Induced Equilibrium Shifts in Labile Racemates. The Nature of the Discriminatory Interactions in the Pfeiffer Effect

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Abstract: A simple thermodynamic model for the shift of an initially racemic equilibrium on adding another chiral species (the solvent being achiral) is proposed as leading to the Pfeiffer activity of labile racemates of metal complexes. The empirical discrimination energy thus defined (which is a characteristic of a given Pfeiffer system, and independent of the physical conditions of the experiment) is postulated to arise either from solvent packing effects, or from discriminations in the intermolecular forces between A and B. The nature of possible discriminating interactions is discussed, and calculations for model complex systems suggest why the effect is observed only for a limited class of metal complexes.

Introduction

If a chiral ion B is added to a racemate (containing equal concentrations of enantiomers A', A") of a labile metal complex A, the resulting solution has a circular dichroism spectrum containing bands that are directly attributable to one of the enantiomers of A. This is known as the Pfeiffer effect.[1-4] As the initial racemate is optically inactive, it has been postulated that one of the possible mechanisms of the effect is the shift of an initially racemic equilibrium to a new equilibrium in which one of the enantiomers is produced in excess because of the different A'-B, A"-B interactions.[2-5] Such discriminating interactions may be either due to diastereoisomer formation, or to differences in long-range interactions (where long range is used in the sense of noncontact interactions).

If the circular dichroism (CD) or optical rotation (OR) at a particular wavelength λ is designated by the general symbol R_λ, the Pfeiffer CD or OR may be defined conveniently as

$$P_R(\lambda) = R_\lambda(\text{obsd}) - R_\lambda(B) \qquad (1)$$

where $R_\lambda(\text{obsd})$ is the measured property of the final solution, and $R_\lambda(B)$ the value of R_λ of a pure solution of B of the same concentration as that of B in the final solution.

The equilibrium shift mechanism has been convincingly demonstrated as leading to the Pfeiffer effect in a range of systems. Data are available for measurement of the equilibrium shifts of a number of labile complexes as functions of the nature of B,[2,3] the concentrations of A and B,[1,3] and the temperature. There is, however, no simple model predicting the interrelationship of these variables and thus no simple quantity that summarizes the Pfeiffer activity of a particular A-B system. An attempt at a simple relationship based on activity coefficients[4] is unsatisfactory as these are still concentration dependent. In the present paper, a simple model is proposed that leads to the definition of a discrimination energy that is independent of the concentrations of A and B, and of temperature, and depends only on the nature of the A-B system. The interactions capable of leading to this experimentally observed discrimination are discussed, and calculated for some model metal complexes. The results suggest that one source of the discrimination is an electric dispersion interaction arising from third-order perturbation theory depending on the separation of the two species as R^{-9}. The theory further suggests that the effect should only be significant for chelate systems with chirally disposed unsaturated ligands—a result that agrees well with experimental observations.

The importance of the Pfeiffer effect has been discussed in a number of recent publications, and may be summarized as follows: (1) the partial resolution of otherwise unresolvable complexes;[6] (2) the measurement of the CD spectra of the excess enantiomer without the necessity of effecting a complete resolution;[7,8] (3) the prediction of absolute configuration of labile metal complexes;[8] (4) the measurement of the discrimination energies in chiral systems. These uses of the Pfeiffer effect will be briefly discussed in the context of the proposed model.

The Equilibrium Shift Model

The free energy of a solution containing a total of X mol of A, X_B mol of B, and X', X'' mol of A', A", respectively (where $X = X' + X''$), will be a function of all of these concentrations. For a given system, X and X_B will be a constant, so that equilibrium is established when X'. X'' adjust so as to minimize the overall free energy. This equilibrium condition may be written

$$\partial G / \partial X' = \partial G / \partial X'' = 0$$

where G is the free energy of the solution. If G is written as a sum of contributions $\Sigma_i G_i$, it follows that we need only extract those contributions G_i that depend on X' or X'', as any others will vanish on differentiation in determining the equilibrium conditions. Two such chiral (chiral referring in this case to the explicit dependence on the relative concentration of the two enantiomers) contributions may be distinguished.

The Racemization Entropy. This contribution to the free energy results directly from the distinguishability of A', A", and is essentially an entropy of mixing.[9] It favors the disordered racemate, and effectively opposes any resolution. It has the form

$$S_R = -RX(X' \ln X' + X'' \ln X'')$$

so that the racemization free energy contribution may be written

$$G_R = -TS_R$$

It is independent of any interactions of A', A" with the environment.

