

Figure 6. Theoretical vibrational spectrum of TiCl_4 . The intensity of each peak has been weighted according to the orbital degeneracy.

magnitude of the coupling constant indicates strong vibronic coupling accompanying photoionization for all valence molecular orbitals. The relative line widths of the first three bands are qualitatively produced by the calculations. Thus the calculated full widths at half-height for the three bands A, B, (C + D) are 0.18, 0.21, and 0.30 eV. The vibrational coupling

constant for the $1e$ orbital is the largest, and the resulting broad line partially explains the large line width for C + D. The shoulders are of course not reproduced because of the neglect of Jahn-Teller and spin-orbit splitting. Taken together with all the other experimental and theoretical evidence in this paper, our assignments must be considered relatively reliable.

Conclusions

For the relatively simple inorganic molecule TiCl_4 , we have obtained high-resolution He I and He II spectra. In combination with $X\alpha$, INDO, cross-section, and vibrational calculations, we have shown that the previous assignment $1t_1 < 3t_2 < (1e, 2a_1) < 2t_2$. However, even with this large amount of experimental and theoretical evidence, we obviously still do not completely understand aspects of the spectrum—the shoulders on bands A, B, and C and the exact position of the $2a_1$ orbital. Valence-band spectra taken with synchrotron radiation along with more elaborate calculations are required to complete the assignments, even on this simple molecule.

Acknowledgment. We wish to thank the generosity of Professor Zerner and Dr. Davenport in furnishing the computer programs used in the present work. The financial support of the NSERC (Canada) is gratefully acknowledged. E.P. wishes to thank Bar Ilan University (Ramat-Gan, Israel) for financial support.

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Studies of the Pfeiffer Effect Developed in Tris(pyridine-2,6-dicarboxylato)terbate(III) by Phenylalkylamines, Phenylalkylamino Alcohols, and Phenylalkylamino Acids

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Optical activity induced in the title complex through outer-sphere complexation with a series of structurally related environment substances has been studied by means of circularly polarized luminescence (CPL) spectroscopy. The substrates were found to fall into four classes, which were determined by trends in the induced optical activity and by the nature of the functional groups on the substrates. For certain of the chiral materials, the observed optical activity was pH independent, but for others, the CPL spectra were found to invert upon ionization of the protonated ammonium group. Systematic variation of functionality on the chiral substrates enables one to conclude that ionic, hydrophobic, and hydrogen-bonding mechanisms can all contribute to the association of complex and environment substance.

Introduction

The development of optical activity in a racemic mixture of a labile metal complex upon addition of certain chiral compounds (termed the environment substance) is known as the Pfeiffer effect^{2,3} and is usually thought to arise from a displacement of the equilibrium existing between the enantiomers of the racemic metal complex. While several theories have been advanced to account for the effect,⁴ most of the reported work has been explained by the existence of complexation between the racemic complex and the environment substance as leading to the observed optical activity. Several attempts have been made to use the Pfeiffer effect as a means to predict absolute configurations of a variety of substances,⁵⁻⁷

but these correlations have been very limited in their scope.

We have recently been using Pfeiffer optical activity to study f-f optical activity in trigonal lanthanide complexes, since these complexes are too labile to be resolved by ordinary physical or chemical means. Our work has centered on the tris lanthanide complexes of pyridine-2,6-dicarboxylic acid (DPA, or dipicolinic acid), as this ligand is known to form very strong complexes with all members of the lanthanide series⁸ and the tris complex is known to possess an approximate D_3 symmetry in fluid solution at room temperature.⁹ The first studies were involved with determinations of conditions under which the effect could be observed, and it was found that the $\text{Tb}(\text{DPA})_3^{3-}$ complex could associate with chiral environment substances through both ionic (resolved tris(ethylenediamine)chromium(III)¹⁰) and hydrophobic (L-ascorbic acid¹¹) mechanisms.

The studies involving hydrogen bonding of environment substances to aromatic portions of the DPA ligands were found to be of extreme interest, and we have recently studied the pH

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dependence of the Pfeiffer effect induced in $\text{Tb}(\text{DPA})_3^{3-}$ by L-histidine and analogues of L-proline¹² and tartrate substrates.¹³ However, in another recent work, we have shown that with certain diamino carboxylic acids the sign of the Pfeiffer optical activity is dependent on solution pH.¹⁴ This sign inversion was not found with monoamino carboxylic acids and short-chain diamino carboxylic acids and clearly demonstrates that the Pfeiffer effect in the $\text{Tb}(\text{DPA})_3^{3-}$ complex (where the metal ion is known to be 9-coordinate¹⁵) is not a reliable indicator of the absolute configuration of the environment of the substance.

In the present work, we report the optical activity induced in $\text{Tb}(\text{DPA})_3^{3-}$ by phenylalkylamines, phenylalkylamino alcohols, and phenylalkylamino acids. As in our previous works,¹⁰⁻¹⁴ we have chosen to use circularly polarized luminescence (CPL) spectroscopy as our chiroptical method rather than circular dichroism. This choice is dictated by the fact that f-f absorption transitions tend to be extremely weak and overlap to a considerable extent, while the luminescence spectrum of the Tb(III) ion is quite strong when sensitized by the DPA ligands and the emission bands are well separated. Since f-electrons are essentially nonbonding in nature, one would predict that information taken on an excited f-f state would be applicable to the ground-state molecule.

