Nuclear Magnetic Resonance Spectra of Cyclopropyl Derivatives[1]

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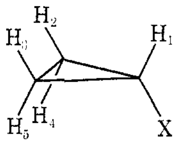
The analysis of the nmr spectra of 22 monosubstituted cyclopropanes is reported. An attempt has been made to estimate the anisotropy of the C–X bond in these compounds. The effect of chemical shift on coupling constants and the relationships between the several coupling constants are also considered. These data should be useful in estimating parameters for other systems.

Our interest in the nmr spectra of cyclopropane derivatives stems from their rigid, well-defined geometry which permits a detailed study of the effects of substituents. Earlier, we reported the analysis of the spectra of cyclopropyl bromide and cyclopropanecarboxylic acid,[2] and studies of other monosubstituted cyclopropanes have also been reported.[3]

The spectra were determined at 60 and 100 MHz with peak positions being measured to ±0.1 Hz. The analysis was initially carried out using the 60-MHz spectra and the NMRIT program.[4] Later, 100-MHz spectra were obtained and a complete reanalysis was performed using LAOCOON III.[5] The average deviation between calculated and observed spectra was 0.06 Hz and in no case were the deviations between observed and calculated line positions greater than 0.20 Hz.

To minimize concentration effects, all spectra were determined in 0.5 *M* (approximately 3–6%) carbon tetrachloride solutions, and tetramethylsilane (TMS) was used as the internal standard. The coupling constants and chemical shifts derived from the analysis of the spectra are summarized in Table I.[6]

The analysis of the spectra does not, of course, specify which protons are cis and trans to the functional group. However, the assignment is easily made since the cis-vicinal hydrogens (with a 0° dihedral angle) will give a large coupling constant whereas the trans-vicinal hydrogens (with a 145° dihedral angle) will give a relatively small coupling constant.[2,7] It can be seen from Table I that the coupling constants to the α-ring proton (indicated as no. 1) fall cleanly into two groups, one of which is 6–8 Hz whereas the other is 3–5 Hz. The former must then be the cis coupling constant whereas the latter must be the trans coupling constant. The sign of the geminate coupling constant is assigned as negative since this leads to a better fit between observed and calculated spectra. The numbering of the protons based on the above assignment is



In most of the cases in which one of these compounds had been analyzed previously,[3,8] our results are in satisfactory agreement with the reported values. However, in the case of *p*-fluorophenyl cyclopropyl ketone and *p*-methoxyphenyl cyclopropyl ketone,[9] the results are markedly different. The previous values appear out of line with those obtained for related compounds and almost certainly are incorrect.

The chemical shifts for cyclopropanol and dicyclopropyl ketone have been obtained in benzene solution by Scherr and Oliver.[3] It is interesting to note that they found differences in chemical shift between the cis and trans hydrogens of 0.246 and 0.466 ppm, respectively. The corresponding values in carbon tetrachloride are 0.079 and 0.170. It seems unlikely that carbon tetrachloride would be oriented in a specific fashion with respect to either compound. On the other hand, benzene has been observed to have such effects,[10] and it seems likely that the differences observed in benzene solution are enhanced by orientation of the solvent.

Let us examine the chemical shifts. The chemical shifts of the α protons with respect to that of cyclopropane is largely determined by the electronegativity of the substituent and the anisotropy of the C–X bond. Thus, attempts to correlate the chemical shifts with electronegativity[11] alone have not been too successful. We have found it of interest to compare the chemical shifts in the cyclopropane series with those for *n*-propyl and isopropyl derivatives (Figures 1a and 1b).[12] Considering the difference in substitution at the carbon in question in cyclopropane and propane, the correlation with *n*-propyl derivatives is fairly good. The slope of the line is 1.33. One might expect a better correlation with the isopropyl derivatives since the substitution pattern is now quite similar. Except for the halogens, a reasonable correlation is found with a slope of 1.34.

The deviation of the halogens with isopropyl probably results from the size of the substituent which will alter the geometry. Since the anisotropy of the carbon–halogen bonds is quite large (see below), a change in geometry will result in a significant change in chemical shift. Iodine would be expected to lead to the largest deviation, and this is the case.

The correlation with methyl chemical shifts (Figure

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[1] This investigation was supported by the U. S. Army Research Office, Durham. The nmr spectrometer was obtained with the aid of a National Science Foundation departmental equipment grant.

