NMR Chemical Shift Reagents in Structural Determination of Lipid Derivatives: IV. Methyl *cis*- and *trans*-9,10-Epoxystearate and Methyl *erythro*- and *threo*-9,10-Dihydroxystearate[1]

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ABSTRACT

Chemical shift reagents were used to expand the amount of structural information obtainable from NMR studies of derivatives of methyl oleate and elaidate: methyl *cis*-9,10-epoxystearate, methyl *trans*-9,10-epoxystearate, methyl erythro-9,10-dihydroxystearate, and methyl threo-9,10-dihydroxystearate. Chemical shift reagent studies of methyl *trans*-9,10-epoxystearate and methyl threo-9,10-dihydroxystearate afforded the most information. Chemical shift reagent studies of methyl *cis*-9,10-epoxystearate and methyl erythro-9,10-dihydroxystearate were decidedly inferior. The series of complementary interpretive techniques previously developed during chemical shift reagent studies of monofunctional fatty esters and model polyfunctional fatty esters were found to be applicable in the current study. However, to avoid ambiguity in several proton assignments, supplementary spin decoupling experiments were necessary.

INTRODUCTION

Previous reports from our laboratory and elsewhere (1-5) have demonstrated that NMR chemical shift reagents (CSR), such as tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)-europium (III)–Eu(fod)$_3$–can considerably increase the amount of structural information obtainable from NMR studies of lipid derivatives. However, due to overlapping NMR signals, increased information often is limited to protons that are within five carbons of a Eu(fod)$_3$ coordination site (2). For unsaturated lipid derivatives, it is theoretically possible to obtain substantially more structural information by introducing additional CSR active functional groups into those molecules through reactions with their double bonds (the carbon-carbon double bond does not complex with CSR).

In testing this hypothesis, we were able to perform successful CSR studies on selected model polyfunctional lipid derivatives, such as methyl ricinoleate (methyl 12-hydroxy-*cis*-$\Delta^{9,10}$-octadecenoate) (MR) and methyl 12-hydroxystearate (MHS) (6). These results encouraged us to extend the interpretive techniques developed with MR and MHS to more complex polyfunctional derivatized lipid systems.

This article describes CSR studies of methyl *cis*-9,10-epoxystearate (MCES), methyl *trans*-9,10-epoxystearate (MTES), methyl threo-9,10-dihydroxystearate (MTDHS), and methyl erythro-9,10-dihydroxystearate (MEDHS).

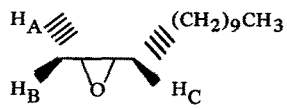
EXPERIMENTAL PROCEDURES

The NMR experimental procedures used already have been described (2). MCES and MTES were obtained from the Eastern Regional Laboratory, USDA, Philadelphia, Pa.; MTDHS was obtained from Applied Science Laboratories, State College, Pa.; MEDHS was obtained from the Hormel Institute, Austin, Minn.; and 1,2-epoxydodecane was prepared by a standard method (7,8). All compounds were greater than 99% pure. A 100-MHz NMR spectrometer, Varian model XL-100, was used through the current study.

RESULTS AND DISCUSSION

Conversions of olefins into epoxides and 1,2-glycols are stereospecific and essentially quantitative (8). Therefore, epoxides and glycols are logical derivatives increasing the number of CSR coordination sites in long chain unsaturated esters. Protons on carbons 11-18 in MCES, MTES, MTDHS, and MEDHS should be affected only by CSR complexation at their respective epoxide or glycol functions. Therefore, induced shift ratios (2) characteristic of complexation with those groups readily can be determined. CSR studies of 1,2-epoxydodecane were carried out first so that induced shift ratios of MCES and MTES could be compared with those of a model epoxide. It was hoped that different induced shift ratios would be observed for each type of epoxide and that these ratios would be characteristic of the stereochemistry of MCES and MTES.

CSR Study of 1,2-Epoxydodecane



Only limited structural information is obtained from the 100 MHz NMR spectrum of 1,2-epoxydodecane in the absence of CSR (only six signals). Letters in parentheses or numbers in brackets refer to chain positions of protons whose signals are observable: (A) δ 2.27, multiplet, 1H; (B) δ 2.54, multiplet, 1H; (C) δ 2.72, multiplet, 1H; [3] δ 1.50, shoulder on δ 1.25 peak; [6-11] δ 1.25, broad singlet; [12] δ 0.87, triplet, 3H [trimethylsilane (TMS) = 0].

