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Chiral Metal Complexes
3*. The pH-Controlled Equilibrium of Diastereoisomeric Pairs of Ternary *Cis*-Ru(II)-Diimine Complexes with *L*-Glutamic Acid

ROBERT S. VAGG**
School of Chemistry, Macquarie University, North Ryde, N.S.W. 2113, Australia

and PETER A. WILLIAMS**
Department of Inorganic Chemistry, University College, P.O. Box 78, Cardiff CF1 1XL, U.K.

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The compounds of general formula Δ,Λ-*[Ru(diimine)$_2$(L-glu)]·nH$_2$O [where L-glu is the L-glutamate di-anion and diimine is 1,10-phenanthroline (n = 6) or 2,2'-bipyridyl (n = 5)] have been isolated and their diastereoisomeric pairs resolved using chromatographic methods. The* Λ*-isomer of each species spontaneously inverts in neutral aqueous solution in the presence of light. The equilibrium constants at 298 K for the reaction*

$$\Delta\text{-}[Ru(diimine)_2(L\text{-}glu)]^{\circ}_{(aq)} \rightleftharpoons \Lambda\text{-}[Ru(diimine)_2(L\text{-}glu)]^{\circ}_{(aq)}$$

are 0.64(5) and 0.56(7) for the phen and bipy complexes respectively. From acidic solutions the compounds of general form

$$\Delta,\Lambda\text{-}[Ru(diimine)_2(L\text{-}gluH)]ClO_4\cdot 3H_2O$$

[where L-gluH is the monohydro-L-glutamate anion] have been obtained. The corresponding equilibrium constants for these cationic species are close to unity, being 1.03(8) and 1.17(17) for the phen and bipy complexes respectively. Equilibrium mixtures of these cationic species, upon deprotonation, deracemize with respect to the metal centre to yield solids enriched in the Δ*-diastereoisomers, consistent with equilibration of the neutral form. Possible contributions to the chiral discriminations observed for these reactions are discussed.*

Introduction

Observations of inversion at the metal centre of Ru(II) complexes of diimines and optically active amino acids have been reported recently [1, 2]. These inversions are light-catalysed and, unlike previous examples [3–5], involve no substitution in the coordination sphere. Steric factors appear to be important in the establishment of the position of equilibrium (1). As is suggested

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

by molecular models [1], the Λ-propellor molecule is favoured for *L*-amino acids which contain bulky side groups such as *L*-tryptophane, [1], *L*-phenylalanine, *L*-proline and *L*-tyrosine [6].

However, it appears that steric factors are not the only important influence on the equilibration of such diastereoisomers. While the Λ-hand of[†] [Ru(phen)$_2$(*L*-ser)]$^+$ shows the expected bias on steric grounds, the Δ-hand of the bipy analogue is observed to be the thermodynamically more stable at room temperature [2]. Consequently both Λ- to Δ- and Δ- to Λ- inversions proceed [2] under the appropriate conditions. Hence dispersion, possible hydrogen bonding interactions and the effects of chiral solvent sheaths [7] associated with the optically active complex ions also may be important in these novel reactions.

One aim of our continuing studies on these systems is to evaluate the possible significance of these effects. We wish to report here our results for related species when *L*-glutamic acid is the coordinated amino acid. Complexes analogous to those above with *L*-glutamic acid are neutral when the carboxylic side chain is deprotonated, (Ia) or are cationic when protonated (Ib). We find that for the proto-

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*Part 2 is reference [2].

**Authors to whom correspondence should be addressed.

[†] phen = 1,10-phenanthroline, bipy = 2,2'-bipyridyl, *L*-ser = *L*-serinate anion, *L*-gluH = monohydrogen-*L*-glutamate anion, *L*-glu = *L*-glutamate dianion, en = 1,2-diaminoethane.

(a) (b)

(I)

nated species the equilibrium constants for (I) of both the phen and bipy complexes are, within experimental error, unity. The position of the equilibrium for each of the neutral species, however, lies on the Δ-side. If, therefore, the mixtures of the protonated diastereoisomers are made basic and exposed to light, the complexes are observed to spontaneously deracemize with respect to the configuration at the metal centre, and to yield finally the appropriate equilibrium mixture of diastereoisomers found for the neutral aquated species.

