Lanthanide-induced Shifts in the Carbon-13 Nuclear Magnetic Resonance Spectra of Some Ketones, Alcohols, and Amines. An Analysis of Contact, Pseudo-contact, and Complex-formation Contributions to the Observed Shifts

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The lanthanide-induced shifts in the carbon-13 n.m.r. spectra of some ketones, alcohols, and amines are reported. The shifts produced upon complex formation with diamagnetic $La(dpm)_3$ are relatively large for carbonyl carbons of ketones, and significant for oxygen-bonded carbons of alcohols, and carbons α to the C–N bond of primary amines $(C$–C–$N)$; appropriate corrections must therefore be made to the measured shifts produced by paramagnetic lanthanide ions. Contact contributions to the ^{13}C shifts in the compounds examined are generally larger in amines than alcohols or ketones, pseudo-contact shifts normally being dominant in the last two classes of compound. For quantitative structural ^{13}C work with shift reagents, $Yb(dpm)_3$ is recommended as it minimises contact contributions without causing adverse line broadening.

IF lanthanide shift reagents are to be used in conjunction with carbon-13 n.m.r. spectroscopy to provide quantitative structural information, then the induced n.m.r. shifts must be shown either to be solely or very largely pseudo-contact in origin[1] or to be analysable to yield the pseudo-contact contributions to the observed shifts. It is these contributions, when the anisotropy of the susceptibility of the shift reagent–substrate complex has axial symmetry,[2] which are proportional to $(3\cos^2\theta_i - 1)r_i^{-3}$, where r_i is the distance from the complexed lanthanide ion to the ith nucleus in the complex, and θ_i is the angle between this radius vector and the principal symmetry axis of the complex. For induced proton shifts, the largely pseudo-contact contribution seems clear.[3] Lanthanide-induced contact shifts have been observed in ^{14}N,[4] [17]O,[5] and ^{31}P,[6] spectra, and, recently, in the ^{13}C spectra of some amines,[7,8] pyridines,[9] and alcohols.[10] The apparently

significant contact contributions even at atoms γ to the site of complexation[11] would seem to prove a severe stumbling block to a potentially powerful method for structure elucidation in solution. It was clear to us that a detailed study of the factors contributing to observed lanthanide-induced carbon-13 n.m.r. shifts was essential before our wider aim of using such shifts to determine molecular structures could be realised.

12 Substrates (I)—(XII) representative of the more common functional groups, ketones, alcohols, and amines, were selected, and in each class of compound, a substrate of rigid, predictable structure was included. The positions of the carbon-13 resonances are listed in Table 1 and the lanthanide-induced shifts [corrected for 'complex formation' shifts caused by $La(dpm)_3$ (Table 3)] are given in Table 2.

Preliminary studies with the spin-paired $La(dpm)_3$ complex indicated that significant 'complex formation' shifts[2,12,13] occur at the carbon atom nearest to the site

[1] E. DeBoer and H. Van Willigen, *Progr. N.M.R. Spectroscopy,* 1967, **2**, 111.

[2] B. Bleaney, C. M. Dobson, B. A. Levine, R. B. Martin, R. J. P. Williams, and A. V. Xavier, *J.C.S. Chem. Comm.,* 1972, 791.

[3] J. K. M. Sanders and D. H. Williams, *Nature,* 1972, **240**, 385.

[4] M. Witanowski, L. Stefaniak, H. Januszewski, and Z. W. Wolkowski, *Chem. Comm.,* 1971, 1573.

[5] W. B. Lewis, J. A. Jackson, J. F. Lemons, and H. Taube, *J. Chem. Phys.,* 1962, **36**, 694.

[6] J. K. M. Sanders, S. W. Hanson, and D. H. Williams, *J. Amer. Chem. Soc.,* 1972, **94**, 5325.

[7] C. Marzin, D. Leibfritz, G. E. Hawkes, and J. D. Roberts. *Proc. Nat. Acad. Sci. U.S.A.,* 1973, **70**, 562.

[8] R. J. Cushley, D. R. Anderson, and S. R. Lipsky, *J.C.S. Chem. Comm.,* 1972, 636.

