Energy Discriminations between the Enantiomers of tris-Chelate Co-ordination Compounds in the Fluid Phase

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Two aspects of the Pfeiffer effect are distinguished. Each of these, enantiomer reequilibration and induced intermolecular optical activity, gives the differential free energy, enthalpy, and entropy of the enantiomers for intermolecular association in fluids. The salts, $M_3[Cr(ox)_3]$, in chiral α-hydroxy ester solutions antiracemise to an enantiomeric excess with a magnitude, up to 70%, dependent upon the particular cation, M^+, and with a sign dependent upon the (R)- or (S)-configuration of the ester solvent. The effect is quenched by the addition of one equivalent per cation of a crown ether. The temperature-variation of the induced intermolecular CD of racemic $[Cr(pd)_3]$ in ethanol solutions of $\Delta-(-)$-$K[As(cat)_3]$ gives a differential enthalpy of 10.7 kJ mol^{-1} for the association of the chiral anion with the two $[Cr(pd)_3]$ enantiomers. The enantiomer in excess is found to form the larger and more stable association with the chiral environmental molecules. The stereochemical and energetic aspects of the homochiral and the heterochiral intermolecular associations are discussed.

Introduction

Optically-inactive substances, both achiral molecules and racemic compounds, give a circular dichroism (CD) associated with the characteristic electronic transitions in their absorption spectrum when dissolved in a transparent chiral solvent [1–9]. The effect is time-independent in the case of achiral solutes and optically-stable racemic compounds, and it is ascribed to the association of a solute molecule with one or more solvent molecules to give a labile complex with a statistically-preferred set of mutual stereochemical relationships between the groups of the solute and the associated solvent molecules. An achiral molecule becomes effectively a 'symmetric chromophore in a dissymmetric molecular environment', namely, that of the particular preferred association with the solvent molecules, and the induced CD originates by the mechanisms established for this general case [10].

The energies of the intermolecular association between the molecules of the chiral solvent and those of a racemic compound are generally unequal for the two enantiomers of the racemate, and the corresponding resolved enantiomers in a chiral solvent give, superimposed upon the intrinsic molecular CD, an induced CD which is not equivalent for the two antipodal isomers. In the case of an optically-labile racemate, the different energies of the intermolecular association of the chiral solvent molecules with the two enantiomers of the racemate result in a time-dependent antiracemisation, attaining an equilibrium in which the concentration-ratio of the enantiomeric solutes differs from unity. The initial induced CD, produced with an equimolecular ratio of the two enantiomers, becomes progressively overlaid by the inherent molecular CD of the enantiomer with an excess relative concentration in the new equilibrium.

The two effects, the induced intermolecular CD and the molecular CD due to the enantiomeric excess at equilibrium in a chiral solvent, are difficult to separate when the rate of antiracemisation is fast, as in the case of the tris(1,10-phenanthroline)zinc(II) and analogous tris-chelate complexes first investigated by Pfeiffer and Quehl [11]. The two aspects of the 'Pfeiffer effect' are separable, however, if the half-life of the enantiomer for racemisation is sufficiently long to allow the quenching of the induced intermolecular CD, by dilution with an achiral solvent, followed by the immediate measurement of the CD due to the enantiomeric excess at equilibrium prior to the dilution. The induced intermolecular CD is directly accessible in studies of optically-stable molecules in a chiral solvent. Each of the two aspects of the 'Pfeiffer effect', appropriately separated, provide a method for the estimation of the chiral discrimination energy between the two enantiomers of a racemate in a fluid-phase chiral environment.

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The half-life for racemisation of the enantiomers of the tris(oxalato)chromium(III) ion, $[Cr(ox)_3]^{3-}$, is reported [12] as 18.4 minutes in aqueous solution at 25 °C, whereas the corresponding half-life for an enantiomer of tris(pentane-2,4-dionato)chromium-(III), $[Cr(pd)_3]$, in chlorobenzene solution at 25 °C is estimated [13] to be some 700 years by extrapolation of the racemisation rates measured over the 96.1 to 135.0 °C temperature range. The dissymmetry ratio of the CD to the isotropic absorption in the visible region is so large, with the maximum $|\Delta\epsilon|/\epsilon$ values of 4.8% and 7.8% for the enantiomers of $[Cr(ox)_3]^{3-}$ and of $[Cr(pd)_3]$, respectively [14], that an enantiomeric excess down to 0.1% can be estimated in each case.

With a chemical stability and a convenient optical lability, the $[Cr(ox)_3]^{3-}$ complex ion is well-suited for measurements of the free energy of the discrimination between the enantiomers by a chiral solvent, from the enantiomeric equilibrium constant, $[\Lambda]/[\Delta]$, established between the antipodal isomers at a given temperature, and the corresponding enthalpy and entropy of the discrimination, from the variation of the enantiomeric equilibrium constant with temperature. With both chemical and optical stability, the $[Cr(pd)_3]$ complex is more suited for measurements of the differential between the enantiomers in the enthalpy of intermolecular association with a common environmental chiral species, from the temperature variation of the CD induced in the visible absorption region of racemic $[Cr(pd)_3]$. A study of each of these systems is reported in the present work.

Enantiomeric Equilibration in Chiral Solvents

The salts of the $[Cr(ox)_3]^{3-}$ complex anion with a number of singly-charged cations are adequately soluble (1–5 m*M*) for spectroscopic measurements in the ethyl esters of the chiral α-hydroxy carboxylic acids, (R,R)-(+)-tartaric acid (1) and (S)-(+)-lactic acid (2), the esters being fluid at ambient temperature. The racemic salts, $M_3[Cr(ox)_3]$, in these solvents give a CD absorption over the visible wavelength region, developing with time and attaining a stationary level after several hours. The CD spectrum corresponds to an enantiomeric excess of the Λ-(+)-$[Cr(ox)_3]^{3-}$ isomer in the solvent (1), as large as 70% for the ammonium salt at 19 °C, and to an excess of the Δ-(−)-isomer in the solvent (2).

