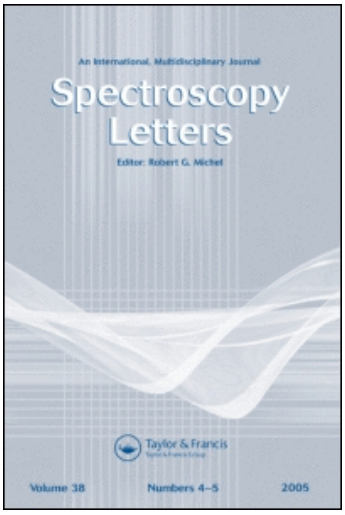


Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

^{1}H NMR Spectral Simplification with Achiral and Chiral Lanthanide Shift Reagents. Methastyridone, 2,2-Dimethyl-5-(2-Phenylethenyl)-4-Oxazolidinone

Joel Ross[a]; Robert Rothchild[b]
[a] Physics Department, St. Michael's College, Colchester, VT [b] Department of Science, The City University of New York, John Jay College of Criminal Justice, Toxicology Research and Training Center, New York, NY

To cite this Article Ross, Joel and Rothchild, Robert(1990) ''H NMR Spectral Simplification with Achiral and Chiral Lanthanide Shift Reagents. Methastyridone, 2,2-Dimethyl-5-(2-Phenylethenyl)-4-Oxazolidinone', Spectroscopy Letters, 23: 7, 923 — 944
To link to this Article: DOI: 10.1080/00387019008054470
URL: http://dx.doi.org/10.1080/00387019008054470

SPECTROSCOPY LETTERS, 23(7), 923-944 (1990)

^{1}H NMR SPECTRAL SIMPLIFICATION WITH ACHIRAL AND CHIRAL LANTHANIDE SHIFT REAGENTS. METHASTYRIDONE, 2,2-DIMETHYL-5-(2-PHENYLETHENYL)-4-OXAZOLIDINONE.

Key Words: Europium, Praseodymium, Optical Purity, Enantiomer, $Pr(FOD)_3$, $Pr(HFC)_3$, $Eu(FOD)_3$, $Eu(HFC)_3$, Analysis

[a]Joel Ross and Robert Rothchild*[b]

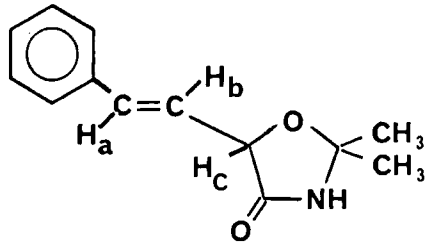
a) Physics Department, St. Michael's College, Winooski Park, Colchester VT 05439; b) The City University of New York, John Jay College of Criminal Justice, Toxicology Research and Training Center, Department of Science, 445 West 59th Street, New York NY 10019-1199

ABSTRACT

The 60 MHz ^{1}H NMR spectra of methastyridone, 2,2-dimethyl-5-(2-phenylethenyl)-4-oxazolidinone, 1, have been studied at 28° in $CDCl_3$ solution with the achiral reagent tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium(III), 2, $Eu(FOD)_3$, and the chiral reagent tris[3-(heptafluoropropylhydroxy-methylene)-d-camphorato]europium(III), 3, $Eu(HFC)_3$.

* To whom correspondence should be sent.

The corresponding achiral and chiral praseodymium reagents, $Pr(FOD)_3$, 4, and $Pr(HFC)_3$, 5, were also employed in these studies. Substantial $\Delta\delta$ values and spectral simplification are achieved with all LSR used. Significant enantiomeric shift differences, $\Delta\Delta\delta$, are observed with 3 that should provide direct optical purity determinations of 1. Results are discussed in terms of LSR binding sites and general structural aspects of 1.



INTRODUCTION

Methastyridone, 1, 2,2-dimethyl-5-(2-phenylethenyl)-4-oxazolidinone, has structural similarities to a broad range of pharmaceuticals of considerable importance. The compound has been examined as a behavioral stimulant (1,2) and more recently was part of an analytical study (3). Considered broadly, 1 can be considered as an example of five- or six-membered ring compounds possessing the amide group, exemplified by hydantoins, barbiturates,

succinimides, glutarimides and related compounds. Many such compounds possess a chiral center in the ring or a sidechain and can exist as a pair of enantiomers, which may differ in their potency, physiological effects or toxicities. The stereochemistry of drugs, including attention to enantiomer configurations, has become of increasing concern, as seen by developments in enantioselective synthesis. Both chromatographic and spectroscopic methods for optical purity determination have been extensively used. Among spectroscopic methods, the NMR method using chiral lanthanide shift reagents (LSR) has proven quite useful. The different techniques should be considered as complementary.

