CHIRAL DISCRIMINATION IN DIASTEREOISOMERIC SYSTEMS OF CADMIUM WITH 1,10-PHENANTHROLINE AND S-AMINOACIDATES

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Abstract—Δ,Λ-[Cd(phen)$_2$(S-aa)]$^+$NO$_3^-$ diastereomeric systems (where phen = 1,10-phenanthroline and S-aa = S-alaninate, S-serinate, S-threoninate, S-prolinate, S-valinate, S-leucinate and S-phenylalaninate) have been prepared in the form of methanolic solutions and characterized by spectral (UV, CD, ORD) and conductance measurements. The CD spectra of these systems in the β' band region of the diimine ligand exhibit residuary exciton splittings, whose intensities and sign patterns suggest the following decreasing order of [Λ]/[Δ] diastereoisomeric equilibrium constants: S-prol > S-phenala > S-val > 1 > S-ala > S-leu > S-ser > S-threo. The same order is inferred from the ORD data over the range 400–600 nm. Comparison with the selectivities observed for some zinc analogues and the analysis of molecular models suggest that in the cadmium systems the chiral discriminations are governed mainly by a balancing between intramolecular steric repulsion, differential solvation and discriminating ion association. Solvent effects on the optical activity of some cadmium and zinc systems in methanol/n-propanol and methanol/benzene mixtures have also been studied. The corresponding results are discussed in terms of the contributions of the above discriminating forces.

The circular dichroism (CD) spectra in the aromatic region of Δ,Λ-[M(diimine)$_2$(aa)]$^{(z-q)+}$ systems, where M^{z+} is a transition or an $(n-1)d^{10}$ metal ion, diimine is 1,10-phenanthroline or 2,2'-bipyridine and aa^{q-} is an optically active α-aminoacidate, in aqueous or methanolic solution, exhibit residuary exciton bands whose intensities and sign patterns can be mainly connected with the particular positions of the respective diastereoisomeric equilibria:[1–4]

$$\Delta\text{-[M(diimine)}_2\text{(aa)]}^{(z-q)+} \Longrightarrow$$

$$\Lambda\text{-[M(diimine)}_2\text{(aa)]}^{(z-q)+}.$$
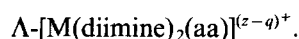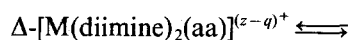
The equilibrium constants for the preceding reactions show, in turn, a clear dependence upon the nature of the side-chain of the chiral ligand. Usually, the chelation of an S-aminoacidate having an apolar side-chain induces an equilibrium shift towards an increase in concentration of the Λ-
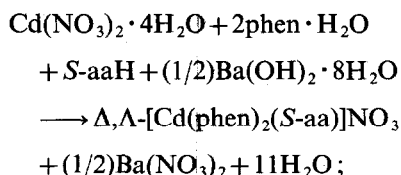
isomer. Here, the origin of chiral discrimination has been ascribed to a prevalence of intramolecular ligand–ligand steric repulsive interactions in the less preferred Δ-isomer.[2–6] On the other hand, the chelation of an S-aminoacidate having a polar side-chain may lead to the predominance of either the Δ- or the Λ-diastereoisomer, depending on the particular metal ion and diimine ligand involved. Thus, concerning the trend to Δ-isomer predominance, for systems containing S-serinate the order Ru^{II} > Co^{III} can be established from the data reported at present.[1,7] The order 2,2'-bipy > 1,10-phen is also observed for the above tendency in systems of ruthenium(II) with S-serinate, S-aspartate or S-glutamate.[1,8,9] This sequence has been ascribed to the greater flexibility of the bipyridine ligand,[8] which should cause a decrease in the intramolecular ligand–ligand steric repulsion, thus enhancing other types of non-covalent interactions that are referred to below. Indeed, for 1,10-phen systems in aqueous solution chiral induction involving $\Delta/\Lambda > 1$ occurs only in Δ,Λ-[Ru(phen)$_2$(S-glu)]^0 and Δ,Λ-