Figure 1 shows additional spectral information that is obtained when the 100-MHz NMR spectrum of 1,2-epoxydodecane is redetermined at a Eu(fod)$_3$/substrate molar ratio of 1.2 (nine signals). Further increments of Eu(fod)$_3$ do not produce additional NMR signals. Note that individual signals now are observed readily for protons on carbon atoms 1-7. Separate signals are not observed, however, for

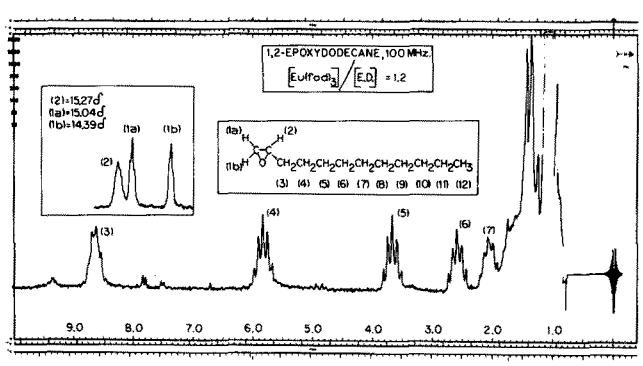


FIG. 1. NMR spectrum of 1,2-epoxydodecane with chemical shift reagent, Eu(fod)$_3$/1,2-epoxydodecane molar ratio = 1.2.

[1]Presented in parts at the AOCS Meeting, Ottawa, Canada, September 1972 and Philadelphia, Pennsylvania, September 1974.

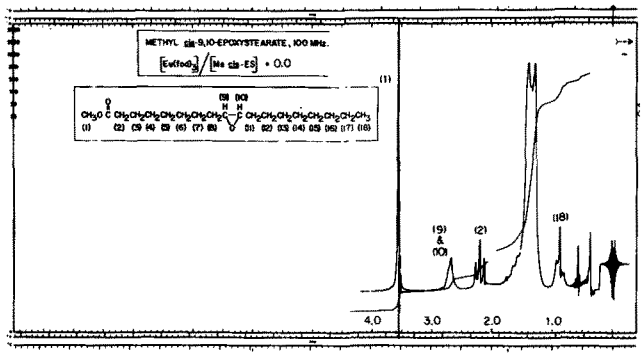


FIG. 2. NMR spectrum of methyl *cis*-9,10-epoxystearate (MCES) in absence of chemical shift reagent. Eu(fod)$_3$/MCES molar ratio = 0.0.

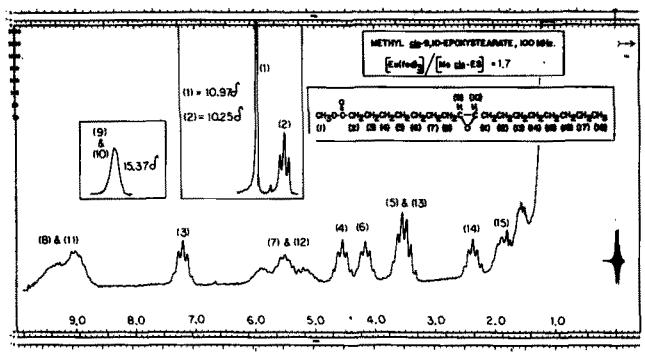


FIG. 3. NMR spectrum of methyl *cis*-9,10-epoxystearate (MCES) with chemical shift reagent. Eu(fod)$_3$/MCES molar ratio = 1.7.

the geminal protons on C-3, even though they are α to the asymmetric center at C-2. The deformation of their multiplicity pattern is attributable to their magnetic nonequivalence. Induced shift ratios (2) have been calculated for 1,2-epoxydodecane from data obtained from an incremental addition study with Eu(fod)$_3$. These values are shown in Table I; they are fairly constant for each chain position over a broad range of molar ratios of Eu(fod)$_3$/substrate. These values are compared below with those obtained for MCES and MTES.

CSR Study of MCES

Since more protons in a long chain compound are affected by complexation at both functional groups, identification of proton signals is potentially more complicated. The CSR active functional groups in MCES are closer together than those in MR and MHS. Therefore, CSR studies of methyl oleate derivatives, such as MCES, are a more realistic test of the ability of CSR to solve NMR problems than our previously reported CSR studies of MR and MHS.

The 100-MHz spectrum of MCES first was determined in the absence of CSR (Fig. 2). Only limited information is obtained (five signals). Numbers in brackets refer to chain positions of proton signals that can be identified: [18] δ 0.88, triplet, 3H; [2] δ 2.21, triplet, 2H; [9] and [10] δ 2.68, broad singlet, 2H; [methoxy] δ 3.55, singlet, 3H; δ 1.15-1.80, overlapping signals, 26H.

