

Pyridyl-Based Pentadentate Ligands: Base-Catalyzed Hydrolysis of *asym*-[Co(dmptacn)Cl]²⁺

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Received March 19, 2004

The [Co(dmptacn)Cl]²⁺ (dmptacn = 1,4-bis(pyridylmethyl)-1,4,7-triazacyclononane) complex has been shown to be the *asym* isomer through 1D and 2D NMR studies, its optical resolution, and the single-crystal X-ray structure of its perchlorate salt. The kinetics of base-catalyzed hydrolysis establishes the usual [OH⁻] dependence ($k_{\text{OH}} = 0.040 \text{ M}^{-1} \text{ s}^{-1}$, 25 °C, $I = 1.0 \text{ M}$, NaCl), but D-exchange experiments reveal that substantial if not complete reaction proceeds via the new pseudoaminate mechanism, i.e., via deprotonation at an α -CH₂ center rather than the NH. The significant kinetic isotope effect ($k_{\text{H}}/k_{\text{D}} = 2.1$) is interpreted in terms of rate-limiting deprotonation followed by reprotonation of the conjugate base at a rate competitive with loss of Cl⁻. NMR and polarimetric studies establish geometric and optical retention for the hydrolysis reaction and exclude even the transient formation of a *sym* isomer intermediate.

Introduction

Octahedral cobalt(III) complexes containing amine ligands are subject to base catalysis, and this catalysis can be enormous, up to a factor of 10¹⁵ faster than the normal so-called acid hydrolysis reaction.^{1,2} While many of the essential features of this catalysis are now understood, an outstanding problem that has resisted resolution is the relative effectiveness of NH deprotonation *cis* or *trans* to the leaving group. The major experimental difficulties have been the following: (i) the synthesis of a ligand with just one deprotonatable NH center; (ii) the synthesis of a pair of [Co(pentaamine)-Cl]²⁺ isomers, one with the sole NH *cis* and the other the NH *trans* to the leaving group. Necessarily such pentadentate ligands must be constructed from tertiary amine and pyridine donors, and this can lead to instability of the Co(III) complex

toward reduction and a susceptibility toward autocatalysis.^{1,3} While pyridine can easily be coordinated to Co(III), no monodentate tertiary amine complexes are known, and the necessary stability must be instilled through a subtle balance of donor atoms and ligand connectivity. A pentadentate ligand (dmptacn, Figure 1) initially prepared for other purposes^{4–7} attracted our attention because it had just the one NH center and its cobalt(III) complex proved stable in base toward reduction. Further, it can exist in two isomeric forms, with the single NH either *cis* or *trans* to the leaving group (Figure 2).

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(1) Jackson, W. G. *Inorg. React. Mech.* **2002**, *4*, 1.

(2) Tobe, M. L. *Adv. Inorg. Bioinorg. Mech.* **1983**, *2*, 1.

(3) Dickie, A. J.; Hockless, D. C. R.; Willis, A. C.; McKeon, J. A.; Jackson, W. G. *Inorg. Chem.* **2003**, *42*, 3822.

(4) Spiccia, L.; McLachlan, G. A.; Fallon, G. D.; Martin, R. L.; Moubaraki, B.; Murray, K. S. *Inorg. Chem.* **1994**, *33*, 4663.

(5) McLachlan, G. A.; Fallon, G. D.; Martin, R. L.; Moubaraki, B.; Murray, K. S.; Spiccia, L. *Inorg. Chem.* **1994**, *33*, 4663.

(6) McLachlan, G. A.; Brudenell, S.; Fallon, G. D.; Martin, R. L.; Spiccia, L.; Tiekink, E. R. T. *J. Chem. Soc., Dalton Trans.* **1995**, 439.

(7) McLachlan, G. A.; Fallon, G. D.; Martin, R. L.; Spiccia, L. *Inorg. Chem.* **1995**, *34*, 254.

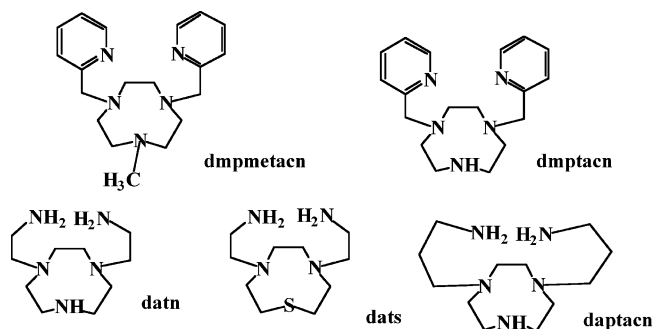


Figure 1. dmptacn and other two “armed” pentadentate ligands derived from tacn and a tacn-like ligand.

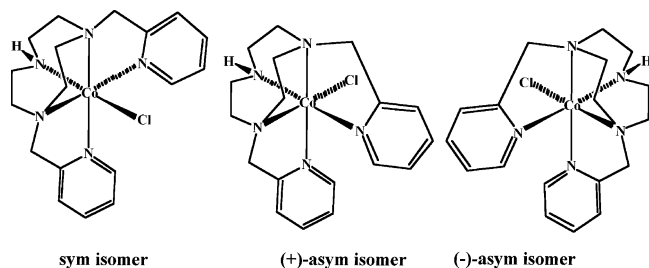


Figure 2. The two geometric isomers for $[\text{Co}(\text{dmptacn})\text{X}]^{n+}$.

Herein we report the synthesis of one of these isomers, its optical resolution, and the kinetics and stereochemistry of base-catalyzed hydrolysis. We also report NMR studies on deuterium incorporation which provide mechanistic information on the role of $\alpha\text{-CH}_2$ deprotonation in the hydrolysis mechanism.^{1,3}

Results and Discussion

Synthesis and Structure. The $[\text{Co}(\text{dmptacn})\text{X}]^{n+}$ complexes are asym isomers (Figure 2), clearly apparent from the 18 line ^{13}C NMR spectra (Figures 3 and 4S (Supporting Information)). This is confirmed by the optical resolution of the chloro complex and the activity of the aqua and hydroxo ions generated from it. The crystal structure of a salt of the aqua complex of dmptacn ion was reported previously.⁶ The ^1H NMR spectra (Figure 5S) for corresponding dmptacn and dmpmetacn complexes are strikingly similar (see also Figure 7 in ref 3, for the ^{13}C spectra; cf. Figures 3 and 4S herein), and the assignments worked out from extensive 2D NMR work on the dmpmetacn compounds³ apply also to the dmptacn analogues (Figure 5S). The four closely spaced $\alpha\text{-CH}_2$ protons (two AB quartets, Figure 4, A) are assigned, but we could not positively identify the deprotonation site in this work; very likely it is the same “trans” proton³ as pinned down for the dmpmetacn complex (H-i, Figure 5).

