Tetrahedron Letters No. 7, pp 493 - 496, 1973. Pergamon Press. Printed in Great Britain.

N.M.R. Lanthanide Shift Reagents : II Solvent Effects.

J. BOUQUANT and J. CHUCHE *

Laboratoire de Chimie Organique Physique
B.P. 347 - Faculté des Sciences - 51062 - REIMS CEDEX (France).

(Received in UK 11 December 1972; accepted for publication 8 January 1973)

We have recently reported an easy method allowing a determination of the "lanthanide induced shift" (LIS) parameter Δ_{S-R} and the equilibrium binding constant K between a shift reagent R and a substrate S$^{(1)}$. The derived equations are only valid for a 1/1 stoichiometry :

$$S + R \rightleftarrows S\text{-}R$$

In connection with our studies concerning the relative importance of the various factors on these parameters, we have studied the solvent effect. Several authors (2) (3) (4) have compared the chemical shift power of lanthanide reagents in different solvents by measuring the induced shifts δ_i. Nevertheless the observed shifts are a function of three parameters (1) :

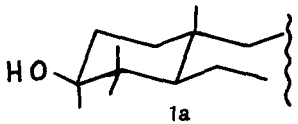
$$\delta_i = f\ (K, \Delta_{S-R}, m)$$

$m = C°_R/C°_S$ ($C°_R$ and $C°_S$ are the respective concentrations for reagent and substrate). It is an experimentaly imposed parameter, therefore, the measurement of Δ_{S-R} and K is required in order to assess the origin of the discrepancy between the induced shifts.

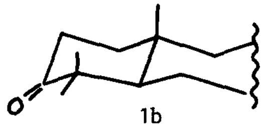
In this preliminary work we have investigated five solvents :

- carbon tetrachloride and chloroform as the most commonly used solvents
- cyclohexane as an inert solvent
- benzene which is magnetically anisotropic
- carbon disulfide in which the shift reagents are more soluble and which can still be used at a low temperature.

-Here the action of Eu(dpm)$_3$ on 3α, 4, 4-trimethyl-5α-cholestan-3β-ol (1a) and 4,4-dimethyl-5α-cholestan-3-one (1b) in these five solvents is reported.



1a



1b

-These molecules offer a number of practical and theoritical advantages : there are several methyl groups near the site of complexation allowing an accurate determination of the chemical shifts, they are very soluble and they differ by the functional group.

-The numerical values for K and Δ_{S-R} reported in this paper (tables I, II and III) were obtained according to the procedure outlined in our previous communication(1). A plot of $\delta_i^{(5)}$ versus $\sqrt{\delta_i/C^{\circ}_S}$ yields straight lines ; from the slope and the intercept of such a straight line the two parameters K and Δ_{S-R} were easily deduced. In every case the correlation coefficients are between - 0.995 and - 1.

-Some remarks can be made concerning K values : (a) the binding constant increases very much from chloroform to cyclohexane (table I) (b) for 1a and 1b all the solvents are classified in the same order (c) the ratio K_{1a}/K_{1b} is between 2,3 and 3 in a given solvent, this is in good agreement with the known relative basicity of alcohols and ketones.

Solvents	$CDCl_3$	C_6H_6	CS_2	CCl_4	C_6H_{12}
$K^{(1)(2)}$ 1a(3)	61.8±0.8	188.1±0.3	303±1	330±5	854±40
1b(4)	26.7±0.3	69.9±0.4	101.1±0.5	126±1	339±3
K_{1a}/K_{1b}	2,5	2.6	3.0	2.6	2.3

1) l. mole^{-1} at 39°. 2) The incertainties are standard deviations.
3) From the 3α, 4α, 4β, 19-methyl shifts. 4) from the 4α, 4β, 19-méthyl shifts.

TABLE I : Binding constants K of 1a and 1b with $Eu(dpm)_3$.

Variations of induced shifts with molar ratio $Eu(dpm)_3$/substrate in C_6H_6, CS_2 and $CD\ Cl_3$ have been plotted (fig.1). The agreement between the calculated and the experimental shifts ($CD\ Cl_3$ and C_6H_{12}) is good. Here, it should be noted that the sequence of observed shifts is identical with the K values although Δ_{S-R} is smaller for cyclohexane.

-Now let us consider Δ_{S-R} values. There are striking LIS differences (tables II and III) if the solvent is changed from benzene to cyclohexane. Differences may attain 1 p.p.m.

