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LANTHANIDE SHIFT REAGENTS. A NOVEL METHOD FOR FITTING THE PSEUDOCONTACT SHIELDING EQUATION TO EXPERIMENTAL INDUCED SHIFTS

J.W. ApSimon and H. Beierbeck
Department of Chemistry, Carleton University, Ottawa K1S 5B6, Canada

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It is generally accepted[1-9] that chemical shifts induced by lanthanide shift reagents are predominantly or entirely due to a dipolar shielding mechanism. Assuming axial symmetry[10] the dipolar shifts Δ_i are given by the McConnell-Robertson equation (1)[11] where C is a proportion-

$$\Delta_i = C(1 - 3\cos^2\theta_i)/R_i^3 \tag{1}$$

ality constant, R_i is the vector from the metal to the i'th nucleus and θ_i is the angle between the principal axis of the chelate and R_i. The principal axis of the complex is usually taken to be colinear with the metal-ligand bond[12]. Structural information is extracted from the induced shifts by fitting the pseudocontact equation (1) to the experimental Δ_i, usually by incremental variations of the proportionality constant C and the lanthanide metal coordinates[1-6].

In this communication we describe a data fitting algorithm using Newton's method[13] where Δ_i is expanded in a Taylor series in C and in the metal coordinates x, y, and z, truncating after the linear terms (equation 2).

$$\begin{aligned}\Delta_{in+1} = \Delta_{in} &+ (\partial\Delta_i/\partial C)_n\,(C_{n+1} - C_n) + (\partial\Delta_i/\partial x)_n\,(x_{n+1} - x_n)\\ &+ (\partial\Delta_i/\partial y)_n\,(y_{n+1} - y_n) + (\partial\Delta_i/\partial x)_n\,(z_{n+1} - z_n)\end{aligned} \tag{2}$$

The deviation between experimental and calculated induced shifts is minimized by the iterative linear least squares optimization of the new variables $(C_{n+1} - C_n)$, $(x_{n+1} - x_n)$, $(y_{n+1} - y_n)$, and $(z_{n+1} - z_n)$.

The chemical shifts of the substrate nuclei, measured after successive addition of aliquots of shift reagent stock solutions, are plotted against the sums of the shifts in each spectrum[14]. The experimental induced shifts Δ_i(exp) used in the calculations are the slopes in these plots, scaled to a value of 10 ppm for the fastest moving signal. The substrate structure is defined in terms of cartesian coordinates. Starting values for the lanthanide metal coordinates are conveniently obtained by specifying a substrate nucleus which, together with the hetero-atom on the substrate, defines a vector pointing to a likely metal position. For instance, the point on the vector C(7) - O, 3 Å from oxygen, served as starting point in the case of borneol. Signals which cannot be identified by their appearance are assigned by comparison with induced shifts predicted with the starting parameters.

The optimization of the parameters begins by evaluating the coefficients in equation (2) with the starting parameters C_1, x_1, y_1, z_1. Least squares optimization of the new variables $(C_2 - C_1)$, $(x_2 - x_1)$, $(y_2 - y_1)$, $(z_2 - z_1)$ gives a new set of parameters C_2, x_2, y_2, and z_2. The coefficients in equation (2) are reevaluated with these parameters and the next set C_3, x_3, y_3, and z_3 is obtained, etc. The calculations are terminated when the $(C_{n+1} - C_n)$ etc. drop below preset limits.

Fig. 1 shows the initial and optimized lanthanide metal positions, relative to the substrate, for the $Pr(fod)_3$ and $Eu(fod)_3$ complexes of borneol and iso-borneol. The present results for the borneol/$Pr(fod)_3$ complex are in satisfactory agreement with those in reference 1 (Fig. 1). The choice of the starting parameters is not critical. Convergence to the best values is rapid (table 1) even if the initial lanthanide location is 2 Å or more from the best position. Typically five or six iterations are necessary, requiring only fractions of a minute of computer time.

The values predicted for the 2n and 2x hydrogens, geminal to the hydroxyl group, are in good agreement with the observed lanthanide induced shifts (table 2). Exclusion of the geminal hydrogens from the calculations did not cause any significant changes in either the predicted shift for the other nuclei or the metal-oxygen distances. The lanthanide-heteroatom bond lengths appear to be too long, as noted by other workers[1].

