanism operates is shown by the study of the racemization rate since this can only occur by the substitution pathway. These results are discussed separately below.

The clue to the anomalously small absorbance changes and the apparently identical rate from **A** (OH) and **B** (OH) can then be explained as follows: Azide-ion anation of **B** ($X = H_2O$) is very rapid, so rapid that it is not initially detected as a rate process but manifests itself as an apparently high 'initial' absorbance. The ensuing small absorbance change is then due to anation of the produced **A** ($X = H_2O$) initially formed in small amount in parallel with the azido complexes. This account accommodates all facts.

This proposal could be tested by quenching the azide anation of reactant **B** very early on in the slow step of the sequence, and looking for copious azido product along with some **A** ($X = H_2O$). The results confirmed the expectation. It could also be verified by slowing the rates to permit the direct observation of the initial faster step. Thus, by working at lower temperature (10°), low [$N_3^-$] (0.05M), and lower pH (where not all the aqua ion is converted to reactive hydroxo complex), we could observe the relatively fast initial increase in absorbance, followed by the slower rise attributable to the second azide anation step. We did not study in detail the azide dependence of the rate of anation of isomer **B**, but qualitatively, the rate from **B** is *ca.* 10-fold faster than that from isomer **A** at the same [$N_3^-$].

The important point is that we now know that the common product distribution is not merely apparent. The *mer-endo*(H)-reactant **B** like the *mer-exo*(H)-reactant **A** is substituted directly. Furthermore, the configuration of the azide-anation products was identical to those found for reactant **A** ($X = OH$), *viz.* 70% of **A** ($X = N_3$) and 30% of **B** ($X = N_3$). The significance of this result is elaborated in the *Discussion.*

*Racemization of* mer-exo*(H)-[Co(OH)(dien)(dapo)]*$^{2+}$ (**A**, $X = OH$). In our interpretation, the racemization rate cannot be smaller than the limiting azide-anation rate since we know that the latter involves an achiral intermediate because the azide products derived from it are racemic. Furthermore, since this is the only reasonable optically inactive intermediate that can be perceived for this reaction, it follows that racemization cannot be faster than the generation of this intermediate. Thus, **A** ($X = OH$) must racemize at exactly its limiting azide-anation rate, if the interpretation given to thc latter is correct. This rate was not precisely measured, but two experiments in which optically active **A** ($X = H_2O$) was reacted in pH 8 buffer for a time corresponding to about a half-life of the limiting anation rate showed considerably reduced but residual optical activity, consistent with these proposals.

*Mutarotation and Racemization of* mer-endo*(H)-[Co(OH)(dien)(dapo)]*$^{2+}$ (**B**, $X = OH$). The epimerization of **B** ($X = OH$) was described previously [6]. It corresponds to a mutarotation if the mechanism is *via* the six-coordinate intermediate but to a racemization if the mechanism is, as we have argued, *via* the substitution pathway. We did not directly measure the racemization rate, but again carried out duplicate experiments whereby optically active **B** ($X = H_2O$) in pH 8 buffer was reacted for a very short period, corresponding to about one half-life of the epimerization **B** ($X = OH$) → **A** ($X = OH$), and acid quenched. The isomers were separated and the optical activities of residual **B** and of product **A** determined. The results show that product **A** is, within the error limit, racemic, consistent with a reaction essentially *via* the substitution pathway and with a symmetrical pentacoordinate intermediate. Furthermore, recovered isomer **B** was optically active but not optically pure, consistent with such a process being operative, and indicating that $H_2O$ entry into the achiral five-coordinate intermediate gives comparable amounts of products **A** and **B** and, moreover, product that is racemic. This account is also consistent with the $N_3^-$ entry path leading to totally racemic product.

*Kinetics of Azide Anation of* mer-exo*(H)- and* mer-endo*(H)-[Co(OH)(dien)(dapo)]*$^{2+}$ (**A** and **B**, $X = OH$) *in the Lower pH Region.* The kinetics of anation by $N_3^-$ was studied in the pH range 4–9 using various buffers. In all these studies, the analysis of the results was complicated by the partial conversion of $N_3^-$ into $HN_3$ below pH *ca.* 5.5, with only the $N_3^-$ anion being apparently active as the nucleophile, and the rate is intrinsically dependent on $[N_3^-]$. Furthermore, the rate diminished as the pH was lowered because the hydroxo ion is converted into the inactive aqua form (see below).

