# Studies of the Pfeiffer Effect induced in Tris(pyridine-2,6-dicarboxylato)terbate(III) by Monosaccharide Aldose Sugars

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Optical activity has been induced in racemic mixtures of $[Tb(pydca)_3]^{3-}$ (pydca = pyridine-2,6-dicarboxylate) upon formation of outer-sphere complexes with monosaccharide aldoses, and studied by means of circularly polarized luminescence spectroscopy. No optical activity could be observed upon addition of D-glyceraldehyde to a solution of $[Tb(pydca)_3]^{3-}$, implying that the presence of a hemiacetal-ring oxygen is necessary for occurrence of the outer-sphere association. The sign of the induced optical activity was found to vary with the identity of the sugar used, but a correlation was established between the configuration at carbon 4 of the sugars (when these were present in the pyranose ring form) and the predominant $[Tb(pydca)_3]^{3-}$ enantiomer. This suggests that an association process does indeed lead to the observed Pfeiffer effects, and that the forces leading to the formation of the outer-sphere complexes are rather specific in nature.

It is well known that optical activity may be developed in racemic mixtures of labile metal complexes upon addition of certain chiral substances,[1,2] a phenomenon which has been termed the Pfeiffer effect. A variety of explanations have been advanced to account for the observed effects,[3,4] but most investigations have been satisfactorily explained with the assumption that some sort of outer-sphere association exists between the racemic metal complex and the chiral substance. In that case the enantiomeric interconversion associated with the racemic metal complex [equation (1)] is thought to be perturbed by the formation of diastereoisomers [equation (2)].

$$\Delta\text{-}[ML_3] \rightleftharpoons \Lambda\text{-}[ML_3] \qquad (1)$$

$$\Delta[ML_3] + \Lambda[ML_3] + 2B \rightleftharpoons \Delta\text{-}[ML_3B] + \Lambda\text{-}[ML_3B] \qquad (2)$$

An unequal diastereoisomer population then yields observable chirality. Since the association is outer sphere in nature, one may assume (to a first approximation) that the observed optical activity would correspond to that of the resolved metal complex. Thus, the Pfeiffer effect may be used to study the chirality of metal complexes too labile to be resolved by conventional means.

The study of chiral lanthanide compounds has lagged far behind analogous studies of chiral transition-metal compounds, which may be partially due to the extremely labile nature of the former compounds. Nevertheless, a careful choice of ligand environments can enable chiroptical studies.[5] The very weak intensities associated with the lanthanide *f–f* absorption bands hinders the use of circular dichroism as a useful chiroptical technique for these compounds, but circularly polarized luminescence (c.p.l.) spectroscopy has proved to be particularly effective in these studies.[5,6]

Only one Pfeiffer-active system has been identified thus far for lanthanide compounds, $[Ln(pydca)_3]^{3-}$ (pydca = pyridine-2,6-dicarboxylate (dipicolinate)]. These complexes are somewhat unique in lanthanide chemistry in that the metal ion experiences trigonal symmetry in the solid state [7] and that the $D_3$ symmetry is preserved in aqueous solution.[8] Each pydca ligand is known to bind lanthanide ions with such efficiency [9] that relatively few ligands (outside of the aminopolycarboxylates) are capable of displacing it. Thus far, it has been demonstrated that optical activity may be induced in aqueous solutions of $[Tb(pydca)_3]^{3-}$ and $[Eu(pydca)_3]^{3-}$ upon outer-sphere co-ordination with L-ascorbic acid,[10] resolved tris(ethylenediamine)chromium(III),[11] proline-type amino acids,[12] monoamino- and diamino-carboxylic acids,[13] phenylalkylamines, -alcohols, and -acids,[14,15] and tartrate substrates.[16]

One exceedingly interesting result to come out of the L-ascorbic acid study was the observation that no optical activity could be induced in $[Tb(pydca)_3]^{3-}$ once the hemiacetal ring was broken.[10] To study the nature of this interaction further, the Pfeiffer optical activity induced in $[Tb(pydca)_3]^{3-}$ by simple aldoses has now been examined in detail. The present study is somewhat unique in that it represents (to my knowledge) the first Pfeiffer-effect studies in which simple sugars have been used as the chiral substances.

