89. Stereoselective Coordination to Chiral Matrices

Cobalt(III) Chemistry of Simple Facially Coordinating Chiral Triamines

by **Peter Comba***, **Aldo Hörmann**, **Lisandra L. Martin**, and **Luc Zipper**

Institut für Anorganische Chemie, Universität Basel, Spitalstrasse 51, CH-4056 Basel

(19.III.90)

Chiral ligands coordinated to metal ions exert a selectivity towards the additional coordination of racemic substrates. Experimentally determined equilibria distributions of $[Co(L^3)_2]^{3+}$ and $[Co(L^3)(L^2)(X)]^{n+}$ are compared with calculated data based on strain-energy minimization (L^3: trap = propane-1,2,3-triamine; 1,2,4-trab = butane-1,2,4-triamine; 1,2,3-trab = butane-1,2,3-triamine; 1,3,4-trpe = pentane-1,3,4-triamine; 1,3,4-tmeb = 2-methylbutane-1,3,4-triamine; 1,2,4-trpe = pentane-1,2,4-triamine; L^2: en = ethane-1,2-diamine; pn = propane-1,2-diamine; X: NH_3, OH_2, OH^-). Equilibration of Co(III) complexes was achieved by oxygenation of aqueous solutions of Co(II) salts in presence of the ligands. Quantitative isomer distribution was investigated with HPLC, and quantitative analysis of the enantiomeric excess (ee) of the racemic substrate (present in a two-fold excess) was studied, after chromatographical recovery, by ^{1}H-NMR analysis of its *Mosher*-acid derivative. There is good agreement between calculated and experimental data. Systems with L = 1,2,4-trab are, as expected, relatively poorly discriminating ($ee([Co(1,2,4\text{-trab})_2]^{3+}) \sim 5\%$; $ee([Co(1,2,4\text{-trab})(pn)(X)]^{n+}) \sim 10\%$). Calculations indicate that Me substitution of the ligand backbone of 1,2,4-trab (and trap) leads to an increased enantioselectivity (with practically constant isomer selectivity), and at the optimum site for substitution ~ 90% ee is predicted.

Introduction. – Our studies of steric interactions of coordinated ligands are aiming at producing chiral discrimination upon coordination of racemic ligands to chiral matrices (formation of stable diastereoisomers) [1–6]. This involves: *i*) ligand design by molecular-mechanics calculations and ligand synthesis; *ii*) stereoselective ligand-exchange reactions, *viz.* equilibration of the chiral matrix with a racemic substrate; *iii*) recovery of the (partly) resolved racemic substrate and analysis of the amount of chiral induction.

The ligand systems described here are summarized in *Fig. 1*. They are based on trap and 1,2,4-trab, which are the smallest achiral and chiral tridentate triamines, respectively.

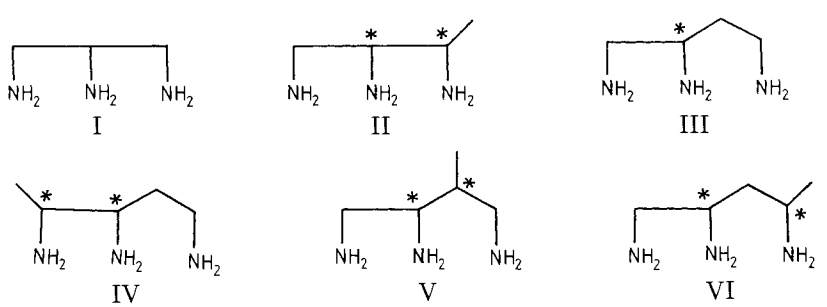

Fig. 1. *Examined ligand systems.* **I:** *Propane-1,2,3-triamine* (trap); **II:** *butane-1,2,3-triamine* (1,2,3-trab); **III:** *butane-1,2,4-triamine* (1,2,4-trab); **IV:** *pentane-1,3,4-triamine* (1,3,4-trpe); **V:** *2-methylbutane-1,3,4-triamine* (1,3,4-tmeb); **VI:** *pentane-1,2,4-triamine* (1,2,4-trpe).

Not surprisingly, the stereoselectivities observed with $[Co(trap)_2]^{3+}$ and $[Co(1,2,4\text{-trab})_2]^{3+}$ are rather small, and the chiral induction exerted by a $[Co(1,2,4\text{-trab})]^{3+}$ fragment is relatively poor [2] [3]. However, the performance of these (and other similar) systems may be enhanced by substitution of the ligand backbone. Strain-energy minimization calculations are particularly well suited for predicting stereoselectivities of this type, since one is mainly interested in strain-energy differences of isomers with roughly identical chromophores, and entropy and solvation effects have been demonstrated to be of minor importance, if innocent solvents and electrolytes are involved [2] [3], *viz.* some of the major problems of and criticism to molecular-mechanics calculations are immaterial [2].

