113. Energy-Minimized Structures and Calculated and Experimental Isomer Distributions in the Hexaamine-Cobalt(III) System $[Co(L)_2]^{3+}$ with the Chiral Facially-Coordinating Triamine (L = Butane-1,2,4-triamine)

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Butane-1,2,4-triamine (trab) is the smallest tridentate aliphatic unsubstituted chiral triamine. With optically pure trab, there are three, with racemic trab five isomers of $[Co(trab)_2]^{3+}$. One of the five isomers is centrosymmetrical, the others are chiral. For one of the isomers, there are four possible conformations (all combinations of chair and skew boat conformations for the chelate six ring of each ligand), for the others there exist only three independent conformers. All sixteen independent structures have been calculated by strain-energy minimization. The calculated isomer distribution, based on total strain energies corrected with statistical entropy contributions (21%:16%:16%:4%:43%, and 40%:30%:30%, for racemic and optically pure trab, respectively) are in excellent agreement with the experimental data based on HPLC and ^{13}C-NMR analyses of equilibrium solutions of the hexaamine-Co(III) compounds prepared by oxygenation of aqueous solutions in presence of activated charcoal. The results are also briefly discussed in relation to possible stereoselectivity upon complexation of optically pure trab and a racemic chiral ligand to a transition-metal center.

Introduction. – We are interested in steric interactions of coordinated ligands and their possible application to chiral discrimination upon coordination of racemic ligands to a chiral matrix [1–3]. Presently, we are exploring hexaamine-Co(III) systems involving chiral facially-coordinating triamines designed by molecular-mechanics calculations [2]. The force-field parametrization used in the strain energy minimization calculations was shown to reproduce transition-metal hexaamine structures with high accuracy [1] [2] [4–9], and aerial oxidation of aqueous solutions containing stoichiometric Co(II)-ligand mixtures in presence of activated charcoal is known to lead to the equilibrium isomer distribution of the binary hexaamine-Co(III) products [10] [11] which are in good agreement with the calculated distribution based on strain energies [2].

We now present a study of hexaamine-Co(III) complexes with a simple, easily accessible chiral facially-coordinating triamine, trab (butane-1,2,4-triamine). The five possible isomers of $[Co(trab)_2]^{3+}$ are shown in *Fig. 1*. Clearly, trab is not the result of, but is a possible basis for a careful design of chiral matrix ligands. Based on the results of the $[Co(trab)_2]^{3+}$ system, implications on the reduction of the number of isomers, on isomer selectivity, and possible chiral induction are analyzed.

Experimental. – *Materials.* All reagents used were of anal. purity. H_2O used for spectroscopy and chromatography was of *MilliQuad* quality. Butane-1,2,4-triol (*Aldrich*, 95%) was used as purchased. Optically pure (–)-(*S*)-butane-1,2,4-triol ($[\alpha]_D^{20} = -28.3$ ($c = 1.0$, MeOH)) and optically pure (+)-(*R*)- and (–)-(*S*)-α-methoxy-α-phenyl-α-(trifluoromethyl)acetyl chloride (MTPA·Cl; $[\alpha]_D^{20} = +135.5$, -135.5, resp. ($c = 5.2$, CCl_4)) were from *JPS Chimie*, Bevaix, Switzerland.

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Syntheses[2]). *Butane-1,2,4-triyl Tris(p-toluenesulfonate)*. A soln. of TsCl (109.60 g, 0.57 mol) in 150 ml of pyridine, cooled to 5°, is added dropwise (1¾ h) and under stirring to a soln. of butane-1,2,4-triol (12.63 g, 0.10 mol) in 100 ml of pyridine, cooled to 0–5° (after addition of about half of the TsCl, a precipitate appeared). The mixture was placed in a refrigerator (4°) overnight and then added under vigorous stirring to 300 ml of ice-cold H_2O. After 2 h, the pinkish white solid (~ 41.5 g) is collected on a filter (in some cases the product did not crystallize directly, and the resulting paste was, therefore, recrystallized twice). This crude product was purified by recrystallization from 200 ml of refluxing MeOH. On cooling to ambient temp. a white solid of the product formed which was filtered and washed with little MeOH and subsequently dried in the oven (70°) until constant weight. Yield: 38.71 g (68.1%). M.p. 98.5°. Anal. calc. for $C_{25}H_{28}O_9S_3$: C 52.80, H 4.96, S 16.91; found: C 52.87, H 5.03, S 16.84.