In both solvents an induced intermolecular CD overlies the molecular CD due to the enantiomeric excess at equilibrium, although it is relatively small. The induced intermolecular CD increases the ratio of the peak heights of the two longer wavelength CD bands, ($\Delta\epsilon$ 630/$\Delta\epsilon$ 552), from the value (0.226) observed for a $[Cr(ox)_3]$ enantiomer in aqueous solution. However the induced CD is quenched by the

TABLE I. The Percentage Enantiomeric Excess (e.e.) of the Λ-(+)- or the Δ-(−)-Enantiomer of the Tris(oxalato)chromium(III) Complex Ion in Solutions of the Salts $M_3[Cr(ox)_3]$ in Diethyl-(R,R)-(+)-tartrate and in Ethyl-(S)-(+)-lactate at 30 °C as a Function of the Cation, M^+, and the Free-Energy of the Discrimination between the Enantiomers in the Chiral Environment ($\delta\Delta G$, kJ mol^{-1}).

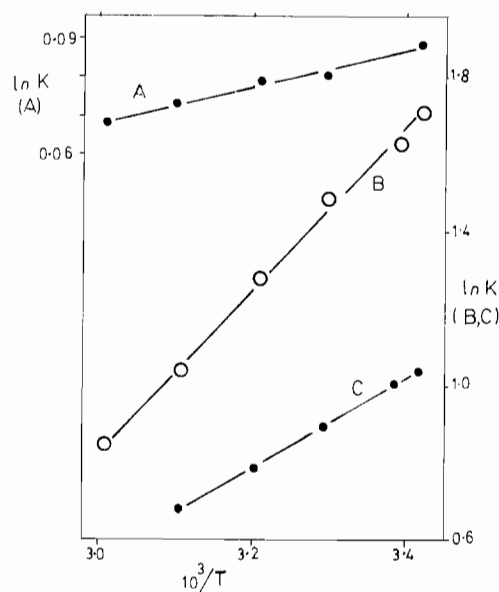| Cation	Diethyl-(R,R)-(+)-tartrate		Ethyl-(S)-(+)-lactate	
	Λ c.e. (%)	$-\delta\Delta G$	Δ e.c. (%)	$-\delta\Delta G$
Li^+	a		10.7	0.54
Na^+	34.6	1.82	12.3	0.62
K^+	60.8	3.55	25.9	1.34
Rb^+	66.0	3.99	26.5	1.37
Cs^+	50.0	2.77	29.3	1.52
NH_4^+	65.5	3.95	a	
$EtNH_3^+$	47.6	2.61	25.1	1.29
Et_3NH^+	7.4	0.37	11.9	0.60
Et_4N^+	3.4	0.17	2.4	0.12
$n\text{-}Bu_4N^+$	6.1	0.31	3.4	0.17

[a]Insufficiently soluble.

Fig. 1. The relationship between the reciprocal absolute temperature (1/T) and the logarithm of the enantiomeric equilibrium constant, $K = [\Lambda]/[\Delta]$, for solutions in diethyl-(R,R)-(+)-tartrate of, (A) $[Ni(phen)_3]Cl_2$, (B) $(NH_4)_3[Cr(ox)_3]$ and (C) $K_3[Cr(ox)_3]$ with 0.2 mole fraction of water in the ester solvent.

dilution of the equilibrated ester solution with ice water, and an immediately subsequent measurement gives the molecular CD due to the enantiomeric excess alone.

TABLE II. The Enantiomer Equilibrium Ratio, $[\Lambda]/[\Delta]$, of Tris-chelate Metal Complexes in Diethyl-(R,R)-(+)-tartrate, or in Mixtures with Water Containing a Mole Fraction, n, of the Diester, at a Temperature, T, and the Differential Enthalpy, $\delta\Delta H$ (kJ mol^{-1}) and Entropy, $\delta\Delta S$ (J K^{-1} mol^{-1}), of the Enantiomers Relative to the Corresponding Racemate, with a Unit Enantiomer Ratio.

Complex	n	T °C	$[\Lambda]/[\Delta]$	$-\delta\Delta H$	$-\delta\Delta S$
$[Co(en)_3]Cl_3$[a]	1.0	25	4.2	14	34
$(NH_4)_3[Cr(ox)_3]$	1.0	30	4.8	18	47
$K_3[Cr(ox)_3]$	0.9	30	3.5	12	30
	0.8	30	2.5	10	26
$[Ni(phen)_3]Cl_2$	1.0	25	1.09	0.5	0.9
$[Cr(pd)_3]$	1.0	20	1.2		