Particularly well studied in terms of molecular-mechanics calculations (structures and isomer distributions, *viz.* comparison with X-ray and thermodynamic data, respectively) are Co(III) hexaamine systems [1–3] [7–21]. Oxygenation of aqueous solutions of Co(II) salts with stoichiometric amounts of ligands in presence of charcoal is known to produce equilibrium isomer mixtures of homoleptic Co(III)-hexaamine systems [2] [22–24]. The situation with mixed ligand systems is rather more complex, since addition of charcoal may lead to preferential formation of mixtures of the respective homoleptic complexes. As in similar published cases, in this study, equilibration is achieved without addition of charcoal [25–27]. The quality of a chiral matrix consisting of an optically pure ligand coordinated to a Co(III) center is analysed by chromatographic recovery of the excess substrate and subsequent analysis of the enantioselection by ^{1}H-NMR spectroscopy of the corresponding *Mosher*-acid derivatives [28].

Clearly, for efficient resolution procedures based on stereoselective ligand-exchange reactions, labile coordination centers have to be used [6]. Therefore, it is of importance to note that we have demonstrated that the force field used in our strain-energy-minimization calculations is also suitable for transition-metal centers other than Co(III) [1]. Moreover, based on the assertion of steric effects being primarily responsible for the stereoselective ligand exchange processes described [2] [3], it is expected that data resulting from Co(III) systems may be extrapolated to other transition-metal ions.

Experimental. – *Materials.* All reagents were of analytical degree. Butane-1,2,4-triamine was prepared as described in [3]. Optically pure propane-1,2-diamine ($[\alpha]_D^{20} = -34.0$ (*R*), $+34.0$ (*S*); 1.0M benzene) and α-methoxy-α-(trifluoromethyl)phenylacetyl chloride ($[\alpha]_D^{20} = -135.5$ (*R*), $+135$ (*S*); 5.2M, CCl_4) were from *JPS Chimie*, Bevaix, Switzerland. Water used for spectroscopy and chromatography was of *MilliQuad* quality.

Syntheses and Recovery of Resolved Substrates. O_2 was bubbled for 2¼ h through an aq. soln. (pH 8, NaOH) containing 179.6 mg (0.75 mmol) $CoCl_2 \cdot 6\,H_2O$, 159.2 mg (0.75 mmol) (*R*)-1,2,4-trab·3 HCl, and 111.2 mg (1.5 mmol) (±)-pn. The product soln. was acidified with conc. HCl (pH 2) and warmed on a water-bath (85°) for 1 h. The resulting purple soln. was diluted with 0.1M NaOH and the pH adjusted to 10, before sorbing it onto a cation exchange column (*Dowex 50W* × 2; 1.4 cm·11 cm; washed with 0.1M NaOH). Uncoordinated pn was eluted with 0.1M NaOH (free ligand in a few drops of the eluate was detected by a purple colour resulting from addition of a few drops of 2.8 mM Cu(II) soln.). The amount of recovered pn (determined spectrophotometrically as its Cu(II) complex) was 0.73 mmol (97.3%)[1]). Before analysing its optical purity (see below), pn was purified by sorbing it onto, and eluting it with 1M HCl from a cation-exchange column (*Dowex 50W* × 2; 1.4 cm·11 cm; H^+ form) and subsequent evaporation of the soln. to dryness. The Co(III) complexes remaining on the first cation-exchange column were eluted with 2M and 3M HCl after washing it with H_2O and then 1M HCl. From the two fractions, 174 mg and 55 mg of a purple and a yellow product (analyzed spectrophotometrically as $[Co((R)\text{-}1,2,4\text{-trab})(pn)Cl]Cl_2$ (yield: 74%, not purified) and a hexaamine-Co(III) salt) were isolated, respectively.

---

[1]) In a blank experiment (chromatography of known amounts of $[Co((R)\text{-}1,2,4\text{-trab})(pn)Cl]^{2+}$ and pn under otherwise identical conditions), (99 ± 1)% recovery was identified.

$[Co(1,2,4\text{-trab})(en)Cl]Cl_2$ was prepared as described above for $[Co((R)\text{-}1,2,4\text{-trab})(pn)Cl]Cl_2$ but using stoichiometric amounts of the diamine.

Analysis of Isomer Equilibria. The product distribution of solns. of the oxygenation of Co(II) in presence of 1,2,4-trab and en was analyzed with HPLC, after ion-exchange chromatography on *SP Sephadex C25* with the same eluent (elimination of org. materials). These solns. contain also some Co(III)-hexaamines and hydrolysis products (^{13}C-NMR). The three signals in the chromatogram are only moderately well separated, but the three products can be identified (VIS spectra) as Co(III)-pentaamines.