(−)-(S)-Butane-1,2,4-triyl tris(p-toluenesulfonate) was prepared as described above starting from (−)-(*S*)-butane-1,2,4-triol. M.p. 107.7°. $[\alpha]_D^{20} = -23.0$ (*c* = 1.0, acetone). Anal. calc. for $C_{25}H_{28}O_9S_3$: C 52.80, H 4.96, S 16.91; found: C 52.65, H 4.94, S 16.97.

1,2,4-Triphthalimidobutane was prepared from the *p*-toluenesulfonate as described for similar compounds [15]. Potassium phthalimide (19.45 g, 105 mmol) were added under stirring and in an Ar atmosphere to butane-1,2,4-triyl tris(*p*-toluenesulfonate) (17.06 g, 30 mmol) dissolved in 30 ml of dry DMF. The mixture is refluxed (~ 165°) for ½ h[3]) and then cooled to ambient temp. The brown solid was filtered and washed with 10 ml of DMF/MeOH mixture 1:1, then with a large amount of H_2O and finally with MeOH and Et_2O. The slightly peach colored product was dried in the oven (~ 70°). The resulting solid (~ 9.9 g) was stirred in refluxing MeOH (75 ml), and the product was filtered after allowing to cool to ambient temp., washed with MeOH and Et_2O, and dried at 70°. Yield: 8.68 g (58.6%). M.p. 234°. Anal. calc. for $C_{28}H_{19}N_3O_6$: C 68.15, H 3.88, N 8.52; found: C 67.86, H 3.98, N 8.66.

(+)-(R)-1,2,4-Triphthalimidobutane was prepared as described above but starting from *(−)-(S)-butane-1,2,4-triyl tris(p-toluenesulfonate)*. M.p. 236°. $[\alpha]_D^{20} = -64.5$ (*c* = 0.4, DMF). Anal. calc. for $C_{28}H_{19}N_3O_6$: C 68.15, H 3.88, N 8.52; found: C 67.80, H 3.90, N 8.48.

Butane-1,2,4-triamine Tris(hydrochloride) (trab·3 HCl). A suspension of 1,2,4-triphthalimidobutane (4.94 g, 10 mmol) and hydrazine hydrate (4.65 g, 93 mmol) in EtOH (300 ml) was refluxed for 2 h under constant stirring. The yellow soln. was allowed to cool to ambient temp., and the addition of 37% HCl (37.5 ml) resulted immediately in a white precipitate. After boiling of the suspension for 1 h, the white solid was removed by filtration, and the yellow filtrate was evaporated to dryness. The residue was extracted with little H_2O and the insoluble white material removed again by filtration. The filtrate was concentrated to 2–3 ml, and the resulting white precipitate was filtrated again and washed with little 37% HCl. After a further filtration, the clear yellow soln. was almost evaporated to dryness and then added to abs. MeOH (10 ml). The resulting suspension was stirred for 2 h and the triamine tris(hydrochloride) was filtrated as a white powder. It was stirred again in abs. MeOH (2.5 ml) for ½ h and then collected on a filter, washed with Et_2O, and dried in the oven (60°). Yield: 0.65 g (30.6%). M.p. 203°. Anal. calc. for $C_4H_{16}Cl_3N_3$: C 22.60, H 7.59, N 19.77, Cl 50.05; found: C 22.97, H 7.65, N 19.75, Cl 49.11.

(+)-(R)-Butane-1,2,4-triamine tris(hydrochloride) ((R)-trab·3 HCl) was prepared from (+)-(*R*)-triphthalimidobutane as described for the racemic analogue. M.p. 240°. $[\alpha]_D^{20} = +1.7$ (*c* = 4.1, H_2O). Anal. calc. for $C_4H_{16}Cl_3N_3$: C 22.60, H 7.59, N 19.77, Cl 50.05; found: C 22.68, H 6.81, N 19.84, Cl 50.81.

1,2,4-Tris[α-methoxy-α-phenyl-α-(trifluoromethyl)acetamido]butane (trab-MTPA, (R)-trab-(R)-MTPA, (R)-trab-(S)-MTPA, (RS)-trab-(R)-MTPA, (RS)-trab-(S)-MTPA) was prepared according to a literature procedure used for the condensation of monoamines with MTPA·Cl [16], using optically pure or racemic trab and (*R*)- or (*S*)-MTPA·Cl, respectively: a stirred soln. of trab·3 HCl (0.106 g, 0.50 mmol) in $ClCH_2CH_2Cl$ (5 ml), to which Et_3N (1 ml) and MTPA·Cl (0.379 g, 1.50 mmol) were added, was refluxed under continuous stirring for 3 h. The product mixture (yellow soln. and white crystals (Et_3N·HCl)) was evaporated to dryness and dissolved in a mixture of Et_2O (6 ml) and 1M HCl (7 ml). The org. phase was washed with NaOH (7 ml) and dried ($NaSO_4$) overnight. Removal of the solvent under reduced pressure produced a yellow oil which was dissolved in (D_6)DMSO for ^{1}H-NMR analysis (see below).