Since the stereochemical environments of the oxirane groups in MCES and 1,2-epoxydodecane are different, we did not expect induced shift ratios obtained for protons affected by oxirane complexation in MCES to match the induced shift ratios determined for protons in 1,2-epoxydodecane, a terminal epoxide. The stereochemical environment of the carbomethoxy group in MCES, however, is similar to that of other esters we have studied using CSR (2, 6). Therefore, unless CSR complexation at the oxirane

TABLE I

Induced Shift Ratios of Protons in 1,2-Epoxydodecane

Eu(fod)$_3$[a]	Induced shift ratios[b]				
1,2-Epoxydodecane	3	4	5	6	7
0.10	0.58	0.37	—	—	—
0.25	0.59	0.38	0.21	—	—
0.40	0.60	0.38	0.20	0.13	—
0.61	0.59	0.37	0.20	0.12	—
0.81	0.59	0.37	0.20	0.12	0.07
1.03	0.58	0.38	0.19	0.10	0.07
1.25	0.57	0.36	0.19	0.11	0.07
Average	0.59	0.37	0.20	0.12	0.07

[a] Molar ratio, CCl_4 solution.

[b] The number at the head of each column refers to carbon chain position.

group significantly changes the conformation of the carbomethoxy portion of MCES relative to the carbomethoxy conformation of previously studied esters (this ia a most unlikely possibility), the induced shift ratios of protons affected by carbomethoxy complexation are expected to be similar to ratios previously determined for monofunctional esters (2).

Induced shift ratios determined for protons affected by complexation at the oxirane group in MCES should be characteristic values that can be used in structural studies of other *cis*-epoxides. Incremental addition studies enable the calculation of these induced shift ratios and also the determination of whether the oxirane or carbomethoxy function is the more effective CSR coordinator.

Figure 3 shows the 100 MHz NMR spectrum of MCES at a Eu(fod)$_3$/MCES molar ratio of 1.7. Further increments of Eu(fod)$_3$ do not produce additional signals. Eleven discrete sets of proton signals are seen. Many of the signals overlap; thus, much less specific information is obtained from CSR studies of MCES than from our previous studies of MR and MHS. Despite the overlap, many proton assignments are possible based upon distance parameters, since the magnitude of an induced shift is proportional to the proximity of protons being shifted to CSR coordination sites. These assignments cannot be made based upon examination of Figure 3 alone. Assignments are possible only from a series of spectra obtained from an incremental addition study. The proton signals affected by CSR complexation can, thereby, be followed through their series of stepwise shifts, and analogies can be drawn between their observed behavior and the behavior of shifted signals in CSR studies of monofunctional esters (2).

The incremental addition study shows clearly that the oxirane group in MCES is a more effective CSR coordinator than the carbomethoxy group. The induced shifts (2) of protons 11 and 2 can be compared usefully, since those protons are substantially equidistant from their CSR complexation sites. Up to and including Eu(fod)$_3$/MCES molar ratios of 0.92, protons 11 undergo larger induced shifts than do protons 2. Beyond this Eu(fod)$_3$/MCES molar ratio, the oxirane group becomes saturated with CSR. Upon addition of further increments of Eu(fod)$_3$, it is obvious that complexation of the carbomethoxy group becomes increasingly more important until, finally, at high Eu(fod)$_3$/MCES molar ratios, the induced shift of protons 2 exceeds that of protons 11. This set of NMR spectra are not shown because of space limitations.

From results obtained during the incremental addition study with MCES, induced shift ratios of protons affected by CSR complexation at the oxirane group can be calculated. These results are not reported here because, due to signal overlap, induced shifts are difficult to measure directly in several cases. The induced shifts used to

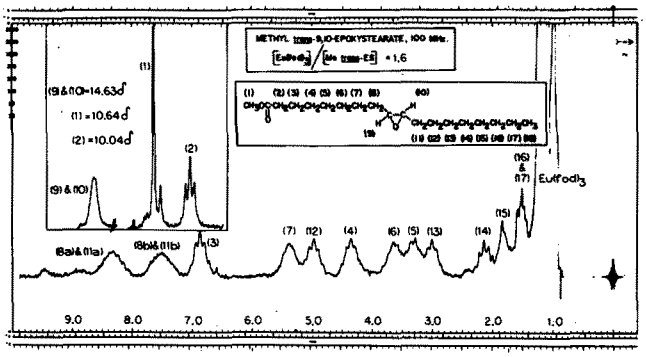


FIG. 4. NMR spectrum of methyl *trans*-9,10-epoxystearate (MTES) with chemical shift reagent. Eu(fod)$_3$/MTES molar ratio = 1.6.

