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198. Energy-Minimized Structures and Calculated and Experimental Isomer Distributions in the Hexaamminecobalt(III) System $[\text{Co}(\text{trap})_2]^{3+}$ (trap = 1,2,3-Propanetriamine)

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The two isomers of $[\text{Co}(\text{trap})_2]^{3+}$ (*meso*- $[\text{Co}(\text{trap})_2]^{3+}$ and *rac*- $[\text{Co}(\text{trap})_2]^{3+}$; trap = 1,2,3-propanetriamine) have been studied by strain-energy minimization. The two isomers have been separated preparatively by fractional crystallization, and fully characterized by ^{13}C -NMR and electronic spectroscopy, and microanalyses. The calculated isomer distribution (*rac/meso* = 60%: 40%) is in good agreement with HPLC analysis of thermodynamic equilibrium mixtures at 298 K and 353 K (*rac/meso* = 55%: 45%). These results are discussed in relation to the approach of calculating isomer distributions of hexaamminecobalt(III) systems by strain-energy minimization neglecting the differences in environmental effects.

Introduction. – We are currently studying steric interactions of coordinated ligands with the aim of producing chiral discrimination upon coordination of racemic ligands to a chiral matrix [1–3]. Our project involves *i)* design of the chiral matrix by molecular-mechanics methods, *ii)* preparation of the chiral matrix (ligand synthesis), *iii)* molecular

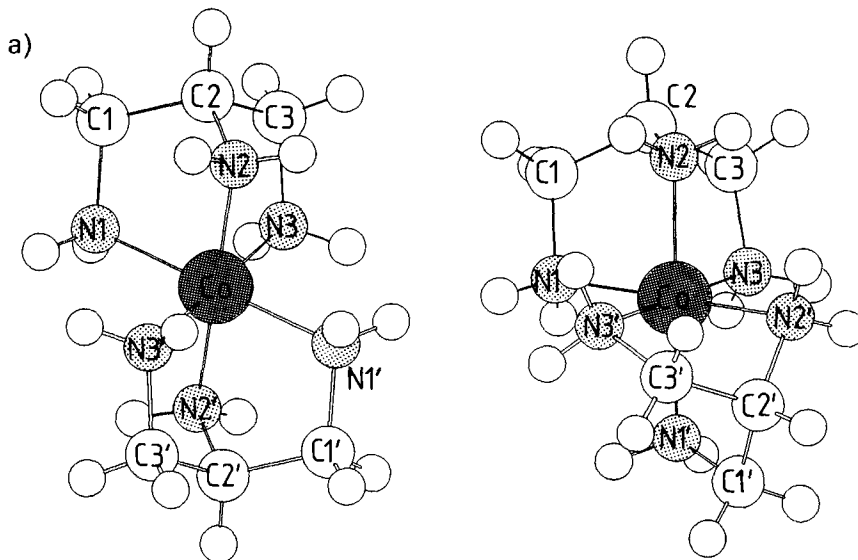


Fig. 1. Strain-energy-minimized structures of (a) *meso*- $[\text{Co}(\text{trap})_2]^{3+}$ and (b) *rac*- $[\text{Co}(\text{trap})_2]^{3+}$

recognition (equilibration of hexaaminocobalt(III) systems), *iv*) product separation and analysis. We have shown that the force field used for the computation of strain-energy-minimized structures [4] [5] leads to an excellent agreement between calculated and experimental structural parameters for transition-metal hexaamine complexes [1]. In the present publication we are focusing on the relation between calculated and experimental equilibrium constants for a pair of hexaaminocobalt(III) isomers. The choice of a hexaaminocobalt(III) system is based on the fact that hexaaminocobalt(III) chemistry is generally well understood, *viz.* there are a number of publications on the equilibration of isomeric mixtures of hexaaminocobalt(III) systems [6–9], and the force field used for the strain-energy minimizations is well established [1] [4] [5] [10] [11]. $[\text{Co}(\text{trap})_2]^{3+}$ (see *Fig. 1*) has the three advantages that *i*) the ligand is easily accessible, *ii*) there are only two isomers in the system (trap, which is the smallest tridentate triamine, coordinates only facially), and *iii*) there is only one possible conformation each, *viz.* the $[\text{Co}(\text{trap})_2]^{3+}$ system is comparably easy to analyze. In the *Discussion*, we analyze possible limitations of the approach.