The chiral LSR method has been successfully applied by us and others to many pharmaceuticals, and this has been reviewed (4). Some structural virtues of the substrate for successful use of chiral LSR would seem to include: (a) presence of a suitable Lewis base binding site in the substrate, located near the chiral center; (b) relatively rigid molecular structure; (c) presence of a suitable "marker group" of nuclei close to the chiral center and the LSR binding site, to provide a high intensity signal of low multiplicity (5,6). The chiral LSR method is based on observation of enantiomeric shift differences for substrate nuclei. The enantiomeric shift difference, $\Delta\Delta\delta$, is the

difference in chemical shift between corresponding nuclei in substrate enantiomers in the presence of chiral LSR.

Our interest in 1 was aimed at extending our understanding of LSR interactions with this broad class of pharmaceuticals and analogs. We employed both achiral LSR for spectral simplification as well as chiral reagents for potential direct optical purity determinations. Principles and theory of LSR have been reviewed (7-13) and use of chiral LSR has been specifically discussed (7,10,11,13). The use of LSR based on europium(III) and on praseodymium(III) was planned since the former reagents normally induce downfield shifts and the latter, upfield shifts. The selected reagents would include tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium-(III), 2, known as $Eu(FOD)_3$; tris[3-heptafluoropropyl-hydroxymethylene)-(+)-camphorato]europium(III), 3, known as $Eu(HFC)_3$ or $Eu(HFBC)_3$; and the corresponding Pr(III) reagents $Pr(FOD)_3$, 4, and Pr(HFC), 5. Reagents 2 and 4 are achiral, and reagents 3 and 5 are chiral. We expected that the rigid ring and ethenyl moieties of 1 should serve to make it a significant model compound.

EXPERIMENTAL

Racemic 1 was obtained from Merck Sharp & Dohme Research Laboratories, Rahway NJ 07065. The sample, L-

580,406-000W013, was used as supplied without further purification. Chloroform-d, (99.8 atom % D), obtained from Aldrich Chemical Corp., Milwaukee WI 53201 or from Norell, Inc., Landisville NJ 08326, was dried and stored over 3A Molecular sieves. Shift reagents were obtained from Aldrich and were stored in a desiccator over P_2O_5. Materials were used as received except as noted.

For runs with shift reagents, an accurately weighed portion of drug was added to $CDCl_3$ [containing about 0.5% tetramethylsilane (TMS) as internal standard] in an NMR sample tube and dissolved by shaking; increments of solid shift reagent were added directly to the sample, dissolved by shaking, and the spectra immediately obtained. Drug concentrations were typically from 0.11-0.20 molal. Spectrometer probe temperature was $28\pm1^\circ$. Chemical shifts are believed accurate to ±0.05 ppm, and apparent coupling constants to $\pm$ 0.2 Hz. Calculations of correlation coefficients and slopes by least squares fits were performed with a Sharp EL-5100 calculator.

RESULTS AND DISCUSSION

The 60 MHz ^{1}H spectrum of 0.1131 molal 1 in $CDCl_3$ showed signals as follows (δ, ppm): 1.57 (6H, br s, two CH_3 groups); 4.97 (1H, d, ^3J = 5.6 Hz, H_a); 6.25 (1H, dd, ^3J=15.7, 5.4 Hz, H_b); 6.82 (1H, d, ^3J = 16.0,

H_a); 7.33 (5H, m, C_6H_5); 8.33 (1H, br s, NH). Distinct long-range (allylic) coupling was not clearly seen. The diastereotopic methyls were nearly isochronous and appeared as a slightly broadened singlet. The magnitude of $J_{a,b}$ is consistent with a trans double bond in the sidechain. Incremental additions of the achiral $Eu(FOD)_3$, 2, resulted in lanthanide-induced shifts (LIS) as shown in Fig. 1. At higher molar ratios of 2:1, the methyls clearly became chemical shift nonequivalent and the aryl ortho protons separated from the other aryl protons. Deviations from linearity in the curves of Fig. 1 were most noticeable for 2:1 ratios greater than ca. 0.5. The relative LIS magnitudes were $H_c > NH > H_b > H_a > CH_3 > H_o > H_{m,p}$ This sequence is qualitatively consistent with predominant or exclusive LSR binding at the carbonyl oxygen. No anomalous ("wrong-way") shifts were seen.

Increments of the chiral $Eu(HFC)_3$, 3, were added to 0.1124 molal 1, and the results are shown in Figs. 2 and 3. Assignments of NH and H_c at 3:1 ratios of 0.520 and 0.783 are tentative. Relative LIS magnitudes were similar to those noted for 2, except that the values for NH and H_b were close, with H_b slightly greater. Enantiomeric shift differences, $\Delta\Delta\delta$, were seen for several of the nuclei of 1 as shown in Fig. 3. Because of lanthanide-induced line broadening or interfering

