A Multisite Model for Lanthanide Shift Reagent Coordination to Monofunctional Substrates. Effects of Rotational and Site Averaging on Shifts and Relaxation Rates

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Abstract: The shifts and line broadenings induced by various Ln(fod)$_3$ shift reagents in the proton spectrum of pinacolone, $(CH_3)_3CCOCH_3$, are analyzed using an approach which combines a two-site model for lanthanide coordination to the carbonyl group with several methods for averaging over internal rotations of the methyl and *tert*-butyl groups within the substrate. The applications of all possible combinations of three rotational averaging schemes (free rotation, restricted rotation, and averaging along the axis of rotation) to evaluate the geometrical parameters for the dipolar shift and relaxation indicate that combinations containing the latter scheme cannot be used satisfactorily to simulate the data. At present, it is difficult to ascertain which of the other combinations is most satisfactory, since all generate similar results. As might be expected from steric considerations, lanthanide binding to the carbonyl takes place at the site nearer the methyl group. The simultaneous application of both shift and relaxation rate data to derive information concerning the shift reagent-substrate complex removes many of the ambiguities present if only one kind of data is employed. Details are given of the approach to the data analysis and the interpretation of the results.

The formation of complexes between lanthanide shift reagents (LSR) and organic molecules bearing lone pairs of electrons (substrates) has been rationalized on the basis of Lewis acid-Lewis base interactions.[1] In such paramagnetic complexes, the electron-nuclear interactions are manifested in two changes in the NMR spectra of the nuclei within the substrate molecule: chemical shift perturbations and enhanced relaxation rates.[2] A large portion of the efforts invested in shift reagent research has been directed at developing computational models, which relate the shift perturbations to some "average" LSR-substrate complex.[3,4] Several strategies for utilizing both the shifts and the relaxation rate enhancements to determine an average LSP-substrate structure have also emerged.[5] In virtually all of these approaches it is tacitly assumed that the central lanthanide ion occupies a unique position in space relative to the substrate molecule. Typically, this position is found by systematically varying the coordinates of the metal atom and assessing the agreement between the observed and calculated shifts until a "best fit" position is reached.[3c,6] More elaborate methods, which incorporate rotation around the lanthanide donor-atom bond in the LSR-substrate complex, have also been suggested.[7-9] The results of such computational schemes are reported as a set of coordinates for the lanthanide atom relative to the donor atom in the substrate along with an agreement factor for the shift data.[6] While the fit of the shift data is satisfactory (agreement factors of 5-10%), the lanthanide atom positions are not always in accord with x-ray crystallographic data or simple chemical intuition.

In general, for substrates containing atoms which bear more than one lone pair of electrons, there are strong chemical reasons to anticipate that more than one coordinating position exists. Specifically, in considering substrates containing carbonyl groups, there is evidence that the assumption of a unique metal position is suspect. Lanthanide-oxygen distances ranging from 1.9 to 3.2 Å have been reported from NMR studies[10,11] while Ln-O distances ranging from 2.4 to 2.6 Å have been obtained by x-ray crystallography.[12,13] Recent preliminary attempts to test the assumption of a unique lanthanide position have led to the conclusion that this assumption may not be valid.[14] Moreover, the molecular-orbital description of the carbonyl bond places the two lone pairs of electrons on the oxygen in geometrically equivalent positions. In formaldehyde, e.g., the two lone pairs are in the plane of the formaldehyde molecule at 55.5° from the carbon-oxygen bond axis.[15] Therefore, it may be more reasonable to treat the carbonyl group as having two distinct sites for coordination of an LSR molecule. For symmetrical ketones, the two sites should be equivalent. Since differences in steric hindrance have been shown to cause differences in LSR binding to different sites in polyfunctional substrates,[4] in nonsymmetrical ketones, differences in binding between the two lone-pair sites might be anticipated. Comparisons between observed and calculated shifts or relaxation rates induced by LSR's will have physical significance only if the calculated values are obtained by averaging the two sites according to their relative populations. In addition, if the substituents on the carbonyl group are subject to internal rotation, averaging of this internal motion must also be considered.