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Table 1. Iterative optimization of the proportionality constant C in the pseudocontact equation (1) and of the lanthanide metal coordinates x, y, and z for the complex borneol/Pr(fod)$_3$.

Iteration	C[x1000]	x	y	z	R^a	error^b
0	-1.00	2.29	1.99	-4.90	3.00	0.901
1	-0.40	1.47	2.68	-4.67	2.92	0.215
2	-0.54	0.94	3.50	-4.44	3.28	0.070
3	-0.54	1.33	3.31	-4.43	3.13	0.039
4	-0.53	1.28	3.29	-4.41	3.09	0.038

a. R = metal-oxygen distance

b. error = $\sqrt{\Sigma[\Delta_i(\text{exp}) - \Delta_i(\text{calc})]^2/\Sigma\Delta_i(\text{exp})^2}$ (ref. 5)

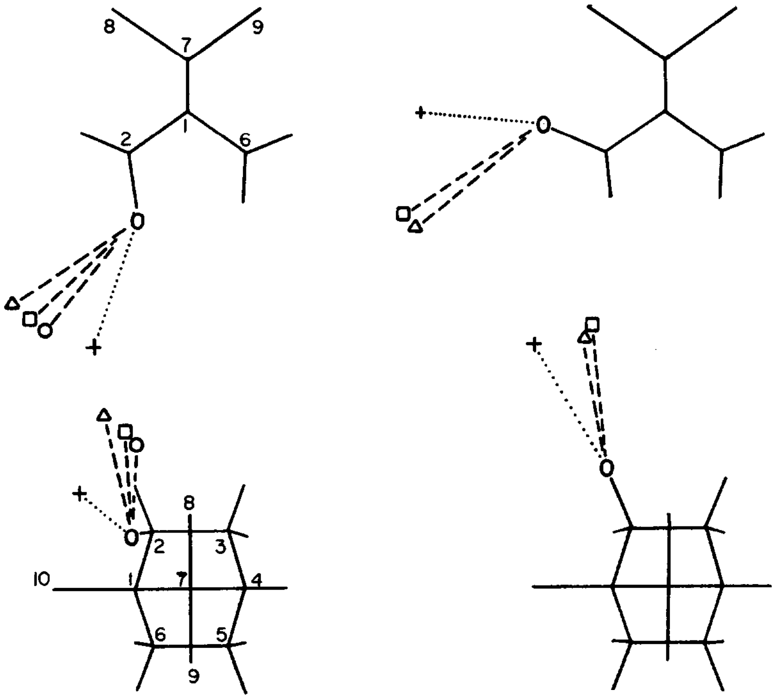

Fig. 1. Initial (+) and optimized metal locations relative to the substrate for the Pr(fod)$_3$ (□) and Eu(fod)$_3$ (△) complexes of borneol (left) and iso-borneol (right). Results of calculations with the experimental data in reference 1 for the borneol/Pr(fod)$_3$ complex are included for comparison (○).

Table 2. Experimental and calculated relative lanthanide induced shifts for the complexes of borneol and *iso*-borneol with $Eu(fod)_3$ and $Pr(fod)_3$. For nuclei whose signals were incompletely resolved only predicted values are given.

	2n/x	3n	3x	4	5n	5x	6n	6x	Me-8	Me-9	Me-10
					borneol/$Eu(fod)_3$						
exp.	10.00	6.64	3.27	2.11	3.48	2.20	6.52	-	1.67	1.52	3.45
calc.	9.95	6.78	3.33	1.91	3.69	2.24	6.56	3.09	1.61	1.62	2.97
					borneol/$Pr(fod)_3$						
exp.	10.00	7.31	3.55	-	3.90	2.08	7.30	3.23	1.79	1.68	3.86
calc.	9.95	7.42	3.45	1.97	3.86	2.33	7.36	3.36	1.89	1.78	3.34
					iso-borneol/$Eu(fod)_3$						
exp.	10.00	3.48	7.00	2.27	-	1.75	2.65	-	4.11	1.81	4.12
calc.	9.98	3.62	6.99	2.21	1.63	1.50	2.46	1.97	4.39	1.94	3.92
					iso-borneol/$Pr(fod)_3$						
exp.	10.00	3.84	7.59	2.40	1.93	1.81	2.59	2.05	4.49	1.87	4.39
calc.	10.01	3.90	7.53	2.34	1.81	1.63	2.71	2.13	4.69	2.06	4.15

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