Chiral Metal Complexes. 11.* Steric Interactions in some Complexes of General Form [Ru(Diimine)$_2$-(*S*-aminoacidate)]$^{n+}$

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A series of complexes of the type Δ,Λ-[Ru(diimine)$_2$(S-aa)]$^{n+}$ have been prepared, where diimine is 1,10-phenanthroline or 2,2'-bipyridyl and S-aa is the anion of 5-hydroxytryptophane or phenylalanine and its substituted congeners. The complexes were resolved using chromatographic methods and equilibration studies carried out at 298 K in aqueous solution to determine the position of the equilibrium

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

Two types of steric interaction are thought to be responsible for the chiral discriminations observed between pairs of diastereoisomers. One is that between an aromatic diimine ligand and the side chain of the coordinated amino acid. The second, evident in complexes of α-methyl-substituted S-amino acids, involves that methyl group and an amine hydrogen atom of the optically active bidentate. The α-methyl substitution results in an energetic preference for the Λ-diastereoisomer by approximately 1.6 kJ mol^{-1}.

Introduction

The photochemical inversion of diastereoisomers of the type [Ru(diimine)$_2$(*aa*)]$^{n+}$, where diimine is phen[‡] or bipy and *aa* is an optically active amino acid has been shown to occur as a result of chiral discriminations of various kinds. These discriminations may be due to steric interactions, intramolecular hydrogen bonding requirements, differential solvation or hydrophobic bonding effects depending upon the particular amino acid involved [1]. The observed direction of the inversion overall depends upon the magnitude of the equilibrium constant for eqn. (1).

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

For complexes of *S*-amino acids with bulky side groups, such as in *S*-tryptophane (I), the Λ-diastereoisomer is considerably more thermodynamically stable than the Δ-isomer at room temperature in aqueous solution [2]. Non-bonded steric interactions between the side chain and a hydrogen atom of one of the phen or bipy rings are probably responsible, in the main, for these observations.

Nevertheless, other discriminating forces may still be important [1], and in an attempt to investigate this possibility, we have studied a series of related complexes based upon the phenylalanine nucleus (II), the results of which are presented below.

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[‡]Phen = 1,10-phenanthroline, bipy = 2,2'-bipyridyl, pheH = phenylalanine, tyrH = tyrosine, trpH = tryptophane, dopaH = 3,4-dihydroxyphenylalanine, alaH = alanine.

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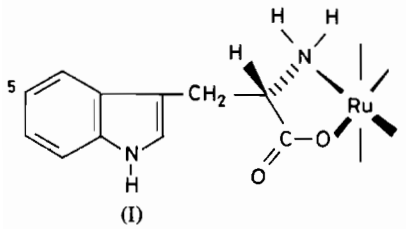
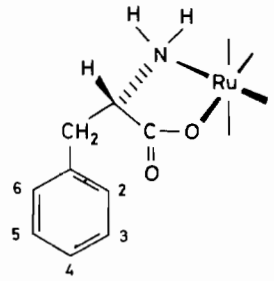
TABLE I. Analytical Data for the Complexes Δ,Λ-[Ru(diimine)$_2$(*S*-aa)]$ClO_4 \cdot nH_2O$.

Diimine	*S*-aa	n	Yield (%)	Calcd. (%)				Found (%)			
				C	H	N	H_2O	C	H	N	H_2O
phen	phe	2	52	52.1	4.1	9.2	4.7	52.2	3.5	9.0	4.4
bipy	phe	2	43	48.8	4.4	9.8	5.1	48.2	4.1	9.6	4.9
phen	tyr	3	49	49.8	4.1	8.8	6.8	50.0	4.0	8.8	7.0
bipy	tyr	2	45	47.8	4.3	9.6	4.9	47.9	4.4	9.8	5.3
phen	O-methyltyr	3.5	48	49.9	4.3	8.6	7.7	49.9	4.0	8.5	7.6
phen	3,5-dibromotyr	2.5	36	42.0	3.1	7.4	4.8	41.9	2.8	7.5	4.6
phen	3,5-diiodotyr[a]	0	64[b]	38.1	2.4	6.3	–	38.4	2.4	6.3	–
phen	α-methyltyr	0	39	54.1	3.7	9.3	–	54.0	3.7	9.3	–
bipy	α-methyltyr	2.5	41	47.8	4.4	9.3	6.0	48.1	4.1	9.6	5.9
phen	3-O-methyldopa	2	68	50.6	4.0	8.7	4.5	50.7	4.0	8.8	4.3
phen	α-methyldopa	2	71	50.6	4.0	8.7	4.5	51.3	3.6	9.1	4.8
bipy	α-methyldopa	4	48	45.3	4.6	8.8	9.1	45.2	3.4	8.7	9.0
phen	5-hydroxytrp	2.5	73	50.9	3.8	8.5	5.5	50.9	4.1	8.8	5.8

[a]Isolated as the S-3,5-diiodotyrosinate salt; see Experimental Section. [b]Based on amino acid content.



