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

Part 2

Structure and Reactivity of the Pentacoordinate Intermediate

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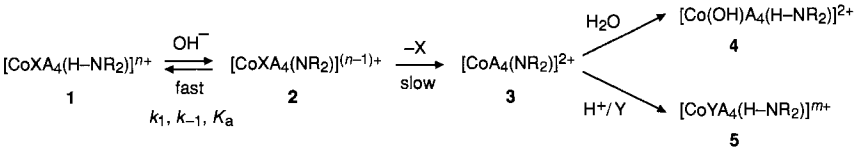
Base hydrolysis of optically pure *mer-exo*(H)- and *mer-endo*(H)-$[CoCl(dien)(dapo)]^{2+}$ (**A** and **B** (X = Cl), resp.; dien = *N*-(2-aminoethyl)ethane-1,2-diamine; dapo = 1,3-diaminopropan-2-ol, $k_{OH} = (1.13 \pm 0.09) \cdot 10^5$ $M^{-1}s^{-1}$ (**A** (X = Cl)), $k_{OH} = (1.18 \pm 0.11) \cdot 10^5 M^{-1}s^{-1}$ (**B** (X = Cl)); $I = 1.0$M ($NaClO_4$ or NaN_3), $T = 298$ K) is accompanied by retention of the *mer*-geometry and by full racemization (99 ± 1%). It is shown that this is not due to racemization of either reactants or products. This result, together with the fact that both **A** and **B** yield the same *mer-exo*(H)/*mer-endo*(H)-product distribution, indicates the intermediacy of a pentacoordinate species **II** which is symmetrical (at least in the time average), *viz.* trigonal bipyramidal with a deprotonated ('flat') secondary-amine moiety. The H-exchange rates of the coordinated amine groups are consistent with this interpretation and indicate that loss of Cl^- is the rate-determining step, in agreement with an S_N1CB mechanism. The reactivity of the *unsym-fac-exo*(OH)- and *unsym-fac-endo*(OH)-isomers **C** and **D**, respectively, is in sharp contrast: base hydrolysis is 3 orders of magnitude slower, and the reaction is accompanied by some change of coordination geometry (**C**, 23%; **D**, 10%), some inversion of configuration (**C**, 15%; **D**, 19%); and much lower acceleration of hydrolysis in base (10^6 *vs.* 10^{10}). Azide competition during base hydrolysis of the *mer*-isomers **A** and **B** is quite large ($R = [CoN_3]_\infty/[CoOH]_\infty[N_3^-] = 1.4 \pm 0.2 M^{-1}$, $I = 1.0$M, $T = 298$ K) and indicates that the coordinatively unsaturated intermediate **II** is highly selective. The ratios of *exo*(H)- and *endo*(H)-azide competition products **A** and **B** (X = N_3), respectively, immediately after the substitution reaction (kinetic control) are independent of the engaged epimer **A** or **B**: 31.7 ± 0.9% of **B** (X = N_3) and 68.3 ± 0.9% of **A** (X = N_3, determined after *ca.* $10 \cdot t_{1/2}$ of the base hydrolysis). This is in agreement with the effective site of deprotonation at the secondary(central)-amine group of dien, *cis* to the leaving group X, and with a common set of intermediates. Epimerization of **A** and **B** (X = Cl, N_3) is shown to proceed solely *via* the pentacoordinate (base hydrolysis) intermediate **II**, *viz.* the direct route involving a six-coordinate deprotonated intermediate is immeasurably slow. For the hydroxo products **A** and **B** (X = OH), the direct route may compete with the H_2O-substitution (exchange) path which can occur by an internal conjugate-base process. The kinetically controlled distribution of complexes **A**/**B** (X = N_3) is different from the quasi-thermodynamic one (19.1 ± 0.8% of **B** (X = N_3) and 80.9 ± 0.8% of **A** (X = N_3)). This is consistent with the differences in the base-hydrolysis rates of the reactants (k_{OH} (**A** (X = N_3)) = $(1.59 \pm 0.04) \cdot 10^2 M^{-1}s^{-1}$; k_{OH} (**B** (X = N_3)) = $(2.89 \pm 0.22) \cdot 10^2 M^{-1}s^{-1}$). Various aspects of the investigated reactions are discussed on the basis of the widely studied reaction of base hydrolysis of pentaaminecobalt(III) complexes. Also, the structure and reactivity of the pentacoordinate intermediate **II** are discussed in relation to various current models.

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

Introduction. – Base hydrolysis of pentaaminecobalt(III) complexes **1** (A = amine, X = leaving group) is a prototype of a substitution process with dissociative activation, and it usually is discussed as an S_N1CB process where loss of the leaving group X from an activated conjugate base **2** (fast pre-equilibrium) is the rate-determining step which leads to a pentacoordinate intermediate **3** of high reactivity (*Scheme 1*) [1] [2]. The

Scheme 1



A = amine ligand, X = leaving group

broad acceptance of this view is based on kinetic analysis [1] [3] [4], competition experiments [1] [3], and the analysis of activation parameters [1] [4–10]. The question of a coordinatively unsaturated intermediate state is more contentious [11–13] and was not considered in the original *Garrick* S_N1CB mechanism. An important aspect in this context is the question of ion-pairing and its influence on the reactivity of the conjugate base **2** and any coordinatively unsaturated intermediate state **3**. The ions in solution are all ion-paired to some extent, but there is evidence that, in reactions at constant and relatively high ionic strength, ion-pairing leads merely to a reduction of the substitution reactivity, probably caused by a reduction of the acidity of coordinated amines [3]. More recent studies performed at very low and variable ionic strength [11] [12] seem to indicate that, at least for $[CoX(NH_3)_5]^{n+}$, the mechanism proceeds *via* hexacoordinate intermediates[2]). Thus, in spite of extensive studies in the field, various points of interest are still contentious: *i*) Although the site of deprotonation is a widely discussed point of interest [1] [11] [12] [16], there exist few examples where it was determined experimentally. *ii*) The question of the stage of back-protonation was only addressed in few cases [12], and in most cases it was unclear whether protonation occurs at the pentacoordinated intermediate, after hydrolysis, or concerted with the capture of nucleophiles. *iii*) There has been continuing discussion concerning the structure of the pentacoordinated intermediate (in cases where it is formed). One approach to know more about the structure of this very short-lived intermediate is the study of the stereochemical course of base hydrolysis, and this was successful in some cases [16] [17]. *iv*) The hydrolysis of pentaaminecobalt(III) is accelerated in base by a factor of 10^5–10^{10}. There is a continuing argument on the reason for this large OH^- catalysis, an important and possibly the most challenging point. Evidently, a determination of the site of deprotonation, the stage of back-protonation, and the structure and approximate lifetime of any pentacoordinated intermediate, as well as the effects of ion-pairing are all substantial components of the puzzle.

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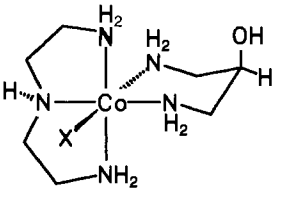
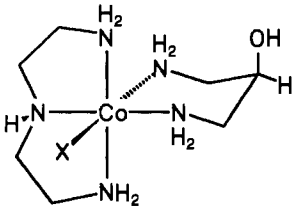
[2]) Our results (see below and [14–16]) are not fully compatible with the interpretation given in [12], *viz.* an I_DCB mechanism would only apply if the proposed hexacoordinate intermediate is allowed to relax stereochemically. Therefore, most of our results are explained by the classical S_N1CB mechanism involving a reduced-coordination-number intermediate, and a careful appreciation of the newer hypotheses in relation to our results is given below (see also [14–16]).

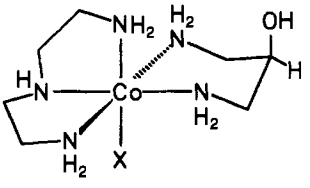
The remarkably fast rates of base hydrolysis were for a long time nearly exclusively discussed based on *Basolo* and *Pearson*'s idea of π-stabilization of the pentacoordinated intermediate by amido 2p to $Co^{III}d_{x^2-y^2}$ bonding [18] [19]. A necessary (but not sufficient) requirement for this model is a trigonal-bipyramidal pentacoordinate intermediate.



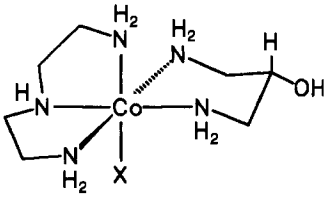
A *mer-exo*(H)



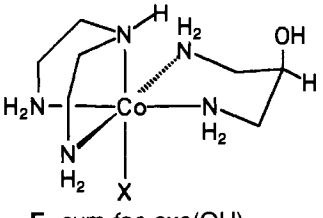
B *mer-endo*(H)



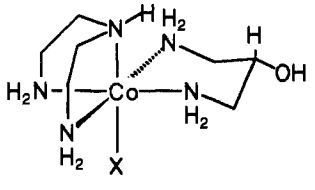
C *unsym-fac-exo*(OH)



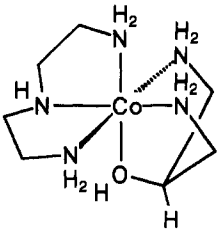
D *unsym-fac-endo*(OH)



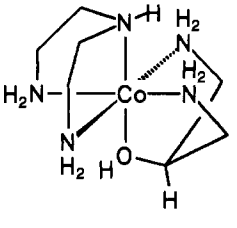
E *sym-fac-exo*(OH)



F *sym-fac-endo*(OH)



G *unsym-fac-N,N′,O*



H *sym-fac-N,N′,O*

However, even this condition was never experimentally substantiated. Moreover, a thorough theoretical analysis of the electronic aspects in support of the π-stabilization model was not presented. Other models, involving a spin change caused by deprotonation of a coordinated amine and level crossing, based on ligand-field studies, were reported some time ago [20–22]. From a recent ligand-field calculation, it emerges that a quintet ($^5E''$) rather than the earlier postulated triplet ($^3A_2'$) state is the groundstate of the trigonal-

bipyramidal intermediate [23] [24][3]). More recently, HMO and MS Xα calculations of the conjugate base and resulting substitution intermediates for the base hydrolysis of penta-aminecobalt(III), -rhodium(III), -chromium(III) complexes were performed [25]. They indicate that, for Co^{III}, deprotonation of a coordinated amine leads to thermal population of a six-coordinate reactive triplet state, which is substitutionally labile, and which, in favorable cases, might lead to a five-coordinate intermediate.

We chose the system $[CoX(dien(dapo)]^{n+}$ (see **A**–**H**)[4]) to shed some light on some of the unsolved problems of base hydrolysis of pentaaminecobalt(III) complexes. The main goal was to obtain information concerning the geometry of the very short-lived coordinatively unsaturated intermediate *via* stereochemical features during base hydrolysis. In the present publication, we will discuss the kinetics and stereochemistry of base hydrolysis of *mer-exo*(H)- and *mer-endo*(H)-$[CoX(dien)(dapo)]^{n+}$ (**A** and **B**, resp.; X = Cl, Br, N_3, and OH), in comparison with that of the *unsymfac*-complexes **C** and **D** (X = Cl), the competition behaviour of the *mer*-isomers **A** and **B**, and the kinetics and thermodynamics of their epimerization and racemization. The syntheses, separation, chiral resolution, and characterization of the geometric isomers of $[CoX(dien)(dapo)]^{n+}$ are reported in [14] and the reactivity of the hydroxo and aqua complexes **A** and **B** in [15].

Experimental. – 1. *General.* See [14]. In addition: All reagents were of anal. purity. H_2O was deionized (syntheses) or doubly distilled (spectroscopy and kinetics). Racemization kinetics: *PE-241* spectropolarimeter. Stopped-flow kinetics. *Dionex-Durrum-D-110* or *Hi-Tech-SF-2L* instrument. H-Exchange kinetics: by ^{1}H- or ^{13}C-NMR on *Bruker-WP-200* or *Varian-XL-300* spectrometer, respectively, at 25°. pH Measurements: *Metrohm-605* pH meter; *Orion-81025C* combined glass electrode (1M $NaClO_4$), calibrated by titrations of standard HCl and NaOH *Titrisol* (*Merck*) solns. (I = 1.0M, $NaClO_4$); reported pH values are, therefore, $p[H^+]$.