The Discrimination Free Energy. This is the component G_D of the free energy which arises directly from the discriminating interactions. In relating this to the discrimination in the intermolecular forces, we employ a vastly simplified statistical-thermodynamic model, as we are ultimately only interested in the general thermodynamic behavior of Pfeiffer systems and in a rough estimate of the discrimination energy. It would be unrealistic to expect accurate estimates of discriminations in the intermolecular forces of such complex systems. The following assumptions are made in establishing our simplified
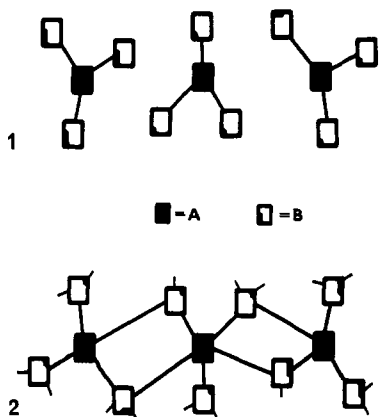
Figure 1. Associated (1) and dissociated (2) solution models. Each solid line connects a discriminating A-B pair.
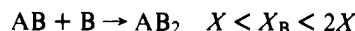
solution model: (1) The free energy G_D contributes additively to the overall free energy of the solution. (2) G_D is assumed to be purely enthalpic, equal to the total interaction energy of the discriminating intermolecular forces. This assumption is consistent with the results of the simple statistical thermodynamic model[10] of A-B mixtures with weak interactions. (3) Any attractive forces leading to A-B nearest neighbors (hereafter referred to as A-B pairs) such as hydrogen bonding are assumed to be independent of the chirality of A and B, and thus do not contribute to the free energy component G_D. (4) The discriminating interaction is assumed to be sufficiently short range so that only nearest-neighbor A-B interactions can contribute to G_D. (5) The discriminating interaction is approximated at some averaged A-B separation, and has a value V_{AB}' per mole of A'-B pairs, and similarly for A''-B.

Perhaps the most contentious yet important of the assumptions is (3), for it excludes those systems in which A' and A'' actually have different association constants with B. Such systems have been studied by Ogino and Saito,[19] and result in an overall CD which is directly a function of the relative association constants. As mentioned in their paper, this is not strictly a Pfeiffer effect, as such rotations do not require any equilibrium shift at all. In such cases, definite diastereoisomers are formed through strong contact interactions, and thus they are not strictly within the scope of this work. It is assumed in this paper that the forces holding A and B relatively close together are not specific; i.e., there is no single relative orientation of A'B and A''B, but rather some degree of disorder in the relative orientations throughout the solution. For example, a single hydrogen bond may hold A and B close together without giving a definite diastereoisomer with a unique A-B orientation, and is thus independent of the chirality of A and B. Recognition of the difference between chiral contact interactions (leading to diastereoisomers) and the achiral association (which does not lead to preferred relative orientations) is vital to the following discussion, where association is used in the latter context. In our model, then, the discriminating interactions are assumed to be quite different from those holding A and B together.
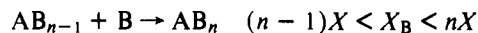
Estimation of the discrimination free energy then proceeds through estimating the number of A'-B, A''-B pairs in the solution. The latter depends crucially on whether definite aggregates are formed in the solution, or whether the species are essentially dissociated so that a given B can interact with a number of species A. We therefore develop two extreme models of the solution, and determine their respective equilibrium conditions. It will then be possible to experimentally determine which is the better description of Pfeiffer systems.

The Associated Model. Suppose that definite aggregates up to AB_n are formed by stepwise association (the interaction

leading to the association being achiral),

$$A + B \rightarrow AB \quad X_B < X$$

$$AB + B \rightarrow AB_2 \quad X < X_B < 2X$$

$$\cdots\cdots\cdots$$

$$AB_{n-1} + B \rightarrow AB_n \quad (n-1)X < X_B < nX$$

and that only the discriminating interactions within the aggregate are important. Then, for $X_B < nX$, the number of moles of A-B pairs is simply

$$n_{AB} = X_B$$

A' and A'' have equal probabilities of association with B, so that the number of A'-B pairs is

$$n_{AB}' = x'X_B$$

where $x' = X'/X$. It follows that

$$G_D = (x'V_{AB}' + x''V_{AB}'')X_B, \quad X_B < nX$$

n may be determined by finding the concentration $\overline{X}_B = nX$ beyond which G_D remains constant. At this point, the system is effectively saturated in B with respect to the discriminating interaction. No further A-B pairs can be established.

