

Secondary Deuterium Kinetic Isotope Effect for Aquation, Solvolysis, and Isomerization Reactions of *trans*-[Co(en)₂(OSMe₂)N₃]²⁺, and the Resolution of a Mechanistic Anomaly

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The two closely spaced NH signals in the ¹H NMR spectrum of *trans*-[Co(en)₂(OSMe₂)(N₃)]²⁺ have been reassigned using 2D NMR and other techniques. Thus, the unusual syn to anti (to Co–N₃) NH rearrangement on base catalyzed substitution of the selectively deuterated complex in ND₃(l) has been reinterpreted as “normal”, with inversion of the effective deprotonation site accompanying the act of substitution. The re-examination of this system required a repeat study of the secondary isotope effect for the acid hydrolysis reaction, previously used to assign syn and anti amine sites, and this has been extended to other solvents (Me₂SO, MeCN). The relative NH proton exchange rates are also reconsidered. A systematic rate reduction for Me₂SO substitution is observed for deuterium incorporation into the *cis*-NH centers, irrespective of whether these are syn or anti, and the effect is much greater in Me₂SO than in water. The results are interpreted in terms of zero point energy effects and coupled vibrations.

Introduction

It is well-known that organic halides or sulfonates on deuteration at the α-carbon substitute more slowly (Figure 1).^{1–3}

These rate effects are easily discerned because rate reductions can be as great as 40%, although typically k_H/k_D is ca. 1.20. This quantity represents the secondary kinetic isotope effect, hereafter “skie”. The effect usually diminishes with distance from the reaction center (α in above example), but β and γ skies are measurable and have assumed significance in precise kinetic studies. The organic chemists have demonstrated that the magnitude and sense of the skie provides a powerful probe on detailed mechanism.¹

Studies on metal ion coordination complexes have been considerably fewer, but the early results were similar. Comparative studies in H₂O and D₂O for the aquation of [Co(NH₃)₅X]²⁺ (X = Cl[−], Br[−]), *cis*- and *trans*-[Co(en)₂Cl₂]²⁺, *trans*-[Co(β-picoline)₄Cl₂]⁺, *cis*- and *trans*-[Co(en)₂(NO₂)Cl]²⁺, as well as *cis*-/*trans*-[Co(en)₂(OH₂)Cl]²⁺

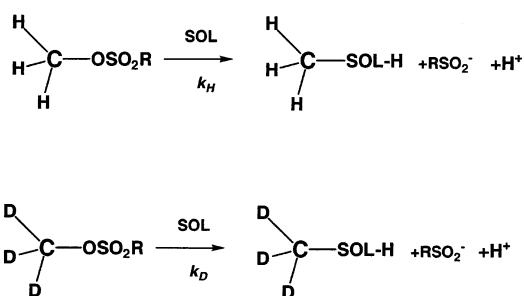


Figure 1. Solvolysis of protic and deuterated alkyl sulfonates (SOL = H₂O or CH₃COOH; R = alkyl or aryl).

isomerization have been reported.^{4–6} The effect of amine deuteration on the hydrolysis rate has also been investigated.^{4,5} However, most work for metal ion systems has focused on the primary kinetic isotope effect (pkie) where, because abstraction of the H or D isotope is directly involved and is rate determining, the effect is large ($k_H/k_D \sim 6$).⁷ The recently reported⁸ base catalyzed hydrolysis of *asym*-[Co(dmpmetacn)Cl]²⁺ (Figure 2) is a good example. Proton

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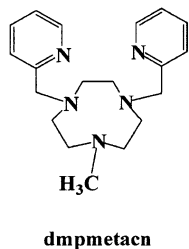


Figure 2.

abstraction of a $-\text{CH}_2-$ proton adjacent to a pyridyl group is rate determining, and this leads to an accelerated hydrolysis through to $\text{asym-}[\text{Co}(\text{dmpmetacn})\text{OH}]^{2+}$ before reprotonation. For this system, $k_{\text{H}}/k_{\text{D}}$ is close to 5.

Our recent publication on the aquation of stereoselectively N-deuterated $[\text{Co}(\text{NH}_3)_5\text{Cl}]^{2+}$ complexes is the first, as far as we are aware, on the stereoselectivity of the *skie*.⁹ Even for the widely studied organic systems there are few data. It is therefore perhaps ironic that a significant stereoselective effect of D-substitution has been found only for this one inorganic system, and we are unaware that any have been observed for the organic systems.

Our work on the $[\text{Co}(\text{NH}_3)_5\text{Cl}]^{2+}$ system was motivated by the study¹⁰ of the aquation of selectively deuterated *trans*- $[\text{Co}(\text{en})_2(\text{OSMe}_2)(\text{N}_3)]^{2+}$ complexes. N-Perdeuteration was reported to reduce the aquation rate by ca. 9%, and moreover, it was claimed that deuteration at only the *syn*-NH centers brought about this reduction (the *syn*-NH protons are defined as adjacent to DMSO or NH_3 , while the NH protons adjacent to the azide group are anti). The work of Buckingham et al.¹¹ was cited¹⁰ as the basis for this assignment, i.e., deuteration *cis* to the leaving group reduces the hydrolysis rate, but that publication¹¹ did not address this issue. Further, all NH protons in the *trans*- $[\text{Co}(\text{en})_2(\text{OSMe}_2)(\text{N}_3)]^{2+}$ complex are *cis* to the leaving group (Figure 3).

The concern¹⁰ was not with the isotope effect per se, but rather the converse, using the observed kinetic isotope effect to determine the preferred site of deuteration in the parent complex. Our re-examination of the isotope effect for the acid hydrolysis of the *trans*-azido-dmsO complex, reported herein, yielded quite different results,¹⁰ and they undermine the previous basis for the assignment of the two different sets of NH protons in the NMR spectra.

Herein we extend this work to reactions of the same complex in other solvents (DMSO and MeCN), to scrutinize the effects of solvation on the magnitude of $k_{\text{H}}/k_{\text{D}}$, and to see if the effect depended upon the type of reaction (solvolysis or isomerization).

