Inversion and Proton Exchange at Chiral Nitrogen Centers of $[Co(acac)_2(Ph\text{-}en)]^+$ (acac = 2,4-Pentanedionate Ion; Ph-en = *N*-Phenylethylenediamine) and $[Co(acac)_2(Me\text{-}en)]^+$ (Me-en = *N*-Methylethylenediamine)

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Abstract

The rates of the base-catalyzed proton exchange and inversion (epimerization) at chiral nitrogen centers of $[Co(acac)_2(Ph\text{-}en)]^+$ (acac = 2,4-pentanedionate ion; Ph-en = *N*-phenylethylenediamine) and $[Co(acac)_2(Me\text{-}en)]^+$ (Me-en = *N*-methylethylenediamine) in aqueous solutions have been measured at 34.0 °C. The Ph-en complex, which has an electron-withdrawing phenyl group on the nitrogen atom undergoes proton exchange about 10^4 times faster than the Me-en complex which has an electron-repelling methyl group. The proton-exchange rates are *ca.* 10^2 and 10^5 times greater than the inversion rates for the Ph-en and Me-en complexes, respectively. The faster rate of inversion for the Ph-en complex was explained by the lower barrier of inversion; an increased stabilization of the intermediate was due to $(p\text{-}p)_\pi$ conjugation between the amide nitrogen atom and the phenyl group.

Introduction

Recently, the kinetics of racemization and proton exchange at chiral secondary amine nitrogen atoms of metal complexes have been studied extensively [1]. However, little work has been reported on the effect of the nature of the substituents bonded to chiral nitrogen centers on the rate.

In this paper, we report the rates of inversion (epimerization) and proton exchange at chiral nitrogen centers of $[Co(acac)_2(Ph\text{-}en)]^+$ (acac = 2,4-pentanedionate ion; Ph-en = *N*-phenylethylenediamine) and $[Co(acac)_2(Me\text{-}en)]^+$ (Me-en = *N*-methylethylenedi-amine).

Experimental

$[Co(acac)_2(Ph\text{-}en)]^+$ and $[Co(acac)_2(Me\text{-}en)]^+$ were prepared and separated into racemic pairs of the

diastereomers ($\Delta(R)\Lambda(S)$ and $\Delta(S)\Lambda(R)$) as described previously [2, 3]. ^{1}H NMR spectra were measured on a JEOL PMX-60 spectrometer using sodium trimethyl-silylpropanesulfonate as the internal reference.

Epimerization Studies

A racemic pair of diastereomers, $\Delta(R)\Lambda(S)$- or $\Delta(S)\Lambda(R)$-$[Co(acac)_2(Me\text{-}en)]ClO_4$ (*ca.* 7×10^{-4} mol dm^{-3}) in an aqueous solution of NaOH–Na$_2$CO$_3$ (pH 9.60–10.72) was epimerized at 34.0 °C. Portions of the reaction mixture were withdrawn at timed intervals and mixed with dilute CH$_3$COOH, which served to stop effectively the epimerization reaction. The mixture was then chromatographed (sample volume: 3×10^{-3} cm^3) with a column (ϕ 0.46 cm × 15 cm) of JASCO Finepack SIL C$_{18}$S and 5×10^{-3} mol dm^{-3} sodium heptanesulfonate in methanol as the eluent. The chromatography was carried out with a JASCO TRI ROTAR V system at a flow rate of 0.5 cm^3 min^{-1}, and the complexes were detected with a JASCO UVIDEC-100 IV spectrophotometric detector at 245 nm where the two isomers give the same molar absorption coefficient. The areas of two bands on the chromatograms were determined by weighing paper cut-outs matching the bands. The kinetics of epimerization of $[Co(acac)_2(Ph\text{-}en)]^+$ was studied in a similar way. The reaction was carried out with a buffered solution (phthalate buffer, pH 4.07– 5.22) at 34.0 °C.

