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Chiral Metal Complexes. 5. Sources of Chiral Discrimination in Aqueous Solutions of the Complexes Δ,Λ-[Ru(diimine)$_2$(*L*-aspartate)]$^\circ$ and their Conjugate Acids

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The complex ternary species Δ,Λ-[Ru(phen)$_2$(L-asp)]$^\circ$, Δ,Λ-[Ru(phen)$_2$(L-aspH)]$^+$ and their bipy analogues (L-aspH$_2$ = L-aspartic acid, phen = 1,10-phenanthroline, bipy = 2,2'-bipyridyl) have been synthesised and characterized, and the various diastereoisomers separated using cation exchange chromatography. Equilibrium constants in H$_2$O solution for the reaction Δ-[Ru(diimine)$_2$(L-aa)]$^{n+}_{(aq)}$ ⇌ Λ-[Ru(diimine)$_2$(L-aa)]$^{n+}_{(aq)}$, L-aa being either [L-asp]$^{2-}$ or [L-aspH]$^-$, are 1.00(1), 1.39(1), 0.88(1) and 1.22(1), respectively at 298.2 K. In D$_2$O, the corresponding values are 1.52(10), 1.50(4), 1.09(3) and 1.21(9). High resolution ^{1}H nmr studies indicate that a strong intramolecular hydrogen bond between the uncoordinated carboxyl group and an amine hydrogen atom of the amino acid exists when the species are deprotonated, and that this effects the relative thermodynamic stabilities of the diastereoisomers. Equilibration differences in H$_2$O and D$_2$O suggest the possibility of hydrophobic bonding being a source of chiral discriminations in complexes of this type. Such discriminations, although small in magnitude, arising from the above interactions and steric effects are discussed.

Introduction

Isolated diastereoisomers of ternary Ru(II) complexes of the type† [Ru(diimine)$_2$(aa)]$^{n+}$, where diimine is phen or bipy and *aa* is an optically active α-amino acid, undergo photochemically controlled inversion at the metal centre to yield solutions enriched in one diastereoisomer [1, 2]. Both Δ- to Λ- and Λ- to Δ-inversions have been observed depending upon the amino acid involved.

Steric influences contribute significantly to the observed selectivities, particularly when the side group of the amino acid is bulky [1]. However, chiral discriminations in these and related complexes may arise from other sources including hydrogen bonding and differential solvation [2–4]. This is evidenced by the fact that Λ-[Ru(phen)$_2$(*L*-ser)]$^+_{(aq)}$ is thermodynamically more stable than the corresponding Δ-diastereoisomer, whereas the converse is true for the bipy analogues [2]. In addition, the values of the equilibrium constants for the phen and bipy complexes as defined by equation (*1*) are each 1.0 when *L*-aa is [*L*-gluH]$^-$, but less than unity for the deprotonated analogues [5]. Again this indicates that

$$\Delta\text{-}[Ru(diimine)_2(L\text{-}aa)]^{n+}_{(aq)} \rightleftharpoons \Lambda\text{-}[Ru(diimine)_2(L\text{-}aa)]^{n+}_{(aq)} \quad (1)$$

steric effects alone, which favour the stability of the Λ-diastereoisomers, may be dominated by other discriminatory forces. The effects of hydrogen bonding were suggested as being significant in the *L*-gluH$_2$ complexes [5], and indeed in the related compound Λ-[Co(en)$_2$(*L*-glu)]ClO$_4$ a structural investigation showed the existence of an intramolecular hydrogen bond between the unbonded carboxyl group of the amino acid and an amine hydrogen atom of an ethylenediamine ligand [6].

In order to explore further the chiral discriminations involved in determining the equilibrium position for equation (1) with these Ru(II) complexes, we

*Part 4 is reference [9].

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†phen = 1,10-phenanthroline, bipy = 2,2'-bipyridyl, *L*-serH = *L*-serine, *L*-gluH$_2$ = *L*-glutamic acid, *L*-aspH$_2$ = *L*-aspartic acid, *L*-asnH = *L*-asparagine, *L*-alaH = *L*-alanine, en = 1,2-diaminoethane.

