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POSITION OF LANTHANIDE ION IN NMR SHIFT REAGENT - LIGAND CHELATES

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In the course of studies on the stereochemistry of Tilidine* 1) and related compounds it became desirable to apply NMR shift reagents quantitatively2-4) rather than in the widely used qualitative way.

The intention was to locate in a first step the position of the lanthanide ion in the chelate formed by the shift reagent (s.r.) complex and the respective ligand molecule, and to determine in a second reverse step the coordinates of those protons, the positions of which are unknown but essential for the elucidation of the structure of the molecule in question.

Although it seems to be accepted now that the chemical shifts of pmr-signals induced by the lanthanide ion are predominantly of pseudocontact origin2,4-6), it remains uncertain whether the contribution of the contact term may be neglected in all cases or should be considered for those protons separated from the site of complexation by a certain number and type of bonds. In order to decide this question by experiment, we developed a computer program7) to calculate the position of the lanthanide ion of the s.r.8) complexed with a ligand molecule on the basis of the McConnell-Robertson expression9) for the induced pseudocontact shifts $\Delta\delta_i$:

$$\Delta\delta_i = k\ (3\ \cos^2\Theta_i - 1)\ /\ r_i^3\ . \qquad (1)$$

r_i is the distance between Eu and the ith proton, Θ_i is the angle formed by this vector and the principal magnetic axis10,11) of the complex, and k is a constant

As input data to the program we used the cartesian coordinates[12]) of the protons and of the heteroatom and the induced shifts $\Delta\delta_i$ of the respective signals taken from the NMR-spectra[13]). The shifts are calculated from (1) for all points within a reticular search area, and the time-averaged position of the Eu is found by minimizing the error function

$$ERR = (\Sigma(\Delta\delta_{calc} - \Delta\delta_{obs})^2)^{1/2} / n \ , \qquad (2)$$

where n is the number of protons used in the respective calculation.

We confined ourselves to rigid two-dimensional model compounds of well known geometry, in order to keep inaccuracies in the input data as low as possible. Some typical results are shown in Table 1 (position of Eu) and Table 2 (shifts)

One-ring systems: Substituents at C2 force the lanthanide complex to one side because of steric hindrance. d (distance heteroatom-Eu) is constant within the precision of measurement (No. 2-6). Remote substituents (at C3,4,5) have little or no influence on the position of the Eu (No. 3,4,6).

Two-ring systems: A second aromatic ring condensed with pyridine introduces a lateral hindrance similar to that of C2-substituents (No. 7,8,9). d is again constant and of the same magnitude as in 2-substituted pyridines, while its angle with the y-axis is adapted so as to make room for the bulky ring.

Three-ring systems: In order to find out what would happen to the Eu in cases of symmetrical or non-symmetrical bilateral hindrance, we calculated its position when complexed with 2,4-dimethyl-quinoline, acridine and fluorenone. Indeed, d is increased from 2.5 Å to 3.2 Å, 4.4 Å and 3.4 Å[14]) respectively.

So as to test the validity of our approach to the problem, we calculated the position of Eu employing different protons of one and the same molecule, including those of methyl groups, the use of which would be of considerable value with respect to the availability of experimental data. The averaged locus of methyl protons was approximated by the center of the circle described by the freely rotating H-atoms.

Protons in remote positions, where the pseudocontact term tends to zero because of the r^{-3} dependance, do not affect results calculated from protons close to Eu and separated from the heteroatom by only 2 or 3 bonds (No. 7a, b; 10a, b; 11a, c).