Proton-exchange Studies

The rates of the proton-exchange at the chiral nitrogen atoms of $[Co(acac)_2(Ph\text{-}en)]^+$ and $[Co(acac)_2(Me\text{-}en)]^+$ were followed by monitoring signal changes in the ^{1}H NMR spectra. The complex per-chlorates were converted into chlorides with a Dowex 1X8 anion exchanger in the chloride form in order to increase the solubility. The Ph-en complex (*ca.* 0.2 mol dm^{-3}) in D$_2$O solution of H$_2$d-tart–NaHd-tart (d-tart = d-tartrate ion; pD 1.21–3.13) was placed in a thermostat at 34.0 °C, and the spectra were recorded at timed intervals at the same temperature. The amine proton signal of the C$_6$H$_5$NH–group at $\delta = 7.0$ (or 7.5) in the spectra of $\Delta(R)\Lambda(S)$- (or

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$\Delta(S)\Lambda(R)$-)[Co(acac)$_2$(Ph-en)]Cl disappears as the result of deuteration, and the rate was followed by monitoring the change in peak area. The change in N–CH$_3$ signal of the Me-en complex in buffered D$_2$O solution (KH$_2$PO$_4$–Na$_2$HPO$_4$) at 34.0 °C was followed. The N–CH$_3$ doublet of $\Delta(R)\Lambda(S)$-[Co-(acac)$_2$(Me-en)]Cl at $\delta = 1.80$ becomes a singlet by deuteration. For the other $\Delta(S)\Lambda(R)$-[Co(acac)$_2$-(Me-en)]$^+$ isomer, the N–CH$_3$ doublet overlaps the C–CH$_3$ signal of the acac ligand, and the proton-exchange rate could not be obtained. Proton-exchange studies at primary amine nitrogens of the Ph-en and Me-en complexes were performed by the same method. The empirical formula, pD = pH meter reading + 0.4 [4], was used to calculate [OD$^-$].

Results and Discussion

For [Co(acac)$_2$(Ph-en or Me-en)]$^+$, two isomers (racemic pairs of the diastereomers), $\Delta(R)\Lambda(S)$ and $\Delta(S)\Lambda(R)$ are possible (Fig. 1)*. Both complexes have been separated into the isomers by fractional crystallization or ordinary column chromatography and characterized by spectroscopy [2, 3]. It has been shown that the complexes isomerize in alkaline solution to give an equilibrium mixture of the isomers, and that the isomerizations proceed by epimerization at the nitrogen centers [2, 3].

Kinetic studies of reversible isomerization (epimerization) between the two isomers of the present complexes were performed in aqueous solutions at 34.0 °C by the high-performance liquid chromatographic method, and changes in the chromatograms with reaction time were followed. This method has the great advantage of a short elution time and only micro quantities of samples [6]. Figure 2 shows a typical set of elution curves obtained at intervals
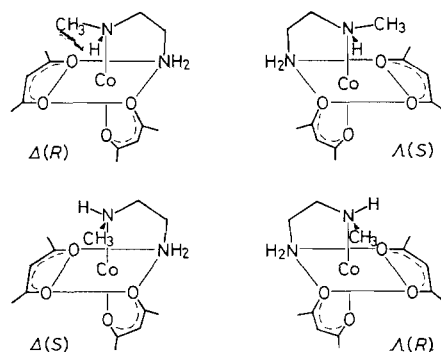

Fig. 1. The four possible isomers of [Co(acac)$_2$(Me-en)]$^+$.