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have examined the species Δ,Λ-[Ru(diimine)$_2$-(*L*-asp)]$^\circ$ and Δ,Λ-[Ru(diimine)$_2$(*L*-aspH)]$^+$ using chiroptical and high resolution nmr techniques. The results of that examination are the subject of this article. We are able to show that both steric effects and intramolecular hydrogen bonding, and possibly also hydrophobic bonding effects, are important factors in the interconversion of the diastereomeric pairs.

Experimental

Electronic and circular dichroism (CD) spectra were obtained using a Beckman DK2A ratio recording spectrophotometer and a Jobin-Yvon CNRS Dichrographe III, respectively. Elemental analyses were carried out by Mrs. A. Dams in the Department of Chemistry (Cardiff). Water of hydration, ruthenium and ethanol analyses were performed using a Stanton Redcroft TG750 thermogravimetric balance. Proton nmr measurements at 200 MHz were made using a Varian XL-200 spectrometer. Chromatographic separations of the diastereoisomeric mixtures were made in the absence of light using Sephadex® C-25 cation exchange resin in the H^+ form, following published procedures [5]. Eluted fractions were collected using an LKB 2070 Ultrorac® II automatic fraction collector.

Δ,Λ-[Ru(phen)$_2$(L-aspH)]ClO$_4$·3H$_2$O

The complex formed as deep red crystals from an aqueous $NaClO_4/HClO_4$ solution following methods previously published for the synthesis of analogous *L*-glutamic acid complexes [5]. [Yield: 60%. *Anal.*: Found; C: 45.1; H: 3.5; N: 9.6; H_2O: 7.0%. Calc. for [Ru(phen)$_2$(*L*-aspH)]ClO_4·3H_2O; C: 45.0; H: 3.8; N: 9.4; H_2O: 7.2%].

Δ,Λ-[Ru(bipy)$_2$(L-aspH)]ClO$_4$·4H$_2$O

Deep red crystals were obtained using a method analogous to that of the phen complex above. [Yield: 65%. *Anal.*: Found; C: 40.5; H: 3.1; N: 9.4; H_2O: 11.0%. Calc. for [Ru(bipy)$_2$(*L*-aspH)]ClO_4·4H_2O; C: 40.2; H: 4.2; N: 9.8; H_2O: 10.1%]. The low hydrogen analysis obtained is due to the loss of the water of crystallization near room temperature prior to combustion for microanalysis [Calc. H: 3.1% under these conditions].

Δ,Λ-[Ru(bipy)$_2$(L-asp)]·5H$_2$O

This compound was isolated as deep red-black glistening crystals following an analogous published procedure [5] after purification of the reaction mixture on Sephadex® C-25 cation exchange resin. [Yield: 56%. *Anal.*: Found; C: 45.5; H: 4.4; N: 11.2; H_2O: 14.0; Ru: 16.0%. Calc. for [Ru(bipy)$_2$-(*L*-asp)]·5H_2O; C: 45.4; H: 4.9; N: 11.0; H_2O: 14.2; Ru: 15.9%].

Δ,Λ-[Ru(phen)$_2$(L-asp)]·0.5EtOH·3H$_2$O

Deep red-black feathery crystals were obtained after recrystallization from ethanol following a procedure similar to that above.[Yield: 71%. *Anal.*: Found: C: 50.6; H: 4.1; N: 9.8; H_2O: 8.0; EtOH: 3.5; Ru: 14.6%. Calc. for [Ru(phen)$_2$(*L*-asp)]·0.5EtOH·3H_2O; C: 52.0; H: 4.5; N: 10.5; H_2O: 8.1; EtOH: 3.4; Ru: 15.1%]. The low carbon and hydrogen analyses obtained may be ascribed to loss of the ethanol of crystallization near room temperature prior to combustion for microanalysis. [Calculated; C: 50.2; H: 4.1% under these conditions]. The stoichiometry of the compound was confirmed both by the thermogravimetric analysis and by integration of the ethanol proton signals in the nmr spectrum in comparison with those arising from the phen and *L*-asp ligands.

Absorption coefficients for λ_{max} in the ultraviolet region of the electronic spectra were calculated to be 6.88 × 10^5 dm^2 mol^{-1} (263 nm) for Δ,Λ-[Ru(phen)$_2$(*L*-aspH)]$^+_{(aq)}$ and 4.49 × 10^5 dm^2 mol^{-1} (292 nm) for Δ,Λ-[Ru(bipy)$_2$(*L*-aspH)]$^+_{(aq)}$. These values were determined after the solutions had equilibrated in the presence of light and after the addition of hydrazine hydrochloride to inhibit photooxidation [1]. The absorption coefficients were used in turn to calculate the concentrations and CD magnitudes for solutions used in equilibration studies and from chromatographic separations after acidification of neutral solutions when appropriate.