2. *Kinetic Measurements.* 2.1. *General.* Kinetics usually were measured using buffered (pyridine, 2,2′,2″-nitrilotris(ethanol) 2,2′-iminobis(ethanol), 2-aminoethanol, aminomethanol, methylamine, *Tris*, N_3^-, OH^-, imidazole, acetate, formiate) thermostated (25 ± 0.1°) aq. solns. ($[Co]_{tot} \approx 2 \cdot 10^{-3}$ M) of fixed ionic strength (I = 1.0M, $NaClO_4$). The fixed wavelengths used for base-hydrolysis kinetics (UV/VIS, CD, or stopped flow) were: **A** (X = Cl): 300, 305, 460, and 491 nm; **B** (X = Cl): 300, 305, and 469 nm; **A** (X = Br): 342 nm; **A** (X = N_3): 390, 490, and 494 nm; **B** (X = N_3): 390 and 467 nm; **C** (X = Cl): 305 and 502 nm; **D** (X = Cl): 310 nm; **C** (X = Br): 334 nm; **C** (X = N_3): 370 nm. When pseudo-first-order kinetics were observed, plots of $\log(D-D_\infty)$ *vs.* time were linear for at least 3 half-lives.

2.2. *Spectrophotometrically Measured Base-Hydrolysis Kinetics.* A known amount of the Co^{III} complexes was dissolved as quickly as possible in the pre-thermostated buffer soln. and transfered to the UV/VIS or CD spectrometer cells, and the fixed-wavelength or full-spectra kinetic runs were started immediately. Alternatively, the soln. of the Co^{III} complexes ($[Co]_{tot} \approx 4 \cdot 10^{-3}$, pH ≈ 3.0 ($HClO_4$)) and of a buffer were placed in separate thermostated syringes of a stopped-flow instrument. Perchlorate salts of the complexes were used rather than $ZnCl_4^{2-}$ salts where possible, because of opulescence caused by $Zn(OH)_2$ formation in base; millipore filtration was used where appropriate.

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[3]) Note, that these calculations [23] [24] were performed for spontaneous aquation, *viz.* all amines were fully protonated. However, it emerges that the activation energy (for the spin-flip and the formation of a trigonal-bipyramidal intermediate of reduced coordination number) decreases with π-donor ligands. This is consistent with an acceleration of hydrolysis in base. Moreover, qualitatively this effect is similar to *Basolo* and *Pearson*'s π-stabilization model [18] [19], where the amido π-donor is also the reason for the accelerated loss of the leaving group. However, we stress that there is a large conceptional difference between the two models.

[4]) Abbreviations: dien = 1,5-diamino-3-azapentane; dapo = 1,3-diaminopropan-2-ol; dpt = 1,7-diamino-4-azaheptane; tn = propane-1,3-diamine; en = ethane-1,2-diamine.

2.3. *Rates of Base Hydrolysis of* **A** *and* **B** *in* N_3^- *Media* were measured with the stopped-flow setup. The competitor (N_3^-) was included in the buffer soln. The kinetics were followed at a wavelength corresponding to an isosbestic point of the azido and hydroxo complexes involved, to eliminate biphasic behavior arising from facile N_3^- anation of the hydroxo products.

2.4. *Kinetics of Base Hydrolysis of* **A** *and* **B** (X = N_3) were measured spectrophotometrically (350 and 300 nm) at relatively low [Co] to avoid the problem (see below) of kinetic mass-law retardation, parallel epimerization *via* hydrolysis-reanation, and net reversibility for the hydrolysis. Runs were initiated by injecting 2.5 µl of a fresh aq. soln. of the appropriate azido complex ($1.1 \cdot 10^{-2}$ M) into 2.5 ml of pre-thermostated buffer soln. (I = 1.0M, $NaClO_4$) contained in a 1-cm cell housed in the cell compartment of the instrument. Three different buffers were used (pH 7.85, 8.35, and 9.94).

2.5. *Loss of Optical Activity from (+)-***A** *and (+)-***B** (X = N_3) was followed polarimetrically (436 nm) using the Y-tube method to initiate the reaction before transfer to the cell thermostated at 25.0 ± 0.1°. Complex concentrations were as follows: *ca.* 25 mg of $ZnCl_4$ salts/15 ml of buffer (pH 8.35; I = 1.0M) using a 1-dm cell and *ca.* 100 mg of $ZnCl_4$ salts/15 ml of buffer using a 2-cm cell. For both isomers, at both high and low [Co] and even in the presence of added N_3^- (up to 1.0M), the decay in optical activity followed a simple first-order rate law, and the final optical activity was always zero. Clearly, we were measuring the base-hydrolysis rate since any N_3^- re-entry leads to racemic epimerized product.

2.6. *Kinetics of Epimerization of* **A** *and* **B** (X = N_3). A known amount of *ca.* 10 mg of optically pure *mer-exo*(H)-[Co(N_3)(dien)(dapo)]$ZnCl_4$ (**A**($ZnCl_4$), X = N_3) was dissolved in 5 ml of aq. pyridine or 2,2′,2″-nitrilotris(ethanol) buffer ([buffer] = 0.1M, [N_3^-] = 1.0M, I = 1.0M ($NaClO_4$)). The kinetics were followed with CD spectroscopy at several wavelengths. The engaged epimer has zero absorption at λ = 432 nm (**A**) or 519 nm (**B**), and the absorption remained at zero throughout the epimerization.

2.7. *Kinetics of Epimerization of* **A** *and* **B** (X = OH). The VIS spectra of the *mer-exo*(H)- and *mer-endo*(H)-[Co(OH)(dien)(dapo)]$^{2+}$ ions (**A** and **B** (X = OH), resp.) and those of the corresponding aqua species are far too similar for a convenient spectrophotometric study of the epimerization. The kinetics were, therefore, followed by a quenching method. *mer-endo*(H)-[Co(H_2O)(dien)(dapo)]$Cl_3 \cdot 1.5H_2O$ (**B** $Cl_3 \cdot 1.5\ H_2O$, X = H_2O; *ca.* 150 mg) was added to one arm of an inverted Y-tube and the appropriate buffer (10 ml, I = 1.0M, 2,2′,2″-nitrilotris(ethanol) buffer, Σ(base) = 0.20M, pH 7.85 or 8.35) to the other arm, and the assembly sealed at the throat. After thermal equilibration (10 min, 25.0 ± 0.1°), the reaction was initiated by rapidly inverting and shaking the Y-tube. The reaction was quenched at a selected time in the range of 1–3 $t_{1/2}$ (8–20 s) by rapid injection of 2M $HClO_4$ (4.0 ml). The products were diluted with H_2O and sorbed on and eluted from *Dowex 50WX2* (200–400 mesh, NH_4^+ form) resin using 2M $NaClO_4$ (pH 2, $HClO_4$). Isomer **A** (X = H_2O) was eluted well in front of **B** (X = H_2O) under these conditions; the relative amounts of **A** and **B** were determined spectrophotometrically using the recorded eluate volumes and previously recorded spectral data [14].

2.8. *H-Exchange Kinetics.* The complexes ($[Co]_{tot} \approx 0.3$M) were dissolved in thermostated D_2O/D_2SO_4 (pD ≈ 4–5). After adjustment of the ^{1}H-NMR instrumental parameters with this soln., the buffer soln. (in D_2O) was added (resulting ionic strength I = 1.0M), and the spectra were registered as a function of time. Where the NH and NH_2 signals were obscured by solvent signals (HOD, *ca.* 4.7 ppm), portions of the reaction mixture were quenched with D_2SO_4 at known time intervals and the spectra recorded subsequently (downfield shift of the HOD signal due to increased [H^+]). Instrumental parameters: field, 200 MHz; sweep width, 2400 Hz; pulse length, 3 µs; aquisition time, 3.40 s; number of pulses, 4; reference, sodium 3-(trimethylsilyl)propane-1-sulfonate (DSS; 0 ppm); positive chemical shift is upfield.

H-Exchange was also followed *in situ* using ^{13}C-NMR spectroscopy with solns. of the complex in D_2O containing dioxane as internal standard. Good-quality spectra were obtained within a few min. The Cl^- salts of the complexes were used to achieve high solubility. Relative exchange rates were accurately obtained using a 1:1 molar mixture of the isomers **A** and **B** in the same NMR tube.

3. *Product Analyses.* 3.1. *Analysis of the Base-Hydrolysis Products* (*unsym-fac*-Complexes). *Unsym-fac-exo*(OH)- and *unsym-fac-endo*(OH)-[Co(Cl)(dien)(dapo)]$ZnCl_4$ (**C** ($ZnCl_4$) and **D** ($ZnCl_4$), X = Cl; 1.0 g) were reacted in 100 ml of 0.1M NaOH at 20° for 5 and 1 min, resp. The reactions were quenched by 2M HCl (100 ml) and heated at 90° for 25 min (reanation to chloro complexes). These solns. were evaporated and the ^{13}C-NMR spectra recorded in D_2O. Alternatively, the solns. were sorbed onto *Dowex 50 WX2* resins, eluted with 1–3M HCl, and each band evaporated and analyzed by VIS and ^{13}C-NMR.

3.2. *Azide-Ion Competition Experiments* (*mer*-Complexes). The rates of formation of azido complexes by competition during base hydrolysis of the chloro and bromo ions and by anation of the hydroxo products are not sufficiently different to determine the competition ratios for the first reaction phase by quenching the product mixtures and analyzing the products directly after their ion-exchange separation. The competition ratios were,

therefore, determined by monitoring the formation of azido products as a function of time. The kinetics were followed to completion of both reaction phases on a stopped-flow instrument at a wavelength (514, 528, or 530 nm) corresponding to an isosbestic point between the reactant ion and the product mixture **A**/**B** (X = OH) 9:1. These experiments were designed to compute the absorbance due to the azido complex isomers (70% **A**/30% **B** (X = N_3)) formed in the initial base-hydrolysis step (see below). The following molar extinction-coefficient data were required for the analysis: **A** (X = Cl) reactant, 514 nm, $\varepsilon_{Cl} = \varepsilon_{OH} = 74$ and $\varepsilon_{N3} = 340\,M^{-1}cm^{-1}$; **B** (X = Cl) reactant, 528 nm, $\varepsilon_{Cl} = \varepsilon_{OH} = 69$ and $\varepsilon_{N3} = 303\,M^{-1}cm^{-1}$; **A** (X = Br) reactant, 530 nm, $\varepsilon_{Br} = \varepsilon_{OH} = 67$ and $\varepsilon_{N3} = 297\,M^{-1}cm^{-1}$. Analysis of the biphasic kinetics allowed the analysis of the two amplitudes of the competition and anation product within a reasonable error limit. The isomeric composition of the competition products was determined in separate experiments.

In stopped-flow kinetics for consecutive reactions, care has to be taken in defining the zero-point of the time axis. This was found to be variable, and the following procedure was used: The value of the optical density of the soln. of starting material (without base) was recorded as a horizontal trace on the oscilloscope. To this was superimposed a kinetic trace of the biphasic reaction sequence in alkaline azide soln., maintaining the oscilloscope settings. The biphasic kinetic trace was fitted to *Eqn. 1*, and the timescale was adjsted iteratively in order to fit the previously measured optical density $D(t = 0)$.

$$D = Ae^{-k1t} + Be^{-k2t} + C \tag{1}$$

3.3. *Quenched Base-Hydrolysis Experiments* (Epimerization of the Reactants, *mer*-Complexes). A known amount of *ca.* 150 mg of either racemic or optically active **A** or **B** (X = Cl) was dissolved in aq. pyridine or imidazole buffer (*ca.* 40 ml, $[Co]_{tot} = 0.1$M, pH 6.16 or 7.40, $I = 1.0$M ($NaClO_4$ or NaCl), 25.0 ± 0.1°). The base hydrolysis was acid quenched after 1–2 half-lives (*ca.* 240 s, 30 s). In one experiment, the CD of the soln. was recorded immediately after acid quenching. The product soln. was diluted and sorbed onto an ion-exchange column (*Dowex 50 WX2*, 1.2 × 10 cm), and the chloro complexes were eluted with 1–2M NH_4Cl and the aqua ions with 2M, $NaClO_4$ (pH 2, $HClO_4$) and analyzed spectrometrically and by CD using the data recorded in [14].

3.4. *Kinetic Epimer Ratio of the Azide* (Competition) *Products* (*mer*-Complexes). A known amount of **A** or **B** (X = H_2O, Br, or Cl) ($[Co]_{tot} \approx 0.008$M) was dissolved in a prethermostated (25.0 ± 0.1°) buffer ($I = 1.0$M ($NaClO_4$), $[N_3^-] = 1.0$M, [buffer] = 0.05M). After 10 half-lives of the base hydrolysis or azide anation, the mixture was acid quenched, diluted, and sorbed onto a *Dowex 50 WX2* column. Elution and product analysis was carried out as described below.