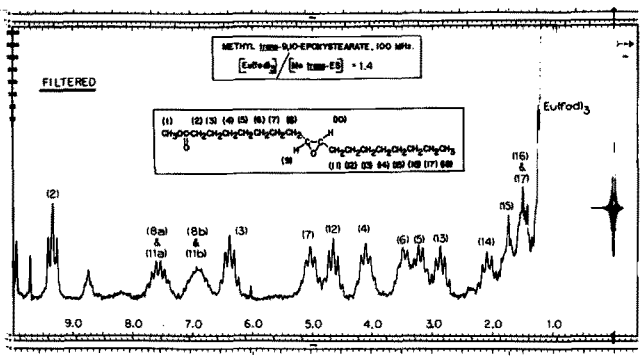


FIG. 5. NMR spectrum of methyl *trans*-9,10-epoxystearate (MTES) with chemical shift reagent. Eu(fod)$_3$/MTES molar ratio = 1.4.

calculate induced shift ratios are, therefore, somewhat speculative. The induced shift ratios obtained are similar to those listed in Table I for 1,2-epoxydodecane. This similarity is consistent with theory, since Eu(fod)$_3$ complexation would be expected, in both cases, to occur predominantly, if not exclusively, on the unhindered side of the molecule.

CSR Study of MTES

The 100-MHz NMR spectrum of MTES in the absence of CSR is similar to that of MCES shown in Figure 2; information of only limited interpretive value is obtained. Comparison of the spectral data obtained during a Eu(fod)$_3$ incremental addition study of MTES with similar data obtained with MCES reveals that the oxirane group in MTES is a less effective CSR coordinator. For example, at Eu(fod)$_3$/MTES ratios which cause protons 2 in MTES to undergo an induced shift of 400 Hz, protons 9 and 10 shift only 565 Hz. On the other hand, when protons 2 in MCES undergo an induced shift of 417 Hz, protons 9 and 10 shift 744 Hz. This difference in coordinating ability can be rationalized by considering substrate geometry. MCES has an unhindered oxirane face with which to form a CSR adduct, whereas both faces of the oxirane group in MTES are hindered by a long alkyl chain.

Figure 4 shows the 100-MHz NMR spectrum of MTES at a Eu(fod)$_3$/substrate molar ratio of 1.6. Obviously, a far greater number of discrete signals (15 signals) are obtained for MTES than for MCES. The number of individual signals is comparable to the number obtained during CSR studies of MR (6).

The assignment of signals for protons 1, 2, 3, 9, and 10 is straightforward and is based upon the position and multiplicity of the signals observed; the relative proximity to CSR coordination sites of protons being shifted also had to be considered. The assignment of other proton signals is more complex and required the decoupling studies described below.

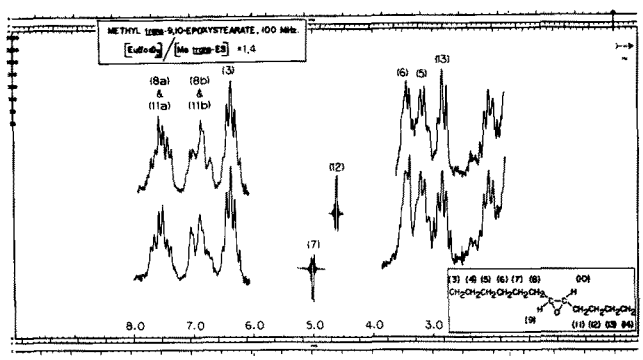


FIG. 6. Decoupling experiment I. Methyl *trans*-9,10-epoxystearate (MTES). Eu(fod)$_3$/MTES molar ratio = 1.4.

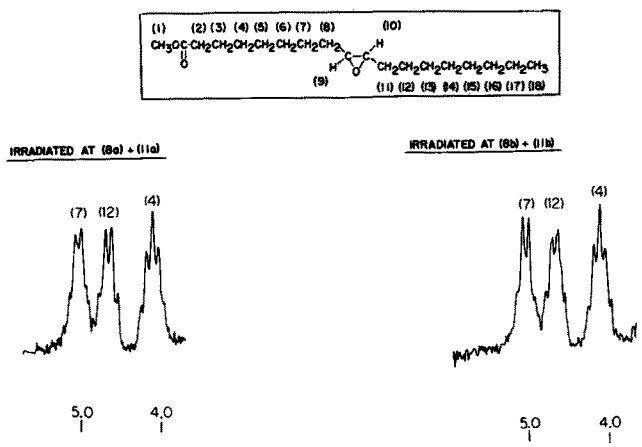


FIG. 7. Decoupling experiment II. Methyl *trans*-9,10-epoxystearate (MTES). Eu(fod)$_3$/MTES molar ratio = 1.4.

Figure 5 shows the 100-MHz NMR spectrum of MTES at a Eu(fod)$_3$/MTES molar ratio of 1.4, but the sample solution has been filtered to remove small quantities of undissolved solids. The improvement in resolution over the spectrum shown in Figure 4 is noteworthy. The indicated proton assignments in MTES have been made using this sample and are based upon the experiments described below.