Experimental Section

The $\text{Tb}(\text{DPA})_3^{3-}$ complexes were prepared by mixing stock solutions of Tb(III) and pyridine-2,6-dicarboxylic acid in a 1:3 stoichiometric ratio. The lanthanide ions were obtained as the 99.9% oxides (Kerr-McGee), and the stock solutions were prepared by dissolving the oxide in the minimum amount of 11.6 M HClO_4 and neutralizing to pH 3 with NaOH. The dipicolinic acid was used as received from Aldrich. In a previous work, $\text{Na}_3\text{Tb}(\text{DPA})_3 \cdot 15\text{H}_2\text{O}$ was prepared and used for the induced optical activity studies, but no difference in results was noted when the two methods of complex were prepared.¹² The concentration of $\text{Tb}(\text{DPA})_3^{3-}$ used in all spectroscopic studies was found to be 14 mM after all dilutions were performed. The final ionic strength of all solutions was adjusted to be 0.15 M with NaClO_4 .

In the absence of a chiral environment substance, no CPL was noted in any of the Tb(III) emission bands at any pH. Addition of a 3- to 10-fold excess of environment substance always led to the observation of measurable Pfeiffer optical activity, which was detected using CPL spectroscopy. For certain environment substances (hydroxyphenyl derivatives in general), it was found that optical activity could be observed at much lower concentrations of chiral material, ratios as low as 0.1 being usable in some cases.

All environment substances were obtained optically pure from either Aldrich Chemical Co., Sigma Biochemicals, or Norse Laboratories. The optical purity of each material was checked by measuring its specific rotation at the sodium D line, and corrections to the substrate concentration were made when the substance was not found to be 100% optically pure. This problem was especially severe for (-)- α -phenylethylamine obtained from Norse; the material received was found to be only 63.4% optically pure. In every case where both enantiomers could be obtained, the Pfeiffer optical activity was measured for each environment substance.

The optical activity of the Tb(III) complexes was monitored by studying the circular polarization within the luminescence bands. For the $\text{Tb}(\text{DPA})_3^{3-}$ complex, the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ transition at 545 nm was studied to the greatest extent since it is now well established that this band exhibits the strongest Tb(III) emission and also shows the most intense CPL spectra. The other Tb(III) emission bands correspond to transitions from the $^5\text{D}_4$ level to the $^7\text{F}_6$ (490 nm), $^7\text{F}_4$ (582 nm), and $^7\text{F}_3$ (622 nm) levels, but these were only examined briefly to compare to earlier work.¹² The existence of axial symmetry in the isomorphous $\text{Eu}(\text{DPA})_3^{3-}$ complex was demonstrated recently by the absence of a luminescence band corresponding to the $^5\text{D}_0 \rightarrow ^7\text{F}_0$ transition.^{13,14}

All CPL and total luminescence (TL) spectra were obtained on a medium-resolution spectrometer constructed in our laboratory for this purpose, whose operation has been described in detail.¹⁶ The $\text{Tb}(\text{DPA})_3^{3-}$ complexes were excited at 295 nm, taking advantage of the fact that the DPA ligand absorbs quite strongly at this wavelength and is capable of sensitizing the lanthanide ion emission. The emission spectra were analyzed by a 0.5-m grating monochromator at 1-nm resolution, and further increases in spectral resolution did not lead to an improvement of the band-shape features. The TL and CPL spectra are obtained in proportional arbitrary units, with the TL being defined as $I = \frac{1}{2}(I_L + I_R)$ and the CPL as $\Delta I = I_L - I_R$; I_L and I_R represent the emitted intensities of left and right circularly polarized light. The ratio of these quantities, $\Delta I/I$, is termed the luminescence dissymmetry factor (g_{lum}), and this quantity is dimensionless. No other absolute quantal parameters were obtained. It was generally found that the TL intensity did not depend strongly on the nature or concentration of added substrate and that the dissymmetry factor was an excellent measure of the degree of induced optical activity in the $\text{Tb}(\text{DPA})_3^{3-}$ complex.

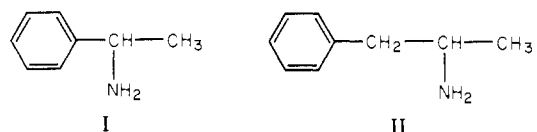
The interaction between the chiral substrates and the $\text{Ln}(\text{DPA})_3^{3-}$ complexes was also investigated by examining the $^5\text{I}_8 \rightarrow ^5\text{G}_6$ absorption of $\text{Ho}(\text{DPA})_3^{3-}$ at 450 nm. This particular band is one of the "hypersensitive" lanthanide transitions, which display intensity and wavelength variations as a function of the metal ion environment. Data were obtained on a Cary 11 UV/VIS recording spectrophotometer.