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[2]) The synthesis of trab has been described previously [12–14]. The route described below is relatively easy and high-yielding, and the reactions described do not lead to racemization of the optically pure building block. Moreover, the procedures do not involve hazardous intermediates as does the more often used route *via* organic azides, *viz.* the synthesis described is convenient and also safe for larger scale preparations.

[3]) The yield of the tris(phthalimide) product does not vary with reaction times between ½ and 2 h. Similar reactions with propane-1,2,3-triyl tris(*p*-toluenesulfonate) and D,L-butane-1,2,3,4-tetrayl tetrakis(*p*-toluenesulfonate) do not lead to the tris- and tetra(phthalimides), respectively [3].

Bis(butane-1,2,4-triamine)cobalt(3+) chloride ($[Co(trab)_2]^{3+}$; isomer mixture). Air was bubbled for 24 h through an aq. soln. (10 ml, pH 7 (NaOH)) of trab·3 HCl (213 mg, 1 mmol), $CoCl_2 \cdot 6\,H_2O$ (119 mg, 0.5 mmol), and charcoal (60 mg). After filtration, small amounts of unreacted starting materials and by-products were removed chromatographically (*Dowex 50WX2*, 2M HCl, 3M HCl). The yellow soln. was then evaporated to dryness and the residue suspended in little abs. MeOH. The product was then collected on a filter and dried at 60°. Yield (monohydrate): 0.11 g (59.2%). ^{13}C-NMR (δ [ppm] (relative intensity), for assignments, see *Fig. 3*): 53.0 (53.1); 52.9 (70.8); 52.8 (34.4); 52.2 (75.3); 52.0 (74.9); 51.8 (15.8); 48.2 (14.2); 47.7 (61.9); 47.5 (35.8); 47.4 (64.5); 47.3 (44.5); 47.2 (59.9); 37.0 (74.2); 36.8 (54.6); 36.7 (48.3); 36.6 (78.9); 36.5 (73.2); 36.3 (17.3); 29.7 (34.0); 29.6 (112.8); 29.5 (44.7); 29.2 (60.6); 29.1 (18.9). Electronic spectrum (λ [nm] (ε_{max} [$l \cdot mol^{-1} \cdot cm^{-1}$])): 464 (75); 336 (75). Anal. calc. for $C_8H_{28}Cl_3CoN_6O$: C 24.66, H 7.24, N 21.87, Cl 27.30; found: C 24.99, H 7.29, N 21.18, Cl 27.07.

Bis[(+)-(R)-butane-1,2,4-triamine]cobalt(3+) chloride ($[Co((R)\text{-}trab)_2]^{3+}$; isomer mixture) was prepared from (*R*)-trab·3 HCl as described above for $[Co(trab)_2]^{3+}$. ^{13}C-NMR (δ [ppm] (relative intensity); for assignments, see *Fig. 3*): 53.0 (54.2); 52.8 (53.4); 52.2 (89.8); 47.5 (44.6); 47.3 (49.4); 47.2 (73.3); 36.8 (57.2); 36.7 (49.9); 36.5 (79.1); 29.7 (39.7); 29.6 (83.8); 29.5 (50.3). Electronic spectrum (λ [nm] (ε_{max} ([$l \cdot mol^{-1} \cdot cm^{-1}$])): 465 (73); 336 (72). Anal. calc. for $C_8H_{28}Cl_3CoN_6O$: C 24.66, H 7.24, N 21.87, Cl 27.30; found: C 24.81, H 7.27, N 21.13, Cl 27.16.

The optical purity of (*R*)-trab was analyzed by two independent methods: *i)* optical purity is demonstrated by the fact that $[Co((R)\text{-}trab)_2]^{3+}$ consists of only three isomers (*I*, *II*, *III*, see *Fig. 1*), *viz.* the two isomers with mixed (*R*/*S*)-configurations of the two coordinated triamines (isomers *IV* and *V*, see *Fig. 1*) are absent (HPLC, ^{13}C-

