

CHEMICAL SPIN-DECOUPLING AND LANTHANIDE REAGENTS

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Utilization of lanthanide complexes in nmr studies has centered around the $(3 \cos^2 \theta - 1/r^3)$ dependence of shifts arising from pseudocontact interactions to provide resolution enhancement and first-order coupling patterns in spectra¹⁻³. In addition to inducing shifts, the paramagnetism associated with the metal also causes line broadening, which has generally been regarded as a nuisance in experiments designed to obtain coupling constants. The purpose of this note is to demonstrate the potential value of a line-broadening or relaxation reagent in the determination of coupling constants and to serve as a caveat for the interpretation of observed splittings using shift reagents.*

The width of a proton resonance is reciprocally related to the average length of time a nucleus resides in a particular spin state. A relaxation time thus corresponds to a reciprocal rate constant for nuclei undergoing a transition from one spin state to another. There is considerable variation in the effectiveness of the paramagnetism of different metals in causing these transitions and the associated relaxational broadening. The suitability of europium and praseodymium complexes as shift reagents is attributable to their relatively ineffectual relaxation of protons, which generally results in narrow resonances. With other lanthanides or with high ratios of Eu or Pr to substrate, line broadening can become substantial. Generally, this is observed as a larger broadening associated with increasing shift of the resonance. This is to be expected because the θ in the dipolar shift expression is generally between 0 and 30°, which leads to an approximate proportionality to the inverse cube of the distance from the metal to the proton, $1/r^3$, whereas the broadening is approximately proportional to $1/r^6$.** Of particular interest here, however, is that the greater broadening

* Paramagnetic complexes have been used previously to effect decoupling of boron and phosphorus nuclei.^{4,5} Homonuclear decoupling of protons in quinoline has also been observed with nickel complexes.⁶

** For gadolinium the broadening shows a very close correlation with $1/r^6$, however, for the other rare earths two additional angular factors must be considered.^{7,8}

of certain resonances in a compound can be attributed to shorter relaxation times or faster rates of transition between $|\alpha\rangle$ and $|\beta\rangle$ spin states of those protons. This increased relaxation rate has the same effect on the spin-spin splittings caused by that proton as does rapid chemical exchange between two environments; i.e., broadening of the lines and collapse to a single line at sufficiently fast rates.

This effect can be readily demonstrated by following the changes in the 3-protons of pyridine induced by the addition of a relaxation reagent. Addition of $\text{Eu}(\text{fod})_3^*$ to a solution of pyridine shifts the 2-protons to 13.04 δ , and produces smaller shifts in the 3- and 4-protons, which appear at 8.66 and 9.06 δ respectively (see Figure). The 4-proton appears as a triplet due to $J_{34} = 7$ Hz; whereas, the 3-protons appear as a doublet of doublets from coupling to the 4-proton as well as coupling to the 2-proton ($J_{23} = 5$ Hz). The addition of one microliter of 0.05 M $\text{Gd}(\text{fod})_3$ to the above solution causes the 2-protons to broaden to a halfwidth of 41 Hz. The rapid relaxation of the 2-protons results in effective decoupling from the 3-protons, thus eliminating the 5 Hz coupling in the 3-H resonance as shown in the Figure. This can be considered as the coalesced spectrum of the resonances at 9.12, 9.07 and those at 9.05 and 8.99 δ , due to rapid exchange between sites associate with $|\alpha\rangle$ and $|\beta\rangle$ spin states of the 2-proton.

