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EVIDENCE FOR THE PRESENCE OF CONTACT TERM CONTRIBUTION TO LANTHANIDE-INDUCED ISOTROPIC SHIFTS IN ^{13}C AND ^{19}F NMR SPECTRA OF ALIPHATIC COMPOUNDS: CAUTION FOR APPLICATIONS OF LANTHANIDE SHIFT REAGENTS

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Evidence for the presence of the contact term contribution besides the dipolar interaction has been presented in paramagnetic shifts induced by lanthanide shift reagents in ^{13}C and ^{19}F NMR spectra of several aliphatic alcohols, ketone, amines, and nitriles. Thus, it is suggested that caution should be exercised in their applications.

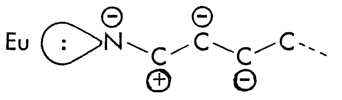
Although applications of some lanthanide chelates as NMR shift reagents have been explosively developed,$^{1)}$ the origin of the paramagnetic-induced shifts remains rather ambiguous.$^{2)}$ The dipolar (pseudocontact) interaction has widely been accepted as a main contributor to the isotropic shift observed in ^{1}H NMR.$^{1,3,4)}$ On the same basis, the shift reagents have successfully been used to assign ^{13}C NMR signals in several compounds.$^{5,6)}$ On the other hand, the large isotropic shifts observed in ^{1}H NMR spectra of complexes of some lanthanide ions with pyridine derivatives were earlier interpreted as originating from both contact and dipolar interactions of nearly equal magnitude but of opposite sign.$^{7)}$ Recently, the abnormal and large upfield shifts of ^{14}N resonances by tris-(dipivalomethanato)europium(III), Eu(dpm)$_3$, and shifts to the opposite direction by Pr(dpm)$_3$ were observed for various compounds.$^{8)}$ Furthermore, abnormal behaviour of ^{31}P NMR shifts induced by Eu- and Pr(NO$_3$)$_3$ was reported for some phosphates.$^{9)}$ Thus, it seems of great importance to obtain further insight into the nature of the induced shifts for various nuclei. We wish to report here some observations on the ^{13}C and ^{19}F NMR shifts caused by tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato)europium(III), Eu(fod)$_3$, and -praseodymium(III), Pr(fod)$_3$, to show that contact interaction is actually involved in the induced shifts.

As model compounds, linear long-chain aliphatic alcohols **1** and **7**, ketone **2**, amines **3** and **4**, nitrile **5**, and the rigid nitrile **6** were studied for the following two reasons. First, although the so-called geometric factors,$^{10)}$ $(3\cos^2\theta - 1)/r^3$, cannot be precisely obtained, the shifts of nucleus N caused by the Eu and Pr complexes, ΔEu(N) and ΔPr(N) respectively,$^{11)}$ due to the pseudocontact interaction are at least expected to attenuate gradually from bond to bond except for nuclei very close to the coordination site; this is actually the case with ^{1}H NMR of linear alcohols.$^{12)}$ Secondly, whether the contact term is actually involved or not can simply be judged by comparing the ΔEu(N)/ΔPr(N) ratios observed for such linear molecules, because the geometric factors for a certain nucleus in a linear compound complexed with Eu- or Pr(fod)$_3$ may be almost equal with regard to the coordination site; in fact, values of ΔEu(^{1}H)/ΔPr(^{1}H) for relevant protons have been found to be considerably constant as seen in Table 1, as expected from the predominance of the pseudocontact term in ^{1}H NMR shift.[1,4]

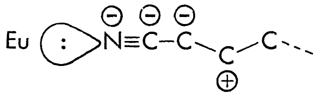
The results obtained are summarized in Table 1. Geometric factors of the i-th proton are almost equal to those of the i-th carbon except for those very close to the functional group in the freely rotating alkyl chain of 1-5. Actually, the values of ΔPr(^{13}C)/ΔPr(^{1}H) obtained for 1 and 2 are fairly constant except for the α-position in each molecule. On the other hand, the ΔEu(^{13}C)/ΔEu(^{1}H) values, and consequently the ΔEu(^{13}C)/ΔPr(^{13}C) ratios, were relatively indefinite. Thus, the present observations, as well as the result reported by Briggs, *et al.*,[5,13] suggest that the contact term contribution of both Pr(fod)$_3$ and Pr(dpm)$_3$ is small except for the α-carbon in aliphatic alcohols and ketones. However, it should always be taken into consideration that the contribution of the Eu ion may be transmitted to the β and further carbons.