Results and Discussion

Resolution of the neutral diastereoisomers of [Ru(phen)$_2$(*L*-asp)]$^\circ$ and [Ru(bipy)$_2$(*L*-asp)]$^\circ$ using chromatographic methods was achieved as previously described [1, 2, 5]. Absolute configurations again have been assigned on the basis of the calculations of Bosnich [7, 8] using exciton theory. Those predictions are entirely consistent with previous studies [1] where the bulky nature of certain *L*-α-amino acids enforce the Λ-absolute configuration as a result of steric requirements.

The diastereoisomers of the aspartate complexes with negative values of $\Delta\epsilon$ for the low-energy, long-axis-polarized $\pi \rightarrow \pi^*$ transition, assigned the Δ-absolute configuration, eluted from the column first. This has been a consistent feature of all of the Ru(II) complexes studied to date. Values of $\Delta\epsilon_{max}$ for the above transitions for the pure diastereoisomers are given in Table I together with $\Delta\epsilon$ for the equilibrated pairs, relevant equilibrium constants with respect to equation (*1*), and calculated chiral discrimination energies.

TABLE I. CD Maxima for the Diastereoisomers and Equilibrium Mixtures in H_2O, with Appropriate Equilibrium Constants and Chiral Discrimination Energies at 298.2 K.

Complex[a]	λ[b]/nm	$\Delta\epsilon$[b]/dm^2 mol^{-1}	K_{eq}[c]	$\Delta G^\circ_{H_2O}$	K_{eq}[e]	$\Delta G^\circ_{D_2O}$
Λ-[Ru(phen)$_2$(*L*-asp)]$^\circ$	271	+1790(8)[d]				
Δ-[Ru(phen)$_2$(*L*-asp)]$^\circ$	272	−1420(7)				
Λ-[Ru(bipy)$_2$(*L*-asp)]$^\circ$	297	+1193(10)				
Δ-[Ru(bipy)$_2$(*L*-asp)]$^\circ$	296	−946(8)				
Λ-[Ru(phen)$_2$(*L*-aspH)]$^+$	271	+1842(8)				
Δ-[Ru(phen)$_2$(*L*-aspH)]$^+$	272	−1399(6)				
Λ-[Ru(bipy)$_2$(*L*-aspH)]$^+$	297	+1034(10)				
Δ-[Ru(bipy)$_2$(*L*-aspH)]$^+$	296	−785(5)				
Δ,Λ-[Ru(phen)$_2$(*L*-asp)]$^\circ$		+186(4)	1.00(1)	0.00	1.52(10)	−1.04
Δ,Λ-[Ru(bipy)$_2$(*L*-asp)]$^\circ$		+52(1)	0.88(1)	0.32	1.09(3)	−0.21
Δ,Λ-[Ru(phen)$_2$(*L*-aspH)]$^+$		+484(6)	1.39(1)	−0.82	1.50(4)	−1.01
Δ,Λ-[Ru(bipy)$_2$(*L*-aspH)]$^+$		+218(3)	1.22(1)	−0.49	1.21(9)	−0.47

[a]Neutral species at pH 10, protonated species at pH 3, NaOH and $HClO_4$, respectively in H_2O. In D_2O solution, corresponding conditions are 0.105 F Na_2CO_3 and 1.5 F CF_2COOH. [b]Low energy $\pi \rightarrow \pi^*$ transition, H_2O solution. [c]In H_2O; $\Delta G^\circ_{H_2O}$ is calculated from equation (*2*) and is given in kJ mol^{-1}. All equilibrium constants refer to equation (*1*) in appropriate solution. [d]Values in parentheses refer to estimated standard deviations derived from multiple analyses. CD and electronic spectra are similar in all respects to those found for corresponding *L*-glutamic acid series of complexes [5]. [e]In D_2O.

