234. Base Catalysed Racemization of Ethylenediamine-N,N,N′-triacetato-aqua-cobalt(III)

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Summary

The kinetics of the base catalysed racemization of $[Co(EN3A)H_2O]$1) were studied polarimetrically in aqueous buffer solution. The reaction rate is first order in OH^- and in complex, in weakly acidic medium. Activation parameters are $\Delta H^{\neq} = 22$ kcal · mol^{-1}, $\Delta S^{\neq} = 26$ cal · K^{-1}. The results are discussed in terms of an S_N1CB mechanism involving exchange of the ligand water molecule.

The *N*-methylated analogue $[Co(ME3A)H_2O]$ does not racemize in the pH-range investigated. Loss of optical activity occurs at a rate which is about 1,000 times slower than the racemization of $[Co(EN3A)H_2O]$(60°) and coincides with the decomposition of the complex.

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1. Introduction. – The racemization of $[Co(EDTA)]^-$ in solution has been described in terms of two mechanisms, a base-catalysed path and a thermal twist [1], possibly with coordination of one solvent water molecule in the transition state [2]. It has been proposed from NMR. studies that a similar heptacoordinated transition state, resulting from chelate ring closure by the predominantly quinquedentate ligands, is formed in the racemization of $[Ni(EDTA)]^{2-}$ and $[Ni(TNTA)]^{2-}$, whereas the nickel(II) complexes of $EDDA^{2-}$ and $ME3A^{3-}$ resisted racemization on the NMR. time scale [3].

Formation of amido nitrogen [4] occurs in the racemization or isomerization of cobalt(III) chelates containing coordinated H-carrying nitrogen centers [5] [6]. For similar aquacobalt(III) amines, a S_N1CB mechanism with exchange of a ligand water molecule has been suggested [7–9], involving a trigonal bipyramidal transition state. The stabilization of a corresponding intermediate by π-bonding with the amido nitrogen has been discussed in detail [10].

We now report the results of racemization studies of aquacobalt(III) complexes with two quinquedentate ligands of the diaminotricarboxylate type.

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1) Abbreviations: $EN3A^{3-} = (^-OOCCH_2)_2N(CH_2)_2NHCH_2COO^-$; $ME3A^{3-} = (^-OOCCH_2)_2N(CH_2)_2N(CH_3)CH_2COO^-$; $EDDA^{2-} = {}^-OOCCH_2NH(CH_2)_2NHCH_2COO^-$; $EDTA^{4-} = (^-OOCCH_2)_2N(CH_2)_2N(CH_2COO^-)_2$; $TNTA^{4-} = (^-OOCCH_2)_2N(CH_2)_3N(CH_3COO^-)_2$; $HETA^{3-} = (^-OOCCH_2)_2N(CH_2)_2N(CH_2COO^-)CH_2CH_2OH$; en $= H_2N(CH_2)_2NH_2$; Meen $= H_2N(CH_2)_2NHCH_3$; sar$^- = {}^-OOCCH_2NHCH_3$.

2. Experimental. – *Ethylenediamine*-N,N,N′-*triacetato-aqua-cobalt(III)*, *[Co(EN3A)H$_2$O]H$_2$O*. The complex was prepared according to the procedure of *Blackmer et al.* [11], modified as follows: the reaction mixture after air oxidation was passed first through a Dowex 1x4 anion exchanger column in acetate form, eluted with water, then through a Dowex 50WX8 cation exchanger in H$^+$ form and eluted again with water. The obtained eluate containing the complex in diluted acetic acid was evaporated to a small volume in a rotary evaporator. The spontaneously crystallizing complex was separated, recrystallized once from hot water and dried *in vacuo* over KOH.

