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CHROMATOGRAPHIC SEPARATION OF THE DIASTEREOMERS OF THE BIS(2,4-PENTANEDIONATO)[2-(METHYLSELENO)ETHYLAMINE]-COBALT(III) ION ON A COLUMN OF SULPHOETHYL-TOYOPEARL AND DETERMINATION OF THE RATE OF INVERSION AT THE SELENIUM ATOM

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SUMMARY

A high-performance liquid chromatographic (HPLC) method was successfully applied to kinetic studies of the inversion at the selenium atom of $[\text{Co}(\text{acac})_2(\text{CH}_3\text{SeCH}_2\text{CH}_2\text{NH}_2)]^+$ (acac = 2,4-pentanedionate ion). The complex was separated into two racemic pairs, $\Delta(R)$, $\Lambda(S)$ and $\Delta(S)$, $\Lambda(R)$, by column chromatography on sulphoethyl (SE)-Toyopearl. The racemate, $\Delta(R)$, $\Lambda(S)$ or $\Delta(S)$, $\Lambda(R)$, was epimerized in $0.05 \text{ mol dm}^{-3} \text{ Na}_2\text{SO}_4$, and then the products, $\Delta(R)$, $\Lambda(S)$ and $\Delta(S)$, $\Lambda(R)$, were separated on SE-Toyopearl packed in an HPLC column. The activation enthalpy obtained, $\Delta H^* = 113 \text{ kJ mol}^{-1}$, is the highest reported so far for inversion of coordinated selenide.

INTRODUCTION

In a previous paper¹, we described the preparation of chiral cation-exchange Toyopearl* derivatives and successfully applied columns of these materials to the chromatographic resolution of cobalt(III) complexes. An achiral cation exchanger, sulphoethyl (SE)-Toyopearl, was also described¹, and it was found that this exchanger is more effective than sulphopropyl (SP)-Sephadex in the separation of diastereomers of uni- and dipositive cobalt(III) complexes². One of the important advantages of Toyopearl derivatives is that they are hard gels³, and they are very suitable for use in high-performance liquid chromatography (HPLC) under a reasonable pressure³.

* Toyopearl, a product of Toyo Soda (Tokyo, Japan), is the same material as Fractogel TSK available from E. Merck (Darmstadt, F.R.G.).

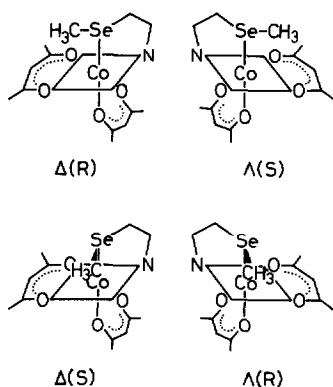


Fig. 1. Four stereoisomers of $[\text{Co}(\text{acac})_2(\text{CH}_3\text{SeCH}_2\text{CH}_2\text{NH}_2)]^+$.

The selenium atom of 2-(methylseleno)ethylamine becomes chiral on coordination to a cobalt(III) ion. In this paper, we describe the separation of the two racemic pairs of diastereomers, $\Delta(R), \Lambda(S)$ and $\Delta(S), \Lambda(R)$, of $[\text{Co}(\text{acac})_2(\text{CH}_3\text{SeCH}_2\text{CH}_2\text{NH}_2)]^+$ (acac = 2,4-pentanedionato) (Fig. 1) by column chromatography on SE-Toyopearl, and application of the HPLC method to kinetic studies of inversion at the selenium atom. The inversion of selenium in this complex is so slow that the two pairs of diastereomers could be separated by ordinary column chromatography. A solution containing the racemate, $\Delta(R), \Lambda(S)$ [or $\Delta(S), \Lambda(R)$], was epimerized, and then the two pairs of diastereomers, $\Delta(R), \Lambda(S)$ and $\Delta(S), \Lambda(R)$, were separated using SE-Toyopearl packed in an HPLC column to study the kinetics. This method has the great advantages that only a short elution time is required and that only micro quantities of samples are necessary.

