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The Isomers of the Bis(1-thia-4,7-diazacyclononane)cobalt(III) Ion: Separation and Characterization

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Abstract

The two geometric isomers *cis* and *trans* of the bis(1-thia-4,7-diazacyclononane)cobalt(III) ion have been separated and crystallized as the pure isomers by fractional crystallization, aided by cation-exchange chromatography on SP-Sephadex. The pure isomers are characterized by ^{13}C NMR and UV–Vis spectroscopy. The isomers undergo a base-catalyzed isomerization to an equilibrium mixture *cis*/*trans ca.* 4/1. This isomerization is unusually facile, and occurs at a significant rate at pH down to about 5 at room temperature, so that chromatographic separations require acidic conditions. Separation by IE-HPLC has been demonstrated as a valuable tool to separate (3+)-charged complexes on an analytical scale, and can indicate the optimum conditions for preparative scale separations on SP-Sephadex columns. The isomerization process has been investigated as a function of temperature and pH using IE-HPLC, and ^{13}C NMR and visible spectroscopy.

Introduction

Various aspects of the chemistry of bis complexes with the macrocyclic ligand 1-thia-4,7-diazacyclononane, $[M(tasn)_2]^{n+}$, have been reported in recent papers [1–6], and comparisons have been made with complexes of the analogous open-chain ligand di(2-aminoethyl)sulfide, $[M(daes)_2]^{n+}$. The structures of these and related ligands discussed in this paper are shown in Fig. 1: 2-aminoethyl-3-aminopropylsulfide (aeaps), 4,7-bis(2-aminoethyl)-1-thia-4,7-diazacyclononane (dats), diethylenetriamine (dien) and 1,4,7-triazacyclodecane (tacd).

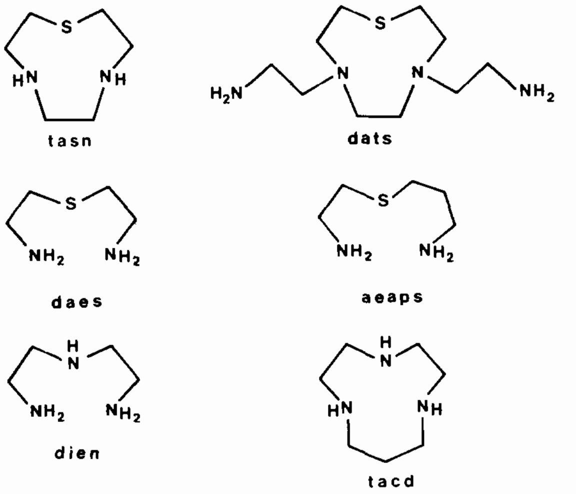

Fig. 1. Ligands discussed in this paper.

For complexes $[M(tasn)_2]^{n+}$ *cis* and *trans* geometric isomers are possible, and these are shown with their symmetries in Fig. 2. However, the separation or isolation of both isomers has not previously been achieved for any one system M = Co(III) [1–3], Ni(II) [4, 5], Cu(II) [6], and the factors determining the apparent stabilities of the isomers are unclear.

The cobalt(III) complex $[Co(tasn)_2]^{3+}$ was first prepared by oxygen oxidation of Co(II) in the presence of tasn [1]. Passage through SP-Sephadex and the use of other chromatographic methods failed to indicate any separation of the two possible isomers [1, 3], although the ^{13}C NMR spectrum of the isolated $[Co(tasn)_2](ClO_4)_3$ run in D_2O showed a number of peaks which was consistent

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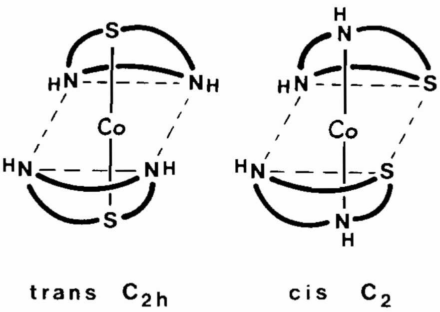

Fig. 2. Geometric isomers of $[Co(tasn)_2]^{3+}$, and their point-group symmetries assuming conformational mobility.

with a mixture of the two isomers, at least in solution [1, 3]. The apparent difficulty in their separation has remained puzzling.

The present work describes analytical separation of the isomers by IE-HPLC, and crystallization and preparative-scale ion-exchange SP-Sephadex chromatography experiments with $[Co(tasn)_2]^{3+}$, which have led to our isolation of the pure geometric isomers. The isomers have been characterized by ^{13}C NMR and UV–Vis spectra, and equilibration. An unusual feature of $[Co(tasn)_2]^{3+}$ is that a base-catalyzed isomerization takes place at relatively low pH. The isomerization was detected by IE-HPLC over the range pH 3–8. Thus the ^{13}C NMR spectra obtained at pH 9 were a superposition of the spectra of the two isomers in equilibrium with the ratio *cis/trans ca.* 4/1.

Experimental

Synthesis of cis-$[Co(tasn)_2]Br_3 \cdot 2H_2O$

A solution of tasn·2HBr (1.04 g) was partially neutralized with NaOH (5.0 ml of 1 M). This mixture was added to a stirred solution of $Co(CH_3COO)_2 \cdot 4H_2O$ (0.40 g, 0.0016 mol). The volume was increased to 60 ml, and CO_2-free air was passed through for 4 h. The deep orange–red solution was filtered and absorbed on a column (3 cm i.d. × 3 cm) of Dowex 50W-X2 resin, 200–400 mesh, H^+-form, and washed on with 0.01 M HCl (or HBr). The column was washed with 1 M HCl (or HBr), then the complex was eluted off with 3 M HCl (or HBr). A brownish presumably highly-charged impurity was left on the column.