[2] K. B. Wiberg and B. J. Nist, *J. Amer. Chem. Soc.*, **85**, 2788 (1963).

[3] P. A. Scherr and J. P. Oliver, *J. Mol. Spectrosc.*, **31**, 109 (1969), have summarized the previously available data.

[4] J. D. Swalen and C. A. Reilly, *J. Chem. Phys.*, **37**, 21 (1962).

[5] S. Castellano and A. A. Bothner-By, *ibid.*, **41**, 3863 (1964).

[6] Some small difference will be noted between these results and those reported previously.[2] This results from the use of the lower concentrations than was possible previously and from additional information available from the 100-MHz spectra.

[7] H. M. Hutton and T. Schaefer, *Can. J. Chem.*, **40**, 875 (1962).

[8] Reference 2 (cyclopropyl bromide and cyclopropanecarboxylic acid), H. M. Hutton and T. Schaefer, *Can. J. Chem.*, **41**, 2774 (1963) (cyclopropylamine); and ref 3 (cyclopropanol and dicyclopropyl ketone).

[9] H. Weitkamp and F. Korte, *Tetrahedron*, **20**, 2125 (1964).

[10] T. Ledaal, *Tetrahedron Lett.*, 1683 (1968).

[11] J. S. Waugh and R. W. Fessenden, *J. Am. Chem. Soc.*, **79**, 846 (1957); H. Spiesecke and W. G. Schneider, *J. Chem. Phys.*, **35**, 722 (1961).

[12] The data for *n*-propyl and isopropyl were taken from ref 13, p 672, and are on the methane reference scale.

[13] J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, Oxford, 1966.

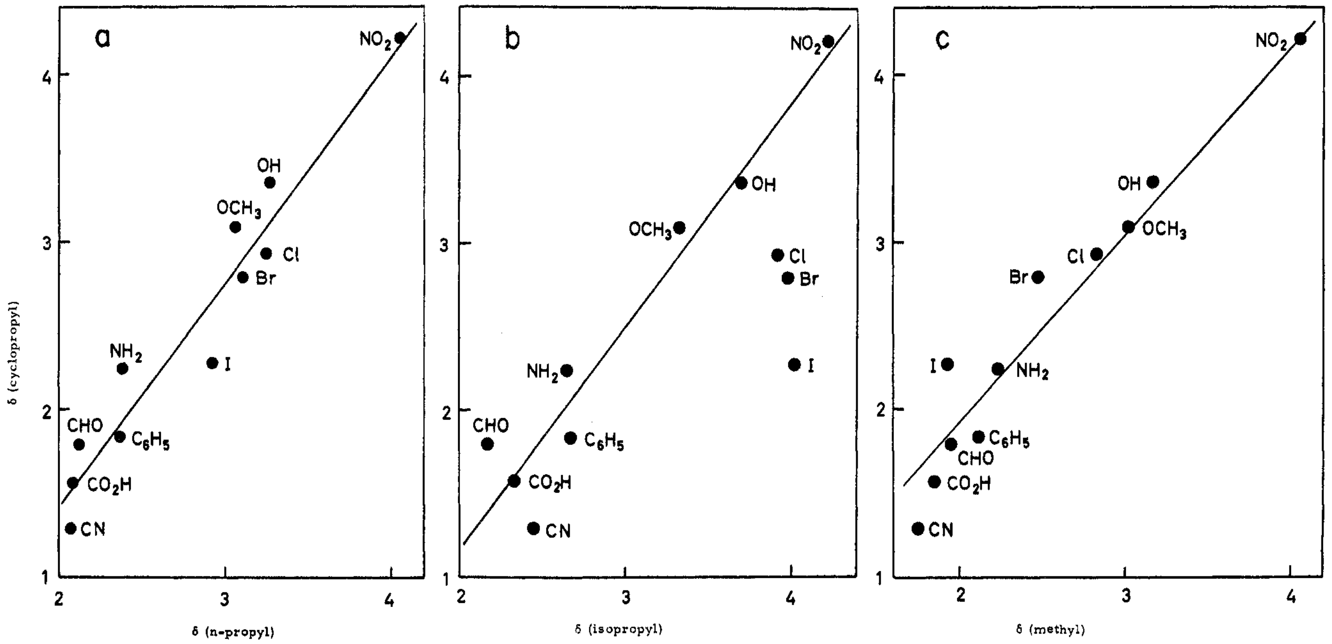

Figure 1.—Relationship between α-chemical shifts for cyclopropyl derivatives and (a) *n*-propyl, (b) isopropyl, and (c) methyl derivatives.