EXPERIMENTAL

Preparation of $[\text{Co}(\text{acac})_2(\text{CH}_3\text{SeCH}_2\text{CH}_2\text{NH}_2)]\text{PF}_6$

To a solution of *trans*- $[\text{Co}(\text{acac})_2(\text{H}_2\text{O})_2]^{4+}$ (0.50 g, 1.71 mmol) in ethanol (30 cm^3) were added acetic acid (2 cm^3) and a solution of 2-(methylseleno)ethylammonium chloride⁵ (0.30 g, 1.71 mmol) and sodium ethoxide (0.29 g, 4.3 mmol) in ethanol (20 cm^3). The resulting purple solution was stirred for 10 min, and then lead dioxide (0.21 g, 0.877 mmol) was added. After stirring for an additional 20 min, the reaction mixture was filtered. The green filtrate was diluted with water (300 cm^3) and applied on a column (6 × 4.5 cm I.D.) of SP-Sephadex C-25. The adsorbed material was eluted with 0.1 mol dm^{-3} NH_4PF_6 , and the eluate containing the green band was collected. The eluate was evaporated to a small volume to yield green crystals, which were collected by filtration and recrystallized from water in a yield of 0.10 g. Found: C, 28.86; H, 4.41; N, 2.65%. Calculated for $\text{C}_{13}\text{H}_{23}\text{NCoF}_6\text{O}_4\text{PSe}$: C, 28.90; H, 4.29; N, 2.59%.

Separation of the diastereomers

About 5 mg of $[\text{Co}(\text{acac})_2(\text{CH}_3\text{SeCH}_2\text{CH}_2\text{NH}_2)]\text{PF}_6$ dissolved in a small amount of water was applied on a column (30 × 1.1 cm I.D.) of SE-Toyopearl

HW-40 {fine; ion-exchange capacity for $[\text{Co}(\text{en})_3]^{3+}$ (ref. 6), 0.45 mmol g^{-1} }. On elution with $0.05 \text{ mol dm}^{-3} \text{ Na}_2\text{SO}_4$, the column showed two green bands, I and II, with an order of elution representing first the racemate of the pair of diastereomers $\Delta(R)$, $\Lambda(S)$ and then $\Delta(S)$, $\Lambda(R)$. The complexes were not isolated because they are likely to epimerize. Each eluate was kept in a freezer at *ca.* -20°C for kinetic studies. The isomers do not interconvert detectably over a period of at least 1 month under the given conditions. When the complex was eluted with $0.05 \text{ mol dm}^{-3} \text{ Na}_2[\text{Sb}_2(d\text{-tart})_2]$, the column also showed two green bands, I and II, in that order of elution. The front (I-1 and II-1) and the tail (I-2 and II-2) of each of the two bands showed enantiomeric CD patterns, indicating partial resolution of the enantiomers.

Kinetics

A solution containing $\Delta(R)$, $\Lambda(S)$ (*ca.* $10^{-4} \text{ mol dm}^{-3}$) in $0.05 \text{ mol dm}^{-3} \text{ Na}_2\text{SO}_4$ was epimerized in the temperature range $40.0\text{--}55.0^\circ\text{C}$. Portions of the reaction mixture were withdrawn at timed intervals and then chromatographed (sample volume: $1 \cdot 10^{-3} \text{ cm}^3$) on a column ($50 \times 0.4 \text{ cm}$ I.D.) of SE-Toyopearl HW-40 {super-fine; ion-exchange capacity for $[\text{Co}(\text{en})_3]^{3+}$, 0.48 mmol g^{-1} ; prepared by the slurry packing technique³} with a 0.05 mol dm^{-3} aqueous solution of Na_2SO_4 as the eluent (flow-rate, $0.2 \text{ cm}^3 \text{ min}^{-1}$; pressure, *ca.* 5 kg cm^{-2}). The chromatography was carried out at ambient temperature with a Shimadzu-DuPont LC-2 HPLC system, and the complexes were detected with a Shimadzu-DuPont STD-1 spectrophotometric detector at 260 nm. The areas of the two bands on the chromatograms were determined by weighing paper cut-outs matching the bands.

Measurements

Absorption and circular dichroism (CD) spectra were measured with a Hitachi 323 spectrophotometer and a JASCO J-40 CS spectropolarimeter, respectively. ^1H NMR spectra were obtained in CDCl_3 with a JEOL PMX-60 spectrometer using TMS as an internal reference.