Analysis of Enantioselectivity. Recovered and purified pn (see above) was condensed with (*S*)-MTPA·Cl, and for comparison, optically pure (*R*)-pn was reacted with (*R*)- and (*S*)-MTPA·Cl each, as described in [3], but using 2 instead of 3 equiv. of MTPA·Cl. The ^{1}H-NMR spectrum of the *Mosher*-acid adduct of recovered pn is shown in *Fig. 2*.

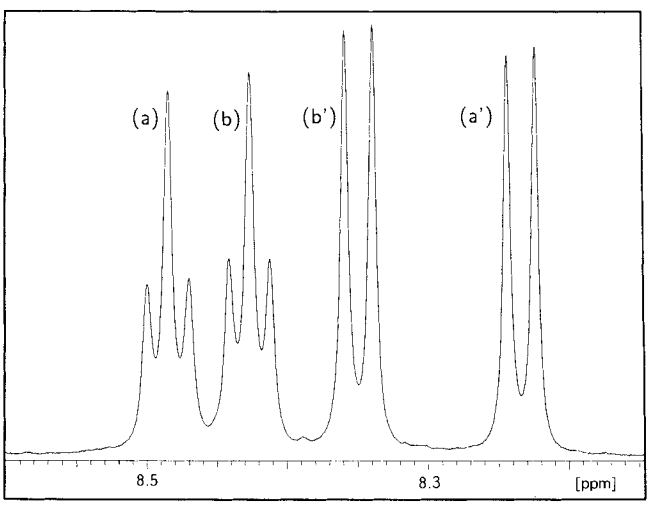

Fig. 2. *^{1}H-NMR Spectrum of partially resolved propane-1,2-diamine condensed with (S)-MTPA·Cl* (amide-proton region). *a*): (*R*)-pn; b): (*S*)-pn (analysis based on similar experiments with optically pure pn); dashed signals; 1-amide of pn residue; undashed signals: 2-amide of pn residue.

Physical Methods. HPLC chromatography was done with a system described in [2]. As stationary phase, we used a *TSK SP-5PW* cation-exchange gel column (7.5·75 mm) and the eluant was 0.2M Na_2 (tartrate) with a flow rate of 0.13 ml/min. Electronic spectra were recorded on *Perkin-Elmer λ15* or *λ2* and *Cary 2300* instruments. ^{13}C- and ^{1}H-NMR spectra, in D_2O or (D_6) DMSO, were measured on a *Varian VXR 400* spectrometer at 101 or 400 MHz, respectively, and chemical shifts (δ [ppm]) are relative to internal dioxane or TSP, respectively.

Strain-Energy Minimizations. Molecular-mechanics calculations were done with *Momec 85* [29] on a *VAX 8830*. The force-field parameters used are based on published data [8] [14] (for details, see also [1–3]). No symmetry restrictions have been imposed on the last cycles of the minimization procedures, and the refinements were allowed to cease when all shifts of positional coordinates were less than 0.001 Å.

Molecular-Mechanics Calculations. – The structures of all isomers of the complexes studied are presented schematically in *Fig. 3*. The six-membered chelate rings of 1,2,4-trab can adopt either chair or skew-boat, and the five-membered chelate rings of pn and en either λ or δ conformations. In consideration of all configurations of the tridentate and bidentate ligands, there are 16, 56, 56, 56, 48, 12 different structures for $[Co(1,2,3\text{-trab})_2]^{3+}$, $[Co(1,3,4\text{-trpe})_2]^{3+}$, $[Co(1,3,4\text{-tmeb})_2]^{3+}$, $[Co(1,2,4\text{-trpe})_2]^{3+}$, $[Co(1,2,4\text{-trab})(pn)(X)]^{n+}$, and $[Co(1,2,4\text{-trab})(en)(X)]^{n+}$, respectively. All independent structures have been calculated with molecular mechanics. The resulting total strain energies have been cor-

