

The Effect of $\text{Eu}(\text{fod})_3$ on the NMR Spectra of Methyl Esters of Some *cis* and *trans* α,β -Unsaturated Mono and Dicarboxylic Acids

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The development of lanthanide NMR shift reagents has provided a new approach to the determination of configurations in geometrical isomers containing a heteroatom with a lone electron pair. Since the paramagnetically induced NMR shift of a proton can be related to its distance r from the lanthanide ion and to the coordination angle χ (cf. Fig. 1), geometrical isomers show characteristic differences in their NMR spectra on addition of a shift reagent. This has been observed with, for example, oximes¹ and α,β -unsaturated aldehydes.² Systematic investigation has so far been mainly confined to monofunctional compounds; no examples have apparently been reported of the use of shift reagents to determine configuration of *cis* and *trans* isomers containing two functional groups, both able to interact with the lanthanide ion. For a few types of bi- and polyfunctional compounds containing, e.g., ester, keto, ether, thioether, and amino groups, the preferred order of coordination has been investigated.³ When the functional groups in a molecule are of the same kind and located in similar but not identical surroundings, the preferred site of coordination is determined mainly by steric effects. These are often difficult to evaluate since the exact position of the lanthanide ion is generally not known. Moreover the configuration of the organic molecule may change on complexation with the lanthanide ion.

In this communication we report the effect of $\text{Eu}(\text{fod})_3$ ⁴ on the NMR spectra of the methyl esters of the following *trans-cis* pairs: crotonic-isocrotonic acid, 1 and 2; tiglic-angelic acid, 3 and 4; fumaric-maleic acid, 5 and 6; and mesaconic-citraconic acid; 7 and 8. This comparative study was performed in an attempt to strengthen the assignments of configuration to the two

geometrical isomers 9 and 10, which have been made on the basis of NMR and electronic spectra.⁵

The induced shifts, reported in δ -values, were measured in ca. 0.5 M solutions of the esters in dry CDCl_3 at 60 MHz. The shifts were plotted against $[\text{Eu}(\text{fod})_3]/[\text{ester}]$ up to molar ratios of 1–2. A linear dependence was obtained for ratios up to ca. 0.5, beyond which saturation gradually occurred resulting in no further change in chemical shift (cf. Ref. 4). The Δ_{Eu} -values⁶ for the olefinic and methyl protons, summarized in Tables 1 and 2, have therefore been calculated as the slope of the straight line for ratios between 0 and 0.5.

Esters coordinate with $\text{Eu}(\text{fod})_3$ at the carbonyl oxygen atom;³ assuming a pseudo-contact shift, a linear dependence between Δ_{Eu} and $(3 \cos^2 \chi - 1)/r^3$ is expected.⁷ The distances r and angles χ for the protons in 1–4 (cf. Fig. 1) were estimated for the *s-cis* and *s-trans* conformations by means of Dreiding models. When the corresponding

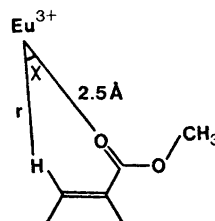


Fig. 1. Model for *s-cis* conformer of the *trans* isomers 1 or 3 coordinated with $\text{Eu}(\text{fod})_3$.

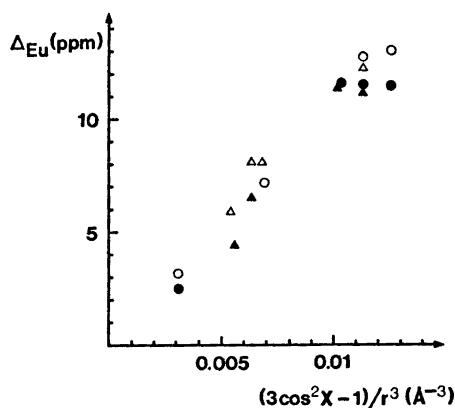


Fig. 2. Δ_{Eu} -values for *s-cis* conformers of 1–4 plotted against $(3 \cos^2 \chi - 1)/r^3$ for $r = 2.5 \text{ \AA}$.

Table 1. Δ_{Eu} -values for the protons in the monocarboxylic esters 1-4.

Monoesters		CH ₃ -ester	H-2	H-3	CH ₃ -2	CH ₃ -3
$\begin{array}{c} \text{H} \quad 3 \quad 2 \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{H}_3\text{C} \quad \text{H} \end{array} \text{COOCH}_3$	(1)	11.5	11.6	11.6	—	2.5
$\begin{array}{c} \text{H}_3\text{C} \quad \text{COOCH}_3 \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{H} \end{array}$	(2)	11.1	11.4	4.4	—	6.5
$\begin{array}{c} \text{H} \quad 3 \quad 2 \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{H}_3\text{C} \quad \text{CH}_3 \end{array} \text{COOCH}_3$	(3)	12.7	—	13.0	7.2	3.1
$\begin{array}{c} \text{H}_3\text{C} \quad \text{COOCH}_3 \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{CH}_3 \end{array}$	(4)	12.3	—	5.9	8.2	8.2

Table 2. Δ_{Eu} -values for the protons in the dicarboxylic esters 5-10.