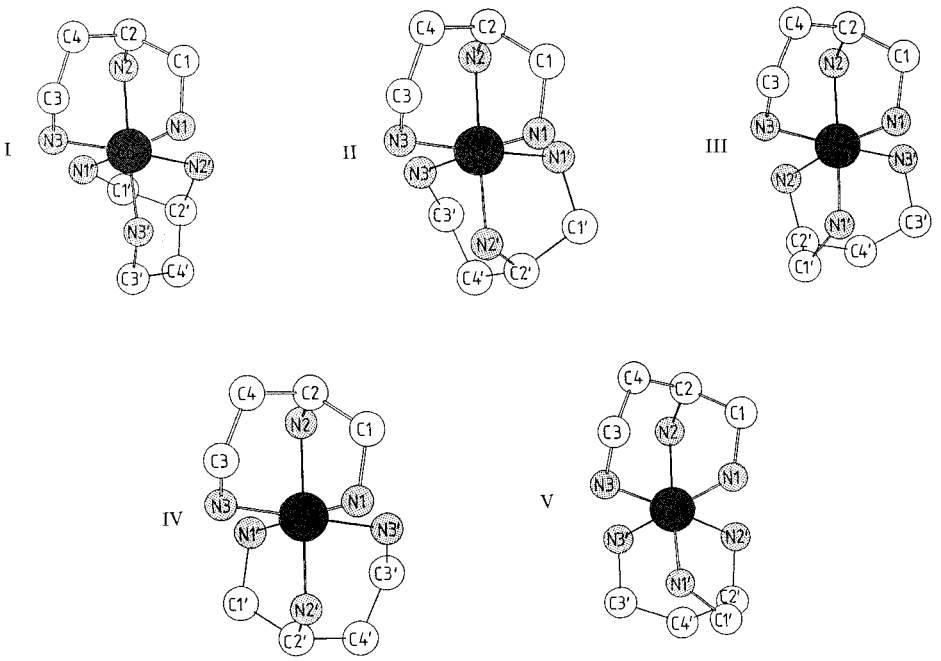

Fig. 1. *Strain-energy-minimized structures of the most stable conformers* (chair–chair) *of the five isomers (I–V) of $[Co(trab)_2]^{3+}$*

NMR). *ii)* The condensation of (*RS*)-trab with (*R*)- or (*S*)-MTPA·Cl leads to two diastereoisomeric enantiomer pairs, *viz.* (*R*)-trab-(*R*)-MTPA, (*S*)-trab-(*S*)-MTPA, and (*R*)-trab-(*S*)-MTPA, (*S*)-trab-(*R*)-MTPA, which exhibit two distinctly different sets of ^{1}H-NMR transitions. The optical purity of trab is best analyzed based on the amide protons (8.2–8.5 ppm, J(H–N(1)) = J(H–N(3)) = 5.8 Hz, J(H–N(2)) = 8.7 Hz), see *Fig. 2*. Therefore, the reactions for the preparation of trab described above are all stereoretentive or lead to full inversion, respectively (optical purity of 99 ± 1%).

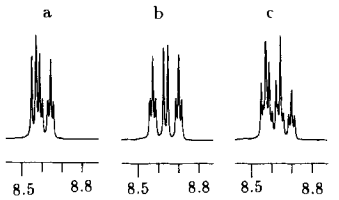

Fig. 2. *Determination of the optical purity* (99 ± 1%) *of trab by ^{1}H-NMR spectroscopy of its condensation product with MTPA·Cl* (amide protons). *a)* (*R*)-trab-(*R*)-MTPA; *b)* (*R*)-trab-(*S*)-MTPA; *c)* (*RS*)-trab-(*R*)-MTPA.

Physical Methods. Electronic spectra were recorded on *Perkin-Elmer λ15* or *λ2* instruments, ^{1}H- and ^{13}C-NMR spectra in (D_6)DMSO and D_2O, respectively, were measured on a *Varian VXR 400* spectrometer at 400 MHz and 101 MHz, respectively, and chemical shifts (δ, [ppm]) are relative to internal TMS or dioxane. HPLC chromatography was done with a system described in [2]. As stationary phase, we used *TSK SP-5PW* cation-exchange gel columns (7.5 × 75 mm or 21.5 × 150 mm) and the eluant was 0.2M Na_2SO_4 with a flow rate of 0.2 or 0.9 ml/min, respectively. The spectral data (diode-array detector) were analyzed on a *Hewlett Packard 200* PC. Microanalyses were done by *Ciba-Geigy AG*, Basel.

Strain-Energy Minimizations. Molecular-mechanics calculations were performed with *Momec85* [17] on a *VAX 8830*. The force field is the same as used before [1] [2][4]) (see also [4] [18]). No symmetry restrictions have been imposed on the last cycles of the minimization processes, and the refinements were allowed to cease, when all shifts of positional coordinates were less than 0.001 Å. All structures minimized to true potential minima. The plotted structures are produced with *ORCHIDEE* [19].

