

Lanthanide-induced Chemical Shifts in Proton NMR Spectra of 5,5-Dimethyl-2-oxo-1,3,2-dioxaphosphorinanes

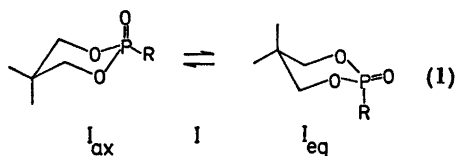
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The conformational preference of the R substituent in twelve 5,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinanes (I) is discussed on the basis of lanthanide shift NMR data. The results show that although lanthanide induced shifts might not be conclusive when considered isolated, they are of great value in connection with other NMR parameters, *i.e.* coupling constants and chemical shifts. In fact, the chemical shifts induced in the substrate upon complexation in some cases indicate the presence of conformers which cannot easily be detected by interpretation of coupling constants and ordinary chemical shifts. As far as only chair conformers are considered, it is concluded that the P=O bond is mainly axial for R=CH₃, CH₂Ph, Ph, C(CH₃)₃, CPh₃, N(CH₃)₂ and mainly equatorial for R=OCH₃, OC(CH₃)₃, OPh, SCH₃, Cl, F. There is evidence, however, that non-chair conformers might contribute to the true average conformation for I, R=C(CH₃)₃, CPh₃.

Information about the conformation in 2-oxo-1,3,2-dioxaphosphorinanes has been obtained by a number of different techniques¹ such as X-ray crystallography, dipole moment studies, IR spectroscopy, NMR chemical shifts and coupling constants. Most of the available information supports a chair conformer with the substituent on phosphorus axial.² There is evidence, however, that a conformational equilibrium exists in solution.³

For 5,5-dimethyl-2-oxo-1,3,2-dioxaphospho-



rinanes (I), the conformational equilibrium is given by (1).

The use of lanthanide shift reagents (LSR) in structural and conformational analysis has been successful in a number of cases.³ The strong electron donor ability of the P=O oxygen in I opens the possibility that equilibrium (1) can be studied by observing the chemical shifts induced in I upon complexation with an LSR. In fact, it was shown previously that lanthanide induced chemical shifts (LIS) allowed qualitative conclusions regarding the stereochemistry around phosphorus in I.⁴ The purpose of this work is to obtain information about the orientation of the substituent at the phosphorus atom.

RESULTS AND DISCUSSION

Existing data on the conformation of I in solution agree with the equilibrium shown in (1).⁵ In the discussion to follow it is presumed, unless otherwise stated, that the chair forms I_{ax} and I_{eq} are the only conformers contributing to the true average conformation of the molecule. On the basis of the available X-ray structural data this is a reasonable assumption.⁶⁻⁷ Non-chair geometries have, however, been shown to exist in a few special cases.^{8,9}

The application of LIS are based on the pseudocontact shift equation¹⁰

$$\Delta\nu_1 = K(3 \cos^2 \theta_1 - 1)R_1^{-3} \quad (2)$$

where K is a constant, $\Delta\nu_1$ is the incremental chemical shift induced in proton H₁ on complex-

ation, R_i the internuclear distance between H_i and the lanthanide atom, and θ_i the angle between the vector R_i and the symmetry axis of the LSR. Although eqn. 2 has been applied quantitatively,¹¹ its approximate nature should be kept in mind.

The chemical shifts induced in the hydrogens in I will depend on the relative contribution from I_{ax} and I_{eq} .⁴ The shifts induced in the methylene protons should be particularly informative with respect to the position of equilibrium (1). A qualitative application of eqn. 2 shows that the difference in the chemical shifts induced in the two types of methylene protons should be larger for conformer I_{ax} than for I_{eq} . Apart from these shifts, additional information can be obtained from the LIS of other protons in the molecule. Useful information regarding the position of the conformational equilibrium is also provided by the POCH coupling constants.^{8,12}

