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LANTHANIDE NMR SHIFT REAGENTS: AN UNEXPECTED TEMPERATURE EFFECT

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Although numerous reports have appeared during the past year on the use of lanthanide shift reagents for clarification of NMR spectra (see Ref. 1 for a recent list of references), effects of temperature variation have received little attention. The only investigations of this subject[1,2] have shown that, in accord with theory, the magnitude of the induced shifts was inversely proportional to temperature. Thus, in the case of a europium shift reagent, lowering the temperature resulted in downfield shifts of the signals.[1] We now wish to report an anomalous temperature effect in $Eu(fod)_3$-shifted spectra of limonoids.*

Fig. 1 shows a typical example of this phenomenon. Here an increase in temperature causes several proton signals of limonin (e.g., 6α, 6β, 15) to move upfield, as expected. However, several other resonances (e.g., 2α, 17) simultaneously move downfield. This shift of signals in opposite directions was observed over a variety of temperature ranges and $Eu(fod)_3$: limonin ratios. It was also seen in the spectra of other limonoids. Fig. 2 shows graphically the variations in $Eu(fod)_3$-induced shifts of three selected protons of obacunone with temperature. Here the 2 and 6α protons, which are almost superimposed at -20°, have moved 4.5 ppm apart at 50°.

This temperature effect can be of great practical value. Although $Eu(fod)_3$ effectively spreads out limonoid spectra, the large number of signals present makes some overlapping inevitable at any given concentration of shift reagent. Varying the temperature provides a simple method for moving signals away from each other, as shown in Fig. 1. We have found that in most cases increasing the temperature gives best results in clarifying spectra, with the added advantage that signals become sharper at higher temperatures.

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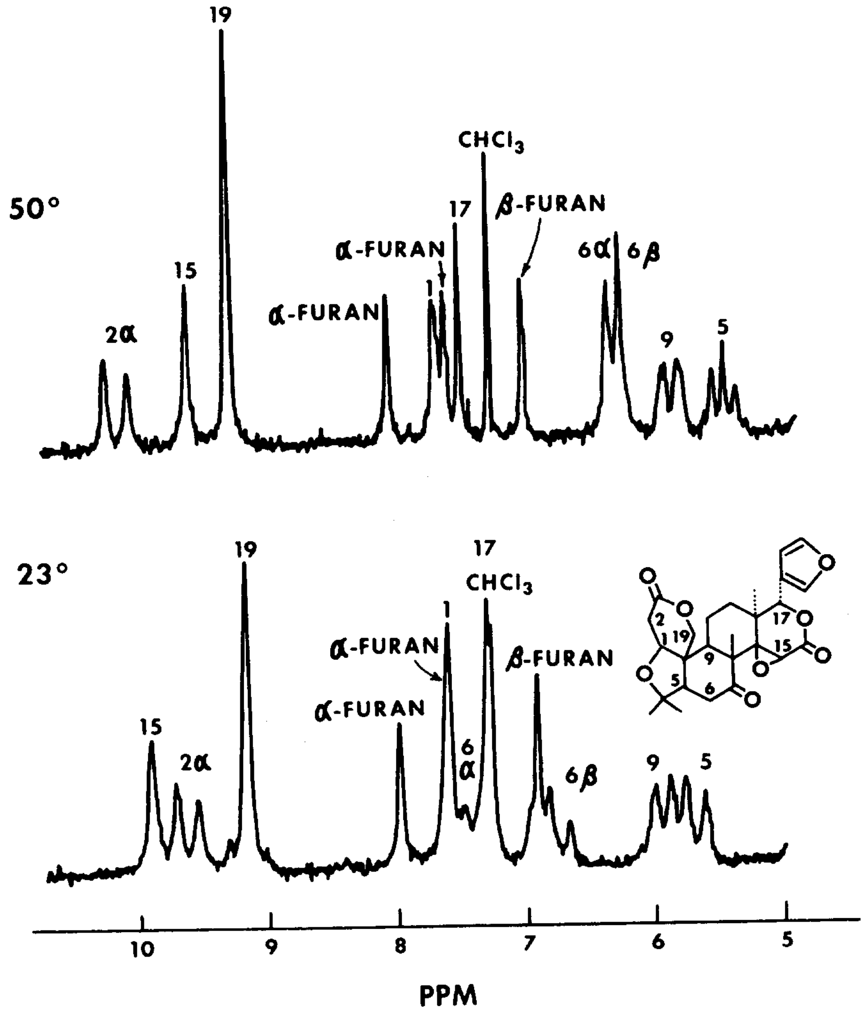

Fig. 1. Portions of NMR spectra of limonin at two temperatures in the presence of 2.2 molar equivalents of Eu(fod)$_3$. Spectra were run in $CDCl_3$ at 100 MHz.