3.5 *Equilibrium Epimer Ratio of the Hydroxo and Chloro Ions* (*mer*-Complexes). A known amount (*ca.* 20 mg) of **A** ($ZnCl_4$) or **B** ($ZnCl_4$) (X = Cl) was dissolved in a pyridine buffer ([pyridine] = 0.1M, pH 6.39, $I = 1.0$M ($NaClO_4$), $T = 25.0 \pm 0.1°$). After 10 half-lives of base hydrolysis (24.5 min), the reaction was quenched by addition of $HClO_4$, diluted, and sorbed onto an ion-exchange column (*Dowex 50 WX2*, Na^+ form, 1.2 × 11 cm). The 4 bands (**A** and **B** (X = H_2O and Cl)) were eluted with 2M $NaClO_4$ (pH 2, $HClO_4$) and analyzed by their VIS spectra.

To better define the **A**/**B** (X = Cl) ratios, the experiments were repeated using *ca.* 200 mg of **A** or **B** (X = Cl) in 5.0M NaCl (*ca.* 20 ml, imidazole buffer, $base_{tot} = 0.2$M, pH 7.4) and equilibrated for 48 h at 25°. The chloride salts of **A** and **B** (X = H_2O) were also directly equilibrated (10–15 min, 25°) in buffer solns. ($I = 1.0$M, $NaClO_4$, 2,2′,2″-nitrilotris(ethanol), $base_{tot} = 0.2$M, pH 7.85 and 8.35), acid quenched, and chromatographed as above.

3.6. *Equilibrium Epimer Ratio of the Azido Ions* (*mer*-Complexes). Buffered aq. solns. ($[Co]_{tot} = 0.01$M, $I = 1.0$M, pH 9.09 (2,2′-iminobis(ethanol)), $[N_3^-] = 1.0$M, 25.0 ± 0.1°) with known amounts of **A** $(ClO_4)_2$ or **B** $(ClO_4)_2$ (X = N_3) were equilibrated for 5–10 half-lives (**A**, 42 min; **B**, 21 min). Then the reaction was quenched by the addition of 2.0M $HClO_4$, diluted, and sorbed onto ion-exchange columns (*Dowex 50 WX2*, NH_4^+ form). The 2 bands of epimers were eluted with 1M NH_4Cl (pH 2.0 (HCl)). The *endo*-epimers eluted first, and the separated isomers were analyzed spectrophotometrically using $\varepsilon_{max}^{510}(exo) = 356$ and $\varepsilon_{max}^{515}(endo) = 305$.

3.7. *Degree of Optical Retention in the Base-Hydrolysis Products* (*mer*-Complexes). *exo*-Hydroxo- and especially the *endo*-hydroxo ions racemize rapidly (at a pH-independent rate), and the *endo*-form also epimerizes smartly. We, therefore, sought to examine the optical activity of azide ion competition products rather than the hydroxo products because the former are very much more stable to racemization (and epimerization) under the conditions of base hydrolysis used for the chloro and bromo ions.

The base-hydrolysis kinetics of optically pure **A** and/or **B** (X = Cl, Br) were followed in different buffered azide media (pH 5.95–6.10, $[N_3^-] = 0.5$–2.0M, $I = 1.0$ or 2.05M). The change in CD intensity was followed at 491 nm at a sensitivity of 0.2 m°/cm. Pseudo-first order, monophasic kinetics were observed in all runs, and Θ_{inf} coincided with the base line in all cases. These measurements were done at the maximum value of Θ on the most sensitive scale. Given the high competition values, an accuracy of at least ±2% may be assigned. The result is, therefore,

99 ± 1% racemization for the azido products. In a blank experiment, the CD intensity of optically active **A** (X = N_3) was monitored at 491 nm in one of the pyridine buffers (pH 5.85). No decrease in CD intensity was found for at least 30 min, and, therefore, in the above experiments, the presence of racemic azido complex is not due to racemization after its formation.

To avoid any possibility that the observed zero optical acitivity arose from compensations from the *exo*- and *endo*-components of the azido product mixture (**A**/**B** 70:30), the products of the competition experiments for **A** and **B** (X = Cl) were acid quenched at $10 \cdot t_{½}$. The products were chromatographed and the azido isomers separated as described before. CD and ORD spectra of the concentrated eluates were indistinguishable from their baselines.

3.8. *Degreee of Optical Retention in the Azide Ion Anation of the Chiral Hydroxo Ions (mer*-Complexes). Optically pure **A** ($ZnCl_4$) or **B** ($ZnCl_4$) (X = N_3; 0.12 g) was dissolved in H_2O (40.0 ml, 25.0°) containing 4.0M $HClO_4$ (0.5 ml). Aq. $NaNO_2$ (0.033 g, *ca.* 2 equiv., 5 ml) was added to convert active azido ion into the corresponding active aqua species (with full retention). The careful addition of aq. NaN_3 (0.031 g, *ca.* 2 equiv., 5 ml) destroyed residual HNO_2. Optical rotations (at 436 nm; 1-dm cell) were recorded immediately following the addition, with stirring, of 2.0M azide buffer (50.0 ml, 2-aminoethanol, pH 7.85 or 8.35, $base_{tot}$ = 0.4M). After 2 min, when the azido species were fully formed, the rotation was indistinguishable from zero ($[\alpha]_D = 0 \pm 0.002$). Controls were performed on optically pure **A** ($ZnCl_4$) and **B** ($ZnCl_4$) (X = N_3). There was only *ca.* 11% racemization in 2 min for the higher pH buffer and for the faster reacting *endo*-isomer **B**. Thus, the loss of activity for the aqua ions in N_3^- is a result of the actual substitution process, and is not due to subsequent racemization.

4. *Stereochemical Experiments* (*mer*-Complexes). The optically pure epimers **A** and **B** (X = N_3) or a known mixture **A**/**B** (2:1, $[azido\ complex]_{tot}$ = 16 mg) was nitrosated as follows. The complex was dissolved in H_2O (40 ml, 25°) containing 4M $HClO_4$ (0.5 ml). Aq. $NaNO_2$ (0.33 g; *ca.* 2 equiv., 5 ml) was added to convert the optically active azido ion into the corresponding optically active aqua species. The product soln. was diluted and sorbed onto a column (*Dowex 50 WX2*, Na^+ form, 1.2 × 10 cm). The aqua complexes were eluted with 2M $NaClO_4$ (pH 2, $HClO_4$) as described above and analyzed by UV/VIS and CD.

The stereochemical course of the anation reaction of **A** and **B** (X = H_2O) by Cl^- was checked as follows: A known amount (*ca.* 20 mg) of optically active **A** ($ZnCl_4$) or **B** ($ZnCl_4$) (X = N_3) was transformed to the corresponding aqua complex by nitrosation as above. To the resulting soln. of the aqua complex was added 37% HCl soln. (4 ml). After 20 h of reaction in the dark, the soln. was diluted to 80 ml and sorbed onto a *Dowex 50 WX2* column (1.2 × 8 cm, NH_4^+ form). The complexes were eluted with 1M NH_4Cl (pH 2, HCl) and analyzed by their VIS and CD spectra.

For the stereochemical cycle $[Co(Cl)A_5] \rightarrow [Co(H_2O)A_5] \rightarrow [Co(Cl)A_5]$, a sample of known mass (*ca.* 15 mg) of **A** ($ZnCl_4$) or **B** ($ZnCl_4$) (X = Cl) was dissolved in aq. 0.2M $Hg(ClO_4)_2$ (pH 2 ($HClO_4$), 5 ml). After 25 min of reaction at r.t. in the dark ($10 \cdot t_{½}$), the soln. was diluted to 10 ml (0.1M $HClO_4$) and sorbed onto an ion-exchange resin (*Dowex 50 WX2*, H^+ form 1.2 × 3 cm), washed with 0.5M $HClO_4$ until the eluate was Hg^{2+}-free, and eluted with 10M HCl. The eluate (10.0 ml) was left for 21 h at 25° in the dark. Then, 1.0 ml of the soln. was diluted with H_2O to 25 ml to record VIS and CD spectra. Another portion of 5.0 ml was diluted to 100 ml and sorbed onto an ion-exchange column (*Dowex 50 WX2*, NH_4^+ form, 1.2 × 7 cm). The complexes were eluted with 1M NH_4Cl (pH 2, HCl) and analyzed spectroscopically.

Results. – *Amino Proton Exchange* (*mer*-Isomers). The deprotonation of one coordinated amine is a fast equilibrium reaction prior to the loss of the leaving group X (*Scheme 1*), and the kinetic and thermodynamic parameters involved (*i.e.* k_1, k_{-1}, and K_a) are clearly of importance in the base-hydrolysis process. It is usually assumed and/or observed that coordinated amines have $pK_a \geq 14$ [1] [2][5]), and the relative acidities can then be estimated from H/D exchange rates as measured by ^{1}H-NMR spectroscopy. The analysis is based on a diffusion-controlled and constant back-protonation rate, and the exchange rate law $k_{obs} = k_{H/D} \cdot [OD^-] + k_{D_2O}$ pertains. The $[OD^-]$-independent term is usually negligible, and under the conditions used in this work, this is true for all *mer*-$[CoX(dien)(dapo)]^{n+}$ complexes.

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[5]) Note, however, that the pK_a values of some cage hexaaminecobalt(III) complexes are considerably lower than 14 [2]. Also, recently some direct measurements of amine acidities of some hexaaminecobalt(III) complexes with $pK_a \approx 13.8$ [27] were obtained.

In buffered solns., clean pseudo-first-order rates were observed, and these were linear in $[OD^-]$, with a zero intercept. The second-order rate constants $k_{H/D}$ of the secondary-amine proton NH and of the amine protons NH_2 *trans* to the leaving group were similar (within one order of magnitude; see *Table 1*) and significantly faster than the respective base-hydrolysis rates, *viz.* the loss of the leaving group is the rate-determining step. The exchange rates of the amine protons NH_2 *cis* to X were by at least two orders of magnitude slower, and definitely slower than the rate of base hydrolysis. For the H/D exchange rates, an isotope effect is expected (the rates are usually *ca.* 2 times slower in D_2O). However, the relative site-exchange rates are unlikely to be dramatically affected.

Table 1. *H-Exchange Rates* ($k_{H/D}$ [$M^{-1}s^{-1}$]) *as Observed by* ^{1}*H-NMR Spectroscopy of the Coordinated Amine Groups of* mer-*[CoX(dien)(dapo)]*$^{n+}$ **A** *and* **B**. I = 1.0M ($NaClO_4$), 293 K, $[Co]_{tot} \approx 0.1$M, $[buffer]_{tot}$ = 1.0 or 0.5M[a]).

	$k_{H/D}$ [$M^{-1}s^{-1}$][b])[c])		
	NH(sec.)[d])	NH_2(*trans*)[e])[g])[h])	NH_2(*cis*)[f])
A (X = Cl)	$(5.97 \pm 0.56) \cdot 10^6$	$(2.06 \pm 0.28) \cdot 10^7$	$\leqslant 10^5$
B (X = Cl)	$(6.60 \pm 0.54) \cdot 10^5$	$(1.24 \pm 0.53) \cdot 10^6$ $(8.72 \pm 0.27) \cdot 10^5$)	$\leqslant 10^5$
A (X = N_3)	$(7.84 \pm 0.17) \cdot 10^6$	$(1.22 \pm 0.14) \cdot 10^5$	$\leqslant 10^5$
B (X = N_3)	$(1.26 \pm 0.31) \cdot 10^6$	$(2.00 \pm 0.21) \cdot 10^5$	$\leqslant 10^5$
A (X = Br)	$(1.09 \pm 0.12) \cdot 10^7$	$(3.12 \pm 0.42) \cdot 10^7$	$\leqslant 10^5$
mer-exo(H)-[Co(Cl)(dien)(tmd)]$^{2+}$	$(2.65 \pm 0.25) \cdot 10^6$	$(2.65 \pm 0.32) \cdot 10^6$	$\leqslant 10^5$

[a]) Formate, acetate, imidazole; $4.5 < pD < 6.2$.
[b]) $pD = pH + 0.4$; $pK_{D2O} = 14.869$ [26].
[c]) The errors given are standard deviations of 3–5 determinations.
[d]) Secondary(central)-amine proton NH of the meridionally coordinated dien ligand.
[e]) Primary-amine protons NH_2 of dapo, *trans* to the leaving group X.
[f]) Primary-amine protons NH_2 of dien and dapo, *cis* to the leaving group X.
[g]) Monophasic exchange kinetics are observed; the reported rate constants $k_{H/D}$ are statistically corrected (factor 2).
[h]) For **B** (X = Cl), the diastereoisotopic dapo NH_2 protons *trans* to Cl^- are resolved in the ^{1}H-NMR spectrum and have significantly different rates.