[a]From ref. [16].
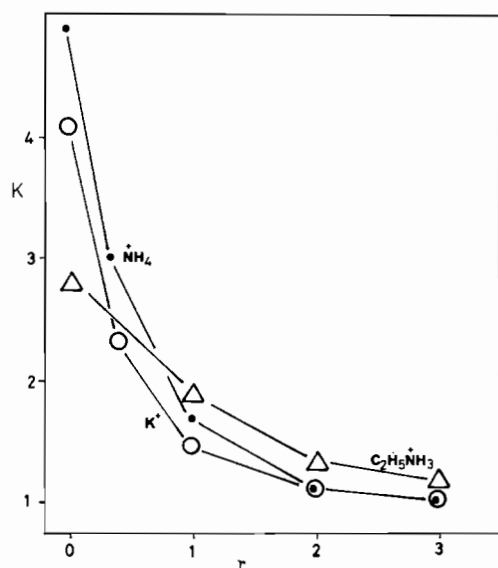

Fig. 2. The relationship between the enantiomeric equilibrium constant, $K = [\Lambda]/[\Delta]$, of the salts, $M_3[Cr(ox)_3]$, in diethyl-(R,R)-(+)-tartrate at 30 °C and the molar ratio, r, of 18-crown-6 to the salt, $M_3[Cr(ox)_3]$, for $M^+ = NH_4^+$, K^+, and $EtNH_3^+$.
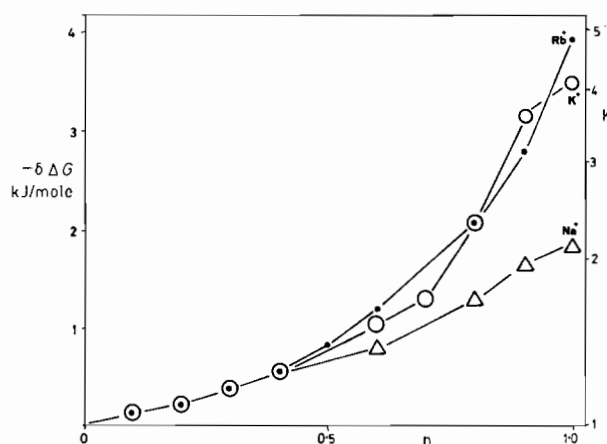

Fig. 3. The relationship between the enantiomeric equilibrium constant, $K = [\Lambda]/[\Delta]$, or the free energy of the discrimination between the enantiomers, $\delta\Delta G = -RT\ln K$, for the salts, $M_3[Cr(ox)_3]$ in mixtures of diethyl-(R,R)-(+)-tartrate, with the mole fraction, n, and water at 30 °C, for $M^+ = Na^+$, K^+, and Rb^+.

At a given wavelength, the ratio of the CD thus measured to that of a single enantiomer of $[Cr(ox)_3]^{3-}$ in aqueous solution gives the fractional enantiomeric excess (e.e.), and thence the enantiomeric equilibrium constant from the relation, $K = (1 + e.e.)/(1 - e.e.)$. The free-energies of the discrimination between the enantiomers of $[Cr(ox)_3]^{3-}$ in the chiral solvents (1) and (2) at 30 °C, recorded with the percentage enantiomeric excess in Table I, were obtained from the relationship, $\delta\Delta G = -RT\ln K$.

Similar CD measurements were carried out on solutions of $M_3[Cr(ox)_3]$ in the chiral solvents (1) and (2) equilibrated at a series of temperatures in the range 19 to 59 °C, followed by a dilution with ice water. The free energies of the enantiomeric discrimination obtained are found to be inversely proportional to the temperature of the equilibration (Fig. 1) and the relation, $\delta\Delta G = \delta\Delta H - T\delta\Delta S$, gives the values recorded of the differential enantiomeric enthalpy ($\delta\Delta H$) and entropy ($\delta\Delta S$) of association with the chiral solvent molecules (Table II).

As the enantiomeric excess of the $M_3[Cr(ox)_3]$ salts in the chiral solvents (1) and (2) at equilibrium proved to be cation-sensitive (Table I) the effects of the incremental addition of 18-crown-6 (Fig. 2) and of water (Fig. 3) to the ester solutions was investigated. The 18-crown-6 molecule forms an achiral 1:1 complex with most of the cations studied [15], and the discrimination by the chiral solvent between the enantiomers of the complex anion goes to zero when each cation of the $M_3[Cr(ox)_3]$ salt is

complexed by the crown ether (Fig. 2). Similarly, a small mole fraction of water in the mixed aqueous-chiral ester solvent substantially reduces both the enantiomeric discrimination and the sensitivity of the discrimination to the particular cation of the M_3-$[Cr(ox)_3]$ salt (Fig. 3).

The enantiomeric discrimination of diethyl-(R,R)-(+)-tartrate as a solvent is large, not only for the complex anion of the salts, $M_3[Cr(ox)_3]$, but also for the complex cation, tris(ethylenediamine)cobalt(III). The solubility of Λ-(+)-$[Co(en)_3]Cl_3$ in the diester (1) is larger than that of the Δ-(−)-isomer by a factor of 3.5 at 35 °C and of 4.2 at 25 °C [16]. The ratios correspond to the enantiomeric equilibrium constants in the solvent (1), and they provide [16] the differential enthalpy and entropy of the discrimination recorded (Table II).

The discrimination of the diester (1) between the enantiomers of tris-chelate complex cations devoid of hydrogen-bonding sites is small, however. The racemic 1,10-phenanthroline complex, $[Ni(phen)_3]$-Cl_2, in (−)-2,3-butandiol solution equilibrates at 25 °C to an enantiomeric excess of 3% of the Δ-(−)-isomer [17]. In diethyl-(R,R)-(+)-tartrate solution at 25 °C the enantiomeric excess of equilibrated $[Ni(phen)_3]Cl_2$ is comparable in magnitude (4%), although opposed in sign, the Λ-(+)-isomer having the major concentration (Table II).

