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Chiral Metal Complexes.
6*. The Kinetically Controlled Stereoselective Synthesis of Ternary Co(III) Complexes of the Type [Co(phen)$_2$(*S*-aminoacidate)]$^{n+}$

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The complexes Λ*-[Co(phen)$_2$(*aa*)]$^{2+}$, where* aa *is the singly charged anion of the α-amino acids* S*-glutamine,* S*-asparagine,* S*-glutamic acid and* S*-aspartic acid, and phen is 1,10-phenanthroline, may be synthesized stereospecifically under certain conditions by the reaction of the amino acid with* Δ,Λ*-[Co(phen)$_2$CO$_3$]$^+$. Kinetic, rather than thermodynamic, influences are responsible for the reaction products observed. It is evident that both diastereoisomers of the* bis*-phen complex form initially, but the rate of decomposition of the* Δ*-isomer is considerably faster than that of the* Λ*-isomer. The results have been used to reinterpret some earlier work on chiral discriminations in related complexes containing 1,2-diaminoethane, and recent results concerning the phen complexes containing glycine,* S*-alanine,* S*-phenylalanine,* S*-leucine,* S*-isoleucine and* S*-valine.*

Introduction

We have previously reported [1] studies of chiral discriminations in complexes of the type Δ,Λ-[Ru(diimine)$_2$(*aa*)]$^{n+}$, where diimine is phen† or bipy and *aa* is an optically active α-amino acid. During the course of these studies, which aim in part to establish the causes of the discriminatory interactions involved, we have had occasion to examine some analogous complexes of Co(III). The results of this study, which concerns the species Δ,Λ-[Co(phen)$_2$(*aa*)]$^{n+}$, where *aa* is the *S*-asparaginate, *S*-aspartate, *S*-glutaminate or *S*-glutamate anion, are presented below. The Λ-diastereoisomer of each of the four complexes was obtained stereospecifically under the chosen synthetic conditions. This result has led us to reinterpret some earlier work on chiral discriminations in the related series of en complexes, Δ,Λ-[Co(en)$_2$(*aa*)]$^{n+}$, and recent results concerning phen complexes of *S*-alaH, *S*-valH, *S*-leuH, *S*-isoH and glycine [2].

Experimental

Analyses were carried out by Mrs. A. Dams in the Department of Chemistry, Cardiff. Circular dichroism (CD) and electronic spectra were recorded using a Jobin-Yvon Dichrographe III, and a Beckman DK2A ratio recording spectrophotometer, respectively. Thermogravimetric analyses were carried out using a Stanton Redcroft TG 750 thermogravimetric balance. All chromatographic separations were performed using a column (60 × 2 cm) of CM Sephadex® C-25 cation exchange resin in the H$^+$ form. Elution with H$_2$O followed by 0.01 mol dm^3 aqueous NaClO$_4$ effected the separation of the desired complexes, fractions being collected with an LKB 2070 Ultrorac® II instrument. Δ,Λ-[Co(phen)$_2$CO$_3$]Cl·5H$_2$O was synthesised from Δ,Λ-[Co(phen)$_2$Cl$_2$]Cl·3H$_2$O using previously published procedures [3, 4].

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*Part 5 is reference [1].

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†Phen = 1,10-phenanthroline, bipy = 2,2′-bipyridyl, en = 1,2-diaminoethane, asnH = asparagine, aspH$_2$ = aspartic acid, glnH = glutamine, gluH$_2$ = glutamic acid, alaH = alanine, valH = valine, metH = methionine, pheH = phenylalanine, serH = serine, leuH = leucine, proH = proline, cysH = cysteine, pipH = pipecolic acid, isoH = isoleucine, thrH = threonine, alloH = allothreonine.

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Λ-[Co(phen)$_2$(S-asn)](ClO$_4$)$_2$·4H$_2$O

To Δ,Λ-[Co(phen)$_2$CO$_3$]Cl·5H$_2$O (0.2029 g, 3.37 × 10^{-4} mol) dissolved in H$_2$O (25 cm^3) was added *S*-asnH (0.059 g, 3.91 × 10^{-4} mol). The mixture was heated for exactly 40 min on a steam-bath during which time its colour changed from pink-orange to yellow-orange. The reaction mixture was cooled quickly to room temperature and loaded immediately on to the cation exchange column. Elution with water developed a broad pink band whose spectral characteristics showed it to comprise isomers of *tris*-(*S*-asparaginato)Co(III), [5, 6]. Elution with 0.1 *M* NaClO$_4$(aq) developed several pink and pink-orange bands, followed by a well separated orange fraction. The former were undoubtedly isomers of [Co(phen)(*S*-asnH)$_2$]$^+$, found in an exactly analogous fashion during the separation of the reaction products of *S*-asnH, *S*-gluH$_2$ and *S*-aspH$_2$ with Δ,Λ-[Co(en)$_2$CO$_3$]$^+$ or *trans*-[Co(en)$_2$Cl$_2$]$^+$, [7, 8]. These species were not investigated further.