Relative H-exchange rates were also determined from high-resolution ^{13}C-NMR spectra. C-Atoms in α-position to the exchanging *NH* atoms resonate *ca.* 0.1 ppm upfield for each deuteron substituted (see *Fig. 1*), and the ^{13}C-NMR signals for all isotopomers (except stereoisotopomers) arising from N-deuteration were resolved. From studies carried out in D_2O solutions ($pD \approx 5$), the following obervations emerge[6]): *1*) The fastest exchanging protons in both **A** and **B** (X = Cl) are the NH_2 protons *trans* to Cl^-, and each of these exchange at comparable rates. Isomer **B** is slower (*ca.* 3-fold) for this exchange than **A**. *2*) For both **A** and **B** (X = Cl) different exchange rates for the (nonequivalent) NH_2 protons *trans* to Cl^- can be discerned (this is not detected in the ^{1}H-NMR study). *3*) The secondary NH moiety is the next fastest to exchange, but there is no detectable

[6]) In most cases, the ^{1}H- and ^{13}C-NMR results were in agreement. Some discrepancies in quantitation could stem from the fact that in the ^{13}C-NMR study, essentially zero ionic strength and relatively low pH values were used, while in the ^{1}H-NMR study the ionic strenght was 1.0M and the pH somewhat higher (this might affect relative rates). In general, the ^{13}C-NMR technique was more sensitive in that each separate isotopomer was observed, while for the ^{1}H-NMR, only the total (for a particular site or coincident sites) was examined.

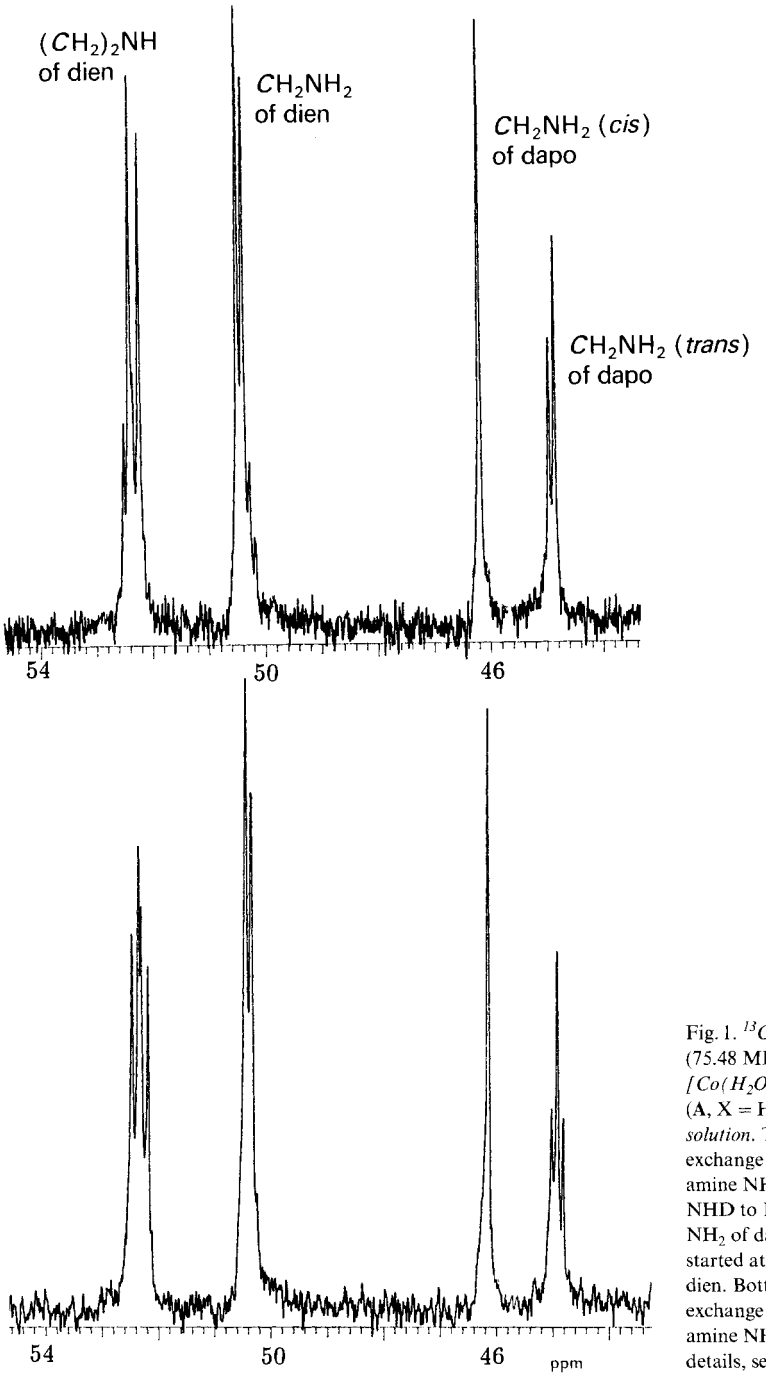


Fig. 1. *^{13}C-NMR spectra* (75.48 MHz) *of* mer-exo*(H)-[Co(H$_2$O)(dien)(dapo)]$^{3+}$* (**A**, X = H_2O) *in dilute DCl solution.* Top: *ca.* $3 \cdot t_{1/2}$ of exchange at the secondary-amine NH of dien and at the NHD to ND_2 stage at the *trans* NH_2 of dapo; some exchange started at one of the *cis* NH_2 of dien. Bottom: *ca.* $1 \cdot t_{1/2}$ of exchange at the secondary-amine NH of dien. For further details, see text.

exchange at this site after *ca.* 75% exchange at the corresponding *trans* site for either **A** or **B** (X = Cl). *4*) The *mer-exo*(H)-epimer **A** (X = Cl) exchanges its secondary NH proton at least 5-fold faster than the *mer-endo*(H)-epimer **B**. *5*) No mutarotation (epimerization) is observed during the exchange of the secondary NH proton, neither for **A** nor **B** (X = Cl), *i.e.* retention predominates over inversion at the secondary NH center during the exchange process. *6*) Exchange of the secondary NH of **A** and **B** (X = Cl) is almost complete before hydrolysis is apparent, *viz.* the secondary-amine exchange rate is faster than base hydrolysis. *7*) For **A** (X = H_2O), the secondary NH is the fastest exchanging proton and considerably faster than in the corresponding chloro complexes **A** (X = Cl).

Base Hydrolysis. Under pseudo-first-order conditions, the base-hydrolysis kinetics obey the usually observed rate law for an S_N1CB substitution mechanism (*Scheme 1*), $k_{obs} = k_{OH} \cdot [OH^-]$ (loss of the leaving group is the rate determining step, $pK_a \geq 14$, $[OH^-] \leq 1$M, $k_{OH} = k \cdot K_b$) [1–4]. For all reactions studied, there was no detectable general-base catalysis.

The rate constants for the base hydrolysis of *unsym-fac*-isomers **C** and **D** (*Table 2*) are the average of ≥ 3 determinations within a large range of $[OH^-]$. Base hydrolysis was followed by slower reactions, and the final product of these processes, for both **C** and **D**,

Table 2. *Base-Hydrolysis Rates of* $[CoX(dien)(dapo)]^{n+}$ *Isomers* **A**–**C** *in Aqueous Solution at 25°. I* = 1.0M ($NaClO_4$)[a]).

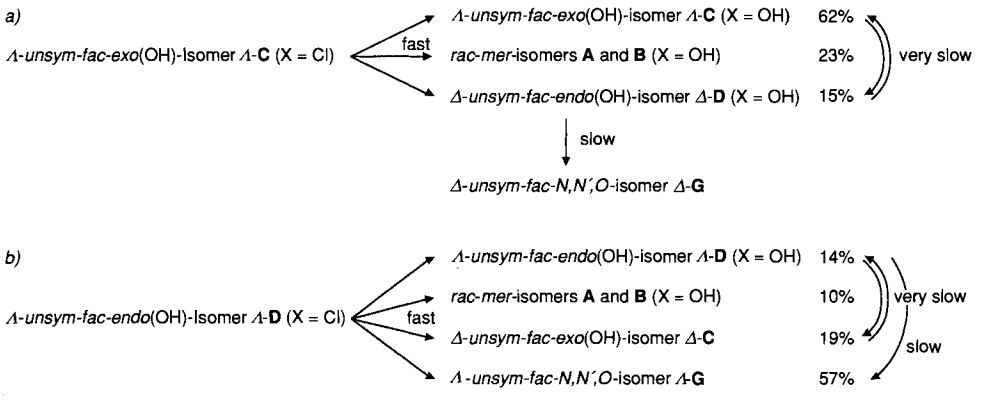
	k_{OH} [$M^{-1}s^{-1}$]	pH range		k_{OH} [$M^{-1}s^{-1}$]	pH range
A (X = Cl)	$(1.13 \pm 0.09) \cdot 10^5$	5.8–11.0	**C** (X = Cl)[c])	$(2.55 \pm 0.31) \cdot 10^1$	9.2–12.7
B (X = Cl)	$(1.18 \pm 0.11) \cdot 10^5$	5.8–11.0	**D** (X = Cl)[c])	$(6.5 \pm 0.46) \cdot 10^2$	5.8–8.5
A (X = Br)	$(1.40 \pm 0.07) \cdot 10^6$	8.2–9.8	**C** (X = Br)[c])	$(1.77 \pm 0.12) \cdot 10^2$	8.3–13.0
A (X = N_3)[b])	$(1.59 \pm 0.04) \cdot 10^2$	8.2–9.8	**C** (X = N_3)[c])	$(5.44 \pm 1.37) \cdot 10^{-2}$	11.0–12.9
B (X = N_3)[b])	$(2.89 \pm 0.22) \cdot 10^2$	8.2–9.8			

[a]) $k_{OH} = k_{obs}/[OH^-]$; $pK_W = 13.77$.

[b]) Base hydrolysis of the azido complexes is a reversible reaction (anation, see also [15]: $[Co(OH)]^{2+} + N_3^- \rightleftarrows [Co(N_3)]^{2+} + OH^-$) with the rate law: $k_{obs} = k_f + k_r = (K \cdot k \cdot [N_3^-] + k_{OH} \cdot [OH^-]) \cdot 1/(1 + K \cdot [N_3^-])$. Under the conditions used, the retardation term $1/(1 + K \cdot [N_3^-])$ is insignificant, and the anation term k_f only leads to, at most, 5% of k_{obs} ($k_r/k_f \approx 20$).

[c]) First phase (base hydrolysis).

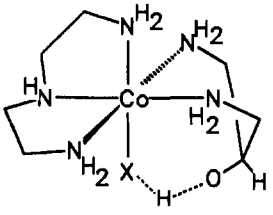
Scheme 2



was pure *unsym-fac*-[Co(dien)(dapo-*N,N',O*)]$^{2+}$ (structure **G**) [28], analyzed by ^{13}C-NMR, UV/VIS and CD spectroscopy. Product analysis after the first reaction phase (base hydrolysis) revealed that the initial products from both **C** and **D** (X = Cl) were mixtures of *mer*-, *unsym-fac-exo*(OH)- and *unsym-fac-endo*(OH)-[Co(OH)(dien) (dapo)]$^{2+}$ (**A**–**D**, X = OH) and *unsym-fac*-[Co(dien)(dapo-*N,N',O*)]$^{2+}$ (**G**) species (see *Scheme 2*).

A qualitative analysis of the biphasic reaction sequences for the two chloro complexes **C** and **D** (X = Cl) revealed pH-dependent specific base-hydrolysis rates (see *Table 2*), followed by roughly pH-independent processes. These must be due to isomerization and cyclization[7]). For *unsym-fac-exo*(OH)-[Co(OH)(dien)(dapo)]$^{2+}$ (**C**, X = OH), these processes were studied at pH > 10 after completion of the base hydrolysis. Monophasic reactions were observed, indicating that the isomerization process is, as expected, rate-determining. Further support for this interpretation came from a comparison of the specific rates of the slow phase of the reaction of **D** (X = Cl; $1.82 \cdot 10^{-3}$ s^{-1}; cyclization) and of **C** (X = Cl; $(4.24 \pm 0.75) \cdot 10^{-5}$ s^{-1})[7]); isomerization).

The first reaction phase (base hydrolysis) was roughly 25 times faster for the *unsym-fac-endo*(OH)-isomer **D** than that for the *exo*(OH)-species **C**. This might indicate a participation of the dapo OH group in the transition state **I**, and if so, it is consistent with



I

the structural assignment of *unsym-fac-exo*(OH)- and *unsym-fac-endo*(OH)-configurations (see **C** and **D**, resp.). Further support for this assignment and interpretation came from the fact that the cyclization of **C** was accompanied by an inversion of the configuration (see *Fig. 2*). The edge-displacement leading from the *exo*(OH)- to the *endo*(OH)-configuration, driven by a stabilization due to OH coordination necessarily inverts the configuration about cobalt(III). Also, product-distribution studies established that only for *unsym-fac-endo*(OH) isomers, OH is captured during the base-hydrolysis process.