*According to the rule [5], the notation of the absolute configurations, R and S, for the chiral nitrogen atoms are reversed for apparently the same configuration of Ph-en and Me-en complexes.
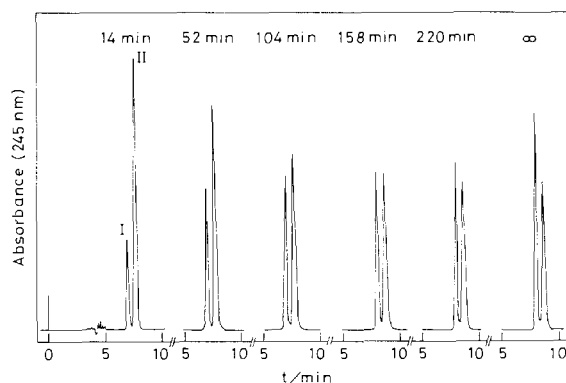

Fig. 2. Change in the elution curve during the epimerization of $\Delta(R)\Lambda(S)$-[Co(acac)$_2$(Me-en)]$^+$ at pH 10.72 and 34.0 °C. Chromatographic conditions: column, JASCO Finepack SIL C$_{18}$S, ϕ 0.46 cm × 15 cm; eluent, 5 × 10^{-3} mol dm^{-3} sodium heptanesulfonate in methanol; flow rate, 0.5 cm^3 min^{-1}; UV detection, 245 nm.

after $\Delta(R)\Lambda(S)$-[Co(acac)$_2$(Me-en)]$^+$ had been dissolved in water at pH 10.72 and 34.0 °C. The area of band I ($\Delta(S)\Lambda(R)$-isomer) increases whereas that of band II ($\Delta(R)\Lambda(S)$-isomer) decreases with time as the result of epimerization. In each kinetic run, the plot of $\ln[S_\infty^I/(S_\infty^I + S_\infty^{II}) - S_t^I/(S_t^I + S_t^{II})]$ versus time gave a straight line (S_∞^I, S_∞^{II}, S_t^I, and S_t^{II} denote the areas of bands I and II at infinite time and at time t). The slope gave the pseudo first-order rate constant, $k_{ep(obs)}$. The $k_{ep(obs)}/[OH^-]$ ($=k_{ep}$) values are constant at 34.0 °C in the pH range of 9.60–10.72, indicating that the reaction is first order in [OH$^-$]. Thus, the rate law was the same as that obtained for racemization (epimerization) of other amine complexes, $R = k_{ep}$[complex][OH$^-$] [1]. The runs starting from either of the isomers gave the same result within the experimental error. From these observations, the reaction can be expressed as

$$\Delta(R)\Lambda(S) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \Delta(S)\Lambda(R)$$
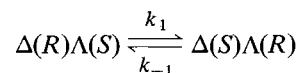
The forward and reverse second-order rate constants, k_1 and k_{-1}, were obtained from k_{ep} ($k_{ep} = k_1 + k_{-1}$) and the equilibrium constant ($k_{eq} = k_1/k_{-1} = 1.16$) as given in Table I.

Kinetics of epimerization for [Co(acac)$_2$(Ph-en)]$^+$ was studied by the same way. The reaction follows the same rate law as the Me-en complex, and the rate constants are given in Table I.

The rates of the proton exchange at amine nitrogen centers of the Ph-en and Me-en complexes were followed by monitoring signal changes in the ^{1}H NMR spectra. From the changes in signal, the pseudo first-order rate constants for the proton exchange, $k_{D(obs)}$ were obtained by a method similar to that for epimerization. The rate law for the proton-exchange reaction is the same as that

TABLE I. A Comparison of Data for the Proton Exchange and Inversion at Chiral Nitrogen Centers of $[Co(acac)_2L]^+$ (L = Ph-en, Me-en) at 34.0 °C:

$$\Delta(R)\Lambda(S) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \Delta(S)\Lambda(R)$$