In a previous communication,[16] we have reported a method for determining relaxation parameters from the line broadenings induced by LSR's in the proton spectrum of pinacolone, $(CH_3)_3CCOCH_3$. Reported here is a computational model which analyzes both the shifts and relaxation rates in terms of the geometry of the LSR-pinacolone complex considering the populations in the two lone-pair sites. Various methods for averaging the methyl and *tert*-butyl group rotations are also presented.

Computational Approach

It has been shown[7,17] that LSR-induced shifts in general obey the axially symmetric form of the dipolar shift equation:

$$\delta = K(3\cos^2\theta - 1)/r^3 \qquad (1)$$

where δ is the observed shift perturbation, K is a constant which depends on the electronic quantum states of the individual lanthanide, r is the internuclear distance between the central lanthanide ion and the nucleus being observed, and θ is the angle between the vector r and the principal magnetic axis of the lanthanide complex. The dipolar relaxation equation, which can be used[16] to analyze the limiting line broadenings caused by lanthanides, is[18]

$$1/T_{2M} = Cf(\tau)/r^6 \qquad (2)$$

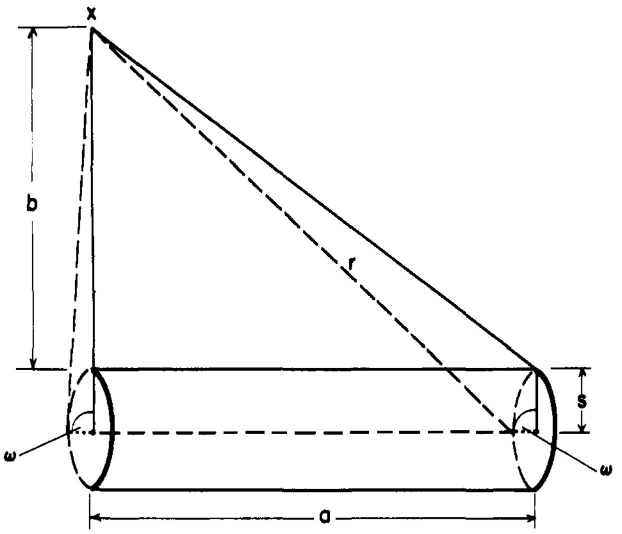

Figure 1. The physical model employed for the averaging procedures.

where $1/T_{2M}$ is the relaxation rate of the nucleus in the paramagnetic complex, C is a constant which depends on the lanthanide ion, $f(\tau)$ is a function of correlation times, and r has the same meaning as in eq 1.

Rotational Averaging. The quantities $[1/r^3]_{av}{}^2$ and $[(3\cos^2\theta - 1)/r^3]_{av}$ were calculated for the simulation of relaxation rate and shift data, respectively.[19] In all of the cases, the *tert*-butyl group was treated by first taking the average position of the protons in each methyl group along the methyl axis of rotation and then averaging for the rotation around the carbon-carbonyl bond by one of the methods described in this section.

Consider the general problem of calculating the average of the quantity $1/r^3$ where r is the distance from a point X in space to a point on a rotating circle as shown in Figure 1. After rotation through ω radians, r^2 is given by

$$r^2 = a^2 + (b + s)^2 + s^2 - 2b(b + s)\cos\omega \qquad (3)$$

where all the symbols are defined in Figure 1. For free rotation (a nonweighted average of all the points on the circle), $[1/r^3]_{av}$ is given by

$$[1/r^3]_{av} = \frac{1}{2\pi}\int_0^{2\pi} \mathrm{d}\omega/(r^2)^{3/2} \qquad (4)$$

The integral in eq 4 was numerically evaluated for both the methyl and *tert*-butyl groups using the trapezoidal rule. An expression for the function $[(3\cos^2\theta - 1)/r^3]_{av}$ was derived in a manner similar to the one described by Armitage et al.[8a] It was integrated over the same limits as in eq 4 and the integral evaluated numerically using again the trapezoidal rule.