Potassium Chloro-(ethylenediamine-N,N,N′-*triacetato)-cobaltate(III)*, *K[Co(EN3A)Cl]0.5H$_2$O* [11] [12]. A solution of the aqua complex in 37% hydrochloric acid was evaporated to dryness on a boiling water bath; the cooled residue was dissolved in ice-cold water and the solution poured into a Dowex 1x4 anion exchanger in Cl$^-$ form. The column was washed with water and the chloro complex was eluted with 0.2M $CaCl_2$ in 0.05M HCl. The calcium salt was precipitated by addition of ethanol in the cold, washed thoroughly with ethanol and dried *in vacuo* over KOH.

The potassium salt was obtained from the calcium salt by cation exchange on Amberlite CG50 in K$^+$ form and isolated by the same procedure.

Resolution of K[Co(EN3A)Cl]0.5H$_2$O. The racemic potassium salt (2.70 g, 7.2 mmol) was reacted with $(+)_D[Co(en)_2C_2O_4]^+$ [13] (3.6 mmol) according to *Van Saun & Douglas* [14].

The crystals of the less soluble diastereomer were collected and the filtrate was passed through a small column of Amberlite CG50 (K$^+$) to eliminate unreacted resolving agent. The eluate was collected in two roughly equal fractions and the potassium salt recovered from each fraction.

The complex from the 1st fraction (0.57 g) was nearly inactive due to racemization in the alkaline elution front. The second fraction gave 0.52 g K-$(+)_{546}$-[Co(EN3A)Cl]H$_2$O, $[\alpha]^{RT}_{546} = +970°$.

The diastereomeric salt (1.48 g) was dissolved in cold water and the resolving agent removed similarly, yielding 0.95 g K-$(-)_{546}$-[Co(EN3A)Cl]H$_2$O, $[\alpha]^{RT}_{546} = -925°$.

$C_8H_{13}ClCoKN_2O_7$ (382.7)	Calc.		C 25.1	H 3.42	N 7.32%
	Found	$(+)_{546}$	,, 24.7	,, 3.27	,, 7.45%
	,,	$(-)_{546}$	,, 24.4	,, 3.22	,, 7.77%

Enantiomers of Ethylenediamine-N,N,N′-*triacetato-aqua-cobalt(III)*; $(-)_{546}$- *and* $(+)_{546}$-*[Co(EN3A)H$_2$O]H$_2$O*. The optically active aqua complexes were obtained by stirring K-$(-)_{546}$- and K-$(+)_{546}$-[Co(EN3A)Cl]H$_2$O respectively with excess 0.1M $Hg(NO_3)_2$ in 1M HNO_3 for 10 min at RT. The aqua complexes were isolated by passing the resulting solution on Dowex 50WX8 (H$^+$) cation exchanger, washing with water, concentrating and precipitating by addition of ethanol in the cold. The complexes were dried *in vacuo* over KOH.

N-*Methylethylenediamine*-N,N′,N′-*triacetate complexes*. The ligand was prepared according to [14] and reacted directly without isolation to form the aqua complex [Co(ME3A)H$_2$O]0.5H$_2$O by the procedure used for the EN3A complex. The racemic and resolved chloro complex and the $(-)_{546}$-aqua complex were obtained by the procedure used for the corresponding EN3A complexes.

	C		H		N	
	Calc.	Found	Calc.	Found	Calc.	Found
[Co(ME3A)H$_2$O]0.5H$_2$O (331.2)	32.6	32.4%	4.87	4.96%	8.46	9.03%
K[Co(ME3A)Cl]H$_2$O (396,7)	27.3	27.1%	3.81	3.80%	7.07	7.15%

Measurements. Electronic spectra were recorded on a *Unicam* SP800 spectrophotometer. Optical rotations were measured on a *Perkin-Elmer* 141 polarimeter using a mercury lamp source (578, 546, 436 and 365 nm). A *Metrohm* Titriskop pH meter equipped with a combined glass electrode was used for pH-measurements.

