

## 혼합 란탄족 Shift Reagents

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## Mixed Lanthanide Shift Reagents

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요약. 란탄족 화합물인  $\text{Ln}(\text{fod})_3$  ( $\text{Ln}=\text{Pr}$ ,  $\text{Nd}$ ,  $\text{Eu}$  및  $\text{Yb}$ )를 사용하여 contact-only (COM) 및 dipolar-only (DOM) 2 성분계 혼합물을 만든 후 기질인 4-picoline의  $F_i$  및  $G_i$  값을 핵자기공명 이동으로부터 측정하였다. 그 결과  $\text{Pr}(\text{fod})_3$  및  $\text{Eu}(\text{fod})_3$ 의 혼합물인 COM 1 및 DOM 1으로 얻은 값들을 단일  $\text{Ln}(\text{fod})_3$ 로 얻은 값들과 잘 일치 하였다. 그러나  $\text{Nd}(\text{fod})_3$  및  $\text{Yb}(\text{fod})_3$ 의 혼합물인 COM 2 및 DOM 2로 얻은 값들을 단일  $\text{Ln}(\text{fod})_3$ 로 얻은 값들과 상당한 오차를 나타내었다. 그 오차는 이테르븀( $\text{Yb}$ ) 착물에 기인하는 것으로 추정되었다.

**ABSTRACT.** Contact-only (COM) and dipolar-only (DOM) mixtures of the lanthanide shift reagents were prepared based on the  $F_i$  and  $G_i$  values deduced using individual  $\text{Ln}(\text{fod})_3$  ( $\text{Ln}=\text{Pr}$ ,  $\text{Nd}$ ,  $\text{Eu}$ , and  $\text{Yb}$ ), and 4-picoline. The  $F_i$  and  $G_i$  values obtained directly by COM 1 and by DOM 1, which were appropriate mixtures of  $\text{Pr}(\text{fod})_3$  and  $\text{Eu}(\text{fod})_3$ , agreed well with those values obtained by experiments using individual  $\text{Ln}(\text{fod})_3$  shift reagents.  $F_i$  and  $G_i$  values obtained directly by COM 2 and by DOM 2, which were mixtures of  $\text{Nd}(\text{fod})_3$  and  $\text{Yb}(\text{fod})_3$ , deviated from the expected values. The error was traced to the behavior of the ytterbium complexes.

### INTRODUCTION

Lanthanide shift reagents (LSR's) have been widely used in structural assignments, configurational assessment, and conformational analysis<sup>1</sup>. The lanthanide-induced shift (LIS) is usually composed of two components, the contact shift (Fermi-contact, through-bond), and the dipolar shift (pseudo-contact, through-space). The contact shift gives information related to the spin density distribution of unpaired electrons, and the dipolar shift gives information

related to the geometric structure. However, for these purposes it is necessary to separate the observed paramagnetic shifts into the contact and dipolar components. This is particularly important for  $^{13}\text{C}$ ,  $^{19}\text{F}$ ,  $^{31}\text{P}$ , etc, spectra.

There is also a third contribution to the total shift, *i.e.*, the complex formation shift. The complex formation shift is a diamagnetic shift and this term is sometimes too large to be ignored in the LIS.

Reilley and coworkers<sup>2-4</sup> have recently presented several structure and electron spin distri-

bution methods to separate the dipolar and contact contributions to the observed LIS, based on shift parameters calculated theoretically. For the axially symmetric complexes, the observed LIS,  $\Delta\delta_{ij}$ , of the nucleus  $i$  is given as the sum of the contact, dipolar, and complex formation (KCF) terms according to eq. 1.

$$\Delta\delta_{ij} = F_i \langle S_z \rangle_j + G_i C^D + K_{CF} \quad (1)$$

In eq. 1  $C^D$  and  $\langle S_z \rangle_j$  depend only upon the lanthanide ion,  $j$ , being used and have been calculated by Bleaney<sup>5,6</sup> and Golding<sup>7,8</sup>.  $G_i$  and  $F_i$  depend upon the geometric location and electron spin density of the nucleus  $i$ , respectively. To determine the  $F_i$  and  $G_i$  values for each nucleus three or more LSRs are needed. If LSRs having  $C^D$  or  $\langle S_z \rangle$  values of zero were available, the observed LIS would be purely contact-only or dipolar-only, circumventing the more elaborated multiple experiments required to calculate the  $F_i$  or  $G_i$  values from the observed shifts. Only Gd complexes, which have been used primarily as relaxation reagents, are known to have a  $C^D$  value of zero<sup>9,10</sup>. Thus the LIS of Gd complexes are purely contact-only but the shifts cannot be determined precisely due to the extensive relaxation broadening effect.