Experimental

Elemental analyses for C, H and N were carried out by Mrs. A. Dams in the Department of Chemistry at Cardiff. Thermogravimetric analyses for water and ruthenium metal were made under N_2 flow using a Stanton Redcroft TG 750 temperature-programmed thermogravimetric balance. Water loss often was observed to be stepwise, with each compound losing three mol equivalents of water in the temperature range 30–50 °C. Observed low H microanalysis values are entirely consistent with the species formed after initial loss of this lattice water in each case.

Electronic and circular dichroism (CD) spectra were obtained using a Beckman DK 2A ratio recording spectrophotometer and a Jobin-Yvon Dichrographe III, respectively. Chromatographic separations of the neutral diastereoisomer species were performed with light excluded on Sephadex® C-25 cation exchange resin in the Na^+ form, and empolying an LKB 2070 Ultrorac® II fraction collector. The reproduceability of electronic and CD spectra showed the effect of light admitted during their recording to be negligible.

The successful separation of the Λ- and Δ-forms of $[Ru(diimine)_2(L\text{-}glu)]^0$ as neutral complexes by cation exchange presumably must rely on the hydrolysis of water to produce protonated cationic species which will compete for exchange sites on the resin. Slow elution is thereby effected with this solvent alone.

Δ,Λ-[Ru(phen)$_2$(L-glu)]·6H$_2$O

Crystalline *cis*-$[Ru(phen)_2Cl_2]$, (0.27 g, 0.5 mmol), [8], was dissolved in hot water (40 cm^3) and to the solution of *cis*-$[Ru(phen)_2ClH_2O]^+$ thus generated was added magnesium *L*-glutamate trihydrate (0.57 g, 2.5 mmol, California Biochem. Research Corp. Reagent) followed by 1.0 mol dm^{-3} sodium hydroxide (2.5 cm^3, 2.5 mmol). The solution was heated to 50 °C and this temperature maintained for one hour, then it was filtered and allowed to stand at room temperature for one day. Half of the deep-red reaction solution was retained for the isolation of the monoprotonated species, described below. The remainder was applied directly to a Sephadex® C-25 column (Na^+ form) which was eluted with deionized water. A small quantity of a yellow species was retained at the top of the column, while another unidentified yellow band moved with the solvent front. The rich ruby-red band containing the required compound developed slowly, was collected, and the combined fractions evaporated to dryness under reduced pressure at 40 °C. Deep red–black crystals were obtained. [Yield: 65%. *Anal.* Found: C, 48.9; H, 9.6; N, 9.9; H_2O, 15.5; Ru, 14.8%. Calc. for $[Ru(phen)_2(L\text{-}glu)]\cdot 6H_2O$: C, 48.7; H, 4.9; N, 9.8; H_2O, 15.1; Ru, 14.1%]. A solution of the compound in deionized water was used for the separation of the diastereoisomers.

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

To the reaction solution retained above was added deionized water (40 cm^3) and conc. HCl (1 cm^3). After heating the reaction mixture to near boiling a solution of $NaClO_4$ (15 g) in H_2O (20 cm^3) was added and the mixture cooled to room temperature and allowed to stand overnight. The red crystalline solid which had formed was collected at the pump, washed with a minimum of ice-cold water, and air-dried. [Yield: 40%. *Anal.* Found: C, 45.7; H, 3.0; N, 9.2; H_2O, 7.0%. Calc. for $[Ru(phen)_2(L\text{-}gluH)]ClO_4\cdot 3H_2O$: C, 45.8; H, 4.1; N, 9.2; H_2O, 7.1%].

Δ,Λ-[Ru(bipy)$_2$(L-glu)]·5H$_2$O

Deep red-black crystals of the compound were isolated, and later used for separation of diastereoisomers, following a procedure identical to that described for the phen analogue above, but starting with *cis*-$[Ru(bipy)_2Cl_2]$, [1]. [Yield: 45%. *Anal.* Found: C, 46.5; H, 4.3; N, 10.7; H_2O, 14.0; Ru, 16.0%. Calc. for $[Ru(bipy)_2(L\text{-}glu)]\cdot 5H_2O$: C, 46.3; H, 5.1; N, 10.8; H_2O, 13.9; Ru, 15.6%].