The second-order rate constants k_{OH} (*Table 2*) for the base-hydrolysis rates of *mer*-[CoX(dien)(dapo)]$^{n+}$ complexes **A** and **B** are among the largest known for pentaaminecobalt(III) complexes, and, significantly, the acceleration of hydrolysis in base is the largest known to date for a pentaaminecobalt(III) complex (see *Table 3*). Also, the rates of racemization and azide anation for the hydroxo complexes were much larger than expected based on the usually observed order of reactivity for pentaaminecobalt(III) complexes ($Br^- > Cl^- > H_2O > N_3^- > OH^-$) [1] [4]. This apparant anomaly is discussed in detail in [15], together with similar observations in other systems [42] [43].

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[7]) The reaction sequence shown in *Scheme 2* indicates that a thorough analysis of this complex system is not warranted on the basis of the experiments reported here. This is also apparent from the relatively large error on the rate of the second reaction phase of *unsym-fac-exo*(OH)-complex **C** (X = Cl; see below) which might be the result of an albeit small pH dependence.

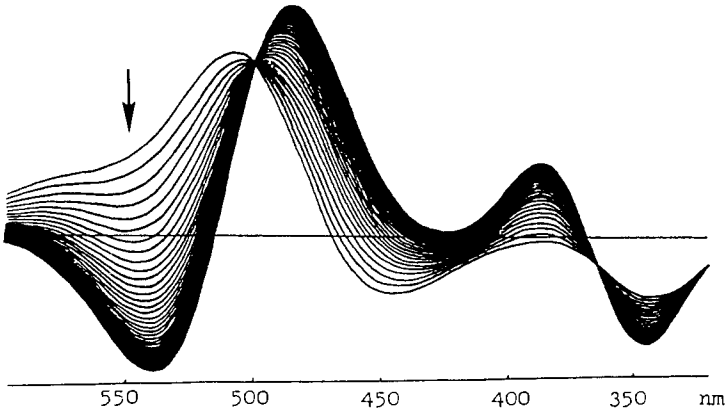


Fig. 2. *Stereochemical change on base hydrolysis* ($t_{1/2} \approx 13$ s) *of* unsym-fac-exo*(OH)-[CoCl(dien)(dapo)]*$^{n+}$ ((**C**, X = Cl) *as shown by the CD spectra* (H_2O) *over 30 min.* pH 11.11, 25.0°).

Table 3. *Acceleration Factors and Azide-Ion Competition for Base-Hydrolysis Reactions of Some Pentaamine-cobalt(III) Complexes.* I = 1.0M ($NaClO_4$), 25°[a]).

	k_{aq} [s^{-1}]	k_{OH} [$M^{-1}s^{-1}$]	k_{OH}/k_{aq}	%$[Co(N_3)]^{2+}$ (1M N_3^-)	Ref.
$[CoCl(NH_3)_5]^{2+}$	$1.8 \cdot 10^{-6}$	0.26	$1.4 \cdot 10^5$	8.5	[4] [19] [29] [30]
$[CoBr(NH_3)_5]^{2+}$	$6.5 \cdot 10^{-6}$	1.4	$2.2 \cdot 10^5$	8.7	[4] [19] [29]
$[Co(MeSO_3)(NH_3)_5]^{2+}$	$2.0 \cdot 10^{-4}$	55	$2.8 \cdot 10^5$	10	[31] [32]
$[Co(SO_4)(NH_3)_5]^{+}$	$8.9 \cdot 10^{-7}$	$4.9 \cdot 10^{-2}$	$5.5 \cdot 10^5$	5.8	[4] [33]
$[Co(Me_2SO)(NH_3)_5]^{3+}$	$2.0 \cdot 10^{-5}$	5.4	$2.7 \cdot 10^5$	13	[34] [35]
cis-$[CoCl(en)_2NH_3]^{2+}$	$4.2 \cdot 10^{-7}$	2.7[d])	$6.4 \cdot 10^5$	24	[4] [33] [36]
cis-$[CoBr(en)_2NH_3]^{2+}$	$1.6 \cdot 10^{-6}$	22[d])	$1.4 \cdot 10^7$	24	[33] [36]
sym-$[Co(MeSO_3)(trenen)]^{2+}$[b])	$2.6 \cdot 10^{-5}$	$7.6 \cdot 10^4$	$2.9 \cdot 10^9$	48	[32] [31]
$[CoCl(MeNH_2)_5]^{2+}$	$3.7 \cdot 10^{-5}$	$3.4 \cdot 10^2$	$9.2 \cdot 10^9$	49	[37]
$[CoCl(bamp)(dapo)]^{2+}$[c])	$1.0 \cdot 10^{-5}$	$3 \cdot 10^3$	$3.0 \cdot 10^8$	6.5	[17] [38] [39]
$[CoBr(bamp)(dapo)]^{2+}$[c])	$4.1 \cdot 10^{-5}$	$1.5 \cdot 10^4$	$3.7 \cdot 10^8$	6	[17] [38] [39]
$[CoCl(bamp)(en)]^{2+}$[c])	$1.6 \cdot 10^{-6}$	$4.8 \cdot 10^2$	$3.0 \cdot 10^8$	9	[17] [38] [39]
mer-exo(H)-$[CoCl(dien)(en)]^{2+}$	$1.8 \cdot 10^{-7}$	$1 \cdot 10^4$[d])	$5.6 \cdot 10^{10}$	–	[40]
mer-exo(H)-$[CoCl(dien)(dapo)]^{2+}$ (**A**, X = Cl)	$5.7 \cdot 10^{-6}$[e])	$1.1 \cdot 10^5$	$2.0 \cdot 10^{10}$	56	this work
mer-endo(H)-$[CoCl(dien)(dapo)]^{2+}$ (**B**, X = Cl)	$5.7 \cdot 10^{-6}$[e])	$1.2 \cdot 10^5$	$2.2 \cdot 10^{10}$	56	this work
unsym-fac-$[CoCl(dien)(tn)]^{2+}$	$4.3 \cdot 10^{-6}$	46	$1.1 \cdot 10^7$	–	[41]
unsym-fac-$[CoCl(dien)(dapo)]^{2+}$ (**C**, X = Cl)	$4.3 \cdot 10^{-6}$[e])	25	$5.8 \cdot 10^6$	–	this work
sym-fac-$[CoCl(dien)(tn)]^{2+}$	$2.2 \cdot 10^{-7}$	3.5	$1.6 \cdot 10^7$	–	[41]
mer-exo(H)-$[CoCl(dpt)(tn)]^{2+}$	$1.7 \cdot 10^{-5}$	$9.2 \cdot 10^3$	$5.3 \cdot 10^8$	–	[41]
mer-exo(H)-$[CoCl(dpt)(en)]^{2+}$	$2.1 \cdot 10^{-5}$	$2.9 \cdot 10^3$	$1.4 \cdot 10^8$		[41]
mer-endo(H)-$[CoCl(dpt)(en)]^{2+}$	$1.2 \cdot 10^{-5}$	$7.3 \cdot 10^2$	$6.3 \cdot 10^7$	–	[41]

[a]) For abbreviations, see *Footnote 4.* [b]) trenen = *N,N,N'*-tris(2-aminoethyl)ethane-1,2-diamine. [c]) bamp = pyridine-2,6-bis(methanamine). [d]) Estimated from different ionic strength. [e]) Estimated from analogous tn complex.

Azide Competition (*mer*-Isomers). At pH values convenient for the study of the base hydrolysis of *mer*-$[CoX(dien)(dapo)]^{2+}$ (**A** and **B**, X = Cl and Br), the rates of base hydrolysis and subsequent azide anation were of the same order of magnitude (see *Table*

Table 4. *Base Hydrolysis* (k_{OH} [$M^{-1}s^{-1}$]) *and Anation Rates* (k_{an}^{OH} [$M^{-1}s^{-1}$]) *of* mer-*[CoX(dien)(dapo)]$^{n+}$ Complexes* **A** *and* **B**. (I = 1.0M ($NaClO_4$), 298 K, $[Co]_{tot} \approx 10^{-3}$ M, [buffer] ≈ 0.1M[a])[b]).

	k_{OH} [$M^{-1}s^{-1}$][a])		k_{an}^{OH} [$M^{-1}s^{-1}$]	
	1M NaN_3	1M $NaClO_4$[b])	1M NaN_3	anation[c])
A (X = Cl)	$(1.03 \pm 0.31) \cdot 10^5$	$(1.13 \pm 0.09) \cdot 10^5$	$(2.91 \pm 0.67) \cdot 10^{-2}$	$(2.02 \pm 0.08) \cdot 10^{-2}$
B (X = Cl)	$(0.97 \pm 0.12) \cdot 10^5$	$(1.18 \pm 0.11) \cdot 10^5$	$(3.02 \pm 0.62) \cdot 10^{-2}$	
A (X = Br)	$(1.54 \pm 0.32) \cdot 10^6$	$(1.40 \pm 0.07) \cdot 10^6$	$(2.10 \pm 0.60) \cdot 10^{-2}$	

[a]) $7.82 < pH < 8.04$; $pK_W = 13.77$.
[b]) Rate constants from *Table 2*.
[c]) See [15].

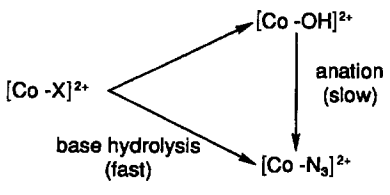
4). Therefore, an analysis of azide competition by spectroscopy or by the usually applied technique of acid quenching followed by ion-exchange chromatography was not feasable.

The base-hydrolysis kinetics of *mer-exo*(H)- and *mer-endo*(H)-[CoX(dien)(dapo)]$^{2+}$ (**A** and **B**, resp.; X = Cl, Br) in the presence of N_3^- (0.2–1.0M) and buffer (pyridine or *Tris*, pH 7.96–8.04, I = 1.0M) at 25.0° were biphasic. Both reaction phases were accompanied by an increase in optical density at 514, 528, or 530 nm for **A** (X = Cl), **B** (X = Cl), or **A** (X = Br), respectively (isosbestic points with the *mer*-hydroxo products), consistent with formation of the *mer*-azido complex. The formation of this compound was verified by ^{13}C-NMR and chromatography and was essentially quantitative at the end of the reaction sequence. The pseudo-first-order rate constants of the two reaction phases were determined by nonlinear regression using *Eqn. 1*. Since the two rate constants were relatively close to each other under the conditions of the experiment (see *Table 4*), the analysis is subject to quite a large error, but rates of the first rapid reaction phase are within the error limit identical with the respective base hydrolysis rates, measured independently (*Table 4*). The slow reaction phase had a rate constant close to that for anation of the hydroxo product and was independent of the leaving group. In general, base hydrolysis of the azido complexes ($k_{OH} = 1.59 \cdot 10^2$ $M^{-1}s^{-1}$, $2.89 \cdot 10^2$ $M^{-1}s^{-1}$ for the *exo*(H)- and *endo*(H)-species, respectively) could be neglected.

We interpret these observations by the reaction sequence shown in *Scheme 3*. Thus the azido complex arises from competition (fast phase) as well as from subsequence anation of the hydroxo complexes (slow phase). Therefore, for the competition ratios, the initial concentration of the azido complex had to be determined at the beginning of the slow phase by extrapolation to $t = 0$.