## Experimental

The $[Tb(pydca)_3]^{3-}$ complexes were normally prepared by mixing stock solutions of $Tb^{III}$ and pyridine-2,6-dicarboxylic acid in a 1 : 3 mol ratio. The terbium(III) solution was prepared by dissolving a suitable amount of $Tb_4O_7$ in a very slight excess of 5 mol dm$^{-3}$ $HClO_4$ (requires boiling the solution for 1—2 h), neutralizing to pH 3 with NaOH, and then diluting to the desired volume. The pydca ligand was used as received from Aldrich, and the aldose sugars were obtained from Sigma. Aqueous stock solutions of the sugars were prepared by dissolution in water, and were allowed to equilibrate for at least 48 h before use. Prepared in this manner, the sugar substrates could be assumed to have reached conformational equilibrium. Several of the sugars were received as syrups, and these could only be removed from their containers as an aqueous solution. In all cases, the D-aldose sugars were used to induce the Pfeiffer effects.

All c.p.l. and total luminescence (t.l.) spectra were obtained on a medium-resolution spectrometer constructed in this laboratory. The $[Tb(pydca)_3]^{3-}$ complexes were excited at 295 nm, taking advantage of the fact that the ligand absorbs strongly at this wavelength and thus acts as an excellent sensitizer of terbium(III) luminescence. The emission spectra were analysed at 1-nm resolution by a 0.5-m grating monochromator. The t.l. and c.p.l. spectra were obtained in proportional arbitrary units, the t.l. intensity being given as in equation (3) and the c.p.l. intensity as in equation (4). The

$$I = I_L + I_R \qquad (3)$$

$$\Delta I = I_L - I_R \qquad (4)$$

unit dependencies of these quantities may be removed by computation of the luminescence dissymmetry factor [equation (5)]. The $g_{lum}$ factor is thus dimensionless, and may be taken

$$g_{lum} = \Delta I/0.5I \qquad (5)$$

as a measure of the degree of optical activity exhibited within a particular emission band. It was found that the t.l. intensity normally was not affected by the outer-sphere association of the $[Tb(pydca)_3]^{3-}$ complex and the sugars.

The pH of each solution was varied between 3 and 9 in increments of 0.5 pH units, with both the t.l. and c.p.l. spectra being recorded at each pH value. The solution pH values were determined on an Orion 701A pH meter, employing a glass microcombination electrode which could be directly inserted into the fluorescence cuvettes. The system was calibrated daily with standard phosphate and phthalate buffers.

## Results

Upon binding three equivalents of pydca, the emission intensity of $Tb^{III}$ is greatly enhanced through a sensitization process in which excitation energy is absorbed by the co-ordinated ligands and transferred non-radiatively to the metal ion.[17-19] The $[Tb(pydca)_3]^{3-}$ compound must be co-ordinatively saturated, as it has been shown that no water molecules are present in the inner sphere of the metal ion.[20] Nevertheless, it has been shown that a wide variety of materials bind to the outer co-ordination sphere of $[Tb(pydca)_3]^{3-}$,[10-16] and there appears to be no direct interaction between the terbium(III) ion and the substrate.

When these materials are chiral in nature, optical activity may be observed in all the $[Tb(pydca)_3]^{3-}$ emission bands corresponding to emission from the $^5D_4$ excited state to the various components of the $^7F_J$ ($J = 1$—6) ground state. The lineshapes of the t.l. and c.p.l. spectra invariably are of the same form, and these have never been found to be a function of the nature of the chiral material inducing the chirality. Thus, it may be contended that the c.p.l. lineshapes are characteristic of $[Tb(pydca)_3]^{3-}$ in a dissymmetric, trigonal environment. Thus, one may concentrate on the trends observed within a single terbium(III) emission band system, as the same trends must be duplicated in all other band systems. The $^5D_4 \longrightarrow {}^7F_5$ transition (centred around 545 nm) is known to exhibit the strongest t.l. and c.p.l. spectra,[21] and consequently all the work which shall be discussed in subsequent sections refers to this transition.

Addition of D-glyceraldehyde to a solution of $[Tb(pydca)_3]^{3-}$ did not yield any observable chirality, but optical activity was obtained upon addition of any one of the pentoses or hexoses derived from D-erythrose or D-threose (*e.g.* see Figure). A very interesting result was that even though D-sugars were used in all the studies, the induced c.p.l. was not always of the same sign. The intensity and sign of the major c.p.l. peaks (as measured by the luminescence dissymmetry factor) were not found to be functions of pH, at least between the limits of 3 and 8. Gradual degradation of the spectra did take place over extended periods of time, and is clearly related to the thermal and photochemical stabilities of the sugars, since the spectra obtained with the less stable sugars were found to degrade at significantly higher rates than those with more robust chiral substances.