The general discrimination of the diester solvent (1) in favour of the Λ-isomer of tris-chelate coordination compounds extends to the neutral pentane-2,4-dionato complexes, $[M^{(III)}(pd)_3]$. The extraction of solutions of the racemic complexes, $[M^{(III)}(pd)_3]$, in the chiral diester (1) with an achiral immiscible solvent, cyclohexane or a toluene-cyclohexane mixture, effects a partial resolution [18]. The achiral solvent layer is enriched with the Δ-isomer, leaving an excess of the Λ-isomer in the chiral diester layer. After some ten successive extractions, no optical activity is detectable in the achiral solvent layer, indicating that enantiomeric equilibrium is established in the chiral diester layer [18]. The dilution of the diester layer with water, in order to quench the induced intermolecular CD, leaves an inherent molecular CD corresponding to an enantiomeric excess of some 10% of the Λ-isomer of the $[M^{(III)}(pd)_3]$ complex (Table II).

Temperature-Variation of the Induced Intermolecular Circular Dichroism

The intermolecular CD induced in a racemate by a chiral solvent arises from the differential optical activity of the diastereomeric associations formed by the enantiomers of the racemates with a single environmental chiral species. An indication of the stoichiometry of the dominant intermolecular association is provided by the concentration-dependence of the induced CD, and of the relative enthalpy of
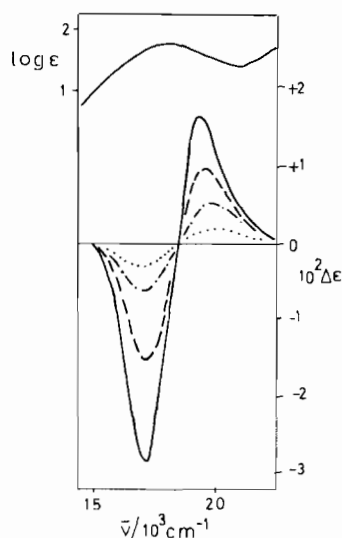

Fig. 4. The absorption spectrum (upper curve) and the intermolecular induced CD (lower curves) of racemic $[Cr(pd)_3]$ (0.01 M) in an ethanolic solution of Δ-(−)-K$[As(cat)_3]$ (0.215 M) at the absolute temperature, 193 (———), 218 (-----), 243 (−·−·−), and 298 K (·······).

that association by the temperature-variation of the induced intermolecular CD.

Racemic $[Cr(pd)_3]$ in an ethanol solution of a salt of Δ-(−)-tris(catechyl)arsenate(V), which is transparent over the visible wavelength region, gives a pair of oppositely-signed induced CD bands in the region of the lowest-energy d–d band of $[Cr(pd)_3]$ at 570 nm (Fig. 4). The induced CD, which appears immediately on mixing the ethanol solutions of the two solutes and is quenched by dilution, is distinguished from the inherent molecular CD of an enantiomer of $[Cr(pd)_3]$ by the peak-height ratio of the lower to the higher-frequency CD band, 1.67 for the induced CD and 0.334 for the molecular CD (Figs. 4 and 5). The CD induced in the region of the 570 nm absorption of racemic $[Cr(pd)_3]$ at 0.01 M is linearly proportional to the concentration of the salt, Δ-(−)-K$[As(cat)_3]$, added, over a concentration range from 0.215 M to 0.860 M of the latter, suggesting that the optically-dominant intermolecular association contains, on the average, one more Δ-(−)-$[As(cat)_3]^-$ ion than the optically less-active association.

On cooling an ethanol solution of racemic $[Cr(pd)_3]$ and Δ-(−)-K$[As(cat)_3]$ from 298 to 193 °K, the peak heights of both the induced CD bands increase by an order of magnitude (Fig. 4). These and additional measurements of the induced CD ($\Delta\epsilon_{ind}$) at 243 and 218 K provide the basis of the linear relationship observed between (1/T) and ($\ln\Delta\epsilon_{ind}$) (Fig. 6). The slope of the relationship corresponds to a differential enthalpy of 10.7 kJ
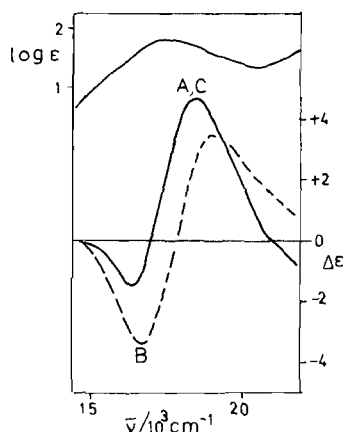
Fig. 5. The absorption spectrum (upper curve) and the CD spectrum (A) of Λ-(+)-[Cr(pd)₃]. The CD spectrum (B) is that given by racemic [Cr(pd)₃] (0.01 *M*) in an ethanolic solution of Δ-(−)-[As(cat)₃] (0.860 *M*) after standing for 7 days at 20 °C. The CD spectrum (C) is that of the [Cr-(pd)₃] recovered from the aged solution by dilution with water followed by a chloroform extraction. The Δε scale refers to the CD spectrum (A), and the values of the CD for spectra (B) and (C) are smaller by the factor of 1/400.
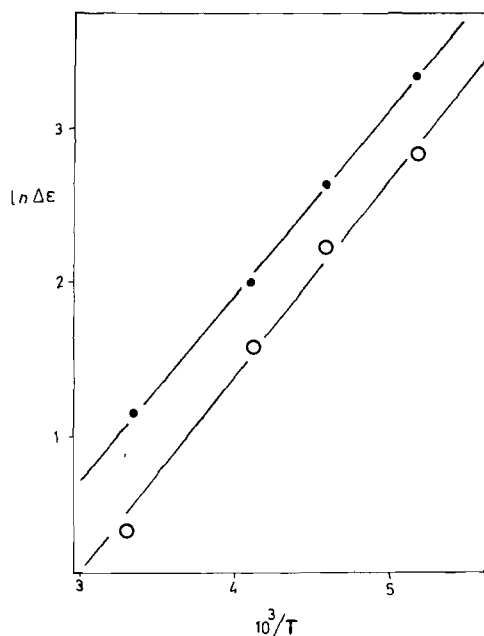

Fig. 6. The relationship between the reciprocal absolute temperature (1/T) and the logarithm of the induced intermolecular CD of racemic [Cr(pd)₃] in an ethanol solution of Δ-(−)-[As(cat)₃] (0.215 *M*). The upper relation refers to the negative lower-frequency CD band of Fig. 4, and the lower relation to the positive higher-frequency CD band.

mol⁻¹ between the optically-active intermolecular associations of Δ-(−)-K[As(cat)₃] with the enantiomers of [Cr(pd)₃].