[9] M. Hirayama, E. Edagawa, and Y. Hanyu, *J.C.S. Chem. Comm.,* 1972, 1343.

[10] G. E. Hawkes, D. Leifbfritz, D. W. Roberts, and J. D. Roberts, *J. Amer. Chem. Soc.,* 1973, **95**, 1659.

[11] G. E. Hawkes, C. Marzin, S. R. Johns, and J. D. Roberts, *J. Amer. Chem. Soc.,* 1973, **95**, 1661.

[12] K. Tori and Y. Yoshimura, *Tetrahedron Letters,* 1973, 3127,

[13] C. D. Barry, C. M. Dobson, D. A. Sweigart, L. E. Ford, and R. J. P. Williams in 'Nuclear Magnetic Resonance Shift Reagents,' ed. R. E. Sievers, Academic Press, New York, 1973, p. 173.

of complexation in ketones and alcohols but that in amines the situation is more complex (Table 3). The magnitude of the effect is greatest in ketones (up to *ca.* 17% of the shifts induced by the paramagnetic lanthanide complexes). This is to be expected since we
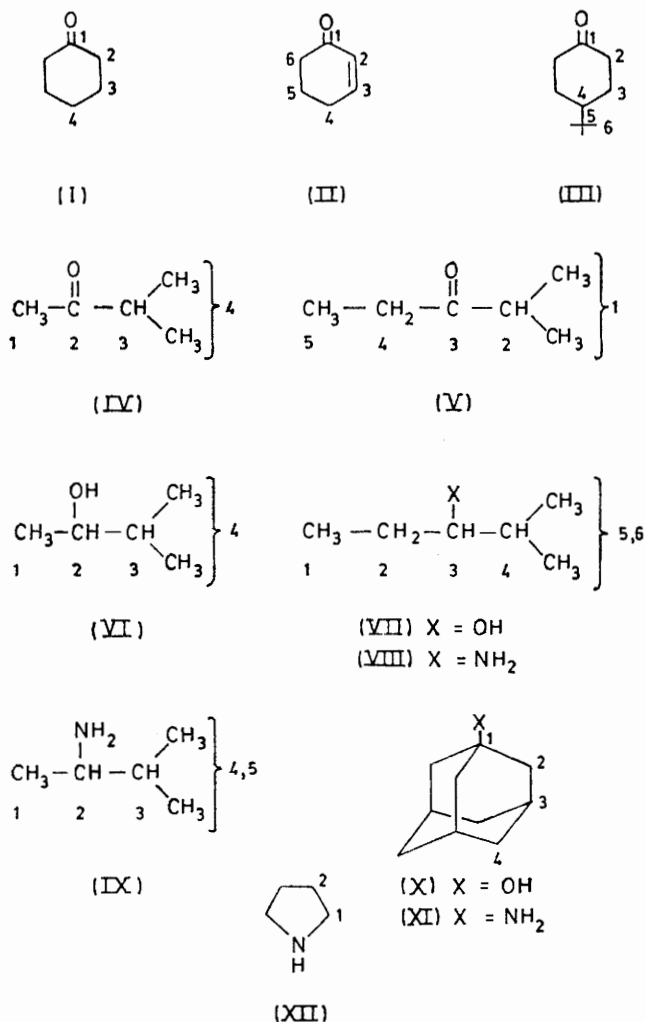

(I) (II) (III)

(IV) (V)

(VI) (VII) X = OH (VIII) X = NH₂

(IX) (X) X = OH (XI) X = NH₂

(XII)

Unsystematic numbering used for convenience in tabulation.

are surely observing electron donation from the carbonyl oxygen to the lanthanide ion, and efficient π-transmission of the resulting electron deficiency to the carbonyl carbon atom leading to magnetic deshielding at this atom and hence a ' downfield ' shift in its resonance. The reduced effect in alcohols must at least in part be a result of the absence of a π-system. In the amines, the effects are extraordinarily substrate-dependent. In (VIII), no significant shift is observed at the carbon atom adjacent to the amino-group, but at both of the carbon atoms β to the amino-group, small *shielding* effects are observed. A similar shielding effect found in (IX) is significant only at one of the two β-carbon atoms. In (XI), a β-shielding effect is again observed but, in addition, there is a deshielding effect at the α-carbon atom, and in (XII) no significant shifts are

observed. We conclude that it is essential to ' correct ' observed lanthanide-induced shifts for ' complex-formation ' shifts, especially in ketones, if erroneous conclusions are to be avoided.