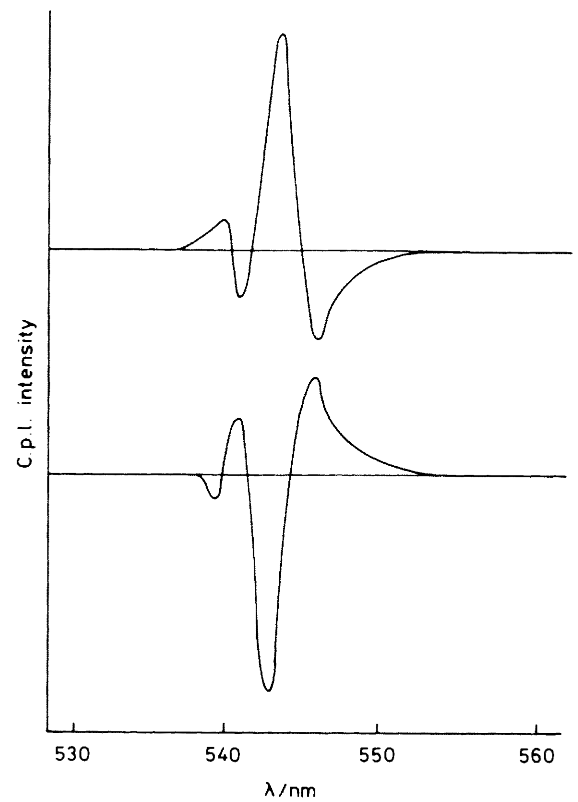


**Figure.** Circularly polarized luminescence spectra obtained within the $^5D_4 \longrightarrow {}^7F_5$ transition of 14 mmol dm$^{-3}$ $[Tb(pydca)_3]^{3-}$. The upper trace represents c.p.l. induced by D-glucose, and the lower trace that induced by D-galactose. The concentration of each sugar was 0.2 mol dm$^{-3}$, and each spectrum was obtained at pH 6.0

While the solution pH did not play an important role in determining the degree of observed optical activity, the concentration ratio of $[sugar]/[Tb(pydca)_3{}^{3-}]$ was found to influence the observed dissymmetry factors. Such an effect is anticipated on the basis of association equilibria of the form (6), with the corresponding equilibrium constant expressed as

$$[Tb(pydca)_3]^{3-} + sugar \rightleftharpoons [Tb(pydca)_3(sugar)]^{3-} \qquad (6)$$

$$K_1 = \frac{[Tb(pydca)_3(sugar)^{3-}]}{[Tb(pydca)_3{}^{3-}][sugar]} \qquad (7)$$

in equation (7). Complete formation of the $[Tb(pydca)_3]^{3-}$–sugar complex would be reflected in a limiting dissymmetry factor at some point in the concentration studies. Knowledge of that factor then would permit a calculation of the association constant for the outer-sphere complex *via* the methods outlined previously.[13]

Unfortunately, this type of limiting dissymmetry factor could not be reached with the Pfeiffer systems in the present work. Addition of extremely large excesses of sugars continued to yield proportionally larger dissymmetry factors, and eventually a different type of upper limit was placed on the induced chirality by the solubility of the sugar. These results are in sharp contrast to several earlier reports, in which it was noted that a limiting dissymmetry factor of ±0.022 (specifically for the 544-nm c.p.l. peak) could be reached *independent* of the nature of the chiral substance.[12-16] The observation that a limiting factor could not be reached with the sugar substrates implies that the outer-sphere interaction is considerably weaker than any of the Pfeiffer-active systems I have examined to date. With the assumption that ±0.022 represents the limiting dissymmetry factor for Pfeiffer optical activity induced in $[Tb(pydca)_3]^{3-}$, the association constants presented in Table 1 were calculated. C.p.l. data were obtained using a minimum of three $[sugar]/[Tb(pydca)_3{}^{3-}]$ ratios in order to