TABLE I

COUPLING CONSTANTS AND CHEMICAL SHIFTS FOR MONOSUBSTITUTED CYCLOPROPANES[a]

R	Registry no.	δ_1	$\delta_2 = \delta_3$	$\delta_4 = \delta_5$	$J_{12} = J_{13}$	$J_{14} = J_{15}$	J_{23}	$J_{24} = J_{35}$	$J_{25} = J_{34}$	J_{45}	δ_6	J_{16}	No. of lines assigned	Rms error of line positions
C_6H_5	873-49-4	1.8346	0.8913	0.6469	8.41	5.13	9.36	−4.56	6.22	9.33			53	0.086
CN	5500-21-0	1.2871	0.9627	1.0391	8.47	5.09	9.42	−4.93	7.02	9.88			49	0.066
CH_2OH[b]	2516-33-8	1.0145	0.4600	0.1747	8.04	4.89	8.93	−4.52	5.70	9.34	3.3430*	6.70*	58	0.060
CH_2OCOCH_3	36982-54-4	1.0779	0.5265	0.2599	8.06	4.83	8.99	−4.71	5.91	9.41	3.8080*	7.24	240	0.068
CH_2CH_2OH[c]	2566-44-1	0.7126	0.4203	0.0431	8.02	4.92	9.06	−4.40	5.59	9.25	1.4070*	6.94	151	0.098
CH_2CH_2Br[c]	36982-56-6	0.8387	0.4914	0.1039	8.06	4.87	9.25	−4.58	5.66	9.43	1.7520*	6.91	164	0.078
$C(CH_2)C_3H_5$[b,d]	822-93-5	1.2448	0.5736	0.4820	8.36	5.29	9.24	−4.26	6.00	9.36	4.4930*		53	0.070
CHO[b]	1489-69-6	1.7895	0.9872	1.0262	7.98	4.56	8.80	−4.46	6.99	9.60	8.9730*	5.00*	51	0.051
$COCH_3$[b]	765-43-5	1.8310	0.7665	0.9305	7.85	4.58	9.16	−3.53	6.98	9.54	2.1625*	0.30*	56	0.046
COC_3H_5	1121-37-5	1.9592	0.7925	0.9630	7.83	4.58	9.16	−3.51	6.96	9.45			54	0.072
COC_6H_5	3481-02-5	2.5759	0.9244	1.1625	7.84	4.58	9.05	−3.37	7.00	9.50			57	0.064
$COC_6H_4OCH_3$[e]	7152-03-6	2.5127	0.8725	1.1130	7.84	4.58	9.12	−3.33	6.91	9.48			56	0.065
COC_6H_4F[e]	772-31-6	2.5327	0.9406	1.1638	7.83	4.56	9.15	−3.41	7.03	9.54			58	0.057
CO_2H	1759-53-1	1.5654	0.8828	1.0453	8.04	4.61	9.17	−3.98	7.12	9.74			58	0.052
NH_2	765-30-0	2.2379	0.3276	0.2220	6.60	3.52	9.77	−4.40	6.15	10.02			53	0.055
NO_2	13021-02-8	4.2144	1.1291	1.6025	7.01	3.42	10.09	−5.52	8.26	11.27			57	0.068
OH	16545-68-9	3.3646	0.4026	0.4814	6.17	2.93	10.08	−5.45	6.78	10.82			47	0.060
OCH_3	540-47-6	3.0857	0.3591	0.4665	6.04	2.98	10.48	−5.52	6.78	11.31			56	0.062
$OCOCH_3$	4606-06-8	4.0500	0.6588	0.6175	6.60	3.07	10.85	−6.26	7.45	11.77			43	0.065
Cl	7393-45-5	2.9325	0.8653	0.7837	7.02	3.59	10.55	−6.08	7.09	10.83			54	0.052
Br	4333-56-6	2.7896	0.9623	0.8536	7.16	3.82	10.27	−6.14	6.98	10.49			54	0.060
I	19451-11-7	2.2690	1.0385	0.7817	7.55	4.37	9.83	−5.94	6.65	9.90			59	0.052

[a] Coupling constants are given in Hz. Chemical shifts are given in ppm downfield from TMS. Starred items are based on direct measurements of spectra and have not been fitted. [b] Protons in R group were irradiated while observing cyclopropyl protons. [c] Side-chain protons α and β to the cyclopropyl ring were irradiated while observing cyclopropyl methylene and methine protons, respectively. [d] 1,1-Dicyclopropylethylene. [e] Para isomer.