In this study the LSR europium(III)-tris-1,1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-oc-tanedione, $Eu(fod)_3$,¹³ was applied to carbon

tetrachloride or deuteriochloroform solutions of I. In all cases the induced chemical shifts were observed as a function of the molar ratio $q = [LSR]/[substrate]$ at a constant substrate concentration, normally at 0.100 M. Representative LIS plots are shown in Fig. 1. Common for all LIS plots obtained is an approximately linear ν vs. q dependence for low values of q . In this region the ν/q slope can be taken as a measure of $\Delta\nu$ caused by complexation. Assuming that the stoichiometry of the complex is one molecule of LSR to two molecules of I, it can be shown that the initial ν/q slope (S) is approximately equal to twice the limiting shift of the 1:2 complex.¹⁴ Whether the stoichiometry of the complex is 1:2 or 1:1 is not essential as the arguments given only depend on the existence of the same type of complex in the series of compounds studied, a reasonable assumption. In addition to geometry, S will depend on the strength of the interaction. While the LIS within a molecule reflects the difference in orientation with respect to the lanthanide in the complex, this need not be the case when comparing S -values obtained for different compounds. However, the qualitative picture of the LIS plots should be similar for compounds of type I if their conformation is the same, even if the strength of the interaction with the LSR differs between the members of the series.

The obtained S -values, chemical shifts and coupling constants are listed in Tables 1 and 2. The indices 1, 2, 3, and 4 denote, respectively, the highfield methyl signal, the low field methyl signal, the high field methylene signal, and the low field methylene signal. For the purpose of internal comparison of chemical shifts, the ratios S_3/S_1 and S_4/S_2 are also included in the table.

$I [R = CH_3, CH_2Ph, Ph, C(CH_3)_3, N(CH_3)_2]$. The qualitative LIS pictures of these compounds are very similar and therefore indicate a common conformation for these molecules in solution.

The LIS behaviour of 5,5-dimethylmethylene-sulfite (II) is very similar to that observed for compounds 1–3.⁴ Since there is compelling evidence for the axial orientation of the S=O bond in this compound,^{15–17} it can tentatively be concluded that I_{ax} is the main contributing conformer for compounds 1–5.

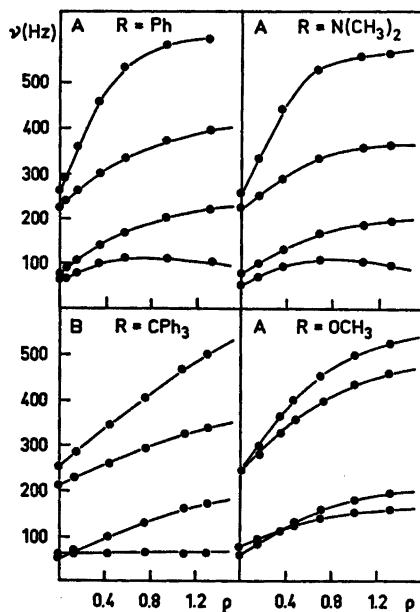


Fig. 1. Examples of ν/q -curves for the methyl (high field) and methylene (low field) protons in compounds of type I. A and B denote carbon tetrachloride and deuteriochloroform, respectively.

Table 1. Initial ν/ρ slopes (S -values)^a for 0.1 M solutions of I at 25 °C.

Compound	R	Solvent ^b	S_1	S_2	S_3	S_4	S_2/S_1	S_4/S_3
1	CH ₃	A	85	155	205	435	1.82	2.12
		B	55	115	145	295	2.09	2.03
2	CH ₂ Ph	A	70	110	150	310	1.57	2.07
		B	50	100	130	250	2.00	1.92
3	Ph	A	110	190	220	600	1.73	2.73
		B	35	135	145	315	3.36	2.17
4	C(CH ₃) ₃	A	110	150	200	490	1.36	2.45
		B	30	120	140	280	4.00	2.00
5	N(CH ₃) ₂	A	110	150	180	490	1.36	2.72
		B	100	110	140	290	1.10	2.07
6	OCH ₃	A	170	110	250	350	0.65	1.40
		B	130	90	~240		0.69	
7	OC(CH ₃) ₃	A	120	80	170	290	0.67	1.70
8	OPh ^c	A	120	80	200	270	0.67	1.35
		B	90	60	~180		0.67	
9	SCH ₃	A	120	90	170	240	0.75	1.41
10	Cl	A	110	160	220	260	1.45	1.18
		B	95	135	160	210	1.42	1.31
11	F	A	130	170	~240		1.31	
12	CPh ₃	B	0	105	120	195		1.63
II		A	160	230	340	770	1.44	2.26

^a In Hz/mol ratio shift reagent. ^b A and B denote carbon tetrachloride and deuteriochloroform, respectively. ^c 0.05 M in carbon tetrachloride solution.

Table 2. Chemical shifts^c (ν) and POCH coupling constants^a for compounds I–12.

