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THE EFFECT OF SHIFT REAGENT ON THE CONFORMATIONAL EQUILIBRIUM OF 3,3'-DISUBSTITUTED DIPHENYLSULFINES[1]

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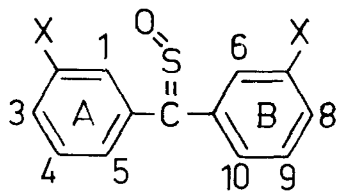
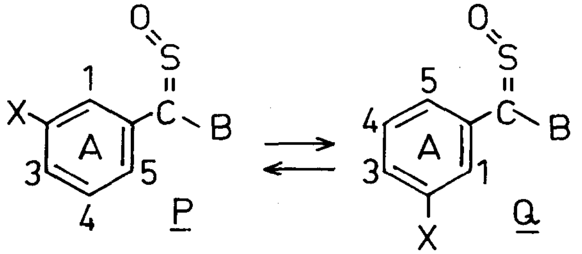
Shift reagents have widely been used in NMR spectroscopy[2], particularly in the determination of molecular geometry. Sofar little attention has been given to its use in the study of mobile conformational equilibria. The use of shift reagents in such mobile systems can give rise to NMR spectra which are difficult to interpret[3]. Some authors[4,5] recognized the possibility that complexation with shift reagents can change the conformational preference, others[6,7] neglected such effects. In one instance[8], *viz.* of the conformational equilibrium of cyclic phosphonates, the perturbation caused by added shift reagents has been treated quantitatively. The sum of the percentages of uncomplexed and complexed conformers was obtained from an analysis of coupling constants.



Ia: X = Cl
Ib: X = NO_2
Ic: X = OCH_3
Id: X = CH_3

In this paper we wish to present an analysis of the conformer populations of 3,3'-disubstituted diphenylsulfines (I) in the complexed state by means of chemical shift differences and to compare these conformer populations with those in the uncomplexed state. In addition, the solvent dependency on the conformational equilibrium in the complexed state is being compared with that in the uncomplexed state.

The system of 3,3'-disubstituted diphenylsulfines can be described[9] as an equilibrium between the two rotamers[10] P and Q, which differ in the relative orientation of the group dipole moments of the substituent X and the CSO group (μ_{CSO} = 3.62 D, directed towards the sulfine oxygen with an angle of 25^o with the carbon sulfur bond[11]).



The proportions of these rotamers in different media have been obtained[9] by an evaluation of the difference in anisotropic deshielding effect of the CSO system on the protons H_1 and H_5. It was found that the rotational equilibrium strongly depends on the polarity of the solvent in the sense that the population of the more polar rotamer (P for X = Cl or NO_2 and Q for X = OCH_3 or CH_3) increases with increasing solvent polarity.

The shift reagent, $Eu(dpm)_3$, complexes with sulfines at the sulfine oxygen[12]. Consequently the LI shifts for the *ortho* protons of the A-ring will be much larger than for those of the B-ring. Furthermore, complexation of $Eu(dpm)_3$ with rotamer P will show a much larger downfield shift for proton H_1, which is situated closest to the CSO system, than for proton H_5. The reverse will be true for the complexed rotamer Q.

The proportions of the rotamers P and Q in the complexed state can be obtained as follows. When z equiv. of shift reagent are added, we assume that for a 1:1 complexation a fraction z of the total amount of sulfine is in the complexed state. This fraction z consists of a proportion a of rotamer P and a proportion b of rotamer Q. The LI shifts of protons H_1 and H_5 (Δ_1 and Δ_5) are expressed by the equations[13] (1) and (2) in which $\delta(H_1)_{free}$ is the δ-value of proton H_1 in the spectrum without $Eu(dpm)_3$ and P_1^{max} is the LI shift of H_1 upon addition of one equiv. of $Eu(dpm)_3$ for $a = 1$. $\delta(H_5)_{free}$, Q_1^{max}, P_5^{max} and Q_5^{max} are defined analogously.

$$(1)\quad \Delta_1 = \delta(H_1)_{exp} - \delta(H_1)_{free} = z\,(aP_1^{max} + bQ_1^{max})$$

$$(2)\quad \Delta_5 = \delta(H_5)_{exp} - \delta(H_5)_{free} = z\,(aP_5^{max} + bQ_5^{max})$$

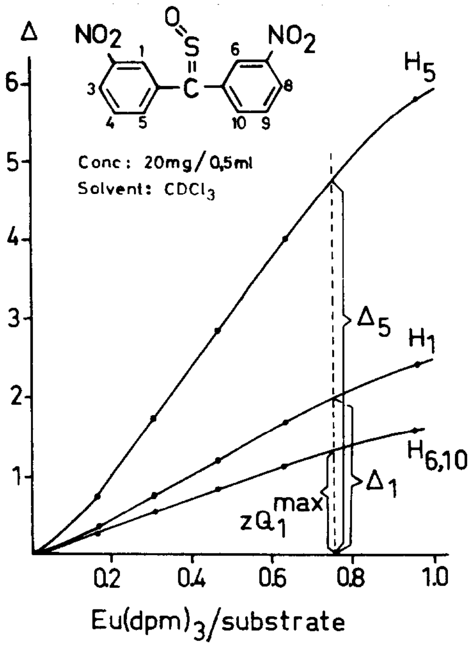
By making the assumptions that $P_1^{max} = Q_5^{max}$ and $P_5^{max} = Q_1^{max}$, which means that the effect of the position of the substituent X on the coordination of $Eu(dpm)_3$ with the CSO group is being neglected, the expression $P_1/(P_1 + Q_5)$ becomes a measure for the proportion a (equation 3).