In a general sense the results parallel those found for the *L*-glutamic acid complexes [5], in that the protonated species equilibrate such that the equilibrium lies further towards the Λ-hand than is the case with each of the neutral diastereoisomers in H_2O. This bias is however more pronounced for all equilibria involving the aspartic acid complexes than was observed to be the case with the glutamic acid analogues. If either Δ-diastereoisomer of [Ru(diimine)$_2$(*L*-asp)]$^\circ$ is isolated in the absence of light then its solution made acidic so as to generate the Δ-[Ru(diimine)$_2$(*L*-aspH)]$^+_{(aq)}$ species, it is observed, upon exposure to light to spontaneously invert with respect to its absolute configuration to yield the respective Λ-biased equilibrium mixture indicated in Table I. Concentration ratios of the Δ- and Λ-neutral phen complexes at equilibrium are equal within experimental error. However, with [Ru(bipy)$_2$(*L*-asp)]$^\circ$ the Δ-diastereoisomer predominates in H_2O solution and a Λ- to Δ-inversion may be observed for this complex under the conditions described. The magnitudes of the chiral discrimination energies involved are small, being no greater than about 1 kJ mol^{-1} (Table I).

As was found with related Ru(II) complexes [2, 5], the equilibrium position for the mixture Δ,Λ-[Ru(bipy)$_2$(*L*-asp)]$^\circ_{(aq)}$ indicates that steric effects may be outweighed by other factors in determining the magnitude of the difference in ΔG°_f between pairs of diastereoisomers of this kind. However, when the uncoordinated carboxyl groups of both sets of diastereoisomers are protonated the concentrations of the aqueous species change to give mixtures quite in accord with those expected on steric grounds alone. These differences in selectivity for the protonated and neutral forms indicate that a rather specific kind of hydrogen bonding may be important in the complexes. Indeed, the energy involved in the formation of one hydrogen bond would be more than sufficient to account for the observed chiral discriminations.

Evidence that hydrogen bonding does play a role in the determination of the equilibrium positions for the various species is provided by high resolution proton nmr studies. Of the four pairs of diastereoisomers examined, that of the phen complexes proved to be the most amenable to analysis since no 'deceptively simple' [18] spectra were encountered and all N–*H* proton resonances could be assigned in both basic and acidic solution.

All relevant chemical shifts and coupling constants for both the bipy and phen systems are given in Table II. Preliminary assignments of signals to Δ- and Λ-hands of the complexes were made on the basis of studies of Δ,Λ-[Ru(bipy)$_2$(*L*-ala)]$^+$, [9]. For this latter complex, the Δ-diastereoisomer elutes first from columns of Sephadex® C-25 exchange resin, and isolated fractions enriched in this hand were found to have the α-methine hydrogen resonance of the *L*-alaH ligand at higher field than the corresponding proton of the Λ-isomer. Accordingly, we have assigned the various signals

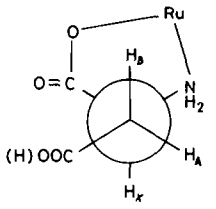
TABLE II. 200 MHz ^{1}H Nmr Spectral Data for the Complexes.[a]