With amines 3 and 4, upfield shifts induced by Eu(fod)$_3$ were observed for the β-carbons. Negative ΔEu(^{13}C) values for the γ-carbons are markedly smaller than expected and the positive ΔPr(^{13}C) values for the β-carbons are smaller even than those for the γ-carbons (see Table 1). With nitriles 5 and 6, it is a little surprising that considerably large *upfield* shifts for the nitrile (α) carbons were induced by Eu(fod)$_3$, and that smaller negative ΔEu(^{13}C) values than those expected for β-carbons were observed. The ΔPr(^{13}C) values for those carbons are also quite small though still positive (see Table 1). Thus, the presence of considerable contact-shift contribution of the shift reagents to these nitrogen-containing molecules becomes quite evident.

It is suggested, as previously reported,[7] that a negative (or positive) spin is induced on the hetero atom by a Eu (or Pr) ion. This suggestion is supported by the results obtained by Witanowski, *et al.*,[8] who observed the upfield (or downfield) shifts of ^{14}N NMR signals in similar amines and nitriles induced by a Eu (or Pr) ion. The negative spin thus induced by the Eu ion on the hetero atom in amines may be transmitted through σ-bonds by σ-electron spin polarization and delocalization mechanisms as in the following schema;[14]



The positive spin induced on the α-carbon strengthens the downfield shift. The negative spin on the β-carbon gives an upfield shift by overcoming the downfield pseudocontact-shift contribution. Further, the positive spin on the γ-carbon tends to weaken the psuedocontact shift contribution. The experimental data also suggest that the negative spin on the nitrogen atom[8] is distributed in nitriles complexed with Eu(fod)$_3$ as in the following schema;



The negative spin delocalized onto the α-carbon to a large extent, has the effect of overcoming the downfield shift by the pseudocontact term. It is suggested that a positive spin is induced on the hetero atom by a Pr ion, but to a lesser extent than the negative spin induced by the Eu ion. Accordingly, much caution should be exercised in the application of the shift reagents, particularly Eu(fod)$_3$, to the assignment of ^{13}C NMR signals or for structural determinations of nitrogen-containing compounds solely on the basis of their pseudocontact term.[17]

The apparent variation of ΔEu(^{19}F)/ΔPr(^{19}F) values in the case of 2,2,3,3,4,4,5,5-octafluoropentanol (7) (see Table 1) must also result from an origin other than the pseudocontact term. It appears to be explained by the fact that the fluorine isotropic hyperfine coupling (hfc) with an unpaired electron on the carbon α to the fluorine is much greater than that of a hydrogen.[15] Even the s-electron spin density slightly delocalized in the fluorine

Table 1. Lanthanide-induced isotropic shift data on various aliphatic compounds[a]