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[Ru(phen)$_2$(*S*-threo)]$^+$, whereas Δ,Λ-[Ru(phen)$_2$(*S*-asp)]^0 and Δ,Λ-[Ru(phen)$_2$(*S*-ser)]$^+$ show no stereoselectivity.[1,8–10] In general, chiral discrimination favouring the stability of one diastereoisomer would arise partly from a balancing between steric repulsive interactions and other intramolecular forces, such as hydrogen bonding and possible hydrophobic bonding interactions.[8,9] Further, some intermolecular factors have also been suggested as sources of stereoselectivity, namely differential solvation[11] and hydrogen bonding interactions with the surrounding chiral solvent sheaths,[12] which are concomitant with the dissymmetry of the complex ions. A structural feature of rather obvious interest for the study of the different kinds of interactions previously mentioned would be the metal ion size. An increase in the metal ion radius should diminish the intramolecular steric repulsion effects, which are usually predominant, thus allowing other discriminating forces to become apparent with relatively higher intensities. This report is concerned with the stereoselective effects of non-resolvable *S*-aminoacidatobis(1,10 - phenanthroline)cadmium(II) complexes in methanolic solution. In these complexes the metal–ligand bond lengths should be nearly 0.2 Å larger than those of the corresponding complexes of zinc or ruthenium(II). Hence, a somewhat different balancing of intramolecular interactions should be expected here regarding the analogues of those metal ions. Similarly to zinc systems, cadmium systems exhibit very rapid diastereoisomeric equilibration rates. This prevents both the use of ordinary resolution procedures and the experimental estimation of the respective Δ/Λ equilibrium constants from optical activity measurements. Notwithstanding the above restraints, these complexes provide in return the certainty of dealing with truly equilibrated diastereoisomeric systems.

EXPERIMENTAL

Nitrate salts of the heterochelated ions Δ,Λ-[Cd(phen)$_2$(*S*-aa)]$^+$ were prepared as 0.007 or 0.018 M solutions in methanol, by means of the following general reaction:

$$Cd(NO_3)_2 \cdot 4H_2O + 2phen \cdot H_2O$$
$$+ \textit{S}\text{-aaH} + (1/2)Ba(OH)_2 \cdot 8H_2O$$
$$\longrightarrow \Delta,\Lambda\text{-[Cd(phen)}_2(\textit{S}\text{-aa)]NO}_3$$
$$+ (1/2)Ba(NO_3)_2 + 11H_2O;$$

where *S*-aaH = *S*-alanine, *S*-serine, *S*-threonine, *S*-valine, *S*-leucine, *S*-phenylalanine or *S*-proline. Stoichiometric amounts of the analytical reagent or CP-grade chemicals were mixed in methanol *pro analysi* as a solvent, and heated at 60°C in stoppered flasks until complete reaction of the amino acid. Once cooled the resulting mixtures were ultrasonically stirred and allowed to stand at room temperature for 2 days. Barium nitrate was discarded by filtration under suction. The resulting solutions were concentrated by boiling and standardized to 0.007 or 0.018 M at 25°C. For the sake of comparison chloride and sulphate salts of similar zinc complexes were also prepared as methanolic solutions (0.007 or 0.018 M in complex ions) by methods previously reported.[4] Electronic spectral measurements in the UV region were performed at room temperature on a Carl–Zeiss DMR-21 spectrophotometer using 5.6×10^{-5} M solutions in 0.1 cm cells. CD spectra were recorded on a Cary 60 spectropolarimeter, at room temperature, using 2.1×10^{-4} or 4.2×10^{-4} M solutions in closed 0.1 cm cells. Optical rotatory dispersion (ORD) spectra were measured at 25°C on a modified Perkin–Elmer 141 polarimeter, using 0.007 M solutions in thermostated closed 2 or 10 cm cells. Conductivity measurements were performed at 25°C with a YSI model 32 conductance bridge and an immersion cell (1.022 cm^{-1}), using 0.007 M solutions. Molar ratio studies of optical rotation at 450 nm of the systems Cd^{II} : phen : *S*-aa = 1 : *x* : 1 were performed at 25°C over the range $1 \leqslant x \leqslant 3$ for *S*-aa = *S*-threo and *S*-val. Moreover, solvent effects of increasing concentrations of n-propanol and benzene on the optical activity of some 0.0018 M cadmium systems were tested over the ranges 0–12 M and 0–10 M, respectively. Some zinc systems were also considered in these experiments. The effects of the relatively small water contents of the complex salt solutions on diastereoisomeric and formation equilibria were assumed to be neglible for comparative purposes.