UV–Visible Spectroscopy. The UV–visible spectral data are displayed in Table 1, together with those of some related complexes. Two bands are generally observed in the UV–visible spectra of Co(III) pentamine complexes, with maxima at approximately 500 and 350 nm. These are due to transitions from the $^1\text{A}_{1g}$ ground state to the upper $^1\text{T}_{1g}$ and $^1\text{T}_{2g}$ states in the parent octahedral species; the lower energy transition is usually observably split in the lower symmetry CoN_5X species, and indeed in all these complexes, the first

ligand field band is appreciatively asymmetric. The visible spectra of the dmptacn and corresponding dmpmetacn complexes indicate that the tertiary amine is a somewhat poorer donor than the *sec*-NH but are generally consistent with what is expected for $\text{Co}^{\text{III}}\text{N}_5\text{Cl}$ or $\text{Co}^{\text{III}}\text{N}_5\text{O}$ chromophores.

Crystallography. Crystal data are given in Table 2. An ORTEP diagram of the cation is shown in Figure 6 along with the atomic numbering scheme. Selected interatomic parameters are listed in Table 3. Additional crystallographic data are accessible from the deposited CIF file.

The complex adopts the same asym stereochemistry as all the dmptacn, dmpmetacn, datn, and dats complexes thus far characterized.^{3,8,9} The Co–N (amine and pyridine) bond lengths vary from 1.929(4) to 1.958(4) Å and, as expected, are similar to those of $[\text{Co}(\text{dmptacn})\text{OH}_2]^{3+}$, which range from 1.906(7) to 1.937(7) Å. $[\text{Co}(\text{daptacn})\text{Cl}]^{2+}$ (Figure 1) shows slightly longer Co–N distances of 1.96–2.01 Å, probably because of the more flexible nature of the aminopropyl pendant arms. The Co–Cl distance of 2.246(3) Å in $[\text{Co}(\text{daptacn})\text{Cl}]^{2+}$ is the same as that for the dmptacn complex (2.249(1) Å). House has tabulated and analyzed Co–Cl bond lengths for a wide range of pentaaminecobalt(III) complexes—no clear correlations emerged.¹⁰ The $\angle\text{NCoN}$ chelate ring angles for the tacn nitrogens in the dmptacn chloro complex are close to 90° (average 87.2°), and the same angles in the related complexes, $[\text{Co}(\text{dmptacn})\text{OH}_2]^{3+}$ and $[\text{Co}(\text{daptacn})\text{Cl}]^{2+}$, are on average 86.9 and 87.6° , respectively, very little different.

The angles subtended by the pyridyl and tacn nitrogens, N(1)–Co(1)–N(4) and N(2)–Co(1)–N(5) (average 84.5°) are also less than 90° . They are smaller than those for the $[\text{Co}(\text{daptacn})\text{Cl}]^{2+}$ complex where such rings are six- rather than five-membered (average 93.9°), which was found to show minimal distortion from a regular octahedral geometry, with trigonal twist distortion angles (θ) of 59.6° for both aminopropyl groups. The average trigonal twist angle (θ) for the 2-pyridylmethyl groups in $[\text{Co}(\text{dmptacn})\text{OH}_2]^{3+}$ is 53° , indicating considerably more distortion from a regular octahedral geometry ($\theta = 60^\circ$), and a similar value (52°) was found in the corresponding chloro complex reported herein. Comparison with the recently reported *asym*- $[\text{Co}(\text{dmpmetacn})\text{Cl}]^{2+}$ complex reveals the same trends as found for *asym*- $[\text{Co}(\text{dmptacn})\text{Cl}]^{2+}$ (twist angle 53°),¹¹ with the only anomaly, not noted earlier, of a long Co–N3 bond for the tacn nitrogen which carries a methyl rather than H substituent (2.005(7) vs 1.929(4) Å, respectively).

Reactivity. The base-catalyzed hydrolysis reaction is single phasic, with three sharp isosbestic points observed in the UV–visible spectra (419, 495, and 560 nm; Figure 9S).

(8) Fortier, D. G.; McAuley, A. J. *Chem. Soc., Dalton Trans.* **1991**, 101.

(9) Gahan, L. R.; Lawrance, G. A.; Sargeson, A. M. *Aust. J. Chem.* **1982**, *35*, 1119.

(10) House, D. A. *Comments Inorg. Chem.* **1997**, *19*, 327.

(11) The twist angle for the “offset” about a 3-fold axis running through two parallel octahedral triangular faces is an average value. There is no strict 3-fold axis—the triangular faces are not equilateral nor are they strictly parallel.

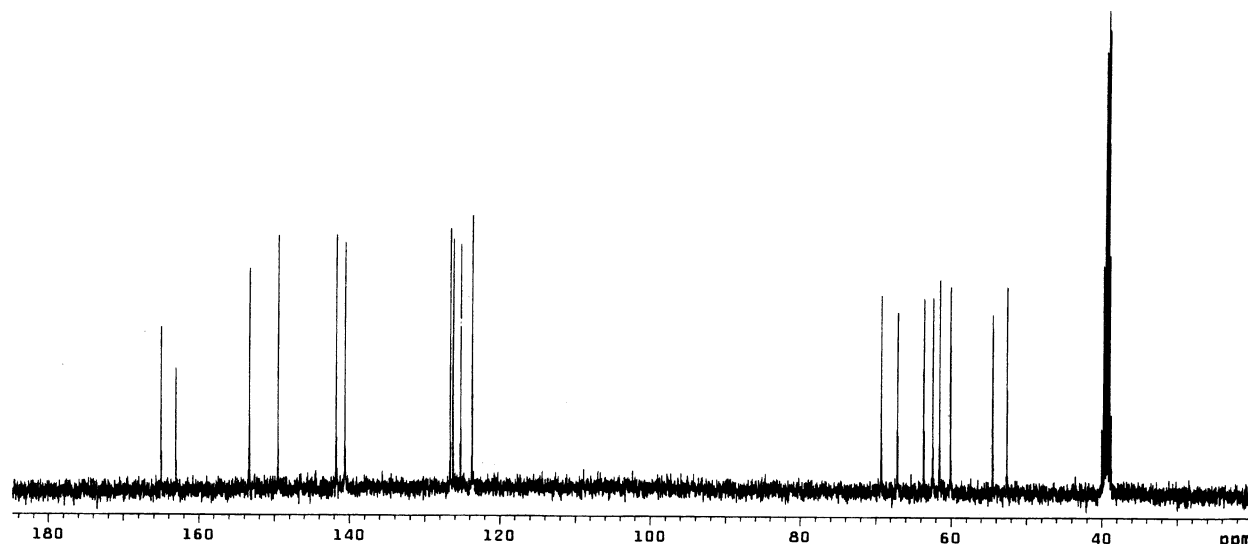


Figure 3. ^{13}C NMR spectrum of *asym*- $[\text{Co}(\text{dmptacn})\text{Cl}](\text{ClO}_4)_2$ in $\text{Me}_2\text{SO}-d_6$.