TABLE 1

¹³C Shifts (p.p.m.) [a] at carbon atoms

Compound [b]	1	2	3	4	5	6
(I) (1·8; a; i; √)	207·6	42·7	28·2	26·3		
(II) (3·0; b; ii; √)	195·1	128·2	147·8	24·8	22·0	37·1
(III) (1·7; c; i; √)	207·6	42·0	28·8	47·7	33·4	28·8
(IV) (2·0; c; i; √)	28·3	208·8	42·3	19·3		
(V) (1·8; c; i; √)	19·6	41·2	211·6	34·3	9·2	
(VI) (2·0; c; i)	20·9	72·7	35·8	19·1		
(VII) (1·9; d; i)	11·4	27·9	78·4	34·1	20·0	18·3
(VIII) (1·7; d; iii; √)	10·9	27·4	58·0	32·8	17·0	19·3
(IX) (1·8; e; iii; √)	20·3	51·9	34·7	18·4	18·1	
(X) (1·1; e; iii; √)	68·2	45·6	31·0	36·3		
(XI) (1·4; e; iii; √)	46·7	45·9	29·5	35·9		
(XII) (6·1; f; i)	47·9	26·5				

[a] Recorded at 25·2 MHz on a Varian XL-100 spectrometer. [b] Arabic numerals give substrate molarity; letters specify the solvent (a, CCl_4–C_6H_6 5 : 1; b, CCl_4–$CHCl_3$ 4 : 1; c, CCl_4–C_6H_6 3 : 1; d, CCl_4–C_6H_6 6 : 1; e, $CDCl_3$; f, C_6H_6); small Roman numerals specify the internal reference from which shifts were measured (i, C_6H_6; ii, $CHCl_3$; iii, $CDCl_3$ centre): shifts were then converted to p.p.m. with respect to Me_4Si assuming $\delta_{Me_4Si} - \delta_{C_6H_6} = 128\cdot7$, and $\delta_{Me_4Si} - \delta_{CHCl_3} = 77\cdot2$ p.p.m., ignoring solvent, concentration, and isotope effects; a tick indicates the addition of $Cr(acac)_3$ (*ca.* 0·06M) to shorten the required pulse delay. Assignments are based on shielding considerations and, where necessary, off-resonance decoupled spectra.

In Table 4, ' corrected ' Eu : Pr shift ratios for the carbon atoms of the cyclic substrates (I)—(III) and (X)—(XII) are listed.

The Eu : Pr induced shift ratios of Table 4 suggest that at carbon atoms remote from the site of complexation to shift reagent (where contact contributions must tend to zero), a ratio of *ca.* −0·7 would be expected. This expectation of a constant shift ratio due to a purely pseudo-contact shift assumes that the differences in geometry of the Eu and Pr complexes are sufficiently small that the term $(3\cos^2\theta - 1)/r^3$ is the same for the two metals. Justification for this assumption is found in proton and carbon shift data for cholesterol,[13] where the shift ratios (ratioed to C-4 of cholesterol) were not changed by more than ±0·01 when Eu^{III} was replaced by Dy^{III}. Substantial deviations from this figure may then be used to diagnose significant contact contributions. In all the compounds in Table 4, contact effects appear to be significant at carbon atoms adjacent to the carbon atoms bonded directly to the complexing atom or group, the effects being especially pronounced in the amines (XI) and (XII). Additional, gross effects are observed at α and γ carbon atoms in the amines and at atoms 3 and 4 in cyclohex-2-enone, the latter presumably a consequence of spin transmission through the π-system. In contrast to the saturated cyclic ketones, where contact effects are in general rather small, the acyclic ketones, at all carbon atoms other than the carbonyl, show large deviations from the expected Eu : Pr shift ratio. The acyclic