RESULTS AND DISCUSSION

Spectral properties and diastereoisomeric equilibria

Results of the molar ratio studies on the systems Cd^{II} : phen : *S*-aa$^-$: NO$_3^-$ = 1 : *x* : 1 : 1 of *S*-valinate and *S*-threoninate are compared in Fig. 1, where the molecular rotations at 450 nm are plotted against $x = [\text{phen}]_{\text{total}} : [\text{Cd}^{II}]_{\text{total}}$. From these data it becomes apparent that the species responsible for the optical activity in the above system are [Cd(phen)$_2$(*S*-aa)]$^+$ diastereoisomeric complexes. This inference agrees with the conductance data listed in Table 1. Although these values are not accurate, they strongly suggest that the cadmium systems prepared consist predominantly of uniu-
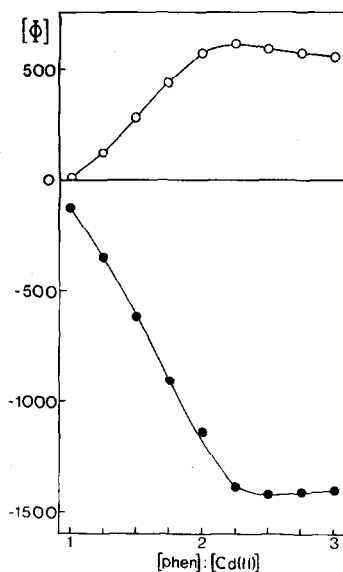
Fig. 1. Variation of molar rotation at 450 nm of systems Cd^{II}:phen: S-aa$^-$:NO$_3^-$ = 1:x:1:1, in methanol, as a function of the [phen]$_{total}$:[Cd^{II}]$_{total}$ molar ratio. [Cd^{II}]$_{total}$ = 0.007 M; 25°C. S-aa$^-$ = S-val$^-$ (○) and S-threo$^-$ (●).
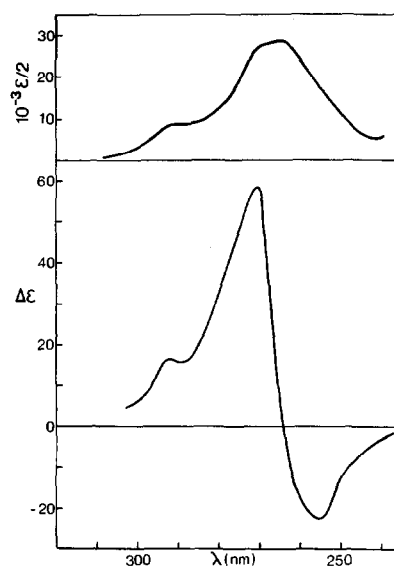

Fig. 2. Absorption and CD spectra in the UV region (p- and β'-bands) of the system Δ,Λ-[Cd(phen)$_2$(S-prol)]NO$_3$, in methanol, at room temperature.

nivalent electrolytes.[13,14] Moreover, the UV absorption spectra in the region of the long-axis-polarized π–π* transitions of the diimine ligand, which are virtually identical for the different cadmium systems, show bathochromic shifts of the β'- and p-bands that are similar to those of Δ,Λ-[Ni(phen)$_2$(S-aa)]$^+$ and Δ,Λ-[Zn(phen)$_2$(S-aa)]$^+$ complexes[4] (Figs 2 and 3). Some features of the CD spectra in the β'-band region of the studied cadmium systems are given in Table 1 and CD

spectra in the β'- and p-band region of some selected systems are shown in Figs 2, 3 and 4. According to these data residuary exciton bands are always present in the CD spectra, their intensities and sign patterns being clearly dependent upon the structure of the side-chain of the chiral ligand. In fact, the typical sign pattern indicating the predominance of the Λ-diastereoisomer is observed only in the systems of S-phenylalaninate, S-prolinate and S-valinate, i.e. in systems of S-aminoacidates having

Table 1. CD data at room temperature and molar conductances at 0.007 M and 25°C of Δ,Λ-[Cd(phen)$_2$(S-aa)]NO$_3$ systems in methanol

S-aa[a]	λ (nm) (Δε)	Λ[b] (Ω^{-1} cm^2 mol^{-1})
S-prol	271 (+58.8); 256 (−22.0)	80
S-phenala	275 (+17.4); 253 (−8.7)	—
S-val	271 (+8.7); 253 (−4.6)	76
S-ala	275 (−6.5); 264 (+7.6)	78
S-leu	273 (−9.3); 259 (+2.9)	78
S-ser	273 (−9.9); 256 (+1.7)	81
S-threo	272 (−13.1); 256 (+2.9)	79

[a] Abbreviations: S-prol = S-prolinate, S = phenala = S-phenylalaninate, S-val = S-valinate, S-ala = S-alaninate, S-leu = S-leucinate, S-ser = S-serinate, S-threo = S-threoninate.

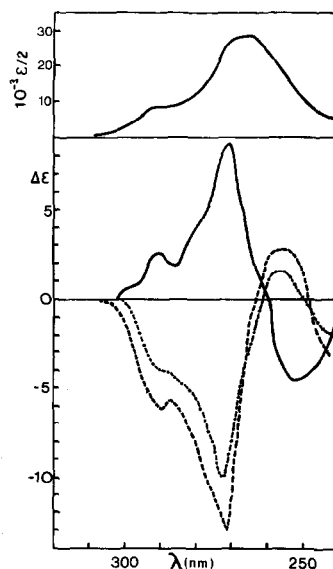[b] Not corrected for the presence of small varying concentrations of barium nitrate.