Examination of a space-filling model of pinacolone indicates that restricted rotation of both the methyl and the *tert*-butyl groups must also be considered. The preferred rotamer, from considerations of the model, seems to be the one in which the methyls of the *tert*-butyl group form dihedral angles of $\pi/3$, π, and $5\pi/3$ radians with the carbonyl bond. In this rotamer the protons of the methyl group form dihedral angles of 0, $2\pi/3$, and $4\pi/3$ radians with the carbonyl bond. Accordingly, the functions $[1/r^3]_{av}{}^2$ and $[(3\cos^2\theta - 1)/r^3]_{av}$ were evaluated for this rotamer as well. For the purpose of comparison, an average of each group was taken along its axis of rotation and the same quantities calculated from these two points.

Two-Site Model. A model for lanthanide binding to the carbonyl group is shown in Figure 2. All of the above described averaging procedures were performed for each site on the carbonyl. The subscripts 1 and 2 are introduced to refer, respectively, to the side nearer the methyl, and to the one remote from it. The population in site 1 is defined as P_1. The population in site 2 is given by $1 - P_1$. The symbols δ_m and δ_t are defined as the calculated values of $[(3\cos^2\theta - 1)/r^3]_{av}$ for the methyl and *tert*-butyl groups, respectively, and D_m and D_t are the calculated values of $[1/r^3]_{av}{}^2$ for the two groups, respectively. The ratio (methyl to *tert*-butyl) between the experimentally observed shift should thus obey the relation

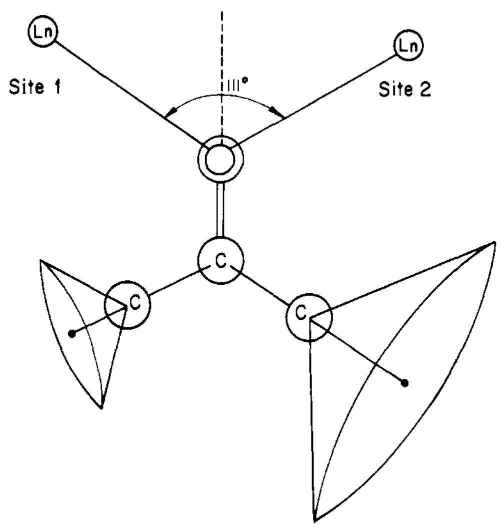

Figure 2. A graphical description of the two-site computational model used in simulations of shift and relaxation data for the various LSR-pinacolone complexes, with the methyl on the left and the *tert*-butyl on the right.

$$R_{\delta,\mathrm{obsd}} = \frac{(1 - P_1)\delta_{m2} + P_1\delta_{m1}}{(1 - P_1)\delta_{t2} + P_1\delta_{t1}}. \qquad (5)$$

Similarly, the observed ratio (methyl to *tert*-butyl) of the relaxation rates should obey the relation

$$R_{D,\mathrm{obsd}} = \frac{(1 - P_1)D_{m2} + P_1D_{m1}}{(1 - P_1)D_{t2} + P_1D_{t1}} \qquad (6)$$

The calculated values of $[(3\cos^2\theta - 1)/r^3]_{av}$ and $[1/r^3]_{av}$ for the two groups are functions of the lanthanide-oxygen distance, d, while the quantities $R_{\delta,\mathrm{obsd}}$ and $R_{D,\mathrm{obsd}}$ are experimentally determined. Therefore, for each distance, d, values of P_1 can be calculated using eq 5 and 6.[20] Curves can now be constructed of the site population, $P_{\delta1}$, determined from eq 5 and P_{D1}, and the site population determined from eq 6, as functions of d. For each lanthanide, the two curves should intersect at a common d, at which point $P_{\delta1} = P_{D1}$. In this way, it should be possible to determine the two-site populations as well as the lanthanide-oxygen distance for each LSR-pinacolone complex.