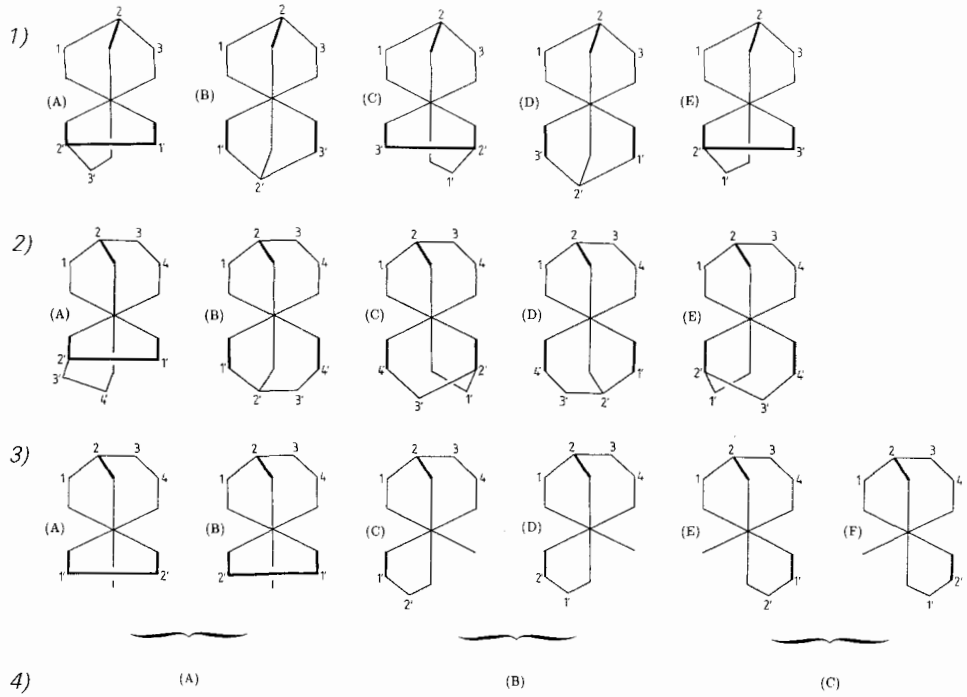

Fig. 3. *Structural formula of all isomers of* 1) *[Co(1,2,3-trab)$_2$]$^{3+}$*, 2) *[Co(1,3,4-trpe)$_2$]$^{3+}$, [Co(1,3,4-tmeb)$_2$]$^{3+}$, [Co(1,2,4-trpe)$_2$]$^{3+}$*, 3) *[Co(1,2,4-trab)(pn)(X)]$^{n+}$, and* 4) *[Co(1,2,4-trab)(en)(X)]$^{n+}$*.

rected for statistical contributions to the entropy (other entropy contributions and environmental effects are neglected, see [2]). The calculation of the isomer distributions is based on the partition function of the system:

$$N_i[\%] = 100 \cdot \frac{e^{-\frac{E_i}{RT}}}{Q_{\text{total}}} \tag{1}$$

$$Q_{\text{total}} = \sum_i e^{-\frac{E_i}{RT}} \tag{2}$$

The total strain energies and the calculated isomer distribution of [Co((S)-1,2,4-trab)((R)/(S)-pn)X]$^{n+}$ are given in *Table 1*[2]).

The calculated *isomer distributions* in [Co(1,2,3-trab)$_2$]$^{3+}$, [Co(1,3,4-trpe)$_2$]$^{3+}$, [Co(1,3,4-tmeb)$_2$]$^{3+}$, [Co(1,2,4-trpe)$_2$]$^{3+}$, and [Co((*S*)-1,2,4-trab)((*R*)/(*S*)-pn)X]$^{n+}$ are roughly independent of the site of the Me substituent and very similar to the distributions observed in the analogous complexes with unsubstituted ligands, *viz.* [Co(trap)$_2$]$^{3+}$ [2], [Co(1,2,4-trab)$_2$]$^{3+}$ [3] and [Co(1,2,4-trab)(en)X]$^{n+}$: *i*) [Co(trap)$_2$]$^{3+}$/[Co(1,2,3-trab)$_2$]$^{3+}$; isomers *rac*/(A + C + E); isomers meso/(B + D): 60:60; 40:40. *ii*) [Co(1,2,4-trab)$_2$]$^{3+}$/[Co(1,3,4-trpe)$_2$]$^{3+}$/[Co(1,3,4-tmeb)$_2$]$^{3+}$/[Co(1,2,4-trpe)$_2$]$^{3+}$; isomers A; B; C; D; E:

[2]) Tables with strain energies and calculated isomer distributions of [Co(1,2,3-trab)$_2$]$^{3+}$, [Co(1,3,4-trpe)$_2$]$^{3+}$, [Co(1,3,4-tmeb)$_2$]$^{3+}$, [Co(1,2,4-trpe)$_2$]$^{3+}$, and [Co(1,2,4-trab)(en)X]$^{n+}$ and tables with calculated stereoselectivities (*Tables S1–S6*) are available as *Supplementary Material*.

Table 1. *Calculated Strain Energies* [kJ/mol] *and Isomer Distribution* (298.15 K) *of [Co((S)-1,2,4-trab)(R)/(S)-pn)(X)]$^{n+}$*