An unprecedented rearrangement of this *trans*- $[\text{Co}(\text{en})_2(\text{OSMe}_2)(\text{N}_3)]^{2+}$ species in which an en chelate is rotated through 180° during base catalyzed solvolysis in $\text{NH}_3(\text{l})$, Figure 4, has also been claimed.¹⁰

We believed this to be a misinterpretation of the facts based on an incorrect assignment^{10,12} for the *syn* or *anti*

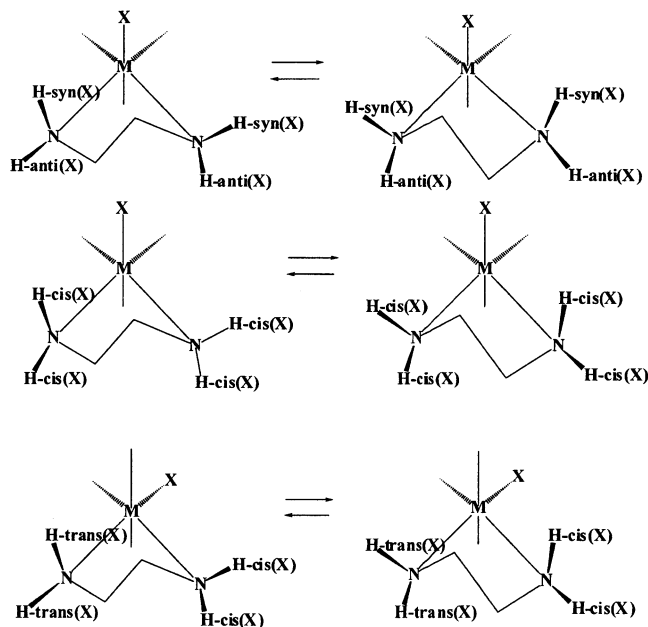


Figure 3. Diagram illustrating the distinction between *syn/anti* and *cis/trans* NH protons. The distinctions are retained under the (usual) conditions of rapid ring flipping.

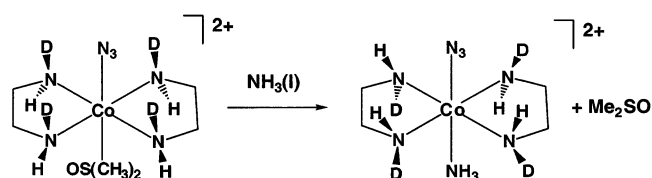


Figure 4. Proposed rearrangement for the base catalyzed substitution of *trans*- $[\text{Co}(\text{en})_2(\text{OSMe}_2)(\text{N}_3)]^{2+}$ in $\text{NH}_3(\text{l})$.

protons in either the reactant *trans*- $[\text{Co}(\text{en})_2(\text{OSMe}_2)(\text{N}_3)]^{2+}$ or product *trans*- $[\text{Co}(\text{en})_2(\text{NH}_3)(\text{N}_3)]^{2+}$ complexes. Herein we redress both these issues.

Experimental Section

All chemicals were AnalaR or an equivalent grade. 1D ^{13}C and ^1H and 2D DQCOY and NOESY NMR spectra were recorded on a Varian Unity Plus 400 MHz instrument at 20°C or 5°C . Solvents used were D_2O with dioxane as the internal reference (^{13}C , δ 69.27 ppm relative to DSS), and $\text{Me}_2\text{SO}-d_6$ with the central peak of the CHD₂ quintet or CD₃ septet as the reference (^{13}C δ 39.37 ppm, ^1H δ 2.50; relative to SiMe₄). Proton NMR spectra recorded for $\text{Me}_2\text{SO}-d_6$ solutions in the presence of Cl^- utilized NH_4Cl rather than NaCl because integration of the NH_4^+ 1:1:1 triplet centered at ca. 7 ppm provided a direct measure of the relative quantities. AnalaR or HPLC grade DMSO and MeCN were used in the kinetic studies without further purification.

Microanalyses were performed by the Microanalysis Unit at the RSC, ANU.

Synthesis. *cis*- $[\text{Co}(\text{en})_2(\text{OSMe}_2)(\text{N}_3)]\text{NO}_3 \cdot \text{ClO}_4$, *trans*- $[\text{Co}(\text{en})_2(\text{OSMe}_2)(\text{N}_3)](\text{ClO}_4)_2$, *trans*- $[\text{Co}(\text{en})_2(\text{N}_3)_2]\text{ClO}_4$, *trans*- $[\text{Co}(\text{en})_2\text{Cl}_2]\text{ClO}_4$, *trans*- $[\text{Co}(\text{en})_2\text{Br}_2]\text{ClO}_4$, *trans*- $[\text{Co}(\text{en})_2(\text{N}_3)\text{Cl}]\text{ClO}_4$, *cis*- and *trans*- $[\text{Co}(\text{en})_2(\text{NH}_3)(\text{N}_3)](\text{ClO}_4)_2$, and *trans*- $[\text{Co}(\text{en})_2(\text{NH}_3)_2](\text{ClO}_4)_2$ were prepared as previously reported.^{13–18}

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$\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)}_2\text{](ClO}_4\text{)}_3$ was synthesized by the strategy developed for other *trans*-solvento complexes,^{15,17–19} namely reaction of a suitable halo reactant with excess $\text{Hg(ClO}_4\text{)}_2$ in DMSO. In the present case, $\text{trans-[Co(en)}_2\text{Cl}_2\text{]ClO}_4$ (or better, $\text{trans-[Co(en)}_2\text{Br}_2\text{]ClO}_4$) was used, and 5 equiv of $\text{Hg(ClO}_4\text{)}_2 \cdot \text{H}_2\text{O}$ (Aldrich). A cobalt concentration of 5 g of reactant in DMSO (50 mL) was employed. The mercuric salt is first dissolved in DMSO (50 mL) in small portions with stirring and cooling, and then added in one lot to the complex. [CAUTION! Heavy metal perchlorates in organic solvents can explode.] After 1 min reaction at 20 °C, the product is precipitated as an oil by pouring into ether (1 L) containing *i*-PrOH (100 mL). After decantation, this oil yields green crystals on addition of solid $\text{LiClO}_4 \cdot 3\text{H}_2\text{O}$ and ethanol and vigorous stirring. The product was filtered, washed with ethanol and ether, and air-dried. Two recrystallizations from saturated solutions in water using a fifth volume of 5 M NaClO_4 as precipitant yielded grass green needles, free of the more soluble *cis* isomer. Anal. Calcd for $\text{CoC}_8\text{H}_{28}\text{N}_4\text{S}_2\text{Cl}_3\text{O}_{14}$: C, 15.2; H, 4.5; N, 8.8; Cl, 16.8. Found: C, 15.2; H, 4.6; N, 8.9; Cl, 16.9%.