The Dissociated Model. The essential feature of the associated model is that a given B can only lead to a discriminatory interaction with the particular A to which it is associated. In the dissociated model, we shall relax this condition, so that a particular B may be nearest neighbor to a number of A, and vice versa. We can retain the simplicity of an averaged, constant discrimination interaction energy by taking a lattice picture of the solution. We consider intially the solution to be saturated in both A and B (where here saturation refers to the point at which further addition of A or B will not lead to any further increase in G_D), with the respective number of moles $\overline{X}$, $\overline{X}_B$. If the average coordination number of A (i.e., the number of nearest-neighbor B's about a particular A) is $\overline{n}$ in this solution, then the number of moles of A-B pairs will be

$$\overline{n}_{AB} = \overline{n}\overline{X}$$

The number of moles of A-B pairs at lower concentrations may be determined approximately by considering the initial removal of δX mol of A, δX_B mol of B. The former will decrease the number of A-B pairs by $\overline{n}\delta X$; the latter will have the effect of reducing the effective coordination number by the factor $(\overline{X}_B - \delta X_B)/\overline{X}_B$. It follows that for concentrations less than the saturation values, we have approximately

$$n_{AB} = \overline{\alpha}X_B X$$

where

$$\overline{\alpha} = \overline{n}/\overline{X}_B$$

The assumption that V_{AB} is independent of concentration may seem somewhat drastic, but is consistent with the idea that the discriminating interactions are of relatively short range, and that weak, achiral attractive forces between A and B maintain some semblance of the lattice structure at lower concentrations. Thus this model is not dissociated in the strictest sense, but only in that a given B cannot be identified with any particular A. The discrimination free energy now has the form

$$G_D = \overline{\alpha}(x'V_{AB}' + x''V_{AB}'')X_B X$$

where $\overline{\alpha}$ must be determined empirically by finding the saturation concentrations of A and B.

The Equilibrium Conditions. The associated and dissociated pictures of the solution lead to different concentration dependences, and thus may be expected to lead to different equilibrium conditions. This is indeed the case, and the general condition

Table I. Estimated Discrimination Energies

A	B	Slope = $\bar{\alpha}\Delta(B)X_B$
$Ni(phen)_3{}^{2+}$	d-BCS	-1300 J mol^{-1}
$Ni(phen)_3{}^{2+}$	d-CCH^a	$+1460$ J mol^{-1}

^{a} d-CCH = d-cinchoninium ion.

$$\partial(G_D - TS_R)/\partial X' = 0$$

reduces to

$$\ln X''/X' = \begin{cases} \Delta(B)X_B/XRT & \text{(associated)} \\ \bar{\alpha}\Delta(B)X_B/RT & \text{(dissociated)} \end{cases}$$

For relatively small equilibrium shifts, we may put $\delta X = X' - X'' \ll X'$. Making the approximation that the logarithmic function $\ln(1 + x) \simeq x$ for $x \ll 1$, the equilibrium conditions become

$$\delta X = \begin{cases} -\Delta(B)X_B/2RT & \text{(associated)} \\ -\bar{\alpha}\Delta(B)X_BX/2RT & \text{(dissociated)} \end{cases}$$

In both these expressions, $\Delta(B)$ is the molar discrimination energy, defined by

$$\Delta(B) = V_{AB}' - V_{AB}''$$

In this case, the Pfeiffer CD or OR has the simple form

$$P_R(\lambda) = P_R{}^m(\lambda)\delta X$$

where $P_R{}^m(\lambda)$ is the molar CD or OR of A' (which is, of course, an intrinsic constant of A). Therefore the Pfeiffer CD or OR has the concentration and temperature dependence of δX.

Comparison with Experimental Data. The expressions for the equilibrium shift and the resulting Pfeiffer CD or OR can now be compared with experimental data on the Pfeiffer effect.

Temperature Dependence. The model presented predicts that the equilibrium shift decreases with temperature as $1/T$. The racemization entropy (the driving force to the racemate) increases with temperature, offsetting the tendency of G_D (which is temperature independent) to lead to the formation of the more stable enantiomer. This agrees well with the temperature studies of the Pfeiffer OR by Brasted and co-workers,[3] and also with the work of Davies and Dwyer,[5] who measured the temperature dependence of the equilibrium shift directly. The latter results are summarized in Figure 2.

Concentration Dependence. This has been studied in detail by a number of workers,[1,3] and good linearity for the Pfeiffer OR vs. X_BX is obtained. This suggests that the dissociated picture is appropriate for such systems, and that definite aggregates of the form AB_n are not formed in solution. Davies and Dwyer[5] have studied the A = $Zn(phen)_3{}^{2+}$, B = d-bromocamphorsulfonate ion (d-BCS) in water system, and measured the equilibrium shift directly as a function only of X_B, keeping X constant at 0.001 M. Good linearity is obtained up to a saturation value (in X_B only) of 0.006 M.

