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Determination of Conformations of Esters with the Use of Lanthanide Shift Reagents

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Synopsis. Lanthanide shift reagents have been used for diagnosis of *s-trans* and *s-cis* conformations of esters. By taking a ratio of lanthanide-induced shift of (H)CH_2C=O protons *vs.* [shift reagent]/[substrate] as a reference, relative ratio of (H)CH_2O- of the *s-trans* form has been found to be almost unity, whereas that of the *s-cis ca.* 0.5.

Following the discovery of Hinckley[1] a large number of papers[2] on the utility of the lanthanide shift reagents have been reported. Structures of organic oxygen compounds were investigated with the aid of shift reagents.[3] Interestingly, however, the use of shift reagents in determination of conformations of esters has not so far been reported to our knowledge.

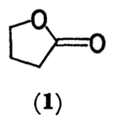
Ester can take either *s-trans* or *s-cis* conformation in principle. Ordinary esters take *s-trans* conformation probably because of the steric and dipolar effects.[4] On the contrary, lactones of small ring size exist as *s-cis* conformation because of the steric requirements.[5] Thus a problem arises whether it is possible to take *s-trans* conformation for a mediumsized lactone or an analogous ring. Hetera-*p*-cyclophanes containing oxygen(s) in an ansa chain, which we have been interested in for some years,[6] is an example of this sort.

It has long been hoped that an infrared carbonyl stretching absorption could be used for diagonsis of the ester conformation. In reality, however, absorptions due to *s-cis* and *s-trans* conformations are so close with each other that they are almost useless for the purpose. Only careful examinations in the presence of both conformations proved to be usefull.[7]

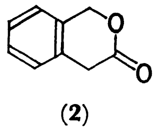
Lanthanide shift reagents are one of the possibilities to solve this problem. If the lanthanide ion is located closely to the carbonyl oxygen, its effect on the ether methylene of the ester group should be different according to its conformation. We now wish to report a successful use of lanthanide shift reagents for determination of conformations of lactones and esters.

Simple esters are known to exist as *s-trans* conformation only[4] and γ-butyrolactone (**1**) must take *s-cis* conformation because of the steric requirement. Thus they were taken as typical examples of *s-trans* and *s-cis* conformations in the lanthanide-induced shift (LIS) measurements. 3-Isochromanone (**2**) was also included as an example of *s-cis* form of 6-membered rings.

PMR spectra of these compounds in deuteriochloroform were determined by adding various amounts of a shift reagent, molar ratio of the shift reagent to the substrate being 0—0.3. LIS was plotted against [L]/[S], where [L] and [S] are the molar concentrations of the shift reagent and the substrate, respectively, to show good linearity. Relative slopes of the straight lines were obtained by taking that of protons at α-position to the carbonyl as a reference and are summarized in Table 1. Changing the shift reagent from Eu(fod)$_3$-d_{27} to Eu(dpm)$_3$ did not seem to give a significant change in the relative slopes. The LIS of the alcoholic methyl signals of methyl acetate was reported by Hart and Love, using Eu(dpm)$_3$.[8] The relative slope was calculated to be 0.96, which is in good agreement with the present datum.



(**1**)



(**2**)

Generally the ether oxygen in an ester group is inactive toward lanthanide shift reagent and preferred site of complexation is the carbonyl oxygen.[3,8,9] If small-sized lactones preferred to form complexes at the ether oxygen, differing from the general tendency of the esters, the relative slopes of the straight lines for the CH_2O would have been larger than unity. Data in Table 1 suggest that the site of complexation is the same for *s-cis* and *s-trans* conformations.

However, the differences in relative slopes concerned with the methylene groups alpha to the ether oxygen do exist; the relative slope of the straight line involving CH_2O group of *s-trans* conformation is almost 1, whereas that of *s-cis* conformation is *ca.* 0.5. In order to discuss the difference of the slopes quantitatively, many factors like pseudo-contact *vs.* contact interactions, symmetry of the anisotropy and the conformational uniformity may have to be considered[10] in the use of McConnell-Robertson equation.[11] Yet this change in relative slopes is distinct and must be useful in diagnosing the conformations of carboxylic esters, provided that they

Table 1. Relative slopes of straight lines obtained from plots of LIS *vs.* [L]/[S] using Eu(fod)$_3$-d_{27}[a)]

Protons	$CH_3CO_2CH_3$	$CH_3CO_2C_2H_5$	$C_2H_5CO_2C_2H_5$	**1**	**2**
(H)CH_2C=O	1.00	1.00	1.00	1.00	1.00
(H)CH_2O-	0.90	1.02	1.03	0.51	0.49(0.54)
(**H**)CH_2CH_2O-		0.41	0.35	0.40	
(**H**)CH_2CH_2C=O			0.56		

a) Numericals in parentheses were obtained by using Eu(dpm)$_3$.