Compound	Solvent	ν_1	ν_2	ν_3	ν_4	ν_{2-1} ^b	ν_{4-3} ^c	$q=0$		$q=1$	
								$J(\text{POCH})_3$	$J(\text{POCH})_4$	$J(\text{POCH})_3$	$J(\text{POCH})_4$
1	A	57.0	71.9	219	254	14.9	35	17	6	20	3
	B	60.7	69.7	227	254	9.0	27	15	8	19	3
2	A	50.2	53.3	214	251	3.1	37	17	5	20	2
	B	49.1	56.4	220	252	7.3	32	15	7	19	3
3	A	62.0	76.8	225	260	14.8	35	17	6	20	3
	B	67.9	71.2	233	259	3.3	26	13	10	19	5
4	A	52.2	74.0	216	261	21.8	41	18	3	19	2
	B	52.5	74.7	222	262	22.2	40	18	3	19	2
5	A	52.6	74.7	219	256	22.1	37	21	2	22	—
	B	53.9	74.2	227	258	20.3	31	19	4	21	—
6	A	55.5	75.3			19.8				~11	~11
	B	54.4	76.1			21.7					
7	A	54.7	73.1			18.4				14	~11
8	A	52.0	80.1			28.1				~11	~13
	B	55.0	80.4			25.4					
9	A	57.2	78.4			21.2				~11	15
	B	53.6	76.7			23.1					
10	A	58.0	82.0			24.0		27	3	27	3
	B	56.6	81.0			24.4		27	3	27	2
11	A	54.2	79.2			25.0					
	B	54.3	78.8			24.5					
12	B	48.7	60.4	209	255	11.7	46	14	6	19	2
II	A	53.2	79.3	199	275	26.1	75				

^a In Hz at 60 Mz. ^b $\nu_{2-1} = \nu_2 - \nu_1$. ^c $\nu_{4-3} = \nu_4 - \nu_3$.

This conclusion is primarily based on the differentiation between the lanthanide induced chemical shifts of the methylene protons, as measured by the S_4/S_3 ratios. As seen from Table 1, this ratio is of similar magnitude for compounds 1–5 and clearly different from the values obtained for other members of the series, as for instance I ($R=Cl$). This is the case whether the solvent is carbon tetrachloride or deuteriochloroform.

Although the methyl protons are not expected to be particularly sensitive to the stereochemistry at the phosphorus atom, their LIS behaviour are in no contradiction to an axial orientation of the $P=O$ bond.

There is generally a change to smaller S_4/S_3 ratios when changing the solvent from carbon tetrachloride to deuteriochloroform. This is in accordance with a change in the conformational equilibrium towards I_{eq} and that conformers like I_{eq} have a larger dipole moment than conformers like I_{ax} .¹⁸ There is also a solvent effect on the S_2/S_1 ratios, which with the exception of compound 5 is towards higher values on going from carbon tetrachloride to chloroform. No attempt will be made to interpret this variation apart from noting that the largest effect is observed for the compound with the bulkiest substituent, $C(CH_3)_3$. The existence of non-chair conformers is therefore indicated.

The stereospecificity of the $POCH$ coupling constants in the 2-oxo-1,3,2-dioxaphosphorinane series is now well documented.³ Typical values for the considered compounds are 2 and 20 Hz, respectively, for axially and equatorially situated methylene protons. The large difference between the $POCH$ coupling constants for compounds 1–5, Table 2, is thus in agreement with the predominance of one conformer. The fact that these values converge when changing the solvent from CCl_4 to $CDCl_3$ corresponds to the observed displacement of the conformational equilibrium towards I_{eq} as was detected by the solvent induced variation of the S_4/S_3 ratios. There is also consistency between the LIS behavior and the $POCH$ couplings in the sense that the smallest coupling constant is found for the low field methylene signal and *vice versa*.

The very small solvent induced variation of the $POCH$ coupling constant for 4 is inter-

pretable in terms of a complete dominance of I_{ax} .

With reference to the anisotropy effect caused by an axially oriented $S=O$ bond in methylenesulfites,¹⁷ it is reasonable to expect an analogous effect of the $P=O$ bond in conformer I_{ax} . The relatively large chemical shift difference for compounds 1–5 can therefore be taken as additional evidence for the domination of the conformer with an axially oriented $P=O$ bond.