Kinetic runs were conducted in buffered solution and the pH measured at the appropriate temperatures. The buffer concentration (acid + base forms) was 0.1M and no other electrolyte was added except when the effect of the buffer concentration or ionic strength had to be checked. Buffers up to pH 5.5 were prepared from acetic acid. Phosphate buffers were used above pH 5.5, as well as α-picoline (pH 5.6 to 6.1) and γ-collidine (above pH 7.0) buffers.

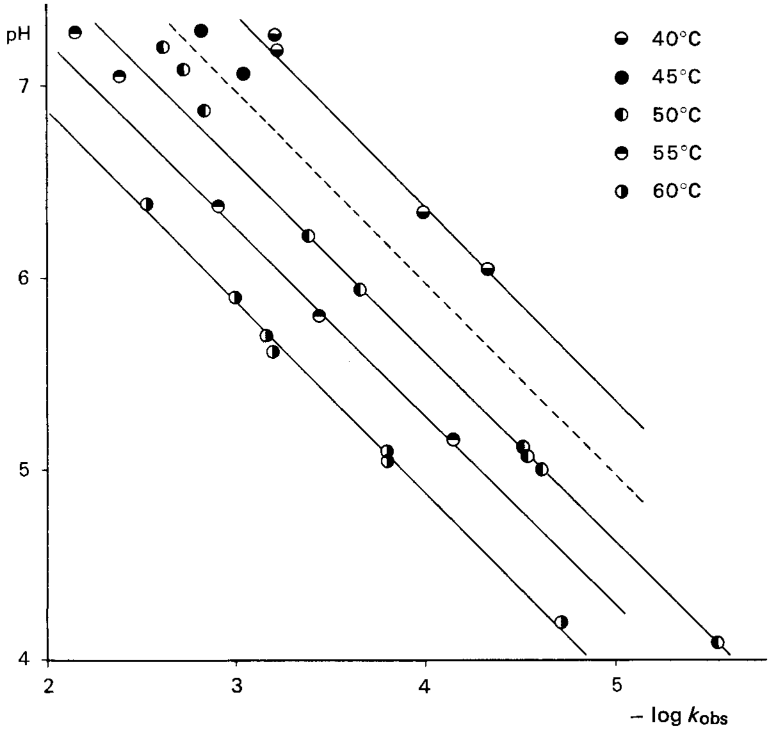


Fig. 1. *Racemization rates of* [*Co*(*EN3A*)H_2O]. (---) *interpolated from values at other temperatures*

3. Results. - The rates of racemization of Co(EN3A)H_2O were measured in buffer solutions at various temperatures and pH values; the results are summarized in *Figure 1.* In most cases, the readings were made at 546 nm. For several runs, however, the change of optical activity was followed also at 436 and 365 nm. The 1st order rate constants obtained at different wavelengths agree within 1%; it can thus safely be assumed that no mutarotation takes place. The plots of log $|\alpha_{546}|$ *vs.* time are strictly linear for at least two half reaction times. Readings were extended in a few cases beyond 4 half reaction times without any deviation from linearity. After completion of the reaction, the solutions showed no optical activity any more at any wavelength. The electronic spectra of the solutions showed no detectable changes at pH $\simeq$ 5 and only minor changes (less than 2% decomposition) at pH $\geqslant$ 6 during the racemization runs.

No ionic strength effect on the rate of racemization could be observed by addition of $NaClO_4$ up to 1 M. General base catalysis does not affect the rates, as was shown by runs done with 0.4 M and 0.8 M buffers. No specific effect of any of the buffers used was evident.

The -log k_{obs} *vs.* pH plot at each temperature is linear within experimental error up to pH $\simeq$ 6.5, implying 1st order dependence on OH^- concentration. Above pH 6.5, deviation from linearity becomes noticeable, the rates being lower (*cf. Figure 1*).