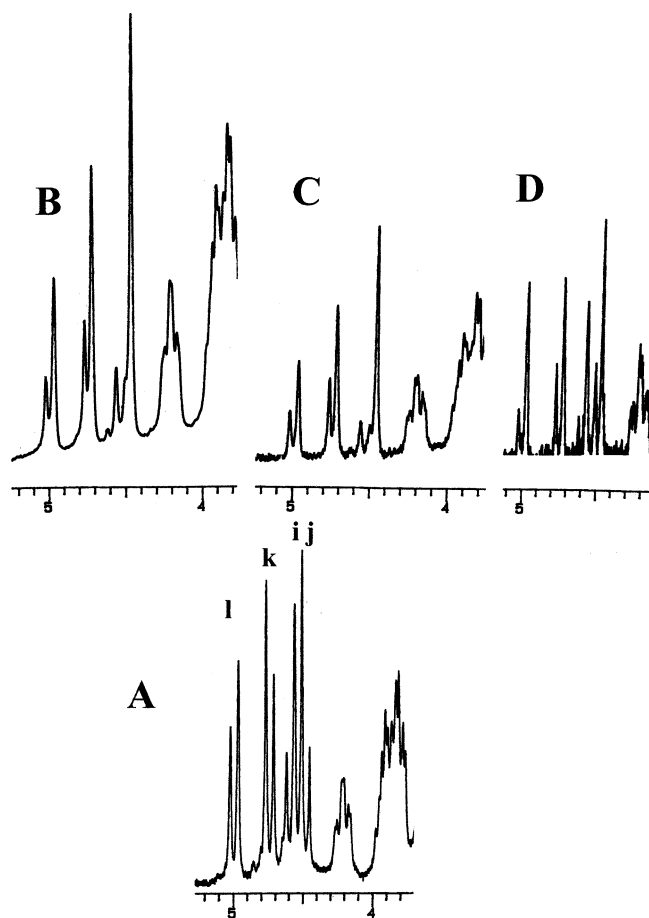


Figure 4. AB quartet portions of the ^1H NMR spectrum for samples of *asym*- $[\text{Co}(\text{dmptacn})\text{Cl}](\text{ClO}_4)_2$ in $\text{Me}_2\text{SO}-d_6$: A, starting material; B, recovered product after 1 half-life of base hydrolysis in $\text{D}_2\text{O}/\text{NaOD}$ (0.1 M)/ NaCl (0.9 M) and converted back to the chloro complex (DCl/Δ); C, recovered reactant after $1 t_{1/2}$ of base hydrolysis (conditions as for (B)); D, aqua complex reacted under the conditions used for (B) and converted back to the chloro complex.

The kinetic data are given in Table 4S and plotted in Figure 7 for the OH^-/Cl^- medium.

The variation is smooth and approximately linear, but there is clear concave curvature. Although this is in the right sense

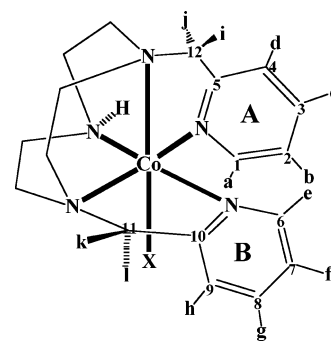


Figure 5. Carbon and proton numbering scheme for the pyridyl pendant arms of *asym*- $[\text{Co}(\text{dmptacn})\text{X}]^{m+}$.

Table 1. UV–Visible Spectra of *asym*- $[\text{Co}(\text{N}_5)\text{X}]$ Complexes Derived from tacn

complex ^a	λ_{max} , nm (ϵ_{max} , $\text{M}^{-1}\text{cm}^{-1}$)	ref
$[\text{Co}(\text{dmptacn})\text{Cl}]^{2+}$	365 (252), 509 (171)	6
$[\text{Co}(\text{dmptacn})\text{OH}_2]^{3+}$	476 (200)	6
$[\text{Co}(\text{datn})\text{Cl}]^{2+}$	366 (152), 521 (165)	9
$[\text{Co}(\text{daptacn})\text{Cl}]^{2+}$	374 (77), 548 (74)	8
$[\text{Co}(\text{dmptacn})\text{Cl}]^{2+}$	366 (186), 513 (152)	this work
$[\text{Co}(\text{dmpmetacn})\text{Cl}]^{2+}$	375 (208), 510 (158)	3
$[\text{Co}(\text{dmptacn})\text{OH}_2]^{3+}$	343 (114), 484 (160)	this work
$[\text{Co}(\text{dmpmetacn})\text{OH}_2]^{3+}$	357 (157), 489 (198)	3

^a The top four spectra are for MeCN as solvent, and the rest for H_2O (pH 3).

for mass law retardation² by Cl^- , this is not the cause; Cl^- is a known¹³ poor competitor in base hydrolysis. Rather, the curvature is due to specific ion activity coefficient variations due to the use of Cl^- rather than the usual ClO_4^- , for solubility reasons. Precisely the same behavior is seen¹⁴ for the base-catalyzed hydrolysis of $[\text{Co}(\text{NH}_3)_5\text{X}]^{2+}$ complexes ($\text{X} = \text{Cl}^-, \text{I}^-$). Ions which best mimic OH^- as the supporting anion are F^- and OAc^- ; Cl^- and N_3^- lead to a discernible

(12) The substitution of NaCl by NaOH as the $[\text{OH}^-]$ is raised leads to a significant medium effect. If m_1 is the second-order rate constant at the lower pH in 1 M NaCl and m_2 the corresponding constant for 1 M NaOH medium, the observed rate constant $k(\text{obsd}) = (m_1)[\text{OH}^-] + (m_2 - m_1)[\text{OH}^-]^2$.

(13) Jackson, W. G.; Begbie, C. M.; Randall, M. L. *Inorg. Chim. Acta* **1983**, *70*, 7.

(14) Angel, R.; Marty, W.; Jackson, W. G. Unpublished results.