The temperature effect can also be used to advantage in assigning proton resonances. In monofunctional compounds protons closest to the site of coordination show the largest induced shifts, and assignments can be made on this basis. Limonoids, however, appear to complex with $Eu(fod)_3$ at two or more sites, and this makes the relation between the magnitude of the induced shift of a particular proton and its position in the molecule ambiguous. It is therefore of significance that the movement of a proton signal caused by temperature change, in terms of direction and magnitude, does seem to be correlated with its position relative to the nearest coordinating site in the molecule. In Fig. 1 the protons close to the 3-carbonyl (1, 2, and 19) all move downfield as the temperature is increased, with the 2α signal moving fastest. Of those protons adjacent to the 7-carbonyl, all three move upfield, but the 6α and 6β signals move much faster than the one at C-5. We have tentatively made assignments for the four methyl resonances of limonin (not shown in Fig. 1) on this basis. This subject, and the question of the influences acting upon the H_{15} signal, will be discussed in more detail elsewhere.

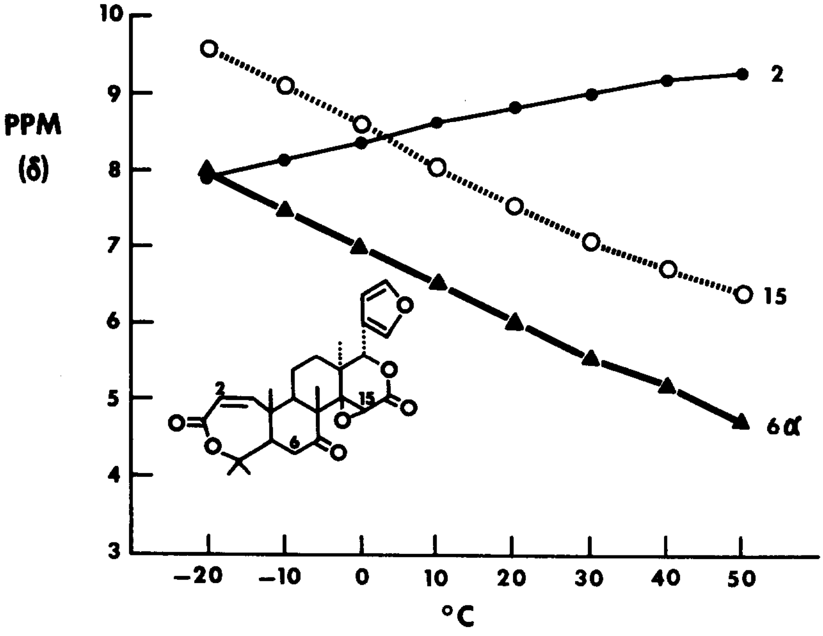

Fig. 2. Chemical shifts of three protons of obacunone in the presence of 0.6 molar equivalent of obacunone as a function of temperature. Spectra were run in $CDCl_3$ at 100 MHz.

Our observations suggest that the competition of two or more coordinating sites in the molecule for Eu(fod)$_3$ may be influenced by temperature changes. Thus, in the example shown in Fig. 2, the 3-carbonyl could be complexing more Eu(fod)$_3$ at higher temperatures, at the expense of other oxygen atoms of obacunone. This effect could be due to temperature dependent changes in the steric requirements of Eu(fod)$_3$ or in relative basicities of the coordination sites of obacunone. It is probably not caused by conformational changes in the limonoids, which are fairly rigid molecules. In the absence of Eu(fod)$_3$, their spectra are not significantly affected by temperature changes. It also seems unlikely that the anomalous temperature effect is related to the phenomenon of upfield shifts with Eu(dpm)$_3$ recently reported (Ref. 3, and references therein). In no case have we observed a net upfield shift of a limonoid resonance relative to its position in the uncomplexed spectrum, i.e., in the absence of Eu(fod)$_3$. For example, the 2-proton of obacunone moves anomalously upfield with decreasing temperature (Fig. 2), but even at -20° it is still far from the original position of this signal (5.97 ppm).

In view of the wide variety of temperatures at which spectrometers are normally operated in different laboratories, our findings further emphasize the need for caution in comparing data on induced shifts.[1] Over a range of 20°, not only the magnitudes of the shifts but also the relative positions of the signals may be drastically changed.

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