The eluate was evaporated, when some green material separated (*ca.* 0.2 g), and this was filtered off at a small volume of the solution and discarded. *Anal.* Calc. for $[Co(C_6H_{14}N_2S)_2]_2[CoBr_4]_3$: C, 15.7; H, 3.1; N, 6.1; S, 7.0. Found: C, 15.7; H, 3.3; N, 6.1; S, 6.8%. The solution was then evaporated almost to dryness to remove most of the HX. The crude product so obtained was dissolved in water, and applied to a large column (4.5 cm i.d. × 40 cm) of SP-Sephadex C-25 cation-exchange resin. On elution with 0.2 M Na_2SO_4/H_2SO_4 pH 2, a number of bands separated: (blue/purple/yellowish) first; orange–yellow of $[Co(tasn)_2]^{3+}$; purple; orange; pink; pink.

The band containing $[Co(tasn)_2]^{3+}$ was collected and applied to a small column (1.2 × 4 cm) of Dowex 50W-X2 resin, H^+-form. The column was washed with 1 M HBr to remove all Na^+, then the complex was eluted off with 3 M HBr. This eluate was evaporated to a small volume (3 ml). Ethanol was added dropwise, and on cooling, the complex started to separate. As the complex crystallized, further ethanol was added gradually to effect a fractionation of the isomers. After refrigeration, the complex as yellow–orange needles was filtered off, washed with ethanol and acetone, and air-dried. Yield 0.51 g, 49%. *Anal.* Calc. for $Co(C_6H_{14}N_2S)_2Br_3 \cdot 2H_2O$: C, 23.0; H, 5.1; Br, 38.2; N, 8.9; S, 10.2. Found: C, 23.0; H, 4.8; Br, 38.2; N, 8.8; S, 10.3%.

The isomeric compositions of the solid thus isolated and the mother liquor were determined from the ^{13}C NMR spectra run in D_2O/HBr (mother liquor first evaporated to dryness). From several syntheses, the isolated solids were *cis*-$[Co(tasn)_2]Br_3$ of high purity. The content of *trans* isomer was highest (*ca.* 5%) when the yield was highest (50%). Mother liquors were enriched in *trans* (typically *ca.* 50% *trans*).

Pure *cis* isomer as the bromide can be obtained from these first crystallized products (95% *cis*) by recrystallization from HBr solution with addition of ethanol. Alternatively, purification can be effected by re-chromatography on SP-Sephadex with acidic conditions maintained throughout (washing on with 0.01 M HCl and elution with Na_2SO_4/H^+) when the small amount of *trans* appears at the tail of the $[Co(tasn)_2]^{3+}$ band and is collected separately (see below). ^{13}C NMR of *cis* bromide in D_2O/HBr: δ 54.7, 53.3, 52.5, 49.9, 38.5, 35.2 ppm.

Crystallization of trans-$[Co(tasn)_2](ClO_4)_3$ *[1, 2]*

The perchlorate salt of the *trans* isomer was obtained by slow precipitation using $NaClO_4$ from a slightly basic solution (pH 9) of *cis*-$[Co(tasn_2)]Cl_3$ isolated after Sephadex chromatography (Na_2SO_4/H_2SO_4 elution, then work-up from Dowex 50W-X2 with 3 M HCl elution). The product from slow crystallization was the pure *trans* isomer from the ^{13}C NMR in D_2O/HCl, δ 55.3, 52.8, 37.4 ppm. The product was recrystallized from water with ethanol vapour diffusion to give crystals suitable for X-ray diffraction work [2].

^{13}C *NMR Spectra*

20.1 MHz ^{13}C NMR spectra in D_2O, broad-band proton decoupled, were recorded on a Bruker

WP80-DS spectrometer locked to deuterium. An 8192 data table was used. For spectra in D_2O, a capillary of t-butyl alcohol provided a reference signal: 618.9 Hz, δ 30.79 ppm for CH_3 downfield from $SiMe_4$. (This reference signal was measured for a t-butyl alcohol capillary in $CDCl_3$ against $SiMe_4$ as internal reference.)

As with other cobalt(III) (3+)-charged complexes previously studied, the chemical shifts of the resonances of the $[Co(tasn)_2]^{3+}$ isomers showed negligible variation with different anions; any variation was similar to that found between different recordings of the same complex.

Ion-exchange High Performance Liquid Chromatography [7]

A Waters HPLC system (M6000A solvent delivery unit, M481 variable-wavelength detector, U6K universal injector) was employed. Columns used were a TSKgel SP-5PW column (Toyo Soda, Japan), or a Protein Pak SP-5PW column (Waters). Both columns had dimensions 7.5 mm i.d. × 75 mm and showed identical performance.

The eluent solutions were prepared using distilled deionized water. All solutions were filtered and degassed before use by passage through an all-glass filter unit fitted with a 0.45 μm membrane (Millipore MF type membrane). Sample solutions were obtained by dissolving the pure compound in water and filtering through a Millex HV4 filter unit (Durapore 0.45 μm) prior to injection.

Separations at different temperatures were achieved by immersing column and inlet in a thermostatted bath. The column was washed initially with distilled water (10 ml, 1.0 ml min^{-1}), then equilibrated with the eluent (30 ml, 1.0 ml min^{-1}). All separations were made with isocratic elution. Samples of 2–25 μl (Hamilton 25 μl syringe) were injected. Chromatograms were recorded from 0–50 min, with full-scale absorbance in the range 0.01–0.5 at different wavelengths.

Separation of $[Co(tasn)_2]^{3+}$ Isomers on SP-Sephadex

From an equilibrium mixture, only a partial separation of the two isomers could be obtained on SP-Sephadex cation-exchange resin. $[Co(tasn)_2]Br_3$ (0.1 g) was applied in water (equilibrium mixture) to a column (2.5 cm i.d. × 40 cm) of the resin. The column was eluted with 0.2 M Na_2SO_4/H_2SO_4 pH 2, and the effluent from the partially separated band was collected in three approximately equal fractions. The complex in each of fractions (1) and (3) was obtained by applying the effluent to a small column of Dowex 50W-X2 cation-exchange resin, H^+-form and eluting off with 3 M HCl as described above. The isomer compositions of these fractions were determined from the ^{13}C NMR spectra in D_2O/HCl to be: fraction (1) orange–yellow, pure *cis*; fraction (3) orange, *ca.* 65% *cis* and 35% *trans*.