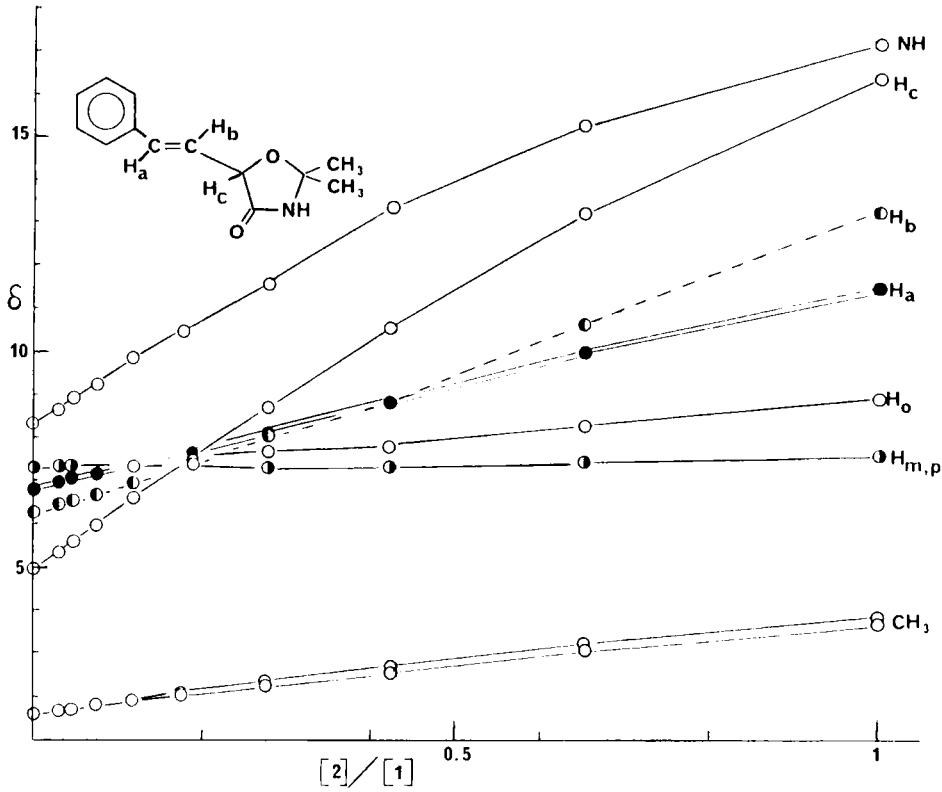


Fig. 1. Variation of chemical shift (in ppm) with molar ratio of 2:1.

peaks, some of the plotted $\Delta\Delta\delta$ values may be uncertain. Nonetheless, our results are quite striking in that four of the five nuclei displaying $\Delta\Delta\delta$ appear to go through maxima in the magnitudes of these values, with the H_a signal being a possible exception. The variations in these values for H_b, H_c and NH are

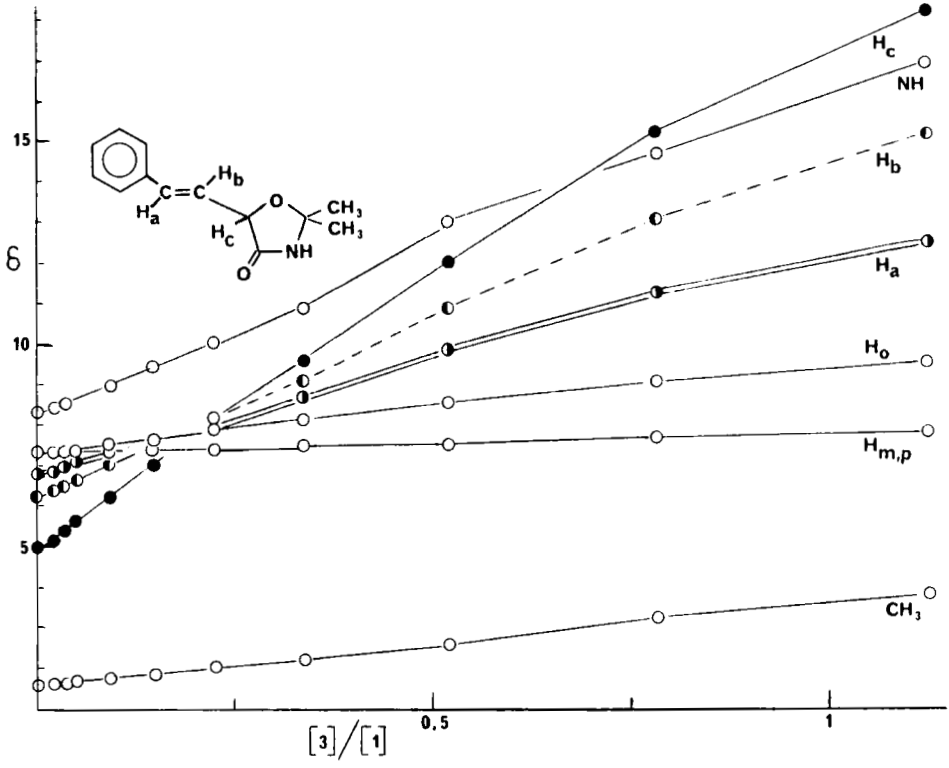


Fig 2. Variation of chemical shift (in ppm) with molar ratio of 3:1. Note: Where enantiomeric shift differences occur, average values of chemical shift are plotted.

especially large. Variations in $\Delta\Delta\delta$ magnitudes often show complex variations, especially with higher molar ratios of LSR:substrate. In some cases, an actual change in the sense of magnetic nonequivalence for a given nucleus may manifest itself in $\Delta\Delta\delta$ appearing to decrease to zero and increasing at higher LSR levels.