The pH of all solutions was obtained with an Orion Model 701A pH meter employing a glass microcombination electrode which could be directly inserted into the spectrophotometer and fluorescence cuvettes. The system was calibrated daily with use of phosphate buffers.

Results

Addition of a chiral phenylalkylamine, phenylalkylamino alcohol, or phenylalkylamino acid to an aqueous solution of $\text{Tb}(\text{DPA})_3^{3-}$ invariably resulted in the development of optical activity, as measured by the appearance of a CPL spectrum. The sign and intensity of the CPL spectra were found to depend on the solution pH, and the trends varied with the nature of the environment substance. CPL spectra could be recorded in all Tb(III) luminescence bands, although the greatest degree of optical activity was measured in the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ band (centered around 545 nm). The optical activity within the other Tb(III) emission bands was examined many times, but trends within these bands always paralleled those obtained in the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ band. As a result, we will restrict our discussions to features obtained only for this most intense band.

Phenylalkylamines. It was found that two chiral phenylalkylamines, α -phenylethylamine (I) and α -methylphenylethylamine (II), led to observable CPL if the solution pH was



sufficiently low. These two environment substances may be considered the simplest members of a series of environment substances built on benzylamine and β -phenylethylamines, respectively. The sign of the CPL within the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ peak proved to be a reliable indicator of the absolute configuration of the environment substance; if the *S* isomer was used, then the major CPL within the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ band was found to be positive in sign. Our previous work^{13,14} has shown that the observation of positive CPL in this band implies that the Λ isomer of the $\text{Tb}(\text{DPA})_3^{3-}$ complex is present in excess. Absolute configurations of the environment substances are available in the literature.¹⁷

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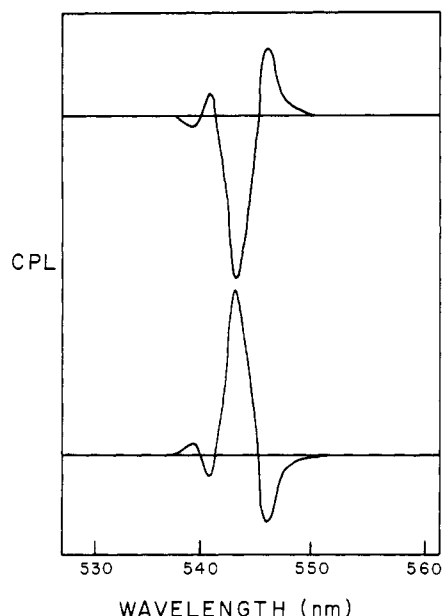


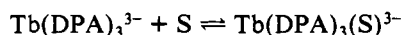
Figure 1. CPL spectra within the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ luminescence band of $\text{Tb}(\text{DPA})_3^{3-}$ complexed with (*R*)-phenylethylamine (upper trace) and (*S*)-phenylethylamine (lower trace). The $\text{Tb}(\text{DPA})_3^{3-}$ in this and all other studies was 14 mM, and both substrate concentrations were 100 mM.

While substrate II could only be obtained as the *S* isomer, substrate I was obtained as the resolved *R* and *S* isomers. CPL spectra obtained upon addition of equal amounts of these to separate $\text{Tb}(\text{DPA})_3^{3-}$ solutions are shown in Figure 1 for the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ transition, and one may easily see that the spectra are exactly equal in magnitude and opposite in sign. The spectra in the $\text{Tb}(\text{III})$ emission bands are essentially identical with those we have presented in our earlier works.¹²

The CPL induced in the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ transition is essentially pH invariant until the solution pH is raised to 8.75, and then a rapid decrease in CPL intensity is noted. This behavior is illustrated in Figure 2, where it should be noted that, while the overall trends are the same for both substrates, substrate I is found to exhibit somewhat higher degrees of CPL than substrate II for equivalent amounts of environment substance. It is known that the acid ionization constant of the primary amines is approximately 9.5,¹⁸ and we therefore conclude that the Pfeiffer effect of CPL is lost when the environment substances are deprotonated. This behavior is not hard to understand when one remembers that the $\text{Tb}(\text{III})$ complex and the protonated amines are oppositely charged, and removal of the positive charge on the amine substrates removes much of the driving force responsible for the association.

We have previously noted that a g_{lum} factor of ± 0.022 (sign depends on the absolute configuration of the environment substance) appears to be the limiting quantity that can be reached¹⁰⁻¹⁴ and have confirmed this observation in the present work by adding 30-fold excesses of environment substances to the $\text{Tb}(\text{DPA})_3^{3-}$ solutions. It is our contention that this limiting dissymmetry factor represents the g_{lum} value of the fully complexed $\text{Tb}(\text{DPA})_3^{3-}$ complex.