**Table 1.** Dissymmetry factors and formation constants associated with the $[Tb(pydca)_3]^{3-}$-aldose complexes *

| Sugar | $10^3 \times g_{lum}$ | $K_1$/dm$^3$ mol$^{-1}$ |
|---|---|---|
| D-Ribose (E) | +1.19 | 0.296 |
| D-Arabinose (E) | +1.31 | 0.345 |
| D-Xylose (T) | +1.28 | 0.320 |
| D-Lyxose (T) | +1.46 | 0.376 |
| D-Allose (E,R) | +1.34 | 0.324 |
| D-Altrose (E,R) | +1.29 | 0.312 |
| D-Glucose (E,A) | +1.31 | 0.347 |
| D-Mannose (E,A) | +0.69 | 0.165 |
| D-Gulose (T,X) | −3.36 | 0.900 |
| D-Idose (T,X) | −0.66 | 0.154 |
| D-Galactose (T,L) | −1.91 | 0.506 |
| D-Talose (T,L) | −1.29 | 0.312 |

* The dissymmetry factors were obtained from solutions of 15 mmol dm$^{-3}$ $[Tb(pydca)_3]^{3-}$ and 0.2 mol dm$^{-3}$ sugar. The formation constants were calculated assuming a limiting dissymmetry factor of ±0.022. For configurational correlations the pentose sugars may be thought of as being derived from either D-erythrose or D-threose, and the hexose sugars from one of the pentoses. The letters following the name of each aldose reflect the parentage of each sugar (E = D-erythrose, T = D-threose, R = ribose, A = arabinose, X = xylose, and L = lyxose).

obtain reproducible results. Dissymmetry factors measured for a given sugar concentration are also provided in Table 1 for reference, as well as configurational correlations for the various aldoses used as chiral substances.

**Table 2.** Configurational and conformational information associated with equilibrium solutions of the aldoses used in the Pfeiffer studies

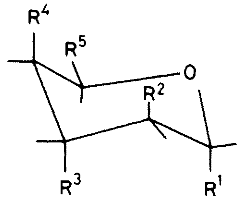
| Sugar | $R^2$ | $R^3$ | $R^4$ | $R^5$ | Furanose/ pyranose ratio | α/β Anomeric ratio of the pyranose isomers |
|---|---|---|---|---|---|---|
| D-Ribose | H | OH | H | OH | 0.32 | 0.36 |
| D-Arabinose | OH | OH | H | OH | 0.09 | 1.85 |
| D-Xylose | H | H | H | H | 0.00 | 0.59 |
| D-Lyxose | OH | H | H | H | 0.00 | 2.57 |
| D-Allose | H | OH | H | $CH_2OH$ | 0.14 | 0.26 |
| D-Altrose | OH | OH | H | $CH_2OH$ | 0.49 | 0.68 |
| D-Glucose | H | H | H | $CH_2OH$ | 0.00 | 0.56 |
| D-Mannose | OH | H | H | $CH_2OH$ | 0.00 | 2.13 |
| D-Gulose | H | OH | OH | $CH_2OH$ | 0.02 | 0.26 |
| D-Idose | OH | OH | OH | $CH_2OH$ | 0.47 | 0.84 |
| D-Galactose | OH | H | OH | $CH_2OH$ | 0.01 | 0.56 |
| D-Talose | H | H | OH | $CH_2OH$ | 0.45 | 1.38 |

## Discussion

The association constants corresponding to the formation of the outer-sphere adduct complexes are considerably smaller than many of those measured in earlier Pfeiffer studies involving $[Tb(pydca)_3]^{3-}$.[12–16] Generally, the presence of an aromatic ring and a positive charge on the chiral substance yield the largest degrees of optical activity.[14] In a study involving L-ascorbic acid considerably stronger Pfeiffer effects were noted, with an association constant of 12.5 dm$^3$ mol$^{-1}$ being calculated for the $[Tb(pydca)_3]^{3-}$–L-ascorbic acid complex.[10] This particular study is of relevance to the present work in that it was established that no Pfeiffer optical activity could be induced in $[Tb(pydca)_3]^{3-}$ once the hemiacetal ring of L-ascorbic acid was broken. This observation strongly suggests that the hemiacetal functionality of the aldose sugars also plays an important role in the outer-sphere complexation. Such a prediction was confirmed by the observation that no optical activity could be induced in $[Tb(pydca)_3]^{3-}$ by D-glyceraldehyde.