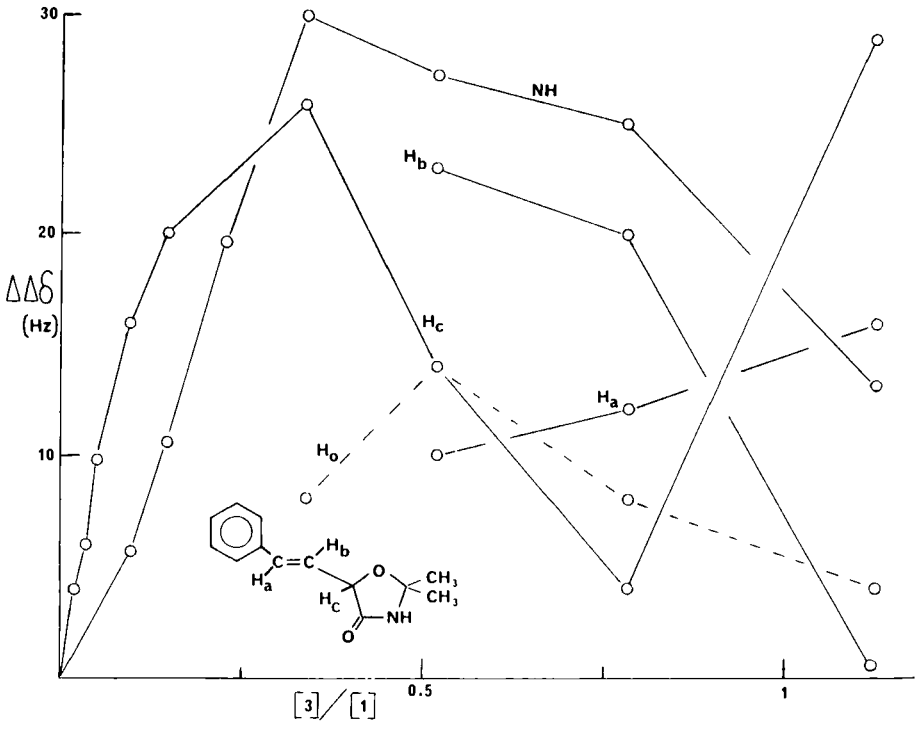


Fig. 3. Variation of enantiomeric shift difference (in Hz) with molar ratio of 3:1.

Such deviations invariably occur at higher molar ratios of LSR. For 1 with added 3, nuclei exhibiting maxima in $\Delta\Delta\delta$ show such maxima near a 3:1 ratio of 0.5. One explanation for such nonlinearities could be a change in stoichiometry or geometry in the bound complex of LSR and substrate (14,15), although the expected corresponding deviations in the plots of chemical shift versus 3:1 ratio are rather modest up to the highest

ratio examined, 1.125. However, the $\Delta\Delta\delta$ values are expected to be more sensitive to such changes since they reflect small differences in chemical shifts for corresponding nuclei in the enantiomeric molecules. The potential for conformational changes in the side chain or in the precise binding sites of LSR at the carbonyl could account for the observed results. The important point is that selection of an appropriate LSR:substrate molar ratio may be absolutely critical for analytical use of the signal of a particular nucleus in determinations of enantiomeric excess.

Using 3, analytical utility for optical purity determinations of 1 appeared optimal using the H_c signal with 3:1 ratios near 0.0927 or 1.125 with $\Delta\Delta\delta$ values of 16 or 29 Hz, respectively, or using the NH signal and a 3:1 ratio near 0.339. For the latter case, $\Delta\Delta\delta$ of 30 Hz was seen, with near-baseline resolution for the signals of each enantiomer. Nearly as good resolution was seen with the H_c signal at the lower 3:1 ratio. Work in these laboratories has suggested that useful $\Delta\Delta\delta$ values for chiral amides are less commonly seen for NH than for CH protons; in part this may reflect intrinsically greater NH linewidth due to broadening resulting from the ^{14}N quadrupole moment.

In an attempt to extend these results, further studies with 1 were performed using the analogous

praseodymium LSRs. The beta-diketonates of Pr(III) normally induce upfield shifts and it was hoped that interferences from the aryl protons with the sidechain signals (encountered with the europium reagents) might be avoided. Unexpectedly, when increments of $Pr(FOD)_3$, 4, were added to 0.2172 molal 1, the relative LIS magnitudes were very different than with 2 or 3. with 4, these LIS magnitudes were NH >> H_c > H_b > H_a > CH_3 > aryl. The relative LIS values for NH and H_c are reversed; the NH value was almost twice that for H_c. These results are summarized in Fig. 4.