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

A portion of the solution from the above preparation was made acidic with conc. HCl to pH ≈ 1 and was then saturated with $NaClO_4$. The red precipitate which formed almost immediately was collected at the pump, washed with a minimum of ice-cold water and dried in air. [Yield: 30%. *Anal.* Found: C, 42.1; H, 3.5; N, 9.9; H_2O, 7.6%. Calc. for $[Ru(bipy)_2(L\text{-}gluH)]ClO_4\cdot 3H_2O$: C, 42.1; H, 4.2; N, 9.8; H_2O, 9.6%].

TABLE I. CD Magnitudes and Equilibrium Constant Results for the Complexes.

Complex[a]	$\Delta\epsilon^{b}_{max}$/dm^2 mol^{-1}	k^{d}_{eq}	ΔG^{o}/kJ mol^{-1} [e]
Δ-[Ru(phen)$_2$(*L*-glu)]^o	−1500(70)		
Δ-[Ru(phen)$_2$(*L*-gluH)]$^+$	−1460(70)		
Δ-[Ru(bipy)$_2$(*L*-glu)]^o	−845(15)		
Δ-[Ru(bipy)$_2$(*L*-gluH)]$^+$	−855(15)		
Λ-[Ru(phen)$_2$(*L*-glu)]^o	+2130(40)		
Λ-[Ru(phen)$_2$(*L*-gluH)]$^+$	+2170(40)		
Λ-[Ru(bipy)$_2$(*L*-glu)]^o	+1220(30)		
Λ-[Ru(bipy)$_2$(*L*-gluH)]$^+$	+1230(30)		
Δ,Λ-[Ru(phen)$_2$(*L*-glu)]^o	−80(8)[c]	0.64(5)	1.1(2)
Δ,Λ-[Ru(phen)$_2$(*L*-gluH)]$^+$	+380(30)[c]	1.03(8)	–
Δ,Λ-[Ru(bipy)$_2$(*L*-glu)]^o	−100(14)[c]	0.56(7)	1.4(3)
Δ,Λ-[Ru(bipy)$_2$(*L*-gluH)]$^+$	+285(40)[c]	1.17(17)	

[a] All as aquated species. [b] Δε of low-energy long-axis-polarized $\pi \rightarrow \pi^*$ transition, with errors estimated from multiple measurements. [c] Δε values of light-equilibrated solutions. [d] Equilibrium constant refers to reaction (1) at 298 K. [e] Calculated from K_{eq} values at 298 K.

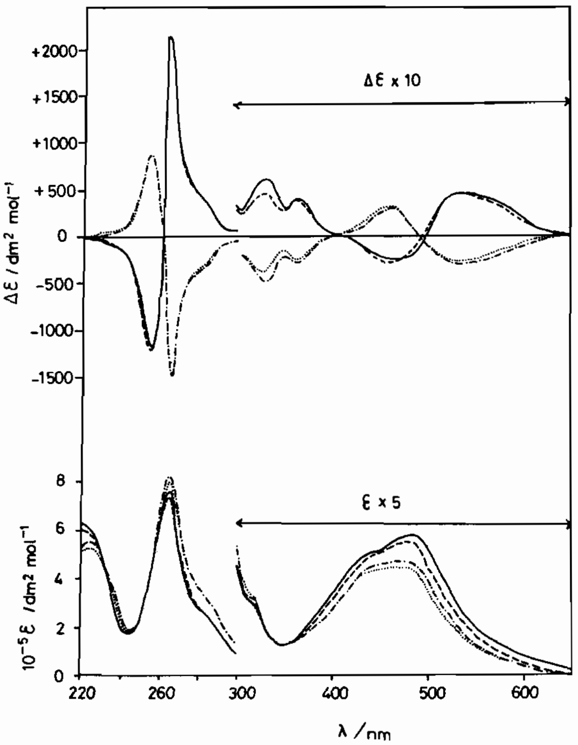


Fig. 1. Electronic and CD spectra of (———) Λ-[Ru(phen)$_2$(*L*-glu)]^o, (– – –) Λ-[Ru(phen)$_2$(*L*-gluH)]$^+$, (–·–·–) Δ-[Ru(phen)$_2$(*L*-glu)]^o, and (······) Δ-[Ru(phen)$_2$(*L*-gluH)]$^+$, in aqueous solution.