Chain positions 8 and 11 are α to asymmetric centers at C-9 and C-10, respectively. Results previously obtained during CSR studies of MR and MHS showed that separate signals for geminal protons α to an asymmetric center may be observed in the presence of CSR. Chain positions 7 and 12 are β to asymmetric centers at C-9 and C-10. Results obtained during CSR studies of MR and MHS demonstrated that separate signals also may be observed for geminal protons β to an asymmetric center in the presence of CSR. On the other hand, results obtained with 1,2-epoxydodecane demonstrated that separate signals are not necessarily observed for geminal protons α to an asymmetric center, even in the presence of CSR. Therefore, it became necessary to demonstrate through decoupling experiments that proposed proton assignments are correct.

Figure 6 (lower curves) shows that irradiation at 501 Hz affects the multiplets at 688 and 754 Hz, as well as the multiplet at 347 Hz. These results are consistent with the assignment of the 501 Hz signal to protons 7, the 688 Hz signal to protons 8b + 11b, the 754 Hz signal to protons 8a + 11a, and the 347 Hz signal to protons 6. Irradiation at 463 Hz (upper curves) similarly affects the 688 and 754 Hz signals but does not affect the 347 Hz signal; instead the pentet at 285 Hz is collapsed to a triplet. These results are consistent wiht the previous assignments of protons 8 and 11, as well as assignment of the 463 Hz signal to protons 12

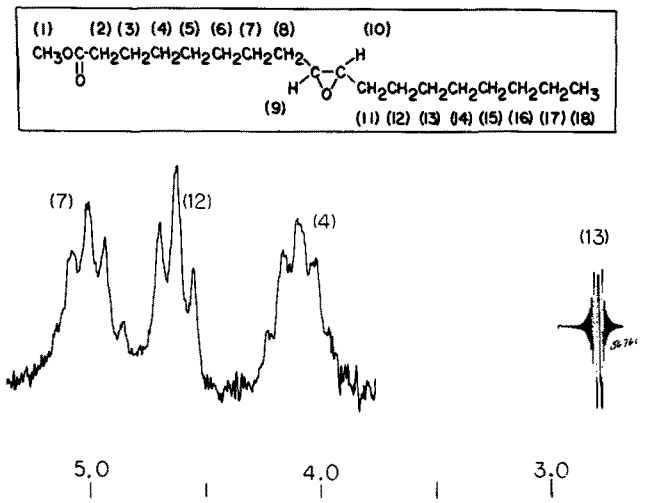


FIG. 8. Decoupling experiment III. Methyl *trans*-9,10-epoxystearate (MTES). $Eu(fod)_3$/MTES molar ratio = 1.4.

and assignment of the 285 Hz signal to protons 13. If the signals at 501 and 463 Hz are due to protons 7a + 12a and 7b + 12b, respectively, then irradiation at either signal should have similarly affected signals assigned to protons 6 and 13. By the same reasoning, if the signal at 754 Hz is due to protons 8, and not to protons 8a + 11a, then irradiation at 7 should affect only this signal and not the one at 688 Hz.

Figure 7 which describes further decoupling studies supports the above conclusions. Irradiation at either 754 Hz (protons 8a + 11a) or at 688 Hz (protons 8b + 11b) similarly affects signals assigned to protons 7 and 12, collapsing their pentets to quartets as predicted by first order multiplicity rules. As Figure 7 also shows, and as would be anticipated, the signal assigned to protons 4 is unaffected by decoupling of protons 8a + 11a and 8b + 12b.

Additional support is provided by Figure 8 which shows that irradiation at 285 Hz (protons 13) collapses the pentet for protons 12 (463 Hz) to a triplet, again as expected by first order multiplicity rules.

These assignments are supported further from a consideration of multiplicity patterns. Signals assigned to 8a + 11a and 8b + 11b are multiplets. Signals assigned to protons 7 and 12 are pentets. If the latter signals are actually due to protons 7a + 12a and 7b + 12b, the $\Delta\nu/J \geqslant 7$ criterion would not be met, and first order multiplicity would not result. The fact that multiplets are observed for protons 5 and 6 supports the above argument.

Since the above decoupling experiments specify proton signal identifications in MTES, it is possible to assign most of the peaks in all the spectra obtained with this compound during the incremental CSR addition study. Since exact chemical shift positions are determinable it is possible to calculate accurate induced shift ratios for MTES. Induced shift ratios attributable to complexation at the oxirane group are shown in Table II. Comparison of these results with those for 1,2-epoxydodecane (Table I) reveal dissimilarities, indicating that the geometry of the complex at the oxirane function is different for MTES than for 1,2-epoxydodecane or MCES.

Induced shift ratios attributable to complexation at the carbomethoxy group are shown in Table III. They are, in fact, comparable to values previously obtained for monofunctional esters (2). This indicates that the geometries of these complexes at the carbomethoxy groups are similar.