Table 2. Crystal Data for *asym*-[Co(dmptacn)Cl](ClO₄)₂

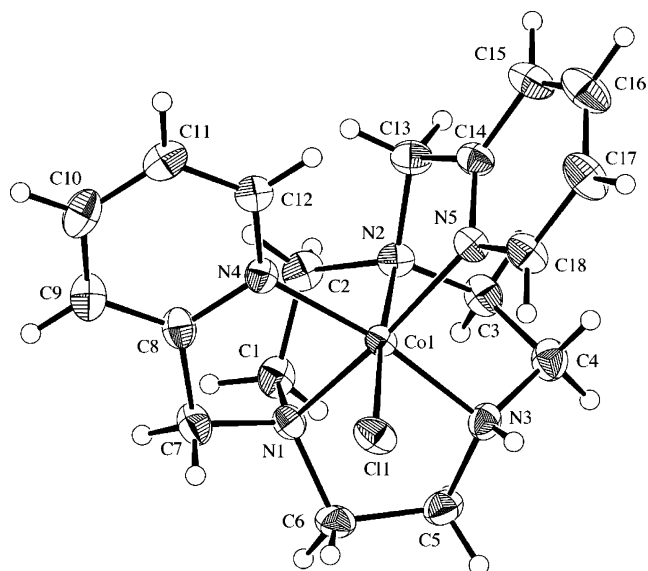
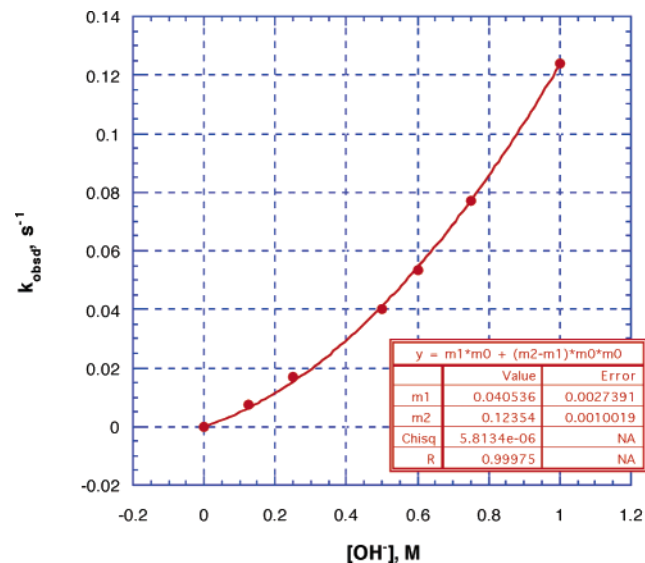
formula	C ₁₈ H ₂₅ Cl ₃ CoN ₅ O ₈
M	604.72
cryst system	monoclinic
space group	<i>P</i> 2 ₁ / <i>c</i>
<i>a</i> /Å	11.162(2)
<i>b</i> /Å	12.934(3)
<i>c</i> /Å	16.724(2)
β /deg	105.34(1)
<i>V</i> /Å ³	2328.3(7)
Z	4
<i>T</i> /K	296
λ (Mo K α)/Å	0.710 73
<i>D_c</i> /g cm ⁻³	1.725
μ /mm ⁻¹	1.138
no. of obsd/unique data	4580/4138 (3004, <i>I</i> > 3 σ (<i>I</i>))
no. of refined params	319
R	0.0434
<i>R_w</i>	0.0468
S	1.929

Table 3. Selected Geometric Parameters (Å, deg)

Co(1)–Cl(1)	2.249(1)	N(5)–C(14)	1.360(6)
Co(1)–N(1)	1.948(4)	N(5)–C(18)	1.342(6)
Co(1)–N(2)	1.945(4)	C(1)–C(2)	1.496(7)
Co(1)–N(3)	1.929(4)	C(3)–C(4)	1.519(7)
Co(1)–N(4)	1.953(4)	C(5)–C(6)	1.518(7)
Co(1)–N(5)	1.958(4)	C(7)–C(8)	1.481(7)
N(1)–C(1)	1.510(6)	C(8)–C(9)	1.377(7)
N(1)–C(6)	1.499(6)	C(9)–C(10)	1.367(8)
N(1)–C(7)	1.484(6)	C(10)–C(11)	1.371(7)
N(2)–C(2)	1.489(6)	C(11)–C(12)	1.379(7)
N(2)–C(3)	1.514(6)	C(13)–C(14)	1.475(7)
N(2)–C(13)	1.490(6)	C(14)–C(15)	1.384(7)
N(3)–C(4)	1.472(7)	C(15)–C(16)	1.370(8)
N(3)–C(5)	1.506(6)	C(16)–C(17)	1.359(8)
N(4)–C(8)	1.350(6)	C(17)–C(18)	1.372(7)
N(4)–C(12)	1.341(6)		
Cl(1)–Co(1)–N(1)	94.4(1)	N(1)–Co(1)–N(5)	170.8(2)
Cl(1)–Co(1)–N(2)	176.0(1)	N(2)–Co(1)–N(3)	86.8(2)
Cl(1)–Co(1)–N(3)	90.0(1)	N(2)–Co(1)–N(4)	95.7(2)
Cl(1)–Co(1)–N(4)	87.8(1)	N(2)–Co(1)–N(5)	83.2(2)
Cl(1)–Co(1)–N(5)	94.7(1)	N(3)–Co(1)–N(4)	170.8(2)
N(1)–Co(1)–N(2)	87.8(2)	N(3)–Co(1)–N(5)	94.1(2)
N(1)–Co(1)–N(3)	87.1(2)	N(4)–Co(1)–N(5)	95.0(2)
N(1)–Co(1)–N(4)	84.2(2)		

mismatch, as also observed here for the dmptacn complex. The rate measured for the dmptacn complex in the OAc[−] medium lies on the straight line connecting the 0 and 1 M OH[−] data points (Table 8S), consistent with this interpretation. The data points in Figure 7 have been fitted to the function $f k_1[\text{OH}^-] + (1 - f)k_2[\text{OH}^-]^2$, the two terms accommodating the activity coefficient mismatch in neat OH[−] (fraction 1 - *f*) and Cl[−] (fraction *f*) media. Given [NaCl] + [NaOH] = 1, 1 - *f* = [OH[−]] and this leads to the expression $k_{\text{obsd}} = k_1[\text{OH}^-] + k_2[\text{OH}^-]^2$. The value for *k*₁ (0.0405 ± 0.003 M^{−1} s^{−1}) corresponds to the rate constant for base hydrolysis in 1 M NaCl and agrees with the value extracted from the more limited data collected for buffers at much lower pH, also for 1 M NaCl (Figure 11S). The *k*_{OH} value for the neat OH[−] medium is 0.124 ± 0.001 M^{−1} s^{−1}, some 2.5-fold larger than for the Cl[−] medium. It needs to be emphasized that such variations for a change in counterion, despite a “constant ionic strength” medium, are more widespread than generally recognized.