RESULTS AND DISCUSSION

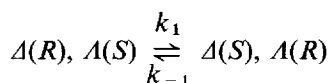
Characterization of the isomers

Four stereoisomers, $\Delta(R)$, $\Delta(S)$, $\Lambda(R)$ and $\Lambda(S)$, are possible for $[\text{Co}(\text{acac})_2(\text{CH}_3\text{SeCH}_2\text{CH}_2\text{NH}_2)]^+$ (Fig. 1). The ^1H NMR spectrum of the isolated hexafluorophosphate salt shows two singlet signals at δ 1.63 and 1.94 ppm, respectively, attributable to the methylseleno group with an intensity ratio of 1.3:1.0. Examination of molecular models indicates that in the $\Delta(R)$ and $\Lambda(S)$ configurations, one of the two acac rings strongly shields the methyl protons on selenium. Column chromatography of the complex on SE-Toyopearl {eluent, $0.05 \text{ mol dm}^{-3} \text{ Na}_2\text{SO}_4$ or $0.05 \text{ mol dm}^{-3} \text{ Na}_2[\text{Sb}_2(d\text{-tart})_2]$ } develops two bands, I and II, in the ratio 1.3:1.0. Accordingly, band I was assigned to the racemate of the pair of diastereomers $\Delta(R)$ and $\Lambda(S)$ and band II to $\Delta(S)$ and $\Lambda(R)$. The eluents were used for kinetic studies of epimerization without isolation of the complexes. The absorbance at 260 nm did not change detectably during epimerization, indicating that the isomers have almost the same absorbance at this wavelength. Hence, the distribution of the isomers in a reaction mixture was obtained from the band areas of the elution curve detected by the absorbance at 260 nm.

In general, the optical activity of a metal complex is explained by the superposition of the configurational (chiral arrangement of ligands around the metal ion) and the vicinal (chiral ligand) effects, the former being the larger⁷⁻⁹. Column chromatography using SE-Toyopearl and 0.05 mol dm⁻³ Na₂[Sb₂(*d*-tart)₂] partly resolved the complex into the enantiomers. The CD spectra of the four isomers changed slightly during epimerization. These observations suggest that the CD change is caused by the inversion at selenium, and that the configuration around the cobalt(III) ion remains unchanged.

Kinetics of the epimerization reaction

Fig. 2 shows the change in the elution curve obtained at intervals during the epimerization of $\Delta(R)$ and $\Lambda(S)$ at 45.5°C. The area of band I decreases whereas that of band II increases with time as the result of epimerization:



where k_1 and k_{-1} denote the forward and reverse rate constants, respectively. Measurements were carried out in the temperature range 40.0–55.0°C. In each kinetic run, the plot of $\ln [S_t^I / (S_t^I + S_t^{II}) - S_\infty^I / (S_\infty^I + S_\infty^{II})]$ vs. time gave a straight line for at least two half-lives (S_t^I , S_t^{II} , S_∞^I and S_∞^{II} denote the areas of bands I and II at time t and at infinite time). The slope gave the first-order rate constant, k_{obsd} (Fig. 3). The rate constants for the epimerization were calculated from the equilibrium constant, K_{eq} , and the observed rate constant:

$$K_{\text{eq}} = k_1/k_{-1} = S_\infty^{II}/S_\infty^I$$

$$k_{\text{obsd}} = k_1 + k_{-1}$$

The K_{eq} value was found to be 1.1, independent of temperature (40.0–55.0°C). The values of k_1 and k_{-1} are given in Table I. The rate was independent of pH in the

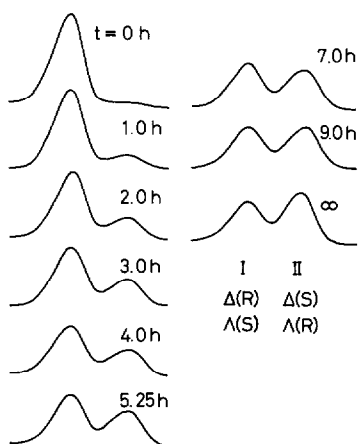


Fig. 2. Change in the elution curve during the epimerization of $\Delta(R)$, $\Lambda(S)$ -[Co(acac)₂·(CH₃SeCH₂CH₂NH₂)]⁺ in 0.05 mol dm⁻³ Na₂SO₄ at 45.5°C.