A saturated solution of $\text{trans-[Co(en)}_2\text{(N}_3\text{)Cl]ClO}_4$ in D_2O containing Tris (0.05M) at 20 °C (pD ca. 10) was reacted for 10 min., and then quenched by the addition of an equal volume of HClO_4 (72%) admixed (1:1) with ice. The blue azido complex crystallized on cooling for 30 min. The reported procedure¹⁰ (45 min reaction time at pD 10) leads to too much loss through hydrolysis. The product was separated from the hydrolyzed material in solution by filtration, and was washed with *i*-PrOH and ether and air-dried.

The NMR spectrum in $\text{Me}_2\text{SO-}d_6$ indicated substantial deuteration (>90%) of both NH sites, and a fractional preferential enrichment in residual NH for the lower field NH resonance. The observation of a slight (60:40) preference for deuteration at the higher field NH at long reaction times suggests that the relative exchange rates at the two sites must be very close to unity in D_2O for the azido-chloro complex.

$\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)}_2\text{(N}_3\text{)](ClO}_4\text{)}_2$ was selectively deuterated *syn* or *anti* to the azide group by several methods. The *syn/anti* selectivity was not pronounced except in the nearly perdeuterated species where the residual *syn-anti*-NH ratio was about 10; the *syn-NH/anti-NH* ratio changes with time. Perdeuterated $\text{trans-[Co(en-}d_4\text{)}_2\text{(OSMe}_2\text{)}_2\text{(N}_3\text{)](ClO}_4\text{)}_2$ was first synthesized from $\text{trans-[Co(en-}d_4\text{)}_2\text{(N}_3\text{)Cl]ClO}_4$ as described.¹⁰ This material and partly deuterated samples were obtained thereafter by direct deuteration through reaction (ca. 20 °C) of a well-stirred slurry in a 0.05 M triethylamine/triethylamineD⁺ buffer (1:1; DCl in D_2O). The reaction was quenched by filtration into ice cold 5 M HClO_4 after a range of trial-and-error reaction times (up to ca. 10 s) which led to the desired degree of deuteration. In other experiments, partly deuterated species were isolated using 1 M $\text{NaF/D}_2\text{O}$ and 0.05 M $\text{Tris/D}_2\text{O}$ solutions. Similar reactions were carried out using $\text{trans-[Co(en-}d_4\text{)}_2\text{(OSMe}_2\text{)}_2\text{(N}_3\text{)](ClO}_4\text{)}_2$ as reactant in $\text{NaF/H}_2\text{O}$ or $\text{Tris/H}_2\text{O}$, to effect partial deuteration with reverse *syn-/anti*-ND ratios.

H/D ratios for the *syn*- and *anti*-N sites were determined by cutting and weighing chart paper from the printed ¹H NMR spectra recorded at high amplitude ($\text{Me}_2\text{SO-}d_6$). The isotope analyses were confirmed from the ¹³C NMR spectra.²⁰ The $\text{CH}_2\text{-NH}_2$, $\text{CH}_2\text{-NHD}$, and $\text{CH}_2\text{-ND}_2$ signals are each separated by ca. 10 Hz and well resolved at 100 MHz. The en carbons in the $\text{trans-[Co(en)}_2\text{-}$

$\text{(OSMe}_2\text{)}_2\text{(N}_3\text{)]}^{2+}$ complex are equivalent, but the expected triplet for the isotopomers was not easily obtained because of rapid isomerization to the *cis* isomer in $\text{Me}_2\text{SO-}d_6$. Samples of the partly deuterated *trans* complex were therefore allowed to isomerize completely to the *cis* form and the spectra of the stable *cis* product analyzed: each of the four inequivalent carbons exhibited the same $\text{CH}_2\text{-NH}_2/\text{CH}_2\text{-NHD}/\text{CH}_2\text{-ND}_2$ distribution.

Kinetics. The kinetics of acid hydrolysis (k_s) of $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)}_2\text{(N}_3\text{)]}^{2+}$ and of several partially deuterated samples of different composition was followed spectrophotometrically as described previously.¹³ Absorbance–time traces at the *cis/trans*- $\text{[Co(en)}_2\text{(OH}_2\text{)(N}_3\text{)]}^{2+}$ isosbestic (538 nm) fitted to a single exponential provided the more accurate rate data because this strategy reduced the analysis for a consecutive reaction to a simple $\text{A} \rightarrow \text{B}$ process. Runs were conducted simultaneously in a 7-cell thermostat housing in the HP8453 diode array spectrophotometer, as described for the $\text{[Co(NH}_3\text{)}_5\text{Cl]}^{2+}$ system,⁹ to minimize temperature fluctuations from run to run.

The rate of isomerization (k_i) in DMSO for the same samples of N-deuterated $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)}_2\text{(N}_3\text{)]}^{2+}$ was followed as previously described.²¹ These data are more accurate than the hydrolysis rate data because of the much larger absorbance changes.

The solvent interchange rates (k_{si}) for reaction of these $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)}_2\text{(N}_3\text{)]}^{2+}$ samples in MeCN were also determined spectrophotometrically (510 and 585 nm). The process leads to a mixture of *trans*- and *cis*- $\text{[Co(en)}_2\text{(NCMe)(N}_3\text{)]}^{2+}$; subsequent *trans/cis* isomerization is very much slower and provided no perturbation on an analysis according to a simple $\text{A} \rightarrow \text{B}$ reaction scheme. Although the isosbestic points were sharp and constant from run to run, the rates of reaction in MeCN were initially hard to reproduce. There was a catalysis of unknown origin which, however, we could eliminate through the use of lower [Co] and low levels of edta (0.001 M) to sequester the likely Co(II) culprit.

Results and Discussion

NH Proton Assignments. The original study¹² argued that the NH chemical shifts should correlate with those for the parent $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)}_2\text{]}^{3+}$ and $\text{trans-[Co(en)}_2\text{(N}_3\text{)}_2\text{]}^+$ complexes. The ¹H NMR spectra are shown schematically in Scheme 1.

The observed shifts are far from their axial azide or axial Me_2SO environment values found for the parent bis complexes, and this method of assignment is unreliable. Balt and Gamelkoorn¹² did not have the *trans*-bis(DMSO) complex to assist with this observation. The chemical shift differences for the *trans*-azido-DMSO ion in $\text{ND}_3(\text{l})$ at low temperature are greater, and the absolute shift for one of the two NH signals is quite close to that for the parent *trans*-diazido complex; this was fortuitously misleading.

Using an unambiguous method (2D NOESY ¹H NMR), the observed NH signals for $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)Cl]}^{2+}$ in $\text{Me}_2\text{SO-}d_6$ are found to be reversed (Scheme 1), as they are also for the related $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)Cl]}^{2+}$ ion.²² A reliable NOESY spectrum for the $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)}_2\text{(N}_3\text{)](ClO}_4\text{)}_2$ ion in $\text{Me}_2\text{SO-}d_6$ could not be obtained because of the overlap in the CH_2 and CH_3 signals in this solvent, and also because of its rapid *trans* to *cis* isomerization at

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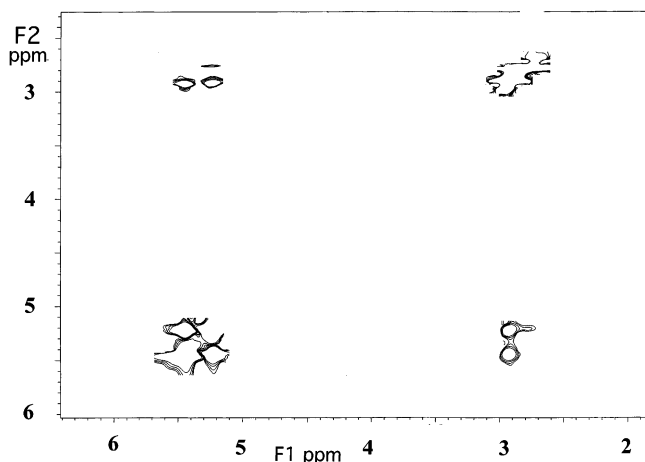
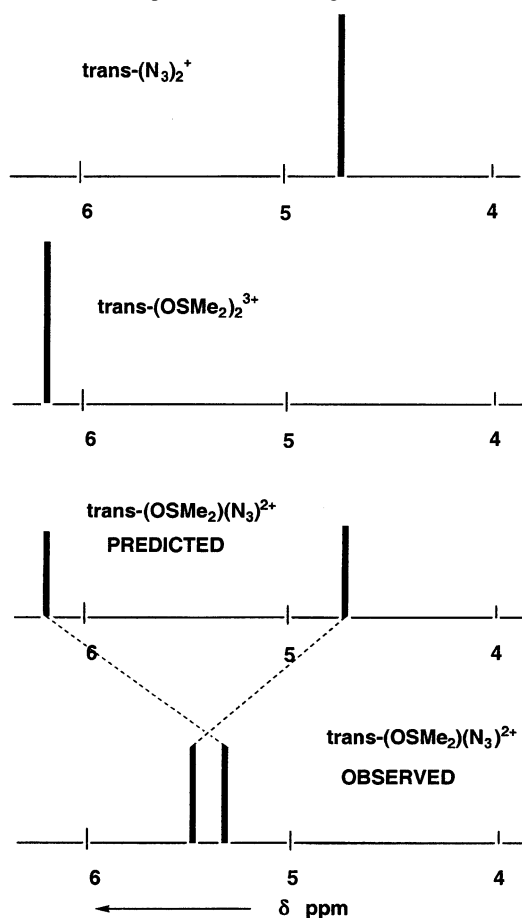


Figure 5. The NOESY spectrum for $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)(N}_3\text{)]}^{2+}$ in dilute DCl at 5 °C; the peaks due to the hydrolysis product have been erased.

Scheme 1 ^1H NMR Spectra in the NH Region ($\text{Me}_2\text{SO-}d_6$)



the lowest temperature possible (ca. 17 °C). However, in $\text{D}_2\text{O/DCl}$ at 5 °C the methyl and methylene signals are distinct, and a weak but real correlation between the higher field NH signal and the methyl group protons of the bound Me_2SO ligand is observed (Figure 5). This establishes that this NH proton is syn to the DMSO ligand. Control experiments established that, for the selectively (and unequally) deuterated complex, the *syn*- and *anti*-NH signals appear at the same relative chemical shifts in both D_2O and $\text{Me}_2\text{SO-}d_6$, and thus, the higher field signal in $\text{Me}_2\text{SO-}d_6$ is

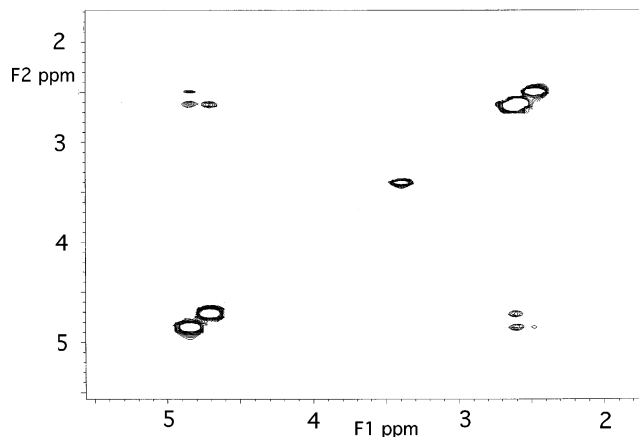


Figure 6. NOESY spectrum for $\text{trans-[Co(en)}_2\text{(NH}_3\text{)(N}_3\text{)]}^{2+}$ in $\text{Me}_2\text{SO-}d_6$.

also the *syn*-NH. Our assignments made previously²¹ based on sound but less direct methods are confirmed.

Addition of NH_4Cl to a $\text{Me}_2\text{SO-}d_6$ solution of this complex results in the selective and substantial downfield shift of this *syn*-NH resonance, remote from anionic N_3^- . The corresponding CH protons and the methyl resonance also move downfield, with preferential ion pairing of Cl^- adjacent to uncharged bound DMSO. This method of assigning *syn* and *anti* protons has been validated using 2D NMR techniques (for $\text{trans-[Co(en)}_2\text{(py)Cl]}^{2+}$, for example^{23,24}

Assignments for the $\text{trans-[Co(en)}_2\text{(NH}_3\text{)(N}_3\text{)]}^{2+}$ species were made using the 2D DQCOSY (figure available as Supporting Information) and NOESY (Figure 6) spectra. The NH signals ($\text{Me}_2\text{SO-}d_6$) for the parent diamine and bis(azido) complexes are at δ 5.10 and δ 4.73 ppm, respectively, compared to δ 4.83 (*syn* to NH_3) and δ 4.75 (*syn* to N_3^-) in $\text{trans-[Co(en)}_2\text{(NH}_3\text{)(N}_3\text{)]}^{2+}$. The corresponding Co– NH_3 signals are at δ 3.19 and δ 2.48 ppm, cementing the point made earlier, namely that changing one axial ligand can significantly affect the chemical shifts for the protons on the other side of the Co(en)_2 “plane”. The lower field NH shows a clear correlation with the axial NH_3 and is therefore the *syn* site (*anti* to azide). The downfield shift of this *syn* signal (the *anti* NH is unmoved) in the presence of NH_4Cl is also consistent with this assignment, since selective ion-pairing occurs adjacent to neutral NH_3 and remote from anionic N_3^- ; the NH_3 signal is also downfield shifted.

Synthesis and Isotopic Analysis. The new $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)}_2\text{](ClO}_4\text{)}_3$ complex has a grass green color much like $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)Cl]}^{2+}$ and $\text{trans-[Co(en)}_2\text{Cl}_2\text{]}^+$, which is consistent with DMSO having a ligand field very similar to Cl^- . The ^1H and ^{13}C NMR data are consistent with the *trans* structure and O-bonded DMSO. The complex isomerizes quantitatively (and rapidly) to the known¹⁶ *cis* isomer in DMSO, as confirmed by the ^1H and ^{13}C spectra.

Five samples of $\text{trans-[Co(en)}_2\text{(OSMe}_2\text{)(N}_3\text{)]}^{2+}$ of varying NH/ND composition were synthesized (Table 1). The *syn*-NH/*anti*-NH ratios were determined by integration of the relevant signals in the ^1H NMR, while individual NH proton

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Table 1. Isotopic Composition and Kinetic Data for Partially Deuterated Samples of *trans*-[Co(en)₂(OSMe₂)(N₃)²⁺ Reacted in Aqueous Acid, Me₂SO, and MeCN (25 °C)^a

sample	% syn-ND	% anti-ND	% total ND	<i>anti</i> -NH/ <i>syn</i> -NH	10 ⁴ <i>k</i> _s (0.1 M HClO ₄)	10 ⁴ <i>k</i> _i (Me ₂ SO), s ⁻¹	10 ³ <i>k</i> _{si} (MeCN), s ⁻¹
1	0.0	0.0	0.0		5.83	7.55	5.20
2	23.3	51.8	37.5	1.60		6.71	
3	18.3	66.8	42.5	2.48	5.64	6.64	4.90
4	68.8	39.8	54.0	0.52	5.54	6.38	
5	100.0	100.0	100.0		4.90	5.55	4.90

^a *k*_s, *k*_i, and *k*_{si} are the specific rates of acid hydrolysis, isomerization, and solvent interchange, respectively.

counts employed the integrated -CH₂- resonances as the internal reference. The ¹³C NMR spectra confirmed the latter. The ¹³C spectra for three samples with different degrees of N-deuteration are shown in Figure 7.

Relative Proton Exchange Rates. The data show that the higher field NH (*syn*) protons are faster to exchange in D₂O, but the *anti* site has already started to deuterate well before all 4 *syn* NH protons have become ND. Partial but incomplete deuteration at each of two sites is only possible if the exchange rates are not greatly different. This is apparent from the data in Table 1. It is also clear from the ¹³C NMR spectra (after complete isomerization to the stable *cis* ion in Me₂SO-*d*₆; Figure 7) which show samples each with comparable amounts of -CH₂-NH₂, -CH₂-NHD, and -CH₂-ND₂, achieved by quenching the sequential exchange processes at the appropriate times. Balt and Gamelkoorn¹⁰ claim that the NH *syn* to azide (now known to be the *anti*-NH) exchanges much more rapidly than the *anti*-NH, such that they could apparently obtain complete *syn* or *anti* site deuteration before the other site had begun to exchange. Although their solvent was NH₃(l) or ND₃(l), it is difficult to understand a solvent effect on the relative exchange rates of this magnitude, but it remains a moot point.

Bergens and Bosnich²⁵ have exposed the observed selectivity problem for consecutive exchange processes of this kind. For parallel reaction involving two different sites, the *syn*-ND/*anti*-ND ratio is initially constant (*k*₁/*k*₂). However, the second phase of reaction (Scheme 2) enhances this ratio as time progresses, and quite radically if *k*₁ and *k*₂ are moderately different (a factor of 5, for example). Indeed, one can obtain product with over 99% site selectivity at a modest expense in chemical yield (ca. 40%).

Such is also the case for the stepwise deuteration of *trans*-[Co(en)₂(OSMe₂)(N₃)²⁺. However, here the intrinsic *syn*/*anti* site selectivity is slight, within a factor of 2 (*k*₁/*k*₂ ≤ 2), and while we have synthesized selectively deuterated samples for which the *residual* *syn*-NH/*anti*-NH (or *syn*-ND/*anti*-ND) ratio is substantial (>10:1), these are unsuitable for the present work since they are either almost fully protic or fully deuterated. We required samples with N-deuteration within the range 25–75% to gauge the relative effect of *syn*- versus *anti*-D substitution on the reaction rate for ligand substitution.

The relative *syn*-/*anti*-NH exchange rates can be achieved in principle with a single measurement of the ¹³C NMR

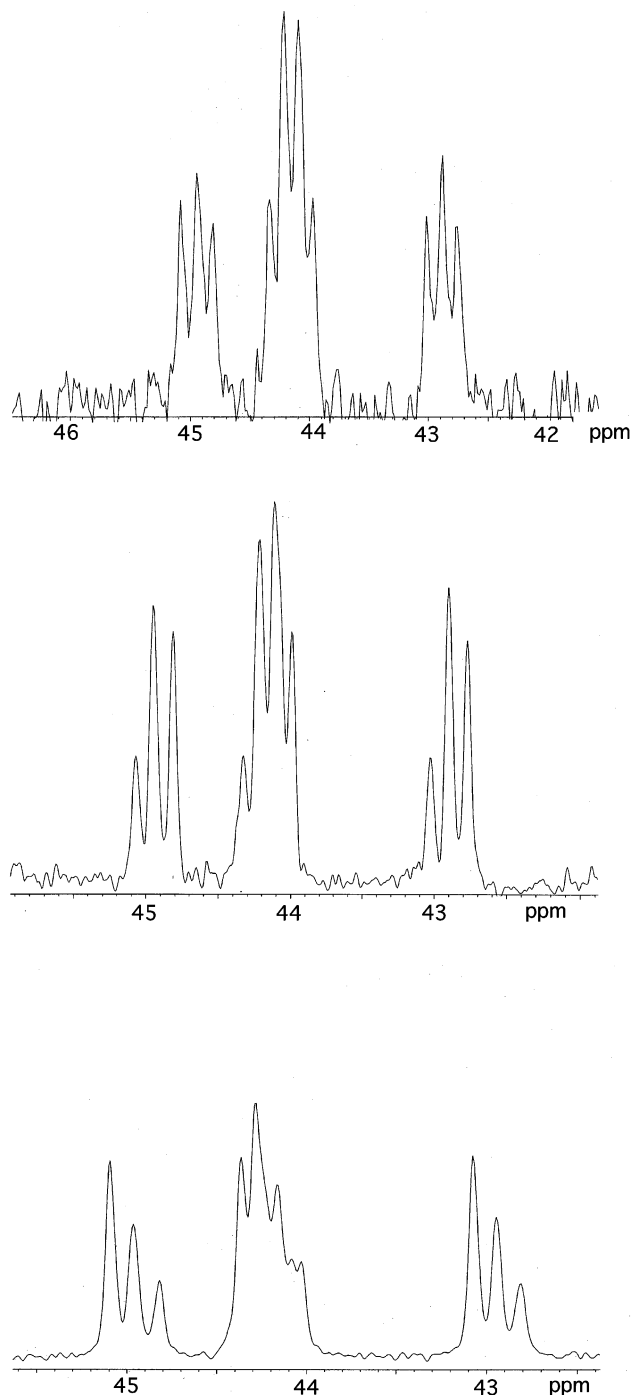
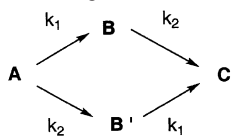


Figure 7. ¹³C NMR spectra for three different partly deuterated samples of *trans*-[Co(en)₂(OSMe₂)(N₃)²⁺ in Me₂SO-*d*₆ made by controlled reaction in D₂O/buffer. Each spectrum comprises four triplets, two of which are overlapped. An upfield shift of ca. 10 Hz is observed for each D substitution at nitrogen (*syn* and *anti* are not distinguished in the ¹³C spectra). The bottom spectrum, for example, indicates the composition -CH₂-NH₂-/-CH₂-NHD/-CH₂-ND₂ - ca. 3:2:1. The comparable amounts of the three isotopomers indicate that the sequential exchange processes are not vastly different in rate.

spectrum for a stage where the signals due to -CH₂-NH₂, -CH₂-NHD, and -CH₂-ND₂ are comparable.

Three cases are presented in Figure 7.²⁶ Peak heights (*h*₁, *h*₂, *h*₃) are proportional to concentration, which a control experiment demonstrated (¹³C NMR spectrum of a 1:1 mixture of fully protic and fully deuterated *cis*-[Co(en)₂-

(25) Bergens, S.; Bosnich, B. *Comments Inorg. Chem.* **1987**, 6, 91.

Scheme 2. Sequential Exchange Processes^a

^a $A = -C^A H^B H^-$, $B = -C^A D^B H^-$, $B' = -C^A H^B D^-$, $C = -C^A D^B D^-$.

(OSMe₂)(N₃)]²⁺). The equations describing the relative peak heights (h_n) for this system (Scheme 2), normalized to sum to 1.0, are

$$A = h_1 = \exp(-(k_1 + k_2)t) \quad (1)$$

$$B + B' = h_2 = \exp(-k_2t) + \exp(-k_1t) - 2 \exp(-(k_1 + k_2)t) \quad (2)$$

Thus, for a hypothetical case where $h_1 = 0.43$, $h_2 = 0.53$ (and $h_3 = 0.04$), elimination of k_2t from eqs 1 and 2 led to the following expression:

$$(0.43 \exp(k_1t) + \exp(-k_1t))/1.39 = 1 \quad (3)$$

This is readily solved numerically to yield $k_1t = 0.078$ or 0.766 . Substitution into the expression for h_1 (eq 1) gives $k_2t = 0.766$ or 0.078 , and thus $k_1/k_2 = 9.82$ or 0.102 . The double solutions for k_1/k_2 , which are reciprocals, arise because the measurement of $B + B'$ cannot distinguish a fast–slow or slow–fast primary reaction sequence. It yields, however, a number for the relative site lability.²⁷ Note that the quench time is not required for this calculation. Also, which site exchanges more rapidly (syn to Me₂SO) is already known from the ¹H NMR measurements.

The real data (Figure 7) reveal a problem, however. The function on the left-hand side of eq 3 is quasiparabolic, which minimizes between the two solutions for k_1t where the function cuts the $y = 1$ axis either side of the minimum. However, none of the functions generated from h_1 , h_2 , and h_3 values for each of the three data sets shown in Figure 7 cut the $y = 1$ axis at all; each lies totally above it. While this might suggest that the second stages of the exchange processes (Scheme 2) are each faster than predicted (the peak due to $-CH_2-ND_2-$ is more intense than is possible under Scheme 2), it is very likely this arises because the complexes were not deuterated under homogeneous conditions. This fact in no way invalidates this new method for extracting relative rate data.

Acid Hydrolysis of Regioselectively Deuterated *trans*-[Co(en)₂N₃(OSMe₂)(N₃)]²⁺. Balt and Gamelkoorn¹⁰ assumed that deuteration on the side of the leaving group (Me₂SO) would lead to a rate reduction in hydrolysis, while deuteration on the azide side would have no effect (Figure 8).²⁸

Their results showed that the complex purported to be deuterated on the azide side hydrolyzed at precisely the same rate as the corresponding protic complex, whereas the species

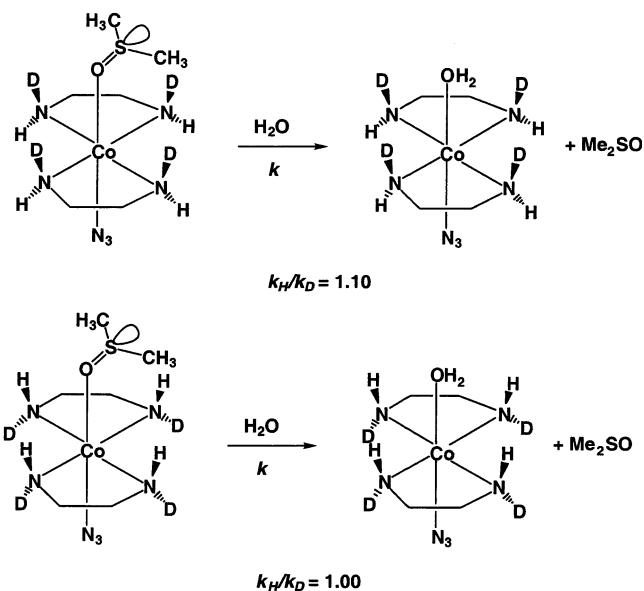


Figure 8. The assumed outcome for the acid hydrolysis of the *syn*- and *anti*-(ND)₄-*trans*-[Co(en)₂(OSMe₂)(N₃)]²⁺ complexes.

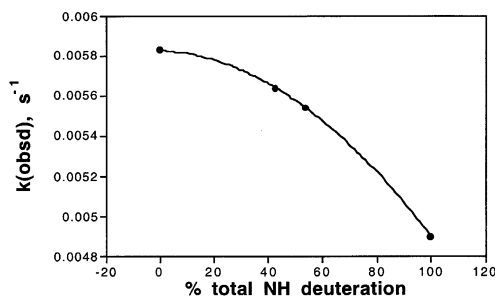


Figure 9. Plot of $k(\text{obsd})$ versus % NH deuteration for the acid hydrolysis of *trans*-[Co(en)₂(OSMe₂)(N₃)]²⁺ in 0.1 M HClO₄ at 25 °C. Note: The 42.5% D point has an anti/syn NH ratio of 2.5:1, whereas the 54% D point has a reverse anti/syn ratio, 0.52:1.

with ND groups only on the leaving group side hydrolyzed at precisely the same rate as the perdeuterated complex, 9% slower.

We have repeated the kinetics of acid hydrolysis of the *trans*-[Co(en)₂(OSMe₂)(N₃)]²⁺ ion in 0.10 M aqueous perchloric acid (25 °C), for undeuterated, a range of selectively deuterated, and fully deuterated species. The ND groups were shown to be unexchanged throughout the acid hydrolysis process, and the 92% *trans*/8% *cis* product stereochemistry¹⁷ was confirmed. Further, the relative *syn*- and *anti*-ND positions were retained for the *trans*-[Co(en)₂(OD₂)(N₃)]²⁺ aquation product.

The results are plotted (Figure 9) to show the effects of cumulative NH deuteration.

The rate reduction with increased deuteration is uniform but not linear, and it is clear that deuteration at either the *syn*- or *anti*-NH sites is effective. Because the overall effect

(26) The sequential exchange of four equivalent protons at rates $4k$, $3k$, $2k$, and k is mathematically equivalent to the exchange of one proton at rate k .

(27) This same strategy can be used to evaluate relative rate constants for consecutive or parallel reaction schemes such as A to B to C, or B to C and B' to C in parallel.

(28) This idea seemed to follow from an early suggestion for the rate reduction for the deuterated complex that arises from a weaker H(D)-bond between the bound amine and incoming water, adjacent to the leaving group. This notion, however, had already been discredited, in that the β -picoline complexes show the usual isotope effect, yet they cannot involve amine–solvent H-bonding effects since there is no N–H group,

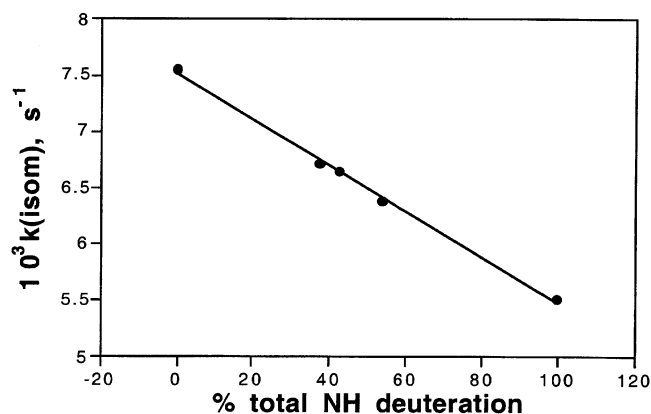


Figure 10. Plot of k_i versus % NH deuteration for the isomerization of $\text{trans-[Co(en)}_2(\text{OSMe}_2)(\text{N}_3)]^{2+}$ in Me_2SO at 25°C . The anti/syn NH ratios for each data point are given in Table 1.

is small ($k_{\text{H}}/k_{\text{D}} = 1.19$), the experimental error in k obscures any detailed assessment. Balt and Gamelkoorn found almost half the skie we observe ($k_{\text{H}}/k_{\text{D}} = 1.10$),¹⁰ and their data showed the effect only for deuteration on what they claimed was the syn site (but now known to be anti).