Results and Discussion

For convenience, we denote the various methods of averaging as FR for free rotation, RR for restricted rotation, and AV as the average along the axis. The numerical values for the averages of the functions calculated with d = 3.0 Å are compiled in Table I. It is clear from Table I that the various quantities vary considerably depending upon the method of averaging used. The most striking difference is observed in the function $[(3\cos^2\theta - 1)/r^3]_{av}$ for the *tert*-butyl group taken from site 2. This quantity not only has different magnitude but may also have a different sign. In addition, as could be anticipated the function $[1/r^3]_{av}{}^2$ varies by more than an order of magnitude depending upon the site from which it is evaluated.

The experimentally observed shift and relaxation rate ratios are summarized in Table II. In all of the cases where the AV method was employed in conjunction with any of the other

Table I. A Comparison of the Values of the Geometrical Functions[a] Obtained from the Various Methods of Rotational Averaging

	Method of averaging	$[1/r^3]_{av}^2$ Methyl	$[1/r^3]_{av}^2$ *tert*-Butyl	r Methyl	r *tert*-Butyl	$[3\cos^2\theta - 1/r^3]_{av}$ Methyl	$[3\cos^2\theta - 1/r^3]_{av}$ *tert*-Butyl
AV	Site 1	2.59×10^{-4}	1.33×10^{-5}	3.96	6.50	10.60×10^{-3}	5.42×10^{-3}
	Site 2	3.46×10^{-5}	2.11×10^{-4}	5.54	4.10	10.50×10^{-3}	3.04×10^{-3}
FR	Site 1	3.53×10^{-4}	1.87×10^{-5}	3.76	6.14	7.83×10^{-3}	7.28×10^{-3}
	Site 2	2.89×10^{-5}	4.79×10^{-4}	5.71	3.58	9.96×10^{-3}	-6.66×10^{-3}
RR	Site 1	3.09×10^{-4}	1.87×10^{-5}	3.85	6.14	7.57×10^{-3}	7.29×10^{-3}
	Site 2	2.89×10^{-5}	7.98×10^{-4}	5.71	3.29	9.95×10^{-3}	-12.4×10^{-3}

[a] r is in units of Å.

Table II. The Observed Shift and Line-Broadening[16] Ratios for LSR-Pinacolone Complexes

Lanthanide[a]	Shift ratio[b]	Line-broadening ratio[b]
Pr	1.62	2.9
Ho	1.54	3.0
Dy	1.63	3.1
Yb	1.45	2.6

[a] The LSR used were the Ln(fod)$_3$ chelates. [b] All ratios are reported as the ratio of methyl to *tert*-butyl at 27 °C. These ratios were measured at 90 MHz on a Bruker HFX-10. For the Yb and Pr ratios, a maximum LSR/pinacolone concentration ratio of 2.5 was reached (the pinacolone concentration was ~0.2 M). For the other two lanthanides a maximum concentration ratio of around 1.0 was reached. Over these ranges, the shift ratio was found to be independent of LSR concentration. The experimental uncertainties are of the order of ±2 and ±10% for the shift and line-broadening ratios, respectively.

Table III. Lanthanide-Oxygen Distances and Site Populations Obtained from the Shift and Relaxation Rate Enhancement Ratios

Lanthanide	Method of averaging CH$_3$	Method of averaging *tert*-butyl	P_1	d, Å
Pr	FR	FR	0.81 ± 0.02	2.82 ± 0.06
Ho			0.82 ± 0.02	2.85 ± 0.06
Dy			0.83 ± 0.02	2.90 ± 0.06
Yb			0.79 ± 0.02	2.60 ± 0.06
Pr	FR	RR	0.88 ± 0.01	2.82 ± 0.04
Ho			0.89 ± 0.01	2.92 ± 0.04
Dy			0.90 ± 0.01	3.10 ± 0.04
Yb			0.86 ± 0.01	2.75 ± 0.04
Pr	RR	FR	0.84 ± 0.02	3.25 ± 0.06
Ho			0.85 ± 0.02	3.00 ± 0.06
Dy			0.86 ± 0.02	3.18 ± 0.06
Yb			0.81 ± 0.02	2.73 ± 0.06
Pr	RR	RR	0.94 ± 0.01	3.40 ± 0.04
Ho			0.94 ± 0.01	3.30 ± 0.04
Dy			0.95 ± 0.01	3.45 ± 0.04
Yb			0.93 ± 0.01	3.10 ± 0.04