Fig. 3. Absorption and CD spectra in the UV region (p- and β'-bands) of systems Δ,Λ-[Cd(phen)$_2$(S-aa)]NO$_3$, in methanol, at room temperature. S-aa = S-val (———), S-ser (—·—·—) and S-threo (————).
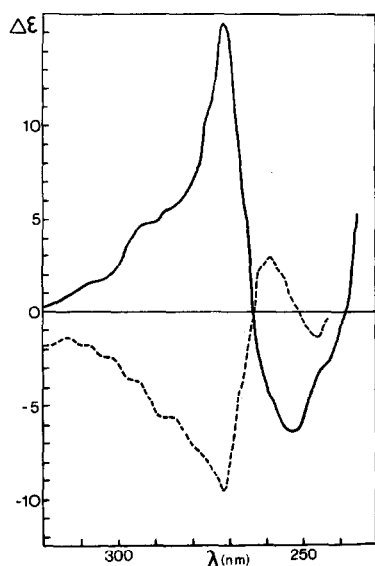
Fig. 4. CD spectra of Δ,Λ-[M(phen)₂(S-leu)]⁺ systems (p- and β'-bands), in methanol, at room temperature. M = Zn (——) and Cd (‐‐‐‐).

bulky, exceedingly rigid or β-substituted side-chains, respectively. Chiral discrimination arising from intramolecular steric repulsive interations must be preponderant in the above systems.[2,5] On the other hand, the exciton CD spectra of the remaining cadmium systems exhibit sign patterns characteristic of Δ-diastereoisomer predominance. Here, discriminating forces other than steric effects would be determinant. Interestingly, two systems containing aminoacidate ligands with apolar side groups are found amongst those exhibiting chiral induction with a preference for the Δ-isomer, viz.

the S-ala and S-leu systems. The exciton CD spectrum of the latter is compared with its zinc analogue in Fig. 4. From a general point of view the above dependences of the CD spectra upon the nature of the side groups of the aminoacidates indicate at least that these ligands are acting as chelating agents.

Molecular rotation values for the cadmium systems are listed in Table 2. As can be seen, these data are in good agreement with the respective CD spectra. This fact is reflected by the plot of the molecular rotation at 450 nm against the maximum of circular dichroism of the low-energy long-axis-polarized π–π^* transition, which gives a fairly good linear correlation ($r = 0.994$). Taking into account the relative intensities of the low-energy exciton CD bands (Table 1) and the molecular rotation values at 450 nm (Table 2), the following sequence of diastereoisomeric equilibrium constants can be proposed for the cadmium systems: $K(S\text{-prol}) > K(S\text{-phenala}) > K(S\text{-val}) > 1 > K(S\text{-ala}) > K(S\text{-leu}) > K(S\text{-ser}) > K(S\text{-threo})$, where $K(S\text{-aa}) = [\Lambda]/[\Delta]$. The preceding sequence differs noticeably from that obtained for analogues of zinc,[3] where steric effects are always predominant and no cases are observed of chiral discrimination enhancing the equilibrium concentration of the Δ-isomer: $K(S\text{-val}) > K(S\text{-prol}) > K(S\text{-threo}) > K(S\text{-ser}) > K(S\text{-leu}) > K(S\text{-ala}) > 1$ (Table 2).

Exciton splitting and hydrophobic interactions

For the sake of comparison the ORD spectra of the cadmium and zinc systems under study were

Table 2. Molecular rotations at 450 nm and Drude equation parameters of Δ,Λ-[M(phen)₂(S-aa)]X₁/q systems of cadmium[a] and zinc[b] in methanol, at 25°C

M	S-aa	$[\Phi]_{450\,nm}^{25°C}$	$\lvert\Sigma\rvert$ (cm⁻¹)	C_1	C_2	$10^3 C_3$
Cd	S-prol	+3693	82.4	+40.260	−39.861	15.3
Cd	S-phenala	+1086	108.0	+11.832	−11.765	4.8
Cd	S-val	+571	97.0	+6.236	−6.181	−2.3
Cd	S-ala	−500	51.0	−5.455	+5.366	1.7
Cd	S-leu	−557	98.5	−6.064	+6.024	−4.8
Cd	S-ser	−829	88.6	−9.044	+8.966	−4.6
Cd	S-threo	−1136	77.0	−12.361	+12.225	−3.8
Zn	S-val	+2179	105.5	+23.764	−23.637	17.2
Zn	S-prol	+2018	91.3	+22.023	−21.857	17.3
Zn	S-threo	+1271	86.4	+13.885	−13.759	5.3
Zn	S-ser	+763	116.0	+8.321	−8.297	9.4
Zn	S-leu	+756	115.0	+8.231	−8.192	2.2
Zn	S-ala	+729	85.0	+7.950	−7.871	0.2