Compound		Carbon position relative to the N or the O atom							
		α	β	γ	δ	ε	ζ	η	θ
n-Octylalcohol (1)	δ_C	62.5	33.3	26.4	30.1	30.0	32.4	23.2	14.4
	$\Delta \mathrm{Pr}(^{13}\mathrm{C})$	+79.9	+32.1	+18.9	+10.4	+ 6.3	+ 3.5	+ 1.9	+ 2.0
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})$	-58.0	- 9.7	- 7.8	- 5.0	- 2.5	- 1.9	- 1.3	- 0.5
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})/\Delta \mathrm{Pr}(^{13}\mathrm{C})$	- 0.73	- 0.30	- 0.41	- 0.48	- 0.41	- 0.53	- 0.69[b]	- 0.24[b]
	$\Delta \mathrm{Pr}(^{1}\mathrm{H})$	+45.9	+26.5	+18.3	+ 9.3	+ 5.5	+ 3.5	+ 2.3	+ 1.1
	$\Delta \mathrm{Eu}(^{1}\mathrm{H})$	-19.0	-11.3	- 8.0	- 4.1	- 2.5	- 1.5	- 1.2	- 0.6
	$\Delta \mathrm{Eu}(^{1}\mathrm{H})/\Delta \mathrm{Pr}(^{1}\mathrm{H})$	- 0.41	- 0.43	- 0.44	- 0.45	- 0.46	- 0.44	- 0.53[b]	- 0.53[b]
	$\Delta \mathrm{Pr}(^{13}\mathrm{C})/\Delta \mathrm{Pr}(^{1}\mathrm{H})$	+ 1.74	+ 1.21	+ 1.03	+ 1.12	+ 1.15	+ 1.00	+ 0.83[b]	+ 1.82[b]
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})/\Delta \mathrm{Eu}(^{1}\mathrm{H})$	+ 3.05	+ 0.86	+ 0.98	+ 1.22	+ 1.00	+ 1.27	+ 1.08[b]	+ 0.83[b]
Di-*n*-butylketone (2)	δ_C	207.9[c]	42.3	26.3	22.7	14.3			
	$\Delta \mathrm{Pr}(^{13}\mathrm{C})$	+36.0	+32.4	+25.3	+11.3	+ 6.8			
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})$	-32.0	-17.4	-15.2	- 6.0	- 1.8			
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})/\Delta \mathrm{Pr}(^{13}\mathrm{C})$	- 0.90	- 0.54	- 0.60	- 0.53	- 0.27[b]			
	$\Delta \mathrm{Pr}(^{1}\mathrm{H})$	--	+21.1	+18.4	+ 7.5	+ 3.2			
	$\Delta \mathrm{Eu}(^{1}\mathrm{H})$	--	-12.1	- 8.9	- 4.0	- 1.4			
	$\Delta \mathrm{Eu}(^{1}\mathrm{H})/\Delta \mathrm{Pr}(^{1}\mathrm{H})$	--	- 0.57	- 0.48	- 0.54	- 0.27[b]			
n-Octylamine (3)	δ_C	42.5	34.3	27.3	30.0	29.7	32.2	22.9	14.2
	$\Delta \mathrm{Pr}(^{13}\mathrm{C})$	+98.0	+12.8	+13.7	+ 9.5	+ 5.5	+ 3.3	+ 1.9	+ 1.5
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})$	-83.6	+22.9	- 4.2	- 4.6	- 2.6	- 2.0	- 1.6	- 0.9
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})/\Delta \mathrm{Pr}(^{13}\mathrm{C})$	- 0.85	+ 1.79	- 0.31	- 0.48	- 0.47	- 0.61	- 0.84[b]	- 0.60[b]
	$\Delta \mathrm{Pr}(^{1}\mathrm{H})$	+52.3	+32.4	+24.8	+17.9	+ 8.2	+ 5.1	+ 2.1	+ 1.5
	$\Delta \mathrm{Eu}(^{1}\mathrm{H})$	-21.5	-14.5	- 8.7	- 4.9	- 3.3	- 1.8	- 1.7	- 0.8
	$\Delta \mathrm{Eu}(^{1}\mathrm{H})/\Delta \mathrm{Pr}(^{1}\mathrm{H})$	- 0.41	- 0.45	- 0.35	- 0.27	- 0.39	- 0.35	- 0.81[b]	- 0.53[b]
n-Hexylamine (4)	δ_C	42.3	34.3	27.0	32.2	23.1	14.3		
	$\Delta \mathrm{Pr}(^{13}\mathrm{C})$	+95.5	+14.1	+15.3	+10.5	+ 6.6	+ 4.8		
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})$	-81.0	+24.3	- 3.9	- 4.1	- 2.1	- 1.2		
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})/\Delta \mathrm{Pr}(^{13}\mathrm{C})$	- 1.07	+ 1.72	- 0.25	- 0.39	- 0.32	- 0.25[b]		
n-Valeronitrile (5)	δ_C	119.0[d]	16.3	27.4	21.8	13.1			
	$\Delta \mathrm{Pr}(^{13}\mathrm{C})$	+24.7	+22.1	+21.6	+11.7	+ 7.1			
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})$	+69.6	- 4.2	-14.6	- 6.2	- 3.4			
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})/\Delta \mathrm{Pr}(^{13}\mathrm{C})$	+ 2.82	- 0.19	- 0.68	- 0.53	- 0.48			
	$\Delta \mathrm{Pr}(^{1}\mathrm{H})$	--	+ 8.8	+ 5.3	+ 4.6	+ 1.9			
	$\Delta \mathrm{Eu}(^{1}\mathrm{H})$	--	- 8.5	- 4.3	- 3.5	- 1.6			
	$\Delta \mathrm{Eu}(^{1}\mathrm{H})/\Delta \mathrm{Pr}(^{1}\mathrm{H})$	--	- 0.97	- 0.81	- 0.76	- 0.84			
1-Adamantanecarbonitrile (6)	δ_C	124.4[d]	30.3	40.1	27.4	35.3			
	$\Delta \mathrm{Pr}(^{13}\mathrm{C})$	+19.6	+17.8	+18.1	+ 7.5	+ 5.8			
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})$	+57.8	- 4.3	-11.3	- 4.5	- 2.9			
	$\Delta \mathrm{Eu}(^{13}\mathrm{C})/\Delta \mathrm{Pr}(^{13}\mathrm{C})$	+ 2.95	- 0.26	- 0.62	- 0.60	- 0.47			
Octafluoro-*n*-pentylalcohol (7)	$\Delta \mathrm{Pr}(^{19}\mathrm{F})$	(+12.0)[e]	+ 8.2	+ 4.1	+ 2.5	+ 1.0 ,	(+ 1.8)[e]		
	$\Delta \mathrm{Eu}(^{19}\mathrm{F})$	(- 8.9)[e]	- 5.8	- 3.3	- 2.5	- 1.6 ,	(- 1.3)[e]		
	$\Delta \mathrm{Eu}(^{19}\mathrm{F})/\Delta \mathrm{Pr}(^{19}\mathrm{F})$	(- 0.75)[e]	- 0.71	- 0.80	- 1.00	- 1.58[b],	(- 0.71)[b,e]		