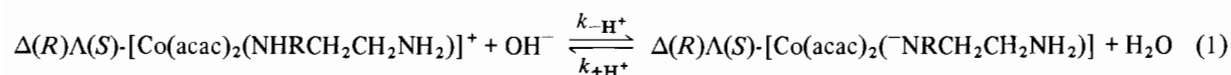| L	Isomer	k_D (M⁻¹ s⁻¹)	(k_1 or k_{-1}) (M⁻¹ s⁻¹)	$k_D/(k_1$ or $k_{-1})$
Ph-en	$\Delta(R)\Lambda(S)$	4×10^7	k_1: 1.4×10^5	2.9×10^2
	$\Delta(S)\Lambda(R)$	5×10^8	k_{-1}: 8.6×10^4	5.8×10^3
Me-en	$\Delta(R)\Lambda(S)$	9×10^3	k_1: 7.0×10^{-2}	1.3×10^5
	$\Delta(S)\Lambda(R)$		k_{-1}: 6.0×10^{-2}	

obtained previously for other amine complexes [1]

$$R = k_D [\text{complex}] [OD^-].$$
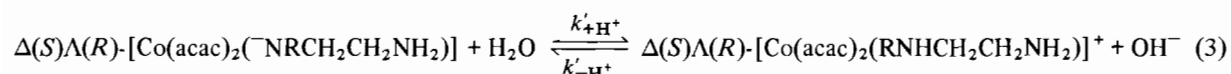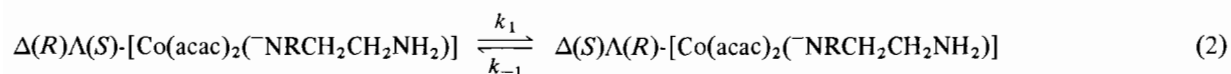
The k_D values at 34.0 °C are given in Table I.

The k_D values for isomers of the Ph-en complex are *ca.* 10^4 times as large as that for the Me-en complex. The large rate difference can be attributed to a difference in electronic effect between the phenyl and methyl substituents. The phenyl group will withdraw electron density from the *N*-phenyl nitrogen atom, creating a more positive center which results in a greater acidity of the *N*-phenyl proton. The rate constants (k_D) of the proton exchange at primary amine nitrogens of $\Delta(R)\Lambda(S)$-$[Co(acac)_2(Me-en)]^+$ (5×10^4 mol⁻¹ dm³ s⁻¹) and $[Co(acac)_2(Ph-en)]^+$ (9×10^4 mol⁻¹ dm³ s⁻¹) are similar, but larger and smaller, respectively, than those at the secondary amine nitrogen in the Me-en and Ph-en complexes. Thus the k_D values for the complexes decrease in the order: secondary amine nitrogen of the Ph-en complex > primary amine nitrogen of the Ph-en and Me-en complexes > secondary amine nitrogen of the Me-en complex. This order may be compared to that of pK_a values: $C_6H_5NH_3^+$ (4.6) < NH_4^+ (9.25) < $CH_3NH_3^+$ (10.6) [7]. Buckingham *et al.* [8] studied the kinetics of proton exchange at the secondary amine nitrogen atom in $[Co(NH_3)_4(Me-en)]^{3+}$ at 34.3 °C. The reported rate constant (3×10^7 mol⁻¹ dm³ s⁻¹) is much larger than that for the $[Co(acac)_2(Me-en)]^+$ complex (9×10^3 mol⁻¹ dm³ s⁻¹ at 34.0 °C), and almost the same as those for the Ph-en com-

plexes. The large rate difference between the two Me-en complexes, $[Co(NH_3)_4(Me-en)]^{3+}$ and $[Co(acac)_2(Me-en)]^+$, can be explained by two factors: the difference in positive charge on the complexes (3+ and +) and the electron-donating effect of the acac chelate ligands. It has been observed that deuteration rates decrease with a decreasing positive charge on the complex (*ca.* 10-fold for each unit of charge) [9]. The electron-donating effect of the acac chelate ligands is suggested from the ¹H NMR spectrum; the $-NH_2$ peak ($\delta = 4.9$) in $\Delta(R)\Lambda(S)$-$[Co(acac)_2(Me-en)]^+$ is shifted upfield by 0.4 ppm from its position in the spectrum of $[Co(NH_3)_4(Me-en)]^{3+}$ [8].