[a] $X^{q-} = NO_3^-$.
[b] $X^{q-} = SO_4^{2-}$.

described over the range 400–600 nm through many-term Drude equations of the form:[4]

$$[\Phi]_\lambda = \frac{10^4}{1.4}\left[\frac{C_1\lambda_1^2}{\lambda^2-\lambda_1^2} + \frac{C_2\lambda_2^2}{\lambda^2-\lambda_2^2} + C_3\right];$$

where subscripts 1 and 2 are the β'-exciton bands, $\lambda_1 > \lambda_2$, and C_3 is a term comprising the weaker contributions. If the same excitation resonance splitting is assumed for both Δ and Λ isomers, the wavelengths of the absorption maxima of the exciton bands become $\lambda_1 = 10^7\lambda_0/(10^7-|\Sigma|\lambda_0)$ and $\lambda_2 = 10^7\lambda_0/(10^7+|\Sigma|\lambda_0)$, where λ_0 is the wavelength in nm of the baricenter of the β'-band and $|\Sigma|$ is the mean absolute value of the excitation resonance energy in cm^{-1}. The parameters C_1, C_2 and C_3 were calculated from the molecular rotation data at 400, 450 and 550 nm by iterating $|\Sigma|$ values until $C_1 \approx 0.1091$ [Φ]$_{450\,nm}$ was obtained. This condition arises from an assumed proportionality between C_1 and [Φ]$_{450\,nm}$. The above proportionality constant was obtained from the previously studied system Δ,Λ-[Zn(phen)$_2$(S-ala)]Cl, for which $|\Sigma| = 100$ cm^{-1} was arbitrarily taken.[4] In other words this approximation implies that in these systems the intensity of the ORD spectrum depends much more upon the position of the Λ/Δ diastereoisomeric equilibrium than on the extent of the excitation resonance splitting. The $|\Sigma|$, C_1, C_2 and C_3 parameters thus obtained are shown in Table 2. The ORD curves calculated with these figures are in excellent agreement with the experimental ones. This fact becomes apparent on plotting the experimental against the calculated molecular rotation values over the range 400–600 nm. Straight lines almost passing through the origin are thus obtained, whose slopes are very close to unity, the corresponding correlation coefficients always being greater than 0.9996. Although the pairs of C_1 and C_2 values listed in Table 2 show the right sign patterns, they do not reflect the relative intensities of the residuary exciton bands (Table 1). However, some uncertainty could also be expected in the magnitudes of the residuary exciton bands since the diimine ligand exerts strong absorption in the aromatic spectral region, rendering the CD measurements difficult in most cases. On the other hand, for both cadmium and zinc systems the variation of $|\Sigma|$ through the aminoacidate series shows no correlation with the remaining Drude equation parameters. Nevertheless, for systems with S-aminoacidates having apolar side-chains amazingly good correlations are observed with a rather rough topological index consisting of the total number of atoms of the side-chain. Such correlations are shown in Fig. 5, where the systems of S-serinate
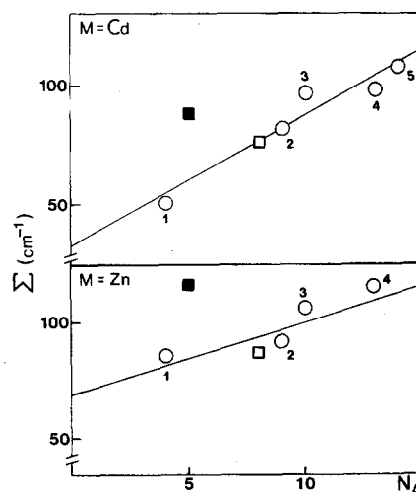

Fig. 5. Correlation of mean excitation resonance energies of Δ,Λ-[M(phen)$_2$(S-aa)]$^+$ systems vs side-chain sizes. N_A = total number of atoms of the side-chain. S-alaninate (1); S-prolinate (2); S-valinate (3); S-leucinate (4); S-phenylalaninate (5); S-serinate (■); S-threoninate (□). M = Cd ($r = 0.97$); Zn ($r = 0.92$).