In calculating the carbomethoxy induced shifts for protons 4, 5, and 6 shown in Table III, induced shift contributions attributable to complexation at the oxirane group have been deducted. The observed chemical shifts for protons 15, 14, and 13 are deducted from the observed chemical shifts for protons 4, 5, and 6, respectively. The result is a calculated "carbomethoxy induced shift." Induced shift ratios then are obtained by dividing these "carbomethoxy induced shifts" by the "carbomethoxy induced shift" for protons 2. The "carbomethoxy induced shift" for protons 2 ordinarily would have been determined by deducting the observed chemical shift for protons 17 (the induced shift contribution attributable to oxirane complexation) from the observed chemical shift for protons 2. Unfortunately, it is difficult to determine accurately the observed chemical shift for protons 17. Consequently, the carbomethoxy induced shift for protons 2 has been determined by dividing the actual methoxy induced shift in MTES by 0.91, the induced shift ratio for methoxy protons in monofunctional esters at high $Eu(fod)_3$/substrate molar ratios (2).

TABLE II

Methyl *trans*-9,10-Epoxystearate (MTES) Induced Shift Ratios Due to Complexation at the Oxirane Group

$Eu(fod)_3$[a]	Induced shift ratios[b]					
MTES	11	12	13	14	15	16
1.11	0.54	0.30	0.14	0.08	0.05	0.03
1.29	0.53	0.30	0.14	0.07	0.05	0.02
1.47	0.53	0.30	0.14	0.08	0.05	0.03
1.65	0.53	0.29	0.14	0.07	0.05	0.03

[a] Molar ratio, CCl_4 solution.

[b] The number at the head of each column refers to carbon chain position.

TABLE III

Methyl *trans*-9,10-Epoxystearate (MTES) Induced Shift Ratios Due to Complexation at the Carbomethoxy Group

$Eu(fod)_3$[a]	Induced shift ratios[b]		
MTES	4	5	6
1.11	0.33	0.16	0.09
1.29	0.32	0.16	0.08
1.47	0.32	0.15	0.08
1.65	0.32	0.15	0.08
Average	0.32	0.16	0.08

[a] Molar ratio, CCl_4 solution.

[b] The number at the head of each column refers to carbon chain position.

CSR Study of MTDHS

The 100-MHz NMR spectrum of MTDHS first was determined in the absence of CSR (Fig. 9). Only limited information is obtained (seven signals). Numbers in brackets refer to chain positions of proton signals that can be identified: [1, methoxy] δ 3.58, singlet, 3H; [2] δ 2.22, triplet, 2H; [9] and [10] δ 3.25, broad singlet, 2H; [18] δ 0.88, triplet, 3H; [3] δ 1.59, shoulder on 1.35 peak; other chain protons at δ 1.34 and 1.28, and [19-20] δ 2.7, singlet, 2H.

Incremental CSR addition studies reveal that, at low $Eu(fod)_3$/MTDHS molar ratios, CSR complexation occurs almost exclusively at the glycol function. For example, at a $Eu(fod)_3$/MTDHS molar ratio of 0.88, the methoxy signal shifts only 40 Hz (0.4 δ), whereas protons 9 and 10 shift almost 1200 Hz (12 δ).

The complexation site(s) either can be considered the glycol function or the two separate -OH groups. The complex at the glycol function could be either a bidentate complex in which both -OH groups are complexed to the europium atom, or it could be an average or rapid

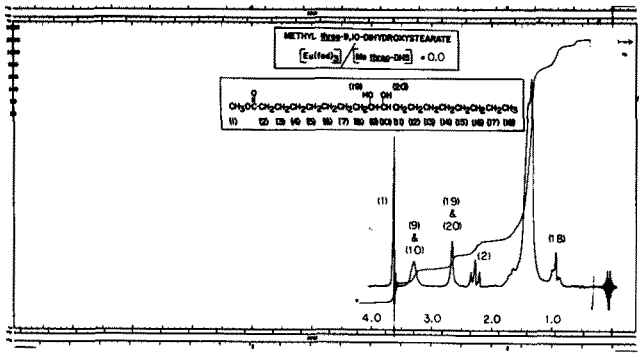


FIG. 9. NMR spectrum of methyl threo-9,10-dihydroxystearate (MTDHS) in absence of chemical shift reagent Eu(fod)$_3$/MTDHS molar ratio = 0.0.