	Λ-[Ru(phen)$_2$(*L*-asp)]$^\circ$	Δ-[Ru(phen)$_2$(*L*-asp)]$^\circ$	Λ-[Ru(phen)$_2$(*L*-aspD)]$^+$	Δ [Ru(phen)$_2$(*L*-aspD)]$^+$
δ_A	2.78[b]	2.84	3.03[c]	3.07
δ_B	2.71	2.56	2.87	2.78
δ_X	4.07	3.48	4.16	3.61
$J_{A,B}$	17.3	17.9	18.2	18.4
$J_{A,X}$	4.9	4.4	4.5	4.6
$J_{B,X}$	3.8	4.0	3.9	3.7
$\delta_{H(h)}$	4.36	5.24	4.13	4.77[d]
$\delta_{H(r)}$	5.15	4.20	5.33	4.48
$J_{H(h),X;H(r),X;H(h),H(r)}$	10.8; 6.7; 9.3	10.0; 6.8; 10.0	H(h),H(r) ill resolved	10.0; 10.0; 10.0[e]
$\delta_{H(2N);H(2O)}$	9.71; 9.52	9.87; 9.44	9.71; 9.49	9.79; 9.43
$J_{2N,3;2N,4}$	5.0; 0.5	5.1; 1.0	5.0; 0.5	5.3; 1.3
$J_{2O,3;2O,4}$	5.3; 1.2	5.4; 1.2	5.3; 0.9	5.3; 1.1
	Λ-[Ru(bipy)$_2$(*L*-asp)]$^\circ$	Δ-[Ru(bipy)$_2$(*L*-asp)]$^\circ$	Λ-[Ru(bipy)$_2$(*L*-aspD)]$^+$	Δ-[Ru(bipy)$_2$(*L*-aspD)]$^+$
δ_A	2.48	2.60	2.79	2.82
δ_B	2.48	2.36	2.65	2.57
δ_X	3.69[3.74][g]	3.16[3.22][g]	3.79	3.28
$J_{A,B}$	not available	17.3	18.0	18.0
$J_{A,X}$	½[$J_{A,X}$ + $J_{B,X}$] = 4.7	4.8	4.9	5.2
$J_{B,X}$		3.7	4.0	3.5
$\delta_{H(h)}$	4.74[f][4.64][g]	3.95[f][4.28][g]		
$\delta_{H(r)}$	[5.01][g]	[5.61][g]		
$J_{H(h),X}$	8.6[f]	8.8[f]		
$\delta_{H(6N);H(6O)}$	8.94; 8.67	9.08; 8.61		
$J_{6N,5;6N,4}$	5.2; 0.6	5.0; 0.6		
$J_{6O,5;6O,4}$	5.8; 0.6	5.2; 0.6		

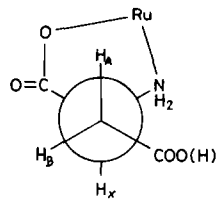
[a]Chemical shifts ± 0.01 in ppm, coupling constants ± 0.1 in Hz. [b]Neutral species spectra recorded in 0.105 F Na_2CO_3 in D_2O. Data except for amine protons recorded after full exchange. [c]As for (b), but recorded in 1.5 F CF_3COOH in D_2O. [d]Partially obscured by HDO peak. [e]±1 Hz. [f]Recorded after H(r) proton had exchanged. [g]Recorded in CD_3OD. Assignments of $\delta_{H(h)}$ and $\delta_{H(r)}$ uncertain.

from solutions of these *L*-aspH_2 complexes on this basis.

A conformational analysis of the compounds was carried out on the spectra obtained after the N–*H* protons had exchanged with those of the deuterated solvent. For each diastereoisomer under these conditions a typical ABX spectrum was obtained save for Λ-[Ru(bipy)$_2$(*L*-asp)]$^\circ$. In this instance a 'deceptively simple' pattern of resonances occurred due to similarities in chemical shifts. With respect to the remaining α-methine and β-methylene protons of the coordinated aspartic acid ligand, the dependence of the vicinal coupling constants on the dihedral angles between protons bonded to adjacent carbon atoms is assumed to generally follow the Karplus equation [10]. Several studies based on this assumption have been reported [11–14] involving amino acids.



(I)



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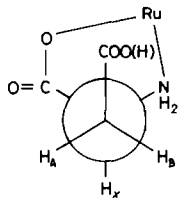


(III)

A consideration of the three possible staggered conformers (I)–(III) leads to the determination of m_I, m_{II} and m_{III}, these being the respective mole fractions of conformers (*I*), (*II*) and (*III*). The coupling constants J_{gauche} = 2.60 and J_{trans} = 13.56 Hz [15] have been used, as in an earlier analysis [12]. These values have been used, in particular, in the analysis of structures and formation constants of Zn(II) complexes of *L*-aspartic acid in aqueous solution [16], with the assumption that both coupling constants remain unchanged upon coordination of the amino acid. We make this same assumption in the present case. Assignments of the overlapping AB positions of the ABX pattern of each amino acid was facilitated by separate spin decoupling of the α-methine hydrogen signals.

The data in Table II have been used to calculate m_I, m_{II} and m_{III} for each diastereoisomer and the results are given in Table III. These are consistent with a conformation taken as a weighted average of the three staggered rotamers with (*III*) being the most

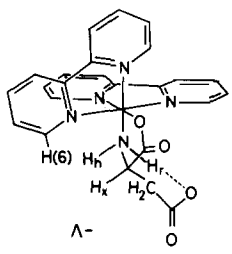
TABLE III. Calculated Mole Fractions of Conformers of the Diastereoisomers at 298.2 K in D_2O.