Experimental. – *Physical Methods.* Electronic spectra were recorded using *Perkin-Elmer-λ15* or *λ2* instruments. ^{13}C -NMR spectra were measured on a *Varian-VXR-400* instrument at 101 MHz. HPLC separations were performed with a system consisting of a *ConstaMetric III* pump fitted with semi-prep. pistons (up to 22.5 ml/min), a *Rheodyne* injection valve, a *TSK-SP-5PW* cation-exchange gel column (7.5 × 75 mm or 21.5 × 150 mm), and a *Hewlett-Packard-1040A-HPLC Diode Array* detection system. The liquid phase was 0.25M or 0.3M Na_2SO_4 with a flow rate of 0.9 or 1.8 ml/min for the small and large column, respectively. For instrumental control and data processing, we used a *Hewlett-Packard-85* and a *Hewlett-Packard-9000-Series-200* PC, respectively. Microanalyses were done by *Ciba-Geigy AG*, Basel.

Syntheses. *1,2,3-Propanetriamine* (trap) was prepared as described in [12]. However, for security, the triazide was not isolated. The Et_2O soln. containing the triazide was added to THF and Et_2O removed under reduced pressure. This soln. was added slowly to LiAlH_4 dispersed in THF. Yield: 55.4% of trap · 3 HCl, based on the propane-1,2,3-triyl tris(methanesulfonate) precursor. Anal. calc. for $\text{C}_3\text{H}_4\text{Cl}_3\text{N}_3$: C 18.15, H 7.11, N 21.17, Cl 53.57; found: C 18.18, H 7.11, N 21.21, Cl 53.17. *Caution:* Organic azides are potentially explosive. Preliminary experiments using phthalimides instead of azides as precursors have not been successful for the synthesis of trap [3].

meso- and rac-Bis(1,2,3-propanetriamine)cobalt(III) Chloride ($[\text{Co}(\text{trap})_2]^{3+}$). An aq. soln. (40 ml) of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (1.92 g, 8 mmol), trap · 3 HCl (3.18 g, 16 mmol), and charcoal (0.96 g) was thermostated to 25° or 80°. The pH was adjusted to pH 7 (NaOH), and air was bubbled through the soln. for 24 h. The charcoal was removed by filtration, and the resulting yellow solns. were used for isomer separation and chromatography as described below.

Isomer Separation. The aq. solns. containing *meso-* and *rac-* $[\text{Co}(\text{trap})_2]^{3+}$ were first passed through a *Dowex-50-W-X-2* ion-exchange column (HCl) to remove small amounts of a red by-product. The resulting soln. was evaporated to dryness, and the yellow powder containing *meso-* and *rac-* $[\text{Co}(\text{trap})_2]^{3+}$ was dissolved in the minimum amount of H_2O . Fractional crystallization was achieved by addition of EtOH to this soln. The less soluble *meso-* isomer was accumulated in the first three of altogether six fractions. This procedure was repeated twice for nearly pure fractions and up to four times for the middle fractions. The three resulting fractions containing pure *meso-*, pure *rac-*, and mixed $[\text{Co}(\text{trap})_2]^{3+}$ were washed with EtOH and Et_2O , and air-dried. Yield (based on 1.94 g $[\text{Co}(\text{trap})_2]^{3+} \text{Cl}_3$): 0.52 g (16.7%) *meso-*, 0.65 g (20.7%) *rac-*, 0.59 g (18.9%) mixed isomers.