With the chiral $Pr(HFC)_3$, 5, added to 0.1995 molal 1, relative LIS magnitudes followed those seen with 4. These results are shown in Fig. 5. Thus, the two Eu reagents are similar to each other but differ from the two Pr reagents. Relative LIS magnitudes for the amide NH signal constitute the major distinguishing parameter. In runs with 5, the highest molar ratio of 5:1 examined was 0.316, since higher LSR levels caused interferences with the signals of 5 itself or with the NH signal, leading to uncertainties in assignments. Over the range of 5:1 ratios employed, the $\Delta\Delta\delta$ values appeared to increase monotonically (Fig. 6) but deviations at higher ratios may occur, as with 3. No conditions were found for analytical utility using 5. Some evidence was seen for $\Delta\Delta\delta$ in one of the two methyl signals.

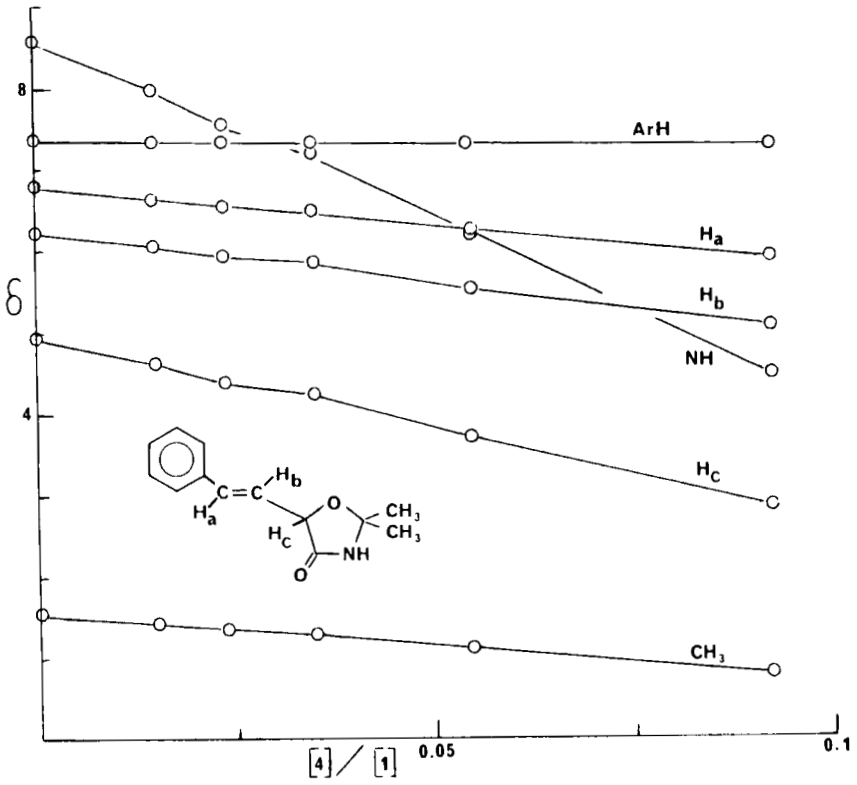


Fig. 4. Variation of chemical shift (in ppm) with molar ratio of 4:1.

Because of the apparent differences in relative LIS magnitudes for the different nuclei of 1 with the LSRs employed, we have attempted to more quantitatively examine these results. In Table 1, the relative ratios of LIS magnitudes versus the molar ratios, [LSR]:[1], are presented for each hydrogen of 1 with each of the four LSRs; these ratios represent least square fits for