Complex[a]	m_I	m_{II}	m_{III}
Λ-[Ru(phen)$_2$(*L*-asp)]$^\circ$	0.11	0.20	0.69
Δ-[Ru(phen)$_2$(*L*-asp)]$^\circ$	0.13	0.16	0.71
Λ-[Ru(phen)$_2$(*L*-aspD)]$^+$	0.11	0.17	0.72
Δ-[Ru(phen)$_2$(*L*-aspD)]$^+$	0.10	0.18	0.72
Λ-[Ru(bipy)$_2$(*L*-asp)]$^\circ$	[0.19][b]	[0.19][b]	[0.62][b]
Δ-[Ru(bipy)$_2$(*L*-asp)]$^\circ$	0.10	0.19	0.71
Λ-[Ru(bipy)$_2$(*L*-aspD)]$^+$	0.13	0.21	0.66
Δ-[Ru(bipy)$_2$(*L*-aspD)]$^+$	0.08	0.23	0.69

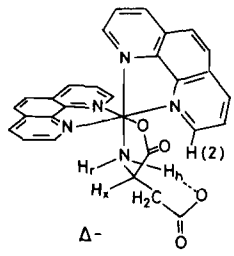
[a]Conditions as given in Table I; all N–*H* protons exchanged. [b]Calculated assuming $J_{AX} = J_{BX} = \frac{1}{2}[J_{AX} + J_{BX}]$.

predominent, but with (*I*) and (*II*) making significant contributions. For all diastereoisomers, the relative weights are approximately m_I = 10%, m_{II} = 20%, and m_{III} = 70%. Indeed, the J_{AX} and J_{BX} values are typical of an essentially *gauche* arrangement of the proton pairs H_A and H_X, and H_B and H_X.

The conformational preference adopted by the aspartic acid ligand is ideal for hydrogen bond formation between the uncoordinated carboxyl group and the amine hydrogen atom located on the same side of the five-membered chelate ring. This is shown in (*IV*) and (*V*). Each two amine protons are also not sterically equivalent, one (H_r) lying in an axial position relative to the plane of one diimine ligand, and the other (H_h) being directed towards the ring hydrogen atom *ortho*- to a heterocyclic nitrogen atom. Thus in each propellor, the proposed hydrogen bond differs, the H_r atom of the Λ- and the H_h atom



(IV)



(V)

of the Δ-species being the ones involved. An analogous intramolecular hydrogen bond exists [17] in the solid state form of Λ-[Co(en)$_2$(*L*-asn)]$^{2+}$.

A consideration of the amine hydrogen resonances in the pmr spectra provides additional evidence that this type of hydrogen bonding is important in these molecules. Not all of the N–*H* resonances could be