(I)



(II)

Experimental

Cis-[Ru(phen)$_2$Cl$_2$] and *cis*-[Ru(bipy)$_2$Cl$_2$] were prepared by published procedures [3].

Δ,Λ-[Ru(diimine)$_2$(S-aa)]$ClO_4 \cdot nH_2O$

With the exception of the *S*-3,5-diiodotyrosine complex, all of the compounds were synthesized in the following way. *Cis*-[Ru(diimine)$_2$Cl$_2$], (0.2 mmol), was refluxed in a mixture of water (10 cm^3) and ethanol (3 cm^3) until all the solid had dissolved to form a deep-red solution. To this solution was added the appropriate *S*-amino acid (0.22 mmol) followed by 0.1 mol dm^{-3} aqueous NaOH (2.2 cm^3). The reaction mixture was heated at 70 °C for 30 min, cooled to room temperature and then filtered. After addition of saturated aqueous $NaClO_4$ (1 cm^3), the reaction mixture was stored in the dark for 48 hours, during which time the compound crystallized. The solid was collected at the pump, washed with ice-cold water and dried *in vacuo* over silica gel at room temperature.

Δ,Λ-[Ru(phen)$_2$(S-3,5-diiodotyr)](S-3,5-diiodotyr)

This compound was prepared in a similar manner to the above except that after filtering the reaction mixture, and prior to the perchlorate addition, the product crystallized as the solution cooled to room temperature.

Elemental analyses were carried out by Mrs. A. Dams in the Department of Chemistry, Cardiff. Water of hydration was determined thermogravimetrically using a Stanton Redcroft TG 750 temperature-programmed thermogravimetric balance. Yields and analytical results are given in Table I.

Resolutions of the diastereoisomeric pairs were achieved using previously described chromatographic methods [2]. For most complexes 1% aqueous sodium perchlorate was used as the eluant except for the species containing *S*-3,5-dibromotyr, *S*-3,5-diiodotyr or *S*-dopa. These all precipitated at the head of the column when elution was attempted with this perchlorate solution. They were resolved using either 0.25 or 0.5% aqueous sodium chloride as eluant. Spectroscopic measurements and equilibrium constants relating to eqn. (1) were carried out and calculated using previously published procedures [2].

TABLE II. Spectroscopic Data for the Complexes Δ-Λ-[Ru(diimine)$_2$(*S*-aa)]$^+$ in Aqueous Solution.

Diimine	*S*-aa	λ^a max(vis) (nm)	10^{-4} ^{a} ε(vis) (dm^2 mol^{-1})	λ^a max(uv) (nm)	10^{-4} ^{a} ε(uv) (dm^2 mol^{-1})	λ_Δ ^{b} (nm)	$\Delta\varepsilon_\Delta$ ^{b} (dm^2 mol^{-1})	λ_Λ ^{b} (nm)	$\Delta\varepsilon_\Lambda$ ^{b} (dm^2 mol^{-1})	λ_{eq} ^{c} (nm)	$\Delta\varepsilon_{eq}$ ^{c} (dm^2 mol^{-1})
phen	phe	482	13.5	264	84.1	272	−1594(4)	271	+1797(7)	271	+655(4)
bipy	phe	489	9.0	292	54.0	296	−1234(3)	297	+1327(6)	297	+137(3)
phen	tyr	481	11.9	264	78.5	272	−1583(6)	271	+1184(3)	271	+290(5)
bipy	tyr	494	9.4	292	61.5	296	−1510(6)	297	+1497(7)	297	+151(3)
phen	O-methyltyr	480	13.2	264	85.1	272	−1595(8)	271	+1689(5)	271	+771(2)
phen	3,5-dibromotyr	480	15.5	264	100.7	272	−2365(10)	271	+1540(7)	271	+402(5)
phen	3,5-diiodotyr	481	15.6	264	107.6	272	−2896(14)	271	+2676(13)	271	+1061(5)
phen	α-methyltyr	482	10.7	264	66.6	272	−1797(8)	271	+1846(3)	271	+1144(4)
bipy	α-methyltyr	494	10.6	292	53.9	296	−1427(3)	297	+1603(4)	297	+693(3)
phen	3-O-methyldopa	482	12.4	264	78.6	272	−1926(6)	271	+2062(8)	271	+829(3)
phen	α-methyldopa	482	9.1	264	86.4	272	−1875(5)	271	+1370(2)	271	+722(7)
bipy	α-methyldopa	492	8.4	292	48.1	296	−1323(4)	297	+1436(5)	297	+397(2)
phen	5-hydroxytrp	485	11.2	264	131.0	272	−1957(6)	271	+2059(8)	271	+1300(4)

[a]Data for solutions of diastereoisomers at 298 K equilibrated in presence of light. [b]Δε of extrema of pure diastereoisomers at the given wavelengths. [c]Wavelengths of extrema and Δε for solutions of diastereoisomers at equilibrium.