meso- $[\text{Co}(\text{trap})_2]^{3+} \text{Cl}_3$: ^{13}C -NMR (H_2O , δ in ppm, relative to internal dioxane): 46.06 (C(1)); 58.01 (C(2)). Electronic spectroscopy (H_2O): $\epsilon_{458.1} = 63.9 \text{ M}^{-1} \cdot \text{cm}^{-1}$; $\epsilon_{330.6} = 53.6 \text{ M}^{-1} \cdot \text{cm}^{-1}$; $\epsilon_{206.9} = 20665 \text{ M}^{-1} \cdot \text{cm}^{-1}$. Anal. calculated for $\text{C}_6\text{H}_{22}\text{Cl}_3\text{CoN}_6$: C 20.98, H 6.46, N 24.46, Cl 30.96; found: C 21.15, H 6.57, N 24.06, Cl 31.41.

rac- $[\text{Co}(\text{trap})_2]^{3+} \text{Cl}_3 \cdot 0.5 \text{H}_2\text{O}$: ^{13}C -NMR (H_2O , δ in ppm, relative to internal dioxane): 46.22, 46.33 (C(1), C(3)); 58.77 (C(2)). Electronic spectroscopy (H_2O): $\epsilon_{460.3} = 66.6 \text{ M}^{-1} \cdot \text{cm}^{-1}$; $\epsilon_{331.7} = 57.9 \text{ M}^{-1} \cdot \text{cm}^{-1}$; $\epsilon_{210.6} = 20313 \text{ M}^{-1} \cdot \text{cm}^{-1}$. Anal. calc. for $\text{C}_6\text{H}_{23}\text{Cl}_3\text{CoN}_6\text{O}_{0.5}$: C 20.44, H 6.58, N 23.84, Cl 30.17; found: C 20.28, H 6.59, N 23.79, Cl 30.07.

Isomer Equilibrations. Aq. solns. (10 ml) of the pure *meso-* and *rac-* isomers of $[\text{Co}(\text{trap})_2]^{3+}$ (0.086 g; 0.25 mmol) at pH 7 and in presence of charcoal (0.03 g) were kept at 80° for 5 weeks (*meso-* isomer) and 3 weeks (*rac-* isomer). The filtered solns. were analyzed by HPLC.

Strain-Energy Minimizations. Molecular-mechanics calculations have been performed with the FORTRAN program MOMECS5 [13] on a VAX 8800. The force-field parameters used are based on a recently developed parametrization [5] (for more details, cf. [1]). No symmetry restrictions have been imposed during the minimization processes. The refinements were allowed to cease when all shifts of positional coordinates were less than 0.001 Å. The plots of the calculated molecules have been produced with ORCHIDEE [14].

Results. – *Synthesis, Isomer Separation, and Equilibration.* Aerial oxidation of an aqueous solution of CoCl_2 and 2 equiv. of 1,2,3-propanetriamine (trap) in the presence of charcoal gives, after 24 h and removal of the charcoal, a yellow orange solution consisting of the two isomers of $[\text{Co}(\text{trap})_2]^{3+}$. Minor amounts of a red side product were removed chromatographically. The isomer distribution was analyzed quantitatively by HPLC, and the two isomers (*meso*- $[\text{Co}(\text{trap})_2]^{3+}$ and *rac*- $[\text{Co}(\text{trap})_2]^{3+}$, see Fig. 1) were separated preparatively by fractional crystallization. The isomers were identified by ^{13}C -NMR spectroscopy, and isomeric purity was confirmed by ^{13}C -NMR spectroscopy and HPLC. A typical chromatogram of an equilibrated isomer mixture is shown in Fig. 2.

In principle, it should be possible to determine the isomer distribution by NMR spectroscopy. However, there is considerable overlap of both the amine and the CH_2 signals in the ^1H -NMR spectra (400 MHz) of the *meso*- and *rac*- $[\text{Co}(\text{trap})_2]^{3+}$ species. An accurate analysis based on ^{13}C -NMR spectroscopy is inappropriate in the present case because of possible inaccuracies due to the variation of relaxation times of the various C-atoms. The HPLC analysis on the other hand is based on the well separated chromatogram and the determination of the ϵ values of both pure isomers.