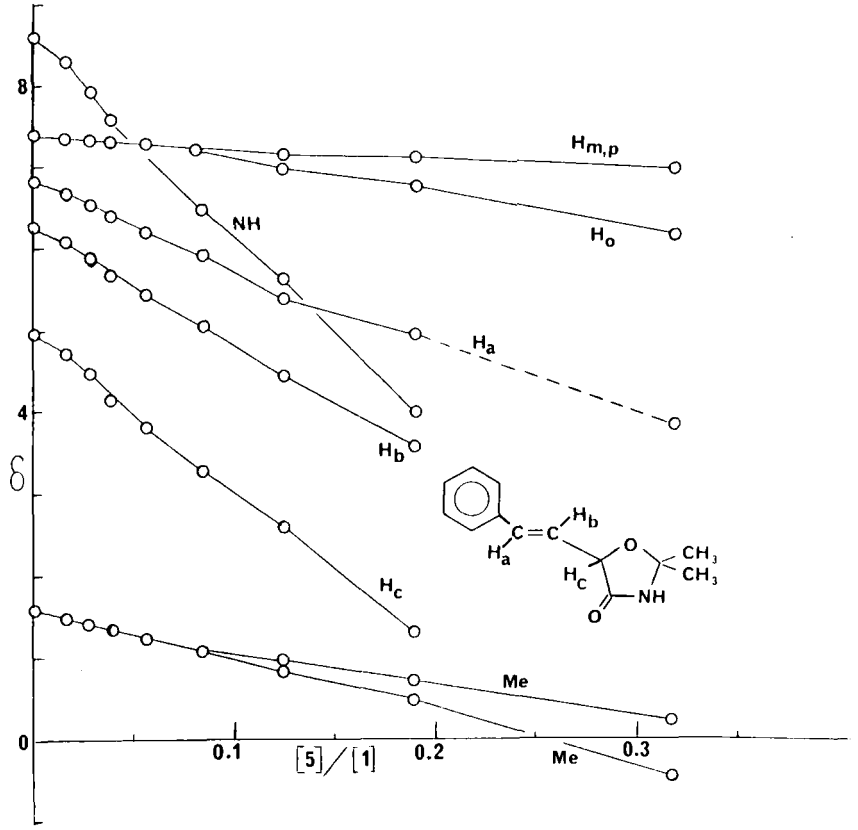


Fig. 5. Variation of chemical shift (in ppm) with molar ratio of 5:1. See Note for Fig. 2.

slopes of the plotted lines in Figs. 1,2,4 and 5. (Negative values denote upfield shifts on addition of LSR.) Since deviations from linearity frequently occur at molar ratios greater than 0.5, the tabulated slopes were determined based on molar ratios near or below this value. Although non-linearities at very low molar

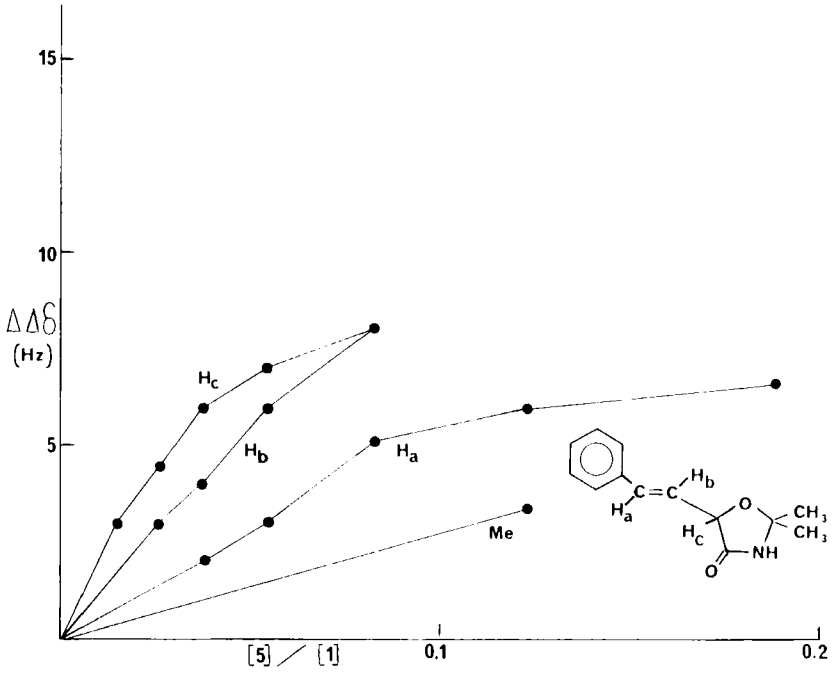


Fig. 6. Variation of enantiomeric shift difference (in Hz) with molar ratio of 5:1.

ratios of LSR:substrate have been observed and attributed to impurities, e.g., traces of H_2O in solvent, this effect was not evident here. Some experimental points were excluded from slope calculations where peak assignments were uncertain. Except for the meta and para protons of the phenyl group, correlation coefficients were equal to or close to unity, indicating good straight lines. Small LIS magnitudes for the meta and para protons contributed to

Table 1. Relative ratios of lanthanide-induced shifts (LIS) to molar ratio, [LSR]:[1], for nuclei of 1[a].

LSR:	2	3	4	5
Nucleus				
[b]CH_3	2.29, 2.68	2.01	-8.59	-4.35,-5.66
H_c	13.23	[d]13.85	-22.70	[e]-19.55
H_b	6.13	8.84	-13.10	[e]-14.47
H_a	4.60	5.77	-10.04	-9.86
$H_{m,p}$	-0.08(-0.51)	0.38(0.96)	-1.19(-0.98)[c]	[f]-1.25(-0.94)
H_o	1.28(0.98)	2.41	-1.19(-0.98)[c]	[f]-3.54(-0.99)
NH	11.85	[d]7.80	-44.69	[g]-26.11

Notes: (a) Data taken from Figs. 1,2,4 and 5. Numbers in parentheses are correlation coefficients where different from ±1.00. Positive ratios refer to downfield shifts (generally seen for 2 or 3) and negative ratios to upfield shifts (seen for 4 or 5). Where peak assignments were uncertain, these experimental points were not used for slope calculations. Generally, data reflect molar ratios of [LSR]:[1] up to 0.424 for 2, up to 0.520 for 3, up to 0.0923 for 4, and up to 0.189 for 5, unless noted.

(b) Where separate signals were assignable for the diastereotopic methyls, values for each are shown, but relative assignments (with 2 and 5) may be interchanged.

(c) Separate aryl signals were not assigned for these levels of 4.

(d) Molar ratios of 3:1 up to 0.339.

(e) Molar ratio of 5:1 up to 0.123.