With knowledge of the limiting dissymmetry factor, it is quite easy to calculate the association constant for the reaction



by varying the concentration of both initial reagents and measuring the degree of induced optical activity. Application of Job's method of continuous variations yields the 1:1 stoi-

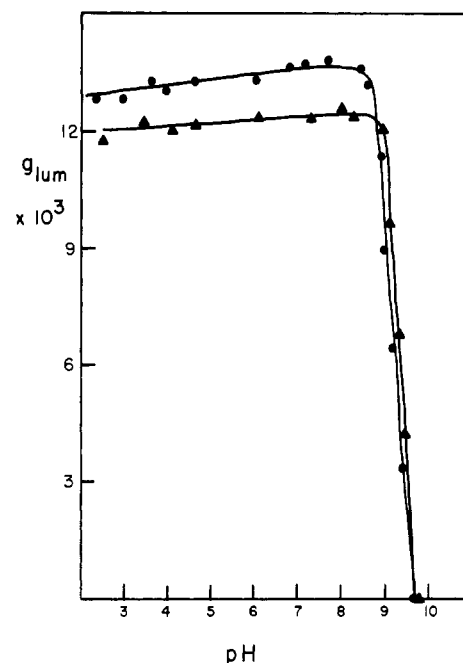


Figure 2. pH dependence of the dissymmetry factors associated with the $\text{Tb}(\text{DPA})_3^{3-}/(\text{S})$ -phenylethylamine (I, ●) and $\text{Tb}(\text{DPA})_3^{3-}/(\text{S})$ -methylphenylethylamine (II, ▲) adducts. The concentrations of both substrates was 105 mM.

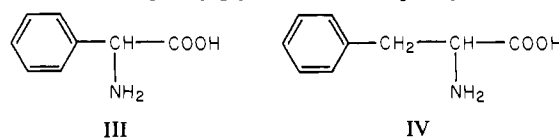
chiometry for the adduct complex and permits the calculation of the association constant:

$$K = [\text{Tb}(\text{DPA})_3(\text{S})] / ([\text{Tb}(\text{DPA})_3][\text{S}])$$

We have previously outlined in sufficient detail how this calculation may be performed.¹⁴

Using our computational procedures, we find that the formation constant of the $\text{Tb}(\text{DPA})_3^{3-}/\text{R-I}$ complex is 21.86, while that of the $\text{Tb}(\text{DPA})_3^{3-}/\text{S-II}$ complex is only 18.63. The constant for the $\text{Tb}(\text{DPA})_3^{3-}/\text{S-I}$ was found to be 21.78, and it is therefore concluded that no stereoselectivity is exhibited when the simple phenylalkylamines bind to the $\text{Tb}(\text{DPA})_3^{3-}$ complex. The formation constant of all environment substances higher than any of those we have reported so far.¹²⁻¹⁴ The formation constant of all environment substances will be found in Table I. The values for the constants obtained here are significantly higher than any of those we have reported so far.¹²⁻¹⁴

Phenylalkylamino Acids. Replacement of the terminal methyl group on substrates I and II by a carboxyl group yield two amino acids, phenylglycine (III) and phenylalanine (IV).



While both of these environment substances yielded CPL when added to a solution of $\text{Tb}(\text{DPA})_3^{3-}$, the pH dependence of this induced optical activity was found to be significantly different from that of the simple amines. In Figure 3 the pH dependence of CPL within the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ transition is illustrated for $\text{Tb}(\text{DPA})_3^{3-}/\text{R-III}$ and $\text{Tb}(\text{DPA})_3^{3-}/\text{R-IV}$.

Several points may be immediately noticed. First, between pH 7.5 and 8.5 the CPL spectra are found to undergo a complete sign inversion. The band shapes that are obtained match those of Figure 1, and it is quite clear that, while the Δ isomer of $\text{Tb}(\text{DPA})_3^{3-}$ is present in excess at low pH, a process takes place near neutral pH which causes the opposite enantiomer to become preferred as a result of some change on the environment substance. This is a highly interesting

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Table I. Formation Constants for $\text{Tb}(\text{DPA})_3^{3-}$ Adducts with Environment Substances That Form Outer-Sphere Complexes^a

substrate	K_1	
(<i>R</i>)- α -phenylethylamine (I)	21.86	
(<i>S</i>)- β -phenyl-2-propylamine (II)	18.63	
(<i>S</i>)-phenylglycine (III)	1.58 (low pH)	30.45 (high pH)
(<i>R</i>)-phenylalanine (IV)	5.76 (low pH)	5.49 (high pH)
(<i>R</i>)-phenylglycinol (V)	1.78 (low pH)	2.27 (high pH)
(<i>S</i>)-phenylalaninol (VI)	2.62 (low pH)	0.96 (high pH)
(1 <i>S</i> ,2 <i>S</i>)-2-amino-1-phenyl-1,3-propanediol (VII)	7.75	
(1 <i>S</i> ,2 <i>R</i>)-norephedrine (VIII)	6.97	
(1 <i>R</i> ,2 <i>R</i>)-norpseudoephedrine (IX)	3.03	
(1 <i>S</i> ,2 <i>R</i>)-ephedrine (X)	2.73	
(<i>R</i>)- <i>p</i> -hydroxyphenylglycine (XI)	22.48 (low pH)	11.47 (high pH)
(<i>S</i>)-tyrosinol (XIV)	14.11 (low pH)	59.26 (high pH)

^a The error associated with each constant is approximately 10%.