The slower-moving orange band, which proved to contain the desired product, was collected in fractions, all of which, within experimental error, had identical optical activities. These fractions were combined and evaporated to dryness *in vacuo* at 30 °C. The residue was triturated with ethanol (25 cm^3), filtered, and left to stand under a further 25 cm^3 of ethanol for 96 hours. The orange solid product was collected at the pump, washed with ethanol, then ether, and air-dried. [Yield: 52 mg. *Anal.* Found: C, 40.6; H, 3.3; N, 10.4%. Calc. for [Co(phen)$_2$(*S*-asn)](ClO$_4$)$_2$·4H$_2$O: C, 40.9; H, 3.8; N, 10.2%].

Λ-[Co(phen)$_2$(S-gln)](ClO$_4$)$_2$·4H$_2$O

This orange complex was prepared in a similar way to the *S*-asnH analogue above, substituting Δ,Λ-[Co(phen)$_2$CO$_3$]Cl·5H$_2$O (0.245 g, 4.06 × 10^{-4} mol) and *S*-glnH (0.062 g, 4.26 × 10^{-4} mol) as reactants. [Yield: 13 mg. *Anal.* Found: C, 41.6; H, 3.8; N, 9.9%. Calc. for [Co(phen)$_2$(*S*-gln)](ClO$_4$)$_2$·4H$_2$O: C, 41.7; H, 4.0; N, 10.1%].

Λ-[Co(phen)$_2$(S-asp)]ClO$_4$·4H$_2$O

To Δ,Λ-[Co(phen)$_2$CO$_3$]Cl·5H$_2$O (0.215 g, 3.56 × 10^{-4} mol) in H$_2$O (25 cm^3) was added *S*-aspH$_2$ (0.047 g, 3.56 × 10^{-4} mol). After heating on a water-bath for 40 min, the reaction mixture was cooled and loaded onto the column. The compound was then isolated by a method similar to that outlined above. [*Yield:* 43 mg. *Anal.* Found: C, 46.8; H, 4.1; N, 9.3%. Calc. for [Co(phen)$_2$(*S*-asp)]ClO$_4$·4H$_2$O: C, 46.6; H, 4.0; N, 9.7%].

Λ-[Co(phen)$_2$(S-gluH)](ClO$_4$)$_2$·8H$_2$O

A solution in water (25 cm^3) of Δ,Λ-[Co(phen)$_2$CO$_3$]Cl·5H$_2$O (0.200 g, 3.30 × 10^{-4} mol) and Na *S*-gluH·H$_2$O (0.070 g, 3.74 × 10^{-4} mol), was heated on a water bath for 40 min. The desired product was isolated by the method outlined above. [Yield: 77 mg. *Anal.* Found: C, 38.2; H, 3.2; N, 7.8; H$_2$O, 16.0%. Calc. for [Co(phen)$_2$(*S*-gluH)]ClO$_4$·8H$_2$O: C, 38.4; H, 4.4; N, 7.7; H$_2$O, 15.9%]. The water is lost in two distinct steps, as found by thermogravimetry, each corresponding to 8% by weight. The first weight loss [–4H$_2$O; calc. 7.9%] occurs at 35 °C in the N$_2$ stream and the second at 90 °C. The low hydrogen analysis reported above is consistent with the loss of four molecules of water prior to analytical combustion. This effect has been observed previously with some Ru(II) analogues [1].

