Origin of Lanthanide Nuclear Magnetic Resonance Shifts and Their Uses

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Summary Series of experimental data on the n.m.r. line shifts of nuclei in ligands bound to lanthanide cations are presented; the agreement between the observed shifts and those predicted by a new theoretical treatment is excellent, and a procedure for the use of the lanthanides in structural studies, as aqueous cations or in shift reagents is outlined.

Recently we have advocated the use of lanthanide cations in the determination of structures of molecules in solution using n.m.r. spectroscopy.[1,2] The procedure is based upon the study of the effect of lanthanide cations, bound to specific groups in an organic molecule, upon position (shift) and half-height width (broadening) of n.m.r. lines followed by an extensive computer-based search for molecular conformations which match the spectroscopic data. The equation used for line broadening has been checked by reference to a known structure.[1] As there was uncertainty about the absolute origin of the line shifts we used ratios of shifts of different resonances. In this paper we give experimental justification for our shift equation based upon a new theoretical treatment.

A detailed theory of n.m.r. line shifts in ligands bound to lanthanides has been submitted for publication.[3] Rather than ascribing dipolar (psuedo-contact) shifts in a lanthanide complex to anisotropic g factors,[4,5] as has been done for transition-metal ions,[6] the new theory accounts for the shifts in solution from anisotropy in the susceptibility arising in less than cubic geometries. At room temperature the g values for lanthanide complexes are isotopic. For an axially symmetric complex the fractional shift in a nuclear resonance frequency of a nucleus of a bound ligand is given[3] by equation (1), where the symbols have their usual meanings.

$$\Delta\nu/\nu_0 = \beta^2/[60(kT)^2] \times [(3\cos^2\theta - 1)/r^3] \times 2A_2^0 \langle r^2\rangle \times g^2 J(J+1)(2J-1)(2J+3)\langle J\|\alpha\|J\rangle \qquad (1)$$

The right hand side of the equation is divided into four factors which are considered in order. The collection of constants in the first factor includes the absolute temperature, T, and varies as T^{-2} instead of T^{-1}. The angular and distance dependence of the second factor is the same as that found for anisotropic g factors[6] in axially symmetric complexes so that comparisons within a complex (or among complexes of similar structure) made using this assumption remain valid. We shall assume in this communication that the crystal-field coefficients of the third factor remain constant for a given complex throughout the lanthanide series.[7] That these coefficients may change sign upon change of symmetry of a complex furnishes a reason in addition to angular dependence for sign reversals of chemical shifts on going from one series of lanthanide complexes to another (see Table).

Relative n.m.r. shifts of ligands bound to lanthanides

	Theory[d]		Experiment[a,b]			
Ln^{3+}	Last term of eqn.	With excited states[b]	$Ln(dpa)_3^{3-}$	$Ln(oda)^+$	$Ln(cmp)^{2+}$	$Ln(dpm)_3P$
La	0	0	0	0	0	0
Ce	−6·6	−6·3				
Pr	−11·4	−11·0	−13	−14·9	−8·2	+20
Nd	−4·5	−4·2	−7·6	−5·6	−3·0	+9·5
Pm	+2·4	+2·0				
Sm	+0·5	−0·7	−1·3	−0·7	−0·2	+2·4
Eu	0	+4·0	+12	+13·4	+5·1	−10
Gd	0	0[c]	not observed			
Tb	−87	−86	−92	−92	−50	+91
Dy	−100	−100	−100	−100	−100	+100
Ho	−39	−39	−51	−30	−42	+71
Er	+33	+33	+31	+38	+16[e]	−27
Tm	+53	+53	+64	+61	(+10[e])	−70
Yb	+22	+22	+23	+26	+12[e]	−33
Lu	0	0				

[a] Scaled to 100 for Dy^{3+} where a minus sign indicates downfield (p.p.m.). [b] At room temperature. [c] Higher-order effects may lead to dipolar shifts.[3] [d] The theory gives only relative not absolute signs. The signs in columns 2 and 3 are chosen to agree with column 4. Reasons for change of sign are given in the text. [e] The low value of the shift in these particular complexes will be discussed in detail in a later paper.

