Temperature Study of the Solution Conformations of Aqueous Lanthanide(III) Complexes containing Monodentate Ligands

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The conformations of the 1 : 1 lanthanide(III)–antipyrine and –tetrafluorophenol complexes in aqueous medium are proposed not to change significantly over the temperature range 5—95 °C. Whilst the Ln^{3+}–antipyrine complexes contain the ligand only weakly bonded *via* a second-co-ordination-sphere interaction, the tetrafluorophenol ligand is proposed to be associated with Ln^{3+} *via* an inner-sphere interaction. Anomalous shift data for Tm^{3+}, Er^{3+}, and Tb^{3+} are interpreted in terms of the assumption of axial symmetry being invalid; such anomalous behaviour decreases with increasing temperature.

The nature of the observed dipolar shifts of ligand n.m.r. spectra using lanthanide ions as paramagnetic reagents has been frequently explored[1–4] but certain problems have not been thoroughly resolved. The outstanding questions concern (*i*) the averaging which occurs due to motion which frequently gives an apparent axial symmetry to the shift and (*ii*) the curious behaviour of one or two lanthanide reagents especially Tm^{III}.

In order to tackle these problems we have looked for ligands which can co-ordinate through one donor atom only so that the direction of one axis of the co-ordination sphere is defined. Ligands binding through such donor groups as carboxylate or phosphate, the most studied cases,[2–4] are obviously unsatisfactory in this regard. The most obvious choice of a ligand is one with a single oxygen-donor group but in general the ionisations of such enols or phenols mean that they do not give anions in sufficient concentration so as to give complexes in a pH range before the lanthanide cation hydrolyses. Such problems can be avoided by using organic shift reagents in organic solvents but it is our desire to use the lanthanide aqua ions in aqueous media, for example to study biological molecules. We have therefore chosen two ligands for investigation. The first, antipyrine, at 30 °C has already been shown[5] to bind in a peculiar manner in the second co-ordination sphere of the lanthanide ions and almost in the geometry of a π complex. The further investigation of this system over a range of temperatures is used in this paper to try to uncover the anomaly of the Tm^{3+} shifts. The second ligand we have chosen is tetrafluorophenol. This ligand is still simpler and has an axis of symmetry. We here used it in the hope that it would behave as a simple monodentate ligand, and in so doing would show, through the nature of the dipolar shifts, the character of the ligand field around Tm^{3+} which produces the well known anomalies. This system was also studied over a range of temperature.

Experimental

Antipyrine (2,3-dimethyl-1-phenyl-3-pyrazolin-5-one; Figure 1) was obtained from BDH, NaOD, DCl, and D_2O from Merck, and the lanthanide(III) oxides from Koch-Light. The lanthanide(III) chloride solutions (pH ≈ 5) were prepared as previously described.[6] 2,3,5,6-Tetrafluorophenol (tfp) was purchased from Sigma.

The ^1H n.m.r. spectra were measured on a Varian FT-80A spectrometer using sodium 3-trimethylsilylpropane-1-sulphonate as internal standard, ^{19}F n.m.r. spectra on a Bruker WH-90 spectrometer using trifluoroacetone as internal standard. The proton and fluorine-19 spin–lattice relaxation times (T_1) were measured using pulsed Fourier-transform techniques (180°–τ–90° sequence). The temperatures reported are those as set on the Varian and Bruker variable-temperature controller accessories of the n.m.r. spectrometers.

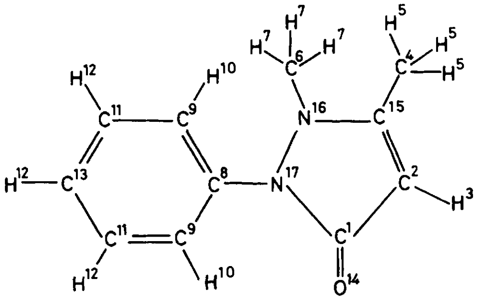

Figure 1. Numbering of atoms in antipyrine

Results

(*a*) *Antipyrine.—Shift studies at* 80 °C. The antipyrine proton resonances in the absence of lanthanide ions are not shifted by pH changes over the region 3.0 < pH < 6.5. Final solutions for n.m.r. measurements had pH values between 4.5 and 5.5 in the case of the Ln^{3+}-containing solutions.

The conformation of the antipyrine complexes at 80 °C was studied by using aqueous lanthanoid(III) ions (Ln = Pr, Nd, Eu, Tb, Dy, Ho, Er, Tm, or Yb) as ^1H n.m.r. shift probes. Titrations were performed at a constant antipyrine concentration (60 mmol dm^{-3}) with the concentration of Ln^{3+} being increased to up to five times in excess.