The rate of racemization for $[Co(NH_3)_4(Me-en)]^{3+}$ has been studied [8]. The reported second-order rate constant, 2.4×10^2 mol⁻¹ dm³ s⁻¹ at 34.3 °C, gives $k_1 = k_{-1} = 1.2 \times 10^2$ mol⁻¹ dm³ s⁻¹, which is *ca.* 10^3 times greater than the k_1 value for $[Co(acac)_2(Me-en)]^+$. However, the k_D/k_1 ratios (retention ratios) are *ca.* 10^5 for both Me-en complexes and imply that the configuration about the chiral nitrogen atom (pyramidal configuration) is retained during most of the time that the proton is off the quarternary *N* site [1]. The retention ratio is only *ca.* 10^2 for $[Co(acac)_2(Ph-en)]^+$. We assume here that the proton-exchange and epimerization reactions proceed by eqns. (1)–(3) [1, 10]. It is generally accepted that amine ligands are bound irreversibly to a cobalt(III) ion and do not dissociate in the lifetime of the above inversion and exchange reactions. If the pK_a values of $[Co(acac)_2(Me-en$ or $Ph-en)]^+$ exceed

$$\Delta(R)\Lambda(S)\text{-}[Co(acac)_2(NHRCH_2CH_2NH_2)]^+ + OH^- \underset{k_{+H^+}}{\overset{k_{-H^+}}{\rightleftharpoons}} \Delta(R)\Lambda(S)\text{-}[Co(acac)_2(^-NRCH_2CH_2NH_2)] + H_2O \quad (1)$$

$$(R = CH_3, C_6H_5)$$

$$\Delta(R)\Lambda(S)\text{-}[Co(acac)_2(^-NRCH_2CH_2NH_2)] \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \Delta(S)\Lambda(R)\text{-}[Co(acac)_2(^-NRCH_2CH_2NH_2)] \quad (2)$$

$$\Delta(S)\Lambda(R)\text{-}[Co(acac)_2(^-NRCH_2CH_2NH_2)] + H_2O \underset{k'_{-H^+}}{\overset{k'_{+H^+}}{\rightleftharpoons}} \Delta(S)\Lambda(R)\text{-}[Co(acac)_2(RNHCH_2CH_2NH_2)]^+ + OH^- \quad (3)$$
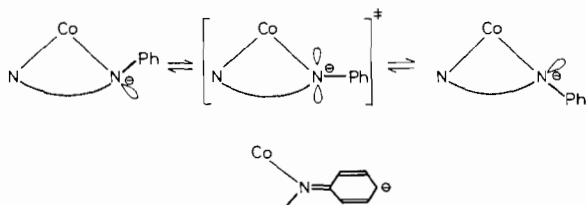
Fig. 3. Inversion at the chiral nitrogen center in the Co–Ph-en complex (upper), and stabilization of the trigonal planar intermediate through $(p-p)_\pi$ conjugation (lower).

14, as has been estimated for other cobalt(III)–amine complexes [1, 11], the reprotonation rates (k_{+H^+}, k'_{+H^+}) must be diffusion controlled for those de-protonated complexes. In that case, the relatively small $k_D/(k_1$ or $k_{-1})$ ratios for the Ph-en complex come from faster rates of inversion. This could result from an increased stabilization of the trigonal planar intermediate of the amide group through $(p-p)_\pi$ conjugation, which will lower the barrier to inversion (Fig. 3). Inversion at nitrogen centers of amide complexes (MNR^1R^2) can be compared to that of tertiary amines. The M–N bond can be considered in the same light as a C–N bond. The effect of the $(p-p)_\pi$ interaction on the rates of inversion in pyramidal $NR^1R^2R^3$ compounds has been studied with N-substituted aziridines [12]. The activation energy of inversion for N-phenyl-aziridine is lower by *ca.* 30 kJ mol^{-1} than that for N-methylaziridine.

Acknowledgements

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