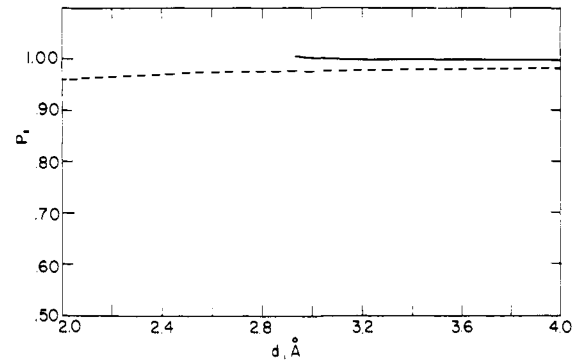

Figure 3. The variation of the site population, derived from shift data (solid line), $P_{\delta 1}$, and relaxation data (broken line), P_{D1}, with the lanthanide-oxygen distance, d, for the Dy-pinacolone complex using the AV and FR methods of averaging the rotations of the methyl and *tert*-butyl groups, respectively.

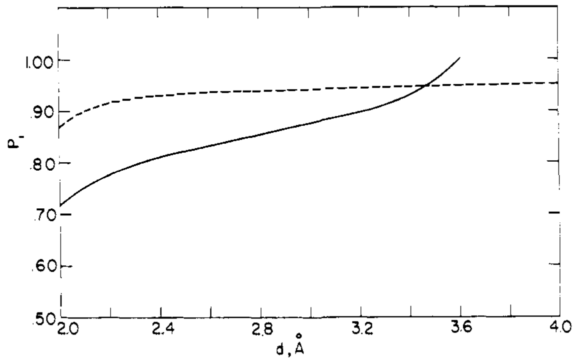

Figure 4. The variation of site population derived from shift data (solid line), $P_{\delta 1}$, and relaxation data (broken line), P_{D1}, with the lanthanide-oxygen distance, d, for the Dy-pinacolone complex using the RR method of averaging the rotations of both the methyl and *tert*-butyl groups.

methods, using the two-site approach, curves of the population against d of the type shown in Figure 3 were obtained. In these cases, the two curves do not intersect but only approach each other to within 1-3% for the range of distances 3.0-4.0 Å. In this particular range neither curve is sensitive to d. In the cases where an averaging process other than AV was employed, curves of the type shown in Figure 4 were obtained. These curves intersect at only one point, for distances between 2.6 and 3.4 Å, depending upon the method of averaging and the observed ratios employed. As can be seen in Figure 4, $P_{\delta 1}$ is now a very sensitive function of d resulting in a rather sharp intersection with P_{D1}. Curves such as the ones shown in Figure 4 were constructed using all sets of data of Table II. The site populations and distances for each set obtained by applying the various computational procedures are summarized in Table III. It is clear that within the series of lanthanides, the distances and site populations are in good agreement for each method of averaging. Moreover, the distances within each series vary in accordance with the trend expected from consideration of the lanthanide ionic-radius contraction. Since no clear-cut distinction between the methods of averaging can be made at this time, it is difficult to ascertain which approach is the most appropriate. However, the fact that all of the schemes employing the AV method do not give as satisfactory results (see Figure 3) as other schemes indicates that for groups which may be free to rotate, more sophisticated methods than the AV method might be called for in the analysis of shift and relaxation data. Of course, more elaborate schemes combining various methods for averaging of individual methyl group rotation within the *tert*-butyl group may also be devised. However, such schemes can be expected to yield results that will qualitatively parallel the ones presented here.