We present here two data sets, one for reactant **A** (X = OH; *Table 2*) and one for **B** (X = OH; *Table 3*), for constant total azide ion (1M) with no added buffer other than the $N_3^-/NH_3$ system itself. The equation governing the azide anation under conditions where the hydroxo complex is not fully formed is given in *Eqn. 11*.

Table 2. *Observed and Corrected Azide-Anation Rates of* mer-exo*(H)-[Co(OH)(dien)(dapo)]*$^{2+}$ (**A**, X = OH) *as a Function of [OH*$^-$*]*. $[N_3^-]_{tot}$ = 1.0, 298 K, $I$ = 1.0M

| pH | $[N_3^-]_{eff}$ a) [M] | $k_{obs}\cdot 10^2$ [s$^{-1}$] | $k_{obs}^{corr,[N_3^-]=1.0}\cdot 10^2$ b) [s$^{-1}$] |
|---|---|---|---|
| 3.94 | 0.24 | 0.032 | 0.059 |
| 4.32 | 0.64 | 0.14 | 0.16 |
| 4.71 | 0.65 | 0.29 | 0.33 |
| 5.14 | 0.83 | 0.72 | 0.76 |
| 5.53 | 0.93 | 1.3 | 1.3 |
| 5.95 | 0.97 | 1.9 | 1.9 |
| 6.18 | 0.98 | 2.3 | 2.3 |
| 6.55 | 0.99 | 2.5 | 2.5 |
| 7.05 | 1.00 | 2.4 | 2.4 |
| 7.16 | 1.00 | 2.5 | 2.5 |
| 7.54 | 1.00 | 2.5 | 2.5 |
| 7.82 | 1.00 | 2.4 | 2.4 |

a) Corrected for partial conversion of $N_3^-$ to $HN_3$, see text.

b) Corrected for the rate variations caused by reduced $[N_3^-]$ (*Eqn. 12*, see text).

Table 3. *Observed and Corrected Azide-Anation Rates of* mer-endo*(H)-[Co(OH)-(dien)(dapo)]*$^{2+}$ (**B**, X = OH) *as a Funciton of [OH*$^-$*]*. $[N_3^-]_{tot}$ = 1.0, 298 K, $I$ = 1.0M.

| pH | $[N_3^-]_{eff}$ a) [M] | $k_{obs}\cdot 10^2$ [s$^{-1}$] | $k_{obs}^{corr,[N_3^-]=1.0}\cdot 10^2$ b) [s$^{-1}$] |
|---|---|---|---|
| 3.65 | 0.14 | 0.017 | 0.045 |
| 3.68 | 0.15 | 0.018 | 0.045 |
| 3.94 | 0.24 | 0.043 | 0.079 |
| 4.17 | 0.35 | 0.090 | 0.13 |
| 4.32 | 0.44 | 0.16 | 0.21 |
| 4.54 | 0.56 | 0.24 | 0.29 |
| 4.69 | 0.64 | 0.35 | 0.40 |
| 4.71 | 0.65 | 0.38 | 0.43 |
| 4.94 | 0.76 | 0.49 | 0.53 |
| 5.14 | 0.83 | 0.81 | 0.85 |
| 5.36 | 0.89 | 1.0 | 1.1 |
| 5.50 | 0.92 | 1.1 | 1.1 |
| 5.53 | 0.93 | 1.4 | 1.4 |
| 5.76 | 0.96 | 1.8 | 1.8 |
| 5.95 | 0.97 | 1.9 | 1.9 |
| 6.18 | 0.98 | 2.4 | 2.4 |
| 6.55 | 0.99 | 2.4 | 2.4 |
| 6.93 | 1.0 | 2.5 | 2.5 |
| 7.05 | 1.0 | 2.6 | 2.6 |
| 7.16 | 1.0 | 2.6 | 2.6 |

a) Corrected for partial conversion of $N_3^-$ to $HN_3$, see text.