Using data and arguments[5] analogous to those offered for the interpretation of the results of the study at 30 °C, the following remarks concerning this study are made: (*i*) the exchange between the free and the bound ligand is fast on the n.m.r. time-scale; (*ii*) the Ln^{3+}–antipyrine complexes are weak; (*iii*) the data are all consistent with the statement that only 1:1 complexes are present; (*iv*) the diamagnetic-corrected lanthanide-induced shifts (l.i.s.; corresponding to Ln:antipyrine 1:1) are

Table 1. Experimental proton shift ratios for antipyrine (relative to C–CH_3 protons) for different lanthanide(III) ions at an Ln^{3+} : antipyrine ratio of 1 : 1 at 80 °C

Lanthanide	CCH_3 (H^5)	CH (H^3)	NCH_3 (H^7)	*o*-H (H^{10})	*m*- and *p*-H (H^{12})
Pr	100 ± 3.0	336.2 ± 4.7	127.0 ± 3.5	160.5 ± 4.7	−6.6 ± 0.4
Nd	100 ± 3.3	327.3 ± 8.5	130.2 ± 3.7	120.9 ± 2.8	−22.3 ± 1.0
Sm	100 ± 5.2	320.1 ± 16.1	115.2 ± 6.9	78.7 ± 6.2	−9.8 ± 3.7
Eu	100 ± 4.9	339.8 ± 16.3	154.0 ± 7.0	143.9 ± 8.1	−44.3 ± 2.1
Tb	100 ± 2.9	338.7 ± 9.4	102.1 ± 2.8	65.0 ± 1.9	−43.4 ± 1.0
Dy	100 ± 2.1	325.6 ± 7.8	122.6 ± 2.5	140.5 ± 2.7	−20.5 ± 0.4
Ho	100 ± 3.8	310.0 ± 8.0	114.9 ± 3.7	100.8 ± 3.0	−38.8 ± 1.0
Er	100 ± 3.9	327.0 ± 12.5	109.0 ± 4.0	78.5 ± 2.8	−54.0 ± 1.8
Yb	100 ± 2.6	259.2 ± 5.8	120.7 ± 3.2	121.4 ± 2.9	−46.2 ± 1.5
Tm	100 ± 4.3	270.6 ± 13.2	103.3 ± 4.2	15.7 ± 1.2	−89.8 ± 3.0

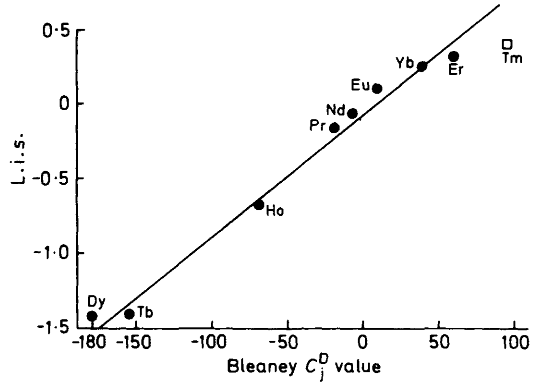

Figure 2. Diamagnetic corrected shifts of the NCH_3 (H^7) protons induced by different Ln^{3+} ions at a 1:1 ratio of antipyrine to cation; [antipyrine] = 60 mmol dm^{-3}

predominantly pseudo-contact in character; (*v*) observed shifts for Tm^{3+} alone deviate substantially from the linear plot of shifts against the Bleaney C_j^D values[7] (Figure 2); and (*vi*) Tm^{3+} shift ratios differ significantly from those of the other Ln^{3+} ions employed in this study (Table 1).

Separation of the contact and pseudo-contact contributions to the induced shifts of atoms close to the metal ion was effected using the method of Reuben and Elgavish.[8] However, because the results for Tm^{3+} were found to be anomalous, they were subsequently not used in the calculation of the pseudo-contact shift ratios to be used in the computerised search procedures. The combined results of all the metals excluding Tm^{3+} thus represent the antipyrine general case (Table 2).

Relaxation studies. Proton T_1 measurements were carried out as previously reported.[5] Tables 2 (for Gd^{3+}) and 3 (for Tm^{3+}) show all the relevant relaxation data expressed as ratios of $1/T_1$ values.

Association-constant study at 90 °C. The praseodymium–antipyrine association constant was determined as previously reported,[5] $K_{assoc.} = 0.81 \pm 0.05$.

Computerised search program: general case at 80 °C. The programs METALSEARCH and CRISTEP were used as previously described.[5] The five unknown spherical polar coordinates r, φ, ψ, α, and β were solved for using 10 experimental parameters, *i.e.* five proton shifts and five Gd^{3+}-induced proton relaxations. Table 4 shows the relevant data for the 'best' solution found for the antipyrine general case. Figure 3 is a stereoscopic view of the general lanthanide–antipyrine complex, together with the principal symmetry axis of the complex lanthanide ion.