Diesters		CH ₃ -ester	H-2;	H-3	CH ₃ -2
$\begin{array}{c} \text{H} \quad 2 \quad 3 \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{H}_3\text{COOC} \quad \text{H} \end{array} \text{COOCH}_3$	(5)	6.7; 6.7	12.5;	12.5	—
$\begin{array}{c} \text{H}_3\text{COOC} \quad \text{COOCH}_3 \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{H} \quad \text{H} \end{array}$	(6)	3.3; 3.3	5.8;	5.8	—
$\begin{array}{c} \text{H}_3\text{C} \quad 2 \quad 3 \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{H}_3\text{COOC} \quad \text{H} \end{array} \text{COOCH}_3$	(7)	6.7; 4.8	—	10.2	6.4
$\begin{array}{c} \text{H}_3\text{COOC} \quad \text{COOCH}_3 \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \\ \text{H}_3\text{C} \quad \text{H} \end{array}$	(8)	4.4; 3.8	—	6.7	3.6
(9)		3.9; 2.8	7.5 (H-10)	—	—
(10)		4.7; 1.9	6.1 (H-10)	—	—

values for the angle-distance expression were plotted against Δ_{Eu} , the best straight-line fit (cf. Fig. 2) was obtained when the europium ion was placed 2.5 Å from the carbonyl oxygen atom in the *s-cis* conformers.

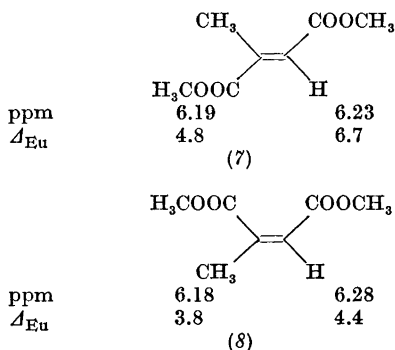
Although the choice of geometrical arrangements and of distances between protons and europium ion in the models is not unequivocal, the Δ_{Eu} -values themselves for the *cis* and *trans* olefinic protons in the esters of the monobasic carboxylic acids differ sufficiently to allow configurational assignments to be made.

The picture for the diesters 5-8 is more complicated, because the europium ion has

two possible sites of coordination. The equilibrium constant for complex formation⁸ for each of these is probably mainly dependent on steric factors. The present measurements were performed at concentrations where dinuclear complexes should not be important. In addition *s-cis* and *s-trans* isomerism is possible at both carbon-carbon single bonds, consequently no obvious position for the europium ion can be proposed with these compounds. Thus no attempts have been made to produce plots of Δ_{Eu} vs. $(3 \cos^2 \chi - 1)/r^3$. In a recent communication,⁹ successful correlations have been reported for bifunctional steroids where the sites of coordina-

tion are far apart. This approach does not lead to interpretable results in our case, probably because the two sites of coordination are too close and also "conjugated" with each other. One can, however, make the following quantitative observations (cf. Table 2). In the pairs 5-6 and 7-8 the Δ_{Eu} -values for the methyl ester protons are always higher in the *trans* isomers. These values are about half of those observed for the same protons in the monoesters, which is conceivable, since the induced shifts at the concentrations used should represent the time average of complexed and free ester groups. The values for the olefinic protons in 1-3 are high when they are either geminal or *cis* to the carbomethoxy group, but much lower when they are 3-*trans* (2 and 4). Similar regularities are found for 5 and 7. It should be noted that the Δ_{Eu} -values for the methyl ester protons in the *cis* compounds 6 and 8 seem difficult to correlate.

In the mesaconic, 7, and citraconic, 8, esters the two nonequivalent ester methyl groups give rise to two different signals at 6.19 and 6.23 ppm in 7 and at 6.18 and 6.28 ppm in 8 (CDCl₃; cf. Ref. 10). To our knowledge no attempts to assign each methyl group to a specific signal in the spectrum have been published. The Δ_{Eu} -values for these methyl protons in 7 and 8 differ (cf. Table 2) and it seems reasonable to assign the ones with the lower Δ_{Eu} -value in each compound to the carbonyl group which is more sterically hindered. This is the one closer to the C-methyl group, and we therefore propose the following assignments:



We had hoped that the use of NMR shift reagents would allow us to distinguish unequivocally between the *E* and *Z* isomers 9 and 10, respectively, in order to support the configurational assignments

proposed for them.⁵ Inspection of the models of *s-trans*, *s-trans* rotational isomers of 9 and 10 (cf. Fig. 3) shows that in 10a the carbonyl oxygen on C-9 is considerably more hindered than is the corresponding oxygen on C-11. The same order of steric hindrance exists in 10b. In 9a and 9b the difference in steric hindrance between the carbonyl oxygens on C-9 and C-11 seems to be less than for the same atoms in 10. The Δ_{Eu} -values (cf. Table 2) are not in disagreement with these speculations. However, conformational uncertainties make the conclusions somewhat debatable.