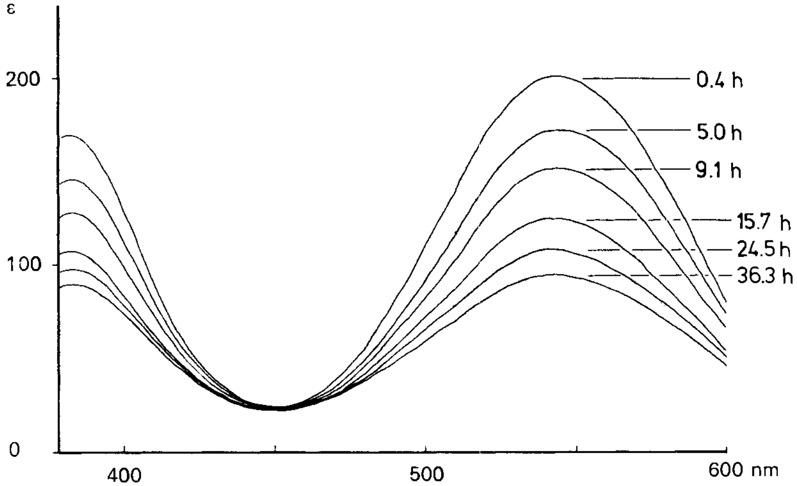


Fig. 2. *Absorption change of* $[Co(ME3A)H_2O]$ *at pH* $\cong 7.0$*, 60°*

Similar measurements were attempted with $[Co(ME3A)H_2O]$ at 60°. However, at pH = 5, the loss of optical activity was too slow to allow a reasonably accurate determination of the rate. At pH $\cong$ 7.0 (phosphate buffer 0.1 M total, initial complex 5×10^{-3} M), a precipitate slowly develops and the pH drops to 6.8 in 15 h. Relatively large concentrations of cobalt(II) are formed and the electronic spectrum (*Figure 2*) shows a monotonous decrease in the 650–380 nm range. These observations show that the complex undergoes complete decomposition.

A 1st order graph can be constructed from the absorption at both maxima in the *d-d* transition bands, using extrapolated values for ε_∞. The obtained rate constants are reported in *Table 1*, together with the values obtained using the same ε_∞ for similar measurements at pH 6.0, combined with the results of polarimetric measurements (*Figure 3*).

Table 1. *Rate constants for the decomposition of* $[Co(ME3A)H_2O]$
All measurements at 60°. Values of k_{obs} in s^{-1}

pH	~7.0	~6.0
Spectrophotometry	1.8×20^{-5}	1.6×10^{-6}
Polarimetry[a]	$\sim 2 \times 10^{-5}$	$\sim 3 \times 10^{-6}$

[a] Upper limiting rate at 578, 436 and 365 nm.

Whereas the plots of log $|\alpha|$ *vs.* time at 365, 436 and 578 nm are similar and give approximately the same limiting rate constant, a lower and steadily increasing rate is obtained at 546 nm. Since the upper limiting rate of loss of optical activity is comparable with the spectrophotometrically obtained rate of decomposition, it can be concluded that the loss of optical activity arises from decomposition and not from a true racemization. The complicated behaviour of the polarimetric measurements is not unexpected, since stepwise dechelation of the complex should yield a number of dissymmetric intermediates.