The *k*_{OH} value [Co(dmptacn)Cl]²⁺ ion is about the most unreactive pentaamminecobalt(III) complex known. Although it bears one NH, *cis* to the leaving group, it is some 20-fold less reactive than *asym*-[Co(dmpmetacn)Cl]²⁺ which has no such NH center;³ this latter ion is also regarded as unreactive.

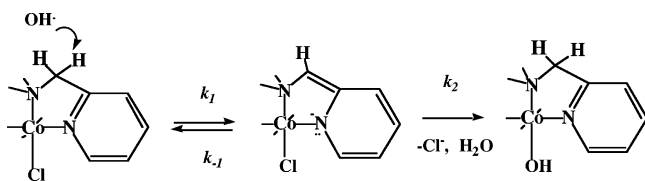
**Figure 6.** ORTEP diagram for the cation *asym*-[Co(dmptacn)Cl]²⁺ (arbitrary enantiomer) with thermal ellipsoids at the 30% level.**Figure 7.** Plot of *k*_{obsd} vs [OH[−]] for the base hydrolysis of *asym*-[Co(dmptacn)Cl]²⁺ in NaOH/NaCl (*I* = 1.0 M) at 25 °C. Solid circles are experimental points, and the curve is the least-squares best fit to the function in the inset. *M*₀ = [OH[−]], and *m*₁ and *m*₂ are as defined in the cited reference.¹²

These facts suggest that both react via α-CH₂ deprotonation and that the methyl substituent alone is responsible for the rate difference. There is a similar rate difference for the corresponding pair of complexes *s*-[Co(trenen)Cl]²⁺ and *s*-[Co(metrenen)Cl]²⁺, where the only difference in structure is a H or Me on the *sec*-N trans to Cl[−] but where base catalysis appears to arise from deprotonation at the same *cis*-NH center.¹⁵

Previously we argued that the *asym*-[Co(dmpmetacn)Cl]²⁺ complex deprotonated at a rate approximately 20-fold slower than the conjugate base lost Cl[−].³ If the corresponding dmptacn conjugate base is now 20-fold less reactive, this

(15) Cresswell, P. J. Doctoral Thesis, Australian National University, 1974; pp 58–60.

Scheme 1



brings the rate of deprotonation into line with the reactivity of its conjugate base. This rationale is entirely consistent with the reduced kinetic isotope effect for the dmptacn species, and the results of the deuterium incorporation experiments, features now discussed.

Kinetic Isotope Effect and Deuterium Incorporation during Base Hydrolysis. The rates of base hydrolysis (k_{OH^-}) for the protic and perdeuterated complexes, the average of triplicate determinations, were determined to be 0.057 ± 0.001 and $0.028 \pm 0.001 \text{ M}^{-1} \text{ s}^{-1}$, respectively, for 0.100 M NaOH ($I = 1.00 \text{ M}$, NaCl) solutions. The kinetic isotope effect, while substantial ($k_{\text{H}}/k_{\text{D}} = 2.1$), is less than that observed for the $\text{asym-}[\text{Co}(\text{dmpmetacn})\text{Cl}]^{2+}$ complex ($k_{\text{H}}/k_{\text{D}} = \text{ca. } 5$). The latter complex base hydrolyses by rate-limiting deprotonation, and if the kinetic isotope effect of magnitude 5 is the benchmark for such a process, then a value of ca. 2.1 could indicate that the dmptacn complex base hydrolyses by both $\alpha\text{-CH}_2$ and NH deprotonation, the former via rate-limiting deprotonation with an isotope effect and the latter via the normal $\text{S}_{\text{N}}1\text{CB}$ process without an isotope effect. There is an alternative explanation for the reduced isotope effect, considered ahead.

For the reaction of $\text{asym-}[\text{Co}(\text{dmptacn})\text{Cl}]\text{Cl}_2$ in $\text{D}_2\text{O}/\text{NaOD}$ both the recovered reactant and the product incorporated deuterium into all four inequivalent sites but to different extents (Figure 4). By comparison there was some but less exchange in the control experiment on the hydroxo complex yet with the same site selectivity.

If base hydrolysis proceeds exclusively via rate limiting $\alpha\text{-CH}_2$ deprotonation, one deuterium should be incorporated into one of the four sites in the product, and the recovered reactant would retain its methylene protons. Such was the case for the methyl derivative, $\text{asym-}[\text{Co}(\text{dmpmetacn})\text{Cl}]^{2+}$. Alternatively more than one site might be effective, in which case the one deuterium would be spread among the effective sites. As noted, however, both reactant and product, even at 1 half-life of reaction, have significant deuterium incorporation into all four sites, although mainly into site H-i (Figure 4). Further, there is less than 1D at each of the sites, which excludes complete reaction via one particular $\alpha\text{-CH}_2$. Moreover, it could be argued that the similar distributions and extent of CH_2 deuteration for reactant and product is consistent with “normal” reaction via NH deprotonation; i.e., exchange at the CH_2 sites is incidental to the base hydrolysis reaction. However, the significant isotope effect indicates only ca. 50% reaction maximum via this route, with the balance coming from deprotonation at a CH_2 center or centers. Also, it seems this pathway is via a preexchanged CH, to accommodate the absence of additional deuterium in the product.

The reactions shown in Scheme 1 with the usual steady-state approximation for the conjugate base lead to the rate law shown in eq 1.

$$k_{\text{obsd}} = k_1 k_2 [\text{OH}^-] / (k_2 + k_{-1}) \quad (1)$$

One limiting case is $k_2 \gg k_{-1}$, which is rate-limiting deprotonation as found for the $\text{asym-}[\text{Co}(\text{dmpmetacn})\text{Cl}]^{2+}$ complex, eq 2.

$$k_{\text{obsd}} = k_1 [\text{OH}^-] \quad (2)$$

The other limiting case is $k_{-1} \gg k_2$, which corresponds to a fast preequilibrium acid–base step in the normal $\text{S}_{\text{N}}1\text{CB}$ process, eq 3.

$$k_{\text{obsd}} = k_1 k_2 [\text{OH}^-] / k_{-1} \quad (3)$$

The large isotope effect ($k_{\text{H}}/k_{\text{D}} = \text{ca. } 5$) is associated with the quantities k_1 and k_{-1} . They compensate in the normal $\text{S}_{\text{N}}1\text{CB}$ process, eq 3, since k_1 and k_{-1} are affected similarly but do not where there is rate-limiting deprotonation, eq 2.

The present value of $k_{\text{H}}/k_{\text{D}} = 2.1$ for base hydrolysis of the $\text{asym-}[\text{Co}(\text{dmptacn})\text{Cl}]^{2+}$ complex is consistent with Scheme 1 where k_{-1} is comparable to and actually larger than k_2 ,¹⁶ and this is also consistent with the observed extent of deuteration found for recovered reactant after one half-life (Figure 4).