Species[a])	U_{total}	ΔG_{rel}	N_i [%]	Species[a])	U_{total}	ΔG_{rel}	N_i [%]
ACDSR	79.70	4.50	2.62	DCDSR	85.80	10.60	0.22
ACLSR	76.67	1.47	8.88	DCLSR	78.76	3.56	3.82
ABDSR	88.95	13.75	0.06	DBDSR	88.27	13.07	0.08
ABLSR	83.18	7.98	0.64	DBLSR	82.37	7.17	0.89
ACDSS	75.22	0.02	15.94	DCDSS	78.36	3.16	4.49
ACLSS	80.70	5.50	1.75	DCLSS	85.55	10.35	0.25
ABDSS	83.80	8.60	0.50	DBDSS	82.09	6.89	1.00
ABLSS	87.98	12.78	0.09	DBLSS	87.97	12.77	0.09
A_{total}			30.5	D_{total}			10.8
BCDSR	79.78	4.58	2.53	ECDSR	85.15	9.95	0.29
BCLSR	76.71	1.51	8.74	ECLSR	78.72	3.52	3.89
BBDSR	88.93	13.73	0.06	EBDSR	91.90	16.70	0.02
BBLSR	83.15	7.95	0.65	EBLSR	84.95	9.75	0.31
BCDSS	75.20	0.00	16.07	ECDSS	79.10	3.90	3.33
BCLSS	80.95	5.75	1.58	ECLSS	84.92	9.72	0.32
BBDSS	83.82	8.62	0.50	EBDSS	85.34	10.14	0.27
BBLSS	88.87	13.67	0.06	EBLSS	91.12	15.92	0.03
B_{total}			30.2	E_{total}			8.4
CCDSR	84.34	9.14	0.40	FCDSR	84.09	8.89	0.45
CCLSR	78.78	3.58	3.79	FCLSR	78.71	3.51	3.90
CBDSR	87.40	12.20	0.12	FBDSR	91.95	16.75	0.02
CBLSR	82.44	7.24	0.87	FBLSR	85.08	9.88	0.30
CCDSS	78.29	3.09	4.62	FCDSS	79.05	3.85	3.40
CCLSS	85.36	10.16	0.27	FCLSS	84.00	8.80	0.46
CBDSS	81.99	6.79	1.04	FBDSS	85.27	10.07	0.28
CBLSS	88.71	13.51	0.07	FBLSS	92.01	16.81	0.02
C_{total}			11.2	F_{total}			8.9
				S-trab/S-pn_{total}			56.4
				S-trab/R-pn_{total}			43.6

[a]) The five-letter abbreviations involve the isomer (A to F, see *Fig. 3*), followed by the chelate ring conformations (C or B for the six-membered ring of 1,2,4-trab, and D (δ) or L (λ) for the five-membered rings of pn) and the configuration at C(2) and C(n) (R or S each).

21:25:20:21; 16:12:16:16; 16:15:16:17; 4:4:4:4; 43:44:44:42. *iii*) [Co(1,2,4-trab)(en)X]$^{n+}$/[Co(1,2,4-trab)(pn)X]$^{n+}$; isomers A/(A+B); isomers B/(C+D); isomers C/(E+F): 58:61; 24:22; 18:17. The calculated *conformational distribution* within each isomer is strongly dependent on the site of the methyl substituents (see below), and this is leading to an appreciable variation of stereoselectivities.

In homoleptic bis-tridentate transition-metal complexes, a chiral matrix, consisting of one ligand coordinated to a metal center, may be defined. The racemic substrate (second ligand) may then be thought to exchange stereoselectively on this fragment. This enantioselection is leading to selective formation of one (or several) diastereoisomers, and it may be determined (experimentally or with molecular-mechanics calculations) even with racemic ligands [3]. In the present case this allows us to determine stereoselectivities exerted by 1,2,3-trab, 1,3,4-trpe, 1,3,4-tmeb, and 1,2,4-trpe, and, therefore, to test the influence of and determine the optimal site for Me substitution to relatively poor chiral

matrix ligands. 1,2,3-trab is, because of the stiff trap backbone [2], as expected, still a relatively unselective ligand (only selectivities at optimum substitution sites are given): chiral matrix, Co((1*S*,2*S*)-1,2,3-trab); racemic substrate, (1*S*,2*S*)-1,2,3-trab *vs.* (1*S*,2*R*)-1,2,3-trab (38% ee) and (1*S*,2*R*)-1,2,3-trab *vs.* (1*R*,2*R*)-1,2,3-trab (38% ee). With 1,3,4-trpe and 1,3,4-tmeb, the substituent in α-position to the tertiary C-atom is still in a relatively inflexible site, and the resulting maximum selectivities are only little improved: chiral matrix, Co((3*S*,4*S*)-1,3,4-trpe); racemic substrate, (3*S*,4*S*)-1,3,4-trpe *vs.* (3*S*,4*R*)-1,3,4-trpe (49% ee) and (3*S*,4*R*)-1,3,4-trpe *vs.* (3*R*,4*R*)-1,3,4-trpe (57% ee); chiral matrix, Co((2*S*,3*S*)-1,3,4-tmeb); racemic substrate, (2*S*,3*S*)-1,3,4-tmeb *vs.* (2*R*,3*R*)-1,3,4-tmeb (60% ee) and (2*R*,3*S*)-1,3,4-tmeb *vs.* (2*R*,3*R*)-1,3,4-tmeb (60% ee). 1,2,4-trpe is a comparably selective ligand with the following optimal enantioselectivities: chiral matrix, Co((2*S*,4*S*)-1,2,4-trpe); racemic substrate, (2*S*,4*S*)-1,2,4-trpe *vs.* (2*R*,4*S*)-1,2,4-trpe (83% ee) and (2*R*,4*S*)-1,2,4-trpe *vs.* (2*R*,4*R*)-1,2,4-trpe (88% ee).