b) Corrected for the rate variations caused by reduced $[N_3^-]$ (*Eqn. 12*, see text).

$$k_{\text{obs}} = \frac{K_a \cdot [\text{H}^+]}{1 + K_a \cdot [\text{H}^+]} \cdot \frac{k \cdot K \cdot [\text{N}_3^-]}{1 + K \cdot [\text{N}_3^-]} \tag{11}$$

$K_a$ is the acidity constant for the aqua complex (actually a weighted average for the 90:10 equilibrium mixture **A**/**B** (X = $H_2O$)), and the other symbols have the same meaning as before. The $[N_3^-]_{tot}$ is 1M in all cases, and the $[N_3^-]$ at the prevailing pH were calculated using the known value for p$K_a$ of $HN_3$ (4.44, $I$ = 1M, 25°). The data sets were analyzed using this equation with just $K_a$ for the aqua complex as the parameter, while $K$ and $k$ were fixed at their previously determined values, 2.8 and $3.6 \cdot 10^{-2} s^{-1}$, respectively. p$K_a$ 5.48 and 5.49 were obtained for **A** and **B**, respectively, and this is in good agreement with the values determined titrimetrically, 5.55 and 5.45, respectively.

The pH dependence of the azide-anation rates are shown graphically in *Fig. 2*. The $k_{obs}$ were corrected back to 1M azide to remove the rate variation with varying azide concentration (*Eqn. 12*).

$$k_{\text{obs}}^{\text{corr}} = k_{\text{obs}} \cdot \frac{1 + K \cdot [\text{N}_3^-]}{K \cdot [\text{N}_3^-]} \cdot \frac{K}{1 + K} = \frac{K_a \cdot [\text{H}^+]}{1 + K_a \cdot [\text{H}^+]} \cdot \frac{k \cdot K}{1 + K} \tag{12}$$

Thus a plot of the $k_{obs}^{corr}$ against pH should reflect a simple acid-base conversion, and indeed the plots in *Fig. 2* show the characteristic sigmoidal titration shape. Note also that the limiting rates at low pH are negligible, consistent with a zero contribution to the anation from the aqua complexes, and also negligible reversibility for the anation, even at low $[N_3^-]$, because of the greatly reduced $[OH^-]$.

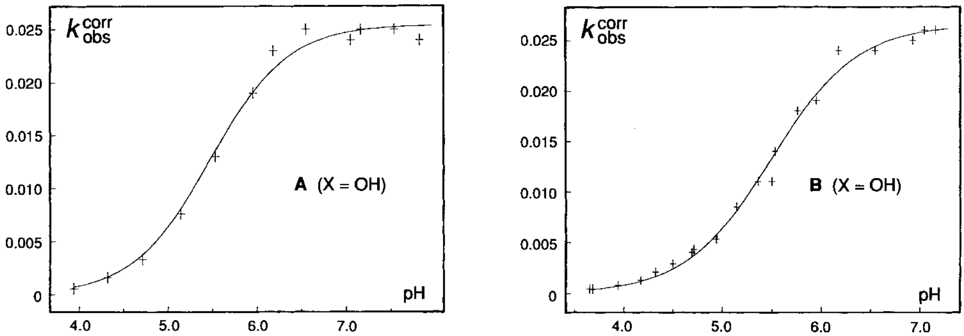


Fig. 2. *Observed specific azide-anation rates* (corrected for protonation of $N_3^-$) *of* mer-exo*(H)- and* mer-endo*(H)-[Co(OH)(dien)(dapo)]*$^{2+}$ (**A** and **B** (X = OH), resp.) *as a function of pH*. $[N_3^-]$ = 1.0, 298 K, and $I$ = 1.0M; fitted to *Eqn. 12* (see text) with p$K_a^{exo}$ = 5.55 or p$K_a^{endo}$ = 5.45, $k = (3.6 \pm 0.1) \cdot 10^{-2} s^{-1}$ and $K = 2.8 \pm 0.3 M^{-1}$ (solid lines).

A weighted fit of all data contained in *Tables 1–3* using the complete rate law *Eqn. 12* yielded p$K_a$ = 5.49, $k = 3.6 \cdot 10^{-2} s^{-1}$, and $K$ = 2.8, values very similar to those separately determined and indicating the internal consistency of all data.