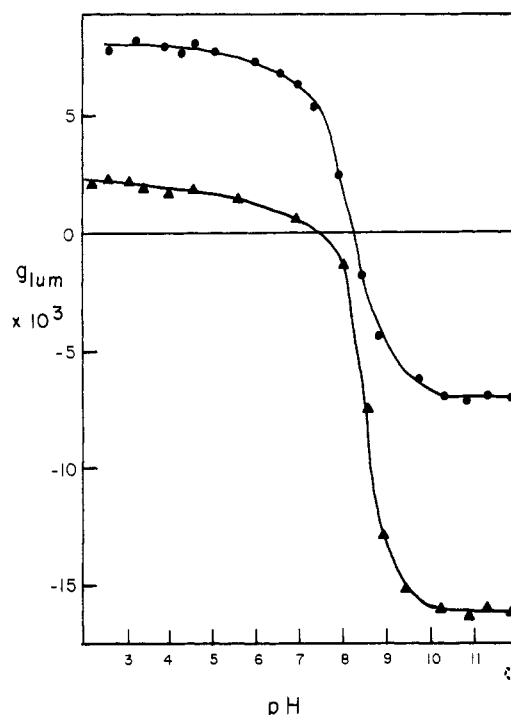


Figure 3. pH dependence of the dissymmetry factors associated with the $\text{Tb}(\text{DPA})_3^{3-}/(\text{R})$ -phenylglycine (III, \blacktriangle) and $\text{Tb}(\text{DPA})_3^{3-}/(\text{R})$ -phenylalanine (IV, \bullet) adducts. The concentration of substrate III was 17.42 mM, while that of IV was 96.25 mM.

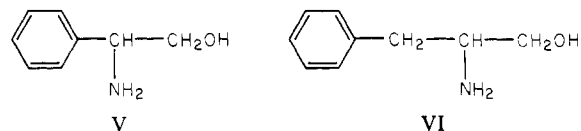
point, since with the simple phenylalkylamines it was the *S* isomer of the environment substance which led to a predominance of the Δ isomer, not the *R* isomer as in the case of the phenylalkylamino acids.

Another important difference is that, while deprotonation of the simple amines led to complete loss of the CPL, performance of the analogous process on the phenylalkylamino acids leads to the appearance of oppositely signed CPL. It is known that the ammonium group of phenylglycine has a $\text{p}K_a$ value of 7.78¹⁹ and phenylalanine has a $\text{p}K_a$ of 9.11,²⁰ and it is not unreasonable to assign the CPL sign inversion as being due to deprotonation of the ammonium group of the amino acids. It is quite significant to note that this deprotonation is more easily effected when the substrates are bound to the $\text{Tb}(\text{DPA})_3^{3-}$ complex; for phenylglycine, the CPL is zero at pH 7.4 and for phenylalanine the CPL crosses zero at pH 8.3.

These crossover points correspond to the situation where we again have an exact racemic mixture of the $\text{Tb}(\text{DPA})_3^{3-}$ complex, and these point out the pH value where equimolar amounts of protonated and deprotonated amino acid substrate exist. Unlike the simple amines, the amino acids continue to bond to the $\text{Tb}(\text{DPA})_3^{3-}$ complex even after the center of positive charge is removed from the environment substance. Our observation that *S*-I, *S*-II, *R*-III, and *R*-IV all lead to enrichment of the solution in the Δ isomer of $\text{Tb}(\text{DPA})_3^{3-}$ at low pH can be taken as proof that the associative mechanism existing between the metal complex and the two classes of environment substances is quite different. We shall return to this point later in the Discussion.

An examination of Figure 3 reveals that, for each amino acid substrate, two pH regions exist where the CPL intensity (as measured by the dissymmetry factor) is essentially constant. This implies that the adduct complex is stable over the pH 3–6 and 10–11.5 ranges and that calculations of the formation constant for the adducts will be more meaningful. For phenylglycine, we find that the binding between $\text{Tb}(\text{DPA})_3^{3-}$ and *R*-III is quite weak ($K = 1.58$) in the low-pH region but becomes dramatically stronger within the high-pH region (where $K = 30.45$). No such dramatic difference is noted for phenylalanine, with formation constant values of 5.76 (low-pH region) and 5.49 (high-pH region) being obtained for *R*-IV. A significantly different association constant was obtained if the *S* isomer of phenylalanine was used, and it was found that the bonding was distinctly weaker ($K = 5.02$ at low pH and 4.37 at high pH). These differences are much greater than the experimental error in the formation constants (which ranges from 0.05 to 0.09 for the values quotes in this paper).

Phenylalkylamino Alcohols. Substitution of a hydroxyl group onto the terminal methyl group of substrates I and II yields two amino alcohols, phenylglycinol (V) and phenylalaninol (VI). Addition of these environment substances to



a solution of $\text{Tb}(\text{DPA})_3^{3-}$ again resulted in the existence of optical activity. This optical activity also was found to undergo a sign inversion around neutral pH.