(f) Molar ratio of 5:1 up to 0.316.

apparent poorer fits; the modest molar ratios employed and the distance of these protons from bound lanthanide result in small induced shifts.

Observed shifts with LSR are expected to include contributions from Fermi contact, dipolar pseudocontact, and diamagnetic complexation shifts. Simple geometric relationships apply only to the

pseudocontact terms. The contact and complexation shifts are expected to be most significant for nuclei other than ^1H which are close to the actual LSR binding site. In 1, the NH and H_c, alpha to the carbonyl binding site, are most likely to exhibit contributions other than pseudocontact. Separations of the three terms for the carbonyl compound, adamantanone, with a series of LSR reagents has been discussed (16,17). Except for the aryl protons of 1, which exhibited relatively small induced shifts, Table 1 reflects substantially greater LIS per mole of LSR for both Pr reagents 4 and 5 relative to the Eu reagents 2 and 3, roughly two times greater for the protons attached to carbon and four times greater for NH. Relatively greater LIS magnitudes had also been reported for all protons of adamantanone with 4 versus 2 (16), but not as dramatic a difference as for 1. The results of Peters and coworkers (16) showed that for adamantanone with 2, the contact shift made a substantial contribution to the observed LIS for the alpha H, more than 10%. It was therefore of interest to examine the relative induced shift magnitudes for 1 with each LSR, 2-5, normalized to the LIS of a proton further from the expected carbonyl binding site, in order to examine predominantly pseudocontact shift ratios (18). It was expected that in 1, the alpha H_c and the NH (in

Table 2. Normalized slopes of nuclei of 1, based on a value for H_b = 1.00 for each LSR (from data of Table 1).

LSR:	2	3	4	5
Nucleus				
CH_3	0.374 0.437	0.227	0.656	0.301 0.391
H_c	2.158	1.567	1.733	1.451
H_b	1.00	1.00	1.00	1.00
H_a	0.750	0.653	0.766	0.698
$H_{m,p}$	-0.013	0.043	0.091	0.086
H_o	0.209	0.273	0.091	0.245
NH	1.933	0.882	3.411	1.804

particular) might be subject to significant Fermi contact and diamagnetic complexation shifts that would otherwise distort the normalized values.

Table 2 shows the normalized values of the slopes for 1 with each LSR using the LIS of H_b (beta to the carbonyl) as the reference. This nucleus should exhibit minimal non-pseudocontact contributions because of greater distance from the LSR binding site. These values reflect very good agreement in the H_a values for the Eu and Pr reagents if identical ligands are compared. Thus, the FOD derivatives for Eu and Pr show normalized LIS values for H_a that agree within about 2%, and the two HFC reagents, 3 and 5, lead to similar

values within about 4%. The relative values of H_a and H_b are of particular interest since they occupy the geometrically rigid ethylene moiety. These results could suggest very similar bound complex geometries (isostructural) for $Eu(FOD)_3$ and $Pr(FOD)_3$ on the one hand, and similar structures for the $Eu(HFC)_3$ and $Pr(HFC)_3$ pair as well, but suggest modest but real differences between the FOD complexes compared to the HFC complexes. In 1, these observations could be accommodated by a different torsion angle of the ethylene sidechain relative to the carbonyl binding site, or possibly different LSR localization near the carbonyl with the different analogs. These effects could reflect different steric constraints and different Lewis acidities of the LSR analogs. Fairly good agreement is also seen for the ortho protons with the HFC reagents, but not for the other aryl protons, possibly reflecting the smaller observed LIS magnitudes and linearity deviations for the more remote protons.

Surprisingly, the normalized relative values for the methyl groups were not especially consistent within the FOD or HFC series of LSR, although larger values were seen for both FOD reagents and for the Pr versus the Eu reagents. Because of the constraints of the ring, it is unlikely that the methyls of 1 could occupy an appreciably different geometry relative to the

carbonyl. Since the methyls are remote enough to avoid appreciable contact or complexation shifts, we suggest that these LSR complexes may not be isostructural due to different positioning of lanthanide relative to the carbonyl oxygen of 1. The Table 2 values for H_c and NH show substantial differences both between the two lanthanides and between the two different ligands, FOD and HFC. The NH values are greater for Pr reagents 4 and 5, and H_c values are greater for Eu reagents 2 and 3, with the FOD reagents eliciting larger values for both nuclei. The very large differences in the NH values and the more moderate differences for H_c may, in part, suggest important contact or complexation shifts for these protons. In addition, subtle changes in binding site or in conformations for flexible multi-functional substrates like 1 can not be ruled out.