and S-threoninate are also included, although they are not considered in the regression analysis. As can be seen these diagrams result in similar arrangements for the systems of both metal ions, even concerning the positions of the systems that contain S-aminoacidates with polar side-chains. Intramolecular non-covalent interactions could also be responsible for this behaviour. These forces should induce small geometrical changes that modify the effective distance between the transition dipoles located at the molecular centres of the adjacent diimine ligands. This assumption agrees with the fact that for each aminoacidate ligand the $|\Sigma|$ value of the zinc system is always greater than that of the cadmium system (Table 2), consistent with the dipole–dipole approximation.[15] Moreover, the $|\Sigma|$ values of systems containing S-aminoacidates with apolar side-chains follow the order S-phenala > S-leu > S-val > S-prol > S-ala, which parallels the hydrophobicity scale for side-chains of aminoacids.[16] Hence, the above defined topological index would also be reflecting the variation in this property through the aminoacidate series. Further, since the variation of the [Λ]/[Δ] equilibrium position of the cadmium and zinc systems through the aminoacidate series does not parallel the aforementioned hydrophobicity scale, it can be concluded that the contributions of intramolecular hydrophobic interactions are not determinant for the observed stereoselective effects. Indeed, intramolecular hydrophobic interactions would rather

enhance the stability of the Λ-isomer, as can be shown from the structure proposed by Sigel *et al.*[17] for the folded form of the species [Zn(phcn)(S-leu)]$^+$.

Solvent effects

It seems reasonable to assume that both polar solvation and ion-pairing interactions of the diastereoisomeric species occur mainly through the amino group, because its hydrogen atoms would carry a substantial fraction of the positive charge of the metal chelates.[18] Thus, both differential polar solvation and discriminating ion association would take place on account of the different intramolecular environments that surround the coordinating amino group in each diastereoisomer. Analysis of molecular models suggests that although the Δ-diastereoisomer must be sterically less favoured than the Λ-form, it should be subjected in turn to better polar solvation on the amino group and stronger ion-pairing interactions, which would obviously contribute to increasing its thermodynamic stability. The above observations are illustrated in Fig. 6, where a comparison is attempted of the intramolecular environment of the assumed main polar solvation sites in the Δ- and Λ-isomers of the S-leucinate system. In these schematic representations the diastereoisomeric chelates are viewed along the H_2N—Cd^{2+} bonds; consequently, the metal ions are eclipsed by the amino nitrogen donors. Moreover, both species are shown in folded form. As can be seen, in the Δ-isomer one of the hydrogen atoms of the NH_2 group remains freely exposed towards the bulk of the solvent, whatever the conformation adopted by the side-chain. Further, such a hydrogen atom would lie nearly 2.6 Å over the molecular plane of the phenanthroline ligand having both nitrogen donors in *cis* positions to the amino group. On the contrary,
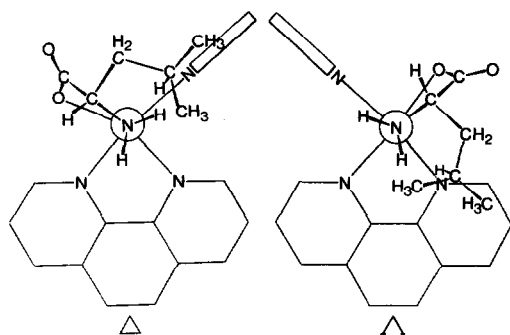
in the folded form of the Λ-isomer polar solvation should be somewhat hindered by the hydrophobic groups of the side-chain. As previously mentioned, in the case of the Λ-isomer the folded conformer would correspond to the "closed" form proposed by Sigel to account for the intramolecular hydrophobic interactions in the [Zn(phen)(S-leu)]$^+$ system.[17] Such interactions would be responsible for the slightly higher stability of the above 1 : 1 : 1 system in comparison with the S-alaninate analogue.[17] From the above considerations it could be proposed that, at least for the cadmium systems containing aminoacidates with apolar side-chains, the position of the $[\Lambda]/[\Delta]$ equilibrium is mainly determined by balancing between polar differential solvation, discriminating ion association and steric repulsive interactions. These factors in combination with hydrophobic solvation could also account for the observed effects that the increasing concentration of n-propanol has on chiral discrimination of cadmium and zinc systems in methanol/n-propanol mixtures (Figs 7 and 8). As can be seen, in systems containing aminoacidates with apolar side-chains the increasing concentration of n-propanol usually induces an equilibrium shift towards an increase in concentration of the Δ-isomer. This fact would be ascribed to the solvating properties of n-propanol. Apart from the ability to solvate the amino group, which is common for both solvents, n-propanol must be more
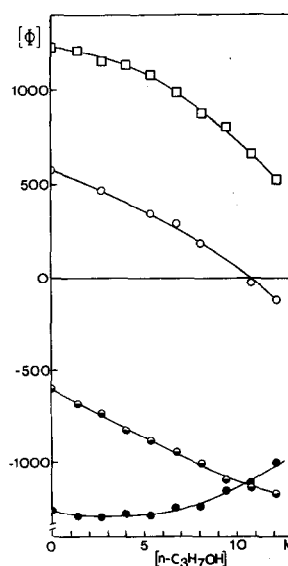