An indication that Λ-(+)-[Cr(pd)₃] associates more intimately with Δ-(−)-[As(cat)₃]⁻ in ethanol solution than its enantiomer is provided by two observations. Firstly, the induced CD of racemic [Cr(pd)₃] in ethanolic solutions of Δ-(−)-K[As-cat)₃] at 20 °C slowly changes in form towards that of the molecular CD of Λ-(+)-[Cr(pd)₃] and, after one week, the peak height of the higher-frequency induced CD absorption is the larger (Fig. 5). The addition of water to the aged solution and an extraction of the mixture with chloroform quenches the induced optical activity, and the chloroform solution gives a CD spectrum corresponding to a 0.25% enantiomeric excess of Λ-(+)-[Cr(pd)₃] (Fig. 5). The enantiomeric excess corresponds to an anti-racemisation of [Cr(pd)₃] with Δ-(−)-K[As(cat)₃] in ethanol at 20 °C with a rate constant of the order of 10⁻⁹ s⁻¹, compared to the extrapolated rate constant of 1.6 × 10⁻¹¹ s⁻¹ for the racemisation of [Cr(pd)₃] in chlorobenzene solution at 25 °C [13]. The second observation refers to the direct measurement of the induced intermolecular CD, superimposed on the intrinsic molecular CD, of Λ-(+)- and Δ-(−)-[Cr(pd)₃] with Δ-(−)-K[As(cat)₃] in ethanol solution. The induced CD, with the form observed for the racemate (Fig. 4), was more substantial for Λ-(+)-[Cr(pd)₃] than for the Λ-(−)-isomer. The optical purity of each of the [Cr(pd)₃] isomers, obtained by an asymmetric synthesis [18],

was limited (25%) and an estimate of the differential free energy and entropy of the enantiomeric discrimination, feasible with the corresponding optically-pure isomers, was precluded.

Discussion

The intermolecular association of chiral molecules generally favours the racemic enantiomer-pair or heterochiral diastereomer pair, (+)-A(−)-B, over the corresponding homochiral pair, (+)-A(+)-B, whether enantiomeric or diastereomeric, in both the solid and the fluid phases. The majority of racemates crystallize as such, and only some 250 cases are known of spontaneous optical resolution by the crystallization of a racemate either from the melt or from solution [19]. The free energy of formation of racemic crystals from an equimolecular mixture of the crystals of the corresponding enantiomers at the temperature of fusion is found to lie in a range from 0 to −8 kJ mol⁻¹, from a thermochemical study of some 50 chiral organic substances [20], and similar free energy differences for coordination compounds are given by the relative solubilities of the enantiomers and the corresponding racemate. At 18 °C Δ-(−)-[Cr(pd)₃] is nine times more soluble in hexane than the corresponding racemate, repre-

senting a free energy preference of 7 kJ mol^{-1} in favour of the racemic crystal lattice.

In the fluid phase, the free energy of the chiral discrimination is usually smaller. A 0.12 M aqueous solution of Δ-$(-)$-[Ni(phen)$_3$]Cl$_2$ extracts, with a preference of 75 J mol^{-1}, the like-configuration isomer, Δ-$(-)$-[Cr(pd)$_3$] from a carbon tetrachloride solution of the corresponding racemate [21]. More generally the discrimination in solution is hetero-chiral, although comparably small. In dioxan-water mixtures at ambient temperature, racemic [Cr-(ox)$_3$]$^{3-}$ and the corresponding tris-malonate, [Cr-(mal)$_3$]$^{3-}$, antiracemise to an enantiomeric excess of some 4% of the Δ-isomer with a co-solute of the Λ-enantiomer of one of some 20 different cobalt-(III) complexes, cis[Co(diamine)$_2$XY]$^{n+}$,· where X and Y are either unidentate ligands or the coordi-nating groups of a chelate ligand [9].

A basis for the general heterochiral trend of enantiomeric and diastereomeric discrimination in the fluid phase is provided by a comparison of the crystal structure of an enantiomer with that of the corresponding racemate. X-ray diffraction studies of aqueous solutions of transition metal [22] and of lanthanide ions [23] show that the local solvent order around the metal ion is analogous to that of the hydrated metal ion in the crystal. Similarly the nearest-neighbour packing in an enantiomeric and a racemic crystal afford a guide to the correspond-ing statistically-preferred intermolecular associations in the fluid phase.

The crystal structures of racemic [Cr(pd)$_3$] [24] and of Δ-$(-)$-[Cr(pd)$_3$] [25] show that the inter-molecular packing of homochiral molecules with a three-bladed propeller shape, that of the D$_3$ tris-chelate metal complexes, is stereochemically inefficient, relative to the corresponding hetero-chiral packing of the racemate. The tris-chelate com-plexes stack economically in homochiral columns with the principal C$_3$ rotation axis of each molecule parallel, or at a small angle to the column axis. Along the direction of a molecular C$_2$ rotation axis, nearest neighbour molecules pack efficiently, with inter-leaving chelate rings and with the principal C$_3$ axes of the molecules maintained parallel to one another, only if the two molecules have antinodal configura-tions, one being a Λ-isomer and the other a Δ-isomer. Thus racemic [Cr(pd)$_3$] and analogous [M(pd)$_3$] complexes, have crystal lattices made up of pairs of homochiral columns, with the molecules of one column antipodal to those of the adjacent parallel column.