The amount of azide competition product was deduced from the following relations (X = Cl, Br), where D_A is the measured optical density at $t = 0$ (see *Exper. Part*) and D_B is

Scheme 3



the optical density resulting form the azide competition product as deduced by extrapolation of the slow reaction phase to $t = 0$ ($l = 1$ cm)[8]).

$$D_A = \varepsilon_{[CoX]} \cdot [[CoX]^{2+}] \tag{2}$$

$$D_B = \varepsilon_{[Co(OH)]} \cdot [[Co(OH)]^{2+}] + \varepsilon_{[Co(N_3)]} \cdot [[Co(N_3)]^{2+}]_{comp} \tag{3}$$

At the isosbestic point between $[CoX]^{2+}$ and $[Co(OH)]^{2+}$, $\varepsilon_{[Co(OH)]} = \varepsilon_{[CoX]}$. At the end of the fast phase, the reaction mixture contained but $[Co(OH)]^{2+}$ and $[Co(N_3)]^{2+}$:

$$[[Co(OH)]^{2+}] = [Co]_{tot} - [[Co(N_3)]^{2+}]_{comp} \tag{4}$$

Thus,

$$D_B = [Co]_{tot} \cdot \varepsilon_{[CoCl]} + [[Co(N_3)]^{2+}]_{comp} \cdot (\varepsilon_{[Co(N_3)]} - \varepsilon_{[CoCl]}) \tag{5}$$

and

$$[[Co(N_3)]^{2+}]_{comp} = \frac{D_B - [Co]_{tot} \cdot \varepsilon_{[CoCl]}}{\varepsilon_{[CoN_3]} - \varepsilon_{[CoCl]}} \tag{6}$$

The competition values were calculated from this formula. An equation of the same type was also derived from the general expression (see *Eqn. 7*) for any system exhibiting biphasic kinetics (A, B, and C, starting material, intermediate, and product, resp.).

$$D = \varepsilon_C[A]_o + (\varepsilon_A - \varepsilon_C)[A]_o\, e^{-k_1 t} + (\varepsilon_B - \varepsilon_C)\frac{k_1[A]_o}{k_2 - k_1}(e^{-k_1 t} - e^{-k_2 t}) \tag{7}$$

The competition ratios $R = [[Co(N_3)]^{2+}]/([[Co(OH)]^{2+}] \cdot [N_3^-])$, where $[[Co(OH)]^{2+}]$ and $[[Co(N_3)]^{2+}]$ are the concentrations of *mer-exo*(H)- and *mer-endo*(H)-products, were

Table 5. *Competition Ratios* R[a]) *of Base Hydrolysis of* mer-*[CoX(dien)(dapo)]$^{n+}$ Complexes* **A** *and* **B** (X = Cl and Br) *in Presence of* N_3^-. $I = 1.0$M ($NaClO_4$), 298 K, $[Co]_{tot} \approx 10^{-3}$ M, $7.82 < pH < 8.25$, [buffer] ≈ 0.1M.

	$[N_3^-]$ [M]	pH	% $[Co(N_3)]^{2+}$ [b])	R [M^{-1}]
mer-exo(H)-[CoCl(dien)(dapo)]$^{2+}$ (**A**, X = Cl)	0.2	7.82	24.2 ± 0.6	1.60
	0.25	8.25	24.8 ± 0.3	1.32
	0.4	7.84	40.9 ± 0.3	1.73
	0.5	8.25	41.3 ± 1.7	1.41
	0.6	7.86	47.9 ± 0.8	1.53
	0.8	7.87	53.5 ± 2.6	1.44
	0.9	7.86	53.5 ± 2.5	1.28
	1.0	8.25	55.8 ± 3.6	1.26
mer-exo(H)-[CoBr(dien)(dapo)]$^{2+}$ (**A**, X = Br)	0.25	8.25	28.5	1.59
	0.5	8.25	36.6	1.15
	1.0	8.25	53.2	1.14
mer-endo(H)-[CoCl(dien)(dapo)]$^{2+}$ (**B**, X = Cl)	0.2	7.82	18.9 ± 0.7	1.17
	0.4	7.84	39.9 ± 0.1	1.66
	0.6	7.86	45.8 ± 0.1	1.41
	0.8	7.87	52.9 ± 1.5	1.40
	0.9	7.86	53.5 ± 5.1	1.28

[a]) $R = [[Co(N_3)]^{2+}]/([[Co(OH)]^{2+}] \cdot [N_3^-]) = 1.4 \pm 0.2 M^{-1}$.

[b]) The errors given are standard deviations for 2–5 determinations.

[8]) The optical density $D_{B'}$ of the competition product obtained by a nonlinear extrapolation of the second exponential to $t = 0$ is $D_{B'} = D_C - k_1/(k_2 - k_1) \cdot (D_B - D_C)$, where D_C is the final absorbance, and k_1 and k_2 are the specific rates for the first and second stages. If $k_1 \gg k_2$ (depending upon the pH) $D_{B'} \approx D_B$.

independent of the leaving group and the configuration of the starting material (see *Table 5*; $R_{av} = 1.4 \pm 0.2 M^{-1}$).

We note that the competition ratios obtained as above are probably a little overestimated (but all to the same extent). This arises because the first formed hydroxo complex no doubt contains both isomeric forms **A** and **B** (like the azido product), and, although the *endo*(H)-form **B** normally epimerizes very rapidly to the *exo*(H)-isomer **A**, in the presence of azide **B** also very rapidly anates to give some azido complex (much faster than does **A**). The net effect is that at the end of the first reaction phase of the base hydrolysis, there will be azido product formed by N_3^- capture plus some azido product derived by subsequent azide anation of any *endo*(H)-hydroxo species.

Stereochemistry and Product Distribution (*mer*-Isomers). Optically active complexes with constant ellipticity were obtained after consecutive resolution procedures. The optical purities were tested using stereoretentive reactions (see *Exper. Part*). Nitrosation of the azido complexes occurred with complete retention of configuration. Chloride anation of the aqua ions led to chloro complexes with full geometric retention. The cycle chloro⇄aqua⇄chloro complexes occurred with complete retention of geometric and optical configuration for the *mer-exo*(H)-species **A** (X = Cl), and with some racemization and epimerization for the *mer-endo*(H)-complex **B** (X = Cl) (74% of **B** (X = Cl) with 76% retention of optical activity and 26% racemic **A** (X = Cl) were found). The conversions azido⇄aqua⇄chloro complexes proceeded with full optical and geometric retention for both *mer-exo*(H)- and *mer-endo*(H)-substrates **A** and **B** (X = N_3).

The **A**/**B** (X = N_3) product ratios were determined at various pH values by chromatographic and ^{13}C-NMR analysis for the base hydrolysis of **A** and **B** (X = Cl) and for the azide-ion anation of the corresponding hydroxo species. Only *mer*-isomers **A** and **B** (X = N_3) were detected (*Table 6*, kinetic distributions[9])). The observed azido-isomer distributions are quite different to the equilibrium values (see *Table 6*, equilibrium distributions). Also, the same results were obtained for different quenching times and pH values of the base hydrolysis and anation, indicating that they are true initial product distributions and not partly (or totally) equilibrated. Note that racemization rates of the azido products are 500 to 10000 times slower than the observed base hydrolysis rates of the chloro and bromo complexes; at a typical pH of 8.0, the half-lives for racemization are $t_{1/2}$ = 3.6, 3.5, 0.3, 2777, and 1584 s, for **A** (X = Cl), **B** (X = Cl), **A** (X = Br), **A** (X = N_3), and **B** (X = N_3), respectively[10]).

The optical activity of azido complexes formed by azide capture in base hydrolysis of (+)-**A** and (+)-**B** (X = Cl) were shown by direct measurements to be zero, both for the total and individual isomers. Similarly, for the products formed by azide anation of both (+)-**A** and (+)-**B** (X = OH), the activity was zero. All these measurements were completed in time scales where the resolved azido complexes do not racemize at an appreciable rate.

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[9]) The values reported in *Table 6* are for competition products *and* products from anation of any hydroxo product. However, the same isomer distribution is observed at relatively short reaction time ($5 \cdot t_{1/2}$ of base hydrolysis at pH 10, *viz.* before anation sets in). The amount of initial azide capture is reported ahead. The isomer ratio from the reaction of the chloro complexes with azide, reported in *Table 6* (kinetic distributions), are exactly the same as observed from the anation of the hydroxo complexes with azide, and thus the *mer-endo*(H)/*mer-exo*(H) ratio **B**/**A** for the direct capture component from the chloro complexes must be the same.

[10]) Calculated from the exper. data presented in *Table 2*.

Table 6. *Equilibrium and Kinetic* mer-*[CoX(dien)(dapo)]$^{n+}$ Isomer Distributions* **A**/**B** (X = Cl, N_3, OH). I = 1.0M ($NaClO_4$), 298 K, $[Co]_{tot} \approx 10^{-3}$ M, [buffer] ≈ 0.1M.

Reactant Product	% **A**	% **B**	Reactant Product	% **A**	% **B**
Equilibrium distributions			Kinetic distributions:		
A (X = H_2O) **A**/**B** (X = OH)[a])	90.4	9.6	**A** (X = Cl) **A**/**B** (X = N_3)[e])	68.7	31.3
A (X = Cl) **A**/**B** (X = OH)[b])	87.6	12.4	**B** (X = Cl) **A**/**B** (X = N_3)[e])	69.9	30.1
B (X = Cl) **A**/**B** (X = OH)[b])	88.4	11.6	**A** (X = H_2O) **A**/**B** (X = N_3)[f])[g])	68.7	31.3
A (X = N_3) **A**/**B** (X = N_3)[c])	81.0	19.0	**B** (X = H_2O) **A**/**B** (X = N_3)[f])[g])	69.9	30.1
A (X = Cl) **A**/**B** (X = Cl)[d])	88.1	11.9			
B (X = Cl) **A**/**B** (X = Cl)[d])	85.3	14.7			

[a]) pH 7.85, 5 min reaction, 95% recovery (including some chloro complex).
[b]) pH 8.35, 5 min reaction, 92.5% recovery.
[c]) pH 9.09, $[N_3^-]$ = 1.0M, 21 min reaction, 99% recovery.
[d]) pH 7.4, 48 h reaction, 5.0M NaCl, *ca.* 20% recovery of chloro species (*ca.* 80% aqua).
[e]) pH 8.35, 5.0 min reaction, 93% recovery.
[f]) pH 7.85 and 8.35, 5.0 min reaction, 94.5% recovery.
[g]) Experiments with optically pure reactant led to fully racemic product.

The optical activities for products **A** and **B** (X = OH) of base hydrolysis of the respective chloro isomers were not determined because these ions (especially the *endo*(H)-form **B**) racemize rapidly (despite the preliminary report of the contrary [16]). Finally, the rates of base hydrolysis of **A** and **B** (X = Cl and N_3) determined spectrophotometrically were identical with the rates of loss of optical activity.

Reactivity of Reactants and Products (*mer*-Isomers). Epimerization of *mer-exo*(H)- and *mer-endo*(H)-[Co(Xdien)(dapo)X]$^{n+}$ (**A** and **B**, resp.; X = N_3, Cl, OH) was studied by quenched base hydrolysis experiments, *viz.* the base hydrolysis of isomerically (and in part of optically) pure **A** or **B** was acid-quenched after *ca.* $1 \cdot t_{1/2}$, and the recovered reactant and any epimer which had formed were determined spectrophotometrically (and polarimetrically) after chromatographic separation.

With X = N_3^- the base hydrolysis (pH 9.90, 2-aminoethanol) was quenched after 20 or 31 s for **A** and **B**, respectively. Starting with either epimer, only two bands (corresponding to recovered azido reactant and aqua product in the expected epimer ratio) were observed. The recovered azido ion was isomerically and optically pure, *viz.* no epimerization had taken place, starting with either epimer, and there was no racemization in the recovered reactant. When similar experiments were done at a lower pH (7.85), base hydrolyses were measurably reversible, *i.e.* the azido complex survived even $10 \cdot t_{1/2}$, and epimerization could be observed. However, when now reactions were quenched after *ca.* $1 \cdot t_{1/2}$ (35 or 59 min for **A** and **B**, resp.), in addition to the reactant, some of its epimer was eluted. Furthermore, the recovered reactant had a reduced optical activity, while the epimer was fully racemic.

With X = Cl^- and racemic reactants, typical product distributions were as follows[11]): reactant **A** (X = Cl), pH 6.2, 22 s reaction time: 83% of **A** (X = Cl), 3.3% of **B** (X = Cl), and 13.1% of **A**/**B** (X = H_2O); reactant **A** (X = Cl), pH 7.4, 30 s reaction time: 36.2% of **A** (X = Cl), 4.5% of **B** (X = Cl), and 59.3% of **A**/**B** (X = H_2O); reactant **B** (X = Cl), pH 7.4, 30 s reaction time: 7.6% of **A** (X = Cl), 28.3% of **B** (X = Cl), and 64.1% of **A**/**B**

[11]) The **A**/**B** ratio of the aqua complexes could not be determined because of rapid subsequent epimerization.

($X = H_2O$); reactant **B** (X = Cl), pH 6.2, 30 s reaction time: 12.9% of **A** (X = Cl), 38.6% of **B** and (X = Cl), and 48.5% of **A**/**B** ($X = H_2O$). With optically pure reactants in similar experiments, the recovered reactant **B** (X = Cl) was still largely optically pure (*ca.* 95%), while the small amount of **A** (X = Cl) was fully racemic. Epimerization results from Cl^- re-entry into the achiral intermediate (see *Discussion*), and the extent depended upon concentration, the reaction time, and the counter-ion (use of $ZnCl_4^{2-}$ for example led to a little more epimerized chloro product).

