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LANTHANIDE INDUCED SHIFTS DUE TO COORDINATION AT PHOSPHORYL AND AMIDE SITES

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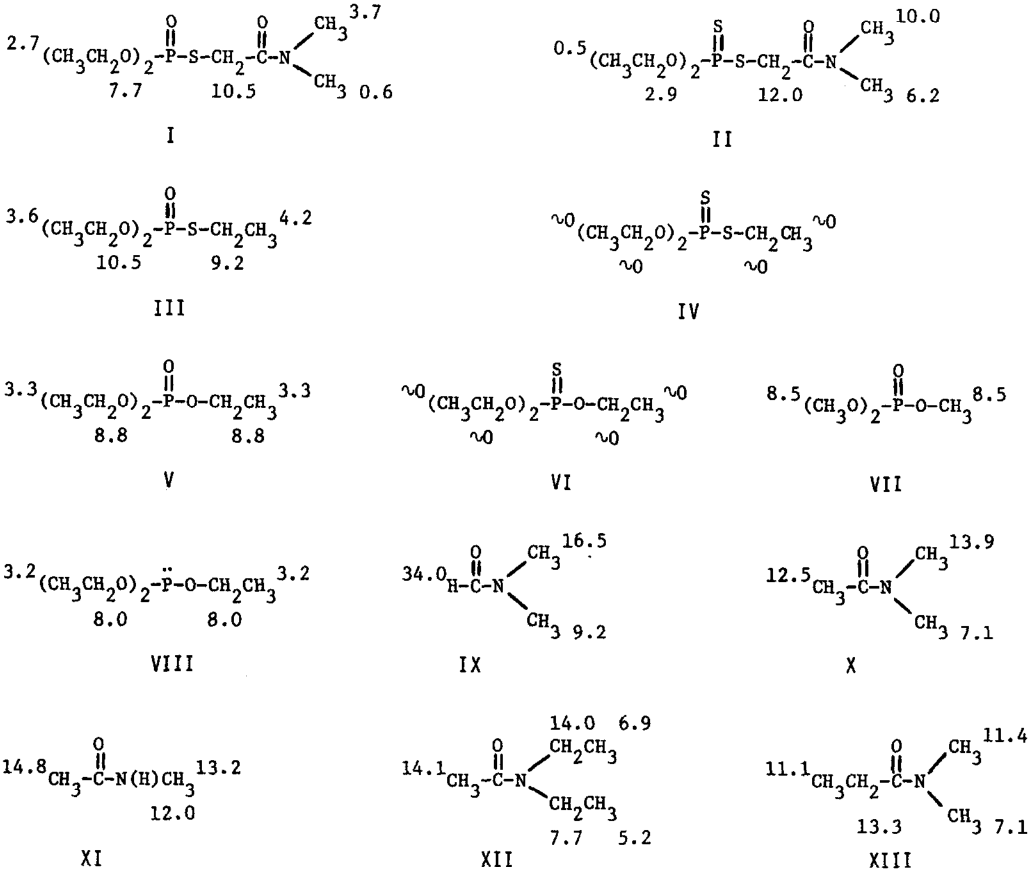
Recently, several complexes of lanthanide ions [Eu(DPM)$_3$[1], Pr(DPM)$_3$[2], Eu(fod)$_3$[3], Pr(fod)$_3$[3], and Yb(DPM)$_3$[4]] have received considerable attention as nmr "shift reagents". The dramatic simplification of nmr spectra resulting from the addition of one of these reagents to a test solution has allowed confident assignment of configuration in diverse systems. In most cases the molecules studied have had only one reactive site likely to complex with the shift reagent. However, Hart and Love[5] have noted recently that intramolecular competition for a shift reagent by different groups in a polyfunctional molecule can lead to preferred bonding orders.

We would like to present results of a study using a series of polyfunctional molecular compounds in which the apparent sensitivity of opposite ends of the molecule can be reversed by a change of one atom in the basic structure. The compounds studied (as ~ 7% (w/v) solutions in CCl_4) were organophosphorous pesticide analogs[6]; O,O-diethyl-S-(N,N-dimethylcarbamoylmethyl)phosphorothiolate(I) and O,O-diethyl-S-(N,N-dimethylcarbamoylmethyl)phosphorodithiolate (II) and certain models containing the functional groups of interest (III-XIII). The shifts (ΔEu) produced in the various hydrogens as a result of Eu(DPM)$_3$ addition, extrapolated to a 1-1 europium to substrate ratio[5,7] are listed near each hydrogen in the figure. The precision of ΔEu values determined from replicate runs on several samples is estimated to be ± 0.5.[8]

It is apparent that when the phosphoryl group is present (I), predominant association with europium occurs at that site rather than at the amide site. Replacement with the thiophosphoryl linkage (II) allows the amide group to successfully compete for the europium. A further comparison of the apparent bonding strengths of the phosphoryl and thiophosphoryl groups can be observed in the proton shifts of compounds III and IV. While the oxygen analog exhibited large shifts, no detectable shifts could be observed in the sulfur compound.

FIGURE



Substantiation of this lack of complexing capacity in thiophosphoryl compounds of this type was obtained by examining the behavior of triethyl phosphorothionate (VI). Once again no shifts could be detected. Evidently the electron density at the sulfur atom in these cases is insufficient for complexation with the shift reagent used here. Bauman[9] has observed a similar effect on replacement of the carbonyl oxygen with sulfur in ethyl acetate.

Comparison of the shifts observed for various amides (IX-XIII) with those of II confirm our assignment of the effect observed in II as due to coordination at the amide site. The generally smaller effects observed for the various hydrogens in II when compared with similar hydrogens in the amides is consistent with a slightly smaller equilibrium constant for the association with Eu(DPM)$_3$. This could be caused by the large steric requirement of the dithiophosphate side chain. This explanation is corroborated by a comparison of the ΔEu values of the N-methyl groups observed for dimethylformamide (IX), dimethylacetamide (X) and dimethylpropionamide(XIII). Such comparisons among these amides are also consistent with other recent results[4,5,10] which indicate that among groups of very similar Lewis basicity, differences in observed ΔEu values are explained best in terms of steric effects. Thus, the more bulky the substrate, the lower the value of the equilibrium constant for substrate • Eu(DPM)$_3$ association and consequently, smaller ΔEu values are expected.

Beaute and co-workers[11] have reported ΔYb values for IX and X which are *approximately* 3.1 times as large as the europium values found in this work. An *estimation* of the decrease in effect to be expected on replacement of the carbonyl oxygen of an amide with sulfur may be obtained by comparing our results on IX with those of Walter et al.[12] for E-N-methyl-N-isopropylthioformamide. The ΔEu values for comparable hydrogens are 1.7-1.8 times as large in the amide as compared to the thioamide. Based on this study and other work cited above it is most likely that of the two possible sites in the amide group (N and O), the carbonyl oxygen is the predominant coordination site. This finding is of some significance since it may allow the use of Eu(DPM)$_3$ as a probe of conformation in biologically significant peptides.

An ordering of preferred coordination sites of the functional groups studied in this work may be written as:

$$P{=}O > C{=}O \text{ (amides)} > C{=}S \text{ (thioamide)} > P{=}S$$

We have not attempted to apply Hinckley's elegant graphical method[13] of estimating the contributions of association to each of several sites due to the conformational flexibility of our systems (I and II) and the uncertainty associated with the angle function[13,14] in the equation for the pseudocontact shift.

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