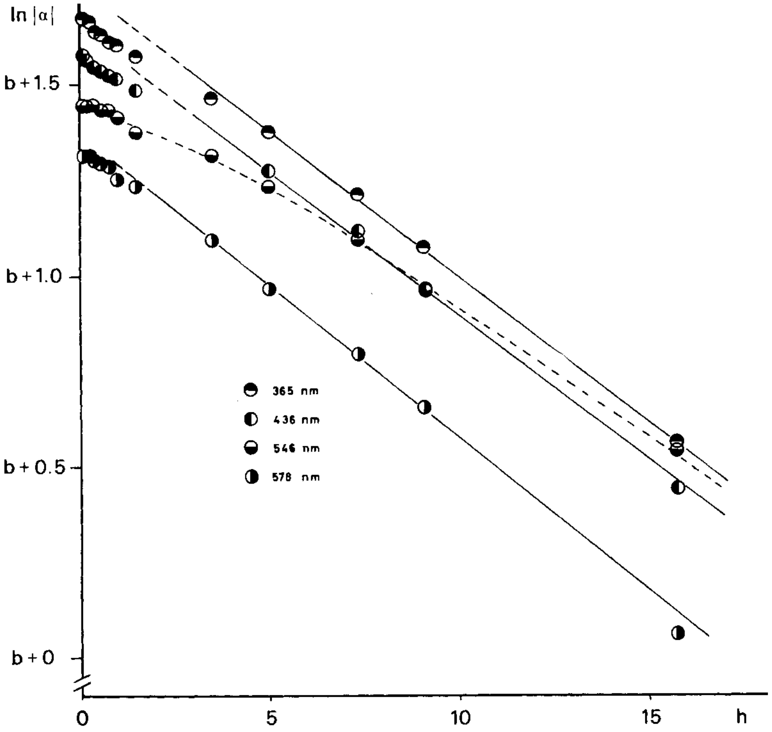
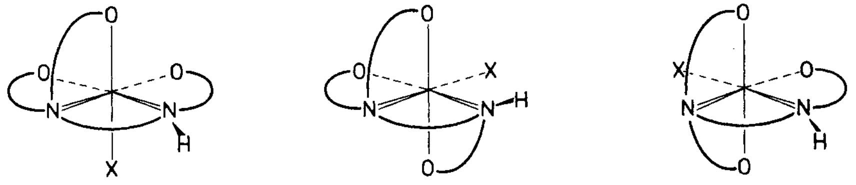


Fig. 3. *Rotatory power changes in the decomposition of* $[Co(ME3A)H_2O]$; *pH 7.0, 60°*; *b = arbitrary origin*

The observed decomposition seems to follow 1st order rate dependence in OH^- concentration and is at least 1,000 times slower than the racemization of $[Co(EN3A)H_2O]$ under the same conditions.

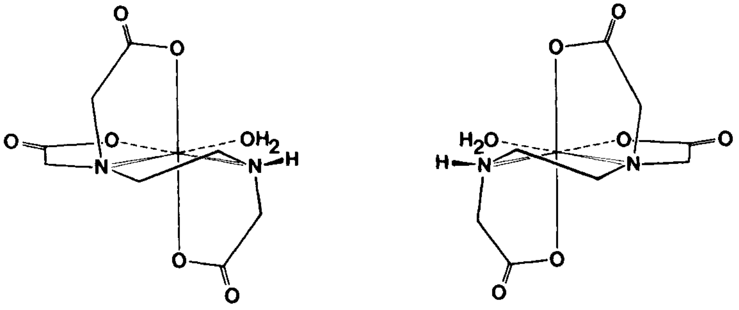


cis-pol. *cis*-eq. *trans*-eq.

Fig. 4. *Geometrical isomers of* $[Co(EN3A)X]$ *complexes*

4. Discussion. – Cobalt(III) complexes with quinquedentate EN3A-type ligands can in principle exist in three geometrical isomeric forms (*Figure 4*). However, disregarding a single example of *trans*-eq. geometry [15] with a ligand having a substituted ethylenediamine backbone, and the existence of some *cis*-polar bromo-complexes [16], all known species are thought to be *cis*-eq. ^{13}C-NMR. measurements on racemic $[Co(EN3A)H_2O]$ show that only the *cis*-eq. isomer is present [17]. Since the *cis*-pol. isomer is also chiral, its presence would cause a complicated kinetic behaviour, whether the complex undergoes preliminary isomerization or racemizes directly. No such complication occurs however, and it can safely be assumed that the complex studied is the pure *cis*-eq. isomer.