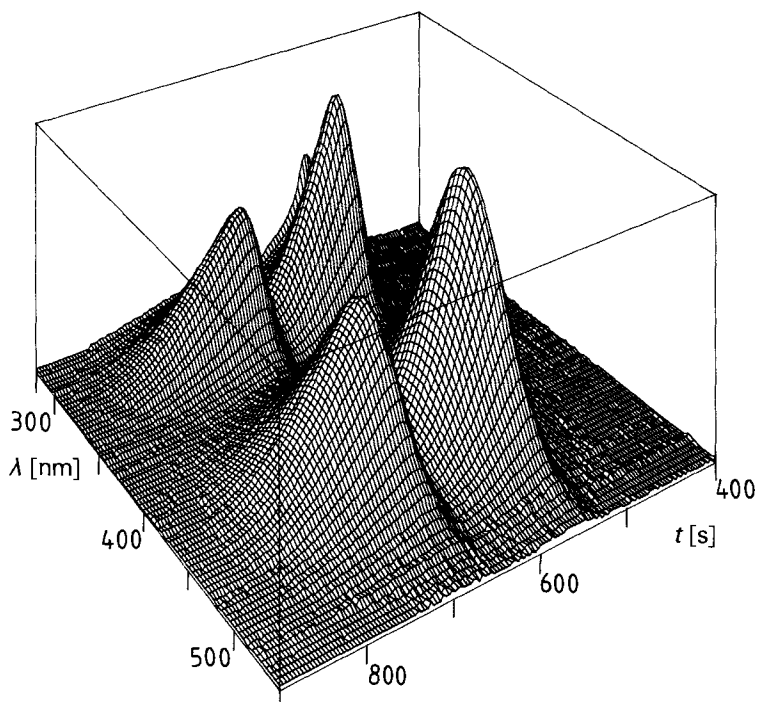


Fig. 2. HPLC chromatogram of an equilibrium mixture of *meso*- $[\text{Co}(\text{trap})_2]^{3+}$ and *rac*- $[\text{Co}(\text{trap})_2]^{3+}$ (arbitrary absorption scale). For experimental conditions and spectroscopic data, see *Experimental*.

Table 1. *Experimental and Calculated Isomer Distributions of meso- and rac-[Co(trap)₂]³⁺*

Experiment	Temp. [K]	<i>meso</i> -[Co(trap) ₂] ³⁺ [%]	<i>rac</i> -[Co(trap) ₂] ³⁺ [%]
Oxidation	298	45	55
Oxidation	353	48	52
Isomerization <i>meso</i>	353	42	58
Isomerization <i>rac</i>	353	45	55
Calc.	298	40	60
Calc.	353	39	61

It is known that aerial oxidation of stoichiometric mixtures of Co(II) salts and an amine ligand in presence of charcoal leads to the equilibrium distribution of the hexaaminocobalt(III) products [6–9]. This was further substantiated by equilibration of both pure isomers of [Co(trap)₂]³⁺ which was achieved in neutral aqueous solution in presence of charcoal. The experimental equilibrium distributions, determined by HPLC chromatography, are presented together with the calculated distributions in Table 1.

Strain-Energy Minimization. The energy-minimized structures of the two isomers are shown in Fig. 1 and the calculated structural parameters appear in Table 2 where the experimental parameters of the crystal structure of the *meso*-isomer are listed for compa-

Table 2. *Structural Parameters of the Energy-Minimized Structures of meso- and rac-[Co(trap)₂]³⁺ (this work) and of the Experimental Structure of meso-[Co(trap)₂]³⁺ [12]*