Table 2. Proton dipolar shift and relaxation ratios for antipyrine at 80 °C [relative to CCH_3 protons (H^5)]: general case

Nucleus	Shift ratio	Relaxation ratio for Gd^{3+}
H^5	100 ± 9.3	100 ± 9.4
H^3	291.5 ± 39.0	1 044 ± 94
H^7	118.9 ± 10.9	97.5 ± 9.5
H^{10}	117.9 ± 14.5	323.9 ± 14.9
H^{12}	−35.9 ± 5.3	139.8 ± 10.4

Table 3. Relaxation ratios [relative to CCH_3 protons (H^5)] of Tm^{3+} for antipyrine

Nuclei	5 °C	30 °C	80 °C
H^5	100.0 ± 9.7	100.0 ± 5.0	100.0 ± 6.6
H^3	592.0 ± 11.0	718.5 ± 51.4	—
H^7	68.7 ± 7.0	78.3 ± 4.0	81.4 ± 11.6
H^{10}	224.0 ± 7.9	322.9 ± 18.8	443.6 ± 4.7
H^{12}	150.2 ± 9.2	135.7 ± 7.2	156.2 ± 5.8

Table 4. Experimental and calculated dipolar shift and relaxation ratios for the solution conformation of Ln^{3+}–antipyrine complexes at 80 °C (Ln = Pr, Nd, Eu, Tb, Dy, Ho, Er, or Yb)

	Dipolar shift ratio		Relaxation ratio		
Nucleus	Exptl.	Calc.	Exptl.	Calc.	Metal–nucleus distance (Å)*
H^5	100.0	100.0	100.0	100.0	5.7 (weighted)
H^3	291.5	286.0	1 044	626.1	4.5
H^7	118.9	113.2	97.5	79.8	6.7 (weighted)
H^{10}	117.9	124.2	323.9	393.7	4.8 (weighted)
H^{12}	−35.9	−36.4	139.8	106.8	5.9 (weighted)

* Values for O^{14}, C^1, C^2, C^{15}, N^{16}, and N^{17} are 3.7, 3.8, 4.4, 5.0, 4.9, and 4.3 Å respectively.

Shift studies from 5 *to* 95 °C. The temperature dependence of the induced shifts by Ln^{3+}, Ln = Pr, Tb, Dy, Ho, Er, Tm, or Lu, was studied over the temperature range 5—95 °C and at fixed Ln^{3+}: antipyrine ratios. For Lu^{3+} no change in the magnitude of the induced shifts was found. For all the other Ln^{3+} ions, the magnitude of the induced shifts increased linearly with increase in temperature; the correlation coefficients for the least-squares linear fits were in all cases better than 0.99. The data for Tb^{3+}, as an example of the more general behaviour of Ln^{3+}, and Tm^{3+} are presented in Tables 5 and 6 respectively.

Interestingly, some of the ratios of the induced shifts (relative to C–CH_3 protons) changed somewhat with temperature. In most cases they increased with increasing temperature (at the lower temperatures) eventually levelling off at an almost constant value at the higher temperatures. Further, plots of $\ln (R_T - R_\infty)$ against temperature in most cases were linear, where R_T is the shift ratio at a given temperature and R_∞ could be obtained for most cases by an iteration procedure (Tables 5—7). Comparison of the experimental proton shift ratios for antipyrine (relative to C–CH_3 protons) at lower,[5] intermediate (Table 1), and higher (Table 7) temperatures also clearly indicates that the antipyrine shift ratios for the various Ln^{3+} becomes more constant with increasing temperature.

Conformational study for Tb^{3+} *and* Tm^{3+} *from* 5 *to* 95 °C. Computerised search procedures were used to arrive at the most probable solution conformation of the Tb^{3+}–antipyrine complex using (*i*) the experimental l.i.s. of Tb^{3+} (Table 5) and/or (*ii*) the induced relaxation ratios of Gd^{3+} (Table 2). The ions Tb^{3+} and Gd^{3+} were taken to represent the more general behaviour of Ln^{3+} while axial symmetry was assumed. The conformations generated using (*a*) relaxation data only, or (*b*) relaxation data together with shift data, or (*c*) shift data only were very similar to that depicted in Figure 3.

The experimental shift ratios (Table 6) and the relaxation ratios (Table 3) induced by Tm^{3+} were similarly used to generate the most probable solution conformation of the Tm^{3+}–antipyrine complex. Conformations generated using Tm^{3+} shift data only were related to, but not necessarily similar to, that depicted in Figure 3. At lower temperatures the Tm^{3+} was placed substantially closer to the phenyl ring with the symmetry axis still passing through the heterocyclic ring of the antipyrine molecule, and making an angle of about 45° with the plane of the heterocyclic ring; in Figure 3 the same angle is about 90°. We consider that this difference between Tm^{3+} and the other Ln^{3+} structures is not real but due to the incorrect application of the assumption of axial symmetry to the Tm^{3+} case. The fact that relaxation data for Tm^{3+} and Gd^{3+} agree closely supports this conclusion strongly. We return to this analysis below.

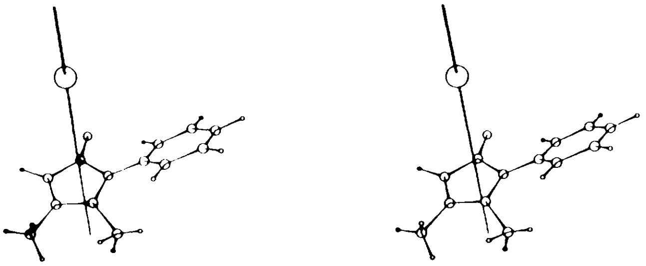

Figure 3. Stereoscopic view of the Ln^{3+}–antipyrine complex in aqueous solution. The symmetry axis is also indicated

(*b*) *Tetrafluorophenol* (*tfp*).—*Shift studies at* 37 *and* 77 °C. At 37 °C the proton and fluorine-19 resonances in the absence of lanthanide ions are shifted by pH changes over the region $3.0 < pH < 8.0$; the pK_a of tetrafluorophenol is about 5.55 based on n.m.r. pH titration data. The pH of all the final solutions for n.m.r. measurements was standardised at 5.0; under these conditions only some 22% of tfp is in the ionic form.