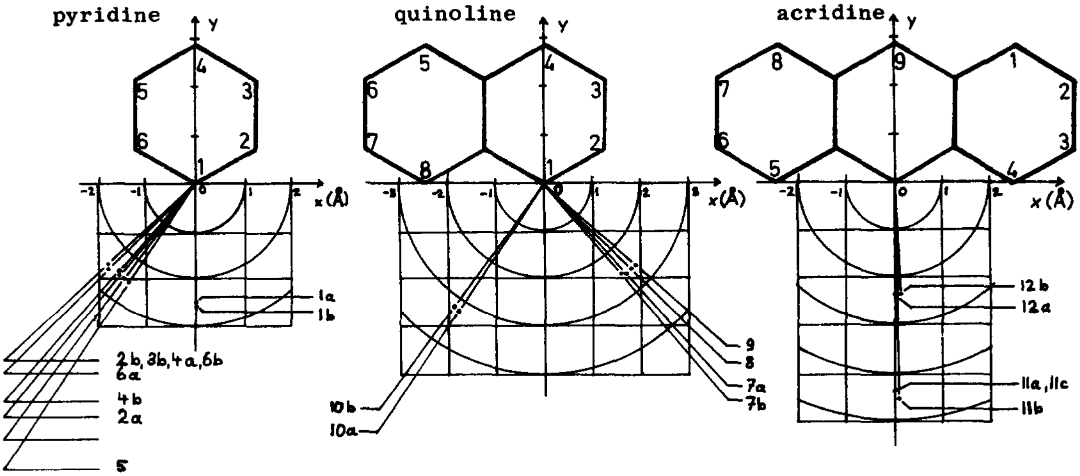

Table 1: Position of Eu (x, y) and distance from heteroatom (d)

No.	Molecule	Protons employed	Position of Eu (A)			Error
			x	y	d	
1a	3,5-dimethyl-pyridine	2,4,6	0.0	-2.5	2.5	0.04
1b	3,5-dimethyl-pyridine	2,3,4,5,6	0.0	-2.6	2.6	0.19
2a	2-methyl-pyridine	3,4,5,6	-1.6	-1.9	2.5	0.88
2b	2-methyl-pyridine	2,3,4,5,6	-1.8	-1.7	2.5	3.48
3a	2,4-dimethyl-pyridine	3,5,6	-1.5	-2.0	2.5	0.22
3b	2,4-dimethyl-pyridine	2,3,4,5,6	-1.8	-1.7	2.5	3.00
4a	2,5-dimethyl-pyridine	3,4,6	-1.8	-1.7	2.5	0.02
4b	2,5-dimethyl-pyridine	2,3,4,5,6	-1.6	-1.8	2.5	3.32
5	2-vinyl-pyridine	3,4,5,6	-1.4	-2.1	2.6	0.15
6a	2-methyl-5-vinyl-pyridine	3,4,6	-1.8	-1.8	2.5	0.82
6b	2-methyl-5-vinyl-pyridine	2,3,4,6	-1.8	-1.7	2.5	3.91
7a	4,7-dichloro-quinoline	2,3,8	+1.7	-1.9	2.5	0.76
7b	4,7-dichloro-quinoline	2,3,5,6,8	+1.6	-1.9	2.5	1.44
8	3-bromo-quinoline	2,4,8	+1.8	-1.8	2.5	3.02
9	8-methyl-quinoline	2,3,8	+1.9	-1.7	2.5	2.98
10a	2,4-dimethyl-quinoline	3,5,8	-1.8	-2.7	3.2	0.10
10b	2,4-dimethyl-quinoline	2,3,5,8	-1.9	-2.6	3.2	3.50
11a	acridine	1 - 9	0.0	-4.3	4.3	0.25
11b	acridine	1,2,3,4,9	+0.1	-4.5	4.5	0.47
11c	acridine	3,4,9,5,6	0.0	-4.3	4.3	0.02
12a	fluorenone[14])	1 - 8	0.0	-2.3	2.3	0.18
12b	fluorenone	1,2,3,4	+0.1	-2.3	2.3	0.46

Table 2: Observed and calculated lanthanide induced shifts (lis) in ppm

No.	5				7a			11b				
H empl.	3	4	5	6	2	3	8	1	2	3	4	9
lis obs.	8.50	6.17	5.33	20.33	25.22	9.00	24.89	1.31	1.15	1.19	9.65	2.12
lis calc.	8.48	6.16	5.18	20.52	24.71	8.41	25.99	1.61	1.03	1.18	9.64	1.95

Results gained from rigid proton calculations are only slightly varied by including methyl protons. The increased error may be attributed to their approximated coordinates (No. 1, 2, 3, 4, 6, 10).

In symmetrical molecules Eu is found along the ordinate, as x-deviations average to zero. The accuracy of the method can be checked by using only one half of the symmetrical set of protons. Comparison of No. 11a, b and of 12a, b shows that x-deviations are very small.

Thus, the position of Eu seems to be independent of the choice of protons selected for the calculation, and induced shifts may well be treated on the basis of mere pseudocontact interaction.

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References and Notes:

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