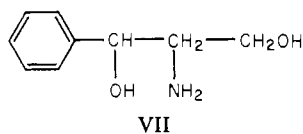
The pH trends are essentially identical with those just described for the phenylalkylamino acids. If *R*-V is used as the environment substance, then the CPL at low pH indicates that the Δ isomer is preferred as a result of the outer-sphere interaction. It was not possible to obtain *R*-VI, but *S*-VI led to enrichment of the solution in the Δ isomer. The dissymmetry factors obtained for the amino alcohols were somewhat smaller than those obtained at corresponding concentrations of amino acids, indicating that the degree of interaction is somewhat smaller for alcohol environment substances. The formation constants of the adducts are found to reflect this difference. Phenylglycinol is found to have an association constant of 1.78 in the low-pH region and 2.27 in the high-pH region, while phenylalaninol exhibits values of 2.62 (low pH) and 0.96 (high pH). The striking change in formation constants found for phenylglycine as the pH was raised is simply not observed for the corresponding amino alcohol.

Examination of the data reveals that the induced CPL of the phenylglycinol complex equals zero at pH 8.3, while that of the phenylalaninol adduct is zero at pH 7.2. These trends are opposite to those found for the amino acids, where the phenylglycine curve crossed zero at lower pH than the phenylalanine curve. These features clearly show that the associative mechanisms are fundamentally different in the two substrate classes. The $\text{p}K_a$ values for the ammonium groups

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in phenylglycinol and phenylalaninol are not available, but a variety of other amino alcohols are known to have $\text{p}K_a$ values ranging from 9.4 to 9.7.¹⁷ It is certain that the change in CPL line shape observed in Figure 4 must be due to ionization of the ammonium group on the environment substances, but the low-pH values at which this occurs indicate substantial promotion of this dissociation by the bound $\text{Tb}(\text{DPA})_3^{3-}$ complex.

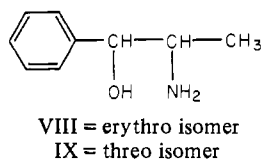
Replacement of one of the methylene protons of phenylalaninol by another hydroxyl group yields 2-amino-1-phenyl-1,3-propanediol (VII). Substrate VII is commercially



available as the *S,S* isomer. Addition of *S,S*-VII to a solution of $\text{Tb}(\text{DPA})_3^{3-}$ led to CPL spectra identical with those just described, but the pH dependence of this optical activity was found to be significantly different from that found for the closely related phenylalaninol substrate. In this system, no sign inversion is observed in the CPL spectra of the $^5D_4 \rightarrow ^7F_5$ transition as the pH is raised from 2 to 9. We do find that the CPL is lost by pH 9, indicating that deprotonation of the ammonium group is responsible for this loss of Pfeiffer optical activity.

With substrate VII, we find that the pattern of induced optical activity established with the simple phenylalkylamine substrates is repeated. We had noted earlier that the CPL induced by (*S*)-phenylethylamine or (*S*)-methylphenylethylamine was positive in sign, and we now find that the CPL induced by *S,S*-VII is also positive in sign. If we use the plateau values of the dissymmetry factors for calculation of the formation constant of the $\text{Tb}(\text{DPA})_3^{3-}/\text{S,S-VII}$ adduct, we find that a value of 7.75 is obtained.

For further investigation of this substitution effect, the CPL induced by (+)-norephedrine (VIII) and (-)-norpseudoephedrine (IX) was investigated. These two environment



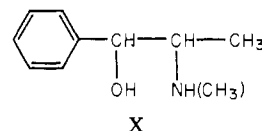
substances are merely the erythro and threo isomers of α -(1-aminoethyl)benzyl alcohol. Comparison of VII (which is also a threo isomer) and IX reveals that the latter substrate is obtained by replacing the terminal CH_2OH group by a simple methyl group. Substrate IX is obtained commercially as the *1R,1R* isomer, and substrate VIII is obtained as the *1S,2R* isomer.¹⁷ The substances were actually obtained as the hydrochloride salts, but we obtained identical results on the salt as on the free base (obtained by a neutralization procedure we have previously described²¹).

The CPL spectra exhibited by $\text{Tb}(\text{DPA})_3^{3-}/1R,1R\text{-IX}$ and $\text{Tb}(\text{DPA})_3^{3-}/1S,2R\text{-VIII}$ were found to follow essentially the same pH dependence as was found for substrate VII. The dissymmetry factors are pH independent between pH 2.5 and pH 6, and above this pH the optical activity decreases rapidly. No optical activity is noted once the pH reaches 9.5, and none is found above this pH. Knowing the approximate ionization constant of the ammonium group, we therefore believe this trend constitutes further proof that removal of the positive charge eliminates the driving force for the association of chelate and environment substance (at least for these benzyl alcohols).