Neighbouring tris-chelate molecules with the same chirality pack economically along the direction of a common C$_2$ rotational axis, with interleaving chelate rings, only if the two molecules are mutually rotated around the line of centres so that the dihedral angle between the two principal (C$_3$) axes has the tetra-
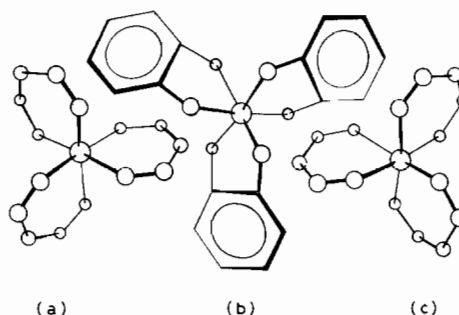

(a)   (b)   (c)

Fig. 7. A projection on the plane perpendicular to the principal C$_3$ rotation axis of, (a) Λ-$(+)$-[Cr(pd)$_3$], (b) Δ-$(-)$-[As(cat)$_3$], and (c) Δ-$(-)$-[Cr(pd)$_3$], illustrating the effi-cient interleaving of the chelate rings along a direction includ-ing a C$_2$ rotation axis of each molecule for a heterochiral pair (a + b), and the steric hindrance to the interleaving, without a mutual rotation, for the homochiral pair (b + c). For clarity, the exocyclic methyl groups of the [Cr(pd)$_3$] enantiomers are omitted.

hedral value, or its supplement. In the crystal of Δ-$(-)$-[Cr(pd)$_3$], three of the four independent angular relationships between the individual molec-ular C$_3$ axes in the unit cell are close to the tetra-hedral value, and the fourth is a near-parallel relation [25].

The relationships are stereochemically imposed, and apply equally to diastereomeric pairs of D$_3$ tris-chelate molecules. In an ethanolic solution of racemic [Cr(pd)$_3$] and Δ-$(-)$-[As(cat)$_3$]$^-$, the stereo-chemically-favoured association of Δ-$(-)$-[Cr(pd)$_3$] with the anion involves intermolecular contact from above or below with the C$_3$ axes of the two species collinear, whereas the more probable association of Λ-$(+)$-[Cr(pd)$_3$] with the anion entails the inter-leaving of the chelate rings along a direction which includes a C$_2$ rotation axis of each species (Fig. 7). As each of the solute species has three C$_2$ axes, but a single C$_3$ axis, the heterochiral association, Λ-$(+)$-[Cr(pd)$_3$] Δ-$(-)$-[As(cat)$_3$]$^-$ is statistically preferred.

Calculations of the intermolecular dispersion energy between two D$_3$ tris-chelate molecules show that the heterochiral pair (Δ,Λ) is generally stabilised relative to the homochiral pair (Δ,Δ), for a given mutual orientation of the two sets of symmetry axes (3C$_2$ and C$_3$), and for a given intermolecular separa-tion beyond the closest approach of intermolecular contact [26]. The point of intersection of the sym-metry axes in two D$_3$ molecules has a separation of closest approach, along a direction including the C$_3$ axes of the two molecules, or a direction contain-ing a C$_2$ axis of each structure, different for the homochiral (Δ,Δ) and heterochiral (Δ,Λ) cases. The smaller separation at contact affords the more negative dispersion energy and, dependent upon the mutual orientation of the two molecules in contact
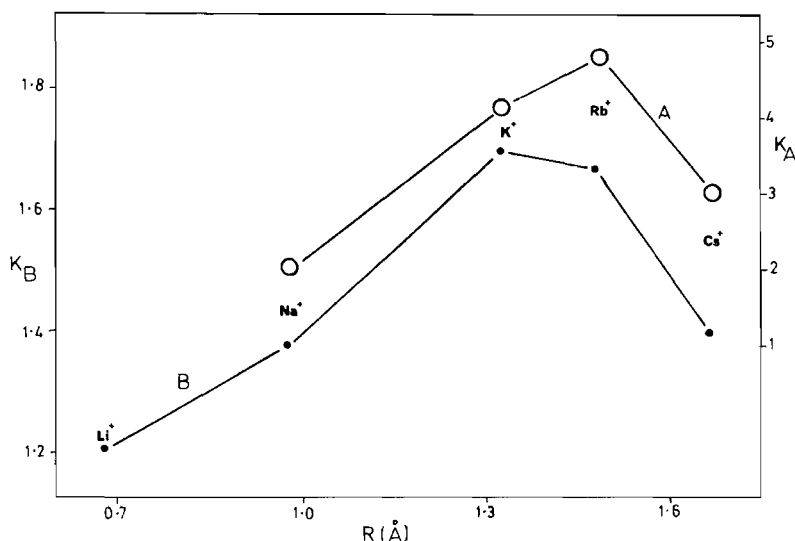
Fig. 8. The relationship between the radius of the alkali metal cation (R) of the salts, $M_3[Cr(ox)_3]$ and the enantiomer equilibrium constant, $K_A = [\Lambda]/[\Delta]$, in diethyl-(R,R)-(+)-tartrate, and $K_B = [\Delta]/[\Lambda]$, in ethyl-(S)-(+)-lactate containing a 0.1 mole fraction of water.

either the homochiral or heterochiral pair has the lower intermolecular energy. The chiral discrimination energies due to the dispersion forces at contact distances are of the order of 1 kJ mol^{-1}, but there is a rapid decrease with increasing intermolecular separation, proportional to R^{-8} [26].