A similar procedure was used to obtain pure *cis* isomer from the first crystallized $[Co(tasn)_2]Br_3$ from the synthesis (>95% *cis*), except that the sample was applied in 0.01 M HCl solution to preclude any isomerization, and the column was lightly loaded (0.5 g on a column 4.5 cm i.d. × 40 cm). The bands were almost separated, the small tailing *trans* band being distinctly more orange than the first yellow *cis* band. A middle fraction was reserved for subsequent recycling. The two isomers were worked up on Dowex resin with elution by 3 M HBr, and precipitated with ethanol. ^{13}C NMR spectra confirmed the isomeric purities of the compounds thus obtained.

Results and Discussion

Synthesis of $[Co(tasn)_2]^{3+}$

The complex was synthesized previously by oxygen oxidation of a mixture of Co(II) + 2tasn, and it was isolated either as the chloride salt [3], or as the perchlorate salt by precipitation from the (neutral) chloride solution [1]. These products were characterized in neutral aqueous solution, where in each case an isomeric mixture of *cis* and *trans* forms in the ratio *ca.* 4/1 was found, as indicated by the ^{13}C NMR spectra run in D_2O only. These equilibrium spectra presumably correspond to the approximately equilibrium isomeric mixtures in the isolated products, since isomerization has been demonstrated to occur only slowly in aqueous solutions of pH 5 or less (see later) in which the ^{13}C NMR spectra were obtained. However, the rate of isomerization depends critically on the pH in this neutral region. Also, it has now been shown that crystallization of the perchlorate from a slightly basic solution gives pure *trans* isomer, so that the formation of *trans* was apparently not great in the previous preparations.

The present synthesis of $[Co(tasn)_2]^{3+}$ is a modification of the method reported earlier. Air-oxidation is now used on a mixture of the following stoichiometry:

$$Co_{aq}^{2+} + 2(tasn{\cdot}2HBr) + 3NaOH + (1/4)O_2 \longrightarrow [Co(tasn)_2]^{3+} + 3Na^+ + 4Br^- + (7/2)H_2O$$

The synthesis was inefficient in that numerous by-products were formed, giving the yield of $[Co(tasn)_2]^{3+}$ as relatively low (50%). One identified by-product was $[Co(tasn)_2]_2[CoBr_4]_3$. Two cation-exchange treatments were necessary, using Dowex 50W-X2 and SP-Sephadex, to separate these impurities. Further degradation products were formed if the work-up was prolonged, suggesting that the

$[Co(tasn)_2]^{3+}$ ions are only moderately stable, a situation paralleling that with the other thioether complexes studied $[Co(daes)_2]^{3+}$ [8] and $[Co(aeaps)_2]^{3+}$ [9].

The following properties of the system underlie the isolation procedure of the two isomers: (1) isomerization occurs rapidly in slightly basic solution (and in warm neutral solution), but is inhibited in acidic solution, $pH < 3$; (2) the equilibrium established in aqueous solution of $pH \approx 9$ has the ratio *cis*/*trans* *ca.* 4/1; and (3) both the perchlorate and bromide salts of the *trans* isomer have lower solubility than the *cis* salts. Thus careful crystallization by gradual evaporation from slightly basic solutions of the mentioned salts yields the pure *trans* isomers.

When the perchlorate salt, which had been previously characterized in neutral solution as largely *cis* [1], was crystallized slowly from a slightly basic solution by addition of ethanol, the resulting crystals consisted entirely of the orange *trans* isomer. This demonstrated that isomerization *cis* → *trans* had occurred in the slightly basic solution, and that the *trans* is the less soluble isomer as the perchlorate.

Salts of the pure *cis* isomer were more troublesome to obtain pure. During synthesis, the equilibrium is established in the slightly basic or neutral solution, and this composition can be frozen by maintaining acidic conditions throughout the subsequent cation-exchange purification (elution from Dowex 50W-X2 with HCl, elution from Sephadex with Na_2SO_4/H^+, and elution from Dowex 50W-X2 with HBr). Some of the *trans* isomer present is removed in the discarded tail of the $[Co(tasn)_2]^{3+}$ Sephadex band, see later. Crystallization from the final HBr eluate gave essentially the predominating *cis*-$[Co(tasn)_2]Br_3$ isomer as indicated by the ^{13}C NMR spectrum. The *cis* isomer crystallizes first because it predominates in the equilibrium mixture (80%) despite its being the more soluble isomer. These products usually contained about 5% *trans* isomer, although this isomer was undetectable in products which were obtained in lower yields (40%).

The high isomeric purity of the isolated, yellow–orange product *cis*-$[Co(tasn)_2]Br_3 \cdot 2H_2O$ was indicated by the ^{13}C NMR spectrum in D_2O/HBr, where the signals from *trans* were weak (δ 55.3, 52.8 as a shoulder on a *cis* peak, 37.6). From the relative integrals of the signals from the two isomers and allowing for the different numbers of carbon atoms per molecule contributing to the peaks (*trans*/*cis* = 2), the mole proportion of *trans* was estimated as <5% for the highest yield product.

^{13}C *NMR Spectral Characterization of the* $[Co(tasn)_2]^{3+}$ *Isomers*

The two isomers, whose isolation is described above, are distinguished and assigned readily from their ^{13}C NMR spectra (Fig. 3), which were run in acidified D_2O to avoid isomerization. The different numbers of resonances reflect their different symmetries: *cis* with molecular symmetry C_2 has six equal resonances, and *trans* with additionally a centre of inversion giving C_{2h} symmetry has only three equal resonances.