Fig. 6. Schematic representation of the assumed main solvation sites of the Δ- and Λ-diastereoisomers of [M(phen)$_2$(S-leu)]$^+$ complexes.
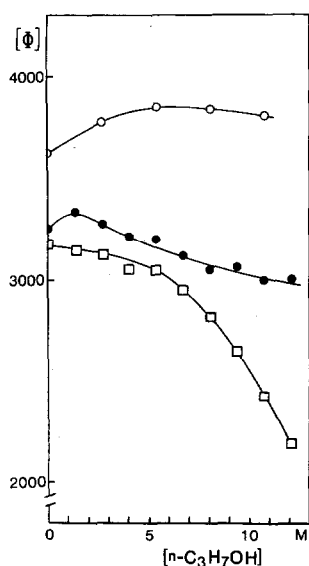

Fig. 7. Variation of molecular rotation at 450 nm of systems Δ,Λ-[M(phen)$_2$(S-aa)]X in methanol/n-propanol mixtures with varying n-propanol concentration, at room temperature. M^{II}, S-aa$^-$, X$^-$ = Zn^{II}, S-leu$^-$, Cl$^-$ ($\square$); Cd^{II}, S-val$^-$, NO$_3^-$ ($\bigcirc$); Cd^{II}, S-leu$^-$, NO$_3^-$ ($\ominus$); Cd^{II}, S-threo$^-$, NO$_3^-$ ($\bullet$).

Fig. 8. Variation of molecular rotation at 450 nm of systems Δ,Λ-[M(phen)₂(S-aa)]X in methanol/n-propanol mixtures with varying n-propanol concentration, at room temperature. M^{II}, S-aa⁻, X^- = Cd^{II}, S-prol⁻, NO_3^- (O); Cd^{II}, S-prol⁻, S-prol⁻ (●); Zn^{II}, S-val⁻, Cl^- (□).

capable than methanol of interacting hydrophobically through its apolar end with the phenanthroline ligand lying almost perpendicular to the H_2N—Cd^{2+} bond (Fig. 6). The simultaneous occurrence of both types of interactions would be more favourable for the Δ-isomer, contributing to its stabilization. Moreover an increase in the discriminating ion-pair effects, favouring the Δ-form, would be expected from the decrease in dielectric constant of the solvent mixture. On the other hand, in the case of the system [Cd(phen)₂(S-prol)]NO₃ the optical rotation varies slightly, exhibiting a tendency to increase with increasing concentration of n-propanol (Fig. 8). This behaviour could be ascribed to the predominance of the unstabilizing effects of intramolecular steric repulsive forces in the Δ-isomer, owing to the extreme rigidity of the side-chain of the S-prolinate ligand. The small ascent in molecular rotation can be attributed to a shift of the formation equilibrium:

$$Δ,Λ-[Cd(phen)_2(solv)_2]^{2+} + S\text{-prol}^- \rightleftharpoons$$

$$Δ,Λ-[Cd(phen)_2(S\text{-prol})]^+ + 2solv$$
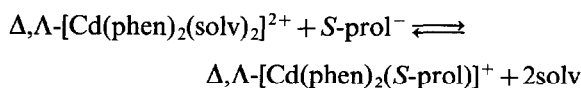
towards the diastereoisomeric species, because of the decrease in dielectric constant of the solvent mixture. This assumption is supported by the fact that on counteracting the effects of such an equilibrium shift, i.e. in the system [Cd(phen)₂(S-prol)]S-prol (Fig. 8), the behaviour of molecular rotation as a function of n-propanol concentration