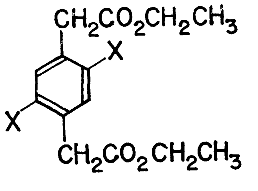
Table 2. Relative slopes of straight lines obtained with compounds **3**, **4**, and dioxa[n]paracyclophanes ($\mathbf{5}_n$) using Eu(fod)$_3$-$d_{27}$$^{a)}$

Compound	$CH_2C{=}O$	CH_2O-	ArH	$ArCH_3$
3	1	1.0	0.59	—
4	1	0.97(1.0)	0.58(0.59)	0.37(0.39)
$\mathbf{5}_{11}$	1	1.1	0.54	0.43
$\mathbf{5}_{12}$	1	1.0	0.52	0.43
$\mathbf{5}_{13}$	1	0.99	0.55	0.43
$\mathbf{5}_{14}$	1	0.95	0.56	0.41
$\mathbf{5}_{15}$	1	0.99	0.53	0.37
$\mathbf{5}_{16}$	1	1.0(0.99)	0.57(0.55)	0.38(0.38)

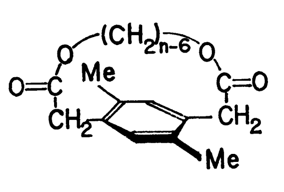
a) Values in parentheses are those obtained by using Eu(dpm)$_3$.

exist as a single conformation. If an ester should exist as a mixture of *s-cis* and *s-trans* conformations and signals due to those conformations should not be resolved it would be natural to expect that an intermediary value between 0.5 and 1 is obtained.

Application of the above findings to complicated systems will be worthwhile to try. We had diester precursors (**3** and **4**) for preparations of hetera-*p*-carbophanes. Testing with these compounds will be worthy because several rotational isomers are possible due to the presence of a RCH_2CO_2R' group$^{12)}$ and two ester groups are present. The results are shown in Table 2.



(**3**): X=H, (**4**): X=Me



($\mathbf{5}_n$)

Relative slopes for the CH_2O group of these compounds are *ca.* 1.0. Doubtlessly, these esters exist as *s-trans* conformations. These observations are in conformity with the idea that the open chain esters take *s-trans* conformation usually and *s-cis* conformation is present in special cases only.$^{13)}$ The results also suggest that the relative slope can be used in such complex esters also for diagnosis of the conformation.

It will be interesting to see the results applied to complex lactones. Dioxa[n]paracyclophanes ($\mathbf{5}_n$)* show only a sharp C=O stretching band at *ca.* 1730 cm^{-1} which is not useful for determination of conformation. Since internal rotations of aromatic rings in the lower members of $\mathbf{5}_n$ are known to be slow on the NMR time scale and rings are strained from the molecular model, a possibility exists that one or both of the ester groups assume *s-cis* conformation. The results of LIS measurements are also shown in Table 2. The relative slopes clearly suggest that these members take *s-trans* conformations irrespective to the ring size.

Usage of lanthanide shift reagents and relative slope of the straight lines obtained by plotting LIS against [L]/[S] of CH_2O signals are powerful tools in determination of conformations of esters. Eu(dpm)$_3$ and Eu(fod)$_3$-d_{27} gave almost the same numerical values. The slope values of methyl groups may be used as well as methylenes.

Experimental

Syntheses. Syntheses of dioxa[n]paracyclophanes ($\mathbf{5}_n$) will be reported elesewhere. γ-Butyrolactone (**1**) was of commercial origin and 3-isochromanone (**2**) was synthesized according to the method of literature.$^{14)}$

*Diethyl 2,5-Dimethyl-1,4-phenylenediacetate (**4**).* A mixture of 10 g (44 mmol) of 2,5-dimethyl-1,4-phenylenediacetic acid, 50 ml of ethanol, 100 ml of benzene, and a few drops of concentrated sulfuric acid was refluxed for several hours and worked up in a usual manner to give 9 g (71.8 %) of pale yellow crystals which were recrystallized from hexane-ether. Mp 55.5—56.5 °C. IR(KBr disk): 1725 cm^{-1} (ν_{CO}). NMR (CCl_4, δ,): 1.22 (6H, t); 2.23 (6H, s); 3.43 (4H, s); 4.04 (4H, q); 6.89 (2H, s). