Racemization and Proton Exchange of the *trans,trans*-Dinitrobis(N-methylethylenediamine)cobalt(III) Ion in Nonaqueous Solutions

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Abstract: The relative rates of proton exchange and racemization for the *trans,trans*-$[Co^{III}(NO_2)_2Meen_2]^+$ ion have been investigated in anhydrous methanol, ethanol, 2-propanol, *t*-butyl alcohol, and a dimethyl sulfoxide–*t*-butyl alcohol mixture. The retention ratio changed by $\sim 10^5$ over this range of solvents, and the results are rationalized to support a common intermediate for racemization and exchange. The large change in the retention ratio is attributed essentially to the change in reprotonation rate in the different solvents.

Kinetic studies of racemization and proton exchange at coordinated asymmetric secondary nitrogen centers in aqueous solution[1-5] have shown that the rate of proton exchange (k_D) exceeds the rate of racemization (k_R) by a large factor, $>10^3$. To account for this property the mechanism in Figure 1 has been proposed. An alternative mechanism was also considered (Figure 2). The first mechanism requires that both proton exchange and racemization proceed through a common deprotonated intermediate. The second proposes that proton exchange occurs principally *via* a cyclic *activated complex* and that racemization occurs when the proton is removed as in mechanism I.

Although the interpretation of the isotope effects for racemization in aqueous solution favors mechanism I,[2] it occurred to us that the cyclic mechanism II for exchange was prohibited if the basic reagent did not contain an abstractable proton. For this reason, the relative rates of proton exchange and racemization of the *trans,trans*-dinitrobis(N-methylethylenediamine)cobalt(III) ion, $[Co(Meen)_2(NO_2)_2]^+$, were investigated in anhydrous methanol, ethanol, 2-propanol, *t*-butyl alcohol, and a dimethyl sulfoxide–*t*-butyl alcohol mixture.

Experimental Section

Instruments. Pmr measurements were made on a Perkin-Elmer R10 spectrometer, which was coupled with a NS544 Northern Scientific computer for the time-averaging experiments. Rotations were measured in either a 1-dm or a 1-cm cell using a Perkin-Elmer P22 polarimeter. Visible spectra were obtained with a Cary 14 spectrophotometer.

Solvents. Methanol and ethanol (Merck AR), 2-propanol (Analar), *t*-butyl alcohol (Univar, AR), and DMSO-d_6 (Fluka) were all dried with type 4A molecular sieve (Union Carbide). The absence of water in the DMSO was verified by using the nmr spectrometer coupled to a time-averaging computer (23 scans). The HOD signal was not detected.

Solutions for Kinetics. Triethylenediamine (1,4-Diazabicyclo-[2.2.2]octane, Aldrich) was dried under vacuum. Solutions of this base in 40% DMSO-d_6–60% *t*-BuOH were made in a drybox by first dissolving the base in DMSO-d_6 and then adding *t*-BuOH. The complex perchlorate, dried and weighed, was dissolved in DMSO-d_6 and the reaction started by adding an equal volume of base solution, all in the drybox. The polarimeter tube (1 cm) was then filled and the rotational change measured at 546 mμ. For the pmr measurements, the complex solution was inserted in the bottom of the nmr tube which was kept horizontal so that the base solution could be added without mixing. After equilibration at the magnet temperature the solutions were mixed and the tube inserted into the probe.

For pmr studies in methanol, solutions (0.026 *M* in complex) were made by adding 0.5 ml of acetic acid solution (0.837 *M* Analar) or solutions diluted from this stock solution with freshly dried methanol to complex bromide (0.005 g) in an nmr tube. For racemization studies, stock solutions of anhydrous sodium acetate (Analar) and LiCl (BDH) were added to $(+)_{500}$-*trans,trans*-$[Co(Meen)_2(NO_2)_2]Br$, and the change in rotation was followed with time in a 1-dm tube at 500 mμ. One solution was made to contain 2.2% by weight water to check the effect of water on the rate.

A concentrated solution of $(-)_{500}$-*trans,trans*-$[Co(Meen\text{-}d_3)_2(NO_2)_2](2\text{-ethylhexyl})_2PO_4$ was made by dissolving it in *t*-butyl alcohol at 34.3° and placing a portion in a 1-cm polarimeter tube. The remainder was kept at 34.3° in a stoppered vessel. After 0.5 and 1.25 hr, aliquots were removed, and glacial acetic acid, lithium perchlorate, and anhydrous ether were added in that order to recover the complex perchlorate. The pmr spectrum of the perchlorate salt in DMSO-d_6 was then recorded. A similar procedure was employed for studies in ethanol and 2-propanol.

Preparation of Complexes. The compounds, $(+)_{500}$-*trans,trans*-$[Co(Meen)_2(NO_2)_2]$-(+)-bromocamphorsulfonate ((+)-BCS), $(+)_{500}$-*trans,trans*-$[Co(Meen)_2(NO_2)_2]ClO_4$, and (±)-*trans,trans*-$[Co(Meen)_2(NO_2)_2]Cl\cdot H_2O$ were prepared as previously described.[3]

(±)-*trans,trans*-$[Co(Meen\text{-}d_3)_2(NO_2)_2]Br$ was prepared as previously reported.[3] *Anal.* Calcd for $[CoC_6H_{14}D_6O_4N_6]Br$: C, 18.71; H + D, 6.78; N, 21.83. Found: C, 18.73; H + D, 7.12; N, 22.02.

(±)-*trans,trans*-$[Co(Meen\text{-}d_3)_2(NO_2)_2]ClO_4$. $[Co(Meen)_2(NO_2)_2]Cl$ (7.6 g) was dissolved in 5 ml of 99.5% D_2O and warmed on a steam bath for 5 min, and then D_2O was evaporated under vacuum at ambient temperature. The process was repeated twice more, the third time with D_2O (10 ml). The residue was then dissolved in dilute $HClO_4$ and $NaClO_4$ was added. The anhydrous complex perchlorate crystallized immediately and was washed with methanol and dried under vacuum. *Anal.* Calcd for $[CoC_6H_{14}D_6N_6O_4]ClO_4$: C, 17.81; H + D, 6.45; N, 20.78. Found: C, 17.73; H + D, 6.58; N, 20.66.

$Ba(PO_4(C_8H_{17})_2)_2$. Fresh $Ba(OH)_2\cdot 8H_2O$ (Fluka) (3.2 g) was dissolved in 75 ml of hot water and filtered into a methanol solution (400 ml) containing 7.2 g of di-(2-ethylhexyl)phosphoric acid (K & K Laboratories). Methanol was added to ensure the formation of one phase, and then water was added dropwise to precipitate the white noncrystalline solid. It was recrystallized twice from warm acetone and dried at 80° for 1 week. *Anal.* Calcd for $BaP_2O_8C_{32}H_{68}$: C, 49.26; H, 8.79. Found: C, 49.46; H, 8.84.

$(-)_{500}$-*trans,trans*-$[Co(Meen\text{-}d_3)_2(NO_2)_2](PO_4(C_8H_{17})_2)$. $(-)_{500}$-*trans,trans*-$[Co(Meen)_2(NO_2)_2]I$ was prepared by adding Na I

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(2) D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *ibid.*, 89, 825 (1967).
(3) D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *ibid.*, 89, 3428 (1967).
(4) D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *Inorg. Chem.*, 7, 915 (1968).
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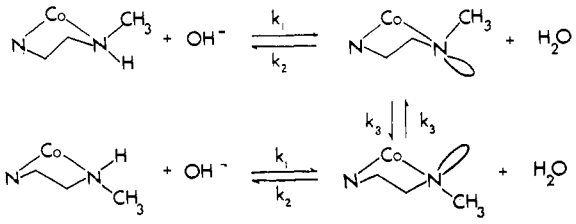


Figure 1. Mechanism I.

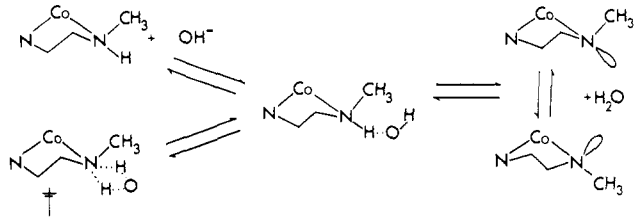


Figure 2. Mechanism II.

to the filtrate from the resolution of $(+)_{500}$-*trans,trans*-[Co(Meen)$_2$(NO$_2$)$_2$]-(+)-BCS[3] instead of LiCl (α_{500} −0.214° for a 0.1% solution of iodide salt in 0.01 *N* $HClO_4$, 1-dm tube). The iodide salt (2.2 g) was shaken with Ag_2SO_4 (0.78 g), filtered, and evaporated to near dryness. An aqueous methanol solution of $Ba(OH)_2 \cdot 8H_2O$ (0.8 g) and di(2-ethylhexyl)phosphoric acid (1.8 g), as above, was added followed by more methanol. The solution was filtered and allowed to stand overnight. It was then decanted from the white precipitate which had formed and was filtered. The methanol was removed under vacuum and the solution extracted with ether to remove excess acid and barium salt. Then the solution was evaporated to dryness and redissolved in D_2O (5 ml), allowed to stand for 1 hr, and evaporated under vacuum. This latter process was repeated twice and the residue was dissolved in acetone (Merck, <0.2% water), filtered, and evaporated to dryness under vacuum. This last procedure was repeated and the hygroscopic powder which remained was stored in a vacuum desiccator.

$(+)_{500}$-*trans,trans*-[Co(Meen)$_2$(NO$_2$)$_2$]Br was prepared by grinding the (+)-BCS diastereoisomer with excess LiBr in a small volume of acidic methanol (acetic acid). *Anal.* Calcd for [$CoC_6H_{20}N_6O_4$]Br: C, 19.10; H, 5.32; N, 22.17. Found: C, 18.72; H, 5.53; N, 22.24.

Results

Preparation of new salts of the racemic and active *trans,trans*-[Co(Meen)$_2$(NO$_2$)$_2$]$^+$ ion was necessary to obtain nonaqueous solutions in the solvents used. The bromide salts were soluble in methanol and the perchlorate salts were soluble in 70% DMSO–30% *t*-butyl alcohol. The common salts Cl^-, Br^-, I^-, ClO_4^-, (+)-BCS^-, and $(C_6H_5)_4B^-$ were insoluble in *t*-butyl alcohol. A general method for getting the complex ion into the organic solvents was therefore developed. The salt $(-)_{500}$-*trans,trans*-[Co(Meen)$_2$(NO$_2$)$_2$]$_2$SO$_4$ was treated with an aqueous methanol solution of barium hydroxide and di(2-ethylhexyl)phosphoric acid; barium sulfate precipitated and the complex dissolved. The di(2-ethylhexyl)phosphate salt of the complex obtained after purification was readily soluble in many organic solvents. The methanol was necessary to dissolve the barium salt of the acid which was otherwise less soluble in water than barium sulfate. It was more convenient to use the methanol solution above than the isolated barium di(2-ethylhexyl)phosphate to effect the conversion.

In neutral methanol the complex exchanged its protons rapidly with the solvent ($t_{1/2}$ < 0.5 min at 25°) but was stable to racemization ($t_{1/2}$ >>1 day). The presence of acetic acid lowered the rate of exchange and this was followed by pmr spectroscopy using the deuterated complex. The singlet due to the methyl group grows into a doublet as the deuterons are exchanged for protons at the N center and this process can be followed (Figure 3), even though the ^{13}C side band of methanol obscures half the doublet signal. Plots of log (peak height$_t$ − peak height$_\infty$) were linear for at least 2 half-lives, and the pseudo-first-order rate constants are given

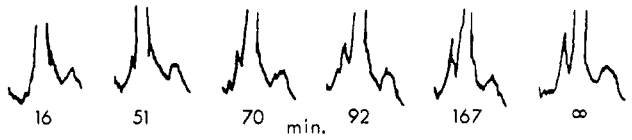


Figure 3. Change in pmr spectrum in methanol (0.042 *M* acetic acid).

in Table I. Clearly they show a first-order dependence on $1/\sqrt{[HOAc]}$. Sodium acetate, however, catalyzes the racemization of the complex ion and plots of log α_{500} against time were linear for at least 3 half-lives. The pseudo-first-order rate constants (Table II)

Table I. Rate Constants for Proton Exchange at 34.3°

Solvent	[Base] or [acid], *M*	k_{obsd}, sec^{-1} × 10^4	$k_{obsd}[H^+]$ × 10^{10}, *M* sec^{-1}
70% DMSO-d_6–30% *t*-butyl alcohol[a]	0.021[c]	38 ± 5	
	0.004[c]	14	
Methanol[b]	0.8370[d]	0.34	9.8[e]
	0.0837[d]	1.0	9.4[e]
	0.0419[d]	1.5	9.6[e]
	0.0251[d]	2.0	10.1[e]

[a] 0.15 *M* in complex. [b] 0.026 *M* in complex. [c] Triethylenediamine. [d] Acetic acid. [e] Calculated using pK_a = 9 for acetic acid in methanol.[7a]

Table II. Rate Constants for Racemization in Methanol at 34.3°

[NaOAc], *M* × 10^2	k_{obsd}, sec^{-1} × 10^3	[OCH_3^-], × 10^5	k_R, M^{-1} sec^{-1} [d]
2.44[a]	1.56	4.4	35
2.44[a]	1.60	4.4	36
2.44[a,b]	1.48	4.4	34
0.483[a]	0.70	1.9	36
0.125[a]	0.367	1.0	37
0.483[c]	1.01	1.9	52

[a] μ = 0.025 *M*. [b] 2.2% H_2O. [c] μ = 0.005 *M*. [d] $k_R = k_{obsd}/[OCH_3^-]$, [Co] = 10^{-3} *M*.

show a first-order dependence on $\sqrt{[OAc^-]}$, and it follows that both racemization and proton exchange obey a rate law of the form

$$R = k[\text{complex}][CH_3O^-]$$

The accuracy of the derived rate constants listed in Tables I and II depends largely on our knowledge of the autoprotolysis constants of the solvents, of the pK_a of acetic acid in methanol, and of the temperature dependence of these constants. The pK for acetic acid at 25° has been taken as 9.0[6] and, since ΔH does not appear to

(6) I. M. Kolthoff and L. S. Guss, *J. Am. Chem. Soc.*, **61**, 330 (1939).

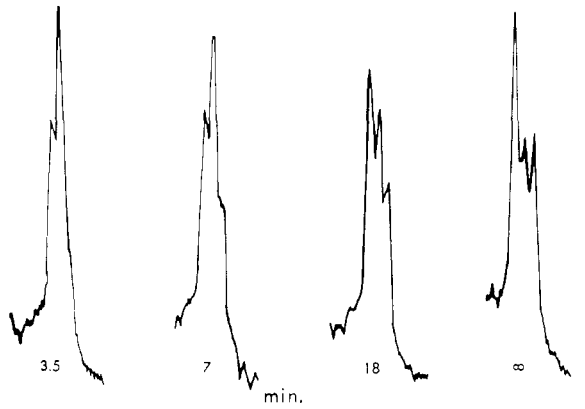


Figure 4. Change in pmr spectrum in 70% DMSO-d_6–30% t-BuOH (0.004 M triethylenediamine).

have been measured, we have assumed that it is zero as for aqueous solutions.[7a] For some carboxylic acids, ΔH for ionization in methanol is close to zero.[7b] The measured autoprotolysis constants for methanol[8] substantially agree, and the value used here is $pK_s = 16.7$ at 25°. We have taken the value for ethanol as $K_s = 1.32 \times 10^{-19}$,[9] since this is the most recent value and was measured by a similar technique to that used for methanol. The same authors also studied 2-propanol, and Table III lists the best K_s values available along with estimates of K_s at 34.3°. Using these data for methanol, a retention ratio may be calculated (Table IV).

Table III. Estimation of Autoprotolysis Constants at 34.3°

Solvent	20°	25°	34.3°
Methanol		2.1×10^{-17} [a]	7.8×10^{-17} [d]
Ethanol	7.1×10^{-20} [b]	1.3×10^{-19} [b]	4.9×10^{-19} [c]
2-Propanol	8.9×10^{-22} [b]	1.6×10^{-21} [b]	5.8×10^{-21} [c]
t-Butyl alcohol			6.0×10^{-22} [e]

[a] Dondon.[8] [b] Teze and Schaal.[9] [c] Estimated from the data at 20 and 25°. [d] Estimated using T dependence for ethanol. [e] Estimated with reference to the McKewen acidity scale: W. K. McKewen, *J. Am. Chem. Soc.*, **58**, 1124 (1936).

Table IV. Rate Constants for H Exchange and Racemization in Neutral Alcohols at 34.3°

Solvent	Exchange: k_{obsd}[b] $\times 10^3$, sec^{-1}	Exchange: k_D, M^{-1} sec^{-1}, $\times 10^{-7}$	Racemization: k_R,[d] M^{-1} sec^{-1}	Retention ratio
Methanol		1.3[e]	36	3.5×10^5
Ethanol	8 ± 2[c]	2.5[a]	0.5×10^4 [a]	5×10^3
2-Propanol	2 ± 0.4	4.1	2.1×10^6	20
t-Butyl alcohol	0.4 ± 0.08	1.5	1.3×10^6	12

[a] Estimated by assuming $E_{a,D} = E_{a,R} \sim 30$ kcal/mole, as for related systems.[1-3] [b] Complex ~0.01 M. [c] 20.0°. [d] Calculated from Table V. [e] Calculated using data in Tables I and III.

In other alcohols (ethanol, 2-propanol, and t-butyl alcohol), the pmr signals of the solvent obscured those of the complex. Aliquots of the reaction solution were quenched by adding acid, the complex was recovered, and the pmr spectrum in DMSO-d_6 was recorded. The variation in the methyl signal with per cent reaction is known from our previous studies of this complex,[3] and a comparison of signal shapes allowed an estimate of half-life, and thus of k_{obsd} (±20%), to be made (Table IV).

The rotational change in the same alcohol solutions was followed polarimetrically. Plots of log α against time were linear for 2-propanol and t-butyl alcohol ($t_{1/2} < 10$ hr) (Table V). However, the complex racemized much more slowly in ethanol, and decomposition interfered with the rate measurement. Initial rate plots were linear for 30% of the total reaction, and the rate constants so obtained were used for comparison with the H exchange rate constants. The values of the retention ratio in these alcohols are given in Table IV, where the retention ratio is defined as the ratio of the second-order rate constant for proton exchange, k_D, to that for racemization, k_R. From our analysis, the proton exchange rate does not vary greatly with the alcohol, but the racemization rate varies enormously (Figure 5). The derived rate constants depend strongly on the K_s values. The latter may not be accurate but their relative values should be reasonable since they have been measured by the same or similar methods. Very small traces of impurity may have a significant effect on [OR$^-$] in the unbuffered solutions used in this study and result in some uncertainty in the derived rate constants.

Table V. Rate Constants for Racemization

Solvent	[Complex], M	k_{obsd}, sec^{-1} $\times 10^5$
Ethanol[a]	0.015	0.16
	0.015	0.18
2-Propanol[b]	0.016	10
	0.009	13
t-Butyl alcohol[b]	0.011	3.3
	0.007	3.5
70% DMSO–30% t-butyl alcohol[b]	0.025[c]	136
	0.075[c]	230
	0.025[d]	55
	0.050[d]	80

[a] 20°. [b] 34.3°. [c] 0.021 M triethylenediamine. [d] 0.004 M triethylenediamine.

In 70% DMSO-d_6–30% t-BuOH, the complex perchlorate does not exchange its N protons readily, and the tertiary base, triethylenediamine, was added to catalyze the exchange. The rate of exchange was obtained by following the disappearance of the methyl singlet for the deuterated complex. The exchange was not complete since there was not a large enough proton store in the solvent, and after several half-lives, the spectrum in the methyl region contains three peaks: (1) the ^{13}C-t-butyl alcohol plus the downfield half of the methyl doublet, (2) the methyl singlet remaining after equilibration, (3) the upfield half of the methyl doublet (Figure 4). A plot of log (peak height$_t$ − peak height$_\infty$) for peak 2 against time was linear over 3 half-lives for the 0.004 M base solution and reasonably linear for the more rapid 0.021 M base solution (Table I). Plots of log α_{546} against time were linear for at least 2 half-lives (Table II). Although the rate of racemization and proton exchange increased with increasing base molarity for a given com-

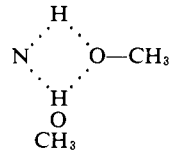
(7) (a) H. S. Harned and B. B. Owen, "Physical Chemistry of Electrolytic Solutions," Reinhold Publishing Corp., New York, N. Y., 1964, p 667; (b) C. D. Ritchie and G. H. Megerle, *J. Am. Chem. Soc.*, **89**, 1452 (1967).
(8) M. Dondon, *J. Chim. Phys.*, **48**, 34 (1951), and references therein.
(9) A. Teze and R. Schaal, *Compt. Rend.*, **252**, 114 (1961).

plex concentration, the rate less than tripled for a five-fold increase in base, suggesting a rate dependence $\propto \sqrt{[\text{base}]}$. This increase in rate is also consistent with a first-order dependence on butoxide ion for both reactions (Table II), similar to the methanol solutions.

For the pure alcohols, the rates of racemization decreased with increasing ionic strength, but the dependence was not great. For the mixed solvent system, the racemization rate increased with complex concentration up to the limit of solubility of $(+)_{500}$-*trans,trans*-$[Co(Meen)_2(NO_2)_2]ClO_4$ (Table V), which was not as soluble as the racemate. The data for racemization were extrapolated to $\mu = 0.15$ *M*, the concentration used in the pmr study, and the retention ratio was estimated from the extrapolated value ($k_{obsd} \sim 1.4 \times 10^{-3}$ sec^{-1}) to be ~ 1.

Discussion

The large retention ratio for methanol appears to support the case for mechanism I (Figure 1) (where OH^- is now replaced by the alkoxide ion) unless the possibility of the intervention of another molecule of solvent is considered. Under those circumstances the cyclic mechanism can be accommodated by the following activated complex



As the alcohol becomes more bulky, this activated complex becomes more difficult to attain and appears sterically impossible for *t*-butyl alcohol. In this alcohol little retention was observed, and this appears on the surface to be consistent with the cyclic mechanism in those instances where it is feasible. However, the pattern of results requires discussion in the light of a more detailed analysis of the retention ratio which is now given.

An analysis of the rate constants for racemization and proton exchange using mechanism I leads to $k_R = k_1k_3/k_2$ and $k_D = k_1$.[1,2] It follows that the retention ratio is k_2/k_3, which is a measure of the ratio of the reprotonation rate of the deprotonated intermediate by the solvent (k_2) to the rate of inversion of this intermediate (k_3). Thus the large change in the retention ratio is accounted for by the two processes, reprotonation and inversion. Other factors being equal, the rate of reprotonation should increase with the acidity of the alcohol in a manner predicted by the Brønsted relationship. The variation of k_3 with solvent is not as easily evaluated, but what little is known about N inversion in aziridines suggests that strongly H-bonding solvents decrease the inversion rate. Assuming the ability of the solvents to H-bond parallels their acidity, the value of k_3 is predicted to follow the sequence $H_2O < CH_3OH < C_2H_5OH < C_3H_7OH < C_4H_9OH$. Since k_2 increases and $1/k_3$ also increases with increasing acidity of the solvent, both effects lead to an increase in retention ratio. Therefore, mechanism I predicts a similar behavior as mechanism II for the retention ratio in the alcohols. However, it appears that the N inversion rates in aziridines are relatively insensitive to solvent. For example, 1-methyl-2,2-dimethylaziridine has inversion rate constants within a factor of 10 in such widely differing solvents as methanol and CCl_4.[10] We infer therefore that the dominant feature in deciding the retention ratio is the rate of reprotonation.

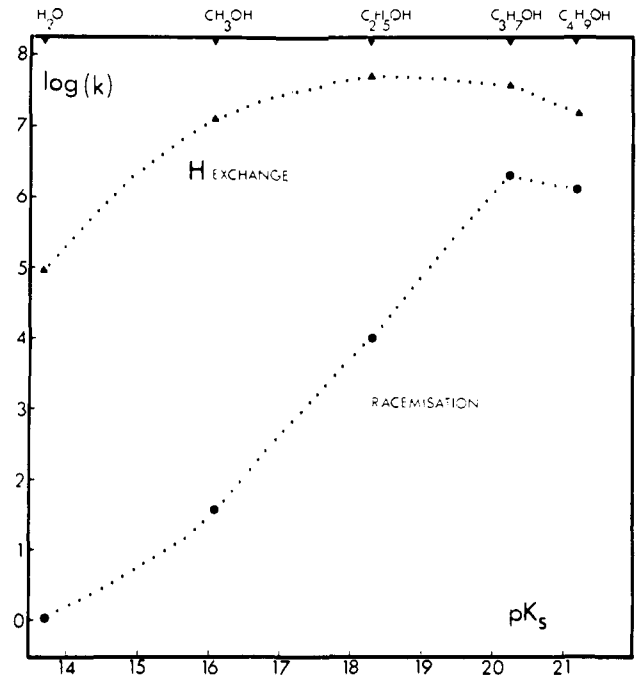


Figure 5. Plot of log k against pK_s for the various alcohols and for water.

It is conceivable also that the low retention ratio measured in *t*-butyl alcohol arises partly from the slower diffusion rate for the bulky molecules leading to a smaller k_2 and a larger lifetime for the deprotonated species and consequently a greater opportunity to racemize. Although ion-pairing effects should become more important as the dielectric constant of the solvent decreases, the uncharged nature of the deprotonated intermediate suggests that such effects on the retention ratio should be small.

The low retention ratio for the DMSO–*t*-butyl alcohol mixture will not be discussed in detail because there is now some controversy whether the dimsyl or butoxide ion is the active agent.[11] The former is not relevant to the situation presented here and the latter does not differ from the pure *t*-butyl alcohol case, except that k_2 may be even smaller due to the lower concentration of butanol.

For mechanism II we have already indicated that the cyclic transition state must contain a molecule of solvent in order to be feasible. In addition the steric problems in forming such a transition state as, RO^- becomes larger, have been emphasized. This factor should manifest itself in a substantially slower rate for H exchange in *t*-butyl alcohol than in methanol. However, approximately the same rate is observed for all four alcohols (Figure 5) and such behavior is difficult to rationalize using mechanism II.

In summary, we propose that the data are best reconciled with mechanism I. The alternative is excluded largely because of the steric problems in forming the

(10) A. Lowenstein, J. F. Neumer, and J. D. Roberts, *J. Am. Chem. Soc.*, **82**, 3599 (1960).
(11) C. D. Ritchie and R. E. Uschold, *ibid.*, **89**, 1721 (1967).

cyclic transition state with *t*-butyl alcohol. This conclusion is consistent with that derived from the H-isotope effects in the related aqueous medium.

Acknowledgment. We wish to thank Dr. J. Fildes and the analytical unit of the John Curtin School of Medical Research, A.N.U., for the microanalyses.

Cobalt(III)-Promoted Hydrolysis of Chelated Glycine Esters. Kinetics, Anion Competition, and O^{18}-Exchange Studies

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Abstract: Kinetic data for the hydrolysis of $[Co(en)_2(glyOC_3H_7)](ClO_4)_3$ in aqueous solution have been obtained, and the results confirm the proposal made by Alexander and Busch[1] that a chelated ester intermediate $[Co(en)_2(glyOR)]^{3+}$ is formed following the Hg^{2+}-induced removal of halide ion from $[Co(en)_2X(glyOR)]^{2+}$ (X = Cl, Br; R = CH_3, C_2H_5, C_3H_7). The same intermediate is generated following the HOCl oxidation of coordinated Br^-. Anion competition results indicate that the chelated ester intermediate is formed directly in the Hg^{2+}-assisted reaction but suggest that some $[Co(en)_2(H_2O)(glyOC_3H_7)]^{3+}$ is generated in the HOCl-promoted reaction. O^{18} studies establish that hydrolysis of $[Co(en)_2(glyOCH_3)]^{3+}$ proceeds without opening of the chelate ring and that the coordinated ester is bound to Co(III) through the carbonyl oxygen.

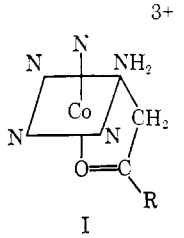
In a recent publication Alexander and Busch have discussed the cobalt(III)-promoted hydrolysis of coordinated glycine esters (reaction 1).[1] Similar, although less detailed information has been obtained for the hydrolysis of small and relatively simple peptide molecules (reaction 2).[2] Both reactions result in a final cobalt(III) product containing the chelated N-amino acid anion, and a marked enhancement in rate, compared to the uncatalyzed reactions, was found for hydrolysis of the ester and peptide bonds, respectively.

$$[Co(en)_2X(glyOR)]^{2+} + Hg^{2+} + H_2O \longrightarrow [Co(en)_2gly]^{2+} + HOR + H^+ + HgX^+ \quad (1)$$

X = Cl, Br; R = CH_3, C_2H_5, *i*-C_3H_7

$$[Co(trien)OH(H_2O)]^{2+} + NH_2CHRCONHCHR'\cdots CO_2R'' \longrightarrow [Co(trien)(NH_2CHRCO_2)]^{2+} + NH_2CHR'\cdots CO_2R'' + H_2O \quad (2)$$

Our interest in the above reactions has been stimulated following the isolation and characterization of chelated amino acid ester, amino acid amide, and dipeptide ester complexes of general structure I.[3] Coordination complexes of this structural type have been invoked in the metal ion catalyzed acceleration in the hydrolysis of such substrates,[4] but, with the exception of $[Co(trien)(glyglyOEt)]^{3+}$ which was isolated from reaction 2,[5] the reported evidence to support the formation of such intermediates either prior to or as a step in the hydrolysis reaction is largely of an indirect kind. For example, Alexander and Busch proposed a chelated ester intermediate $[Co(en)_2(glyOR)]^{3+}$ as the reactive intermediate (structure I) in the Hg^{2+}-promoted hydrolysis (reaction 1). The evidence for this species was obtained primarily from the change in the >C=O stretching frequency as the monodentate ester (1735 cm^{-1}) was first chelated (1610 cm^{-1}) and then hydrolyzed to $[Co(en)_2gly]^{2+}$ (1640 cm^{-1}).



I

R = OR, NRR', NHRCHR'CO_2R''

As the $[Co(en)_2(glyOR)](ClO_4)_3$ compounds have now been isolated,[3] the hydrolysis rates can now be compared with those attributed to this intermediate by the previous authors. Other mechanistic aspects of this reaction which merit consideration are the following. (a) Does opening of the chelate ring precede hydrolysis? (b) Does removal of halide ion from the monodentate ester complex lead to initial incorporation of solvent at the vacated coordination site prior to chelation? (c) What properties does the monodentate ester aquo complex have? Some of these questions are potentially soluble using O^{18}-tracer techniques, and this paper presents some results obtained from such investigations.

Experimental Section

Analar reagents were used throughout without further purification.

O^{18}-Labeled glycine methyl ester hydrochloride was prepared as follows. Glycine hydrochloride was enriched by refluxing the salt for 24 hr at pH 0.5 (HCl) with 1.5 atom % O^{18}-enriched water.[6]

(1) M. D. Alexander and D. H. Busch, *J. Am. Chem. Soc.*, **88**, 1130 (1966).
(2) D. A. Buckingham, J. P. Collman, D. A. R. Happer, and L. G. Marzilli, *ibid.*, **89**, 1082 (1967).
(3) D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *ibid.*, **89**, 4539 (1967).
(4) (a) H. Kroll, *ibid.*, 74, 2036 (1952); (b) M. L. Bender and B. W. Turnquest, *ibid.*, **79**, 1889 (1957); (c) an excellent review of this subject is given by M. L. Bender, Advances in Chemistry Series, No. 37, American Chemical Society, Washington, D. C., 1963, p 19.
(5) J. P. Collman and E. Kimura, *J. Am. Chem. Soc.*, **89**, 6096 (1967).