Table 7. Values of R_x for an Ln^{3+}–antipyrine ratio of 2.0:1

Lanthanide	H^{12}	H^{10}	H^3	H^7	H^5
Pr	−6.0	153.4	—	124.8	100.0
Tb	−29.1	129.5	331.0	—	100.0
Dy	−21.6	142.15	—	122.8	100.0
Ho	−32.85	121.5	282.4	118.4	100.0
Er	−39.3	103.4	—	110.0	100.0
Yb	−29.4	116.7	273.6	115.5	100.0
Tm	−57.6	52.4	333.5	101.5	100.0

Table 5. Temperature study at a Tb:antipyrine ratio of 2.08:1

Temp.	Shift changes					Shift ratios				
(°C)	H^{12}	H^{10}	H^7	H^3	H^5	H^{12}	H^{10}	H^7	H^3	H^5
5	—	−0.51	−1.74	−5.90	−1.75	—	29.1	99.4	337.1	100.0
25	1.09	−0.83	−2.07	−6.98	−2.08	−52.4	39.9	99.5	335.6	100.0
45	1.16	−1.22	−2.45	−8.23	−2.45	−47.4	49.8	100.0	335.9	100.0
65	1.24	−1.64	−2.82	−9.37	−2.80	−44.3	58.6	100.7	334.6	100.0
85	1.30	−2.09	−3.21	−10.53	−3.15	−41.3	66.4	101.9	334.3	100.0
95	1.32	−2.31	−3.40	−11.05	−3.31	−39.9	69.8	102.7	333.8	100.0
R_x						−29.1	129.5		331.0	

Table 6. Temperature study at a Tm:antipyrine ratio of 2.0:1

Temp.	Induced shifts					Shift ratios				
(°C)	H^{12}	H^{10}	H^7	H^3	H^5	H^{12}	H^{10}	H^7	H^3	H^5
5	−0.53	−0.26	0.36	0.32	0.27	−196.3	−96.3	133.3	118.5	100.0
15	−0.55	−0.20	0.44	0.57	0.37	−148.6	−54.1	118.9	154.1	100.0
25	−0.57	−0.16	0.52	0.85	0.46	−123.9	−34.8	113.0	184.8	100.0
30	−0.58	−0.16	0.55	0.98	0.50	−116.0	−32.0	110.0	196.0	100.0
35	−0.60	−0.11	0.63	1.18	0.58	−103.4	−19.0	108.6	203.4	100.0
45	−0.62	−0.04	0.71	1.54	0.68	−91.2	−5.9	104.4	226.5	100.0
55	−0.62	0	0.74	—	0.71	−87.3	0	104.2	—	100.0
65	−0.65	0.06	0.83	—	0.80	−81.3	7.5	103.8	—	100.0
75	−0.67	0.13	0.91	—	0.89	−75.3	14.6	102.2	—	100.0
85	−0.69	0.24	1.01	—	0.99	−69.7	24.2	102.0	—	100.0
95	−0.71	0.33	1.10	—	1.08	−65.7	30.6	101.9	(>250)*	100.0
R_x						−57.60	52.4	101.5	333.5	100.0

* Extrapolated by comparison with H^{12}.

Titrations were performed at a constant tfp concentration (44 mmol dm^{-3}) with the Ln^{3+} concentration being increased to up to eight times in excess; the aqueous lanthanide ions used were Pr^{3+}, Nd^{3+}, Eu^{3+}, Tb^{3+}, Dy^{3+}, Ho^{3+}, Er^{3+}, Tm^{3+}, and Yb^{3+}. Addition of solutions containing both Ln^{3+} and tfp at pH 5 to solutions of tfp at pH 5 did not effect a change in pH. However, addition of neat solutions of Ln^{3+} at pH 5 to solutions of tfp at pH 5 resulted in a decrease in the pH of the resultant solution.

Aqueous La^{3+} ions were used to make diamagnetic blank corrections to the induced shifts. These corrections for the proton shifts were less than 10% of the induced shifts in all cases. The diamagnetic corrections to the induced fluorine shifts were less than 30% for all cases except for Nd^{3+} and Eu^{3+}; the magnitude of the relatively small l.i.s. by Nd^{3+} and Eu^{3+} is comparable to that induced by La^{3+}.

The sharpness of the tfp spectra for the lanthanides Pr^{3+}, Eu^{3+}, and Tb^{3+} indicates that under all experimental conditions used the exchange between the free and the bound ligand is fast on the n.m.r. time-scale. The plots of diamagnetic-corrected induced shifts *vs.* lanthanide concentration were in certain cases linear, but in most cases slightly curved without, however, completely levelling off at the fully bound (limiting) shift value even at Ln^{3+} concentrations up to eight times in excess. It is thus concluded that the lanthanide–tfp complexes are very weak.