is similar to those of the cadmium systems of S-leucinate or S-valinate (Fig. 7). The cadmium system containing S-threoninate, where the effects of polar differential solvation and discriminating ion association are predominant (Fig. 7), also exhibits a slight variation in optical rotation as a function of n-propanol concentration. Moreover, such a variation tends to be opposite to those observed for the remaining systems. This behaviour can be explained by assuming that the decrease in the dielectric constant of the solvent mixture causes the polar group of the side-chain to draw near the carboxylate or amine groups; thus, CO---HO or NH---OH hydrogen bonding would be promoted. The conformational changes involved here would be sterically more favourable in the Λ-isomer, as can be recognized from the analysis of molecular models. Hence, an increase in concentration of the Λ-isomer would be responsible for the slight rise in optical rotation observed on increasing the concentration of n-propanol above 6 M. The results obtained for the cadmium system with S-threoninate in methanol/benzene mixtures seem to be in support of the validity of the above assumptions (Fig. 9). In this case a conspicuous rise in optical rotation is observed with an increase in benzene concentration above 3.5 M; the greater intensity of this effect being in agreement with the more drastic decrease in dielectric constant involved here.
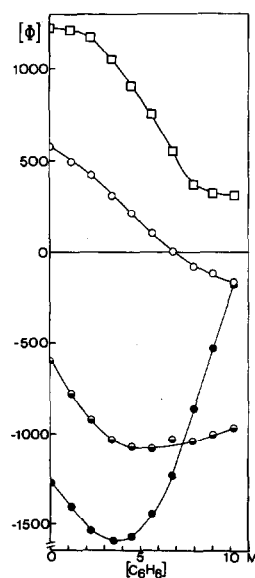

Fig. 9. Variation of molecular rotation at 450 nm of systems Δ,Λ-[M(phen)₂(S-aa)]X in methanol/benzene mixtures with varying benzene concentration, at room temperature. M^{II}, S-aa⁻, X^- = Zn^{II}, S-leu⁻, Cl^- (□); Cd^{II}, S-val⁻, NO_3^- (O); Cd^{II}, S-leu⁻, NO_3^- (◒); Cd^{II}, S-threo⁻, NO_3^- (●).
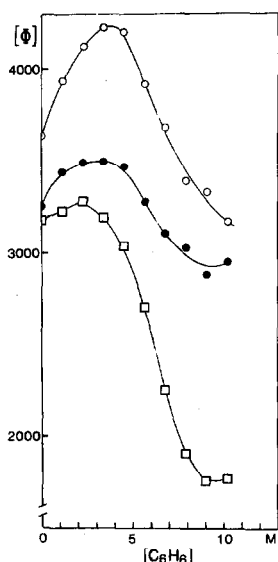
Fig. 10. Variation of molecular rotation at 450 nm of systems Δ,Λ-[M(phen)$_2$(S-aa)]X in methanol/benzene mixtures with varying benzene concentration, at room temperature. M^{II}, S-aa$^-$, X$^-$ = Cd^{II}, S-prol$^-$, NO$_3^-$ (O); Cd^{II}, S-prol$^-$, S-prol$^-$ (●); Zn^{II}, S-val$^-$, Cl$^-$ (□).

leucinate, the effects of the polar differential solvation and discriminating ion association on the [Λ]/[Δ] ratios seem to predominate in almost all the concentration range considered, or at least above 3.5 M. The different behaviour of the cadmium system containing S-leucinate (Fig. 9) would be ascribed to a predominance above 5 M of the effects of an apolar differential solvation, which would arise from a more favourable hydrophobic solvation of the folded form of the Λ-isomer.[19] These effects would also be responsible for the changes in curvature or slight rises in optical rotation observed above 8 M benzene for the remaining systems containing S-aminoacidates with apolar side-chains (Figs 9 and 10).

From a general point of view, for the systems in methanol/benzene mixtures (Figs 9 and 10) the observed effects of the increasing concentration of benzene could be ascribed in part to the fact that the polar groups of the chiral ligand, mainly the amino group, tend to keep the polar ends of the methanol molecules clustered at the solvation sites of the metal chelates, making polar differential solvation prevail as the discriminating factor. Moreover, discrimination arising from differential ion pairing should become more operative on decreasing the dielectric constant. Thus, for the cadmium system containing S-threoninate the above effects would predominate at least up to 3.5 M benzene. However, in all of the systems under study, both in methanol/benzene and methanol/n-propanol mixtures, chiral discriminating effects are obviously superposed with the effects arising from equilibrium shifts towards the formation of 1 : 2 : 1 diastereoisomeric species. Such equilibrium shifts would account for the more negative slopes of variation in optical rotation observed in the concentration range 0–3.5 M of benzene for the cadmium systems of S-leucinate or S-threoninate, as compared with the cadmium system containing S-valinate or the zinc system containing S-leucinate (Fig. 9). Instead, for the systems of cadmium and zinc containing S-prolinate and S-valinate, respectively, the effects of the formation equilibrium shifts clearly predominate in the range 0–4 M (Fig. 10). For the systems containing S-aminoacidates with apolar side-chains, except that of cadmium with S-

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