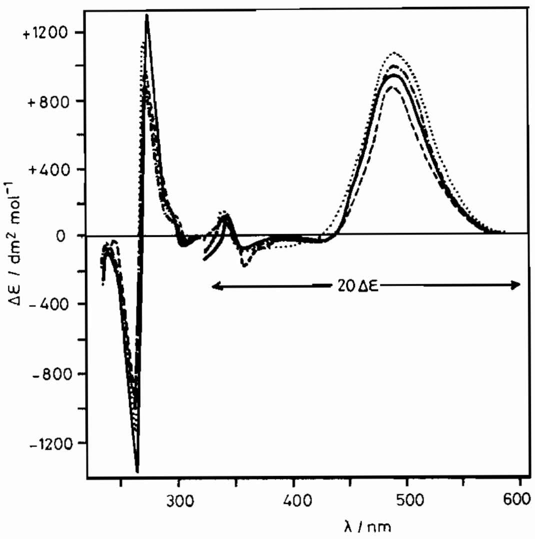


Fig. 1. CD spectra of (——) Λ-[Co(phen)$_2$(*S*-gluH)]$^{2+}$, (------) Λ-[Co(phen)$_2$(*S*-aspH)]$^{2+}$, (–·–·–) Λ-[Co(phen)$_2$(*S*-gln)]$^{2+}$ and (······) Λ-[Co(phen)$_2$(*S*-asn)]$^{2+}$.

At the end of each chromatographic separation a yellow band remained at the top of the column which could be eluted with 1 mol dm^{-3} aqueous HCl. Electronic spectra indicated that the species was [Co(phen)$_3$]$^{3+}$, [9]. Yellow crystals were isolated from these fractions by addition of concentrated HClO$_4$. [*Anal.* Found: C, 45.4; H, 3.1; N, 8.7%. Calc. for [Co(phen)$_3$](ClO$_4$)$_3$·3H$_2$O: C, 45.4; H, 3.2; N, 8.8%]. The eluted fractions containing this species were optically inactive.

Results and Discussion

The electronic and CD spectra of the four diastereoisomers isolated are shown in Figs. 1 and 2, and spectral details are given in Table I. The species separated by chromatographic methods are optically pure and no traces of the Δ-diastereoisomers were found, *under the reaction conditions given above.*

TABLE I. Electronic and CD Spectral Details of the Complexes.

Complex	λ/nm	$\Delta\epsilon_{max}$/dm^2 mol^{-1}	λ_{max}/nm	10^{-5} ϵ/dm^2 mol^{-1}
Λ-[Co(phen)$_2$(*S*-gluH)]$^{2+}_{(aq)}$	497	+46.5(1.3)	488	0.016
	282	+1330(70)	349	0.29
	271	−1400(100)	333sh	0.42
			318sh	0.92
			305sh	1.97
			273	8.25
Λ-[Co(phen)$_2$(*S*-aspH)]$^{2+}_{(aq)}$	497	+42.4(1.1)	490	0.012
	282	+920(30)	347	0.17
	271	−920(30)	332sh	0.25
			315sh	0.59
			300sh	1.26
			275sh	4.56
			270	5.03
Λ-[Co(phen)$_2$(*S*-gln)]$^{2+}_{(aq)}$	498	+48.7(1.9)	481	0.011
	280	+990(11)	347	0.18
	270	−990(11)	332sh	0.24
			303sh	1.01
			271	4.32
Λ-[Co(phen)$_2$(*S*-asn)]$^{2+}_{(aq)}$	499	+52.8(1.7)	499	0.024
	280	+1120(75)	346	0.22
	271	−1140(75)	332sh	0.29
			316sh	0.61
			302sh	1.46
			278sh	5.20
			272	5.71

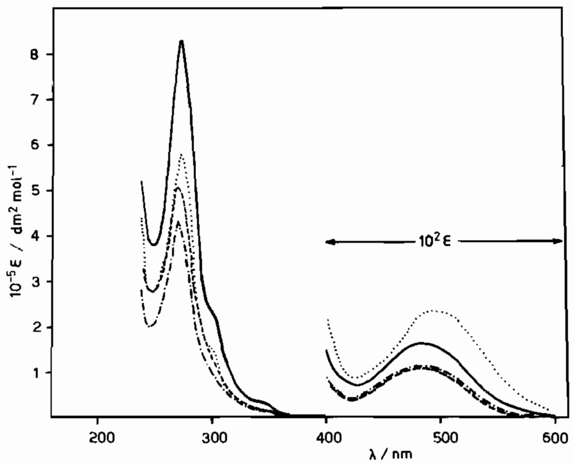


Fig. 2. Electronic spectra of (———) Λ-[Co(phen)$_2$(*S*-gluH)]$^{2+}$, (-----) Λ-[Co(phen)$_2$(*S*-aspH)]$^{2+}$, (—·—·—) Λ-[Co(phen)$_2$(*S*-gln)]$^{2+}$ and (·····) Λ-[Co(phen)$_2$(*S*-asn)]$^{2+}$.