Calculation of $\Delta(B)$. For the dissociated model, the estimation of the discrimination energy $\Delta(B)$ requires the empirical determination of the saturation concentrations $\bar{X}$ and $\bar{X}_B$. No such data are available in the literature. A rough estimate of this energy may be obtained from the results of Davies and Dwyer. By measuring the slopes of the equilibrium shift vs. $1/T$, the following results (Table I) may be obtained from Figure 2. Putting $X_B \simeq \bar{X}_B$ and letting $\bar{n} = 6$ for a cubic lattice type distribution, the discrimination energy is found to be of the order of 200 J/mol of A–B pairs; i.e., about 1–10% of RT at room temperature.

In summary, then, the comparisons between the available experimental data and the results predicted by the simple
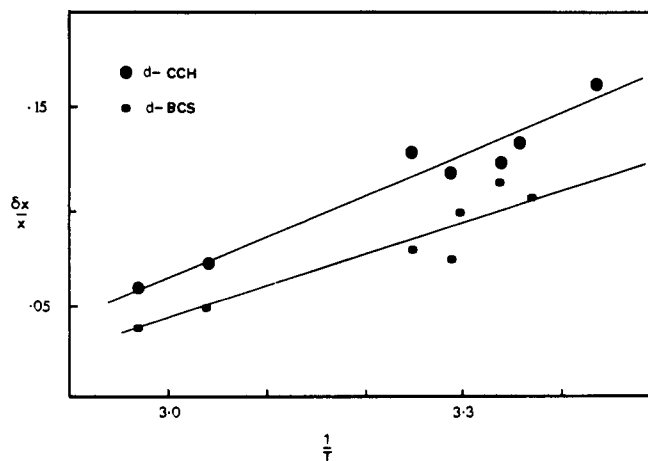

Figure 2. Equilibrium shifts as a function of temperature in Pfeiffer systems. A = $Ni(phen)_3{}^{2+}$, with [A] = 0.001 M. [B] = 0.006 M in water.

models discussed in this paper lead to the following conclusions: (1) Simple diastereoisomers are not formed, so that a given B can lead to discriminatory interactions with a number of A. (2) The equilibrium shift can be thought of as a balance between the two opposing forces of the racemization entropy (favoring the racemate) and the discrimination free energy (favoring the enantiomer with the lowest free energy). (3) The discriminating interactions may be taken to be of relatively short range, being finite only for nearest-neighbor A–B pairs. (4) The types of discriminating interactions responsible for the equilibrium shifts must have a value in the vicinity of 1–10% of RT at room temperature.

Another feature that is found empirically is that the effect is appreciable only for metal complexes with chirally disposed unsaturated ligands.

Microscopic Source of the Discrimination Energy

The exact nature of the discriminating interactions has as yet been unspecified, and in this section we shall discuss the two principal contenders: (1) chiral perturbation of the water lattice structure; and (2) direct chiral interactions between A and B.

Solvent Effects. Although the experimental evidence suggests that the discrimination does not have its source in the different contact interactions of A', A'' with B, it is possible that the interaction of the solvent sheaths about A and B leads to a discrimination energy of the right magnitude. If the solvation sheath about A', for example, retains some of the chiral structure of A', then there will be a chiral component in the interaction of these solvent molecules with the solvent sheath about B. If this were the predominant contributor to the discrimination energy, the following conclusions could be made: (1) The sign of the discrimination energy would not necessarily be the same for different solvents, as it would be a function of the exact nature of the solvent packing. (2) The discrimination energy would increase with the "lattice energy" of the solvent, and also with the specificity of the interaction between the solvent and the species A and B. (3) G_D would be both enthalpic and entropic in nature, leading to a more complex temperature dependence. (4) The effect of the nature of the ligand would be merely its ability to order the solvent structure about the complex. (5) The discrimination from such a picture may be expected to decrease as the solvent becomes smaller, and thus becomes less able to feel the chirality of the overall complex.