The diamagnetic-corrected l.i.s. used in this study is the fully bound (limiting) shift (Δ) calculated according to the method of Shapiro and Johnston.[9] The use of only a portion of the titration data produces l.i.s. (δ) corresponding to a Ln^{3+} : tfp ratio of 1:1 in solution. A comparison of the shift ratios generated using either δ or Δ is shown in Table 8 and indicates an acceptable agreement. The Shapiro and Johnston method[9] also generates the appropriate association constant values; the $K_{assoc.}$ values for 1:1 complexes, and other relevant data, are presented in Table 9. The constancy of the shift ratios for all Ln^{3+} except Tm^{3+} and Er^{3+} at 77 °C makes it extremely probable that only 1:1 complexes are present for the lan-

Table 8. Experimental ^{1}H and ^{19}F shift ratios for tetrafluorophenol (relative to the *para*-proton) for different lanthanide(III) ions at 37 °C. δ = shift ratio at Ln^{3+} : tfp of 1:1, Δ = fully bound shift ratio

	p-H	*m*-F		*o*-F	
Lanthanide	δ/Δ	δ	Δ	δ	Δ
Pr	100	47.7	53.7	135.3	146.6
Nd	100	36.1	41.7	37.9	45.7
Eu	100	106.1	103.2	71.1	67.1
Tb	100	31.1	59.7	92.8	129.7
Dy	100	87.1	73.8	258.9	216.0
Ho	100	44.3	53.8	167.6	180.6
Yb	100	37.6	46.0	51.1	60.2
Er	100	70.0	68.7	−24.7	−25.8
Tm	100	52.2	49.1	−154.3	−150.8

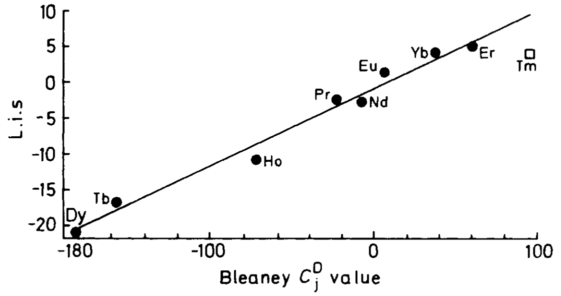

Figure 4. Diamagnetic-corrected shifts of the *para*-H induced by different Ln^{3+} at 77 °C

Table 9. Diamagnetic-corrected ^{1}H and ^{19}F shifts (△) and $K_{assoc.}$ values as generated by the Shapiro and Johnston method[9]

	37 °C			77 °C		
	Δ	Shift ratio	$K_{assoc.}$	Δ	Shift ratio	$K_{assoc.}$
Pr: H	−20.01	100.0		−3.07	100.0	
m-F	−10.74	53.7	0.32	−1.25	40.85	6.90
o-F	−29.34	146.6		−4.56	148.9	
Nd: H	−1.82	100.0		−2.10	100.0	
m-F	−0.76	41.7	1.97	−1.14	54.2	2.35
o-F	−0.83	45.7		−2.26	107.7	
Eu: H	2.76	100.0		0.96	100.0	
m-F	2.85	103.2	1.35	0.52	53.9	10.62
o-F	1.85	67.1		1.06	110.1	
Tb: H	−17.06	100.0		−16.63	100.0	
m-F	−10.18	59.7	5.4	−7.73	46.5	9.0
o-F	−22.12	129.7		−23.49	141.3	
Dy: H	−60.59	100.0		−21.07	100.0	
m-F	−44.69	73.8	2.35	−11.83	56.1	22.6
o-F	−130.9	216.0		−39.69	188.4	
Ho: H	−33.65	100.0		−10.65	100.0	
m-F	−18.09	53.8	1.25	−4.52	45.2	13.7
o-F	−60.76	180.6		−19.88	186.6	
Yb: H	9.74	100.0		3.53	100.0	
m-F	4.48	46.0	2.07	1.25	35.5	12.83
o-F	5.86	60.2		2.65	75.5	
Er: H	13.94	100.0		5.80	100.0	
m-F	9.57	68.7	—	3.07	52.8	—
o-F	−3.59	−25.8		1.10	18.9	
Tm: H	9.21	100.0		3.85	100.0	
m-F	4.52	49.1	—	1.73	45.0	—
o-F	−13.89	−150.8		−1.09	−28.3	
			K(mean) = 2.1 ± 1.6			*K*(mean) = 11.15 ± 6.3

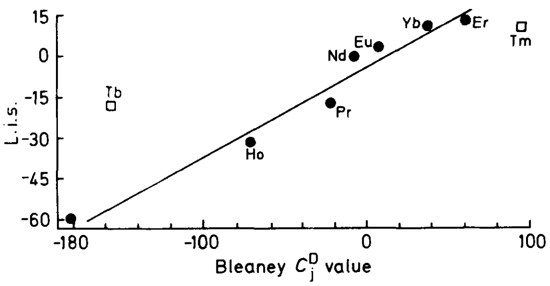

Figure 5. Diamagnetic-corrected shifts of the *para*-H induced by different Ln^{3+} at 37 °C