[a] NMR spectra were recorded on a Varian XL-100-12 spectrometer in the frequency-swept and deuteron-locked mode at normal probe temperature; the observed frequencies were 100.1, 94.1, and 25.2 MHz for ^{1}H, ^{19}F, and ^{13}C resonances, respectively. A C-1024 time-averaging device and the proton noise decoupling technique were used for the ^{13}C NMR measurements. ^{13}C NMR signals were unambiguously assinged by the off-resonance single-frequency decoupling method using each sample containing a shift reagent at 0.3 molar ratio of metal/substrate. The ^{13}C chemical shifts, δ_C, are expressed in ppm downfield from internal TMS (accuracies, ±0.08 ppm). The ^{13}C, ^{1}H, and ^{19}F NMR measurements were carried out using 2M solutions in C_6D_6, 0.6M solutions in $CDCl_3$, and a 0.5M solution in $CDCl_3$, respectively. Values for ΔLn(N) are represented as the slopes of the linear parts of the curves of shift values plotted against the molar ratio of shift reagent/substrate [accuracies are about ±0.5 (^{13}C) and ±0.1 (^{1}H and ^{19}F)]. Positive sign denotes an upfield shift. [b] These values may involve considerable errors because of the small induced shift values. [c] Data on the carbonyl carbon. [d] Data on the nitrile carbon. [e] Data on ^{1}H NMR spectra.

orbitals gives large hfc's.[16] As an NMR phenomenon, this difference should be reflected in greater sensitivity to the contact interaction for a fluorine nucleus than for a proton. Consequently, caution should also be exercised in the application of the shift reagents to the interpretation of ^{19}F NMR spectra.

A systematic study of paramagnetic induced shifts in ^{1}H, ^{13}C, and ^{19}F NMR spectra of aromatic compounds complexed with lanthanide shift reagents afforded results similar to those presented here, and will be published elsewhere.

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