The evidence supporting this solvent effect as the source of the discrimination energy is somewhat contradictory, and definitely warrants further investigation. The effect seems largest in water. This could be due to its effective interaction

with the metal complex, as in the phenanthroline complexes it is well known that a number of solvent molecules can squeeze in between the ligand blades, and thus establish an effective chirality in the water structure about the complex. However, the water molecule is small compared to the overall complex, and thus it is questionable how far this chirality is transmitted to other solvent molecules about the ion. It could simply be that the highly polar water allows for closer A–B pairs than in other solvents, so that the discriminating direct A–B interactions could be maximized. It is difficult to see why the effect only occurs for unsaturated ligand systems if the solvent effect is responsible for the discrimination, although the effect has been correlated with hydrophobic bonding in Pfeiffer systems by some authors.[3,20]

The effect of other solvents such as alcohols and acetic acid is essentially to reduce considerably the size of the effect, and in the case of glacial acetic acid, to also change the sign of the effect.[1,3] In glacial acetic acid, the sign change suggests the importance of the solvent sheath in determining the effect, which would not be expected on the grounds of direct discriminating interactions between A and B. If the solvent mechanism leads to the discrimination energy, then we would have to conclude that water has a much more ordered lattice structure than either of these solvents, and thus is most chirally perturbed by the solute molecules. On the other hand, if direct A–B interactions are responsible for the effect in water, these results suggest that (1) the addition of other solvents to water does not allow sufficiently close A–B pairs to lead to the large discriminations found in pure water; and (2) the effect in acetic acid (glacial) is due to a solvent packing effect which leads to the discrimination energy and at the same time precludes close A–B pairs.

The chirality of solvent sheaths thus remains an open questions. However, it is worth pointing out that the simple model developed in this paper may be expected to apply in principle to discriminations which have this source. It is merely necessary to include the respective solvent sheaths in the definition of A and B. Thus the agreement of the simple thermodynamic model with observed experimental studies does not strictly preclude this as the predominant source of the discrimination. However, it does suggest that A–B diastereoisomeric interactions are not responsible for the discriminations.

Discriminations in Direct A–B Interactions. The contribution of the direct A–B interactions is fortunately more tractable, and in this section we discuss those interactions which could potentially lead to discriminations of the order of magnitude found experimentally. It is assumed that the discriminating interaction between A and B is not orientationally specific; i.e., even if the A–B species are loosely held together by, for example, a single hydrogen bond, the interaction energy leading to the discriminations may be averaged over all orientations of A and B. The average may generally be taken over all the relative orientations of A and B throughout the solution, rather than over time. The averaged discrimination energy $\Delta(B)$ is then defined as the difference in the averaged interaction energies of A' and A'' with B.

Two types of averaged interactions may be shown to lead to significant discriminations in orientationally uncorrelated systems.[11] The first, which we shall refer to as μm discrimination, was first pointed out by Mavroyannis and Stephen,[12] and has since been studied by Craig and co-workers.[13] This discrimination energy has the form

$$\Delta^{\mu m}(B) = -\frac{4}{3}\left\{\frac{1}{4\pi\epsilon_0}\right\}\left\{\frac{\mu_0}{2\pi}\right\}(R_{AB})^{-6}\sum_{\substack{s,u \\ \neq 0}}\frac{R_A{}^{0s}R_B{}^{0u}}{\epsilon_s + \epsilon_u}$$

where

$$R_A{}^{0s} = \mathrm{Im}\,\mu_A{}^{0s}\cdot\mathbf{m}_A{}^{s0}$$

$$\mathbf{m}_A{}^{s0} = \langle\phi_A{}^s|\,\mathbf{m}_A|\phi_A{}^0\rangle$$

and so on. μ_A, $\mathbf{m}_A$ are the electric and magnetic dipole moment operators on A', respectively, $\phi_A{}^0$ the ground state and $\phi_A{}^s$ an excited state on A', the latter with a transition energy ϵ_s relative to the ground state, and so on. R_{AB} is the separation of A' and B. The quantities $R_A{}^{0s}$, $R_B{}^{0s}$ also appear in the circular dichroism of A' and B as the rotatory or CD strengths of the s transition, so that therse terms can in principle be estimated from CD data.

The second type of discriminatory interaction, which we shall refer to as $\mu\mu\mu$ discrimination, has been suggested by this author[11] as being more important than the above contribution, the μm discrimination being relatively small because of the dependence on magnetic dipole–dipole interactions, which are intrinsically weaker than electric ones. This $\mu\mu\mu$ discrimination arises from third-order perturbation theory (normal dispersion interactions as well as the μm discrimination arise in second order) but is a purely electric dipole term. It has the form

$$\Delta^{\mu\mu\mu}(B) = \frac{16}{9}\left(\frac{1}{4\pi\epsilon_0}\right)^3(R_{AB})^{-9}\sum_{\substack{s,t \\ u,v}}\Lambda_A(s,t)\Lambda_B(u,v)$$

$$\times\frac{\Delta\epsilon_{ts}\Delta\epsilon_{vu}}{\epsilon_{su}\epsilon_{tv}\epsilon_{sv}\epsilon_{tu}}$$