In this paper we show that contact-only and dipolar-only shift reagents can be prepared by mixing appropriate  $\text{Ln}(\text{fod})_3$  reagents in certain concentration ratios. These mixed shift reagents were used to determine the  $F_i$  and  $G_i$  values for proton and carbon atoms in 4-picoline.

## EXPERIMENTAL SECTION

**Materials.** The lanthanide complexes of 1, 1, 1, 2, 2, 3, 3-heptafluoro-7, 7-dimethyl-1, 4, 6-octanedione (Hfod),  $\text{Ln}(\text{fod})_3$  ( $\text{Ln}=\text{Pr}$ ,  $\text{Eu}$ , and  $\text{Yb}$ ) were purchased from Norell Inc.  $\text{Nd}(\text{fod})_3$  and  $\text{La}(\text{fod})_3$  were synthesized as described by Sievers<sup>11</sup>. All of the shift reagents were stored

in desiccators over  $\text{P}_2\text{O}_5$ . The substrate, 4-picoline, was purchased from Aldrich Chemical Co., distilled, and stored over Molecular Sieve 4A. The NMR solvent,  $\text{CDCl}_3$ , was also stored over Molecular Sieve 4A.

**Preparation of Contact-Only and Dipolar-Only Mixtures of LSR.** The preparation of the LSR mixtures whose effective net  $C^D$  or  $\langle S_z \rangle$  values are zero required great care. Table 1 lists the mole ratios of  $\text{Ln}(\text{fod})_3$  used to prepare contact-only (COM 1 and COM 2) or dipolar-only (DOM 1 and DOM 2) mixtures; the individual lanthanides were weighed into a vial and shaken vigorously on a mixer/mill (Spex 5100).

**NMR Spectra.** NMR samples were prepared by pipetting 3ml aliquots of 0.5M stock solution of the substrate in  $\text{CDCl}_3$  into 10mm NMR tubes and adding weighed quantities of individual  $\text{Ln}(\text{fod})_3$  shift reagents or the COM or DOM mixtures. Five samples for each LSR-substrate were prepared where the mole ratio of the LSR-substrate (typically 0, 0.05, 0.1, 0.15, and 0.2) was varied to obtain the observed LIS. The NMR spectra were recorded on a Varian XL-100 FT spectrometer that was run at 100MHz for proton and at 25.16MHz for  $^{13}\text{C}$ . The chemical shifts were measured using tetramethylsilane as the internal reference.

Table 1. Mole ratios of  $\text{Ln}(\text{fod})_3$  for contact-only (COM) and for dipolar-only (DOM) mixtures.<sup>a</sup>

Mixture	Mole ratio		net $\langle S_z \rangle$	net $C^D$
	$\text{Eu}(\text{fod})_3 / \text{Pr}(\text{fod})_3$	$\text{Yb}(\text{fod})_3 / \text{Nd}(\text{fod})_3$		
COM 1	2.75	—	-7.04	0
COM 2	—	0.191	3.36	0
DOM 1	0.278	—	0	-7.73
DOM 2	—	1.73	0	12.4

<sup>a</sup>Computed from Bleaney's data (6) scaled to  $D_j$  value and from Golding's data (8) scaled to -100 for  $D_j$ .

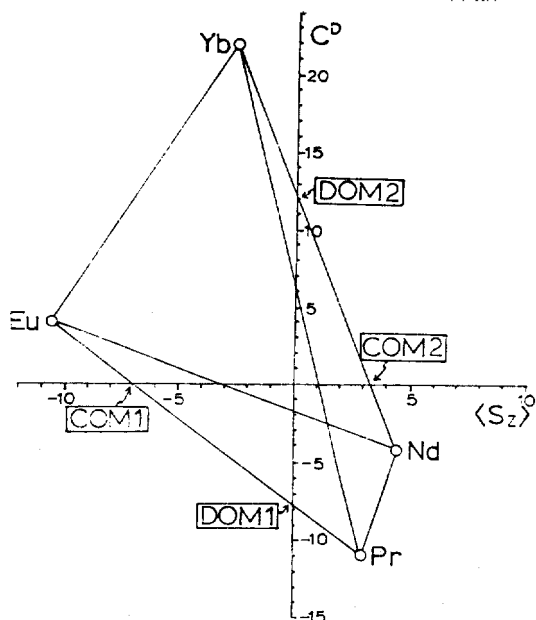


Fig. 1.  $C^D$  and  $S_z$  values for binary mixtures of lanthanide shift reagents.