CONCLUSIONS

We have examined the 60 MHz ^{1}H NMR spectra of methastyridone, 1, with $Eu(FOD)_3$, $Eu(HFC)_3$, $Pr(FOD)_3$ and $Pr(HFC)_3$ and compared LIS values and, for the chiral reagents, enantiomeric shift differences. $Eu(HFC)_3$ produces $\Delta\Delta\delta$ values for the NH signal with a 3:1 molar ratio near 0.339 that should be analytically useful for direct optical purity determinations. Comparisons of relative LIS values with the four LSRs and the normalized values (using H_b as a reference)

showed some evidence for different bound complex geometries between the FOD versus the HFC reagents, possibly consistent with differing conformations of the sidechain ethylenic moiety. Normalized LIS values for the alpha protons, H_c and NH may indicate contact or diamagnetic shift contributions as well as different bound complex geometries. Our results suggest that isostructural bound complexes may not be trivially assumed for flexible multi-functional substrates when differing LSR reagents are employed.

ACKNOWLEDGMENTS

Samples of 1 were kindly provided by Merck, Sharp & Dohme Research Laboratories, Rahway NJ 07065. These studies were supported, in part, by the National Science Foundation Instrumentation and Laboratory Improvement Program grant no. USE-8851684, U.S. Department of Education Minority Science Improvement Program grant no. G008641165, Hewlett-Packard Co. grant no. 0017-80769, U.S. Department of Energy Energy-Related Laboratory Equipment grant no. AL-89-169, Hoffmann-La Roche Inc. and the Sandoz Research Institute (to R.R.)

LITERATURE REFERENCES

1. Kurland A.A., Arbona L., McCusker K. Clinical trial of methastyridone (MK-202) with chronic anergic schizophrenics. J. Nerv. Ment. Dis. 1961; 133(2): 174-175.

2. Bicking J.B., Kwong S.F., Fisher M.H., Nicholson W.H. Behavioral stimulants. 4-Oxazolidinones. J. Med. Chem. 1965; 8(1): 95-100.

3. Kuhnert-Brandstatter M.; Geiler M., Wurian I. Sci. Pharm. 1980; 48(3): 250-258.

4. Aboul-Enein H.Y. NMR methods for optical purity determination of pharmaceuticals. Analytical Lett. 1988; 21(12): 2155-2163.

5. Avolio J., Thomson Eberhart S., Rothchild R., Simons P. ^{1}H NMR spectral simplification with achiral and chiral lanthanide shift reagents. Part II: Ethosuximide, 3-ethyl-3-methyl-2,5-pyrrolidinedione, and comparisons with analogs. Appl. Spectrosc. 1986; 40(4): 531-537.

6. Thomson Eberhart S., Hatzis A., Jimenez J., Rothchild R., Simons P. ^{1}H NMR spectral simplification with achiral and chiral lanthanide shift reagents - IV. Thiopental and barbiturate analogs. J. Pharm. Biomed Anal. 1987; 5(3): 233-245.

7. Fraser, R.R. Nuclear magnetic resonance analysis using chiral shift reagents. Asymmetric Synth. 1983; 1: 173-196.

8. Rinaldi P.L. The determination of absolute configuration using nuclear magnetic resonance techniques. Progr. Nucl. Magn. Reson. Spectrosc. 1982; 15: 291-352.

9. Cockerill A.F., Davies G.L.O., Harden R.C., Rackham D.M. Lanthanide shift reagents for nuclear magnetic resonance spectroscopy. Chem. Rev. 1973; 73(6): 553-588.

10. Sullivan G.R. Chiral lanthanide shift reagents. In: Eliel E.L., Allinger N.L. eds. Topics in Stereochemistry, vol. 10, New York: John Wiley - Interscience 1978: 287-329.

11. Kutal C. Chiral shift reagents. In: Sievers R.E., ed. Nuclear Magnetic Resonance Shift Reagents, New York: Academic Press 1973: 87-98.

12. Morrill T.C. ed. Lanthanide Shift Reagents in Stereochemical Analysis. New York: VCH, 1986.

13. Wenzel T.J. NMR Shift Reagents. Boca Raton FL: CRC Press, 1987.

14. Goering H.L., Eikenberry J.N., Koermer G.S., Lattimer C.J. Direct determination of enantiomeric compositions with optically active nuclear magnetic resonance lanthanide shift reagents. J. Amer. Chem. Soc. 1974; 96(5):1493-1501.

15. McCreary M.D., Lewis D.W., Wernick D.L., Whitesides G.M. The determination of enantiomeric purity using chiral lanthanide shift reagents. J. Amer. Chem. Soc. 1974; 96(4): 1038-1054.

16. Peters J.A., Nieuwenhuizen M.S., Raber D.J. Analysis of multinuclear lanthanide-induced shifts. 1. Investigations of some approximations in the procedure for separation of diamagnetic, contact, and pseudocontact shifts. J. Magn. Reson. 1985; 65: 417-428

17. Raber D.J., Peters J.A., Nieuwenhuizen M.S. Analysis of multinuclear lanthanide-induced shifts. Part 2. The geometry of ketone binding to lanthanides. J. Chem. Soc. Perkin Trans. II 1986; 853-859.

18. Morrill T.C. An introduction to lanthanide shift reagents. In: Morrill T.C. ed. Lanthanide Shift Reagents in Stereochemical Analysis. New York: VCH, 1986: 1-17, and references cited therein.

Date Received: 04/17/90
Date Accepted: 05/21/90