Experimentally Determined Isomer Ratios. – Coordination of both enantiomers of a racemic chelate to a chiral matrix consisting of a chiral (optically pure) ligand coordinated to a transition-metal ion leads to a number of (at least two) diastereoisomers. Under thermodynamic control, the selectivity of such a ligand-exchange reaction is the result of the free-energy differences between the various isomers which usually are dominated by steric intramolecular interactions (provided that the diastereoisomers have basically identical chromophores) [1–3]. Strain-energy-minimization calculations are well suited to predict such stereoselectivities, if one accepts the error limits based on a number of assumptions and simplifications inherent to the molecular-mechanics formalism [1–3], *viz.* the ligand systems of the chiral matrix may be designed in order to minimize elaborate organic syntheses.

For a meaningful comparison between calculated selectivities and experimentally determined isomer ratios and enantioselective coordination of a racemic substrate to a chiral matrix, the equilibrium position has to be determined. For the inert Co(III) systems this is usually done in presence of activated charcoal [2]. However, in the present systems with en and pn as racemic substrates, formation of Co(III)-hexaamines during oxygenation in presence of charcoal is obscuring the tiny amounts of ternary complexes formed. Therefore, equilibrium mixtures were obtained by oxygenation without addition of charcoal. Our confidence in this reaction is based on precedents [6] [25–27] and the good agreement between experimental and calculated data[3]).

The isomer ratio of $[Co(1,2,4\text{-trab})(en)X]^{n+}$ has been determined by HPLC[4]) and enantioselective coordination of (±)-pn was determined by ^{1}H-NMR of the *Mosher*-acid derivative of recovered excess ligand (see *Table 2*). Polarimetric determination of the enantiomeric excess of (±)-pn to the Co((R)-1,2,4-trab) fragment is less precise but gave qualitatively identical results. Falsification by the unrecovered ~3% of pn can be excluded since formation of $[Co(pn)_3]^{3+}$ is not enantioselective, and no 1,2,4-trab was detected in the ^{1}H-NMR of the *Mosher*-acid adduct of pn.

Conclusions. – In general, an increase in stereoselectivity by substitution of the backbone of a matrix ligand may be achieved by *i*) an increase of the steric crowding exerted towards the substrate ligand or *ii*) an enforced change of the conformational

[3]) Clearly, this agreement might be accidental, and it is also based on the generally observed good agreement between calculated and experimental results based on the presently used force field [1–6].

[4]) An unambiguous assignment of the chromatographic peaks to the isomers A, B, C is not possible (see also [3]).

equilibrium. Substitution of the trap and 1,2,4-trab backbones are clearly leading to effects of the second typ, since C-substituents of simple facially coordinating triamines are generally poised away from the coordination sphere. Here, a less stable conformation may be enforced by a preferred conformation of higher priority (larger energy difference). The classes of conformations applicable to our present problems involve δ and λ conformations of five-membered chelated, *chair* and *boat* conformations of six-membered chelates and *equatorial* and *axial* substituents to chelate rings. Based on a number of calculations of Co(III) hexaamines [1–3] [6], the following order of preferences is deduced: *lel* is more stable than *ob* by $\sim$ 1 kJ/mol, *chair* is more stable than *boat* by $\sim$ 4 kJ/mol, and *equatorial* is more stable than *axial* by $\sim$ 15 kJ/mol (for six-membered chelates, the difference for five-membered rings is a little smaller [12]). Clearly, a quantification of such effects is dependent on the exact geometry of a particular molecule, and also on the force-field on which the calculation of the energy differences is based[5]), and it, therefore, has to be considered with caution. Although an increased crowding in the neighbourhood of the substrate ligand might be expected to lead to an even larger selectivity, the enforced conformations by appropriate placements of methyl substituents are, according to our calculations leading to enantiomeric excesses of up to 90%.