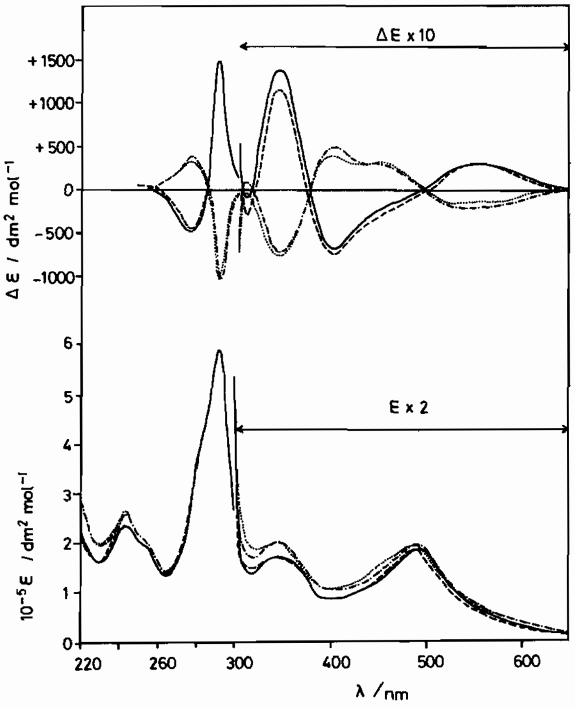
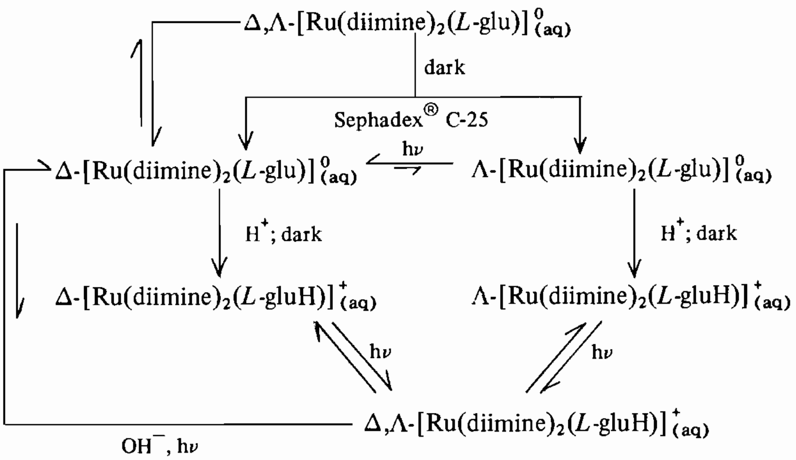


Fig. 2. Electronic and CD spectra of (———) Λ-[Ru(bipy)$_2$(*L*-glu)]^o, (– – –) Λ-[Ru(bipy)$_2$(*L*-gluH)]$^+$, (–·–·–) Δ-[Ru(bipy)$_2$(*L*-glu)]^o, and (······) Δ-[Ru(bipy)$_2$(*L*-gluH)]$^+$, in aqueous solution.

Results and Discussion

Resolution of the neutral diastereoisomeric pairs was indicated by separation profiles similar to those obtained for the *L*-tryptophane [1] and *L*-serine [2] cationic complexes reported earlier. Again in each case the Δ-isomer eluted first from the column as has been observed for all related Ru(II) species investigat-



Scheme

ed thus far [1, 2, 6]. Assignments of the absolute configurations are made on the basis of the calculations of Bosnich [9, 10], and these assignments agree with those predicted from models in which the side-group of the amino acid is bulky [1].

The CD and electronic spectra of the neutral species were recorded immediately after elution, then these same solutions were made acidic (pH ≈ 2) with $HClO_4$, and the corresponding spectra of the cationic monoprotonated complexes were obtained. Definitive spectra are shown in Figs. 1 and 2.

The magnitude of the lower energy long-axis-polarized $\pi \rightarrow \pi^*$ transition of all diastereoisomers is observed to be considerably greater for the Λ-isomer compared with the corresponding Δ-species (Table I). This pattern of spectral magnitudes was found also in the analogous *L*-serinato complexes [2] and, to a lesser extent, in the *L*-tryptophanato congeners [1].

Such differences may originate from structural distortions in the diastereoisomers resulting from varying steric interactions.