Results. – *Complex Synthesis, Chromatography, and Spectroscopy.* $CoCl_2 \cdot 6\ H_2O$ and trab were oxidized with a stream of air for 24 h, and the filtered yellow solutions were analyzed by HPLC chromatography (*TSK SP-5PW* columns, 0.2M Na_2SO_4). Electronic and ^{13}C-NMR spectra and microanalyses were obtained from solid samples, produced by chromatographical removal of unreacted starting materials and side products (*Dowex 50WX2*, 2.0M HCl, 3.0M HCl); and subsequent evaporation to dryness (the $[Co(trab)_2]^{3+}$ isomer distribution in product solutions and solid samples is identical, HPLC).

In the isomers *I*, *II*, and *III*, both trab ligands have the same configuration ((*S*), see *Fig. 1*), in the isomers *IV* and *V*, the top ligand has (*S*)-, the bottom ligand (*R*)-configuration. Isomer *IV* is centrosymmetrical, all others are chiral. The isomers *I–III* have a C_2 axis each (perpendicular to N(1)–N(1), N(2)–N(2), and N(3)–N(3), respectively), interconverting both trab units. Isomer *V* is asymmetrical, *viz.* it consists of two independent ligand units coordinated to Co(III). Since interconversion of conformers is fast in the NMR time scale [20], there are 4, 4, 4, 4, and 8 ^{13}C-NMR signals from independent C-atoms for isomers *I*, *II*, *III*, *IV*, and *V*, respectively. The experimental data *(Fig. 3)* agree with this prediction: there are four sets of transitions (attributed to C-atoms of the type *1*, *2*, *3*, and *4*, see *Fig. 1* for the nomenclature) with three signals each (three $[Co((R)\text{-trab})_2]^{3+}$ isomers with symmetrically related (*R*)-trab units, see above) or six signals per set (five $[Co(trab)_2]^{3+}$ isomers; one isomer (*V*) has two symmetrically independent trab units, see above), respectively. Based on similar relaxation times for the same C-atoms in different isomers, the distribution based on ^{13}C-NMR intensities are (average of sets *1–4*, both spectra): 21%:15%:15%4%:45% for the signals labelled A:B:C:D:E. The signals labelled E can unambiguously be assigned to the asymmetrical isomer *V*, and

[4]) It is important to note that the results presented are not based on force-field parameters adjusted to this particular system, *viz.* the parameters used in our past and present studies are general for (at least) hexaamine-Co(III) systems.