the summation being over all s,t (where none of $s,t,0$ can be the same), and over all u,v with similar constraints. The energy terms are defined as

$$\Delta\epsilon_{ts} = \epsilon_t - \epsilon_s$$

$$\epsilon_{su} = \epsilon_s + \epsilon_u$$

and the *inducing powers* of A' and B, respectively, as

$$\Lambda_A(s,t) = \mu_A{}^{0t}\times\mu_A{}^{ts}\cdot\mu_A{}^{s0}$$

$$\Lambda_B(u,v) = \mu_B{}^{0v}\times\mu_B{}^{vu}\cdot\mu_B{}^{u0}$$

These quantities also arise in theories of induced circular dichroism, from which the term inducing power derives.[15]

Rough numerical comparisons suggest that at short range, the $\mu\mu\mu$ discriminations will be significantly greater than the μm discriminations, despite the origin of the latter in a lower order of perturbation theory. The reason is the weakness of magnetic interactions previously mentioned. The exact relative magnitude of these discriminations depends on the nature of the systems in question, but in the next section, we shall show that for the types of systems that exhibit the Pfeiffer effect, this predominance of the purely electric term seems to be valid.

Discriminations in Chiral Metal Complexes. Metal complexes with chirally disposed unsaturated ligands are characterized by both large rotatory strengths and large inducing powers of the ligand system. Both types of discrimination may thus be expected to be maximized for such systems. Both properties result from the coupling of a strongly electric dipole allowed transition on each of the ligands, the collective excitation manifesting the chirality of the ligand system.

We consider each ligand to have a predominant transition which is strongly electric dipole allowed, and long axis polarized. The states of the entire ligand system may then be determined using simple exciton theory.[14] Each ligand is characterized by a single excited state r, so that the ligand states of the complex may be written as

$$|0\rangle = |000\rangle = |0\rangle_1|0\rangle_2|0\rangle_3$$

$$|S\rangle = \frac{1}{\sqrt{3}}(|r00\rangle + |0r0\rangle + |00r\rangle)$$

$$|T_i\rangle = \frac{1}{\sqrt{2}}(|r00\rangle - |0r0\rangle)$$

$$|T_j\rangle = \frac{1}{\sqrt{2}}(2|00r\rangle - |r00\rangle - |0r0\rangle)$$

where 1, 2, 3 index the separate ligands, 0 refers to the ground state, and S, T_i, T_j refer to the excited exciton states with transition energies ϵ_S, ϵ_T relative to the ground state, the two T states being degenerate.

For simplicity, we first estimate the self-discrimination energy of A', A'' with a given enantiomer $B = A'$ of the same complex. Expansion of the dipole operators in the usual way, and defining $\Delta\epsilon_r = \epsilon_T - \epsilon_S$, the two self-discriminations take the form

$$\Delta^{\mu m}(A') = \frac{1}{12}\left(\frac{1}{4\pi\epsilon_0}\right)\left(\frac{\mu_0}{2\pi}\right)R_{ab}{}^{-6}r_L{}^2|\mu^{0r}|^4\frac{(\Delta\epsilon_r)^2}{\epsilon_r}$$

$$\Delta^{\mu\mu\mu}(A') = 2\left(\frac{1}{4\pi\epsilon_0}\right)^3 R_{AB}{}^{-9}|\mu^{0r}|^4|\mu^{rr} - \mu^{00}|^2\frac{(\Delta\epsilon_r)^2}{\epsilon_r{}^4}$$

where the exciton splitting ($\Delta\epsilon_r$) is assumed small compared to the energies $\epsilon_S \simeq \epsilon_T \simeq \epsilon_r$, and ϵ_r is the unperturbed ligand transition energy. r_L is the ligand center to metal distance, and μ^{0r}, μ^{rr}, μ^{00} the free ligand transition dipole moment, the permanent dipole moment of the excited state, and the permanent dipole moment in the ground state, respectively. The expressions are derived by identifying S, T with the states $\phi_A{}^s$, $\phi_A{}'$ in the interaction expressions, and substituting for the exciton wave functions in terms of the free ligand functions. The permanent moments of the ligands will be directed along r_L. Although the above expressions are for a long axis polarized transition, similar expressions may be derived for any other polarization. Ligand polarizations toward the metal ion are coplanar, and cannot contribute to the discrimination.