Solvents	C_6H_{12}	CS_2	$CDCl_3$	CCl_4	C_6H_6
$\Delta^{3\alpha}$	19.07	19.19	19.67	20.00	20.37
$\Delta^{4\beta}$	12.34	12.72	12.84	13.07	13.30
$\Delta^{4\alpha}$	11.20	11.52	11.67	11.90	12.01
Δ^{19}	4.80	4.93	4.98	5.13	5.15
$\Delta^{4\beta}/\Delta^{19}$	2.57	2.58	2.58	2.55	2.58
$\Delta^{4\alpha}/\Delta^{19}$	2.33	2.34	2.34	2.32	2.33

TABLE II : Isotropic shifts Δ(p.p.m.) for 1a

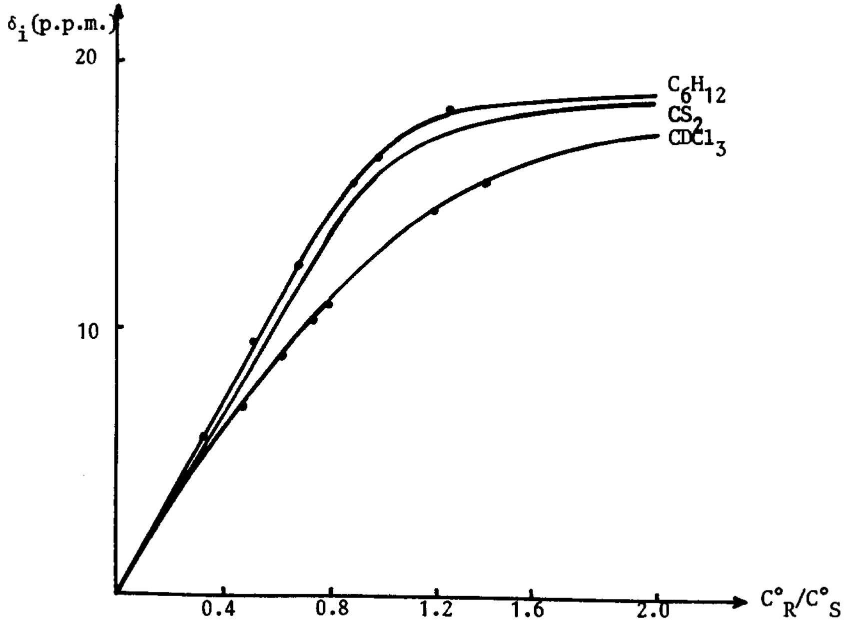
Solvents	C_6H_{12}	CCl_4	CS_2	$CDCl_3$	C_6H_6
$\Delta^{4\alpha}$	11.88	12.75	12.82	12.99	13.12
$\Delta^{3\beta}$	9.79	10.45	10.49	10.57	10.87
Δ^{19}	4.64	5.00	5.05	5.06	5.27
$\Delta^{4\alpha}/\Delta^{19}$	2.56	2.55	2.54	2.57	2.49
$\Delta^{4\beta}/\Delta^{19}$	2.11	2.09	2.08	2.09	2.06

TABLE III : Isotropic shifts Δ(p.p.m.) for 1b

near this site whereas they are smaller than 0.2 p.p.m. with a pure substrate. A second significant feature derived from the data is that the classification of the solvents with respect to increasing Δ values is the same for all the hydrogen atoms of a given molecule (7). Moreover similar results are obtained with carbon disulfide, carbon tetrachloride and chloroform whereas they differ significantly with cyclohexane and benzene.

For axially symmetric secondary fields (8) dipolar shifts are proportional to the product of a magnetic anisotropy factor and a geometric factor (9) :

$$\Delta = \text{constant (Magnetic anisotropy factor) (Geometric factor).}$$



- theoritical lines obtained with K and Δ values from tables I and II.

• experimental.

Figure 1 : Graph of δ_i versus $C°_R/C°_S$ ($C°_S$ = 0,09 mole.l^{-1}) for 3 -methyl(1a)

In every case the shift ratios for the methyl groups based on the 19-methyl resonance (tables I and II) are in reasonable mutual agreement, so that one can assume that the geometric factor remains constant in various solvents (10). It is possible that the magnetic anisotropy factor is somewhat modified by solvents. All the solvents used in this study except for cyclohexane are Lewis bases so that we can imagine a solvent-complex interaction is responsible for the Δ_{S-R} and K discrepancies observed (12). At this point of our study it is impossible to consider the interaction as a solvation rather than a complexation.

REFERENCES

1. J. BOUQUANT and J. CHUCHE, Tetrahedron Letters, 2337 (1972)
2. J.K.M. SANDERS and D.H. WILLIAMS, J. Amer. Chem. Soc., 93, 641 (1971)
3. D.B. WALTERS, Anal. Chim. Acta., 60, 421,(1972)
4. C. FREPPEL, J.C. FLORENCE, J.C. RICHER, Chem. and Ind., 553 (1972)
5. $\delta_i = \delta_{obs.} - \delta_o$ (δ_{obs} and δ_o are the chemical shifts with and without reagent). In several cases δ_o have been obtained by plotting δ_{obs} versus δ_i of a known hydrogen resonance which yields straight line whose intercept is δ_o (6).
6. Unpublished results.
7. Scattering of δ_o values are observed.
8. Nevertheless for a number of S-R systems with lower symmetry we can use the axially symmetric case (9).
9. R. VON AMON and R.D. FISCHER, Angew. Chem. Internat. Edit., 11, 675 (1972)
10. Benzene is the only exception but an ASIS effect may be considered (11)
11. E.M. ENGLER and P. LASZLO, J. Amer. Chem. Soc., 93, 1317 (1971)
12. Weak interactions with substrate are not excluded.