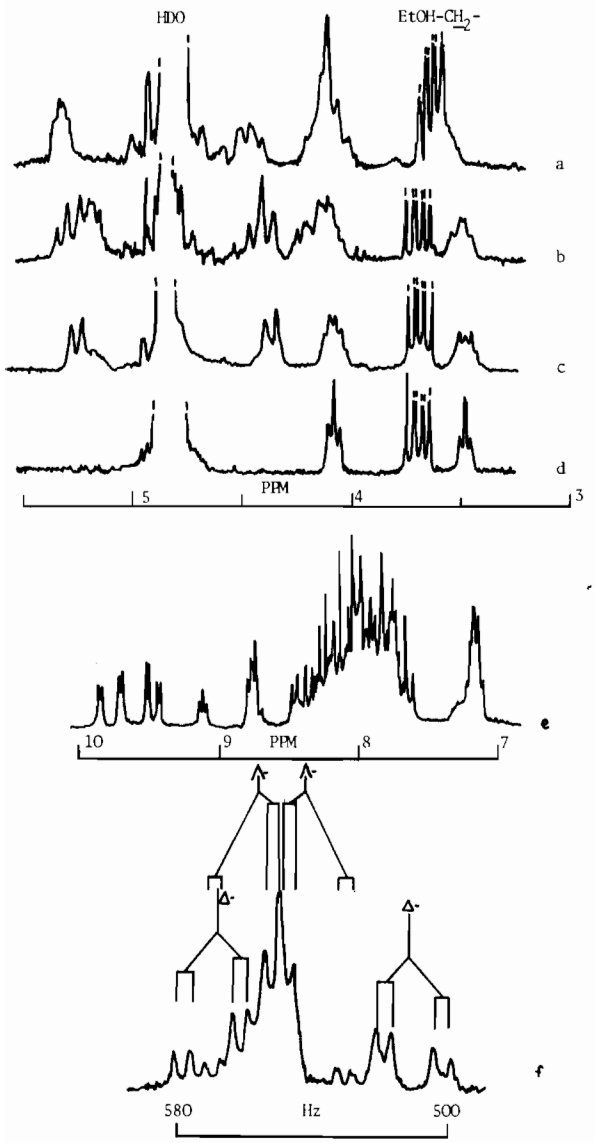


Fig. 1. ^{1}H nmr spectra of Δ,Λ-[Ru(phen)$_2$(*L*-asp)]·0.5EtOH·3H$_2$O; (a): shortly after dissolution in 1.5 F CF_3COOH in D_2O; (b): shortly after dissolution in 0.105 F Na_2CO_3 in D_2O (a similar spectrum is obtained on dissolution of the complex in D_2O alone); (c): as for (b), but when partial N–*H* proton exchange has occurred; (d), (e), (f): as for (b), but when N–*H* exchange is complete. Respective spectra shown for these latter three cases are those of the α-*CH* atoms, the aromatic region and the β-methylene region for the two diastereoisomers.

assigned for bipy diastereoisomers (Table II) due to overlap with the HDO signal, but the spectra of the phen complexes show no such overlap. Here, all four N–*H* resonances were observed on initial dissolution in either 0.105 F Na_2CO_3 or 1.5 F CF_3COOH in D_2O. Spin decoupling experiments afforded the assignments of the pairs of N–*H* resonances to each diastereoisomer in the first instance. Like the alanine species [9], the N–*H* protons are neither chemically nor magnetically equivalent and hence are observed to exchange for deuterons in the solvent at different rates. Molecular models [see (*IV*) and (*V*)] show the H_h protons to be sterically crowded whereas the H_r protons are exposed to the solvent and therefore are more susceptible to facile exchange. We have thus made amine proton assignments on the basis of differential exchange rates.

Figure 1 shows the changes in relevant sections of the spectrum of Δ,Λ-[Ru(phen)$_2$(*L*-asp)]° with time, together with the spectrum of the fully exchanged species. In the absence of light one N–*H* proton of each diastereoisomer is observed to exchange completely before the other. Deshielding of one N–*H* proton by hydrogen bonding is not responsible for the differential exchange rates; the downfield N–*H* of the Δ-diastereoisomer (δ 5.24) exchanges at a slower rate than the higher field one (δ 4.20). Since the protons downfield are expected to be those involved with hydrogen bonding [9, 18], the assignments made above are entirely consistent. With time however, all N–*H* protons do exchange and the spectrum (d) shown in the Figure is obtained.

Upon protonation of the terminal carboxyl group considerable changes occur in the positions of the N–*H* resonances. In acidic solution (1.5 F CF_3COOH) stereoselective exchange is observed and assignments have again been made based on the differential exchange. Although such a detailed analysis of the spectra of the bipy complexes was not possible, the same exchange properties are evident. After a short time in 0.105 F Na_2CO_3 and in the absence of strong lighting only two N–*H* resonances are observed, both being sharp doublets. Each corresponds to one diastereoisomer and is split by coupling to the α-methine hydrogen atom of the amino acid. All N–*H* resonances for Δ- and Λ-[Ru(bipy)$_2$(*L*-asp)]° are observed in CD_3OD solution (Table II) and the marked differences in chemical shifts compared with those in D_2O solution also are indicative of hydrogen bond formation of the type described above.

In related studies of Δ,Λ-[Co(en)$_2$(*L*-asp)]$^+$, Kojima and Shibata [19] found evidence for hydrogen bonding of this type. The positions of the aspartic acid amine hydrogen atom resonances were highly susceptible to pH changes. These results compliment those above, and those of the structural analysis of Λ-[Co(en)$_2$(*L*-asn)]$^{2+}$, [17].