Absolute configurations were assigned as Λ according to the signs in the CD spectra of the lowest energy A → E transitions [10, 11] and on the basis of the signs of the low energy π → π* transitions [12, 13] at 280–282 nm. The absolute configurations predicted are entirely self-consistent and the rotational strengths observed in the exciton region are also in accord with calculations [12] and observations on related species [13, 14]. The spectra of the complexes containing *S*-aspH$_2$ and *S*-gluH$_2$, were measured in 0.01 mol dm^{-3} aqueous HClO$_4$ and hence refer to the mono-protonated species. The *S*-asn and *S*-gln complex spectra were measured in H_2O.

The stereospecific synthesis of the Λ-[Co(phen)$_2$-(*aa*)]$^{n+}$ diastereoisomers is in marked contrast to those related complexes of Ru(II) for which both isomers are obtained. Furthermore, for the latter metal, and when the diimine is either phen or bipy, equilibration studies [1, 16] have shown that the

TABLE II. Reported Ratios of Diastereoisomers of the Type Δ,Λ-[Co(en)$_2$(S-aa)]$^{n+}$.

Amino Acid	Starting Complex	Solvent	T/°C	Time/hr	Method^a	[Λ-S]/ [Δ-S]	Ref.
alaH	Λ-[Co(en)$_2$(S-ala)]$^{2+}$	H_2O	34.3	0.9	A	50/50	25
alaH	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	100 3	~0.2 ~18	B	50/50	26
alaH	c[Co(en)$_2$Cl$_2$]$^+$	H_2O	~100	NS^b	C	~50/50^c	27
alaH	c-[Co(en)$_2$(H$_2$O)(OH)]$^{2+}$	H_2O	100	NS	C	~50/50^c	28
valH	Λ-[Co(en)$_2$(S-val)]$^{2+}$	H_2O	34.3	1.3	A	39/61	25
valH	c-[Co(en)$_2$(H$_2$O)(OH)]$^{2+}$	H_2O	100	NS	C	~50/50^c	28
aspH$_2$	[Co(en)$_2$CO$_3$]$^+$	H_2O	40 70	0.3 0.5	D^d	60/40	29
aspH$_2$	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	~25	NS	D^d	60/40	7
aspH$_2$	Λ-[Co(en)$_2$(S-asp)]$^+$	D_2O	37	NS	A^e	77/23	30, 31
aspH$_2$	Δ-[Co(en)$_2$(S-asp)]$^+$	D_2O	37	NS	A^e	11/89	30, 31
aspH$_2$	Λ-[Co(en)$_2$(S-asp)]$^+$	D_2O	37	NS	A	50/50	31
aspH$_2$	Λ-[Co(en)$_2$(S-asp)]$^+$	H_2O	25	120	A	53/47	32
gluH$_2$	[Co(en)$_2$CO$_3$]$^+$	H_2O	40 70	0.3 0.5	D^d	70/30	29
gluH$_2$	[Co(en)$_2$CO$_3$]$^+$	H_2O	80–100	NS	D^d	53/47	21
gluH$_2$	[Co(en)$_2$CO$_3$]$^+$	H_2O	80–100	NS	D^f	49/51	21
gluH$_2$	Λ-[Co(en)$_2$(S-glu)]$^+$	H_2O	25	NS	A	53/47	21
gluH$_2$	[Co(en)$_2$CO$_3$]$^+$	H_2O	~100	NS	E^g	100/0^h	17–20
asnH	Λ-[Co(en)$_2$(S-asn)]$^{2+}$	D_2O	37	NS	A	50/50	31
asnH	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	50	0.3	D	81/19	8
glnH	Λ-[Co(en)$_2$(S-glu)]$^+$	D_2O	37	NS	A	50/50	31
glnH	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	50	0.3	D	59/41	8
metH	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	~100	NS	B	>50/50	33
pheH	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	100 3	~0.2 ~18	B	50/50	26
pheH	c-[Co(en)$_2$(H$_2$O)(OH)]$^+$	H_2O	100	NS	C	~50/50^c	28
serH	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	~100	NS	B	50/50	33
leuH	c-[Co(en)$_2$(H$_2$O)(OH)]$^{2+}$	H_2O	100	NS	C	~50/50^c	28
leuH	c-[Co(en)$_2$Cl$_2$]$^+$	H_2O	~100	NS	C	~50/50^c	27
leuH	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	~100 3	0.2 18	B	50/50	26
proH	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	~100	NS	B, D	0/100	33
proH	t-[Co(en)$_2$Cl$_2$]$^+$	MeOH	80 40 ~25	~0.1 4 ~18	E	0/100	34
proH	Δ,Λ-[(Co(en)$_2$(S-pro)]$^{2+}$	H_2O	25	>1	F	22/78 23/77	35
proH	t-[Co(en)$_2$Br$_2$]$^+$	MeOH	100	0.75	D	26/64	35
pipH	t-[Co(en)$_2$Cl$_2$]$^+$	MeOH	80	1	B	100/0	34
S-CH$_3$-cysH	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	50 ~25	0.5 4			
isoH	c-[Co(en)$_2$(H$_2$O)(OH)]$^{2+}$	H_2O	100	NS	C	~50/50^c	28
thrH	t-[Co(en)$_2$Cl$_2$]$^+$	H_2O	~100	NS	B	>50/50	33
thrH	Λ-[Co(en)$_2$gly]$^{2+}$	H_2O	25	3	G	58/42	37