The fact that quenched base hydrolysis experiments with pure and optically active azido complexes led to their fully racemic epimer, while the reactant largely retained its optical activity, indicates that the hydrolysis route of epimerization is much faster than the direct route and, therefore, preferred exclusively (see below, *Scheme 4*). Support for this interpretation came from kinetic experiments, where base hydrolyses of the two epimers of the azido complexes were sufficiently different and followed clear monophasic pseudo-first-order rate laws.

Equilibrium isomer distributions (*Table 6*) were obtained for the chloro, azido, and hydroxo complexes in the appropriate medium by allowing sufficient time to complete $10 \cdot t_{½}$ of the epimerization. For the azido isomers, 1M N_3^- was used to eliminate net hydrolysis under equilibrium conditions, but for the chloro species, 5M Cl^- was required to generate a sufficient amount of both **A** and **B** (X = Cl) to define the isomer ratio. The same results were obtained commencing from either side of the equilibrium, *i.e.*, using both the *exo*(H)- and *endo*(H)-isomers as substrates.

For the hydroxo-isomer epimerization kinetics, first-order rate constants by 'one-point' calculations were obtained from the expression $[endo(H)] - [endo(H)]_\infty = ([endo(H)]_o - [endo(H)]_\infty) \cdot e^{-k_{obs} \cdot t}$, where [*endo*(H)] at times 0, t, and ∞ were those determined from mass balance and by chromatographic analysis for a given quench time t. The value of k_{obs} so obtained was checked for constancy by using different quench times in the range $1–3 \cdot t_{½}$, and it is of course the sum of forward ($k_{k'k}$) and reverse ($k_{kk'}$) specific rates of epimerization (*i.e.* $k_{obs} = k_{k'k} + k_{k'k}$; $k_{k'k}/k_{kk'} = 90:10$, see *Table 6*).

Discussion. – *The Site of Deprotonation and General Aspects.* In base hydrolyses of pentaaminecobalt(III) complexes, the site of deprotonation is an important point of discussion, since the conjugate base is responsible for the enormous increase in substitution reactivity. However, there are very few studies with experimental results establishing the site of deprotonation (unless, of course, where there is only one site, *e.g.*, *cis* to chloride in *trans*-$[Co(en)_2Cl_2]^+$). Based on various arguments, one school of thought is that deprotonation *cis* to the leaving group leads to the most reactive conjugate base [1] [25]. An intriguing result in this context, that might be regarded as contradicting a *cis* deprotonation, is the fact that the only structurally characterized aminecobalt(III) complex with a deprotonated coordinated amine is a cage hexaaminecobalt(III) complex which exhibits a lengthening of the aminecobalt(III) bond *trans* to the deprotonated amine, consistent with a labilization of the leaving group *trans* to the deprotonated site (*trans* effect) [2]. Incidentally, kinetically a similar result emerges from *mer*-$[CoCl(dien)(dapo)]^{2+}$ where the *trans* NH_2 proton exchanges fastest. However, the most acidic amine does not necessarily lead to the most reactive conjugate base that loses the leaving group, *viz.* the relative acidity of the coordinated amines is not necessarily product controlling (as long as proton exchange is faster than loss of the leaving group).

In the *mer-exo*(H)-/*mer-endo*(H)-[CoX(dien)(dapo)]$^{n+}$ system **A**/**B** a fact that indicates that deprotonation occurs *cis* to the leaving group (at the secondary 'flat' NH of dien) to give the most reactive conjugate base is, that the acceleration of hydrolysis by base of *mer*-[CoX(dien)(dapo)]$^{n+}$ is roughly three orders of magnitude larger than for the corresponding *fac*-isomers (*Tables 2* and *3*). This difference cannot be due to additional steric strain in the *mer*-isomers [44] (see also [45–47]), and it might, therefore, be related to the configuration of the conjugate base, *viz.* for the *mer*-isomers it is deprotonated at the secondary NH group. This also follows from the following detailed discussion of the base hydrolyses of **A** and **B**.

Both isomers **A** and **B** (X = Cl) were hydrolyzed rapidly and, indeed, at experimentally indistinguishable rates. The latter is fortuitous (the two isomers did not rapidly mutarotate, a circumstance which could lead to apparently identical hydrolysis rates). These are the fastest rates of base hydrolysis for chloropentaaminecobalt(III) complexes that were reported to date (*Table 3*; the base-hydrolysis rate for the structurally related *mer*-[CoCl(dien)(tn)]$^{2+}$ ion is comparable (tn = propane-1,3-diamine)).

The products of base hydrolysis were **A** and **B** (X = OH), observed in their equilibrium ratio. Starting with the optically active chloro complexes, the hydroxo products were racemic. The loss of optical activity from the chloro complexes corresponded to the spectrophotometrically determined base-hydrolysis rates. However, in separate experiments, we showed that the epimerization and racemization of these hydroxo isomers were fast on the time scale of base hydrolysis, and hence this observation did not comment on the immediate configuration of the base-hydrolysis products. The complexes **A** and **B** (X = N_3) were found to be relatively stable to epimerization, base hydrolysis, and racemization under the conditions of base hydrolysis of **A** and **B** (X = Cl). Thus, by doping solutions with azide and observing its capture during the base hydrolysis of **A** and **B** (X = Cl) we could directly determine the stereochemistry of substitution. These experiments proved to be complicated by the unusually rapid azide-ion anation of the complexes **A** and **B** (X = OH). However, the primary base hydrolysis for the chloro species could be largely separated kinetically from the subsequent anation, and we were able to show with some precision that the initially formed azido species were optically inactive when derived from optically pure **A** and **B** (X = Cl). We also found that **A** and **B** (X = N_3) were formed in a nonequilibrium ratio, and the same isomer ratio was observed starting with either **A** or **B** (X = Cl)[12]). A similar but less extensive set of results was obtained for the base hydrolysis of **A** and **B** (X = Br), and finally, the azide anation of pure **A** and **B** (X = OH) gave a common azido-isomer distribution which was identical with that observed for the other substrates[13]).

The results show quite clearly that the configuration of the secondary NH is partly inverted during substitution, and that a common symmetrical intermediate must be involved, unless epimerization and racemization occur prior to substitution (*i.e.* the optically active *mer-exo*(H)- and *mer-endo*(H)-substrates are rapidly equilibrated and racemized). The fact that the base-hydrolysis rates were identical hinted at this possibility,

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[12]) The same isomer ratios were observed at relatively short reaction times ($5 \cdot t_{1/2}$ at pH 10), before anation sets in. The numbers in *Table 6* are for first formed products *and* products from anation of any hydroxo complex.

[13]) In the following publication it is shown that this anation is in fact base hydrolysis of **A** or **B** (X = H_2O) with effective deprotonation at the secondary N-center [15].

and it is not difficult to conceive the epimerization *via* the usual process of deprotonation, inversion, and reprotonation while in the six coordinate state, but it is important to note that such a process cannot result in racemization as well (see below, *Scheme 4*).

If rapid pre-equilibration of **A** and **B** (X = Cl) occurs, it has to be faster than base hydrolysis. Also, since it requires H-exchange, H-exchange at the secondary-amine center has to be faster than base hydrolysis. It is faster indeed, but apparently not sufficiently. At asymmetric N-centers, reprotonation with retention is usually strongly preferred to reprotonation with inversion (*ca.* 1000-fold), and thus it seems very unlikely that epimerization could compete with base hydrolysis. Supporting experiments, therefore, were those conducted for the quenched base hydrolysis of optically pure **A** or **B** (X = Cl). Recovered chloro complex was fully optically active, and little or no epimerization was observed, except in the presence of free chloride, and here the material was racemic. Thus, epimerization can only occur in the presence of free chloride by anation of the base-hydrolysis product (or by chloride capture in the five-coordinate state). In summary, the inversion at the secondary NH observed on base hydrolysis of **A** and **B** (X = Cl) does not occur prior or subsequent to but rather during substitution.

Another conclusion that can be drawn is that a single reaction pathway is followed, *viz.* only one deprotonated amine center is involved in base hydrolysis. This follows from the same product distribution, independent of the leaving group, and the fact that reaction *via* any other route must lead to some optically active product, which is contrary to observation.

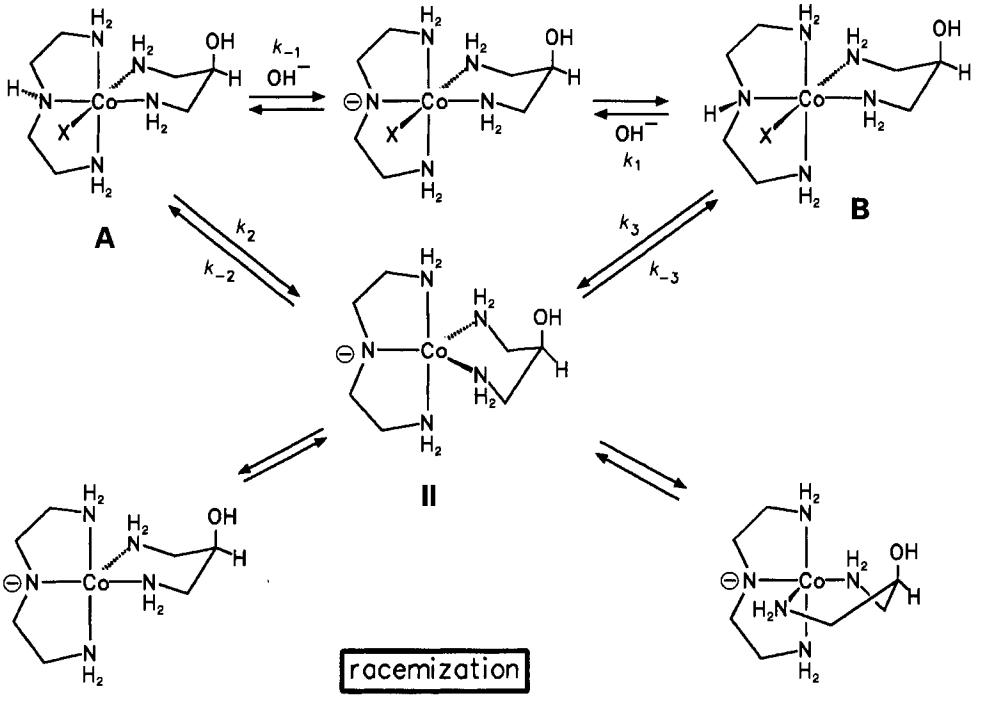
Before dealing with the nature of the intermediate, the H-exchange rate data should be reconsidered in the light of the results above. First, H-exchange at any of the NH_2 groups *cis* to the leaving group X is too slow to accommodate the base hydrolysis, but exchange at the secondary NH or at NH_2 *trans* to X is sufficiently rapid. In the case of **A** (X = Cl), the most abundant conjugate base must be that generated by deprotonation at NH_2 *trans* to X, since that site is the fastest to exchange. Yet base hydrolysis clearly proceeds by effective deprotonation at the secondary NH which is much slower to exchange. Although long recognized as a possibility, this is the first time that base hydrolysis is established to proceed *via* a less abundant conjugate base. Another point to note is that although base hydrolysis does not occur *via* the fastest exchanging site, exchange at the secondary NH center is still faster (perhaps 10-fold) than base hydrolysis, and thus we do not have an example of rate-limiting deprotonation which is usually associated with very reactive conjugate bases such as we have here.

The H-exchange rate at the active site and the base-hydrolysis rate are correlated, but it is interesting to note that this is not a strong 1:1 correlation. This follows from the fact that **A** (X = Cl) is faster to exchange at the secondary NH center, yet the base-hydrolysis rates do not show a corresponding difference. A similar result is found for **A** and **B** ($X = N_3$) (see above) and **A** and **B** (X = OH) (see [15]).

The ions **A** and **B** ($X = N_3$) are much more stable towards hydrolysis than their chloro analogues, and the study of their base hydrolysis had to be carried out in dilute solution to avoid the reverse reaction. Under such conditions, there was no competitive epimerization commencing with either isomer, and the rates of base hydrolysis and loss of optical activity were identical. Thus, the same achiral intermediate is involved, as discussed above for the chloro complexes. At higher Co-concentrations or in the presence of added N_3^- epimerizations is observed, and above *ca.* 0.1M N_3^- and below pH 9, observable base

hydrolysis is not competitive. However, the essential reaction is the same because the racemization rate is the same, *viz.* the rate-determining step in both the hydrolysis and epimerization is formation of the same achiral intermediate. Water entry leads to hydrolysis, while azide entry leads to racemization of the starting isomer and epimerization.