TABLE 2

Shifts (p.p.m.) [a] induced at carbon atoms

Compound [b]	Shift reagent [d]	1	2	3	4	5	6
(I)	Eu(dpm)₃	48·9	17·2	11·5	7·5		
	Pr(dpm)₃	−65·9	−27·9	−14·9	−10·5		
	Yb(dpm)₃	146·2	61·6	28·6	21·2		
(II)	Eu(dpm)₃	48·4	14·9	17·7	8·5	10·7	18·6
	Pr(dpm)₃	−66·1	−26·2	−14·1	−8·5	−13·5	−28·9
(III)	Eu(dpm)₃	47·9	16·0	9·5	5·3	2·5 [c]	0·9 [c]
	Pr(dpm)₃	−60·3	−23·9	−13·3	−8·7	−2·9 [c]	−1·8 [c]
	Yb(dpm)₃	149·7	61·7	28·4	20·7	9·0	5·5
(IV)	Eu(dpm)₃	25·9	42·4	11·4	16·0		
	Pr(dpm)₃	−28·8	−58·3	−21·6	−18·8		
(V)	Eu(dpm)₃	15·7	20·1	29·4	21·9	17·8	
	Pr(dpm)₃	−16·0	−22·1	−40·1	−22·1	−20·1	
(VI)	Eu(dpm)₃	23·5	60·1	15·3	14·1		
	Pr(dpm)₃	−42·3	−92·1	−36·0	−23·6		
(VII)	Eu(dpm)₃	13·7	19·2	51·5	16·6	14·5	12·5
	Pr(dpm)₃	−22·4	−35·1	−79·3	−34·6	−22·9	−21·4
(VIII)	Eu(dpm)₃	24·0	33·6	82·3	−11·8	17·6	18·3
	Pr(dpm)₃	−31·1	−53·8	−114·1	−31·7	−28·5	−31·3
(IX)	Eu(dpm)₃	52·9	116·2	−30·7	18·8	19·6	
	Pr(dpm)₃	−72·1	−143·3	−31·5	−31·9	−28·4	
(X)	Eu(dpm)₃	53·7	22·6	9·6	8·4		
	Pr(dpm)₃	−72·3	−32·6	−13·1	−11·1		
	Yb(dpm)₃	127·7	63·7	27·5	21·7		
(XI)	Eu(dpm)₃	44·3	12·7	7·4	7·3		
	Pr(dpm)₃	−71·2	−28·9	−12·8	−10·3		
	Yb(dpm)₃	110·0	57·0	24·4	19·1		
(XII)	Eu(dpm)₃	142·8	−8·2				
	Pr(dpm)₃	−149·5	−40·0				

[a] Determined by sequential addition of shift reagent to substrate solution and linear least squares extrapolation (correlation coefficients generally >0·99) to 1 : 1 molar ratios, and corrected where necessary for the ' complex formation ' shifts given in Table 3. [b] Concentrations and solvent systems as before (Table 1). [c] Subject to larger errors (±0·3 p.p.m.) than other values because of small shifts and overlap with dpm-ligand resonance. [d] Shift reagents are commercial (Eu and Pr) or synthesised (La and Yb) (K. J. Eisentraut and R. E. Sievers, Inorg. Synth., 1968, 11, 94) and were stored over P_4O_{10} in vacuo.

alcohols and, in particular, the amines (see, in addition, ref. 7), also show larger deviations than are apparent in adamantan-1-ol (X) and 1-aminoadamantane (XI), and ' wrong way ' shifts are observed in (VIII), (IX), and (XII).

In a further effort to quantify contact contributions,

TABLE 3

' Complex formation ' shifts with La(dpm)₃ [a]

Shifts (p.p.m.) at carbon atoms

Compound [b]	1	2	3	4
(I)	10·1	-	-	-
(II)	7·3	-	-	-
(III)	10·8	-	-	-
(IV)	-	11·5	-	-
(V)	-	-	8·4	-
(VI)	-	4·4	-	-
(VII)	-	-	3·1	-
(VIII)	-	−2·7	-	−4·3
(IX)	−4·5	-	-	-
(X)	4·8	-	-	-
(XI)	3·0	−1·4	-	-
(XII)	-	-	-	-

[a] Determined by sequential addition of La(dpm)₃ to substrate solution and linear least squares extrapolation to molar ratios. A hyphen indicates that the ' complex formation ' shift of that carbon is sufficiently small to be ignored (<1 p.p.m.). [b] Concentration and solvent systems as before (Table 1).