## RESULTS AND DISCUSSION

4-Picoline was chosen as substrate because this compound has rigid structure and has already been studied widely in NMR spectroscopy<sup>10,12</sup>.  $\text{Ln}(\text{fod})_3$  employed in our studies have been the most popular shift reagents because of their high coordinating power and large solubilities in organic solvents. The relative shift

abilities of  $\text{Ln}(\text{fod})_3$  ( $\text{Ln}=\text{Pr}$ ,  $\text{Nd}$ ,  $\text{Eu}$ , and  $\text{Yb}$ ) and their mixtures may be best visualized with a plot of  $\langle S_z \rangle$  against  $C^D$  (Fig. 1). Each line connecting two lanthanides represents the continuum of binary LSR mixtures. If rapid association and dissociation of LSR-substrate occurs in the solution at room temperature and if adduct formation is nearly complete as would be likely for the strong Lewis acid fod reagents and at low LSR-substrate ratios, the effective net  $C^D$  and  $\langle S_z \rangle$  values for the  $\text{Ln}(\text{fod})_3$  reagents employed and the points crossing the axes will represent mixtures where contact-only (COM 1 and COM 2) and dipolar-only (DOM 1 and DOM 2) shifts are to be expected. The mole ratios of individual  $\text{Ln}(\text{fod})_3$  for contact-only and for dipolar-only mixtures are shown in Table 1. Some authors<sup>9,13,14</sup> have utilized LSR mixtures, but not for contact-only or dipolar-only purposes.

The observed lanthanide-induced shifts of the 4-picoline are summarized in Table 2. These values were obtained by extrapolating linearly the chemical shifts observed at low ratios of the  $\text{Ln}(\text{fod})_3$ -substrate to a value corresponding to a 1:1 ratio ( $\Delta\delta_{ij}$ ). From these extrapolated shifts the  $F_i$  and  $G_i$  values of the nuclei in the substrate were calculated in a least square

Table 2. Observed lanthanide-induced shifts of 4-picoline.

$\text{Ln}(\text{fod})_3$	Shift (ppm) <sup>a</sup>						
	$C_{2,6}$	$C_{3,6}$	$C_4$	$C_{ME}$	$H_{2,6}$	$H_{3,6}$	$H_{ME}$
La	-1.12	0	3.96	0	0	0	0
Pr	-109.03	-24.32	-30.28	-11.02	-57.81	-19.73	-11.96
Nd	-61.04	1.47	-16.72	-3.98	-26.32	-8.40	-6.33
Eu	85.85	-20.45	34.10	3.57	28.11	8.96	8.33
Yb	139.98	50.68	46.66	19.82	92.41	32.31	17.25
COM 1	36.60	-22.05	17.91	-0.20	5.76	1.47	3.12
COM 2	-26.85	10.23	-5.68	0.38	-5.49	-1.46	-2.29
DOM 1	-68.15	-23.84	-16.76	-7.98	-39.93	-13.79	-7.74
DOM 2	76.95	36.67	27.11	12.78	56.63	19.34	9.65

<sup>a</sup> Positive downfield.

Table 3. Data obtained from observed LIS of 4-picoline.

Nucleus	$F_i^a$			INDO <sup>b</sup> 4-picoline <sup>c</sup>	$G_i^d$			Yb(fod) <sub>3</sub>	Calc'd $G_i^e$
	Ln(fod) <sub>3</sub>	COM 1	COM 2		Ln(fod) <sub>3</sub>	DOM 1	DOM 2		
C <sub>2,6</sub>	-5.20 (-1.64)	-5.36 (-1.71)	-7.67 (-2.51)	(-1.47)	8.42 (2.76)	8.67 (2.81)	6.29 (2.13)	(2.78)	(2.44)
C <sub>3,5</sub>	3.17 (1.00)	3.13 (1.00)	3.05 (1.00)	(1.00)	3.05 (1.00)	3.08 (1.00)	2.95 (1.00)	(1.00)	(1.00)
C <sub>4</sub>	-2.01 (-0.63)	-1.98 (-0.63)	-2.87 (-0.94)	(0.59)	2.58 (0.85)	2.68 (0.87)	1.86 (0.63)	(0.84)	(0.78)
CME	0.6 (0.02)	0.03 (0.01)	0.12 (0.04)	(0.43)	1.02 (0.33)	1.03 (0.33)	1.03 (0.35)	(0.39)	(0.36)
H <sub>2,6</sub>	-0.95 (-0.30)	-0.82 (-0.26)	-1.64 (-0.54)	(0.38)	5.01 (1.64)	5.17 (1.68)	4.55 (1.54)	(1.82)	(1.34)
H <sub>3,5</sub>	-0.21 (-0.07)	-0.21 (-0.07)	-0.44 (-0.14)	(0.13)	1.74 (0.57)	1.78 (0.58)	1.56 (0.53)	(0.64)	(0.54)
HME	-0.46 (-0.15)	-0.44 (-0.14)	-0.68 (-0.22)	(0.03)	0.96 (0.31)	1.00 (0.32)	0.78 (0.26)	(0.34)	(0.29)