In summary, reaction appears to proceed via $\alpha\text{-CH}_2$ deprotonation, likely via loss of the proton H-i (Figure 5) but not proven; a contribution from an NH deprotonation pathway cannot be excluded. Further, in this system reprotonation of and loss of Cl^- from the conjugate base derived from $\alpha\text{-CH}_2$ deprotonation are comparable in rate, and this alone can accommodate the reduced isotope effect. There seems no way to confirm this because the NH proton is completely exchanged before any detectable base hydrolysis (which is normal).

Stereochemistry of Base-Catalyzed Hydrolysis. The NMR results gave no indication of the presence of any sym isomer either in the reactant $[\text{Co}(\text{dmptacn})\text{Cl}]^{2+}$ or the product $[\text{Co}(\text{dmptacn})\text{OH}]^{2+}$. Clearly there is retention of stereochemistry. Moreover, the optically resolved asym isomer withstood a base/acid cycle, showing that there is no appreciable loss of activity for both the base-catalyzed hydrolysis and reverse Cl^- anation reaction in acid. These results therefore exclude the sym structure as a transient intermediate and any symmetrical five-coordinate species.

There was some discernible loss in optical activity in the base/acid/heat cycle, ca. 10%, and this is attributed to some racemization of the aqua product under the forcing conditions of the slow anation reaction in strong HCl solution (4 h, 95 °C). When the anation time was limited, the activity was determined to be 95% rather than 90%, approaching complete retention.

(16) Using eq 1, $k(\text{obsd}) = k_1 k_2 [\text{OH}^-] / (k_2 + k_{-1})$, and assuming the full isotope effect $k_{\text{H}}/k_{\text{D}}$ for each of k_1 and k_{-1} , the observed isotope effect of 2.1 leads to the expression $2.1 = 5(k_2 + 0.2k_{-1}) / (k_2 + k_{-1})$. This solves as $k_{-1}/k_2 = 2.6$.

The results parallel those described for the *asym*-[Co(dmpmetacn)Cl]²⁺ system where retention was established³ through the use of selectively C-deuterated species for which there was no scrambling of the label on base-catalyzed hydrolysis of the Cl⁻ leaving group.

Conclusions

It is believed the bis(pyridylmethyl)tacn complexes ions base hydrolyze via α -CH₂ deprotonation; this is certain for the methyl derivative³ and very likely for the dmptacn analogue, given the substantial isotope effect. In principle one can force the dmptacn complex to react via NH rather than α -CH₂ deprotonation by improving the leaving group, for example through the use of *asym*-[Co(dmptacn)O₃-SCF₃]²⁺. This arises because *k*₂ is very dependent on the leaving group (eq 3) whereas *k*₁ (eq 2) is not expected to be. The triflate leaving group is in other pentaaminecobalt(III) systems known to be >10⁵ more reactive than chloride in base-catalyzed hydrolysis.¹⁷

The stereochemically related series of complexes derived from datn, dats,⁹ dmptacn, dmpmetacn (Figure 1),³ and daptacn⁸ all strongly prefer the *asym* configuration. Further, all base hydrolyze with geometric and optical retention, despite the different active sites for deprotonation, although the rates are very site dependent. However, the properties of any intermediates for reaction via NH vs α -CH₂ deprotonation may well be different, e.g., N₃⁻ ion competition,¹⁸ and this idea is under active pursuit to give better definition to the pseudoaminate mechanism.

Experimental Section

All chemicals were AnalaR or an equivalent grade. Carbon-13 and proton NMR spectra were recorded on Varian XL-300 and Unity Plus 400 MHz instruments at 20 °C or Bruker AC200 or AM300 spectrometers. Solvents used were D₂O with dioxane as the internal reference (¹³C, δ 69.27 relative to Na(DSS)) and Me₂-SO-*d*₆ with the central peak of the CD₃ septet as the reference (¹³C, δ 39.37 relative to SiMe₄). Full visible absorption spectra and absorbance–time traces were recorded on a HP8452A diode array UV–visible spectrophotometer thermostated to 25.00 ± 0.05 °C with use of a Lauda RM6 circulating water bath. Infrared spectra were obtained for KBr disks on a Biorad FTIR instrument. Electrospray ionization mass spectra were recorded on either a Micromass Platform QMS with electrospray source or a Bruker BioApex 47e FTMS with a 4–7 T superconducting magnet and Analytica electrospray source. Optical rotations were measured with use of a Perkin-Elmer model 241 polarimeter and a 1 dm cell. Cation exchange media used were Dowex 50Wx2 (H⁺ form, 200–400 mesh; Biorad) and SP-Sephadex C25 (Na⁺ form; Pharmacia). Carbon dioxide free Milli-Q water was used for all physical measurements.

[Co(dmptacn)Cl]Z (Z = (ClO₄)₂·0.5H₂O, Cl₂, ZnCl₄·H₂O), dmptacn made according to the published procedure from tacn (1.0 g) and 2 equiv of 2-picoyl chloride yielded a brown oil (0.70 g).⁴ The ¹³C NMR spectrum indicated that it comprised mostly of the

pentadentate dmptacn, but also some mptacn (one “arm”) and tmptacn (three “arms”). Purification was conveniently carried out through complexation and ion exchange chromatography. The direct product mixture (pH readjusted to ca. 8), or the free base dmptacn (0.6 g, free base) extracted with CH₂Cl₂ from this basic mixture, was dissolved in 1:1 water/methanol (50 mL), and 1 mol equiv of CoCl₂·6H₂O (0.53 g) was added. Air was drawn through the mixture for 16 h to form a dark brown solution (bridging peroxo complex). On addition of HCl (12 M) and heating on a steam bath, a red solution resulted. This was diluted, sorbed onto a Dowex exchange column, and eluted (1–3 M HCl) to give well-separated purple, yellow, orange, and red bands. These correspond respectively to [Co(mptacn)(OH₂)Cl]²⁺, [Co(tmptacn)]³⁺, [Co(dmptacn)OH₂]³⁺, and [Co(dmptacn)Cl]²⁺. The elution order (2+ ion last) is abnormal but matches that for the corresponding dmpmetacn system.^{3,4} By heating of the aqua product at 90 °C in HCl (10 M) for 4 h more, chloro product was obtained. Combined eluates were taken to dryness and the chloride salt crystallized by addition of an equal volume of methanol to a concentrated aqueous solution and careful dilution with acetone. The perchlorate salt of the chloro product was crystallized from a saturated aqueous solution of the residue by addition of a fifth volume of HClO₄ (70%); it is sparingly soluble in water. The tetrachlorozincate salt was also isolated, using “H₂ZnCl₄” (2 M) as the precipitant. The salts were collected, washed with ethanol and ether, and air-dried. Average yield: 75%. ¹³C NMR (400 MHz; Me₂SO-*d*₆): δ 165.0 (1C), 163.0 (1C), 153.1 (1C), 149.5 (1C), 141.7 (1C), 140.6 (1C), 126.6 (1C), 126.2 (1C), 125.2 (1C), 123.6 (1C) (aromatic); 69.2 (1C), 67.0 (1C) (“elbow” CH₂); 63.6 (1C), 62.4 (1C), 61.5 (1C), 60.1 (1C), 54.4 (1C), 52.5 (1C) ppm, (ring CH₂). Anal. Calcd for CoCl₁₈H₂₅N₅Cl₃O₈·0.5H₂O: C, 35.2; H, 4.3; N, 11.4; Cl, 17.3. Found: C, 34.8; H, 4.1; N, 11.2; Cl, 17.3. UV–visible (H₂O): ϵ _{513(max)} 152.0, ϵ _{478(sh)} 134.0, ϵ _{366(max)} 186.0 M⁻¹ cm⁻¹.