As would be expected, the CPL induced by *1R,1R*-IX is always negative in sign and is opposite to that found if *1S,1S*-VII was used as the environment substance. The optical activity induced by the *1S,2R*-VIII substrate was found also to be negative in sign, indicating that for these benzyl alcohols the favored enantiomer of the $\text{Tb}(\text{DPA})_3^{3-}$ complex is selected by the absolute configuration of carbon-2. For substrates VII, VIII, and IX we can formulate a rule that, if the absolute configuration at carbon-2 is that of the *S* isomer, then the Δ isomer of $\text{Tb}(\text{DPA})_3^{3-}$ will be present in the larger excess.

Calculation of the formation constants for the adduct complexes by the usual methods yields a value of 6.97 for norephedrine and 2.03 for norpseudoephedrine. One would have expected the constant of the two threo isomers to be of similar magnitude, but the greater value obtained for substrate VII undoubtedly reflects the extra protection of the terminal hydroxyl group present on this substrate.

Further verification of this trend was obtained by using ephedrine (X) as the environment substance. This substrate

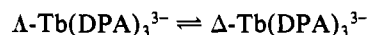


is available as the *D* and *L* isomers, the *D* isomer having the *1S,2R* configuration and the *L* isomer having the *1R,2S* configuration.¹⁷ The CPL spectra within the $^5D_4 \rightarrow ^7F_5$ band are never found to change sign as the pH is raised, and the curves are almost superimposable with those obtained for norpseudoephedrine. It was found that the CPL of *1R,2S*-X was positive in sign, while the CPL of *1S,2R*-X was always negative in sign. These trends confirm the earlier observation that, if the absolute configuration of carbon-2 was *S* in nature, then the Δ isomer of $\text{Tb}(\text{DPA})_3^{3-}$ was favored as a result of the association.

The formation constants of the adducts are found to be 2.01 for the *1R,2S*-X complex and 2.73 for the *1S,2R*-X adduct. This stereoselectivity has been noted before with the phenylalanine adduct complexes, but there it was the *R* isomer that formed the more stable adduct. These data show that the absolute configuration of carbon-2 not only determines the sign of the induced CPL but also affects the stability of the adduct; more stable adducts are formed when carbon-2 is of the *R* configuration.

Discussion

The results obtained in the present investigation are consistent with those of our earlier studies¹⁰⁻¹⁴ in which we established the associative mechanism as being responsible for the Pfeiffer optical activity in the $\text{Tb}(\text{DPA})_3^{3-}$ complex. These earlier studies required that some hydrogen-bonding mechanism was probably necessary to perturb the enantiomeric equilibrium



and this perturbation leads to the observed optical activity. Of greatest interest was our observation (obtained from an examination of the induced chirality caused by monoamino and diamino carboxylic acids of varying chain length) that a hydrophobic "pocket" exists between the DPA rings, and this site could provide extra stabilization for the adducts. The existence of a positive charge on the environment substance provided a driving force for the complex formation, and this force was assisted if the substrate contained a functionality capable of binding at the hydrophobic site.

It is quite clear from examination of the association constants obtained during the course of the present work (and shown in Table I) that the phenyl ring of the phenylalkylamino

acids must fit into the hydrophobic pocket of the $\text{Tb}(\text{DPA})_3^{3-}$ complex. The formation constants of the aliphatic amino acids¹⁴ are significantly smaller than those we report now, and this difference in bonding is most likely due to the extra stability brought about by the hydrophobic bonding. At the same time, we find that this hydrophobic bonding is not sufficient in itself to cause chelate/substrate binding (deprotonation of the simple amines causes loss of the optical activity) and that additional forces are necessary. These other binding forces appear to be associated with the ionic portion of the environment substances, and our previous NMR studies have shown that this region of the substrates is not close to the central lanthanide ion.¹⁴

All of the environment substrates studied in the present work can be grouped into four main classes, depending on their functionality and effect on the $\text{Tb}(\text{DPA})_3^{3-}$ complex. The first of these consists of the two simple amines, substrates I and II. With these substances, CPL is found when the ammonium group is protonated and lost when the ionization takes place. The *R* isomer of these amines always yields negative CPL in the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ Tb(III) band, which we take to imply the existence of an excess of the Δ isomer of the $\text{Tb}(\text{DPA})_3^{3-}$ complex. While the amine is protonated, the substrate contains a center of positive charge, and the ionic attraction between the positively charged environment substance and negatively charged Tb(III) complex provides a driving force of association. The phenyl ring then is able to slip into the hydrophobic site and enables extra stabilization of the adduct to take place. Deprotonation of the amine removes the ionic attraction and permits the adduct to dissociate.