*H-Exchange in* mer-exo*(H)- and* mer-endo*(H)-[Co(OH)(dien)(dapo)]*$^{2+}$ (**A** and **B**, X = OH). The exchange of the NH protons was monitored by $^{13}$C-NMR spectroscopy. The $\mathit{C}H_2NH_2$, $\mathit{C}H_2NHD$, and $\mathit{C}H_2ND_2$ signals are all clearly resolved at 75 MHz, similarly for the two diastereoisotopic C-atoms in $\alpha$-position to the secondary NH of dien, with the substitution of each H by a D resulting in an upfield shift of *ca.* 0.1 ppm. The results for **A** and **B** (X = $H_2O$) in $D_2O$ at several pH's in the acidic region confirmed the usual [$OH^-$] dependence, and this H-exchange is considerably faster than for the corresponding proton in **A** and **B** (X = Cl). The $NH_2$ protons *trans* to the aqua group exchanged at comparable rates (**A** (X = $H_2O$): *k*(*sec.* NH) = *k*(*trans* $NH_A$) + *k*(*trans* $NH_B$), and *k*(*trans* $NH_A$) = *k*(*trans* $NH_B$); **B** (X = $H_2O$): *k*(*sec.* NH) = *k*(*trans* $NH_A$) + *k*(*trans* $NH_B$), and *k*(*trans* $NH_A$) = *k*(*trans* $NH_B$)). These exchange rates refer of course to the hydroxo complexes exchanging *via* its internal conjugate base.

With respect to exchange at the important secondary NH center, isomer **B** was a little faster, consistent with the relative rates of internal base-catalyzed azide substitution, and exchange was complete before detectable epimerization (or anation), *viz.* retention predominates over inversion which is usual, and exchange is faster than substitution, and again this is usual.

**Discussion.** – Anation processes of pentaamine cobalts(III) are, in contrast to base hydrolyses, not particularly well studied. In general, anation kinetics in function of [$X^{n-}$] are not linear, *i.e.* at increasing [$X^{n-}$], saturation occurs [15–19]. This behavior implies a fast pre-equilibrium which usually was interpreted in terms of ion-pairing followed by a rate-determining interchange of the leaving solvent molecule with the anating anion. There are at least two problems with such an interpretation: *i*) The rate of interchange within the ion-pair cannot be faster than the $H_2O$-exchange rate $k^{H_2O}$, in fact a ratio $k^{N_3}/k^{H_2O}$ of *ca.* 0.2 is expected [17]. This actually is the ratio observed for most anions investigated in the (aqua)(pentaamine)cobalt(III) system, except for $N_3^-$ where a ratio of 1.0 emerges [16] [17]. *ii*) The ion-pairing constants $K_{IP}$ resulting from anation kinetics usually are unexpectedly large (*ca.* 2–5 $M^{-1}$) [15–17], *viz.* in disagreement with expectation ($K_{IP} \approx 0.1 M^{-1}$) [2] [11] [20].

The replacement of $H_2O$ by an anion in **A** and **B** (X = $H_2O$) is very slow, and this behavior is quite typical of pentaaminecobalt(III). However, the substitution of $OH^-$, which should be at least two orders of magnitude slower again, is surprisingly much faster in the case of entering $N_3^-$ (over $10^3$-fold). This is quite unusual cobalt(III) chemistry, and indeed unusual metal-ion chemistry in general.

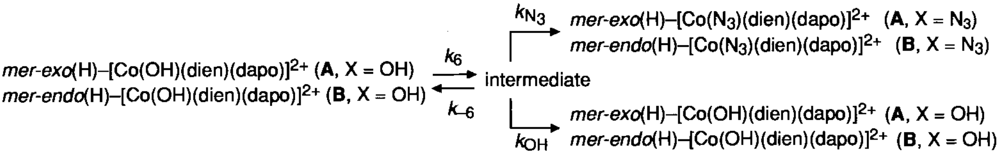
We showed that inversion at the secondary NH center occurs during $N_3^-$ substitution and that the rate is independent of external [$OH^-$]. This result excludes a conventional base-catalyzed pathway for the hydroxo complex which would have accommodated the N-inversion and pinpoints the reaction as being internally base-catalyzed. A like non-equilibrium distribution of 70% of **A** (X = $N_3$) and 30% of **B** (X = $N_3$) was observed starting with either reactant **A** or **B** (X = OH), indicating a common intermediate for azide incorporation and consistent with N-inversion occurring during substitution. The like results exclude the possibility of inversion prior to or after azide substitution, although these processes were independently observed. The latter is much slower than azide substitution of the hydroxo complex, but the former is comparable in rate.