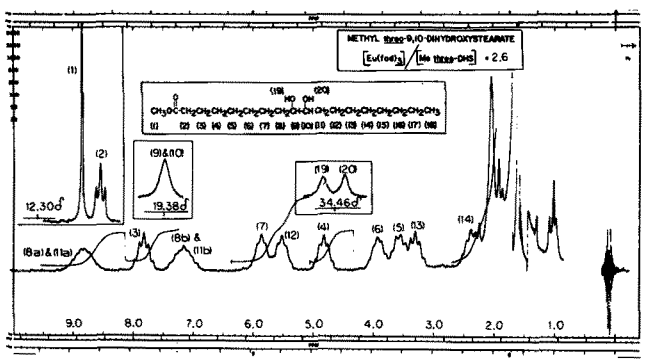


FIG. 10. NMR spectrum of methyl threo-9,10-dihydroxystearate (MTDHS) with chemical shift reagent. Eu(fod)$_3$/MTDHS molar ratio = 2.65.

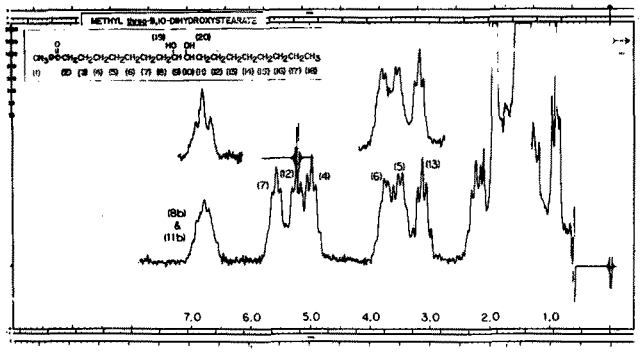


FIG. 11. Decoupling experiment IV. Methyl threo-9,10-dihydroxystearate (MTDHS). Eu(fod)$_3$/MTDHS molar ratio = 2.65.

TABLE IV

Methyl threo-9,10-Dihydroxystearate (MTDHS) Induced Shift Ratios Due to Complexation at the Glycol Function

Eu(fod)$_3$[a]	Induced shift ratios[b]			
MTDHS	11	12	13	14
0.29	0.59	0.32	—	—
0.58	0.46	0.30	0.15	0.07
0.88	0.44	0.29	0.14	0.07
1.18	0.43	0.28	0.11	—
1.50	0.42	0.27	0.13	0.07
1.78	0.42	0.26	0.12	0.06
2.05	0.41	0.26	0.12	0.06
2.65	0.41	0.26	0.12	0.06

[a]Molar ratio, CCl_4 solution.

[b]The number at the head of each column refers to carbon chain position.

equilibration of europium between the two -OH groups. Either mechanism would produce the same effect. Molecular models suggest that the CSR is too bulky to permit separate CSR molecules to coordinate with each of the two -OH groups. The CSR incremental addition study supports this hypothesis. At a Eu(fod)$_3$/MTDHS molar ratio of 2.05, the molecule virtually is saturated with CSR, even though it contains three potential CSR active functional groups.

Figure 10 shows the 100-MHz NMR spectrum of MTDHS at a Eu(fod)$_3$/MTDHS molar ratio of 2.65. The number of individual signals observed (15 signals) is comparable to those observed in the CSR study of MTES. Moreover, the chemical shift positions of MTDHS protons are similar to those of MTES protons in the presence of CSR. This suggests that the geometries of the CSR complexes of MTDHS and MTES are similar.

Assignments of protons 1, 2, 3, 9, 10, 19, and 20 are based upon signal multiplicity and correlations between their observed chemical shift positions and their proximity to CSR coordination sites. Assignment of remaining protons signals is much less straightforward. Several tentative assignments were made for protons near the glycol function. Since carbon atoms 9 and 10 are asymmetric, assignment of signals due to protons 8a + 11a and 8b + 11b were made by analogy with CSR data obtained for MTES (Fig. 5). Figure 11 demonstrates that irradiation of signal 12 affects the multiplet observed for signal 8b + 11b, and also collapses the pentet observed for signal 13 to a triplet. This result substantiates the proposed assignments.

At high Eu(fod)$_3$/MTDHS molar ratios, the glycol function becomes saturated with CSR and further complexation occurs predominantly at the carbomethoxy group. Therefore, at higher Eu(fod)$_3$/MTDHS molar ratios, the signals for protons 5, 6, and 7 shift downfield from signals for protons 14, 13, and 12, respectively. Since exact chemical shift positions can be determined for these latter protons, accurate induced shift ratios can be calculated. Since each of the geminal protons on C-11 absorb at different chemical shift positions, the average of these positions was used in calculations of their induced shift ratios. Induced shift ratios attributable to complexation at the glycol function are shown in Table IV. A comparison of these results with average induced shift ratios obtained for simple alcohols (2) reveals dissimilarities which indicate that the geometry of the CSR-glycol adduct differs from the geometry of a simple CSR-alcohol adduct.