Table 10. Proton and ^{19}F dipolar shift ratios for tfp (relative to the *para*-hydrogen): general cases

Nucleus	Shift ratio 37 °C	 77 °C
p-H	100 ± 47.2	100 ± 16.9
m-F	53.2 ± 26.2	41.2 ± 8.9
o-F	118.9 ± 73.7	117.8 ± 33.9

Table 11. Proton and ^{19}F relaxation ratios for tfp (relative to the *para*-hydrogen)

Nucleus	Relaxation ratio 37 °C	 77 °C
p-H	100 ± 50.8	100 ± 58.2
m-F	143.5 ± 58.4	149.5 ± 72.4
o-F	1 682 ± 674	2 057 ± 876

Table 12. Experimental and calculated dipolar shift and relaxation ratios for the solution conformation of Ln^{3+}–tfp complexes (*a*) at 37 °C, Ln = Dy, Ho, Pr, Nd, Eu, or Yb; (*b*) at 77 °C, Ln = Dy, Tb, Ho, Pr, Nd, Eu, Er, or Yb

	Dipolar shift ratio		Relaxation ratio		
Nucleus	Exptl.	Calc.	Exptl.	Calc.	Metal–nucleus distance (Å)
(*a*) *p*-H	100.0	100.0	100.0	100.0	8.3
m-F	53.2	53.2	143.5	162.6	7.5 (weighted)
o-F	118.9	118.8	1 682	1 717	5.0 (weighted)
O	—	—	—	—	3.2
(*b*) *p*-H	100.0	100.0	100.0	100.0	7.8
m-F	41.2	41.5	149.5	164.8	7.1 (weighted)
o-F	117.8	118.0	2 057	1 997	4.6 (weighted)
O	—	—	—	—	3.0

thanides involved in this study. Even though the shift ratios at 37 °C are not so constant for the same Ln^{3+} it is nevertheless assumed that 1:1 complexes are present. The validity of this assumption will be discussed later.

Plots of Δ against the relative calculated pseudo-contact n.m.r. shift values (Bleaney C_j^D values[7]) at 77 °C are linear; the exceptions are Tm^{3+} (all nuclei) and Er^{3+} (*ortho*-F). Figure 4 illustrates this relationship for the *para*-H induced shifts. Figure 5 illustrates the equivalent case but at 37 °C. From the latter figure as well as Table 9 it is observed that (*i*) for Dy^{3+}, Ho^{3+}, Pr^{3+}, Eu^{3+}, Nd^{3+}, Eu^{3+}, Yb^{3+}, and Er^{3+} the plot at 37 °C is approximately linear, but it is a poorer fit relative to 77 °C, (*ii*) Tm^{3+} is the usual exception, and (*iii*) Tb^{3+} and Er^{3+} are additional exceptions compared to the antipyrine case.

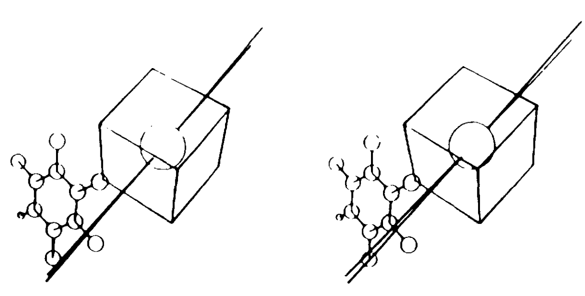

Figure 6. Stereoscopic view of the Ln^{3+}–tfp complex in aqueous solution. The water molecules in $[Ln(H_2O)_7L]^{2+}$ are not shown for clarity

It is proposed that the diamagnetic-corrected l.i.s. is predominantly pseudo-contact in character for all Ln^{3+}, including Tb^{3+}, Er^{3+}, and Tm^{3+} at both temperatures. The reason for the deviations of Tb^{3+}, Er^{3+}, and Tm^{3+} will be discussed later. It should also be noted that with increase in temperature Δ decreases in magnitude (Table 9).

Separation of the contact and pseudo-contact contributions to the induced shifts of atoms close to the metal was effected using the method of Reuben and Elgavish;[8] at 37 °C, the results for Tb^{3+}, Er^{3+}, and Tm^{3+} and at 77 °C, Tm^{3+} and Er^{3+}, were not used in the calculation of the pseudo-contact shift ratios to be used in computerised search procedures. The combined results for the metals that were used thus represent the tfp general cases (Table 10).

Relaxation studies. Proton T_1 measurements were carried out as previously reported[5] using Gd^{3+} as a relaxation probe at both 37 and 77 °C (Table 11). Relaxation data were not obtained for the other Ln^{3+} ions since in our experience they all behave similarly in this respect.