Solvent Effect. The skie has been studied for the solvents DMSO and acetonitrile as well as aqueous solution, using the same series of selectively deuterated starting materials. The observed reactions are isomerization (k_i) and solvent interchange (k_{si}), respectively.

The kinetic data for DMSO as solvent (Table 1) are plotted in Figure 10.

The skie here ($k_{\text{H}}/k_{\text{D}} = 1.37$) is much larger than for water, almost 2-fold. The rate versus %ND correlation is linear, despite the quite marked variations in *syn*- and *anti*-NH distributions for the reactants used. Thus, there appears to be no regioselectivity in *syn*- versus *anti*-NH deuteration as regards the skie. These data corroborate the results for water as solvent.

We have also determined the rates for the same series of complexes in MeCN. Here catalyzed substitution intervenes, and the accuracy of the rate data became a problem, but data obtained at low [Co] and in the presence of edta (both factors essentially eliminate the source of the catalysis) suggest a very modest rate reduction on amine deuteration ($k_{\text{H}}/k_{\text{D}} = 1.06$). With only a 6% rate variation from fully protic to fully deuterated species (Table 1), it is impossible to reliably assess *syn* versus *anti* regiospecific effects.

Rearrangement of $\text{trans-[Co(en)}_2(\text{OSMe}_2)(\text{N}_3)]^{2+}$ in Liquid Ammonia. Balt and Gamelkoorn followed the kinetics and stereochemistry of the ammoniolysis reaction by ^1H NMR spectroscopy in $\text{ND}_3(\text{l})$.¹⁰ They presented data showing that the kinetics were consistent with “normal” base catalyzed substitution (deprotonation and reprotonation faster than loss of Me_2SO , rather than rate limiting deprotonation). Also, they observed that the four residual NH protons in the half-deuterated reactant were not immediately exchanged during the ammoniolysis, and became redistributed in the $\text{trans-[Co(en)}_2(\text{NH}_3)(\text{N}_3)]^{2+}$ product, 3NH on one side of the Co(en)_2 “plane” and one NH on the other. Further, they argued that the base catalyzed substitution must have

occurred via deprotonation at one of four equivalent ND sites, since no further deuteration occurred. All these arguments are sound, but the reversed *syn*-/*anti*-NH assignment for the reactant Me_2SO complex now should be interpreted to mean that the ammoniolysis of this complex leads to three retained and one inverted NH, rather than the converse. Inversion at the deprotonated *anti*-NH center is clear, and such an event is analogous to the base catalyzed hydrolysis of complexes²⁹ such as *syn*- and *anti-mer*- $[\text{Co}(\text{dien})(\text{dapo})\text{Cl}]^{2+}$ in aqueous systems. Balt and Gamelkoorn’s case for a 180° rotation of one en chelate during the act of base catalyzed substitution in $\text{NH}_3(\text{l})$ therefore can no longer be sustained.

It is possible that these authors also reversed the assignments for the ammoniolysis product, $\text{trans-[Co(en)}_2(\text{NH}_3)(\text{N}_3)]^{2+}$, a double error which would ironically make good the case for the en rotation mechanism. Their ^1H NMR spectrum in $\text{NH}_3(\text{l})$ (higher field NH is *syn*) is the reverse of ours for Me_2SO as solvent (lower field NH is *syn*), but they based the NH proton assignments on the selective downfield shift of the NH protons *syn* to the bound NH_3 on addition of Cl^- , and, as we have shown, this method of assignment is sound. The swapover in the *syn*- and *anti*-NH signals for $\text{Me}_2\text{SO}-d_6$ and $\text{ND}_3(\text{l})$ as solvents is not unexpected, given that the chemical shift differences are intrinsically small.

Summary and Conclusions

The *syn*- and *anti*-NH protons have been unambiguously assigned for the $\text{trans-[Co(en)}_2\text{Y}(\text{N}_3)]^{2+}$ complexes ($\text{Y} = \text{OSMe}_2$ and NH_3) using 2D NMR techniques and selective ion-pairing methods. This work reverses the previous assignment for the Me_2SO complex. This important result shows now that base catalyzed ammoniolysis of $\text{trans-[Co(en)}_2(\text{OSMe}_2)(\text{N}_3)]^{2+}$ is “normal”, and that it occurs via deprotonation at a *syn*-NH (to Me_2SO) which becomes inverted (*anti*) during the process.

The previously proposed regioselective *syn*- versus *anti*-ND effects have been discredited. D-substitution at NH_2 sites *cis* to the leaving group (Figure 3) leads to a systematic rate decrease, irrespective of their *syn* or *anti* configuration, and in both water and Me_2SO as solvents.

Solvent is clearly important in determining the magnitude of the skie. Water is both a H-bond donor and acceptor, while Me_2SO is more polar than water but aprotic and lacking in a H-donor capacity. It is a stronger H-bond acceptor nonetheless, and nonspecific solvation factors may be related to this since the skie is greater in this solvent. However, the limited data so far and the magnitude of the effect make it difficult to pinpoint the source. It may be even more fundamental, as previously suggested,⁹ if the N–H (N–D) vibrations are weakly coupled to Co-X vibrations ($\text{X} =$ leaving group) to different extents, and the effect resides in the quite different (H vs D) vibrational zero-point energies. Such a view is consistent with the idea that ligand substitution is largely the result of an aberrant Co-X vibration for a dissociative reaction.

(29) Comba, P.; Jackson, W. G.; Marty, W.; Zipper, L. *Helv. Chim. Acta* **1992**, *75*, 1147.

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Supporting Information Available: Additional figure. This material is available free of charge via the Internet at <http://pubs.acs.org>.
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