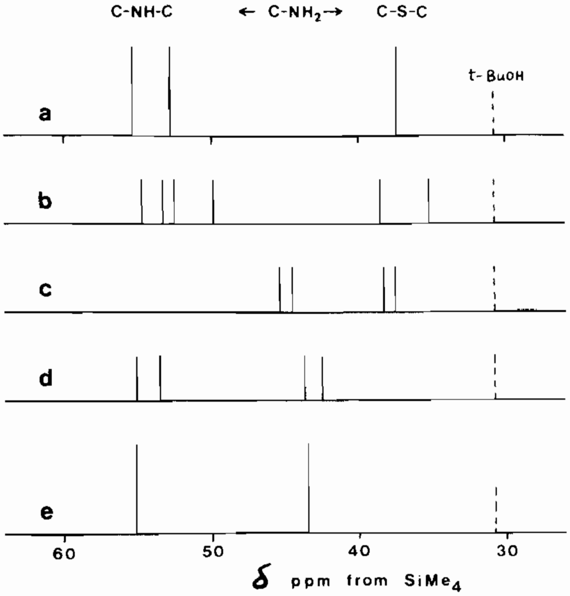

Fig. 3. 20.1-MHz ^{13}C NMR spectra in acidified D_2O: (a) *trans*-$[Co(tasn)_2](ClO_4)_3$; (b) *cis*-$[Co(tasn)_2]Br_3$; (c) *u-fac*-$[Co(daes)_2]Br_3$; (d) *u-fac*-$[Co(dien)_2]Cl_3$; (e) *s-fac*-$[Co(dien)_2]Cl_3$. The reference is a t-BuOH capillary, δ 30.8 ppm.

The isomers of $[Co(tasn)_2]^{3+}$ have two chemically different types of carbons, C–NH and C–S (in the ratio 2/1), and the resonances fall into two sets accordingly. Those in the downfield set at δ 49–56 ppm are assigned as C–NH since they correspond to resonances in the two facial $[Co(dien)_2]^{3+}$ isomers *s-fac* and *u-fac* but have no correspondence with resonances from *u-fac*-$[Co(daes)_2]^{3+}$. The upfield resonances at δ 35–39 are assigned as C–S, having correspondence in *u-fac*-$[Co(daes)_2]^{3+}$ but not in facial $[Co(dien)_2]^{3+}$, Fig. 3 [9, 10].

Isomer Separation by Ion-exchange High Performance Liquid Chromatography

The chromatographic separation of an equilibrium mixture of the $[Co(tasn)_2]^{3+}$ geometric isomers in water obtained by elution with 0.194 M sodium sulfate at pH 5 is shown in Fig. 4 for three different temperatures. The separations were achieved in less than 20 min at a flow rate of 1.0 ml min^{-1}. The first band (*cis* isomer) is approximately three times as large as the second band (*trans* isomer). Notwithstanding different possible light absorptions by the isomers, the first eluted band must be the major isomer, and the other studies (particularly the ^{13}C

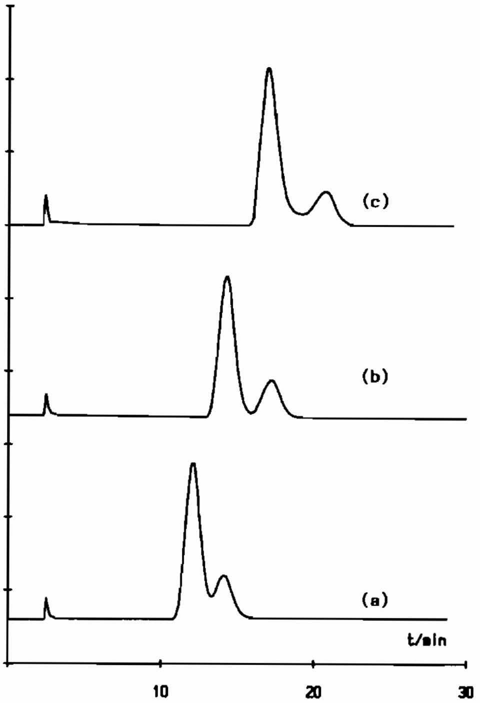

Fig. 4. Chromatograms for the IE-HPLC separation of the $[Co(tasn)_2]^{3+}$ isomers with eluent 0.19 M Na_2SO_4 pH 5 at different column temperatures: (a) 0 °C; (b) 22 °C; (c) 44 °C. Detection at 450 nm, ordinate division 0.05 absorption units; amount applied 40 nmol in 5 μl.

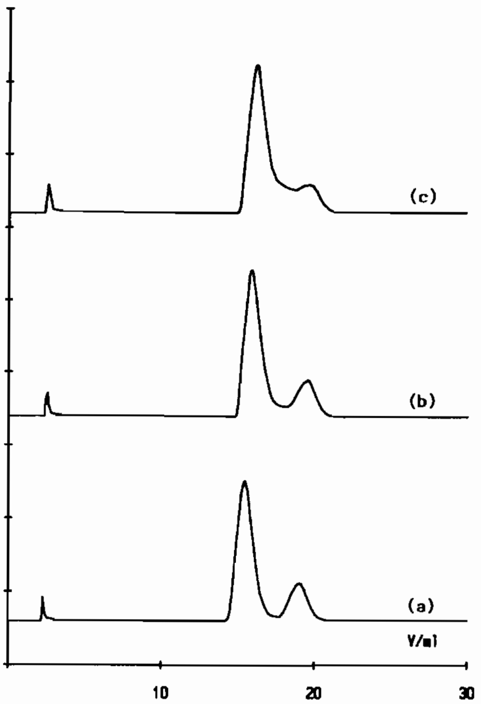

Fig. 5. Chromatograms for the IE-HPLC separation of the $[Co(tasn)_2]^{3+}$ isomers with eluent 0.19 M Na_2SO_4, pH 5, at different flow-rates: (a) 1.0; (b) 0.5; (c) 0.2 ml min^{-1}. Other parameters were column temperature 43 °C; detection at 450 nm, ordinate division 0.05 absorption units; amount applied 40 nmol in 5 μl.