Experiments using resolved **A** and **B** (X = OH) showed that each of the isomeric azido products was racemic, indicating an achiral intermediate. Furthermore, qualitative studies of racemization of resolved **A** and **B** (X = OH) in the same media but containing no azide confirmed that the optical activity was lost in the $H_2O$ dissociation step, *viz.* the same achiral intermediate was involved, and racemization occurred *via* a base-catalyzed

$H_2O$-exchange process. This feature was part of the design of the *mer*-[CoX(dien)(dapo)]$^{n+}$ system.

For the complete reaction (see *Scheme 3*), it can be shown that the specific rates for racemization, epimerization, and limiting azide anation are related. Thus $k_{rac} = k$ for isomers **A** and **B**, and $k_{epim}$ for $\mathbf{B} \rightarrow \mathbf{A}$ (X = OH) is smaller than $k$ for **B** ( = $(k_{OH}/k_{-6}) \cdot k$) by a factor reflecting the stereochemistry of $H_2O$ re-entry into the intermediate. This analysis is consistent with our measured $k_{epim}$ (0.13 $s^{-1}$) and our estimation that at 1M $N_3^-$, the rate for isomer **B** (X = OH) is *ca.* 10 times (or more) that for **A** (X = OH; *i.e. ca.* 0.36 $s^{-1}$). We

*Scheme 3*



can now actually calculate the stereochemistry for $H_2O$ entry and quantify this. The corresponding expression for epimerization of **A** (X = OH) is the same ($(k_{OH}/k_{-6}) \cdot k$), but here $k_{OH}/k_{-6}$ is the fraction of $H_2O$-entry events which lead to rearrangement (product **B** in this case). We deduced earlier that $k_{epim}$ for $\mathbf{A} \rightarrow \mathbf{B}$ is $0.1 \cdot k_{obs}$, since $k_{obs}$ is the sum of forward and reverse rates and the equilibrium comprises 10% of **A**. Thus, $k_{epim} = 0.1 \cdot 0.13 = 0.013$ $s^{-1}$. But $k = 0.036$ $s^{-1}$ for **A**, thus $k_{OH}/k_{-6} = 0.013/0.036 = 0.37$. Hence, $H_2O$ entry into the intermediate yields 37% of **B** (X = OH) and 63% of **A** (X = OH). This then leads to a calculated $k$ for **B** of $0.9 \cdot 0.13/0.63 = 0.19$ $s^{-1}$. Thus, **B** (X = OH) dissociates its bound $H_2O$ *via* its internal conjugate base 5–6 times faster than **A** (X = OH). Recalling that the total rate of disappearance of **B** has two components, azide anation and epimerization ($k_4 + k_5'$), whereas the rate for **A** has just the azide-anation component ($k_5'$), the conclusion can be drawn that **B** is more reactive than **A** by at least a factor of 10, especially at lower $N_3^-$ concentrations, and this is in accord with our estimate from other observations.

The internal conjugate base process established here may well be more general than is widely appreciated. It was proposed for various other systems [1] [9] [21], but never proven. The criteria for its effective operation were considered here, and it is clear that ions having especially reactive conjugate bases coupled with ions bearing a coordinated base such as $OH^-$, imidazolate, or phenoxide ion are especially suited to react in this manner, and we are pursuing the study of reactions of this kind. Pentaaminecobalt(III) complexes having 'flat' secondary-amine moities *cis* to the bound base are likely candidates [5] [6], and the *exo*(H)- and *endo*(H)-$\alpha\beta$-[Co(tetraen)(salicylate)]$^{2+}$ system is presently under active investigation [10].

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