<sup>a</sup>The values in parentheses are normalized to 1.00 at C<sub>3,5</sub> position. <sup>b</sup>From Reference 4. <sup>c</sup>From Reference 11, assuming a Ln-nitrogen distance of 2.60Å.

manner using the linear relationship of eq. 2

$$\Delta\delta'_{ij}/\langle S_z \rangle_j = F_i + G_i(C^D/\langle S_z \rangle_j) \quad (2)$$

where the intercept and slope gave  $F_i$  and  $G_i$ .  $\Delta\delta'_{ij}$  is the chemical shift that is corrected with complex formation shift. The complex formation shifts were measured from La(fod)<sub>3</sub>-induced shifts assuming that these shifts were the same for all the other Ln(fod)<sub>3</sub>. Data and parameters for three Ln(fod)<sub>3</sub> (Ln=Pr, Nd, and Eu) reagents were utilized and the  $F_i$  and  $G_i$  values computed are compared in Table 3 with those obtained directly from the experimental shifts using contact-only and dipolar-only mixtures. We excluded the Yb(fod)<sub>3</sub> data in calculating  $F_i$  and  $G_i$  values because of the large inconsistency of the Yb(fod)<sub>3</sub> data relative to that from the other three lanthanides as described later. The  $F_i$  and  $G_i$  values obtained by COM 1 and DOM 1, which consisted of Pr(fod)<sub>3</sub> and Eu(fod)<sub>3</sub> mixtures, agreed well with those computed by eq. 2 using a composite of data from experiments employing individual Ln(fod)<sub>3</sub> (Ln=Pr, Nd, and Eu) reagents. The  $F_i$  and  $G_i$

values obtained by COM 2 and DOM 2 however, differed much more widely. COM 2 and DOM 2 are not contact-only and dipolar-only respectively because of the behavior of Yb(fod)<sub>3</sub>.

**Behavior of Yb(fod)<sub>3</sub>.** The correlation coefficients in calculating the slopes and intercepts by eq. 2 were considerably improved by excluding the ytterbium data. To illustrate the shift behavior of Yb(fod)<sub>3</sub> toward the substrate, a plot of  $\Delta\delta'_{ij}/\langle S_z \rangle_j$  against  $C^D/\langle S_z \rangle_j$ , according to eq. 2, was made (Fig. 2). The points corresponding to the Yb(fod)<sub>3</sub>-induced shifts deviated substantially from the straight lines which pass through the points obtained from Ln(fod)<sub>3</sub> (Ln=Pr, Nd, and Eu) data. In general, the points for Yb(fod)<sub>3</sub> fell below the lines and also the points for  $\alpha$ -carbons, which are closest to the lanthanide ions, deviated the most. The characteristic deviation of ytterbium data was also apparent in the other data from the literature<sup>10</sup>, where more lanthanides were used, as evidenced in plots made according to eq. 2.

The deviation of ytterbium shift data may come from one or more of the following:

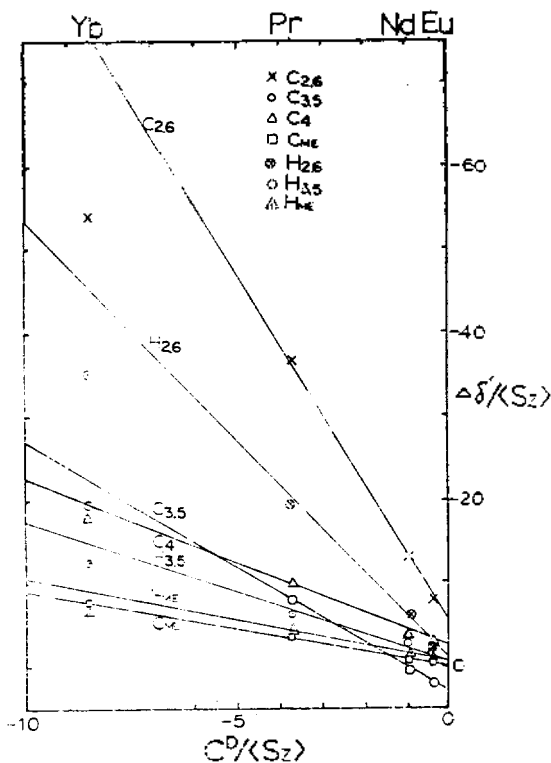


Fig. 2. Plot of the observed LIS of 4-picoline according to eq. 2.