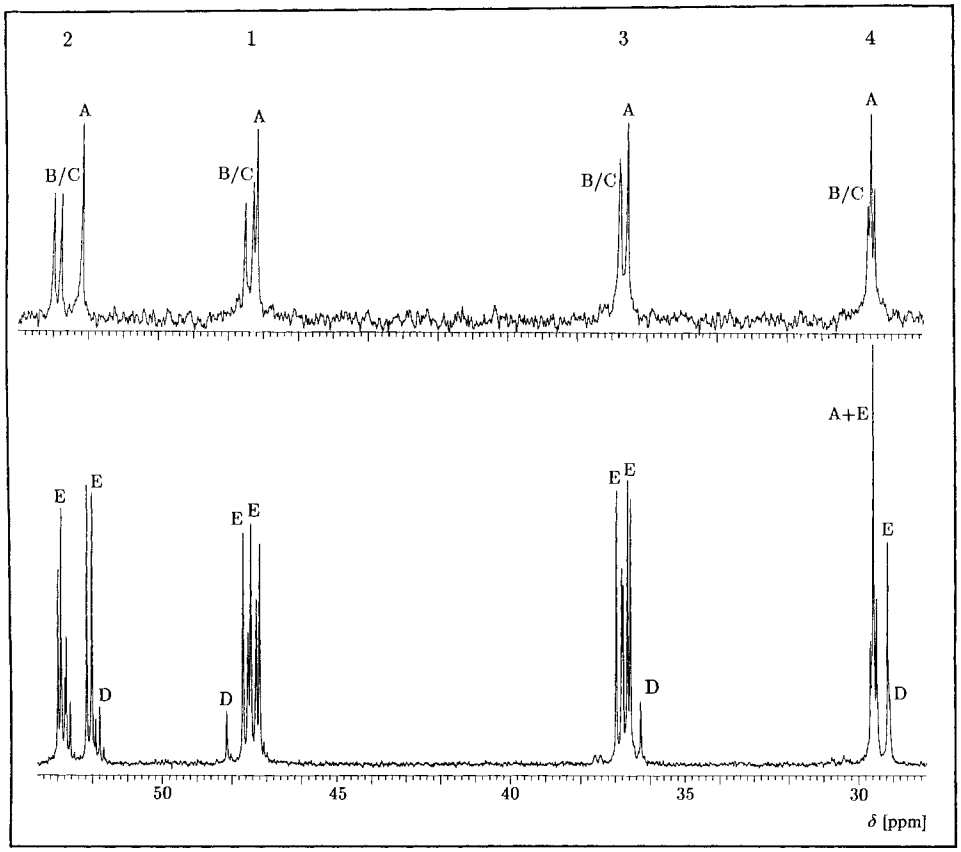

Fig. 3. *^{13}C-NMR Spectra of the equilibrium mixtures of [Co((R)-trab)$_2$]$^{3+}$* (top) *and [Co((R/S)-trab)$_2$]$^{3+}$* (bottom). For nomenclature and assignments, see text.

the signals labelled D, therefore, correspond to the other (*R*/*S*)-isomer *IV*. An unambiguous assignment of the signals A, B, C to the three (*R*/*R*)-isomers *I*, *II*, and *III* is not possible[5]).

The five isomers of $[Co(trab)_2]^{3+}$ were not separated preparatively, and the molar extinction coefficients of the isomers are, therefore, not known quantitatively. However, the different chromophores are very similar, and the errors resulting from an analysis of the HPLC data based on averaged extinction coefficients (solid isomer mixture) is, therefore, negligible. This emerges also from a similar study with $[Co(trap)_2]^{3+}$ (trap = propane-1,2,3-triamine) where the isomers have been separated preparatively [2]. Typical HPLC chromatograms of equilibrated $[Co(trab)_2]^{3+}$ isomer mixtures are shown in *Fig. 4*. Minor amounts of unreacted ligand and side products are eluted well before the $[Co(hexaamine)]^{3+}$ cations[6]). The expected five (racemic trab) and three (optically pure

[5]) Some additional small signals (most visible in set 2 of the spectrum of $[Co(trab)_2]^{3+}$) are presumably due to hydrolysis products.

[6]) These impurities were removed by preparative chromatography for microanalyses, electronic spectra, and some HPLC experiments.

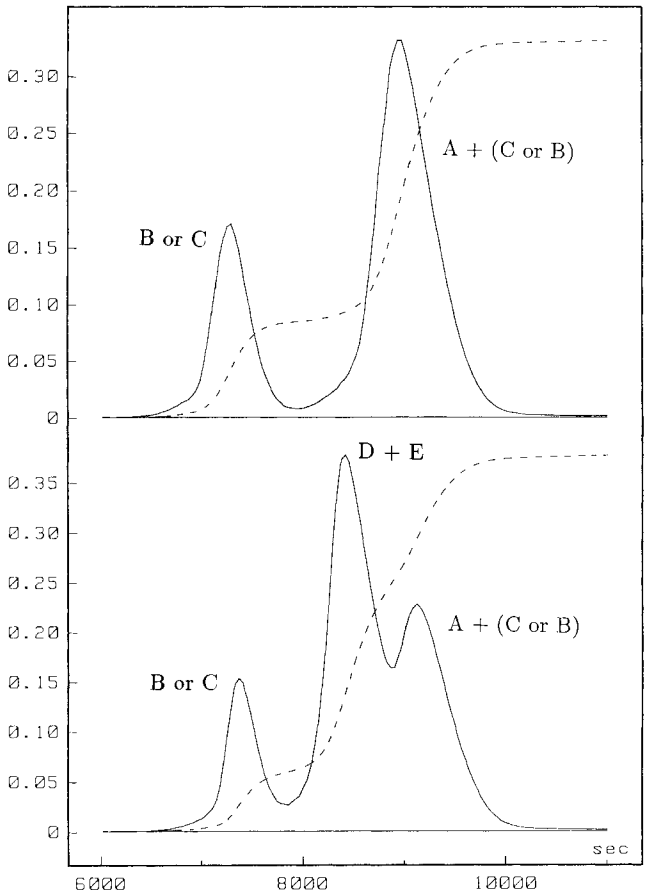

Fig. 4. *HPLC Chromatograms* (absorption at 229 nm (arbitrary scale) *vs.* t_R in s; integrals: dotted lines) *of the equilibrium isomer mixtures of* $[Co((R)\text{-}trab)_2]^{3+}$ (top) *and* $[Co((R/S)\text{-}trab)_2]^{3+}$ (bottom). For nomenclature and assignments, see text.

trab) peaks are not well resolved in the chromatograms. HPLC of a mixture of $[Co((R)\text{-trab})_2]^{3+}$ and $[Co((R/S)\text{-trab})_2]^{3+}$ reveals that the second (central) peak in the chromatogram of $[Co(trab)_2]^{3+}$ is due to the (*R*/*S*)-isomers *IV* and *V*. Based on integration of the chromatograms, the proportions are 14.5%:49%:36.5% for the signals labelled (B or C): (D + E): (A + C or B). These ratios are fully consistent with the abundances observed in the ^{13}C-NMR spectra (see above).