Structural parameter	<i>meso</i> -Isomer (exper.)	<i>meso</i> -Isomer (calc.)	<i>rac</i> -Isomer (calc.)
<i>Bond length [Å]</i>			
N(1)(N(1'))–Co	1.961(2)	1.956	1.954
N(2)(N(2'))–Co	1.942(2)	1.941	1.945
N(3)(N(3'))–Co	1.964(2)	1.956	1.958
N(1)(N(1'))–C(1)(C(1'))	1.491(3)	1.497	1.497
N(2)(N(2'))–C(2)(C(2'))	1.496(3)	1.493	1.493
N(3)(N(3'))–C(3)(C(3'))	1.492(3)	1.497	1.497
C(1)(C(1'))–C(2)(C(2'))	1.521(3)	1.509	1.509
C(3)(C(3'))–C(2)(C(2'))	1.512(3)	1.509	1.508
N–H (average)	0.847(13)	0.911	0.911
C–H (average)	0.978(13)	0.973	0.973
<i>Angle [°]</i>			
N(1)(N(1'))–Co–N(2)(N(2'))	84.9(1)	86.8	86.6
N(1)(N(1'))–Co–N(3)(N(3'))	85.9(1)	85.9	86.5
N(1)(N(1'))–Co–N(2')(N(2))	95.1(1)	93.2	179.1
N(1)(N(1'))–Co–N(3')(N(3))	94.1(1)	94.1	93.1
N(2)(N(2'))–Co–N(3)(N(3'))	83.9(1)	86.8	86.1
N(3)(N(3'))–Co–N(2')(N(2))	96.1(1)	93.2	94.4
Co–N(1)(N(1'))–C(1)(C(1'))	109.4(1)	107.1	107.5
Co–N(2)(N(2'))–C(2)(C(2'))	100.6(1)	97.9	98.2
Co–N(3)(N(3'))–C(3)(C(3'))	109.9(1)	107.1	107.7
N(1)(N(1'))–C(1)(C(1'))–C(2)(C(2'))	107.8(2)	108.3	108.4
N(3)(N(3'))–C(3)(C(3'))–C(2)(C(2'))	107.5(2)	108.3	108.1
N(2)(N(2'))–C(2)(C(2'))–C(1)(C(1'))	105.4(2)	106.6	106.6
N(2)(N(2'))–C(2)(C(2'))–C(3)(C(3'))	105.5(2)	106.6	106.4
C(1)(C(1'))–C(2)(C(2'))–C(3)(C(3'))	112.2(2)	111.9	112.0

Table 3. *Minimized Strain Energies of meso- and rac-[Co(trap)₂]³⁺ [kJ·mol⁻¹]*

Isomer	E_b	E_{nb}	E_θ	E_ϕ	U_{total}	rel. ΔH	rel. ΔG^{298}
<i>meso</i>	7.97	45.47	12.22	20.51	86.17	0.0	0.99
<i>rac</i>	8.16	45.86	11.72	21.15	86.89	0.72	0.0

ri¹). There is good agreement between calculated and experimental parameters, and this is generally observed for calculations with the force field used [1] [5] [9–11].

The strain energies of [Co(trap)₂]³⁺ are presented in Table 3. We stress that comparison of strain energies is only valid between isomers with basically identical chromophores (e.g. *meso*- and *rac*-[Co(trap)₂]³⁺). However, on a qualitative basis, it appears that *meso*- and *rac*-[Co(trap)₂]³⁺ are more strained than, for example, [Co(en)₃]³⁺ ($\Delta U_{total} \approx 86$ kJ·mol⁻¹, 690 interactions *vs.* ~ 60 kJ·mol⁻¹, 750 interactions, identical force field [3]). This is reflected in the contributions to the total strain from angle deformation and torsional strain. The Co–N(2)–C(2) angles in both isomers are reduced to $\sim 98^\circ$ and the conformations around N(1)–C(1) and N(3)–C(3) bonds are nearly eclipsed ($\sim 12^\circ$). The strain due to non-bonded interactions between NH₂ groups is similar for both isomers and there is little overall isomer selectivity. The difference in strain energy ($\sim \Delta H$) is a mere 0.7 kJ·mol⁻¹ in favor of the *meso*-isomer. For the calculation of the isomer distribution, ΔG rather than ΔH (from calculated strain energies) are needed ($K = 10^{-\Delta G/2.3RT}$). From the various possible contributions of ΔS , only statistical factors are usually taken into account [9] (see Discussion). For *rac*-[Co(trap)₂]³⁺, there are two enantiomers (shown in Fig. 1 is the \bar{A} form), the *meso*-isomer is achiral. At 298 K, there is, therefore, a statistical contribution to ΔS of the *rac*-isomer of $RT \ln 2 = 1.7$ kJ·mol⁻¹. The calculated isomer distribution is in excellent agreement with the experimental data (Table 1).