These effects can be computed from the standard line shape expressions normally used for chemical exchange.⁹ The rate constant for $|\alpha\rangle$ to $|\beta\rangle$ transitions of protons associated with a resonance which is broadened can be determined from W_b , the line width at half-height corrected for the natural line width from

$$k \approx \pi \cdot W_b . \quad (1)$$

The additional width of the decoupled resonance due to $|\alpha\rangle \rightarrow |\beta\rangle$ transitions, W_d , can therefore be obtained by substitution from the fast exchange limit expression giving

$$W_b \cdot W_d \approx J^2/2. \quad (2)$$

Thus, the ~ 40 Hz broadening of the 2-protons decouples the 5 Hz coupling to the 3-protons and leaves a residual ~ 0.3 Hz broadening of the coalesced peaks. W_d can naturally be decreased by increasing W_b ; however, the addition of more $\text{Gd}(\text{fod})_3$ only results in narrowing of the 3-proton resonances up to the point that dipolar relaxation significantly broadens the 3-protons due to the $1/r^6$ dependence.

* The acronym, fod, indicates the anion of 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione.

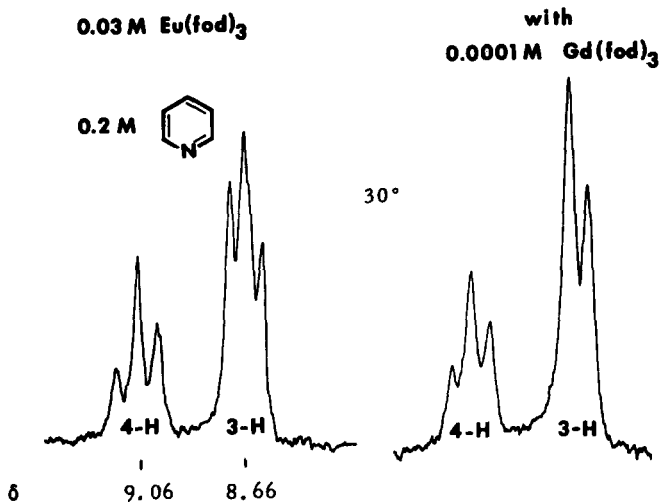


Figure. Left. The 3- and 4-proton resonances of pyridine at 100 MHz in presence of $\text{Eu}(\text{fod})_3$ in deuteriochloroform solution. The resonances appear at 8.66 and 9.06 respectively and the individual lines of the 3-H appear at 899, 905, 907 and 912 Hz downfield from TMS. Right. The effect of addition of $\text{Gd}(\text{fod})_3$ to the solution containing pyridine and $\text{Eu}(\text{fod})_3$.

Lanthanide reagents have excellent potential in the elucidation of couplings between protons in complex molecules; however, there are two points which suggest that the values obtained should be interpreted with discretion. First, the couplings observed in the shifted spectra are the average of those of the free and complexed substrate. Therefore, changes in conformation due to steric requirements of complexation or changes in charge distribution due to coordination to the positively charged metal ion can alter the values of the splittings. Second, the relaxation effects of the more commonly used shift reagents, such as Eu and Pr complexes, can cause pronounced decoupling and their influence on measured coupling constants should not be overlooked. For instance, equation (2) indicates that a 4 Hz broadening of a proton coupled to another with a coupling constant of 2 Hz would reduce the second from a doublet to a singlet broadened by 0.5 Hz. Mixtures of $\text{Gd}(\text{fod})_3$ and $\text{Eu}(\text{fod})_3$ are superior to

other rare earths which both broaden and decouple because the amount of broadening associated with a given shift can be controlled.

In order for the broadening to roughly parallel the magnitude of the shifts, the relaxation must be induced by the Gd while the substrate is attached to the metal via the donor atom. Induced relaxation of nuclei in the second coordination sphere by uncoordinated Gd-complex or by a Gd-substrate complex would tend to produce indiscriminate broadening of all resonances. Therefore, it is essential to have a large Gd complex-substrate formation constant; hence fluorinated ligands are desirable to increase the acidity of the metal, particularly with studies of weak substrates, such as alcohols or ketones. The great effectiveness of gadolinium in causing relaxation and the greater Lewis acidity associated with fod complexes, suggests that $\text{Gd}(\text{fod})_3$ should have excellent potential as a spin decoupling reagent for use in conjunction with shift reagents for obtaining coupling constants.

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