Strain-Energy Minimization. The strain-energy-minimized structures of the chair–chair conformers of the five isomers of $[Co(trab)_2]^{3+}$ are depicted in *Fig. 1* (calculated bond lengths and angles of all conformers are available as *Supplementary Material*)[7]).

[7]) Note that, in a recent report on electron-transfer barriers of hexaamine-Co(III/II) systems as a function of the ligand structure, which involved the $[Co(trab)_2]^{3+/2+}$ system, the configurational isomerism of this system was completely neglected [14]. Based on our results and the error limits on the published correlations [14], these simplifications do not seem to interfere with the earlier conclusions (Co–N bond lengths vary between 1.947 and 1.974 Å, however, the average Co–N distance is constant in all five isomers (1.961(1) Å); the electronic spectra of isomer mixtures *I–III* and *I–V* are identical within the error). A similar comment applies to the $[Co(trap)_2]^{3+/2+}$ system (X-ray structure of one of the isomers, see [21]; analysis of the electron-transfer properties, see [14] [22]; analysis of both isomers, see [2]).

Bond lengths and bond angles for all isomers are very similar, *viz.* based on the structural parameters alone an isomer selectivity is not obvious. The most important distortion from generally observed geometry is for all isomers emerging from the large six-membered chelate rings involving the N(2)–Co–N(3) and this results in considerably flattened Co–N(3)–C(3) angles of up to $\sim 119°$ and, in the chair conformation of the six-membered chelate rings, to close intramolecular contacts involving one of the N(1) and C(3) protons of the same ligand ($H \cdots H \sim 2.08$ Å).

The strain energies of the sixteen structures involving all independent conformations of the five isomers are given in the *Table,* which also includes the calculated and the experimentally determined isomer distributions (the calculated enthalpies have been corrected for statistical contributions to the entropy, other entropy contributions and environmental effects are neglected [2]). The calculated abundances of isomers *IV* and *V* are in excellent agreement with the experimental values resulting from the uniquely assigned ^{13}C-NMR signals D and E, and from the HPLC signal (D + E). Assuming that the prediction of abundances is equally good for isomers *I–III*, the calculated isomer distribution strongly suggests assignment of the remaining ^{13}C-NMR and HPLC signals A, B, and C to isomer *I*, *II*, and *III*, respectively. However, we realize that the calculated values for isomers *I–III* are very close, and small inconsistencies in the force-field parametrization might change their sequence.

Table. *Minimized Strain Energies* [kJ·mol^{-1}] *and Calculated and Experimental Population of All Independent Isomers and Conformers of* $[Co(trab)_2]^{3+}$

Structure	E_b	E_{nb}	E_θ	E_ϕ	U_{total}	rel ΔH	rel ΔG	Isomer distribution [%]		
								Calc.	^{13}C-NMR[a])[b])	HPLC[a])[b])
Isomer I										
chair–chair	12.29	59.33	13.05	12.33	96.99	0	1.6	17.7	21	22
chair–skew boat	12.12	59.71	13.86	17.73	103.41	6.42	6.32	2.6		
skew boat–skew boat	12.03	60.55	14.47	23.23	110.27	13.28	14.82	0.1		
Isomer II										
chair–chair	11.77	59.23	14.02	12.72	97.74	0.75	2.35	13.1	15	14.5
chair–skew boat	12.08	59.82	14.04	17.48	103.41	6.42	6.32	2.6		
skew boat–skew boat	11.47	58.18	13.95	22.90	106.50	9.51	11.11	0.4		
Isomer III										
chair–chair	12.09	60.02	13.12	12.22	97.46	0.47	2.07	14.7	15	14.5
chair–skew boat	12.19	60.91	14.15	17.87	105.12	8.13	8.03	1.3		
skew boat–skew boat	12.11	61.06	14.09	22.69	109.96	12.97	14.57	0.1		
Isomer IV										
chair–chair	12.79	61.79	15.36	12.32	102.26	5.27	6.87	2.1	4	5
chair–skew boat	12.23	60.73	14.02	17.34	104.32	7.33	7.23	1.8		
skew boat–skew boat	11.82	60.33	13.81	23.53	109.49	12.50	14.10	0.1		
Isomer V										
chair–chair	11.94	59.17	13.76	12.22	97.09	0.1	0.0	33.8	45	44
skew boat–chair	11.69	58.35	13.37	17.47	100.88	3.89	3.79	7.3		
chair–skew boat	11.96	60.08	14.36	17.97	104.36	7.37	7.27	1.8		
skew boat–skew boat	12.06	60.15	14.17	22.76	109.15	12.16	12.06	0.3		