1c)[12] also is reasonable, but the slope (1.13) is significantly less than for the *n*-propyl and isopropyl cases. One factor which may affect the slope is the amount of s character in the bond. According to the CNDO molecular orbital calculations,[14] the fraction of s character in the C–H bond is 0.22 for isopropyl, 0.25 for methyl, and 0.29 for cyclopropyl.

In considering the chemical shifts of the β protons, it is convenient to divide the substituents into two groups, those which are saturated and those which are unsaturated. We shall first consider the former group. If the effect of the O–H and N–H bonds are neglected,[15] the substituent effects may be considered in a simple fashion. The chemical shift due to the difference in anisotropy between the C–X bond and a C–H bond is approximately given by[16]

$$\delta_{C-H} - \delta_{C-X} = \frac{\Delta\chi}{3R^3}(1 - 3\cos^2\theta)$$

where δ_{C-X} is the observed chemical shift, δ_{C-H} is the chemical shift which would be found if the X group was replaced by H with geometry unchanged, *R* is the distance between the proton in question and the electrical center of gravity of the C–X bond, and θ

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[14] K. B. Wiberg, *Tetrahedron*, **24**, 1083 (1968).

[15] To a certain extent, their effect will be minimized because of the essentially free rotation about the C–O and C–N bonds.

[16] H. M. McConnell, *J. Chem. Phys.*, **27**, 226 (1957).

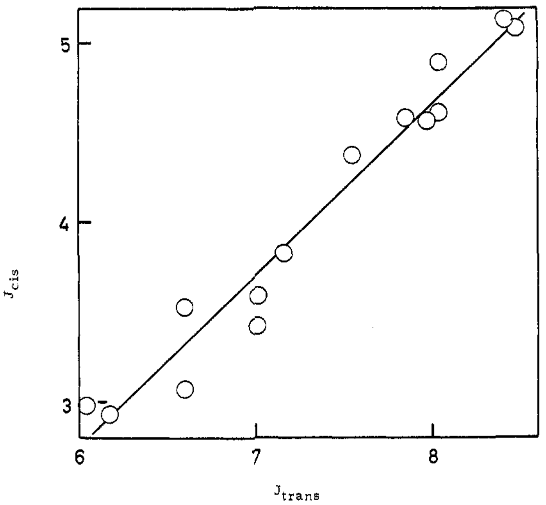

Figure 2.—Relation between J_{cis} and J_{trans} for the β-cyclopropyl protons.

is the angle between the line defining *R* and the axis of the C–X bond. The quantity $\Delta\chi$ is given by

$$\Delta\chi = (\chi_{\parallel} - \chi_{\perp})_{C-X} - (\chi_{\parallel} - \chi_{\perp})_{C-H}$$

where $\chi_{\parallel}$ is the magnetic susceptibility along the *z* (bond) axis and $\chi_{\perp}$ is the magnetic susceptibility along the *x* or *y* axis of the given bond.

Separate expressions may be written for the cis and trans protons (with respect to X) giving two equations and two unknowns (δ_0 and $\Delta\chi$).[17] It is assumed that the chemical shifts of the two protons would be the same if there were no contribution from the anisotropy of the bond to the substituent. The geometry of the compounds was assumed to be the same as for cyclopropyl chloride,[18] except for the C–X bond length. The terms were evaluated for each of the compounds making the assumption that the electrical center of gravity is at the carbon covalent radius (0.772 Å) and are summarized in Table II. It must be emphasized that the anisotropies calculated in this manner are not pure quantities but probably contain a significant contribution from the difference in field effect at the two protons in question. However, the ordering of the values should be correct. The contribution of the field effect to the chemical shift will be considered in detail at a later time in connection with the nmr spectra of monosubstituted cyclobutanes.