The racemization of $[Co(EN3A)H_2O]$ may be discussed in relation to the racemization of $[Co(NH_3)_4(Meen)]^{3+}$ and $[Co(NH_3)_4(sar)]^{2+}$, reported by *Sargeson et al.* [5]. The present system differs however in two main respects. The specific buffer effect observed by these authors with phosphate buffers is absent in the racemization of our neutral complexes. Secondly, whereas the only source of dissymmetry in the complexes studied by *Sargeson et al.* is the asymmetric nitrogen center and the induced conformation of the chelate ring, the entire chelation skeleton of $[Co(EN3A)H_2O]$ is chiral. Nevertheless, the preferred gauche conformation of the ethylenediamine chelate ring correlates all the asymmetry elements univocally with the absolute configuration of the secondary nitrogen donor (*Figure 5*)[2]. The racemization then involves a transition state in which the configuration of all the stereogenic elements of the complex invert. The pH dependence of the racemization rate constant shows two opposite effects. At pH $\lesssim$ 6.5, the reaction rate law is:



Δ'-S(N)-λ Λ'-R(N)-δ

Fig. 5. *Configurations and conformations in* $[Co(EN3A)H_2O]$

$$\text{rate} = k_{\text{obs}}[Co(EN3A)H_2O^*] = k_{\text{rac}}[OH^-][Co(EN3A)H_2O^*]$$

where $[Co(EN3A)H_2O^*]$ is the excess concentration of optically active aqua complex. In neutral or weakly basic medium, the observed rates are lower than predicted according to this expression. The aqua complex is a weak acid, $pK_a \simeq 8.0$ at 25°. Adjusting the pK_a values for the analogous complex $[Co(HETA)H_2O]$, determined by *Tanner & Higginson* [18], over the temperature range used here, the amount of hydroxo complex $[Co(EN3A)OH]^-$ formed can be estimated. Assuming as a 1st approximation that the hydroxo complex does not racemize at an appreciable rate, corrected log k_{obs} values are obtained, which coincide within ± 0.07 log k units with the experimental values. The actual racemization rate of the hydroxo complex cannot

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[2] The IUPAC ring pairing proposal (Inorg. Chem 9, 1 (1970)) for the nomenclature of chiral chelates fails to give a net chirality in this case. Δ' and Λ' relate to ΔΔΛ and ΛΛΔ-EDTA-type skeletons respectively.

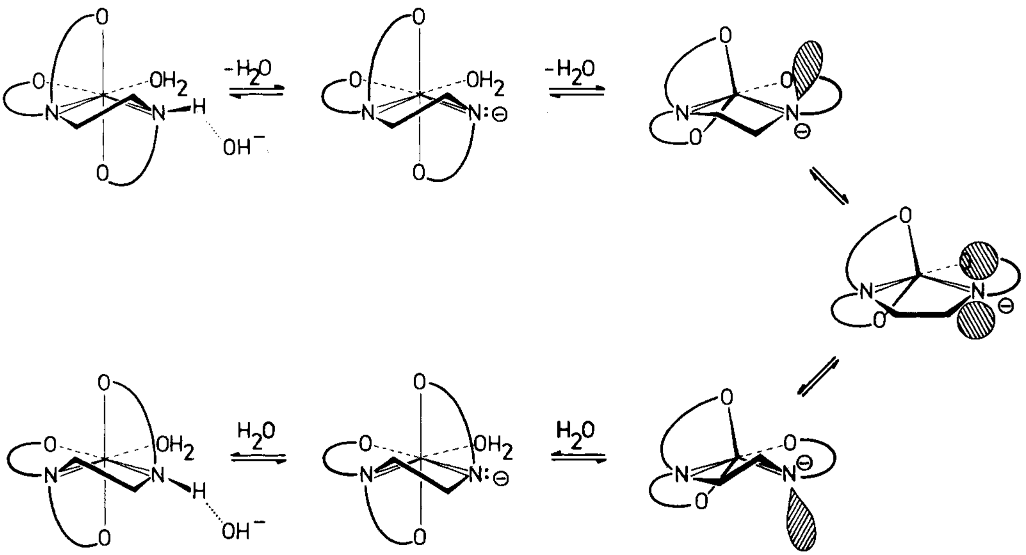

Fig. 6. *Proposed racemization mechanism for* [*Co*(*EN3A*)*H_2O*]

be deduced from these data, since measurements should be extended to higher pH values, where the racemization would compete with the decomposition of the complex. In any case, the rate of racemization of the hydroxo complex must be low, compared to the rate of racemization of the aqua complex. Similar observations on dihydroxo- and hydroxo-aqua-cobalt(III) tetramine complexes have been reported [8].