[a]) See text for assignment of signals A–E to isomers *I–V*.
[b]) Sum of all conformers.

Discussion. – Molecular-mechanics calculations with the force field we are using have been applied successfully to a number of systems, reproducing structural as well as thermodynamic parameters satisfactorily [1–9]. Our aim is to use molecular-mechanics methods in the design of systems used for molecular recognition in terms of chiral selectivity based on the discrimination between stable diastereoisomers produced by the reaction of a chiral matrix with the two antipodes of a racemic ligand. In the present study based on $[Co(trab)_2]^{3+}$ our intention was not to give a valuable example of chiral induction but to demonstrate possible ways leading there: *i)* trab is not the result of but a possible basis for careful ligand design. However, it is the simplest facially-coordinating chiral triamine, and its optically pure form is easily accessible. *ii)* Obviously there cannot be any chiral induction in binary hexaamine-Co(III) complexes produced by oxygenation of Co(II) salts in presence of the ligand. However, the selectivity of a chiral triamine-Co(III) fragment (*e.g.* $[Co((R)\text{-trab})]^{3+}$) towards one antipode of the triamine ((*R*)-trab or (*S*)-trab) can be determined based on the isomer selectivity (*i.e.* $[Co((R)\text{-trab})_2]^{3+}/[Co((S)\text{-trab})_2]^{3+}$ (isomers *I–III*) *vs.* $[Co((R)\text{-trab})((S)\text{-trab})]^{3+}/[Co((S)\text{-trab})((R)\text{-trab})]^{3+}$ (isomers *IV* and *V*), and this may help in the future development of systems for chiral recognition, *viz.* for the evaluation of a chiral matrix system it is not necessary to work with optically pure ligand systems[8]). *iii)* Due to their inertness hexaamine-Co(III) complexes are not predestinate for racemate separations based on selective ligand exchange. However, for the same reason they are clearly very useful in terms of product analysis and due to the large amount of published molecular-mechanics studies [23] also in terms of strain-energy minimizations. Therefore, we have been focussing on hexaamine-Co(III) systems in order to find encouraging examples of molecular recognition which might then be developed further.

The calculation of isomer distributions from strain energies is based on a number of assumptions, and the error limit is quite large [2]. This is especially important in cases as in part of the present one, where the strain-energy differences are small. Therefore, the excellent agreement between calculated and the experimentally determined stabilities for $[Co(trab)_2]^{3+}$ is encouraging. Also, there is good agreement between calculated and experimental enantiomeric excesses ($\%ee = |\%R - \%S|$; 6% and 2%, respectively), *viz.* $[Co((R)\text{-trab})]^{3+}$ is preferentially coordinating (*R*)-trab but the selectivity is poor[9]). The small selectivity is not unexpected, since *i)* there are many isomers in the system, and a possible selectivity based on one strained isomer (*e.g.* isomer *IV*) may, therefore, be diminished by population of another isomer involving the same antipode of the substrate (*e.g.* isomer *V*, and *ii)* the steric crowding induced by trab is rather small.

The stereoselectivity of trab and similar ligands may be enhanced by substitution of the ligand backbone, and the effects of various substituents may be predicted by molecular-mechanics calculations ('fine tuning'). Preliminary results with Me-substituted trab indicate that enantiomeric excesses of up to 90% may be realized, although the isomer selectivity remains practically unchanged [3]. However, such optically pure triamines are preparatively far less easily accessible. Alternatively, the number of isomers may be

[8]) Note that the 'selectivity' of a chiral matrix system (*e.g.* the $[Co((R)\text{-trab})]^{3+}$ fragment) is not a general quantity, *viz.* the enantiomeric excess is different for each substrate. However, it clearly is possible to extrapolate qualitatively the results from one substrate to another.

[9]) We note, and this is an important general result of the present study, that the isomer and enantiomer selectivities are the result of virtually all terms involved in the determination of ΔG (see the *Table* and [1]).

reduced by using symmetrical chiral matrix ligands which are now developed in our laboratory [3].

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