Effect of Lanthanide Shift Reagents on the Nuclear Magnetic Resonance Spectra of Secondary Amides

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Summary It is shown that lanthanide shift reagents induce in the spectra of simple amides unexpected additional peaks and that this effect depends on the nature of the shift reagent used.

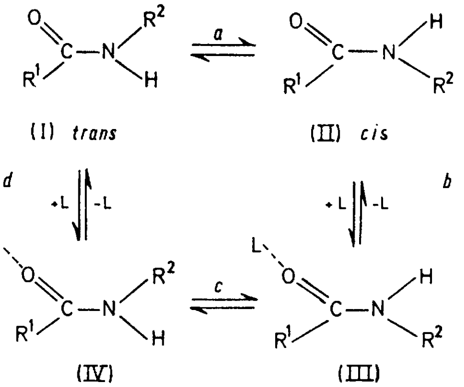
WE have found that the lanthanide shift reagents Eu(dpm)$_3$ and Eu(fod)$_3$ can induce in the n.m.r. spectra of simple secondary amides, which normally show peaks for the *trans*-isomer alone, additional peaks that can possibly be assigned to a *cis*-isomer. The 60 MHz ^{1}H n.m.r. spectra of 0·25M-solutions in CDCl$_3$ (34°) of *N*-methylacetamide (**1**), acetanilide (**2**), and phenacetin (**3**), with a lanthanide–substrate molar ratio ([L]/[S]) $>$ 0·1, contained in each case, in addition to the expected peaks,[1] signals for a minor component, the molar percentage of which increased with increase in [L]/[S]. This minor component displayed a different dependence of induced shift on [L] and gave chemical shift/[L] plots that at low [L] values were not rectilinear.

When Eu(fod)$_3$ was used the *N*-methyl protons for the major component of (**1**) and the *ortho*-aromatic protons for the major components of (**2**) and of (**3**) showed larger induced shifts (*e.g.*, *ca.* 6·7, 6·8, and 6·7 p.p.m., respectively, for [L]/[S] = 1) than did those for the corresponding minor components (*e.g.*, *ca.* 2·3, 1·7, and 1·7 p.p.m., respectively), and the molar percentages of the minor components approached constant values (*ca.* 26, 45, and 57, respectively) at [L]/[S] = 1. Eu(dpm)$_3$ induced slightly smaller shifts and gave rise to smaller amounts of the minor component than did Eu(fod)$_3$. Because of the lower solubility of Eu(dpm)$_3$, [L]/[S] values $>$ 0·5 could not be achieved, but at [L]/[S] = 0·5 the molar percentages of the minor components for (**1**), (**2**), and (**3**) were *ca.* 10, 23, and 31, respectively.

Since simple secondary amides exist in solution largely as the *trans*-isomer (I)[2] it is reasonable to suppose that the major and minor components are associated with complexed *trans*- (IV) and *cis*-isomers (III), respectively. This would accord with our observations that the *N*-methyl protons of (**1**) and the *ortho*-aromatic protons of (**2**) and of (**3**), which are closer to the lanthanide atom in (IV) than they are in (III), show a larger induced shift for the major (*trans*) component than for the minor (*cis*) component and that the molar percentages of *cis*-isomer are greater for (**2**) and (**3**) than they are for (**1**), where steric interactions between the lanthanide and substituent R^2 would be smaller.

It is to be expected that only rotational equilibria *a* and *c* will be significant on the n.m.r. time scale and that, of these, *c* will be slower because of increase in the double bond character of the C–N linkage on complexing with the Lewis acid (L). Thus, the rate of rotation *a* remains the determining factor for the observation of rotational isomers in the complexed substrate. However, if the complexed *trans*-isomer (IV) is destabilised relative to the complexed *cis*-form (III) by steric interaction between the lanthanide group and the substituent R^2, detectable amounts of both isomers may be present in solution. The n.m.r. spectrum will correspond with the population-weighted means of (I) and (IV) and of (II) and (III) for the *trans*- and *cis*-isomers, respectively, and, if the concentration of (III) is appreciable, the spectrum will show peaks for both isomers; this will occur even when the concentration of (II) is too small for (III) to be observed.

The possibility of self-association between substrate molecules must be considered. A study of the ^1H n.m.r. behaviour of (**1**) over the concentration range 0·05—1·0M, although providing some evidence (acetyl peak shifts 0·02 p.p.m.) for self-association, showed that the attainment of association equilibrium was rapid in comparison with the rate of *cis–trans*-interconversion.



A Referee has pointed out that the rates of equilibria *a* and *c* are not exclusively the controlling factors for the observation of *cis* isomers. The 'coalescence temperature' of n.m.r. signals depends not only on rate, but also on the difference in chemical shift of the protons involved; this difference is likely to be much greater with a shift reagent effectively raising the 'coalescence temperature'. It is, alternatively, suggested that the observations could be due to relatively slow complexing of one conformational isomer, either separately or simultaneously at the two weak donor sites oxygen and nitrogen. Further work is being undertaken to clarify this.

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