While the molecules of racemic [Cr(pd)$_3$] and Δ-(–)-[As(cat)$_3$]$^-$ are probably hydrogen-bonded to the achiral ethanol solvent molecules in solution, there are no inter-solute hydrogen bonds to provide a discrimination between the homochiral and heterochiral associations of the anion with the enantiomers of [Cr(pd)$_3$]. All D$_3$ molecules lack a permanent dipole moment. Moreover, an intermolecular dipole-dipole potential cannot give rise to a chiral energy discrimination, which requires a dipole-quadrupole or a higher even-odd multipole potential [27]. Thus the preferred heterochiral association, Λ-(+)-[Cr-(pd)$_3$] Δ-(–)-[As(cat)$_3$]$^-$, in ethanol solution probably owes its differential stabilization to the discrimination in the dispersion energy, mediated by the stereochemical factors favouring the close association of heterochiral D$_3$ species (Fig. 7).

The sign of the discrimination between the enantiomers of the tris-chelate metal complexes studied by chiral solvent molecules of the esters (1) and (2) is dependent upon the (R)- or the (S)-configuration of the asymmetric centre or centres in the ester. Diethyl-(R,R)-(+)-tartrate (1) gives rise to an enantiomeric excess of the Λ-isomer of the tris-chelate complex, whether the discrimination is large, as in the case of (NH$_4$)$_3$[Cr(ox)$_3$], or small, as for [Ni(phen)$_3$]Cl$_2$, while ethyl-(S)-(+)-lactate (2) produces an enantiomeric excess of the Δ-isomer

(Tables I and II). The differential entropy values obtained indicate that the preferred solute enantiomer orders the chiral solvent molecules more effectively than its antipode, forming the larger solute-solvent intermolecular associations (Table II).

Other evidence points to the same conclusion. Solutions of Λ-(+)-[Co(en)$_3$]Cl$_3$ in diethyl-(R,R)-(+)-tartrate are more viscous than the corresponding solutions of the Δ-(–)-isomer [16], and conductivity measurements indicate that the ionic mobility of Λ-(+)-[Co(en)$_3$]$^{3+}$ in aqueous solutions of sodium (R,R)-(+)-tartrate is smaller than that of the Δ-(–)-isomer [28]. The ion association constants of both (R,R)-(+)-tartrate and antimonyl-(R,R)-(+)-tartrate with Λ-(+)-[Co(en)$_3$]$^{3+}$ are larger than the corresponding constants for the Δ-(–)-isomer of the complex cation [29].

Determinations of the crystal structure, by X-ray diffraction, of the less-soluble isomer, Λ-(+)-[Co(en)$_3$]·[(R,R)-(+)-tartrate]·Br·5H$_2$O [30] and of the corresponding chloride [31] show that three N–H groups nearly parallel to the C$_3$ rotation axis of the complex cation hydrogen-bond to the two hydroxyl and one carbonyl group of the tartrate ion, while the second carboxyl group of the anion acts as a steric discriminator, economically accommodated by the Λ-(+)-cation but not by the Δ-(–)-isomer [32]. An analogous hydrogen-bonding association between diethyl-(R,R)-(+)-tartrate and [Co(en)$_3$]Cl$_3$ as a solute probably provides the observed discrimination [16] between the Λ-(+)- and Δ-(–)-isomers of the complex cation (Table II).

A notable feature of the discrimination of the chiral solvents (1) and (2) between the enantiomers

of the complex anion, $[Cr(ox)_3]^{3-}$, is the sensitivity of the magnitude of the enantiomeric excess at equilibrium to the particular cation of the salt solute, $M_3[Cr(ox)_3]$. The relationship between the radius of the cation and the constant of the equilibrium between the enantiomers of the complex anion in the salts, $M_3[Cr(ox)_3]$, at 30 °C (Fig. 8) has a form similar to the corresponding relation between the cation radius and the stability constant for complex formation with crown ethers [15, 33, 34] or cryptates [35]. The addition of 18-crown-6 to a solution of a $M_3[Cr(ox)_3]$ salt in the chiral diester (1) suppresses the enantiomeric discrimination, presumably by competing with the chiral solvent molecules in the formation of a coordination complex with each cation, M^+. It is inferred that the chiral cationic complex, $[M(solvent)_n]^+$, provides the effective discrimination between the enantiomers of the $[Cr(ox)_3]^{3-}$ anion. The discrimination is the larger for the more stable chiral cationic complexes, $[M(solvent)_n]^+$, and the stability is a function of the cation radius and of the particular chiral solvent. In the case of ethyl-(S)-(+)-lactate the discrimination is an optimum at K^+ and Cs^+ for a mole fraction of 0.9 and 1.0, respectively, whereas the optimum obtains with Rb^+ as the cation in the salt, $M_3[Cr(ox)_3]$, when diethyl-(R,R)-(+)-tartrate is employed as the solvent (Table I, Fig. 8).