$$(3)\quad \frac{P_1}{P_1 + Q_5} = \frac{\Delta_1 - zbQ_1^{max}}{\Delta_1 - zbQ_1^{max} + \Delta_5 - zaP_5^{max}} = a$$

P_1 stands for the LI shift of proton H_1 in the conformer P upon addition of z equiv. of $Eu(dpm)_3$. Q_5 represents the LI shift of proton H_5 in conformer Q for a given amount of shift reagent. However, the parameters to calculate a from equation (3) are experimentally only partly available. The expression (4) also equals to a provided that the assumptions $P_1^{max} = Q_5^{max}$ and $P_5^{max} = Q_1^{max}$ are incorporated.

$$(4)\quad \frac{\Delta_1 - zQ_1^{max}}{\Delta_1 + \Delta_5 - 2\,zQ_1^{max}} = a$$

In good approximation[14] for the quantity zQ_1^{max} may be taken the shift difference for the *ortho* protons H_6 and or H_{10} of ring B resulting from complexation of the sulfine with z equiv. of $Eu(dpm)_3$. By means of equation (4) the proportion of rotamer P in the complexed state can be obtained[15] from the observed LI shifts. The figure shows these shifts as they were found for sulfine Ib in $CDCl_3$. The results thus obtained for the four sulfines in different solvents are listed in the Table, which also includes the rotamer populations in the uncomplexed state[9].



The data in the Table reveal that in the three different solvents studied the proportion of conformer P in the complexed state is much smaller[17] than in the uncomplexed state. Thus, as well for sulfines Ia and Ib for which rotamer P is the more polar one, as for sulfines Ic and Id for which rotamer Q is the more polar one, complexation with $Eu(dpm)_3$ leads to a larger preference for rotamer Q. This effect cannot be due to changes in polarity of the medium caused by the presence of the shift reagent because the behaviour of the sulfines Ia and Ib towards changes in medium polarity is opposite to that of the sulfines Ic and Id *(vide supra)*. A likely explanation for the effect of $Eu(dpm)_3$ on the conformational

T A B L E

Compd.	Ia			Ib			Ic			Id		
Solvent	Δ_1	Δ_5	$\Delta_{6,10}$	Δ_1	Δ_5	$\Delta_{6,10}$	Δ_1	Δ_5	$\Delta_{6,10}$	Δ_1	Δ_5	$\Delta_{6,10}$
CCl_4	5.57	9.35	2.70				9.40	6.80	2.90	7.81	8.79	3.00
$CDCl_3$	3.47	5.72	1.60	2.14	5.05	1.40				5.16	6.03	1.90
CH_2Cl_2	2.80	4.30	1.25	1.21	2.55	0.70	3.46	3.17	1.15	3.80	4.77	1.45

	Ia		Ib		Ic		Id	
	% P_c	% P_u	% P_c	% P_u	% P_c	% P_u	% P_c	% P_u
CCl_4	29	45			63	100	45	72
$CDCl_3$	31		19	16			43.5	
CH_2Cl_2	34	70[a]	22	40[a]	54		41	
CH_3COCH_3		100		80		83		56

% P_c = percentage of conformer P in the complexed state; % P_u = percentage of conformer P in the uncomplexed state. Δ-values in ppm obtained upon addition of 0.8 equiv. of $Eu(dpm)_3$. Spectra recorded at 60 Mhz. Conc. 20 mg/0.5 ml. a: see note 16.

equilibrium is that steric interactions between the *meta* substituent X and the coordinated shift reagent result in a larger proportion of rotamer Q in which such interactions are minimized. The data in the Table show further that in the complexed sulfines the proportion of the more polar conformer (P for Ia and Ib, Q for Ic and Id) becomes larger in a solvent of a higher dielectric constant. Thus, in the complexed as well as in the uncomplexed state the conformational equilibrium shifts to the more polar rotamer with increasing solvent polarity. For the sulfines Ic and Id the difference in solvent effect on the conformer population in the complexed and uncomplexed state is small. However, in the uncomplexed sulfines Ia and Ib the effect of solvent polarity on the conformational equilibrium is large while in the complexed state this effect has become much smaller. Apparently, in the latter sulfines the steric effects caused by complexation with the shift reagent are dominating over the solvent effect.

In conclusion this study shows that mobile conformational equilibria can considerably be perturbed by complexation with lanthanides and that utmost care should be taken in studying such equilibria with the use of shift reagents.

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10. The position of phenyl ring B cannot be specified, because H_6 and H_{10} do not show up sufficiently different in the spectra for reasons that the anisotropic effect of the CSO system on these protons is negligible.
11. A. Tangerman and B. Zwanenburg, *J.C.S. Perkin II*, submitted for publication (part 24 in this series).
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13. Δ_1 reflects the LI shift of proton H_1 for the same proportion of rotamers in the uncomplexed and complexed state, which *a priori* will not be the case. However, the formulation as given in the equations (1) and (2) is allowed, because in comparison with the magnitude of the LI shift $\delta(H_1)_{free}$ will vary only little when the rotamer ratio in the uncomplexed state becomes different from that in the complexed state.
14. The distance of the coordinated $Eu(dpm)_3$ to proton H_1 in the Q conformer or to proton H_5 in the P conformer is about the same as the distance of $Eu(dpm)_3$ to the *ortho* protons of ring B. Moreover, the value of Q_1^{max} is small in comparison with that of P_1^{max} or Q_5^{max}, which means that a rather large deviation in Q_1^{max} leads to only a small change in α.
15. The percentage of P in the complexed state has been calculated for different amounts of added shift reagent. The same value was obtained as is predicted from equation (4).
16. These percentages are derived from the spectra in dichloromethane in the manner as described in ref. 9 without making a correction for the solvent effects.
17. An exception is sulfine Ib in $CDCl_3$ which has already predominantly conformation Q in the uncomplexed state.