The carbomethoxy induced shift ratios for MTDHS are shown in Table V. They were calculated using the same procedure described above for MTES. Ratios for protons 4 could not be obtained, because the chemical shift position for the C-15 protons (protons 4 and 15 are equidistant from the glycol function) could not be determined.

When a Eu(fod)$_3$/MTDHS ratio of 1.50 is reached in the CSR incremental addition study, the signals for each of the two -OH protons (19 and 20) begin to separate. We assume that at this Eu(fod)$_3$/MTDHS molar ratio, complexation at the carbomethoxy group now has become significant and the C-9 -OH proton consequently is shifted further downfield than the C-10 -OH proton (proximity effect). At a Eu(fod)$_3$/MTDHS ratio of 2.65 hydroxyl protons 19 and 20 are separated well and have been shifted ca. 32 δ downfield. The possibility exists, therefore, that the separation of the -OH signals in a glycol-ester may be diagnostic for the position of the olefinic double bond from which the glycol was derived. To determine whether this is the case it would be necessary to prepare threo-glycols from a series of unsaturated fatty esters and then perform CSR studies to develop a relationship between double bond position and the chemical shift difference between the -OH proton signals of the glycol at Eu(fod)$_3$/glycol molar ratios of 1.50-2.00.

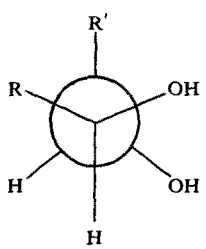
CSR Study of MEDHS

The NMR spectrum of MEDHS in the absence of $Eu(fod)_3$ is similar to that of MTDHS: only limited information can be obtained.

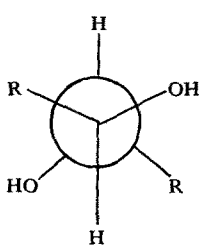
MEDHS is not sufficiently soluble in carbon tetrachloride to permit CSR studies to be performed in this solvent. Deuterochloroform was substituted; it was distilled before use and stored over Linde 4A molecular sieve to remove traces of acidic impurities which might decompose the CSR.

Because MEDHS dissolved in deuterochloroform might not have the same conformational mobility, conformation stability, rotamer population distribution, or CSR complex stability as MEDHS dissolved in carbon tetrachloride, an unequivocal comparison of the effectiveness of MTDHS and MEDHS as CSR coordinators cannot be made. However, Figure 12 which shows the 100-MHz NMR spectrum of MEDHS in deuterochloroform at a $Eu(fod)_3$/MEDHS molar ratio of 2.9, demonstrates that the erythro-glycol is not as suitable as substrate for CSR studies as MTDHS. With the former, fewer discrete signals are obtained; signals are broader, and a complete structural analysis cannot be made. The hydroxyl protons (19 and 20), for example, are not separated clearly, even at the molar ratio of CSR/MEDHS of 2.9.

The similarity of NMR spectra obtained during CSR studies of MCES and MEDHS indicates that the geometries of the CSR complexes of these molecules are quite similar. For this to be the case, the conformation that MEDHS must assume in the CSR complex is represented below by rotamer A. Rotamer B is known to be the most stable



Rotamer A



Rotamer B

conformation for MEDHS in the absence of CSR. It is, therefore, obvious that CSR studies of conformationally mobile systems reveal conformational information about the CSR complexed species only. Uncomplexed substrate molecules may assume completely different conformations.

TABLE V

Methyl threo-9,10-Dihydroxystearate (MTDHS) Induced Shift Ratios Due to Complexation at the Carbomethoxy Group

$Eu(fod)_3$[a] / MTDHS	Induced shift ratios[b] 5	6
1.78	0.14	0.07
2.05	0.13	0.06
2.65	0.14	0.07

[a]Molar ratio, CCl_4 solution.

[b]The number at the head of each column refers to carbon chain position.

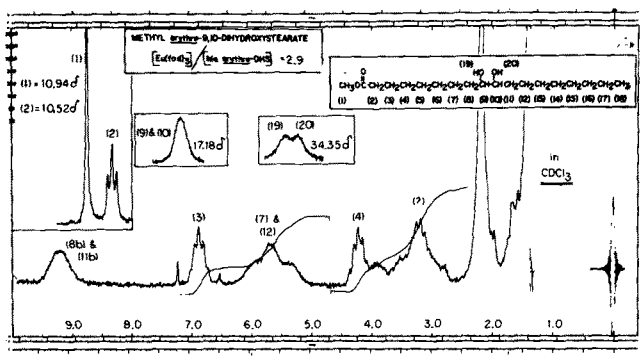


FIG. 12. NMR spectrum of methyl erythro-9,10-dihydroxystearate (MEDHS). $Eu(fod)_3$/MEDHS molar ratio = 2.9.

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