Computerised search program; general case at 37 *and* 77 °C. Table 12 shows the relevant data for the 'best' solution found for the tetrafluorophenol general case. Figure 6 is the resultant stereoscopic view of the cubic complex, $[Ln(H_2O)_7L]^{n+}$. The principal symmetry axis of the complexed lanthanide ion as generated by METALSEARCH and the C_4 axis of rotation of the cube are shown; the angle between the two axes is 8°. The water molecules are not shown for clarity.

Discussion

(*a*) *Antipyrine.—General case* (*excluding* Tm^{3+}) *at* 80 °C. This study has shown that the shift ratios of different nuclear resonances are less dependent on the lanthanide cation at 80 °C than at 30 °C; at 30 °C the shift ratios for the various lanthanides had been found to be approximately constant.[5] Further, the diamagnetic-corrected shifts do follow Bleaney's predicted pseudo-contact shift values (Figure 2). There is thus excellent reason[5] to assume that (*a*) the shifts have their origin in dipolar coupling, (*b*) the Ln^{3+}–antipyrine complexes are isostructural, and (*c*) the Ln^{3+}–antipyrine complexes have axial symmetry.

The specific conformation shown in Table 4 and Figure 3 represents the best fit to the experimental data bearing in mind the limitations associated with the computer search method as previously described;[5] the structure must be seen as an 'ensemble average' around a mean due to vibration and/or rotation. Effective axial symmetry is then again proposed to result from a free rotation of the ligand molecule about the symmetry axis shown in Figure 3. The fact that for this study the Ln–O(antipyrine) bond distance of 3.7 Å is less than the 4.0 Å found for the analogous study at 30 °C is not regarded as significant. All the atoms of the heterocyclic ring of the antipyrine molecule are still at a distance from the metal ion consistent with the proposal of one antipyrine ligand weakly bonded to the hydrated Ln^{3+} ion *via* a second-co-ordination sphere interaction.[5] The fact that there is no significant change in the antipyrine data, and thus the structure, in going from 30 to 80 °C means that we have one average electronic and geometric structure at both temperatures.

The Tm^{3+} *case.* Thulium(III) was found to become less anomalous with increasing temperature (Tables 6 and 7). The most dramatic illustration of the effect temperature has on Tm^{3+} is provided by the H^{10} protons. The apparent move, on average, of the H^{10} protons from outside the cone defined by $(3\cos^2\theta - 1)$ to the inside as temperature increases suggests (assuming axial symmetry) either a conformational change or a change in symmetry axis (or both) in the average Tm^{3+}–antipyrine structure. Given the very close similarity in properties of all the Ln^{3+} ions we reject these possible explanations and state rather that the Tm^{3+} ion fails to give rise to axial symmetry for some reason.

Effect of temperature on induced shifts. Theoretical treatments of the nature of induced shifts in n.m.r. spectroscopy by various authors differ in approach and conclusion, the most readily apparent difference being the temperature dependence predicted for the induced shift.[10] The pseudo-contact shifts are, however, expected to follow a predominantly T^{-2} dependency and the contact shifts a T^{-1} dependency;[3] the l.i.s. should thus decrease with an increase in temperature. For this study, in contrast, it was found that the l.i.s. was directly proportional to temperature! Because the solution n.m.r. experiments can be complicated by a variety of temperature-dependent processes including ligand exchange and stoicheiometric equilibria, it is proposed that such processes obscure the temperature dependence of the l.i.s. The association constant for the formation of the 1 : 1 Pr^{3+}–antipyrine complex at 90 °C was found to be 0.81 ± 0.05. At 30 °C a value of 0.2 ± 0.1 was reported.[5] As temperature, and consequently $K_{\text{assoc.}}$, increases, the fraction of bound ligand increases and the l.i.s. increases sufficiently to mask any decreases in l.i.s. the temperature change should have effected.

Effect of axial symmetry. It has been established that the l.i.s. observed in this study is predominantly pseudo-contact in origin. This pseudo-contact (dipolar) through-space shift, due to the paramagnetic ion, is given by equation (1)[4] where D'

$$\begin{aligned}\delta_{pc} &= \frac{D'(3\cos^2\theta - 1)}{r^3} - \frac{D''(\sin^2\theta\cos 2\varphi)}{r^3} \\ &= \text{Axial} \qquad\qquad - \text{Rhombic}\end{aligned} \tag{1}$$

and D'' can be related to ligand-field parameters (predominantly T^{-2} dependency) and r, θ, and φ are spherical co-ordinates of a nucleus relative to the metal as origin. This equation reduces to equation (2) in the case of either true or effective axial

$$\delta_{pc} = D'\frac{(3\cos^2\theta - 1)}{r^3} \tag{2}$$

symmetry.[3] As for the Ln^{3+}–antipyrine complex in solution at 30 °C, it is proposed that the present Ln^{3+}–antipyrine complexes (Figure 3) also have effective axial symmetry resulting from rotational averaging and ligand exchange. When the reduction of rhombic to effective axial symmetry is due to averaging by motions of ligands then the process should be temperature dependent and for such cases all lanthanide(III) ions should have effective axial symmetry at high temperatures. Thulium(III) does not fit this condition and it is proposed that even at 95 °C in aqueous medium the contribution of the rhombic term to the l.i.s. for Tm^{3+} is still observable; at 30 °C it is quite significant. It is thus concluded that there are extra problems associated with Tm^{III} which are not associated with cationic size only.[5,11a] This observation will be discussed again later. In conclusion the study of the antipyrine case has not solved the problem mentioned in the Introduction.