The quantity in the last factor of the equation has been tabulated for all tripositive lanthanides[3] and the results are presented in the second column of the Table where the values are scaled to −100 for Dy^{3+}. Because only ground states have been considered at this point, the predicted value for Eu^{3+} ($J = 0$) is zero.

It is known that Sm^{3+} and Eu^{3+} have low-lying excited J states. A more refined theory[3] has included interaction terms involving excited states for all the lanthanides and the results are listed in the third column of the Table. Refined values in the third column differ from those in the second column by only a few percent except for Sm^{3+}, where the sign is reversed, and Eu^{3+}, where inclusion of the thermally populated states ($J = 1$) results in a predicted non-zero shift with a maximum value at very low temperatures.[3]

Provided that the structure of a lanthanide complex with a given ligand and the crystal-field coefficient are constant throughout the series, it is possible to compare the predictions of the refined new theory in the third column of the Table with results for several types of ligands in the succeeding columns. The fourth column of the Table lists results for the tris-complexes of the inflexible ligand 2,6-dipicolinate (dpa).[8] The close agreement between theory and experiment extends to more flexible ligands such as oxodiacetate (oda) and cytidine-5′-monophosphate (cmp), where the lanthanide is bound solely at the protonated phosphate group. Included in the last column of the Table are the relative shifts for the 2-hydrogen of a 4-vinylpyridine adduct of tris(dipivaloylmethane) (dpm) lanthanide(III) complexes.[9] The exact correlation of the relative signs for different metal ions between the theoretical prediction in the third column and all experimental results along with the close agreement in magnitudes suggest strongly that the theory accounts for the chemical shifts in principal detail.

Knowing the origin of the lanthanide n.m.r. shifts we can see immediately the conditions which constrain their use in studies of structure. Before listing such conditions we stress that if only a 'spread-out' spectrum is desired, as the expression *shift-reagent* implies, then there can be no objection to using any reagent in any desired manner.[5] However for conformational conclusions to be put on a firm basis it is essential that observed spectral shifts should be shown to have arisen through an interaction which quantitatively relates shift with the space co-ordinates of the nucleus under study.[2] We know of few cases in the literature where the appropriate experimental procedures have been followed. Examination of the above equation indicates that the following procedure is satisfactory.

(1) Lanthanide 'reagents' which shift to both high and low field must be used.

(2) The observed shifts must be corrected by observing shifts due to complex formation with diamagnetic lanthanides, La^{3+} and Lu^{3+}.

(3) Ratios of shifts at different proton sites should then be compared for the different lanthanides so eliminating effects due to changes in A_2^0. If these ratios are independent of the lanthanide cation then the shifts have their origin in dipolar coupling, and, to a good approximation, the anisotropy of the susceptibility has axial symmetry.

(4) In general the dependence of the shift ratios on the concentration of lanthanide and its ligand must be followed so that the stoicheiometry of the complex is proved.

(5) A computer search for the best fit of the n.m.r. shift data to a structure presents obvious advantages. The search should include positioning of the metal ion and the orientation of the magnetic axis.

(6) The search can best be made if data from line broadening or relaxation times are also incorporated as the line-broadening depends upon $1/r^6$, using Gd^{3+} as a relaxation probe.

It may well be the case that the computer will fail to find a solution. In such a case the temperature dependence of the shift ratios should be examined for the shift data could arise through an averaging of the shifts of a molecule which had several configurations in thermal equilibrium. If there is more than one possible binding site for metal ion attachment then the position of the metal ion must be ascertained using the computer search.

The line broadening in the case of fast exchange will be anisotropic as there is a contribution to $1/T_2$ from the total shift which is itself anisotropic. Thus only the broadening due to metal cations which give isotropic broadening, Gd^{3+} and Eu^{2+}, can provide useful structural information. Provided that shift and relaxation data are shown to be consistent with a structure there can be little danger that this structure is incorrect.

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