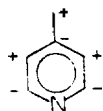
(1) Stoichiometry of LSR adducts. The  $\Delta\delta_{ij}$  were calculated from the slopes of the initial portions in LSR-substrate mole ratios and the shifts could be attributed to at least two complex series, 1:1 and 1:2-substrate<sup>15-22</sup>. At the concentration of excess substrate used in the study the 1:2 stoichiometry may be more probable. The ytterbium ion has the smallest radius along the lanthanide series and may have a preferred tendency to form the 1:1 adduct in addition to the 1:2 adduct. Because the shifts of 1:1 adducts are not twice those of 1:2 adducts, the deviation observed may occur.

(2) Structural changes. Inherent in our model is the feature that the lanthanide complexes of the same substrate would have the same structure. Because of the lanthanide contraction

the structure of ytterbium complexes (ytterbium being a late member in the lanthanide series) may be different from that of the other lanthanide complexes (which are early members of the series), and as a result the ytterbium-induced shifts show the observed deviation. One would expect that the ytterbium complexes would have the largest metal-nitrogen distances of the lanthanide complexes because of ytterbium's small ionic radius, crowding of the fod ligands, and the increased steric hindrance between the fod ligands and substrate molecule. As a result, the dipolar shifts for the ytterbium complexes would be decreased, and the shift at  $\alpha$ -carbon would be affected most. Also the deviation of ytterbium data may occur from a change in effective axial magnetic symmetry<sup>23-25</sup>. From high resolution luminescence studies, particularly the  $^5D_0 \rightarrow ^7F_1$  transition of  $\text{Eu}^{3+}$ , nonaxial crystal field splitting dominates and the three electron-dipole allowed lines are observed for the solution species<sup>26,27</sup>. Effective axial symmetry with respect to the substrate nuclei may result from rapid intramolecular motions or rearrangements which can effectively average out or significantly reduce the contribution of the nonaxial symmetry<sup>28</sup> in the NMR experiments.

(3) Degree of covalency. Dipolar shifts are not very sensitive to small variations in geometry while as little as 1% covalent character will give observable contact interaction<sup>28,29</sup>. The degree of covalency in the lanthanide-nitrogen bond decreases as the  $\text{Ln}^{3+}$  ionic radius decreases<sup>30</sup>, leading to a decrease in contact shift. Ytterbium has the smallest ionic radius and hence could be less accessible to covalent bonding from the substrate.

**Contact Shifts.** The sign of the unpaired electron spin density on the carbon atoms, which is proportional to the  $F_i$  values obtained from the observed LIS, is as follows:



The sign alternations in 4-picoline have the same pattern predicted by a dominant spin polarization mechanism. For pyridine-typed substrate the unperturbed cation radical appeared to be the best model for the INDO computation of the net unpaired spin density distribution in the substrate bound to lanthanide complexes<sup>4</sup>. As shown in Table 3, the  $F_i$  values obtained by COM 1 or  $\text{Ln}(\text{fod})_3$  ( $\text{Ln}=\text{Pr}$ ,  $\text{Nd}$ , and  $\text{Eu}$ ) agreed roughly with the INDO-calculated  $C_{2s}$  spin densities of the cation radical for 4-picoline.

Proton spectra usually exhibit little contact interactions, unlike  $^{13}\text{C}$  spectra, because spin in the  $1s$  orbit of hydrogen has only a small density at the proton nucleus.

**Geometric Factors.** Next we compared the  $G_i$  values obtained by DOM1 or  $\text{Ln}(\text{fod})_3$  ( $\text{Ln}=\text{Pr}$ ,  $\text{Nd}$ , and  $\text{Eu}$ ) with those calculated from the geometry of the complex where the lanthanide-nitrogen bond axis passed the center of the carbocyclic ring. The observed  $G_i$  values agreed well with those calculated for picoline (Table 3). The geometry of the  $\text{Ln}(\text{fod})_3$ -4-picoline adduct is as follows:



Because of the large  $C^D/\langle S_z \rangle$  value for  $\text{Yb}(\text{fod})_3$  the observed shifts using this reagent alone should be principally dipolar. Scaled shift values corresponding to this reagent and tabulated in Table 3 illustrate this point.

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