As a ligand, (S)-(+)-lactic acid, like (S)-(+)-alanine or (S)-(+)-1,2-propylenediamine, forms a chelate ring with a preferred δ-conformation, and a six-coordinate tris-chelate metal complex with a preferred Λ-configuration. The larger alkali metal cations, M^+, in the ester solvents (1) and (2), are expected to form chiral complexes, $[M(solvent)_n]^+$, which on a time and a molecule average have a statistical majority of Λ-isomer forms in the case of ethyl-(S)-(+)-lactate for n = 3 if tris-chelate, or n = 4 with two chelate and two unidentate solvent molecules in the complex cation. Similarly a dominance of the Δ-isomer forms of the solvated cation complex is expected for the salts, $M_3[Cr(ox)_3]$, in diethyl-(R,R)-(+)-tartrate solution with a carboxyl group and the α-hydroxy group of the diester chelating the cation.

The formation of such chiral chelate complexes with the solvent molecules by the cations of the salts, $M_3[Cr(ox)_3]$, is consistent with the sign of the observed discrimination between the enantiomers of the complex anion on the basis that heterochiral pair-associations of tris-chelate or cis-bis-chelate molecules (Δ,Λ) are generally preferred on stereochemical and dispersion-energy grounds. The formation of cis-bis-chelate complex cations by ethyl-(S)-(+)-lactate, with the unidentate solvent molecules coordinated to M^+ through the carboxyl group, leaves the α-hydroxy group free for hydrogen-bonding to the $[Cr(ox)_3]^{3-}$ complex anion, a function available for each solvent ligand in the tris-chelate

cation complex in diethyl-(R,R)-(+)-tartrate solution, where the magnitude of the discrimination between the enantiomers of the $[Cr(ox)_3]^{3-}$ complex anion is the larger (Table I). The effects of the addition of 18-crown-6 to the $M_3[Cr(ox)_3]$ solutions indicate that direct hydrogen-bonding of the chiral solvent molecules to the complex anion produces little discrimination (Fig. 8).

The hydrogen-bonding of the solvent hydroxy-groups to the coordinated oxygen atoms of the $[Cr(pd)_3]$ complex is expected to be largely responsible for the enantiomeric discrimination observed, however. An analogous, but weaker, hydrogen-bonding to the π-systems of the aromatic ligands in the $[Ni(phen)_3]Cl_2$ solutions may contribute to the small discrimination found in this case, although the differential intermolecular dipole-induced dipole and dispersion energies are likely to be of comparable or greater significance (Table II).

Experimental

Materials

The salts, $K_3[Cr(ox)_3] \cdot 3H_2O$, $Na_3[Cr(ox)_3] \cdot 3H_2O$ and $(NH_4)_3[Cr(ox)_3] \cdot 2H_2O$, were prepared by the method of Bunton et al. [36]. The ion-exchange of these salts with Dowex 50W-X8 in the appropriate cation form gave, $Li_3[Cr(ox)_3] \cdot 3H_2O$, $Rb_3[Cr(ox)_3] \cdot 2.5H_2O$, $Cs_3[Cr(ox)_3] \cdot 2.5H_2O$, $(EtNH_3)_3[Cr(ox)_3] \cdot 0.5H_2O$, $(Et_3NH)_3[Cr(ox)_3] \cdot H_2O$, $(Et_4N)_3[Cr(ox)_3] \cdot 1.5H_2O$, and $(n-Bu_4N)_3[Cr(ox)_3] \cdot H_2O$. Each salt gave a satisfactory analysis corresponding to the composition indicated. The salt, $K_3[Cr(ox)_3] \cdot 3H_2O$ was optically-resolved by the method of Vaughn and coworkers [37] and an aqueous solution of the Λ-(+)-isomer gave the CD values, $\Delta\epsilon = -0.70$, $+3.10$, and -0.70, at 630, 552 and 415 nm, respectively.

The salt, $[Ni(phen)_3]Cl_2$, was prepared and resolved into its enantiomers by the method of Kauffman and Takahashi [38], and Δ-(−)-K$[As(cat)_3] \cdot 1.5H_2O$ was synthesised by the procedure of Mann and Watson [39]. Racemic $[Cr(pd)_3]$, 18-crown-6, ethyl-(S)-(+)-lactate ($[\alpha]_D^{20} - 12°$, neat), and diethyl-(R,R)-(+)-tartrate ($[\alpha]_D^{20} + 8.3°$, neat), were commercial materials (Aldrich).

Measurements

Weighed quantities of the finely-ground salts, $M_3[Cr(ox)_3] \cdot xH_2O$, were dissolved by stirring over 3 dys in a known volume of the freshly-distilled ester (1) or (2), or an ester-water mixture with a pre-determined mole-fraction composition. An aliquot of the clear solution was diluted twofold with ice water, and the absorption spectrum of the mixture over the visible wavelength region was measured in order to check the solute concentration and to

detect subsequent chemical decomposition by similar absorption measurements after equilibration. The original solution was maintained in a thermostat for 12–20 hrs, after which the absorption and CD spectrum of another aliquot diluted twofold with ice water was measured. The fractional enantiomeric excess was estimated from the ratio of the dissymmetry factor, $(\Delta\epsilon/\epsilon)$, for the diluted equilibrated solution to the corresponding factor for the Λ-(+)-[Cr(ox)$_3$] isomer at the wavelengths of the CD maxima. A similar procedure was adopted for the estimation of the enantiomeric equilibrium of [Ni-(phen)$_3$]Cl$_2$ in diethyl-(R,R)-(+)-tartrate at a series of regulated temperatures, except that the solutions were left to equilibrate over 4–7 days.

Absorption spectra were measured with a Cary 17 spectrophotometer and the corresponding CD spectra were determined with a Jouan CD185 and a Jasco J40-CS instrument. The measurements of the CD induced in the visible absorption bands of racemic [Cr(pd)$_3$] by Δ-(−)-[As(cat)$_3$]⁻ in ethanol solution at regulated low temperatures were carried out with a Jouan cryostat.

Acknowledgements

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