attempts were made by computer[14] to determine the positions of the complexed lanthanide ions from the

TABLE 4

Eu : Pr Shift ratios at carbon atoms

Compound	1	2	3	4	5	6
(I)	−0·74	−0·62	−0·77	−0·71		
(II)	−0·73	−0·57	−1·26	−1·00	−0·79	−0·64
(III)	−0·79	−0·67	−0·71	−0·61		
(X)	−0·74	−0·69	−0·73	−0·76		
(XI)	−0·62	−0·44	−0·58	−0·71		
(XII)	−0·95	+0·21				

proton lanthanide-induced shifts * for 4-t-butylcyclohexanone (III),[15] adamantan-1-ol (X), and 1-aminoadamantane (XI) (Table 5) assuming only a pseudocontract interaction. The program scans the metal over spheres, specified by two angles (φ and ψ) and a

* Proton complex-formation shifts were sufficiently small to be ignored.

[14] Program ' METALSEARCH ' provided by L. O. Ford, Laboratory of Molecular Biophysics, University of Oxford, and modified by us for use with an I.B.M. 370 computer.

[15] Preliminary communication, D. J. Chadwick and D. H. Williams, J.C.S. Chem. Comm., 1974, 128.

variable radius (R) (see Figure). The principal symmetry axis of the metal is also allowed to vary, being given two angular variables.[13] In the absence of an X-ray crystal structure for (III), the Cartesian co-ordinates used here are those described by Tai and

inferior and false solutions are obtained where the metal is constrained to lie on the C-2 axis (a region which is not significantly occupied by orbitals extending from the oxygen atom!).

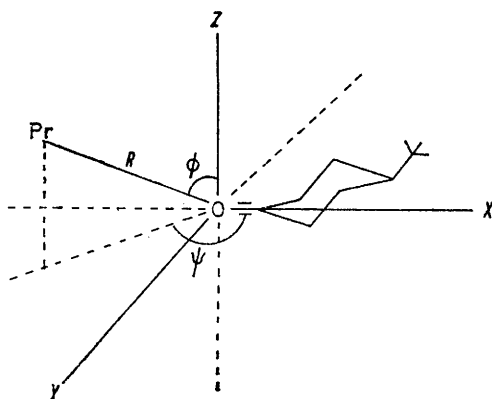The carbon-13 induced shifts predicted for (III) for

TABLE 5

Shifts in p.p.m. [a] induced at hydrogen atoms

Compound	Shift reagent	2		3		4		6
		eq	ax	eq	ax	ax		
(III)	Eu(dpm)₃	19·0	15·9	4·7				1·7
	Pr(dpm)₃	−26·7	−20·1	−7·2	−11·3	−7·6		−2·1
	Yb(dpm)₃	53·4	41·4	16·2				5·2
						eq	ax	
(X)	Eu(dpm)₃	19·3		6·3		6·8	4·9	
	Pr(dpm)₃	−23·6		−7·2		−7·6	−6·0	
	Yb(dpm)₃	50·2		16·4		18·4	13·0	
(XI)	Eu(dpm)₃	21·6		6·4		7·4	5·3	
	Pr(dpm)₃	−35·3		−10·4		−11·1	−8·7	
	Yb(dpm)₃	54·8		17·3		19·3	13·9	

[a] Determined on a Perkin-Elmer R32B spectrometer as in Table 2.

Allinger[16] with the corrections that the Y and Z co-ordinates and the co-ordinates for equatorial and axial substituents at C-4 have been interchanged. The

Model for computer-assisted attempt to determine the position of lanthanide ions from proton lanthanide-induced shifts for 4-t-butylcyclohexanone

co-ordinates for (X) and (XI), derived by vector analysis assuming tetrahedral bond lengths and angles,[17] are listed in Table 6.