(continued on facing page)

TABLE II. *(continued)*

Amino Acid	Starting Complex	Solvent	T/°C	Time/hr	Method[a]	[Λ-*S*]/ [Δ-*S*]	Ref.
thrH	Δ-$[Co(en)_2gly]^{2+}$	H_2O	NS	NS	G	54/46	38
alloH	Λ-$[Co(en)_2gly]^{2+}$	H_2O	25	3	G	89/11	37

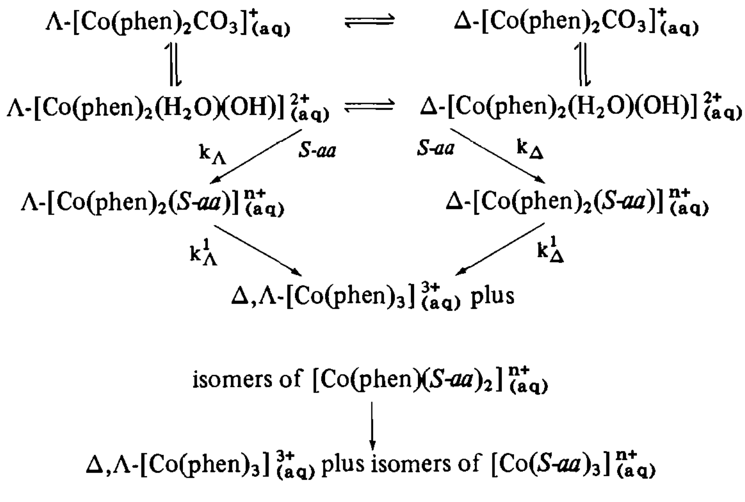
[a] A: Equilibration of isomers in H_2O/OH^- or D_2O/OD^-; B: Recrystallization of iodides and comparison of CD spectra with resolved compounds, or integration of ^1H NMR signals; C: Resolution of complexes; D: Chromatographic separation of reaction products; E: Crystallization of perchlorate or perchlorate chloride from solution; F: Equilibration of isomers over active charcoal; G: Reaction with acetaldehyde and base followed by separation of reaction products. [b] NS = not stated. [c] Not specified, but no discrimination reported. [d] Reaction carried out in presence of charcoal. [e] Equilibrated only until α-methine hydrogen atom exchanged for deuterium. [f] pH = 6–6.5. [g] pH = 4. [h] Λ-*S* diastereoisomer isolated by crystallization. Possible kinetic control on course of reaction. The terms *t*- and *c*- refer to *trans*- and *cis*-, respectively.

chiral discrimination energies between pairs of diastereoisomers are small in aqueous solution. Arguing by analogy, we might expect a similar pattern of reaction products to obtain for the Co(III) complexes, if thermodynamic equilibrium were to be established. It is thus apparent that in each case equilibrium is not attained and that the nature of the reaction of Δ,Λ-$[Co(phen)_2CO_3]^+$ with the four amino acids must be subject to kinetic control.