TABLE III. Equilibrium Constants[a] and Calculated Chiral Discrimination Energies[b] for the Complexes Δ,Λ-[Ru(diimine)$_2$(*S*-aa)]$^+$ in Aqueous Solution at 298 K.

Diimine	*S*-aa	K_{eq}	$\Delta G°$/kJ·mol^{-1}
phen	phe	1.97(2)	−1.68(2)
bipy	phe	1.15(1)	−0.35(2)
phen	tyr	2.09(2)	−1.83(3)
bipy	tyr	1.23(1)	−0.51(2)
phen	O-methyltyr	2.58(4)	−2.35(4)
phen	3,5-dibromotyr	2.44(4)	−2.21(4)
phen	3,5-diiodotyr	2.45(4)	−2.21(4)
phen	α-methyltyr	4.19(9)	−3.55(5)
bipy	α-methyltyr	2.33(2)	−2.10(2)
phen	3-O-methyldopa	2.23(3)	−1.99(3)
phen	α-methyldopa	4.01(8)	−3.44(5)
bipy	α-methyldopa	1.67(2)	−1.27(3)
phen	5-hydroxytrp	4.19(9)	−3.55(5)

[a]With respect to eqn. (1). [b]With respect to eqn. (2).

Results and Discussion

Electronic and circular dichroism data for the complexes are collected together in Table II. The CD spectral curves for the pure diastereoisomers are generally analogous to those found previously for related complexes [1, 2]. Assignments of absolute configurations have been made on the basis of the sign of the low-energy long-axis-polarized $\pi \rightarrow \pi^*$ transitions [4, 5]. This is consistent with results of NMR studies on related complexes [1, 6]. Equilibrium constants for eqn. (1) calculated from CD and electronic spectral measurements of solutions of each complex equilibrated in aqueous solution in the presence of light are listed in Table III, together with the calculated chiral discrimination energy for each pair of diastereoisomers. This quantity is represented by eqn. (2).

$$\Delta G° = \Delta G_{f\{\Lambda\text{-isomer}_{(aq)}\}}° - \Delta G_{f\{\Delta\text{-isomer}_{(aq)}\}}° \qquad (2)$$

The results obtained reveal several trends concerning chiral discriminations between diastereoisomeric pairs. At equilibrium, in aqueous solution at 298 K, the Λ-isomers of both phen and bipy complexes containing *S*-phenylalanine (I) are thermodynamically more stable than the corresponding Δ-species. Consequently Δ → Λ inversions may be observed when aqueous solutions of the less-stable diastereoisomers are exposed to light [1] to yield solutions enriched in the Λ-isomer. These discriminations are less pronounced for the bipy complexes and this fact may be attributed to the greater flexibility of this diimine ligand, compared with phen, resulting in some relief of strain in the Δ-diastereoisomer.

Distortions of the ligand sufficient to account for these observations have been shown to occur in the crystal structure of Δ,Λ-$[Ru(bipy)_2(S\text{-ala})]ClO_4 \cdot \frac{1}{2}H_2O$ [7]. It is also apparent that substitution on the aromatic ring of phenylalanine has little effect on the magnitudes of the resulting equilibrium constants. The phen complexes all have K_{eq} values of about 2.0–2.5 at 298 K whereas the bipy analogues show only minor discriminations similar to that observed with *S*-alanine [6].

Little change is seen in the equilibrium direction for a wide variety of β-substituents and this leads us to conclude that the steric effects described previously [2] are in the main responsible for the observed discriminations. If a bulkier amino acid side chain is present, as is the case [2] with *S*-tryptophane (I) or its 5-hydroxy-derivative, the effects are more pronounced.

A considerable difference is found, however, for the complexes containing α-methyl-amino acids, as may be ascertained from the data in Table III. These results too have as their origin steric requirements, but of a different kind and which lead to even greater stabilization of the Λ-diastereoisomers with *S*-amino acid ligands.

In the species Δ-$[Ru(bipy)_2(S\text{-ala})]^+$, the steric interaction between the methyl group of the amino acid and an H(6) atom of one of the bipyridyl rings was shown to be somewhat compensated for by rotations about the Ru–nitrogen and α-carbon–nitrogen bonds [7]. As a consequence, one N-hydrogen atom and the α-hydrogen atom of the amino acid were observed to approach an eclipsed conformation. The corresponding atoms are nearer to staggered in the Λ-diastereoisomer.

It is only to be expected that repulsive interactions of the kind induced by the twisting described above would be considerably increased in the α-methyl-amino acid complexes. Such effects would serve to further decrease the relative stability of the Δ-isomer. This is indeed what is observed to occur for the appropriately substituted complexes listed in Table III. Equilibrium constants are approximately double those obtained with pairs of analogous isomers containing the normal α-amino acid ligands. The increased preference for the Λ-diastereoisomers is of the order of 1.6 kJ mol^{-1}.

This cooperative steric effect is observed for both the phen and bipy series of complexes and is obviously a significant discriminatory interaction in compounds of this type.

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