While it is clear that the presence of the hemiacetal ring is necessary for the observation of a Pfeiffer effect, the variable sign of the induced optical activity implies that other contributions to the observed effects are equally important. In most of the systems, the major c.p.l. component at 544 nm was found to be positive in sign, but with four of the hexoses a negative peak was observed. In previous work [13,16] it has been established that when considering the 544-nm component within the $^5D_4 \longrightarrow {}^7F_5$ terbium(III) transition the observation of a negative c.p.l. peak implies that the Δ isomer of $[Tb(pydca)_3]^{3-}$ is present in the largest amount.

Correlations involving the sign of the induced chirality must be made on the basis of solution-phase conformations of the aldoses (when these adopt the cyclic furanose or pyranose ring structures), and thus the conventional aldehydo sugar structures are of little help in this regard. However, this situation is not a problem, since n.m.r. studies performed on equilibrium mixtures have permitted the determination of all pertinent stereochemical information.[22] All of the pentoses and hexoses we have used exist in the pyranose ring form to at least 70%, and many of these contain less than 1% of the furanose isomers. Each system also contains an equilibrium mixture of α and β anomers, but the distribution of these is known as well.[22] This stereochemical information is summarized in Table 2, and employs the following numbering system:



Comparison of the stereochemical data in Table 2 with the c.p.l. results of Table 1 enables the final conclusions to be drawn regarding the nature of the $[Tb(pydca)_3]^{3-}$–sugar interactions. There is clearly no correlation between the sign of the c.p.l. and the α/β anomeric ratios. The only correlation which emerges is that when the hydroxyl group on carbon 4 is in an axial position (as it is in D-gulose, D-idose, D-galactose, and D-talose) the induced c.p.l. is negative in sign. On the other hand, when this hydroxyl group is in an equatorial position (as it is in D-ribose, D-arabinose, D-xylose, D-lyxose, D-allose, D-altrose, D-glucose, and D-mannose) the induced c.p.l. is positive in sign. It therefore seems quite clear that the interaction between $[Tb(pydca)_3]^{3-}$ and the aldoses involves the hemiacetal-ring oxygen and the hydroxyl group at carbon 4.

The variability in the observed c.p.l. intensities and computed formation constants indicates that the other hydroxyl groups provide further perturbations of the degree of outer sphere interaction. It is interesting that, almost without exception, corresponding pentoses and hexoses (*e.g.* D-xylose and D-glucose, or D-ribose and D-allose) have essentially the same affinity for $[Tb(pydca)_3]^{3-}$. This suggests that the additional $-CH_2OH$ group present in the hexose sugars does not play a significant role in the bonding. The magnitude of these association constants is comparable to those obtained in earlier work [13] in which highly branched amino acids were used as the chiral substances. These parallels suggest that the low degrees of interaction noted between $[Tb(pydca)_3]^{3-}$ and the aldose sugars originate from substantial steric interference (on the part of the sugar substrates) in the bonding process.

Much attention has focused in the past on the nature of the processes leading to measurable Pfeiffer effects.[3] The results obtained in the present and previous [10-16] studies have amply demonstrated that the detection of measurable induced optical activity in $[Tb(pydca)_3]^{3-}$ requires the formation of intermolecular complexes. Schipper [4] has found that the observed Pfeiffer effects are essentially determined by a balance between the racemization entropy favouring the racemate and the discrimination energy favouring the more stable enantiomer of the racemic metal complex. My work has shown that the discrimination energy may arise from a combination of hydrogen-bonding, hydrophobic, and electrostatic effects,[10-16] and that often combinations of these are needed to create strong Pfeiffer effects. In the present work it is quite likely that only hydrogen bonding between the sugar hydroxyl groups and the $\pi$-electron density of the pydca ligands contributes to the intermolecular association. In this respect, the attractive forces are comparable in nature to those already studied in the interaction of $[Tb(pydca)_3]^{3-}$ with L-ascorbic acid [10] and tartrates.[16]

A final note concerns the prediction of absolute configurations by means of the Pfeiffer effects. As mentioned earlier, the absolute configuration of the $[Tb(pydca)_3]^{3-}$ enantiomer predominantly present is predictable from the sign of the induced c.p.l. but great care must be exercised in such correlations. In fact, with diaminocarboxylic acids, the preferred enantiomer changes with the pH of the solution.[13] The results obtained with the lanthanide systems are in rather sharp contrast to those obtained with transition-metal complexes, where there is a correlation between the chirality of the environment substance and the preferred enantiomer of the metal complex.[2] These observations indicate that more work is required to detail further the nature of Pfeiffer effects in lanthanide complexes, and such studies are being actively pursued in this laboratory.

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