NMR spectrum of an equilibrium mixture in water) show this to be *cis*.

The separation shows some temperature dependence, with the largest separation of the two peaks being achieved at 44 °C. However, the cleanest separation with respect to the baseline was at 22 °C. This result is not in accordance with earlier IE-HPLC results on related systems, where the separation of particular pairs of complexes or isomers has been shown to change in positive and negative directions when the temperature is raised [7]. However, the number of effective plates for this type of column has been shown to increase with temperature, thus producing smaller bandwidths, and for the particular column used here, we have found the number of effective plates to be 1400 at 0 °C, 2000 at 22 °C, and 2600 at 44 °C.

This unexpected behaviour of the $[Co(tasn)_2]^{3+}$ isomers is explained by some isomerization occurring on the column. For evidence of this, a series of separations with 0.194 M Na_2SO_4 (pH 5) at 43 °C at different flow rates was carried out. The decreasing separation as flow rate is decreased (1.0, 0.5, and 0.2 ml min^{-1}), Fig. 5, indicates that isomerization between the two isomers is occurring, over a time scale of hours.

The pH dependence of the isomerization was examined in separations at 43 °C using 0.194 M Na_2SO_4 at different pH values, and the results are shown in Fig. 6. The chromatogram for the separation at pH 8.5 shows only one band, and this probably contained the two $[Co(tasn)_2]^{3+}$ isomers in admixture, with rapid equilibration between them being established during the chromatographic run. Rather small differences are observed for the separations at pH 3–5, but it seems clear that the isomerization is less pronounced at lowest pH. In more acidic solutions, $pH < 3$, we believe that cobalt(III) complexes may be reduced by the metal tubing in the IE-HPLC equipment, and this could affect isomerizations in some cobalt(III) systems.

Attempts to separate the enantiomers of the dissymmetric *cis* $[Co(tasn)_2]^{3+}$ isomer and thereby distinguish it from the achiral *trans* isomer by using optically active eluents sodium di-μ-(*R*,*R*)-tartrato-(4–)diantimonate(III) and acidified sodium (*R*,*R*)-tartrate pH 4 were unsuccessful. The elution with sodium tartrate gave two bands in comparable manner to the sulfate, but only one band was produced with the antimonate. This non-separation of the *cis* enantiomers is probably due to a poor discrimination by these eluent anions, although an especially fast racemization (faster than the *trans* → *cis* isomerization) cannot be excluded.

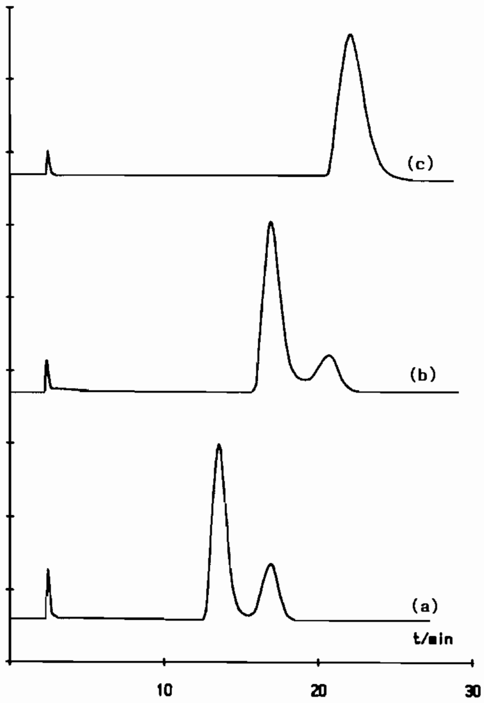

Fig. 6. Chromatograms for the IE-HPLC separation of the $[Co(tasn)_2]^{3+}$ isomers with 0.19 M Na_2SO_4 at different pH: (a) eluent pH 3.0; (b) 5.0; (c) 8.5 buffered with 5 mM tris-sulfate. Other parameters were column temperature 43 °C; flow-rate 1.0 ml min^{-1}; detection at 450 nm, ordinate division 0.05 absorption units; amount applied 40 nmol in 5 μl.

The utility of IE-HPLC for separating the $[Co(tasn)_2]^{3+}$ isomers was investigated concurrently with the column separations on SP-Sephadex (below). With both of these cation-exchange techniques, the separation of these isomers is difficult because the discrimination is small, but with acidified Na_2SO_4 as the most effective eluent the isomers can be almost completely separated under optimized conditions in both methods. The *cis* isomer elutes ahead of the *trans* in both methods, as expected for similar separation mechanisms.

The isomerization has been more readily apparent with the IE-HPLC work. Here, the degree of separation is optimized by higher temperature (44 °C), and at eluent pH 5 isomerization is apparent after about 30 min (Fig. 6). However, isomerization should be obviated by using room temperature, low eluent pH (pH 3), and high flow rates (1 ml min^{-1}) giving shorter elution times. With SP-Sephadex, isomerization is negligible at the room temperature and pH 2 used. In both forms of chromatography, isomerization occurring during runs carried out under less acidic conditions is manifested by a coalescence of the separate isomer peaks.

This work demonstrates that the IE-HPLC method offers outstanding advantages for separations of cationic complexes on an analytical scale: rapid separations, small quantities of material required, immediate detection, hardcopy output of detection, detection is readily quantified. For a new complex system like $[Co(tasn)_2]^{3+}$, optimum separation conditions can be readily determined by IE-HPLC, and then translated more or less directly to Sephadex column separations for preparative scale work.