Exposure to light allowed equilibration of the neutral and protonated aqueous species, as described previously [1, 2]. Equilibrium $\Delta\epsilon$ values for the mixtures of isomers are also given in Table I, together with calculated equilibrium constants and ΔG° values for the reactions as written in (1), at 298 K. As a consequence of these results, the following stereochemical changes, which are summarized in the Scheme, are indicated.

When either propellor of the protonated species is allowed to reach equilibrium in the presence of light the concentrations of the two diastereoisomers are equal within experimental error. Thus, with respect to the metal centre, the complex ions racemize. Aqueous solutions of Δ,Λ-$[Ru(diimine)_2(L\text{-}glu)]^\circ$, on exposure to light, show a bias towards the Δ-isomers after equilibration, and this is reflected in some novel effects in other equilibration studies. The pure Δ-$[Ru(diimine)_2(L\text{-}glu)]^0_{(aq)}$ isomers partially racemize at the metal, but the isolated Λ-diastereoisomers, when exposed to light, spontaneously invert with retention of the coordination sphere to give equilibrium solutions in which the ratio of Δ- to Λ-isomers is approximately 3:2 in each case. As a result of this phenomenon, when equal mixtures of diastereoisomers of the cationic species are deprotonated with mild base (pH ≈ 9), the complexes spontaneously de-racemize with respect to their absolute configuration at the metal centre. These epimerizations are akin to changes of optical activity such as occur with the Pfeiffer effect [11–13], when certain kinetically labile metal complexes are dissolved in aqueous solutions which contain other optically active species, classically alkaloidium ions. Also related are asymmetric transformations of the first kind, such as the equilibration in dry acetone solution of (+)-bromochloromethanesulphonic acid with (–)-hydroxyhydrindane [14], and the work of Bosnich and Watts [15, 16] concerning the enantiomerization of $[Ni(phen)_3]^{2+}$ and $[Co(en)_2Cl_2]^+$ in (–)-2,3-butanediol. However, to our knowledge, the de-racemization effects reported here are, as such, unique in coordination chemistry.

There is little, if any, chiral discrimination between the isomers of the protonated species in aqueous solution. This result is not surprising on steric grounds since in similar studies [2] on related complexes of *L*-serine the Δ-diastereoisomer of the bipy complex and the Λ-diastereoisomer of the phen analogue are each the thermodynamically more stable in aqueous solution, and the associated equilibrium constants are considerably smaller than were found [1] with complex cations containing the much more bulky *L*-tryptophane ligand.

However, the marked preference for the Δ-hand in the neutral complexes of *L*-glutamic acid indicates again that steric factors need not be the predominant determinant of the chiral discriminations involved. Indeed, the present results suggest that hydrogen bonding interactions, possibly with the diimine ligands, but more probably with the surrounding solvent sheaths (which themselves will be chiral), [7], may be at least as significant as steric ones. In this respect it is interesting to note that Buckingham *et al.* [17] have suggested that slightly differing solvation energies could be the source of the chiral discrimination observed in reactions involving the mutarotation of amino acids coordinated to optically active complexes of Co(III) with 1,2-diaminoethane. Their studies on cations of the form $[Co(en)_2(L\text{-aa})]^{2+}$ with *L*-aa = *L*-alanine and *L*-valine found no discrimination for the former, while equilibirum mixtures of diastereoisomers of the latter consisted of significantly different amounts of *L*- and D-amino acid. Conformation calculations for the pairs of complexes showed negligible differences between corresponding alanine and valine isomers.

Only minute differences in contact terms might be expected between the pairs of diastereoisomers described in this work, their only difference being the presence or absence of a proton on the carboxylic group remote from the metal centre, and thus from the aromatic ring hydrogen atoms which are thought to be important in steric terms. The discrimination energies observed for the neutral species, approximating 1 kJ mol^{-1}, are of the order predicted for electrostatic discriminations, although Craig and Mellor [7] have noted that relayed chiral influences might be propagated over several solvent diameters. This would appear to be the case in the present work.

If hydrogen bonding interactions within the solvent sheaths of these kinds of molecules are important, then equilibration studies on related amino acid complexes which have approximately the same steric characteristics, but which contain less bulky side groups than those present in proline, tryptophane or phenylalanine, should display discriminations dependent upon their hydrogen bonding capacities. We are pursuing these ideas at present, and will communicate our results in the near future.

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