A solvent induced variation of the ν_{3-1} and ν_{4-3} values clearly exists for compounds 1, 2, 3, and 5, Table 2. This is in accordance with a displacement of the conformational equilibrium, *i.e.* in correspondence with the effect of solvent on the LIS parameters and $POCH$ coupling constants. In the case of compound 4, however, no significant solvent effect is observed. This finding parallels the virtual constancy of the $POCH$ coupling constants on variation of the solvent. If only conformers I_{ax} and I_{eq} are considered for compound 4, it seems that the conformational equilibrium is totally displaced to the left. However, because of the steric requirements of the $C(CH_3)_3$ group, non-chair conformers cannot be excluded.

The dominant contribution of I_{ax} to the conformation of compounds 1–5 in solution agrees with infrared studies by Majoral *et al.* on derivatives 3 and 5.^{19,20}

Where meaningful comparison is possible, the axial preference of the $P=O$ bond in the solution state is, with the possible exception of 5,³ in contrast to results obtained from X-Ray crystallography. Compound 3, for instance, exists in the solid state in the form of a chair with an equatorially oriented $P=O$ bond.⁵ While there thus appears to be a lack in correspondence between the conformations adopted by 3 in the solid and the solution state, this is not the case for the phosphorus-sulfur analogue of 1. 1H , ^{13}C and ^{31}P NMR showed this compound to have the same conformation in solution²¹ as in the solid state,²² namely a chair with an axial $P=S$ bond.

I [$R=OCH_3$, $OC(CH_3)_3$, OPh , SCH_3]. As can be seen from Fig. 1 and Table 1, the LIS behaviour of compounds 6–9 is very similar, indicating a common solution conformation for these compounds. The crossing of ν/q -curves for the methyl signals is characteristic.

The small LIS discrimination of the methylene protons, as measured by the S_4/S_3 ratio, is another feature which is different from that observed for compounds 1–5. On this basis it can be concluded, if only chair conformers are considered, that the contribution from I_{ax} cannot be dominant. Due to the small chemical shift separation between methylene protons, the effect of solvent on the S_4/S_3 ratio could not be measured. However, the S_2/S_1 -values are not markedly affected by changing the solvent from CCl_4 to $CDCl_3$. Contrary to what was observed for compounds 1–5, this observation indicates that the conformational equilibrium is not drastically changed upon solvent variation.

Due to the small chemical shift difference of the methylene hydrogens in compounds 6–9, the *POCH* coupling constants could not be determined by first order analysis of the NMR spectrum. The values obtained in the presence of $Eu(fod)_3$ in CCl_4 solution are, however, of the same magnitude and therefore indicate competing contributions from I_{ax} and I_{eq} . Because of the possible effect of $Eu(fod)_3$ on the conformational equilibrium (as discussed below), the conformer ratio I_{ax}/I_{eq} might very well be smaller in the absence of the shift reagent. That this is at least the case for derivatives 7 and 8, is shown by the available *POCH* coupling constants for these compounds, obtained by detailed analysis of their NMR spectra. The pairs of coupling constants were found to be (21.0 Hz, 3.3 Hz)⁸ and (22.5 Hz, 1.7 Hz),²³ respectively, for 7 and 8 in deuteriochloroform solution, *i.e.* in agreement with an equatorially oriented P=O bond.

In analogy with the S_2/S_1 ratios, the ν_{2-1} values are very similar in the solvents CCl_4 and $CDCl_3$. This is in contrast to the solvent variation observed for compounds 1, 2, 3, and 5 and indicates that the conformational equilibrium is not significantly changed upon solvent variation.

The fact that the chemical shifts for the methylene protons cannot be resolved is in agreement with the absence of an anisotropy effect of the P=O bond and consequently with a nonpredominating contribution of I_{ax} .

The P=O stretching frequencies observed in the infrared spectrum of 6 and 8 have by Majoral *et al.* been interpreted in terms of

relative contributions from conformers I_{ax} and I_{eq} .¹⁹ It was concluded that the compounds in benzene and pyridine solution were present largely in the form of I_{eq} , *i.e.* in agreement with the results above.