Isomer Separation by Cation-exchange Chromatography on SP-Sephadex

The possible separation of the $[Co(tasn)_2]^{3+}$ isomers was tested on small columns of SP-Sephadex. Of the eluents Na_3PO_4, sodium tartrate and Na_2SO_4 which have been found to be the most discriminating with other complexes [11], only Na_2SO_4 (pH 5) effected a separation, and this was only partial with the columns used. It is clear from the subsequent work that isomer separation in this system is not possible under the basic conditions of Na_3PO_4 elution due to the rapid isomerization at pH 12, and the ineffectiveness of sodium tartrate may also be due to relatively rapid isomerization at the pH 6 used (by comparison with the IE-HPLC results), as well as to the relatively poor discrimination effected by the tartrate anion.

With acidic Na_2SO_4 there was no separation into distinct bands of the two isomers, but the single band graded in colour from orange–yellow (*cis*) at the head to orange at the tail (*trans*). The chromatographic discrimination between the $[Co(tasn)_2]^{3+}$ isomers seems unusually poor for isomeric cobalt(III) systems [11, 12]. Such discrimination is held to be largely a function of the relative ion-associations between the eluent anions and the N–H hydrogens on the isomeric complex cations, and is presumably unrelated to the facility of the isomerization in this system since isomerization (in solution at least) is precluded at the pH 2 used in the preparative chromatographic work.

This SP-Sephadex/Na_2SO_4 pH 2 procedure was unable to separate cleanly an equilibrium mixture of the isomers in a 40 cm long column. This was demonstrated by collecting the effluent from the single lengthened band of $[Co(tasn)_2]^{3+}$ in fractions, when pure *cis* was obtained in the initial fraction of the effluent, and the final fraction of the effluent was an isomer mixture (65% *cis*).

This Sephadex procedure was especially valuable however, for purifying the isomers, particularly for obtaining the pure *cis* from the first crystallized material from the synthesis (<5% *trans*). Provided that the column was relatively lightly loaded, the separation of the isomers on elution with Na_2SO_4/H^+ was almost complete, enabling cuts to be made to contain pure *cis* in the large first fraction and the pure *trans* in a small last fraction. A middle fraction containing a mixture was recycled subsequently.

Vis–UV Spectra

The absorption spectra were obtained in 0.01 M hydrochloric acid as solvent, wherein the spectra remain constant over days (Fig. 7). For the absorption peaks in the visible region, which are due to d–d transitions on the cobalt, it is expected that the molar absorbance in this region for the *cis* isomer may be a little larger than that for the *trans* isomer, since the latter contains a centre of symmetry. The fact that the absorption wavelength maxima and the band widths for the two isomers are similar indicates that the thioether and the imine group are close in the spectrochemical series as found also for other amine–thioether cobalt(III) complexes [9, 13, 14]. The slightly lower wavelength of the *cis* maximum absorption (475 nm) than the *trans* maximum (484 nm) accounts for the more yellow colour of the *cis* isomer.

The UV spectra of both isomers exhibit two allowed charge-transfer bands. The band at higher energy for both isomers is at 234 nm (ϵ 11 900 mol^{-1} dm^3 cm^{-1} for *cis*, 14 400 for *trans*). This band is always found in UV spectra of cobalt(III)–amine complexes and is due to an electronic transition from a σ-bonding orbital on the nitrogen to an empty d(σ^*) orbital on cobalt. A lower energy charge-transfer band is found at 284 nm (ϵ 14 300) for the *cis* isomer and at 316 nm (ϵ 13 100) for the *trans* isomer. These bands in the near-UV region are characteristic for cobalt(III) complexes with coordinating thioether sulphur atoms, and the transition is best described as from an orbital with 3p-character on sulphur (a σ^* orbital having π-symmetry with respect to the Co–S bond direction) to an empty cobalt d(σ^*) orbital [9].

The energy of the Co–S charge-transfer bands in cobalt(III) complexes with chromophores of the type CoN_4S_2 is sensitive to the geometry *cis* or *trans* of the coordinating thioether groups. For all reported examples of cobalt(III) thioether complexes the S → Co charge-transfer transition is located at considerably higher energy (about 3000 cm^{-1} higher) for a *cis*-CoN_4S_2 chromophore than for the *trans* chromophore [9, 15, 16]. The $[Co(tasn)_2]^{3+}$ isomer first eluted in the cation-exchange chromatography exhibits the Co–S charge-transfer band at higher energy than the second eluted isomer, so that on this evidence alone the *cis* configuration can be assigned to the first eluted isomer.

Equilibration of the Isomers, and Crystallization Conditions to Obtain Pure cis

The equilibrium observed in the chromatography experiments was further investigated by ^{13}C NMR and visible spectra.

An orange solution of pure *trans*-$[Co(tasn)_2](ClO_4)_3$ in D_2O was basified (1 M NaOH added dropwise) to the first appearance of a dark red-brown colour which occurred at pH 9–9.5. Accumulation of the ^{13}C NMR spectrum was started immediately, and after 1.5 h at 25 °C, the spectrum showed resonances of both isomers in the peak ratio *cis*/*trans* *ca.* 2, giving a mole ratio of 4/1. No further change in the peak ratio was evident when the solution was further basified to pH 11, allowed to stand, and the spectrum rerun. The solution was