The quite soluble chloride salt was conveniently obtained from the purified perchlorate by adding some HCl (10 M) to a slurry of the salt in acetone/water (1:1) and then carefully diluting with excess acetone.

The sample crystallized for the X-ray structure proved to be anhydrous, but under some conditions the hemihydrate or monohydrate was obtained. Anal. Calcd for [Co(C₁₈H₂₅N₅)Cl](ClO₄)₂·H₂O: C, 34.7; H, 3.7; N, 10.5. Found: C, 34.4; H, 4.4; N, 10.9. Electron microprobe: Cl/Co ratio 3:1. UV–visible (CH₃CN) [λ _{max}, nm (ϵ _{max}, M⁻¹ cm⁻¹): 365 (252), 509 (171). IR (KBr, cm⁻¹): 3230 m, 3090 w, 2922 m, 2854 m, 1612 m, 1569 w, 1480 m, 1465 m, 1377 m, 1307 w, 1295 m, 1272 w, 1246 w, 1214 w, 1156 m, 1098 vs, 995 s, 931 s, 864 w, 844 w, 831 m, 786 m, 762 w, 720 m, 627 s, 514 m, 439 w.

Method 2. This was carried out as above except for the use of excess hydrogen peroxide (30% w/w) as the oxidant which was added dropwise over ca. 5 min to completely oxidize Co(II) to Co(III). The deep brown peroxo complex was cleaved with HCl as before. Yield: 65%.

Method 3. The free base (1.44 g) in excess aqueous HCl was rota-evaporated to dryness under reduced pressure to yield the hydrochloride salt. This was dissolved in a small volume of water and added to freshly synthesized sodium tris(carbonato)cobaltate(III) (1.5 g).¹⁹ The product mixture was heated for 15 min and then treated with HCl and worked up as in method 1. Yield: 85%.

Method 4. To a solution of *trans*-[Co(py)₄Cl₂Cl]·6H₂O (2.0 g, 3.4 mmol) in methanol was added free base dmptacn (1.0 g, 3.4 mmol) in methanol (5 mL), and the mixture was heated to 60 °C

(17) Curtis, N. J.; Lawrance, G. A.; Lay, P. A.; Sargeson, A. M. *Inorg. Chem.* **1986**, *25*, 484.

(18) Jackson, W. G.; Sargeson, A. M. In *Rearrangement in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 2, p 273.

(19) Bauer, H. F.; Drinkard, W. C. *J. Am. Chem. Soc.* **1960**, *82*, 5031.

for 15 min. The product mixture was quenched with 1 M HCl, diluted with water, and sorbed on and eluted from Dowex as before. It was crystallized as the perchlorate or tetrachlorozincate salts from water using HClO₄ or "H₂ZnCl₄" as precipitants. Yield: 1.7 g, 80%; ZnCl₄²⁻ salt.

[Co(dmptacn)OH₂](ClO₄)₃. A slurry of the chloro derivative (perchlorate) in a minimum volume of 2 M NaOH was warmed to effect dissolution and hydrolysis. The solution was filtered and acidified by addition of an equal volume of HClO₄ (70%). On cooling, orange crystals deposited. These were filtered off, washed with *i*-PrOH and ether, and air-dried. Yield: ca. 70%. Anal. Calcd for CoC₁₈H₂₇N₅Cl₃O₁₃: C, 31.5; H, 4.0; N, 10.2; Cl, 15.5. Found: C, 31.3; H, 4.0; N, 10.0; Cl, 15.6%. UV-visible (0.01 M HClO₄): ε(max) 175.5, ε₃₅₂ (max) 145.5 M⁻¹ cm⁻¹. UV-visible (0.01 M NaOH): ε₄₈₄ (max) 159.5, ε₃₇₈ (max) 111.0, ε₃₄₃ (max) 114.0 M⁻¹ cm⁻¹.

Perdeuterated Complex. A solution of *asym*-[Co(dmptacn)Cl]-Cl₂ (1.0 g) in D₂O (20 mL) which was 2 M NaOD was allowed to react at 25 °C for 2 h before quenching with HClO₄ (70%, 5 mL). On cooling, the *d*₄ aqua complex crystallized. The corresponding *d*₄ chloro ion was made by heating samples of the aqua species in HCl (10 M; steam bath, 2 h). It was crystallized as the perchlorate and recrystallized as the chloride from water/HCl/acetone to remove traces of aqua complex (¹H NMR spectrum, Figure 12S).

Partially Deuterated Complexes. The reaction of *asym*-[Co(dmptacn)Cl]Cl₂ in D₂O/NaOD (0.1 M)/NaCl (0.9 M) at 25 °C was followed spectrophotometrically to determine the half-life for hydrolysis in this medium (ca. 80 s). The experiment was repeated on a preparative scale using the inverted Y-tube mix and quench method.³ A sample of the complex (0.5 g) was base hydrolyzed for ca. 1 half-life, and the reaction was quenched in acid. The product mixture was chromatographed, and the product aqua complex (band 1) and residual chloro complex (band 2) were recovered. The aqua complex was anated in hot HCl (5 h) to regenerate the chloro species, and both were analyzed by ¹H and ¹³C NMR to determine the D-content and distribution across the four possible sites. A control experiment showed that there was no loss of deuterium in the anation reaction in HCl. Another control experiment was the reaction of the aqua (hydroxo) complex in NaOD under identical conditions, to determine the extent of deuteration after base hydrolysis.

In an alternative method of workup, the quenched base hydrolysis was cooled and unreacted starting material precipitated and filtered off. Later, after addition of 2-propanol, the aqua product precipitated. The solids were washed with ethanol and ether and air-dried.