Two trends may be seen. First, there is an increase in the anisotropy on going down the periodic table from fluorine to iodine and, second, there is a decrease in anisotropy in going across the periodic table from carbon to fluorine. The effect on the chemical shifts is quite marked. For the cases having a positive value of $\Delta\chi$, the trans protons are found at lower field than the cis protons. The chemical shifts are reversed when the sign of $\Delta\chi$ is negative.

TABLE II

NEIGHBORING BOND ANISOTROPY FOR CYCLOPROPYL DERIVATIVES

Substituent	δ_{C-H}	$\Delta\chi^a$
F	0.49	-13.33^b
Cl	0.82	2.58
Br	0.91	3.44
I	0.90	8.13
C	0.31	9.03^c
	0.22	11.94
	0.29	12.27
N	0.27	3.34^d
O	0.44	-2.49^e
	0.42	-3.40
F	0.49	-13.33^b

[a] Anisotropy units are 10^{-30} cm^3 molecule^{-1}. [b] Based on the values for cyclopropyl fluoride of ref 3. These data were obtained in benzene solution rather than in carbon tetrachloride and may not be strictly comparable to the other values. [c] Based on the values for cyclopropylcarbinol, 2-cyclopropylethanol, and 2-cyclopropylethyl bromide, respectively. [d] Based on the values for cyclopropylamine. [e] Based on the values for cyclopropanol and cyclopropyl methyl ether, respectively.

The larger values of $\Delta\chi$ are associated with atoms having higher polarizability. Polarizability increases on going down the periodic table and decreases on going across the table from left to right. Since the magnetic susceptibility is associated with the circulation of electrons in the bonds, it is not surprising that a relation with polarizability is found.

The compounds which possess double bonds represent a quite different problem. The double bond generally assumes a preferred geometry with respect to the cyclopropane ring.[19] The chemical shifts should be temperature dependent since the proportions of the conformers change with changing temperature. Thus, it is not profitable to consider in detail the experimental chemical shifts at any one temperature. It is generally found that the cis-β protons are at lower field than the trans protons. The one exception is the phenyl ring.

We should now like to consider the coupling constants. An examination of Table I indicates that there is a relationship between the cis and trans coupling constants for the β protons. We have noted this previously and suggested a relationship with electron density.[2,20] This has indeed proved to be the case.[3]

The correlation may now be examined in more detail using only monosubstituted derivatives (Figure 2). A very good correlation is found. Since the origin of the change in coupling constants might be related at least in part to the origin of the chemical shifts, the correlation between these quantities was examined giving the data in Table III. Except for the geminate coupling constant ($J_{2,4}$), reasonable correlations were found. These proved useful in estimating coupling constants as starting points for the analysis of new cyclopropane derivatives.

The correlation of coupling constants with electronegativities was found to give essentially the same slope as found by Scherr and Oliver[3] using substituents having a wider range of electronegativity values.

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(17) This method was used in considering the difference between axial and equatorial substituents on a cyclohexane ring (L. M. Jackman, "Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, London, 1959, p 117) and in other cases (*cf.* ref 9, Chapter 10). Problems associated with the calculation of magnetic spectroscopy by this method have been discussed by A. A. Bothner-By and J. A. Pople, *Ann. Rev. Phys. Chem.*, **16**, 43 (1965).

(18) R. H. Schwendeman, G. D. Jacobs, and T. M. Krigas, *J. Chem. Phys.*, **40**, 1022 (1964).

(19) L. S. Bartell and J. P. Guillory, *ibid.*, **43**, 647 (1965); R. Hoffmann *Tetrahedron Lett.*, 3819 (1965).

(20) *Cf.* R. E. Glick and A. A. Bothner-By, *J. Chem. Phys.*, **25**, 362 (1956).

TABLE III

CORRELATION OF COUPLING CONSTANTS WITH CHEMICAL SHIFTS[a]

$J = a\delta_1 + b\delta_2 + c\delta_4 + d$

J	a	b	c	d	R^b	Error[c]
1,2	−0.700	1.221	0.289	7.990	0.937	0.271
1,4	−0.751	0.891	0.284	5.074	0.939	0.273
2,3	0.662	1.095	−1.321	8.251	0.887	0.299
2,4	−0.917	−4.363	3.746	−2.185	0.824	0.582
2,5	0.304	−0.186	1.128	5.353	0.963	0.190
4,5	0.786	0.135	−0.676	8.653	0.895	0.366

[a] δ_1 is the chemical shift for the α proton, δ_2 is the shift for the β proton trans to the substituent, and δ_4 is the shift for the β proton cis to the substituent. [b] Correlation coefficient. [c] Standard error.