(*b*) *Tetrafluorophenol.*—Since the pH of tfp solution decreases upon addition of Ln^{3+} ions, it is proposed that it is the phenoxide ion, rather than the tfp molecule, which binds to Ln^{3+}. Equilibrium calculations using the pK_a of tfp and $K_{\text{assoc.}}$ substantiate this proposal. It is also proposed that the aromatic ring is flipping rapidly since the two aromatic *ortho* fluorines possess the same resonance frequency; the same also applies to the two aromatic *meta* fluorines.

The general case (*excluding* Tm^{3+} *at* 77 °C *and excluding* Tm^{3+}, Er^{3+}, and Tb^{3+} *at* 37 °C). It is proposed that the same reasons as those described in the antipyrine case at both 30 and 80 °C apply to the tfp system such that (*a*) the l.i.s. has its origin in dipolar coupling and (*b*) the Ln^{3+}–tfp complexes are isostructural and have axial symmetry.

The specific conformation shown in Table 12 and Figure 6 again represents the best fit to the experimental data at both 37 and 77 °C. Whilst bearing in mind all the previous limitations mentioned concerning the interpretation of any static model of a complex's conformation in solution, we have to realise further that the tetrafluorophenol molecule suffers an additional limitation compared to antipyrine; it is smaller than antipyrine with fewer moieties that can act as unique structural and n.m.r. reference points. We thus believe that the data in Table 12, together with Figure 6, should only be used to infer, for example, that: (*i*) the Ln^{3+}–tfp conformation in solution does not change significantly with a change in temperature; (*ii*) the bonding of tfp to Ln^{3+} is of a more classical co-ordination nature compared to the bonding of antipyrine to Ln^{3+}; the angle between the plane of the tfp molecule and the metal *via* the oxygen atom is 167°; and (*iii*) the Ln^{3+}–tfp interaction is stronger than that of antipyrine with Ln^{3+}; the greater $K_{\text{assoc.}}$ values for Ln^{3+}–tfp, the shorter proposed Ln^{3+}–O bond distance for tfp, and the fact that the titration plots are curved (not linear as for antipyrine) support this proposal.

The average inner-sphere water co-ordination number of rare-earth-metal ions in aqueous solution is taken as eight[5] and it is further assumed that $[Ln(H_2O)_8]^{3+}$ has an average cubic structure. If $[Ln(H_2O)_7(C_6F_4HO)]^{2+}$ also has an essentially cubic structure, then 'average' axial symmetry arises with fast ligand exchange since all eight co-ordination sites are equally occupied on the n.m.r. time-scale. To a good approximation the data are in accord with the structure depicted in Figure 6.

The Tm^{3+}, Er^{3+} *and* Tb^{3+} *cases.* Whilst all three of these metals are exceptions to the general case at 37 °C, only Tm^{3+} and Er^{3+} remain the exceptions at 77 °C. For the last two metals it is, however, observed that with an increase in temperature from 37 to 77 °C the l.i.s., and thus the shift ratios, change substantially towards that which would be expected of a general/normal Ln^{3+} ion. The change in shift ratios with temperature could again be due to (*i*) a conformational change and/or, (*ii*) a change in the symmetry axis or, (*iii*) the assumption of axial symmetry being invalid.

It is proposed that the latter argument should be used to explain the exceptional behaviour of Tm^{3+}, Er^{3+}, and Tb^{3+} With an increase in temperature all three metal ions assume axial symmetry; Tb^{3+} first, then Er^{3+}, and finally Tm^{3+}. When the ligand is loosely associated with Ln^{3+}, *e.g.* antipyrine, only Tm^{3+} appears not to be an effective axial symmetry case. When the ligand is more strongly associated with the Ln^{3+} ion, *e.g.* tfp, then Tm^{3+}, Er^{3+}, and Tb^{3+} appear not to be effective axial symmetry cases. This is also true of complexes of carboxylate and phosphate ligands. The problems we face are thus not resolved using monodentate axial ligands.

Thulium(III) has the longest electron-spin relaxation time,

τ_S, of all Ln^{3+} and τ_S of this aqua-ion has the largest temperature dependence.[11b] This anomaly of Tm^{3+} has again been associated[11c] with the 4*f* core of the cation, *i.e.* in larger ligand-field splitting energies of Tm^{3+} compared to those of the other Ln^{3+} ions. Similarly, the nature of the internal splittings of the *f* levels of Tm^{3+} is proposed to be associated with the anomalous behaviour reported above.

In summary we have tried to find an explanation for the different behaviour of some Ln^{3+} ions as probes of structure by using ligands which should have but one donor atom. The structure of the antipyrine complexes did not meet this requirement but that of the tetrafluorophenol did. The anomaly of the Ln^{3+} shifts in the case of Tm^{3+} remained! We shall, however, consider the anomalous Ln^{3+} in more detail in a future paper.

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