The presence of such intramolecular hydrogen bonding partly explains variations in the equilibrium constant values for equation (*1*) as presented in Table I. It is apparent that the O- -H_h–N interaction in the neutral Δ-diastereoisomers serves to stabilize the Δ-

hand. On protonation of the terminal carboxyl group, intramolecular steric interactions become more predominant and consequently the Λ-form is favoured. This is not to say that differential solvation and hydrogen bonding is still not important however. At equilibrium, stabilization of the Δ-isomer in H_2O solution is seen to be more pronounced with Δ,Λ-[Ru(bipy)$_2$(*L*-asp)]$^\circ$ than with the phen analogue. This, we suggest, arises simply from the more flexible nature of the bipy ligand, which could accommodate the appropriate intramolecular hydrogen bond more easily. Steric contributions would also be less significant because of this flexibility.

Exposure of solutions used in the ^{1}H nmr studies to light allows equilibration of the diastereoisomers in the normal way. It should be remembered however that the species in D_2O solution are different from those in H_2O solution, being Δ,Λ-[Ru(diimine)$_2$-(*N*-^{2}H$_2$-*L*-asp)]$^\circ$ and the corresponding deuterocations. Also worth mentioning is the fact that in both the basic and acidic solutions used in all of the experiments described, no exchange of the α-methine hydrogen was observed. This process and its associated epimerization of the coordinated amino acid are considerably slower than the corresponding reactions involving Co(III) complexes [20, and refs. therein].

Equilibrium constants for the neutral and protonated phen diastereoisomers in D_2O were found to be 1.52(10) and 1.50(4), respectively. Corresponding values for the bipy complexes are 1.09(3) and 1.21(9). These calculations (Table I) were based on integration of the ^{1}H nmr signals of the α-methine hydrogen atoms of the *L*-aspH_2 ligands and the deshielded *H*(2) and *H*(6) signals of the phen and bipy residues, respectively. These protons are each magnetically non-equivalent in any diastereoisomer or isomeric pair (Table II, Fig. 1) since they each lie in different steric environments. We have assigned the individual resonances for these pyridyl ring hydrogen atoms assuming Van der Waals deshielding [21] results from the steric interactions described. All of the equilibrium constants obtained in D_2O reflect mixtures enriched in the Λ-isomers. This pattern of results, quite different from that found in H_2O solution, may arise from differences in hydrogen bonding.

It is also possible that they reflect effects of hydrophobic bonding associated with the greater 'structuredness' of D_2O than H_2O [22]. Entropy differences arising from hydrophobic solvation [23] have been suggested as the source of equilibrium shifts of propellor populations of Δ,Λ-[Zn(phen)$_3$]$^{2+}$ in solutions containing strychninium ion [24]. Other manifestations of the Pfeiffer effect [25] have also been associated with hydrophobic bonding [26]. That effect is akin to the diastereoisomeric equilibrations described in this work.

Chiral discrimination energies calculated from the equilibrium constants for the diastereoisomeric pairs are also given in Table I, and refer to equation (*2*) at 298.2 K. There is little free energy difference

$$\Delta G^\circ_{f[\Lambda\text{-isomer,solvent}]} - \Delta G^\circ_{f[\Delta\text{-isomer,solvent}]} \qquad (2)$$

($\Delta G^\circ_{H_2O} - \Delta G^\circ_{D_2O}$) with solvent change from H_2O to D_2O for the protonated diastereoisomers and these species appear to be influenced mainly by steric requirements. For the neutral species, however, the corresponding difference amounts to about 1 kJ mol^{-1} for the phen and 0.5 kJ mol^{-1} for the bipy complexes, respectively. This again suggests that structuring involving labile protons (*viz.* hydrogen bonding effects) are significant in the neutral, but less so in the protonated forms.

The chiral discrimination energies associated with the complexes investigated here are small and of the order of 1 kJ mol^{-1}. Thus, quite subtle effects may have sufficient influence on the thermodynamic stability of individual diastereoisomers so as to become predominant under favourable conditions. We have been able to show for these ternary complexes containing *L*-aspartic acid that steric interactions, intramolecular hydrogen bonding, and quite possibly hydrophobic bonding forces, all contribute to the stability of any particular species in aqueous solution. The relative importance of contributions from any of the above sources varies from complex to complex and, as has been shown here and in previous studies [1, 2, 5, 9], depends upon the particular amino acid involved.

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