Experimental Section

Materials.—Cyclopropylamine, cyclopropyl bromide, cyclopropylcarbinol, cyclopropanecarboxylic acid, cyclopropyl cyanide, cyclopropyl methyl ketone, cyclopropyl phenyl ketone, cyclopropyl 4-fluorophenyl ketone, cyclopropyl 4-methoxyphenyl ketone, 1,1-dicyclopropylethylene, and dicyclopropyl ketone were commercial samples (Aldrich). Cyclopropyl acetate,[21] cyclopropanol,[22] cyclopropyl methyl ether,[23] 2-cyclopropylethanol,[24] cyclopropyl chloride,[25] cyclopropyl iodide,[26] cyclopropanecarboxaldehyde,[27] nitrocyclopropane,[28] and phenylcyclopropane[29] were prepared using previously reported methods. All samples were purified by preparative scale vpc using a 20-ft 20% Carbowax 20M column.

Samples of 2-cyclopropylethanol and 2-cyclopropylethyl bromide were supplied by Dr. Elliot Barber. A sample of nitrocyclopropane was provided by Dr. Gary Lampman, and a sample of cyclopropylcarbinyl acetate was provided by Dr. Gunther Szeimies.

Spectra.—All spectra were taken using a Varian HA-100 nmr spectrometer in the frequency sweep mode. The peak positions were determined by stopping the frequency sweep at the peak maximum and counting the difference in frequency between the observing and locking oscillators. The compounds were examined as 0.5 M solutions in carbon tetrachloride and were degassed using three freeze–thaw cycles. Tetramethylsilane was generally used as the internal standard. In those cases for which this overlapped the cyclopropyl protons, the reference and locking signals were obtained using concentric capillaries containing either benzene or methylene chloride.

The analysis of the spectra were performed using LAOCN3.[30] The coupling constants which are obtained are not unique since the calculated spectra are not affected by interchanging the cis-β-β' coupling constants. All of the calculated and observed spectra are reproduced in the Ph.D. thesis of D.E. Barth.

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Dipolar Nature of Lanthanide-Induced Shifts. Detection of the Angular Dependency Factor

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The contribution of the angular dependency factor can be clearly seen in the improvement of the pseudocontact shift correlations with the Eu(dpm)$_3$, Eu(fod)$_3$, and Pr(fod)$_3$ induced shifts in the symmetrical and rigid ethers, 1,4-dihydronaphthalene 1,4-oxide (**1**), 1,2,3,4-tetrahydronaphthalene 1,4-oxide (**2**), and benzonorbornadiene *exo*-oxide (**3**). The lanthanide positions in the complexes were determined through a least-squares fit. These improvements upon inclusion of this geometric factor support the contention that the lanthanide-induced shifts are largely dipolar in origin.

The pseudocontact nature of the lanthanide-induced paramagnetic shifts in the pmr spectra of a large number of organic compounds is generally accepted although it has not been rigorously established. The observed shift is a weighted average reflecting the rapid equilibration of a lanthanide shift reagent, Ln(Y)$_3$, and the organic substrate, RX:. The size of the induced

$$\mathrm{Ln(Y)_3} + \mathrm{RX{:}} \rightleftharpoons \mathrm{RX{:}Ln(Y)_3}$$

shift obviously depends on these relative concentrations as well as the value of the equilibrium or binding constant, which in turn is related to the basicity of the coordination site in the organic molecule.

The magnitude of a lanthanide-induced pseudocontact shift within a given molecule can be expressed as[1]

$$\Delta\delta_i = \delta_i[\mathrm{Ln}{\neq}0] - \delta_i[\mathrm{Ln}{=}0] = k(3\cos^2\theta_i - 1)(1/R_i^3)$$

where δ_i is the chemical shift of the ith proton, k represents[2] a collection of constants, R_i is the proton–lanthanide distance, and θ is the angle between the crystal field axis of the complex and the radius vector from the lanthanide ion to the ith proton. A vast amount of evidence already suggests a reasonable correlation of the paramagnetic shift with $1/R_i^3$, a correlation that tends to substantiate the importance of the pseudocontact contribution to these induced shifts.[3] Small discrepancies from the $1/R_i^3$ dependency possibly reflect contact contributions[4] or the failure to consider

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