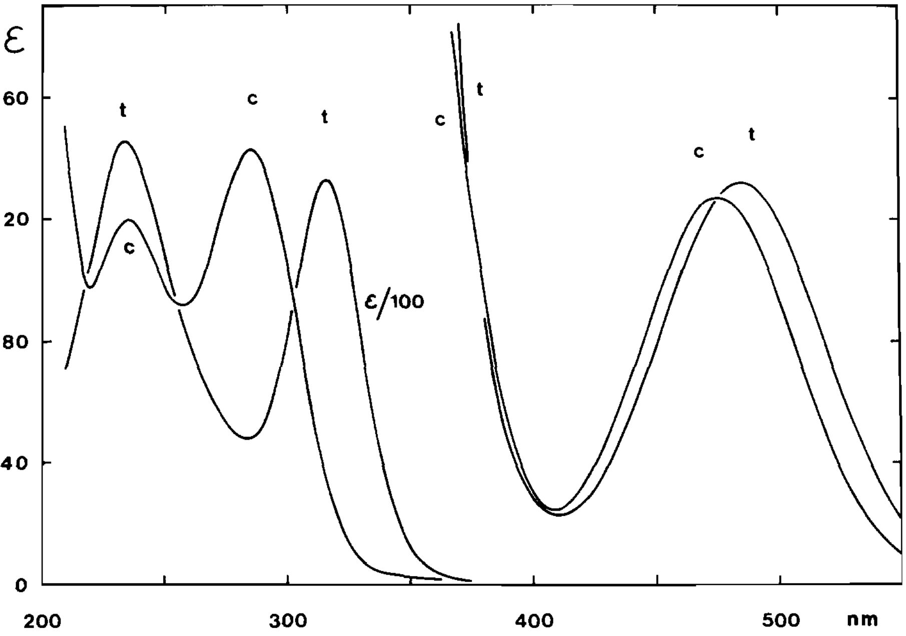

Fig. 7. The UV–Vis absorption spectra of the $[Co(tasn)_2]^{3+}$ isomers in 0.01 M HCl. t is the *trans* isomer; c is *cis*.

acidified with HCl (pH 1), and the now more yellow solution showed the predominance of *cis*-$[Co(tasn)_2]^{3+}$, and the spectrum of this solution was essentially the same as those run in base.

A corresponding experiment was carried out starting with a solution of pure *cis*-$[Co(tasn)_2]Br_3$ basified to pH 9, and a similar equilibrium ^{13}C NMR spectrum was obtained. Thus the above isomer ratio represents equilibrium, and this must have been established in a time considerably less than 1 h at pH 9 at room temperature.

An equilibrated basic solution of the bromide salt was evaporated to dryness, when a yellow–orange solid of pure *trans*-$[Co(tasn)_2]Br_3$ was obtained, as shown by the ^{13}C NMR spectrum run in D_2O/HBr. When this now acidic solution (as used for the ^{13}C NMR spectrum) was again basified to pH 9, the ^{13}C NMR spectrum then showed that the equilibrium had been reestablished. Thus when the complex is crystallized as the bromide or perchlorate under slightly basic conditions wherein isomerization can occur readily, the pure *trans* isomer is obtained showing that in these salts the *trans* is the less soluble isomer.

This equilibrated solution of $[Co(tasn)_2]Br_3$ was acidified using conc. HBr to freeze the equilibrium, and was then fractionally crystallized by concentration and addition of ethanol into two fractions. Fraction (1) was very largely *cis* (*ca.* 5% *trans*), and in fraction (2) the *trans* was enhanced (30%), demonstrating that fractionation of the equilibrium mixture of the bromide salts from HBr solution yields the *cis* isomer first.

The isomerization of $[Co(tasn)_2]^{3+}$ was also studied by spectral changes in the visible range. A solution of orange *trans*-$[Co(tasn)_2](ClO_4)_3$ in 0.01 M HCl (max. λ 484 nm, ϵ 132 mol^{-1} dm^3 cm^{-1}) was basified with 1 M NaOH to generate the dark brown base form (max. λ 519, ϵ 330). The spectrum changed rapidly (minutes) to eventually become essentially constant (max. λ 544, ϵ 422) of colour dark purple–brown, which represented the equilibrium mixture of the base forms of the two isomers. For the particular conditions (pH *ca.* 10.5, temperature 22 °C) $t_{1/2}$ for *trans* to approach equilibrium was about 4 min, and equilibration was reached by 30 min. On acidification (using 3 M HCl), the solution 'instantly' became orange–yellow and this equilibrium spectrum (max. λ 476, ϵ 130; shoulder at λ 370) agreed closely with that of $[Co(tasn)_2]Cl_3$ measured in water [3].

The isomerization was also followed in the reverse manner by starting with a yellow solution of pure *cis*-$[Co(tasn)_2]Br_3$ in 0.01 M HCl (max. λ 475, ϵ 126). Basification then gave a purple solution of the base forms, and the spectrum changed to become approximately constant. $t_{1/2}$ for the approach to equilibrium was estimated as about 10 min at pH 10.5, temperature 22 °C. After reacidification, the spectrum of the orange–yellow equilibrium mixture was obtained again. These approximate rates and equilibrium spectra are consistent with the equilibrium ratio *cis*/*trans* *ca.* 4/1 as estimated from the ^{13}C NMR spectra.

The isomerization was also observed in neutral water, albeit slowly. The visible spectrum of pure *trans*-$[Co(tasn)_2](ClO_4)_3$ in water (max. λ 485, ϵ 139) changed over days to that of the equilibrium mixture (max. λ 478, ϵ 134), and $t_{1/2}$ was estimated as 15 h at pH 5 at 22 °C.

The isomerization is facile in base but is inhibited in acidic solution (occurring negligibly at pH *ca.* 3.5), so that it is clearly base-catalyzed. The rate is significant in water pH *ca.* 5 at room temperature (hours), and at the elevated temperature in a rotary evaporation isomerization must be quite rapid at pH 5, which should enable the *trans* salt to precipitate from an equilibrium solution of the two isomers. It is now appreciated that conditions should be distinctly basic or distinctly acidic for the pure *trans* or *cis* isomers to precipitate respectively, as in the intermediate 'neutral' pH region either or both isomers may precipitate depending on the precise pH and temperature. The previous difficulties in obtaining the isomers have undoubtedly been associated with working in this intermediate region.