Because of extensive overlap of resonances in (III), shifts for all protons could only be determined accurately with the upfield shift reagent Pr(dpm)₃. Using these data, acceptable solutions were found with the Pr^{III} ion sited near to the oxygen atom's lone-pair orbitals $\phi = 80$—$90°$, $\psi = 130$—$150°$ and 210—$230°$ and at distances of from 3 to 4 Å from the oxygen, with the metal complex symmetry axis parallel to the direction of the Pr–O axis. It is important to note that such solutions result only when the calculated shifts for protons symmetrically situated about the C-2 axis are averaged; i.e., when the metal ion is allowed to populate equally sites symmetrical with respect to the X–Z plane. If this procedure is not carried out,

the 'best' metal position (assuming that the three metals occupy similar positions) (Table 7) show poor

TABLE 6

Cartesian co-ordinates for adamantane

Carbon Atom	Hydrogen Atom	X	Y	Z
1		0	0	0
21		0·514	0	1·452
22		0·514	−1·258	−0·725
23		0·514	1·258	−0·725
	211	0·150	0·890	1·965
	212	0·150	−0·890	1·965
	221	0·150	−2·147	−0·212
	222	0·150	−1·257	−1·754
	231	0·150	2·147	−0·212
	232	0·150	1·257	−1·754
31		2·054	0	1·452
32		2·054	−1·258	−0·725
33		2·054	1·258	−0·725
	311	2·418	0	2·480
	321	2·418	−2·147	−1·240
	311	2·418	2·147	−1·240
41		2·568	−1·258	0·727
42		2·568	0	−1·450
43		2·568	1·258	0·727
	411	3·658	−1·258	0·727
	412	2·204	−2·147	1·240
	421	3·658	0	−1·450
	422	2·204	0	−2·479
	431	3·658	1·258	0·727
	432	2·204	2·147	1·240

TABLE 7

Predicted C-13 lanthanide-induced shifts (p.p.m.)

Shift reagent	C-1	C-2	C-3	C-4
Eu(dpm)₃	51·1	22·8	9·8	7·6
Pr(dpm)₃	−71·8	−32·0	−13·8	−10·7
Yb(dpm)₃	143·5	64·0	27·6	21·4

agreement with the observed shifts at C-1 and especially C-2 for the Eu^{III} and Pr^{III} complexes, but agreement is excellent at all carbon atoms for the Yb^{III} complex. This last complex was selected because it was thought that the more penetrating character of the f orbitals

[16] J. C. Tai and N. L. Allinger, *J. Amer. Chem. Soc.*, 1966, **88**, 2179.

[17] R. V. Winsor and G. H. Cady, *J. Amer. Chem. Soc.*, 1948, **70**, 1500.

in later members of the lanthanide series would lead to a lower induced contact shift than is found in earlier members. Also, the pseudo-contact shifts induced by Yb^{III} are much larger than those induced by Eu^{III} and Pr^{III}, and line broadening is not severe.[18]

Because of the high symmetry of the adamantane system, it was not possible to locate metal ion positions uniquely. For reasonable lanthanide–substrate geometries, however, the pseudo-contact shift ratio for C-1 : C-2 should be *ca.* 2. The observed ratios (Table 2) are 3·5 : 1 [Eu(dpm)$_3$], 2·5 : 1 [Pr(dpm)$_3$], and 1·9 : 1 [Yb(dpm)$_3$] [1-aminoadamantane (XI)], and 2·4 : 1 [Eu(dpm)$_3$], 2·2 : 1 [Pr(dpm)$_3$], and 2·0 : 1 [Yb(dpm)$_3$]

[18] See also D. A. Gansow, P. A. Loeffler, R. E. Davis, M. R. Willcott, and R. E. Lenkinski, *J. Amer. Chem. Soc.*, 1973, **95**, 3389.

[adamantan-1-ol (X)]. These results are compatible with the Eu : Pr shift ratios of Table 4, and indicate the presence of contact contributions in Eu^{III} and Pr^{III} induced shifts, especially in 1-aminoadamantane.

We conclude that the carbon-13 n.m.r. shifts induced in ketones, alcohols, and amines by paramagnetic lanthanide(III) ions are summations of contact, pseudo-contact, and complex-formation contributions. The relative importance of these contributions varies considerably with the type of functional group present, the substrate structure, and the shift reagent. Yb^{III} Complexes seem most useful for structural studies based on the pseudo-contact shift since contact contributions to the observed shifts appear to be small.