Steric Course of Base Hydrolysis. A sample (ca. 80 mg) of *asym*-[Co(dmptacn)Cl]Cl₂ was dissolved in D₂O containing dioxane as an internal reference, and the ¹³C NMR spectrum was recorded. Two drops of NaOD (10 M) were then added, and the ¹³C NMR spectrum was recorded for the hydroxo ion that formed within several seconds. The product solution was acidified by addition of a few drops of DCl (10 M) until the solution just became orange, and the ¹³C NMR spectrum was again recorded. In each case the product was a single species—the *asym* isomer.

A sample of the optically resolved salt *D-asym*-[Co(dmptacn)-Cl]ZnCl₄ (ca. 0.2 g) was dissolved in water (50 mL) and divided roughly into two. Half was retained while the other half was treated with aqueous NaOH (5 M) to achieve 1 M OH⁻ after mixing, allowed to react for 10 *t*_{1/2} at 25 °C, and then quenched with an equal volume of HCl (11 M). After being heated on a steam bath for 4 h, this was diluted with water and chromatographed on Dowex along with, and separately from, the untreated sample. The chloro ions were recovered with 3 M HCl, and the absorption spectra and

optical rotations were recorded for each in 5 cm and 1 dm cells, respectively. The ratio α₃₆₅/D₅₈₀ was used as a measure of activity. The values obtained were, averaged for duplicate experiments, 0.90 and 0.88 for treated samples relative to untreated. By reduction of the anation time to 1.5 h, this measure rose to 0.95 for the chloro ion, separated by ion exchange chromatography from the unreacted aqua complex.

Optical Resolution of *asym*-[Co(dmptacn)Cl]²⁺. A saturated solution of the chloride salt was treated with 1 equiv of NH₄(+)-BCS (Aldrich) and 1 equiv of Na(+)-AsO-tart, synthesized by the published method.²⁰ Crystals deposited within days at 2 °C; these were collected at intervals. The diastereomer was not characterized, but it seemed to require both chiral anions for its crystallization. When deposition ceased, the filtrate was chromatographed on Dowex to recover the one enantiomer as the chloride salt. The diastereomer was treated with sufficient concentrated HCl to remove the chiral anions and solubilize the complex. It was then recovered from Dowex using HCl as eluant and crystallized as the chloride salt. Both enantiomers were refractionated to optical purity as tetrachlorozincate salts using "H₂ZnCl₄" and *i*-PrOH to effect crystallization. The less soluble diastereomer yielded the *D* isomer. UV-visible (0.01 M HClO₄): ε₅₁₃(max) 151.5 M⁻¹ cm⁻¹. Molar rotations (H₂O): *D* form [M]₅₈₉ = +370, [M]₅₇₈ = +210, [M]₅₄₆ = -990, [M]₄₃₆ = -1740, [M]₃₆₅ = -3650 deg mol⁻¹ dm²; *L* form [M]₅₈₉ = -349, [M]₅₇₈ = -170, [M]₅₄₆ = +1040, [M]₄₃₆ = +1805, [M]₃₆₅ = +3900 deg mol⁻¹ dm².

Buffer Solutions. The buffers employed consisted of ethanolamine (0.40 M) solutions that had been partly neutralized (0.1–0.9 equiv) with HCl, with the ionic strength adjusted to 2.00 M with NaCl. They were diluted 1:1 for use. The pH determinations were performed as described previously.^{3,21}

Base Hydrolysis Kinetics. The kinetics of hydrolysis of the chloro species (Cl⁻ salt) were measured in a series of ethanolamine buffers and also in NaOH/NaCl (*I* = 1.0 M) at 25.00 ± 0.05 °C. Spectrophotometric data were collected as full spectra (650–300 nm) vs time, in triplicate, and analyzed as described previously.³

Kinetic Isotope Measurements. These were performed as described previously³ using both *h*₄- and *d*₄-*asym*-[Co(dmptacn)-Cl](ClO₄)₂ as reactants, with runs performed in parallel to provide a direct comparison of *k*_H/*k*_D. The medium was 0.1 M NaOH and *I* = 1.0 M (NaCl).

Crystallography. Red crystals of *asym*-[Co(dmptacn)Cl](ClO₄)₂ suitable for X-ray crystallographic analysis were grown by slow evaporation of an aqueous solution. An orange-pink plate crystal of [Co(dmptacn)Cl](ClO₄)₂ having the approximate dimensions of 0.40 × 0.32 × 0.08 mm was mounted on a glass fiber. All measurements were made at 23 °C on a Rigaku AFC6R diffractometer with graphite-monochromated Mo Kα radiation. Crystal data are given in Table 2; the complex crystallizes as the racemate.

The structure was solved by direct methods and expanded using Fourier techniques.^{22,23} All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included at calculated positions, except H on N(3) which was refined positionally. The final cycle of the full-matrix least squares refinement was based on the numbers given in Table 2. Neutral atom scattering factors

(20) Schlessinger, G. *Inorg. Synth.* **1970**, *12*, 267.

(21) Jackson, W. G.; McKeon, J. A.; Marty, W. *Inorg. React. Mech.* **2002**, *4*, 125.

(22) Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Crystallogr.* **1994**, *27*, 435.

(23) North, A. C. T.; Phillips, D. C.; Mathews, F. S. *Acta Crystallogr.* **1968**, *A24*, 351.

were taken from Cromer and Waber.²⁴ Anomalous dispersion effects were included in F_{calc} ; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley.²⁵ The values for the mass attenuation coefficients are those of Creagh and Hubbel.²⁶ All calculations were performed using the teXsan crystallographic software package of Molecular Structure Corp.²⁷

(24) Cromer, D. T.; Waber, J. T. *International Tables for X-ray Crystallography*; The Kynoch Press: Birmingham, England, 1974; Vol. IV, Table 2.2 A.

(25) *International Tables for Crystallography*; Wilson, A. J. C., Ed.; Kluwer Academic Publishers: Boston, MA, 1992; Vol. C, Table 4.2.6.8, pp 219–220.

(26) *International Tables for Crystallography*; Wilson, A. J. C., Ed.; Kluwer Academic Publishers: Boston, MA, 1992; Table 4.2.4.3, p 200.

Acknowledgment. We thank the Australian Research Council for financial support.

Supporting Information Available: Kinetic data (Table 8S), NMR spectra (Figures 4S, 5S, and 12S), UV–visible scans (Figure 9S), rate data plot (Figure 11S), and a crystallographic file in CIF format for *asym*-[Co(dmptacn)Cl](ClO₄)₂. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(27) *teXsan. Single-Crystal Structure Analysis Software*, version 1.7; Molecular Structure Corp.: 3200 Research Forest Drive, The Woodlands, TX 77381, 1992–1997.