Scheme 4



The six specific rates in *Scheme 4* are not all independent – the principle of detailed balance requires the relationship of *Eqn. 8* between them.

$$k_{-1}/k_1 = (k_2/k_{-2}) \cdot (k_{-3}/k_3) \tag{8}$$

For identical (or similar) basicities of the coordinated amines for the *exo*(H)- and the *endo*(H)-species, the epimer ratio **A**/**B** may now be calculated: k_3/k_2 gives the relative rates of base hydrolysis of the two isomers which is 2.89:1.59 = 1.82. Since k_1/k_{-1} is simply the equilibrium isomer ratio which we also know (81:19), we can calculate the isomer ratio for entry into the intermediate (k_{-2}/k_{-3}), and this is 2.34 (70:30), in excellent agreement to that observed (69:31). A similar analysis can be made for other isomeric pairs, and it is a useful device to obtain the steric course when it is otherwise difficult to determine. For the chloro complexes, *e.g.*, the steric course for Cl^- entry is *ca.* 87% of **A**

and 13% of **B**, and for the hydroxo complexes, the steric course for H_2O entry is estimated to be 63% of **A** and 36% of **B**. This analysis reveals that, although the form **A** is in most cases preferred, the steric course depends clearly on the nature of the nucleophile which is not surprising. The same was observed for H_2O and N_3^- ion entry on base hydrolysis of other pentaaminecobalt(III) complexes, although the case for a genuine intermediate in these reactions is not as strong.

The Structure of the Intermediate. The S_N1CB process (*Scheme 1*) involves rate-determining loss of the leaving group X from the conjugate base **2**, resulting in a five-coordinate intermediate **3**. Recently, experiments involving base hydrolysis of pentaaminecobalt(III) at very low and variable ionic strength led to the conclusion that, at least in that case, base hydrolysis is not a true limiting dissociative process but may rather be described as an I_DCB reaction [11] [12]. These date were in good agreement with earlier results, where competition ratios were found to vary slightly but significantly with the leaving group [29] [48]. In contrast, base hydrolysis of **A** and **B** involves a *true five-coordinate intermediate*. This interpretation is based on the result of full racemization during base hydrolysis, and the fact that racemization does not occur prior or subsequent to substitution, *viz.* it is related to the substitution intermediate which has to be common to all substitutions studied. The intermediate can only be symmetrical (*i.e.* able to lead to fully racemic products) when it is deprotonated at the secondary NH of dien (see above) and when the Co–X bond is broken and X departed, *viz.* the process is S_N1CB. Also, the solvation sphere about the intermediate must have relaxed sufficiently to destroy the original chirality associated with it, and X, if still present in this solvation sphere, can no longer be asymmetrically disposed, *viz.* the entity (intermediate plus solvation sphere) must be achiral.

The life-time τ for the *hexa-coordinate intermediate* in the case of pentaaminecobalt(III) was calculated to be $\geqslant$ 200–1500 ps [12]. We do not have any direct evidence for the lifetime of the pentacoordinate intermediate[14]). The formation of the trigonal bipyramid might be a concerted process or the result of an equilibration of initally formed square pyramids (*Scheme 4*). The rearrangement from square-pyramidal to trigonal-bipyramidal geometry clearly is a fast process (probably in the order of 1–10 ps). At this stage, based on the experimental results, it is not possible to know whether the trigonal-bipyramidal structure is a true intermediate or just a transition state between two enantiomeric square pyramids, *viz.* the answer to the question whether the square-pyramidal or the trigonal-bipyramidal species are capturing competing nucleophiles is not unambiguous.

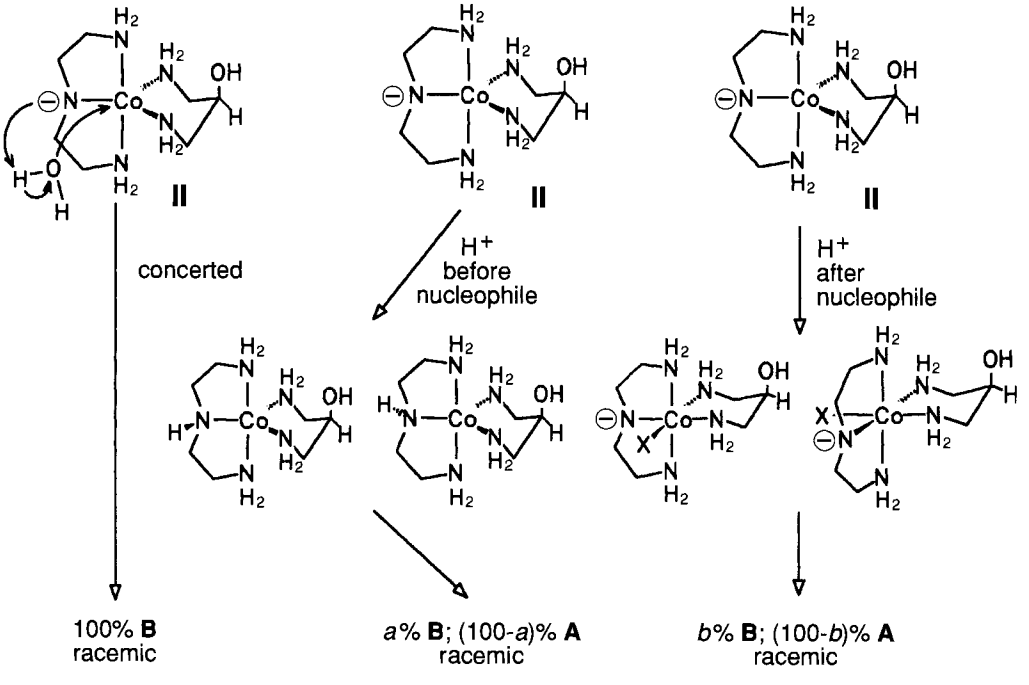
Inherent in the design of the $[CoX(dien)(dapo)]^{n+}$ system was the fact that the pentacoordinate structure (see **II** in *Scheme 4*) is the only possible achiral intermediate. From the fact that N-inversion at the secondary NH center and racemization occur *during* base hydrolysis, it follows that the secondary NH must be, at least in the time average, fully symmetrical, *i.e.* planar. If this results from two enantiomeric trigonal bipyramids with sp^3 secondary NH, N-inversion needs to be extremely rapid or the intermediate extraordinarily long-lived. Usual N-inversion rates (*ca.* 10^4 sec^{-1}) compared to the lifetime of the

[14]) The selectivity of the intermediate (competition ratios) is not directly related to its lifetime but to its structural and electronic properties.

intermediate in the order of ns suggest that the trigonal-bipyramidal intermediate has a fully planar secondary N-center (sp^2).

The Stage of Back-Protonation. In base-catalyzed substitutions, a proton is removed an returned at some stage. If there is an intermediate, the timing of the return is an important question which has rarely been addressed. There are three limiting mechanistic possibilities for back-protonation in base hydrolysis, *viz. i*) the five-coordinate intermediate is protonated before capturing OH^- or competitors, *ii*) the two processes are concerted, or *iii*) protonation occurs subsequent to the capture of the nucleophile. In a recent study on pentaaminecobalt(III) [12], back-protonation was calculated to occur subsequent to the capture of nucleophiles. This was based on the idea that back-protonation must be rather slow ([intermediate] $\leq 10^{-10}$ M, $[H^+] \leq 10^{-7}$ M, diffusion-controlled protonation), *viz.* of the order of s, while the capture of nucleophiles is 5–10 orders of magnitude faster.

Scheme 5



If, in the **A**/**B** system, protonation and capture of OH^- would occur at the same stage (*i.e.* concerted capture of H_2O), this would give the *endo*(H)-product **B** exclusively (see *Scheme 5*) which is not the case. For the base hydrolysis of **A**/**B** we established the occurrence of a common symmetrical intermediate, *i.e.* **II**. Subsequent back-protonation before or after capture of the nucleophile should lead to racemic products **A** and **B**, and their ratio should depend upon the nature of the nucleophile in either case (*Scheme 5*). Exactly this was observed. From the experimental stereochemical results, it is not possible to unequivocally decide whether back-protonation occurred before or after capture of the

nucleophile. However, microscopic reversibility would require reprotonation subsequent to re-entry of the leaving group and infer it for other nucleophiles.

The Stabilization of the Intermediate. The possibly most intriguing question concerning base hydrolysis of pentaaminecobalt(III) is why the conjugate base is so much more reactive than the protonated reactant. A comparison of competition ratios, hydrolysis rates, and acceleration ratios of a number of systems indicates that the main reason for base catalysis is a stabilization of the substitution intermediate, and not a destabilization of the conjugate base. The **A**/**B** system is unique in terms of stereochemical informations. The question arises, whether the enhanced reactivity of the **A**/**B** system is the result of steric or electronic effects. Based on the observation that the accelerated loss of the leaving group only occurs in base (*i.e.* the acceleration ratios and not only the base-hydrolysis rates are high), and based on comparative kinetic studies with *unsym-fac*-[CoX(dien)(dapo)]$^{n+}$ (**C** and **D**), steric strain may be excluded as a major reason for the stabilization of the [Co(dien – H)(dapo)]$^{2+}$ intermediate **II**. Also, using the less reactive *unsym-fac*-reactants, some *mer*-products are formed, whereas *mer*-reactants retain their configuration fully, *viz.* the *mer*-geometry cannot be sterically less favorable. This aspect is also supported by molecular-mechanics calculations [44].

A comparison of base-hydrolysis kinetics and acceleration and competition ratios (*Table 3*) indicates that deprotonation at a 'flat' amine storngly stabilizes the substitution intermediate. Since $k_{OH} = k \cdot K_b$ is a composite constant, either K_b or removal of the leaving group (k), or both, might be responsible for the acceleration. A comparison of H-exchange rates implies that K_b alone cannot be responsible for the effect of 'flat' amines, *viz.* the acceleration is based on a further stabilization of the intermediate. A similar reactivity pattern is found for various other pentaaminecobalt(III) with multidentate ligands exhibiting a 'flat' amine, *e.g. sym*-[CoX(trenen)]$^{n+}$ [31] [32] (trenen = *N*,*N*,*N*′-tris(2-aminoethyl)ethane-1,2-diamine), $\alpha\beta$-[CoX(tetraen)]$^{n+}$ [49–51][15]) (tetraen = *N*-(2-aminoethyl)-*N*′-{2-[(2-aminoethyl)amino]ethyl}ethane-1,2-diamine), *mer*-[CoX(dien)(AA)]$^{n+}$ [40] [53] (AA = diamine), *mer*-[CoX(dpt)(AA)]$^{n+}$ [54], *etc.* (see also *Table 3*). However, none of the above systems allowed the determination of the site of deprotonation and of the structure of the coordinatively unsaturated intermediate state. Stereochemical reactant-product relations similar to the ones described for the *mer*-isomers **A** and **B** were used to determine the steric course of base hydrolysis for [CoX(bamp)(dapo)]$^{n+}$ [17] (bamp = pyridine-2,6-bis(methanamine)) and [CoCl(tri)(en)]$^{2+}$ [53] (tri = *N*-(2-aminoethylidene)ethane-1,2-diamine). For the first system (bamp), full retention of chirality was observed, and the stability of square-pyramidal configuration of the pentacoordinate intermediate[16]) was attributed to electronic effects due to the pyridine donor. In the latter system (tri), there were some ambiguities which precluded a thorough analysis in terms of the site of deprotonation and structure of the intermediate.

Traditionally, the interpretation of the stabilization of the five-coordinate intermediate was based on *Basolo* and *Pearson*'s π-stabilization model ($R_2N^-_{3p} \rightarrow Co^{III}_{3d_{x^2-y^2}}$ π-bonding) [18] [19]. It is tempting to interpret our results of the **A**/**B** system with this model,

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[15]) The enhanced reactivity for base hydrolysis of $\alpha\beta$-[Co(salicylate)(tetraen)]$^+$ was explained by an intramolecular H^+ transfer from the secondary 'flat' amine to deprotonated coordinated salicylate [50] [51]. In the light of the above discussion, it is questionable whether the rate of this tautomerism is relevant to the enhanced reactivity, and this is presently being tested [52].

[16]) The term 'five-coordinate intermediate' might not be appropriate in that case, *vide infra.*

because it is, to our knowledge, the first time that a system fulfills all the necessary conditions for *Basolo* and *Pearson*'s model. Of importance is not only the fact that the substitution intermediate is trigonal bipyramidal, but that the secondary amine moiety is planar, *i.e.* sp_2-hybridized (see above). However, recent theoretical studies based on ligand-field [23] [24] and SCF MS-Xα [25] calculations indicate that a low-spin (singlet) to high-spin (triplet or quintet) or to a formally reduced Co^{II} state might be involved, leading to the enhanced substitution reactivity[17]).

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