A search for a unique metal position was carried out for all of the data presented in Table II employing combinations of the methods of averaging. This search was made with the lanthanide–oxygen bond oriented in the plane of the two lone pairs of electrons as shown in Figure 1, at angles of between 0 and ±55° to the carbonyl-bond axis. In general no such unique position could be found, which would simultaneously conform to both the shift and the relaxation data. The behavior of the praseodymium complex is typical. Using the RR method of averaging for both groups, a fit for the shift data was found at a distance of 2.1 Å at 15° toward the methyl group. For this position, the calculated relaxation data fits to within ±10% of the observed values. The relaxation data gave a position with a distance of 3.1 Å at an angle of 20° toward the methyl group. For this position, there was now a 10% discrepancy between the calculated and observed shift values. The only exception to this trend was observed for the ytterbium complex in conjunction with the application of the FR method of averaging for both groups. In this particular case an Yb–O distance of 4 Å was obtained, oriented at 18° toward the methyl group. Good fits of shift data for oxygen-containing substrates with LSR's have been reported.[2] For unsymmetrical ketones,[9,10] these fits are for unique positions which resemble the one obtained now for praseodymium. However, it is clear from the above discussion that these unique positions may in fact be fictitious. We suggest that a more rigorous way of arriving at LSR–substrate geometries is by the simultaneous fitting of both shift and relaxation data along the lines presented here.

Conclusions

The multisite approach should be applied in analyzing LSR data for substrates containing atoms with more than one lone pair of electrons; e.g., the carbonyl group should be treated as having two sites for LSR coordination. The population in each site is sensitive to steric effects of the substituents. In simulation of the shift or relaxation data from LSR experiments, appropriate rotational averaging must be carried out for substrates where rotation can occur. The simultaneous application of both shift and relaxation rate data to derive information concerning the LSR–substrate complex removes many of the ambiguities present if only one kind of data is employed.

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(19) The relaxation rate due to dipolar interaction is normally given by the square of local field components modulated by reorientation processes with a correlation time τ_c. The local field is proportional to $1/r^3$. If r can assume a range of values an average has to be taken. The average of $1/r^3$ has to be taken when the averaging process is fast compared to τ_c, since an average local field is established before reorientation has taken place. If the averaging process is slower than τ_c, the average of $1/r^6$ has to be computed since in this case relaxation occurs at different local fields. In choosing to calculate $[1/r^3]_{av}{}^2$ we have assumed that internal rotation is the fastest process.

(20) Note that for eq 5 or 6 to be valid the mean residence time at each site has to be short compared to the reciprocal of the chemical shift or of the line-width differences between the two sites.

Conformational Studies of 1,3-Dienes

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Abstract: The relative energies of trans, cis, and gauche conformers of butadiene, glyoxal, and acrolein and their fluoro-, chloro-, and cyano-substituted derivatives have been investigated using single determinant ab initio molecular orbital theory. In all cases the s-trans conformer was found to be the most stable form. The second stable isomer is either s-cis (acrolein and its derivatives, glyoxal itself) or gauche (substituted glyoxals, butadiene, and substituted butadienes). The fluctuations of the cis-trans energy difference and the tendency of the cis form to distort away from planarity are rationalized by perturbationally building up the π-orbital manifold of the various molecules from the π MO's of their constituent fragments.

The most stable conformer of butadiene,[2] acrolein,[3] and glyoxal[4] is planar s-trans. With a few exceptions[5] this rule also holds for the mono- and disubstituted parents of these three basic dienes.[6-8] The second stable conformer, when sufficiently close above the trans form so as to make its experimental detection possible, appears to s-cis,[4,7b,d-g] s-cis or gauche,[2f,7g,h] or gauche.[2f,8a-d] Three questions therefore arise: Are electronic effects responsible for the s-trans form being generally the most