The next substrate class consists of the amino alcohols and acids that contain one asymmetric atom: substrate III, V, XI, IV, VI, and XIV. With the *R* isomer of these environment substances, the CPL is found to be positive while the ammonium group is protonated and negative when it is not. Thus with these bifunctional substrates, it is the *S* isomer that yields $\Delta\text{-Tb}(\text{DPA})_3^{3-}$ while the ammonium group is protonated and not the *R* isomer, which had been the case for the simple amines. These trends clearly indicate that the bonding between chelate and substrate is fundamentally different in both cases. We propose that at pH values below the ionization point of the ammonium group, the substrate binds to the chelate through the usual ionic (ammonium group) and hydrophobic (phenyl ring) mechanisms and this bonding is assisted by further hydrogen bonding between the DPA rings and the carboxyl or hydroxyl functionality. The formation constants demonstrate that binding by the hydroxyl group is much weaker than binding by the carboxyl group, and we believe this observation would suggest involvement of solvent water in the bridging process. When the ammonium group is deprotonated, dissociation of the adduct need not occur as the hydrophobic bonding is still assisted by the carboxyl or hydroxyl hydrogen bonding. However, this bonding change apparently stabilizes the other enantiomer of the $\text{Tb}(\text{DPA})_3^{3-}$ complex, and we observe a complete CPL sign inversion in the $^5\text{D}_4 \rightarrow ^7\text{F}_5$ band. This new mode of bonding must be substantial, as the adduct is stable up to pH 11.5.

The last environment substance class consists of amino alcohol substrates containing two asymmetric atoms. Here, the CPL was found not to invert sign at neutral pH, correlated with the absolute configuration of the carbon binding the ammonium group, and disappeared when the ammonium group was ionized. These substrates behave like the simple amines in their pH trends, and it is also found that the *R* isomer (at carbon-2) leads to enrichment of the Δ isomer of $\text{Tb}(\text{DPA})_3^{3-}$. We believe that the hydroxyl group at carbon-1

must be involved in the bonding somehow; for otherwise the binding trends of 1S,1S-VII would have had to be the same as for phenylalaninol. For this class, the assistance provided by the hydroxyl at carbon-1 must not be highly significant, however, as the CPL is lost with deprotonation of the ammonium group.

To verify that all observed optical activities were indeed due to outer-sphere complexation, we undertook a study of changes within the hypersensitive absorption bands of the $\text{Ho}(\text{DPA})_3^{3-}$ complex. As observed in a previous study of this type,¹³ the spectra within the $^5\text{I}_8 \rightarrow ^5\text{G}_6$ transition of $\text{Ho}(\text{DPA})_3^{3-}$ were identical with those for $\text{Ho}(\text{DPA})_3^{3-}$ /substrate. Given the sensitivity of this band to environment, these results show that the nature of the complexation is predominantly outer-sphere.

Additional evidence that the chelate/substrate interaction was outer sphere in character was obtained by examining the reversibility of the observed changes in CPL with solution pH. It was found that with substrates I-X, the pH of the solution could be swept from very low to very high as many times as desired without substantially altering the luminescence properties. However, other substrates were found (e.g., tyrosine) where inner-sphere bonding was detected and the pH changes were totally irreversible. We will report on these other systems in a later publication.²²

The CPL exhibited by the Tb(III) ion is determined by the absolute configuration of the asymmetric atom on the substrate, but it is clear that other bonding modes (already discussed) dictate exactly which isomer of the Tb(III) complex will be favored. For the amino acid substrates (XII and XIII), the *S* isomer is found to lead to a greater concentration of $\Delta\text{-Tb}(\text{DPA})_3^{3-}$. On the other hand, with amino alcohol substrates (XV and XVI), it is the *R* isomer that yields $\Delta\text{-Tb}(\text{DPA})_3^{3-}$. We propose that the different modes of hydrogen bonding associated with the carboxyl and hydroxyl groups account for this difference.

Conclusions

In the present and earlier works¹²⁻¹⁴ we have presented evidence that the Pfeiffer effect in these 9-coordinate lanthanide complexes arises from the associative mechanism and that this mechanism can contain ionic, hydrophobic, and hydrogen-binding contributions. Unfortunately, the sign of the CPL cannot be used to infer the absolute configuration of the environment substance, as certain substrates are found to exhibit different signed optical activity as the solution pH is systematically varied. Certain limited correlations are possible, however, for a restricted functionality grouping on the environment substances. Given the extreme lability of the $\text{Tb}(\text{DPA})_3^{3-}$ complex, the Pfeiffer effect may be the only method whereby one can obtain the optical activity of this trigonal lanthanide complex in solution.

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Registry No. R-I, 3886-69-9; S-I, 2627-86-3; S-II, 51-64-9; S-III, 2935-35-5; R-III, 875-74-1; R-IV, 673-06-3; R-V, 56613-80-0; S-VI, 3182-95-4; 1S,2S-VII, 28143-91-1; 1S,2R-VIII, 37577-28-9; 1R,2S-IX, 492-41-1; 1S,2R-X, 321-98-2; 1R,2S-X, 299-42-3; R-XI, 22818-40-2; S-XIV, 5034-68-4; $\text{Tb}(\text{DPA})_3^{3-}$, 38682-37-0.

Supplementary Material Available: Figures 4-6, showing the pH dependence of the luminescence dissymmetry factors obtained in the interaction of $\text{Tb}(\text{DPA})_3^{3-}$ with substrates V-IX (4 pages). Ordering information is given on any current masthead page.

(22) Brittain, H. G.; Copeland, R. R.; Yan, F., unpublished results.