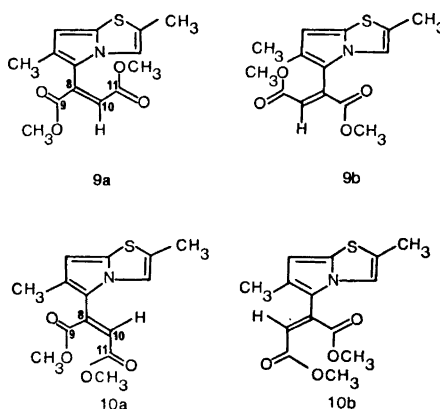


Fig. 3. *s-trans*, *s-trans* Rotational isomers of 9 and 10.

We conclude that Eu(fod)₃ can be applied successfully to the determination of configuration of α,β -unsaturated monocarboxylic esters. The Δ_{Eu} -values for the corresponding dicarboxylic esters are more difficult to interpret but they probably allow a configurational correlation when both isomers are available. The lanthanide shift method should therefore be a very valuable and convenient complement to other spectral and chemical methods for determining geometrical configurations of fumaric-maleic-type esters.

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**Studies on Flavin Derivatives.
X-Ray Structure Investigation of
1',2',3',4'-Tetraacetyl-3-ethyl-
riboflavin Zinc-chelate
Perchlorate**

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This work is part of a series of systematic studies of flavin derivatives, currently in progress at this institute. The crystal structure of 1',2',3',4'-tetraacetyl-3-ethyl-riboflavin zinc-chelate perchlorate, $(C_{27}H_{32}N_4O_{10}ClO_4H_2O)_2Zn$, has been determined by X-ray diffraction methods in order to obtain information about isoalloxazine interaction with metals. The studies were carried out on red single crystals selected from material kindly provided by S. Ghisla, P. Hemmerich and J. Lauterwein, University Konstanz, Germany.

X-Ray diffraction data. Preliminary rotation and Weissenberg photographs indicated monoclinic symmetry with systematic absence of reflections with $h+k=2n+1$. Therefore, possible space groups were $C2/m$, $C2$, and Cm . The non-centric

space group $C2$ was assumed, which was subsequently confirmed to be correct by the determination of the structure. Powder photographs, taken in a Guinier-Hägg type focusing camera with strictly monochromatized $CuK\alpha_1$ radiation ($\lambda=1.54056$ Å) and with KCl ($a=6.2930$ Å) as an internal standard, were used for the determination and least-squares refinement of the lattice parameters. The following result was obtained: $a=20.438 \pm 3$ Å, $b=7.673 \pm 2$ Å, $c=21.389 \pm 4$ Å, $\beta=104.40 \pm 2^\circ$. There are two formula units in the unit cell. The calculated and observed density is 1.471 g/cm³ and 1.465 g/cm³, respectively. The intensity data were collected by integrated multiple-film Weissenberg technique using Ni-filtered CuK radiation. The 640 observed independent intensities were corrected for Lorentz and polarisation effects. Correction for absorption was not made, in view of the small size of the specimen and the low absorption coefficient, 21 cm⁻¹.

Determination of the structure. The general positions of the space group $C2$ are fourfold. The zinc atoms must be on twofold special positions, since there are two formula units in the cell. The approximate position of the isoalloxazine ring system was deduced from a three-dimensional Patterson synthesis. The isoalloxazine was treated as a rigid body, and the position was refined by a least-squares program kindly supplied by Sheringer.¹ The remaining non-hydrogen atoms were found from subsequent iterative Fourier calculations. From a three-dimensional difference electron density map it was found that four peaks, arranged tetrahedrally around the chlorine atom position, stood out clearly from the background. Accordingly, these sites were adopted as alternative positions for the oxygen atoms of the perchlorate ion, keeping the chlorine atom position unchanged. A least-squares refinement of the occupancies of the eight oxygen positions revealed that the oxygen sites have occupancies close to 0.5. Owing to the large number of atoms in the unit cell, leading to 152 positional parameters for the non-hydrogen atoms, and the small number of observed reflections, it has not been found possible to make a detailed structure refinement. Therefore, the structure was refined isotropically by least-squares treatment keeping groups of parameters constant in a step-wise manner. When the refinements were terminated a discrepancy index $R=0.14$ ($R = \sum ||kF_o| - |F_c|| / \sum |kF_o|$) was cal-