Possible pathways in the reaction systems are shown in Scheme. Pure Λ-diastereoisomers may be obtained if $k_\Lambda \gg k_\Delta$. Such a case has been suggested [17–20]. But disputed [21] for the formation of Λ-$[Co(en)_2(S\text{-glu})]^+$. Alternatively if $k_\Lambda \cong k_\Delta$, but $k^1_\Delta \gg k^1_\Lambda$, the Λ-diastereoisomers could be isolated under controlled conditions. There is some evidence to suggest that this latter proposal is correct.

The ligand scrambling observed in all of the reactions is parallelled by that found in the reaction of $[Co(en)_2(H_2O)(OH)]^{2+}$ with optically active amino acids [22], and may involve transient Co(II) intermediates [23]. Indeed, the species here isolated are not thermodynamically stable in aqueous solution at room temperature. Even though the Λ-diastereoisomers are sufficiently stable to allow their isolation and characterization, if any of them is dissolved in 0.1 mol dm^{-3} aqueous $NaClO_4$ at room temperature, crystals of racemic $[Co(phen)_3](ClO_4)_3 \cdot 3H_2O$ are observed to deposit during several days, leaving a mixture of isomers of $[Co(S\text{-}aa)_3]^{n+}$ and $[Co(phen)(S\text{-}aa)_2]^{n+}$, and ultimately only the former. As expected, reaction to form the complexes at steam-bath temperatures for periods longer than 40 min markedly decrease the yield of Λ-$[Co(phen)_2(S\text{-}aa)]^{n+}$, as does carrying out the reaction in the presence of charcoal.

Significantly, however, if the reactions are carried out for much shorter times or at room temperature



Scheme

TABLE III. Equilibrium Constants[a] and Chiral Discrimination Energies[b] Calculated for $[Co(en)_2(S\text{-}aa)]^{n+}$].

Complex	Solvent	T/°C	K_{eq}	$\Delta G°/kJ\ mol^{-1}$	Ref.
$\Delta,\Lambda\text{-}[Co(en)_2(S\text{-ala})]^{2+}$	H_2O	34.3	1.00	0	25
$\Delta,\Lambda\text{-}[Co(en)_2(S\text{-val})]^{2+}$	H_2O	34.3	0.64	1.14	25
$\Delta,\Lambda\text{-}[Co(en)_2(S\text{-asp})]^{+}$	D_2O^{c}	37	1.00	0	31
	H_2O	25	1.13	−0.30	32
$\Delta,\Lambda\text{-}[Co(en)_2(S\text{-gln})]^{2+}$	D_2O^{c}	37	1.00	0	31
$\Delta,\Lambda\text{-}[Co(en)_2(S\text{-asn})]^{2+}$	D_2O^{c}	37	1.00	0	31
$\Delta,\Lambda\text{-}[Co(en)_2(S\text{-glu})]^{+}$	H_2O	25	1.13	−0.30	21
$\Delta,\Lambda\text{-}[Co(cn)_2(S\text{-pro})]^{2+}$	H_2O	25	0.31^{d}	2.93^{d}	35

[a] For reaction (1). [b] ΔG° calculated for reaction (1) at the given temperature. [c] α-methine and N–*H* protons exchanged. [d] Average of three values (see Table II).

during the same period as that employed in this study, both Δ- and Λ-diastereoisomers are obtained. This is evidenced by the fact that the leading fractions of the band developed during the chromatographic separation of the reaction mixtures show CD spectra which are almost mirror images of those of the Λ-diastereoisomers. This pattern of isomer separation is analogous to that found for related Ru(II) complexes [1]. Unfortunately, the yields were always so small as to make the isolation of the Δ-isomers impractical, but these results offer conclusive proof that both diastereomers form in the reaction initially, and that the Δ-isomer disproportionates at a significantly faster rate than the Λ-species. It is also worth noting that the kinetically less stable Co(III) diastereoisomers correspond to the less thermodynamically stable Ru(II) analogues, based on steric effects [1, 16]. Thus the possibility exists that the increased reactivity of the Δ-isomers of the Co(III) complexes may be due to steric interactions in the transition state.