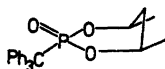
Available structural data on compounds related to $I(R=OR')$ together with the results above, indicate that the conformational situation is not drastically changed on going from solution to the solid state. In particular, 2-oxo-2-phenoxy-1,3,2-dioxaphosphorinane, was in the solid state shown to exist as a chair with an equatorial P=O bond.⁷

I (R=Cl, F). The S_4/S_3 value for compound 10 indicated a very small, if any, contribution from I_{ax} , and must therefore, if only chair conformers are considered, be present in solution as I_{eq} . The domination of one conformer is strongly supported by the very different *POCH* coupling constants, Table 2. Further evidence for this conclusion is provided by the near constancy of ν_{2-1} , the invariance of coupling constants on changing the solvent from CCl_4 to $CDCl_3$ and the fact that its infrared spectrum shows only one band which can be assigned to the P=O stretching frequency.¹⁹

Addition of LSR to a carbon tetrachloride solution of 11 did not result in chemical shift separation between methylene protons large enough to allow determination of S_3 and S_4 . This small chemical shift discrimination induced by the LSR is similar to the situation for compound 10 in which case S_4/S_3 was found to be 1.18. The nearly identical values of ν_{2-1} for 10 and 11 are also consistent with a common conformation for these two compounds. By analogy therefore, it is concluded that 11 exists in solution as I_{eq} .

I (R=CPh₃). For solubility reasons compound 12 could not be studied in carbon tetrachloride solution. The S_4/S_3 value is in correspondence with a predominant contribution from I_{ax} . This is also consistent with the observed *POCH* coupling constants and the chemical shift difference between the methylene protons in the absence of shift reagent. However, the LIS behavior of the methyl signals, which are different from that observed for the other compounds studied whether the P=O bond is axially or equatorially oriented, indicates the presence of non-chair conformers. It is interesting to note that the type of LIS

behaviour observed for the methyl groups in **12** is also observed for **4** in CDCl_3 solution, although to a smaller degree. The fact that a bulky substituent is present in both these compounds supports the assumption of a contribution from non-chair conformers to the average conformation of the molecule. The relevance of steric effects for this type of substituents is demonstrated by the solid state conformation of compound **III**. X-Ray structural studies showed this compound to exhibit a "chaise longue" conformation.²⁴



III

The effect of shift reagent on the conformational equilibrium. From the observation that a change of solvent from CCl_4 to CDCl_3 might result in displacement of the conformational equilibrium (1), the possible influence of the shift reagent on this equilibrium should be considered. Such an influence has previously been noted for **1-3**⁴ and some related compounds.²⁵⁻²⁷ As seen from Table 2, the difference in the observed POCH coupling constants for compounds **1-5** and **12** is increased upon addition of the shift reagent. Similarly, a convergence of coupling constants was noted for derivatives **7** and **8**. In both cases this means that equilibrium (1) is displaced towards I_{ax} . The effect can be explained in terms of a non-negligible difference in the basicity of the $\text{P}=\text{O}$ oxygens in conformer I_{ax} and I_{eq} . Support for this explanation is provided by the fact that the $\text{P}=\text{O}$ stretching frequency for compounds of the considered type have been shown to be lower for I_{ax} than for I_{eq} .¹⁹ This is in correspondance with a greater polarity of the $\text{P}=\text{O}$ bond in I_{ax} , a result which is in agreement with molecular orbital CNDO/2 calculations.²⁰ The effect of $\text{Eu}(\text{fod})_3$ on equilibrium (1) can therefore be interpreted in terms of a larger equilibrium constant for the interaction of the LSR with I_{ax} as compared to I_{eq} , thus leading to a displacement of (1) to the left.

This finding is related to the effect of BF_3 on the relative contribution from conformers I_{ax} and I_{eq} .²⁸ Thus for compounds **3**, **5** and **8**

it was shown that addition of BF_3 induced changes in the ^1H and ^{31}P NMR parameters which were consistent with displacement of equilibrium (1) towards I_{ax} .

Although quantitative results cannot be obtained in the cases where the applied shift reagent distorts the equilibrium under study, the qualitative conclusions drawn above should still be valid. It can therefore be concluded that lanthanide induced chemical shifts can be a valuable tool for gaining information about the solution conformation in compounds of type I.

EXPERIMENTAL

Synthesis and reagents. Compounds **1-12** were prepared according to well-known procedures³⁰ and characterized by their melting points and ^1H NMR spectra.

Spectroscopic grade carbon tetrachloride and deuteriochloroform were stored over molecular sieves. The shift reagent $\text{Eu}(\text{fod})_3$ was kept over P_2O_5 in vacuum before use.

Instrumentation. ^1H NMR spectra were recorded on a JEOL JNM-C-60H spectrometer operating at 60 Mz.

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