Discussion. – Molecular-mechanics calculations allow structures of coordination compounds to be calculated with relatively high accuracy (Table 1, see also [1] [16]). However, it has to be remembered that the calculated structures are usually of isolated ('naked') molecules, *viz.* environmental effects are not taken into account. Apparently, crystal-lattice (comparison with X-ray data), solvation, and ion-pairing effects (general interest in (aqueous) solutions) do not influence the structures of the complex ions significantly.

However, an important problem is the comparison of calculated strain energies of these naked complex ions with experimentally determined thermodynamic parameters, and this clearly is a major consideration in view of our aim of stereoselective ligand coordination. The problem is twofold: *i*) on the experimental side, there has to be a (general) reaction leading to thermodynamic equilibrium of the (hexaamincobalt(III)) products. *ii*) The calculated strain energy represents the enthalpy terms which have to be corrected for entropy effects, ion-ion and ion-solvent interactions²).

For homoleptic hexaamincobalt(III) systems, aerial oxidation of stoichiometric amounts of Co(II) salts and amine ligands in aqueous solution and in presence of

¹) A molecular-mechanics study of *meso*-[Co(trap)₂]^{3+/2+} was recently published [15]. However, the data of that study are not directly comparable with the present one, since *i*) only one of the two possible isomers was considered and *ii*) a slightly different force field was used.

²) The strain-energy differences in our systems are relatively small ($\Delta U_{total} = 0.72$ kJ·mol⁻¹ in the present case), and, therefore, relatively small errors may lead to wrong predictions [17].

charcoal leads to equilibrium distribution of the product isomers (thermodynamic equilibration is assumed to be by electron-transfer catalysis involving the Co(III) products and activated charcoal [7]). It has been shown previously [6] [7] and is confirmed by our results that this reaction is general. Equilibria depend, in principle, on temperature, solvent, anions, *etc.* Our results indicate that on a qualitative basis the *meso-/rac*-[Co(trap)₂]³⁺ equilibrium is temperature-independent. Given these results, and given a structural similarity of the surface of the complexes, one might be tempted to conclude that the *differences* (not the absolute values) between the two isomers in terms of non-statistical contributions to ΔS , solvation, and ion pairing are *negligible*. This is consistent with data on other hexaminecobalt(III) systems (*e.g.* [6]). However, a cancellation of errors arising from slightly inadequate force-field parameters and the neglect of environmental factors and entropy terms cannot be excluded³⁾. In any case, our results indicate that at least for the [Co(trap)₂]³⁺ system, this crude and rather pragmatic treatment is valuable. Considering the simplifications of the model, a discrepancy of *ca.* 5% between calculated and experimental isomer distribution is acceptable and encouraging for our further studies which aim primarily at optimizing the selectivity. Currently, we are extending this type of studies to a number of hexaminecobalt(III) systems including chiral ligands and ternary systems.

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³⁾ There are reports on the computation of entropy effects including vibrational, translational, rotational and statistical factors [18–20]. This approach is not adopted here, because it requires additional assumptions, agreement between calculated and experimental entropies tends to be poor, and because calculated and experimental entropy differences between various isomers of hexaminecobalt(III) systems are usually small in comparison to statistical entropy corrections and enthalpy differences.