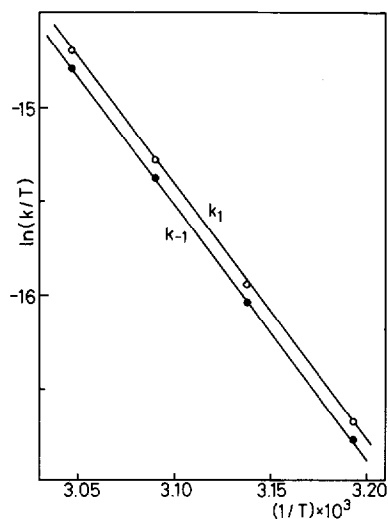
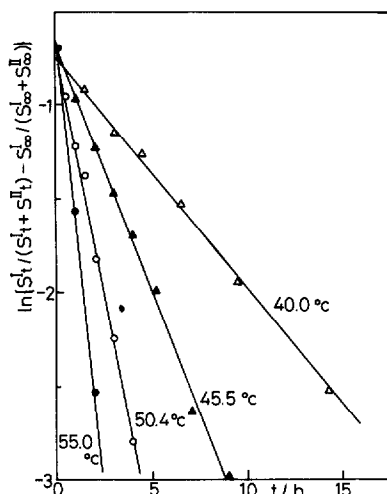


Fig. 3. Plots of $\ln[S_I^I/(S_I^I + S_I^{II}) - S_{\infty}^I/(S_{\infty}^I + S_{\infty}^{II})]$ against time at 40.0, 45.5, 50.4 and 55.0°C.

Fig. 4. Eyring treatments of $\ln(k_1/T)$ vs. T^{-1} (○) and $\ln(k_{-1}/T)$ vs. T^{-1} (●).

range 4.1–5.6. Eyring treatments of $\ln(k_1/T)$ and $\ln(k_{-1}/T)$ vs. T^{-1} (Fig. 4) yielded the activation parameters given in Table I.

Inversion at a coordinated selenide site has been investigated over the last decade, and it has been found that it is too rapid for the resolution of complexes of Pt^{II} , Pt^{IV} and Pd^{II} to be accomplished. The kinetics have been studied by the dynamic NMR method¹⁰. However, recently we resolved *trans*(tertiary amine nitrogen, Se)- $\{\text{Co}(\text{RSeCH}_2\text{CH}_2\text{NH}_2)[\text{N}(\text{CH}_2\text{CH}_2\text{NH}_2)_3]\}^{3+}$ ($\text{R} = \text{CH}_3, \text{C}_2\text{H}_5, \text{C}_6\text{H}_5\text{CH}_2$), in which the configuration of the selenium atom is the sole source of chirality, and studied the kinetics of racemization^{11,12}. The activation enthalpies obtained were almost the same for the three complexes, $\Delta H^* = 95 \text{ kJ mol}^{-1}$ ¹². Thus, a ΔH^* of

TABLE I

RATE CONSTANTS AND THERMODYNAMIC PARAMETERS FOR EPIMERIZATION OF $[\text{Co}(\text{acac})_2(\text{CH}_3\text{SeCH}_2\text{CH}_2\text{NH}_2)]^+$ IN $0.05 \text{ mol dm}^{-3} \text{ Na}_2\text{SO}_4$

$$\Delta(R), \Delta(S) \frac{(1) k_1}{(2) k_{-1}} \Delta(S), \Delta(R)$$

| Temperature (°C) | $k_{\text{obsd}} (10^{-5} \text{ sec}^{-1})$ | $k_1 (10^{-5} \text{ sec}^{-1})$ | $k_{-1} (10^{-5} \text{ sec}^{-1})$ |
|------------------|----------------------------------------------|---------------------------------------------------------------|------------------------------------------------------|
| 40.0 | 3.39 ± 0.09 | 1.78 ± 0.06 | 1.61 ± 0.06 |
| 45.5 | 7.18 ± 0.14 | 3.76 ± 0.10 | 3.42 ± 0.10 |
| 50.4 | 14.2 ± 0.04 | 7.44 ± 0.03 | 6.76 ± 0.03 |
| 55.0 | 25.8 ± 0.06 | 13.5 ± 0.04 | 12.3 ± 0.04 |
| | $\Delta H^* (\text{kJ mol}^{-1})$ | $\Delta S^* (\text{J mol}^{-1} \text{ } ^\circ\text{K}^{-1})$ | $\Delta G^* (25^\circ\text{C}) (\text{kJ mol}^{-1})$ |
| (1) | 113.2 ± 1.8 | 25.2 ± 5.6 | 105.7 ± 2.5 |
| (2) | 113.3 ± 1.8 | 25.1 ± 5.7 | 105.8 ± 2.5 |

113 kJ mol⁻¹ as obtained in this study is by far the largest activation enthalpy reported so far for inversion of coordinated selenide.

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