It has been recently reported [2], during the course of this study, that both Δ- and Λ-isomers of $[Co(phen)_2(aa)]^{2+}$, with *aa* being glycine, *S*-alaH, *S*-pheH, *S*-leuH, *S*-isoH and *S*-valH could be isolated from the reaction of $\Delta,\Lambda\text{-}[Co(phen)_2Cl_2]^{+}$ with the appropriate amino acid in methanol. It was also noted that the yields from the reaction were considerably higher than if the synthesis was carried out in water. Ratios reported for the concentrations of the Λ-S upon the Δ-*S* diastereoisomers varied from 2.1 for the *S*-alanine complexes to 5.4 for the *S*-valine complexes. In this study [2], however, it was assumed that equilibrium had been attained. These measurements of chiral discriminations between the appropriate diastereoisomers yield values considerably in excess of those found [1, and refs. therein] in analogous Ru(II) complexes where thermodynamic equilibrium *is* established. The observation [2] of higher concentrations of Λ-diastereoisomers containing *S*-aminoacidates is thus most probably due to exactly the same kind of kinetic influences as those found to be significant in the *S*-gluH$_2$, *S*-glnH, *S*-aspH$_2$ and *S*-asnH systems.

Observing that kinetic phenomena play an important role in the distribution of products in these reactions, we have also been prompted to re-examine some published results concerning complexes of general form $\Delta,\Lambda\text{-}[Co(en)_2(aa)]^{n+}$. Many studies have concentrated on chiral discriminations of this type [24] and numerous workers [7, 8, 17–21, 25–38] have examined ratios of products obtained from suitable precursors with a view to calculating the discriminatory energies involved. Some of the results are collected in Table II. A few of the reactions were carried out with complexes of Δ absolute configuration, or with *R*-amino acids. Use has been made then of the thermodynamic relationship between enantiomers and the ratios listed in Table II, [Λ-*S*]/[Δ-*S*], refer to the equilibrium constant (or apparent equilibrium constant) for eqn. (1). As is obvious from the data,

$$\Delta\text{-}[Co(en)_2(S\text{-}aa)]^{n+} \rightleftharpoons \Lambda\text{-}[Co(en)_2(S\text{-}aa)]^{n+} \qquad (1)$$

widely varying ratios of diastereoisomers have been reported for the same amino acid.

Some of these apparent anomalies may be simply explained, however, in terms of solubility differences between diastereoisomeric salts. It has been shown [35] that the perchlorate and iodide salts of $\Delta\text{-}[Co(en)_2(S\text{-pro})]^{2+}$ are much more insoluble than the Λ-salts. This may explain the absence of the latter isomer in some cases, although Hall and Douglas [33] reported that no Λ-diastereoisomer could be detected chromatographically in their reaction products. A similar result was found for the Λ-isomer of $[Co(en)_2(N\text{-}CH_3\text{-}S\text{-ala})]^{2+}$ [34], which was crystallized optically pure from solutions containing potentially four diastereoisomers. It was shown subsequently that both hands of the complex could be obtained with the nitrogen atom of the coordinated amino acid having the *R*-configuration [35, 39]. Solubility differences between diastereoisomers also may explain the apparent stereoselective nature of the reaction of $[Co(en)_2CO_3]^+$ with *S*-gluH$_2$ [17–20]. Although a later study suggested that this was not the case [21], the experimental conditions employed differed from the earlier work.

The widely varying ratios of [Λ-*S*]/[Δ-*S*] for the *S*-aspH$_2$ complexes derived from epimerization measurements in D_2O/OD^- solution are clearly the result of kinetic influences. The rate of hydrogen exchange at the α-carbon is considerably faster than the rate of epimerization of the coordinated amino acid.

From these results, and those above, it is evident that very few of the ratios listed in Table II represent equilibrium concentrations. The elegant work of Buckingham, Sargeson and co-workers on some of the complexes has established reliable chiral discrimination energies, and values for a few other species are known with certainty. These are gathered together in Table III. Chiral discrimination energies in these complexes are small, being less than 3 kJ mol^{-1} at near room temperature.

If kinetic factors control the distribution of isomers in the products of the reactions to form Δ,Λ-$[Co(en)_2(S\text{-}aa)]^{n+}$, as seems probable from the results concerning the phen complexes, and since ligand scrambling is known to occur during the formation of these species, the anomalies in Table II are more apparent than real. Depending upon the solvent, ionic strength, starting material, pH, temperature and length of reaction-time, it is almost inevitable that differing ratios of Δ- and Λ-diastereoisomers may be obtained. The situation is further complicated by solubility differences between diastereoisomeric salts. In order to quantify some of the processes involved, we have begun a detailed kinetic study of some of the systems, and our results will be communicated in the near future.

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