As for $[Co(trap)_2]^{3+}$ [2] and $[Co(1,2,4\text{-trab})_2]^{3+}$ [3], the five-membered chelate rings involving N(1) and N(2) are highly strained. This is reflected in nearly eclipsed torsion angles around N(1)–C(1) axes ($\sim$ 12°), and for the trap backbone in Co–N(2)–C(2) angles which are reduced by $\sim$ 10°. In general, the move from two fused five-membered chelates to a five- and a six-membered ring (trap *vs.* 1,2,4-trab) leads to a relaxation of the torsional strain around the C(4)–N(3) axis and to a relaxed Co–N(2)–C(2) angle ($\sim$ 106°, depending on the conformation, *vs.* $\sim$ 97°). On the other hand, the Co–N(3)–C(4) angle the 1,2,4-trab backbone is considerably strained (up to $\sim$ 125°, depending on the conformation), and the Co–N(3) bond is lengthened (up to $\sim$ 1.99 Å, depending on the conformation, *vs.* $\sim$ 1.95 Å). These contributions to the total strain are general and roughly independent of the site of the Me substituent. This is not surprising, since the substituents are pointing away from the second coordinated triamine ligand. Therefore, the *isomer distribution* is in these cases nearly independent of the substitution of the ligand backbone. However, the *conformational distribution* (*i.e.* the distribution within a particular isomer) and, therefore, the *enantioselectivity* are clearly dependent on the site of the Me substituents. Two effects are responsible for this dependency: *i*) there is considerable repulsion of Me substituents by the amine N(2), if the Me group is exo with respect to N(2). The effect is especially pronounced with Me substituents at five-membered chelate rings ($[Co(1,2,3\text{-trab})_2]^{3+}$, $[Co(1,3,4\text{-trpe})_2]^{3+}$), where the *exo*-Me groups are forced into nearly eclipsed conformations with respect to the N(1)–C(1) axis ($\sim$ 0° in $[Co(1,2,3\text{-trab})_2]^{3+}$ *vs.* $\sim$ 12° in $[Co(trap)_2]^{3+}$ [2]). The most relevant contributions to the total strain energy based on this effect are to torsional strain and non-bonded interactions (repulsion of the Me substituent by the *syn*-H of N(1)). *ii*) The conformations of the six-membered chelate rings are the result of a compromise between the preference of chair conformation and the propensity of the Me substituents for axial conformation. It is well

---

[5]) Energy differences obtained with other force fields [12] [19] [30] *are* different, although the general trends are very similar. The numbers presented here are based on a relatively large number of studies with the same force field, and with generally good agreement between calculated and observed data.

known that coordinated six-membered chelate rings are less stable in boat than in chair conformation [3] [7] [12] [19], and the contribution to the torsional strain is most important here. The contribution of axial substituents to the total strain is primarily *via* repulsion of the substituent by neighbouring *syn*-protons and coupled angle distortions.

The matrix ligand used for our experimental studies is the simple facially coordinating and easily accessible chiral triamine 1,2,4-trab. Strain energy minimization calculations have shown that Me substitution of the trap and 1,2,4-trab backbones leads to chiral ligands with enhanced stereoselectivities. In view of the good agreement between calculated and experimentally determined isomer and enantiomer distributions with trap and 1,2,4-trab *(Table 2)*, it might be an obvious task to calculate the selectivities with these

Table 2. *Comparison of Calculated and Experimental Isomer Distributions*[a])

Complex	Isomer	Temperature [K]	N_i^{exp} [%][b])	N_i^{calc} [%]
$[Co(trap)_2]^{3+}$	*meso*	298	45 (*A*)	40
	rac		55 (*A*)	60
	meso	353	48 (*A*); 44 (*B*)	40
	rac		52 (*A*); 56 (*B*)	60
$[Co(1,2,4\text{-trab})_2]^{3+}$	A	298	21 (*A*)	21
	B		15 (*A*)	16
	C		15 (*A*)	16
	D		4 (*A*)	4
	E		45 (*A*)	43
$[Co(1,2,4\text{-trab})(en)(X)]^{n+}$	A	298	~ 60 (*C*)	58
	B		~ 22 (*C*)	24
	C		~ 18 (*C*)	18
[Co((*R*)-1,2,4-trab) ((*R*)/(*S*)-pn)(X)]$^{n+}$	(*R*)-pn	298	54 (*C*)	56
	(*S*)-pn		46 (*C*)	44

[a]) For $[Co(trap)_2]^{3+}$ and $[Co(1,2,4\text{-trab})_2]^{3+}$ see [2] and [3], resp.
[b]) Experiment: (*A*) oxygenation (charcoal); (*B*) equilibration (charcoal); (*C*) oxygenation, see *Experimental.*

improved matrix-ligand systems and a variety of substrates, and to prepare such chiral tridentates and test them experimentally. However, the substituted systems are preparatively far less accessible than trap and 1,2,4-trab, and they have the disadvantage of leading to a large number of isomeric products (see above). Therefore, we are currently developing syntheses of a number of chiral symmetrical ligands [4–6]. The data on improvement of the stereoselectivity of matrix ligands by substitution of the ligand backbone of the simple facially coordinating triamines will certainly be very useful in the design of these new systems.