The absence of general base catalysis and the 1st order rate dependence on OH^- concentration suggests a *S_N1CB* mechanism (*Figure 6*). Proton exchange at a secondary nitrogen coordinated to cobalt(III) is known to occur significantly faster than configurational inversion [5] [8] in weakly acidic, neutral or basic media. This mechanism is supported by the configurational stability of [Co(ME3A)H_2O], which has no dissociable proton available at the asymmetric nitrogen. On the other hand, the higher configurational stability of $[Co(EN3A)OH]^-$ can be accounted for by the much slower exchange of OH^- compared to H_2O.

The reaction can then be described with the following scheme:

$$H\Delta + OH^- \rightleftharpoons \Delta^- + H_2O \underset{k^*}{\overset{k^*}{\rightleftharpoons}} \Lambda^- + H_2O \rightleftharpoons H\Lambda + OH^-$$

where $H\Delta$, $H\Lambda$ are the enantiomeric aqua complexes, the pair Δ^-, Λ^- being the corresponding *N*-deprotonated conjugate bases. The acidity of the proton bound to coordinated nitrogen in $[Co(en)_3]^{3+}$ has been measured, $pK_N \simeq 15$ [19]. Assuming rapid initial dissociation, the true racemization rate constant k^* becomes:

$$k^* = k_{rac}\, k_W / K_N$$

Typically, $\log k^* = 4.2 \pm 0.5$ (40°); 4.7 ± 0.5 (50°); 5.1 ± 0.5 (60°) with $-\log K_N = 15 \pm 0.5$, where it is assumed that the ratio K_W/K_N remains constant over the temperature range studied.

Table 2. *Activation parameters*

Racemization of	$\Delta H^{\ddagger}$ (kcal · mol^{-1})	$\Delta S^{\ddagger}$ (e.u.)
$[Co(EN3A)H_2O]$	22	26
$[Co(NH_3)_4(Meen)]^{3+}$ [5]	24	30
$[Co(NH_3)_4(sar)]^{2+}$ [5]	19	21

The obtained k_{rac} values are intermediate between racemization rates of $[Co(NH_3)_4(sar)]^{3+}$ [5a] and $[Co(NH_3)_4(Meen)]^{2+}$ [5b]. The activation energy was determined from a log k_{rac} *vs.* 1/T plot, whence $E_a = 22.7$ kcal/mol, $\Delta H^{\ddagger} = 22$ kcal/mol, $\Delta S^{\ddagger} = 26$ e.u. It is interesting to compare these activation parameters (*Table 2*) with those for the racemizations of the above tetramines. The chelate ring conformation effect found in the Meen complex appears in the EN3A complex also and could be explained in terms of strain in the symmetric transition state, where the ethylenediamine ring is planar. On the other hand, stabilization of the trigonal bipyramidal intermediate by π-bonding through the amido group, as suggested in *Figure 6*, can account for the relatively low activation enthalpy. It may also be noted that positive activation entropy in the spontaneous aquation of *trans*-diacido-tetramine-cobalt(III) complexes has been interpreted as evidence for trigonal bipyramidal, as opposed to tetragonal pyramidal transition states [20]. The comparison with $[Co(NH_3)_4(Meen)]^{3+}$ and $[Co(NH_3)(sar)]^{2+}$ finally suggests that the rate determining step in the present case is the configurational inversion of the quinquedentate intermediate and not the departure of the ligand water molecule.

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