The base-catalysis of the isomerization implies that proton abstraction could be involved in the mechanism. This does not accord easily with an intramolecular twist mechanism for which there is no obvious proton abstraction requirement, but it is in accord with a dissociative mechanism SN_1CB [17]. However, so far we can not exclude an associative mechanism involving formation of some hydroxo intermediate and subsequent cleavage of a Co–S bond. The Co–S bond is the weaker bond [8], and evidence that this is the bond cleaved (by whatever mechanism) is the demonstrated base-catalyzed cleavage of the Co–S bond in *unsymm*-$[Co(dats)Cl]^{2+}$ to generate *cis*-$[Co(dats)(OH)_2]^+$ [1]. A Co–S cleavage mechanism has been favoured for the charcoal-catalyzed racemization of (–)-*u*-*fac*-$[Co(daes)_2]^{3+}$ [8] and for the homogeneous geometric isomerization in $[Co(aeaps)_2]^{3+}$ occurring in neutral solution [9]. The analogous mechanism but with Co–N cleavage has been proposed for isomerizations with $[Co(tacd)_2]^{3+}$ [18] and $[Co(hexacyclen)]^{3+}$ (hexacyclen = 1,4,7,10,13,16-hexaazacyclooctadecane) [19] occurring in basic solution.

It is intriguing that the (–)-*u*-*fac*-$[Co(daes)_2]^{3+}$ with all five-membered chelate rings is highly optically stable in water under homogeneous conditions [13], whereas the analogous system $[Co(aeaps)_2]^{3+}$ where each ligand forms one six-membered ring and one five-membered ring shows facile isomerization

[9] like the present $[Co(tasn)_2]^{3+}$ complex. Such facile isomerizations are quite unusual for CoN_6^{3+} complexes. Ring size and macrocyclic linking clearly influence reaction rates with the thioether complexes, although it is not yet clear whether reaction routes for racemizations are fundamentally different from those for geometric isomerizations [8].

On basifying, some of these complexes generate darkly coloured 'base forms'. The colour changes occur sharply at pH values characteristic for each complex, and are apparently reversible (except for possible isomerization). Undoubtedly these 'base forms' are intermediates leading to isomerization, and it is probably not coincidental that $[Co(tasn)_2]^{3+}$ forms the dark species at a relatively low pH (*ca.* 9.5) correlating with its greatest facility towards isomerization. This rapid and reversible change is consistent with deprotonation of an imine group to the conjugate base as the precursor to the Co–S dissociation, and support for this intermediate is the characterization of deprotonated species such as $[Co(en)_2(en\text{-}H)]^{2+}$ and $[Co(diNOsar\text{-}H)]^{2+}$ [20, 21]. However, a hydroxo species intermediate is an alternative possibility for the present 'base form', and experiments are proceeding to clarify this issue.

A Re-examination of the $[Co(daes)_2]^{3+}$ *System*

Although three geometric isomers are possible for $[Co(daes)_2]^{3+}$, the complex apparently exists only as the *u-fac* isomer [10, 13, 22] both in isolated solids and in solution, as the other isomers *s-fac* and *mer* have not been detected by ^{13}C and ^1H NMR spectra [10, 13], Sephadex chromatography [11, 13], or IE-HPLC [7]. $[Ni(daes)_2]^{2+}$ [4] and $[Rh(daes)_2]^{3+}$ [23] have also been obtained only as the *u-fac* isomers.

The high preference of the *u-fac* isomers in these systems finds some rationale in force field calculations [24]. However the apparent exclusion of the *s-fac* isomer is less clear [22], since the calculations give a small enthalpy difference between *u-fac* and *s-fac* for $[Co(daes)_2]^{3+}$ 6 kJ mol^{-1}, and also because *s-fac*-$[Cu(daes)_2]^{2+}$ is formed (although stabilization of the *s-fac* with Cu(II) has been associated with the Jahn–Teller effect) [6]. The existence of both geometric isomers of $[Co(tasn)_2]^{3+}$ in comparable proportions (4/1) and their poor chromatographic discrimination on SP-Sephadex now raises the question whether both the facial isomers of $[Co(daes)_2]^{3+}$ might have been obtained in various preparations previously but were not separated because of rapid isomerization or their closely similar properties, and this possibility has now been checked.

$[Co(daes)_2]^{3+}$ forms a dark brown 'base form' in 0.1 M NaOH, and by comparison with $[Co(tasn)_2]^{3+}$ should be labilized towards isomerization at $pH > 12$. (If this base form is a deprotonated amine, the lower acidity of $[Co(daes)_2]^{3+}$ than $[Co(tasn)_2]^{3+}$ can be related to the lower acidity of the $-NH_2$ than $-NH-$ protons.) To test whether the resulting equilibrium mixture might contain a second isomer, a solution of $[Co(daes)_2]Cl_3$ in 1 M NaOH was allowed to stand for 1 h at 20 °C, to the point where some hydrolysis was evident. The solution was then chromatographed down SP-Sephadex using 0.2 M Na_2SO_4/H_2SO_4 pH 2, with the acidic conditions presumably precluding any equilibration during the separation. The substantial hydrolysis was shown by the various purple and brown bands which separated, but $[Co(daes)_2]^{3+}$ appeared in a single orange band. This was collected in fractions, but the first and last fractions both contained the *u-fac* isomer only (^{13}C NMR spectra in D_2O/HCl).

Because (+)-*u-fac*-$[Co(daes)_2]^{3+}$ is highly optically stable in water, it is implausible that geometric isomerization could be so rapid in the acidic conditions in which the Sephadex chromatography was conducted as to preclude a separation if another isomer was present. Even under charcoal conditions in which the *u-fac* racemizes rapidly and consequently wherein equilibration between the geometric isomers should also occur (charcoal in water, charcoal in 0.1 M NaOH) [8, 13], there also has been no evidence for the formation of the other isomers, and the apparent high thermodynamic specificity for the *u-fac* thus remains perplexing.

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