Supplementary Material Available. Tables with strain energies and calculated isomer distributions of $[Co(1,2,3\text{-trab})_2]^{3+}$, $[Co(1,3,4\text{-trpe})_2]^{3+}$, $[Co(1,3,4\text{-tmeb})_2]^{3+}$ $[Co(1,2,4\text{-trpe})_2]^{3+}$, and $[Co(1,2,4\text{-trab})(en)X]^{n+}$, and tables with calculated stereoselectivities *(Tables S1–S6)* are available as *Supplementary Material.*

We are grateful to the *Foundation of the Portlandcement Fabrik Laufen* (HPLC pump), the *Ciba Foundation* (HPLC columns and chiral reagents), and the *Swiss National Science Foundation* (grant 20-5597.88) for financial support.

REFERENCES

[1] P. Comba, *Inorg. Chem.* **1989,** *28,* 426.
[2] P. Comba, T. W. Hambley, L. Zipper, *Helv. Chim. Acta* **1988,** *71,* 1875.
[3] P. Comba, M. Maeder, L. Zipper, *Helv. Chim. Acta* **1989,** *72,* 1029.
[4] P. Comba, T. W. Hambley, G. A. Lawrance, L. L. Martin, P. Renold, K. Várnagy, submitted to *J. Chem. Soc., Dalton Trans.*
[5] P. Comba, L. L. Martin, K. Várnagy, L. Zipper, submitted to *Helv. Chim. Acta.*
[6] P. Comba, work in progress.
[7] J. R. Gollogly, C. J. Hawkins, *Inorg. Chem.* **1969,** *8,* 1168.
[8] M. R. Snow, *J. Am. Chem. Soc.* **1970,** *92,* 3610.
[9] D. A. Buckingham, I. E. Maxwell, A. M. Sargeson, M. R. Snow, *J. Am. Chem. Soc.* **1970,** *92,* 3617.
[10] D. A. Buckingham, P. J. Cresswell, R. J. Dellaca, M. Dwyer, G. J. Gainsford, L. G. Marzilli, I. E. Maxwell, W. T. Robinson, A. M. Sargeson, K. R. Turnbull, *J. Am. Chem. Soc.* **1974,** *96,* 1713.
[11] B. F. Anderson, J. D. Bell, D. A. Buckingham, P. J. Cresswell, G. J. Gainsford, L. G. Marzilli, G. B. Robertson, A. M. Sargeson, *Inorg. Chem.* **1977,** *16,* 3233.
[12] L. J. De Hayes, D. H. Bush, *Inorg. Chem.* **1973,** *12,* 1505.
[13] C. J. Hilleary, T. F. Them, R. E. Tapscott, *Inorg. Chem.* **1980,** *19,* 102.
[14] T. W. Hambley, C. J. Hawkins, M. A. Palmer, M. R. Snow, *Aust. J. Chem.* **1981,** *34,* 45.
[15] T. W. Hambley, C. J. Hawkins, M. A. Palmer, M. R. Snow, *Aust. J. Chem.* **1981,** *34,* 2525.
[16] T. W. Hambley, G. H. Searle, M. R. Snow, *Aust. J. Chem.* **1982,** *35,* 1285.
[17] T. W. Hambley, G. H. Searle, *Aust. J. Chem.* **1984,** *37,* 249.
[18] A. M. Bond, T. W. Hambley, M. R. Snow, *Inorg. Chem.* **1985,** *24,* 1920.
[19] S. R. Niketic, K. Rasmussen, *Acta Chem. Scand., Ser. A* **1978,** *32,* 391.
[20] T. W. Hambley, *Inorg. Chem.* **1988,** *27,* 2496.
[21] G. R. Brubaker, D. W. Johnson, *Coord. Chem. Rev.* **1984,** *53,* 1.
[22] F. P. Dwyer, A. M. Sargeson, *Nature (London)* **1960,** *187,* 1022.
[23] F. R. Keene, G. H. Searle, *Inorg. Chem.* **1974,** *13,* 2173.
[24] G. H. Searle, F. R. Keene, S. F. Lincoln, *Inorg. Chem.* **1978,** *17,* 2362.
[25] M. Shibata, *Topics Curr. Chem.* **1983,** 110.
[26] G. H. Searle, T. W. Hambley, *Aust. J. Chem.* **1982,** *35,* 1297.
[27] G. H. Searle, T. W. Hambley, *Aust. J. Chem.* **1982,** *35,* 2399.
[28] J. A. Dale, D. L. Dullm H. S. Mosher, *J. Org. Chem.* **1969,** *34,* 2543.
[29] T. W. Hambley, Department of Chemistry, The University of Sydney, Australia, Momec 85, a fortran program for strain energy minimizations.
[30] S. R. Niketic, K. Rasmussen, F. Woldbye, S. Lifson, *Acta Chem. Scand., Ser. A* **1976,** *30,* 485.