Some important features follow readily from these results. The discriminations depend on the exciton splitting and the intensity of the free ligand transition, so that they will be largest for strongly coupled, intense ligand transitions, such as for unsaturated chelates. The relative magnitude of the two terms may be shown to be

$$\Delta^{\mu m}/\Delta^{\mu\mu\mu} \simeq 3 \times 10^{-21}R_{AB}{}^3\epsilon_r{}^3r_L{}^2/(|\mu^{rr} - \mu^{00}|^2)$$

where distances are in Å, dipole moments in eÅ, and energies in cm^{-1}. Simple substitution of realistic values shows that the purely electric discrimination term should predominate, and that the other may be safely neglected.

The problem remains as to the absolute magnitude of the discrimination due to purely electric terms relative to RT at room temperature, which may be shown to have the value, using the same units as above, of about

$$1.5 \times 10^{13}R_{AB}{}^{-9}|\mu^{0r}|^4|\mu^{rr} - \mu^{00}|^2(\Delta\epsilon_r)^2/\epsilon_r{}^4$$

and, for a general B,

$$-6.0 \times 10^{13}R_{AB}{}^{-9}|\mu^{0r}|^2|\mu^{rr} - \mu^{00}|\Lambda_B(u.v)\frac{\Delta\epsilon_r\Delta\epsilon_{vu}}{\epsilon_{ru}{}^2\epsilon_{rv}{}^2}$$

For tris(bidentates), R_{AB} as defined in the above model will be measured from the central metal ion, and is thus relatively large even for loosely associated species A and B. A better picture of the interaction may be developed by supposing that B is sufficiently close to A so that it only "sees" two of the ligands. Exciton wave functions may be developed for the two-ligand system analogously to the method discussed above, and the electric discrimination has exactly the same form as for the tris(bidentate), with two minor exceptions: (1) a factor of $^2/_9$; (2) the separation R_{AB} is now measured from an origin between the two ligand dipoles to that of B. Realistic values of R_{AB} can then lead to discriminations of the observed magni-

tude provided that A and B are relatively close nearest neighbors. Of course, the exact definition of R_{AB} is tempered by the use of the multipole expansion in the derivation of the form of the interaction; we should therefore not expect anything more from the model than the form of the interaction, and a rough estimate of its magnitude. These calculations are, however, strongly suggestive that electric discriminating interactions arising from the dispersive coupling of the chirally disposed ligand transition moments to the electric transition on B can lead to those found experimentally.

The best test of the model is the dependence of the discrimination on the intensity of the free ligand transitions. Tris(bidentates) should thus have discriminations roughly varying as the ligand transition intensities, which is qualitatively in agreement with the observation of the effect for unsaturated chelate systems, and also for the effect in phenanthroline complexes being larger than that in dipyridyl complexes.

Induced Circular Dichroism

In the interpretation of Pfeiffer CD or OR, it is important to recognize that contributions other than that arising from the equilibrium shift may appear. The simplest manifestation of this is the appearance of appreciable Pfeiffer activity in kinetically inert racemates.[17] Two effects may be distinguished: (1) the dependence of the CD and OR on the ionic strength of the solution; and (2) induced optical activity. The former has been investigated elsewhere,[3] so that we shall confine this discussion to the latter.

A theory of the induction of optical activity in an achiral chromophore by interaction with other chiral species has been developed.[15,18] Two limits may be defined: that where there is no orientational correlation between the species A and B involved in a pair interaction (dispersion- or dissociate-induced CD, DICD[15]); and that where A and B are rigidly associated (AICD, associate-induced CD[18]). In applications to metal complexes,[16] in either case the CD of the d–d transitions depends only on the achiral metal ion–ligating atoms chromophore. The total CD of the d–d transitions has its source in two perturbations: (1) AICD due to the chiral distribution of the ligands (which leads to the CD of the resolved complex, and vanishes for the racemate); and (2) DICD due to the ions B in the solution. The latter is the *same* for both enantiomers, and thus leads to an overall CD activity of the racemate independent of the relative A'/A'' concentrations. This induced CD contribution to the Pfeiffer CD of the d–d transitions could be appreciable in some cases, and should if possible be distinguished from the CD arising from the equilibrium shift, especially if the Pfeiffer effect is used to investigate the CD of the enantiomer produced in excess.[7]

The CD of the ligand system has a quite different source, the ligand system being intrinsically chiral. The induced CD in these ligand bands may be expected to be relatively small compared to the intrinsic CD, so that the change in the ligand system CD should be safely attributable to the equilibrium shift. As the OR at the sodium D line is largely due to the optical activity of the ligand system,[8] the Pfeiffer OR at the sodium D line may be expected to be a more reliable measure of the equilibrium shift than the d–d CD spectra.

Conclusions

An attempt has been made in this paper to use both thermodynamic arguments and calculations of intermolecular forces in order to elicit the source of the Pfeiffer effect in inorganic systems. The complexity of Pfeiffer systems has necessitated the use of relatively simple models, but a consistent picture of the Pfeiffer effect in general agreement with experimental studies emerges.

Pfeiffer systems in achiral solvents may be thought of as

nondiastereoisomeric systems in which the A–B discriminations arise from nearest-neighbor interactions such that a particular B can interact with a number of A and vice versa. The equilibrium conditions are determined by a balance between the racemization entropy favoring the racemate, and the discrimination energy term favoring the more stable enantiomer of A.

The source of the discriminations is postulated to be twofold: chiral perturbation of local solvent lattice structure between A and B; and purely electric dispersion terms varying with separation as R_{AB}^{-9}. It is hoped that future experimental studies will be directed to eliciting which of these two mechanisms leads to the predominant discrimination in aqueous systems.

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Base-Catalyzed Isotopic Exchange of Molecular Hydrogen. 4.[1] Hydrogen Isotope Effects in the Dimethyl Sulfoxide–Water System
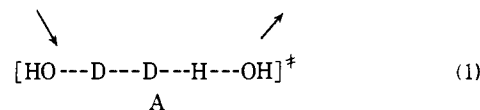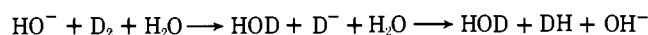
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Abstract: Isotope effects for the hydrogen reacting as a hydride ion in the exchange reaction $HO^- + D_2 + H_2O \rightarrow$ (HOD + $D^- + H_2O$) $\rightarrow$ HOD + DH + OH^- in H_2O-Me_2SO mixtures vary smoothly in the range 1.18–1.65 between 0 and 96.9 mol % Me_2SO, passing through a maximum at 65 mol % Me_2SO. Despite the smallness of the effects. model calculations suggest that they are consistent with rate-determining hydrogen transfer. The low zero point energy difference between isotopically substituted hydrogen molecules can give maximum isotope effects lower by a factor of 3 than in reactions of C-H, O-H, or N-H bonds. For reaction via a hydride intermediate the hydrogen separating as a hydride ion is not subject to tunnelling or a Westheimer effect, while k_H/k_D for the transferred hydrogen, which is also small, should be sensitive to the low equilibrium isotope effect for its reaction ($K_H/K_D = 0.26$). In the more probable single step exchange mechanism, concerting hydrogen transfer reduces k_H/k_D, and a nonlinear configuration for the transition state may reduce it further. The possibilities of "hydride character" in the concerted transition state, $[HO-H-H-H-OH]^{\ddagger}$. and of formation of H-H-OH$^-$ as an intermediate are considered.

Investigation of isotopic exchange between molecular hydrogen and H_2O in the condensed phase is of interest both from a theoretical viewpoint and also in the potential that the method could offer for separation of the deuterium isotope.[5] The exchange is extremely slow in pure water, even at elevated temperatures, but it is catalyzed by the hydroxide ion.[6-8] We have found that the catalyzed reaction is accelerated by using dimethyl sulfoxide (Me_2SO) as a cosolvent,[9,10] although the increase in rate with increased Me_2SO content is not as large as in the case of many reactions involving rate-determining proton transfer.[11,12]

The mechanism of hydroxide catalysis, both of the isotope exchange and of the related para- to ortho-hydrogen conversion, has been extensively investigated,[1,6-10,13-16] but the detailed course of the reaction remains unsettled. Wilmarth[6] suggested that reaction occurs via a hydride intermediate (eq 1) or by a single concerted step through transition state A. He preferred the stepwise mechanism on the grounds that exchange is not subject to acid catalysis, and that the estimated

$$HO^- + D_2 + H_2O \longrightarrow HOD + D^- + H_2O \longrightarrow HOD + DH + OH^-$$

$$[HO\text{---}D\text{---}D\text{---}H\text{---}OH]^{\ddagger} \qquad (1)$$
$$A$$

energy of formation of H^-(aq) from H_2 was less than the activation energy of 24 kcal for the reaction.[6] Olah et al. have more recently reported[17] that exchange does occur slowly in "magic acid" systems.

Subsequently, Ritchie reestimated the energy of formation of the hydride ion as 55 kcal, which would favor a concerted mechanism.[14] However, Ritchie also noted[14,18] that the observed activation energy corresponds to estimates of the energy for removing one water molecule from the solvation shell of the hydroxide ion.[19] Calculations of the potential energy surface for reaction of H_2 with a hydroxide ion in the gas phase show an initial reaction without activation energy and exothermic by 12 kcal/mol to form a stable HHOH$^-$ ion.[14] Ritchie sug-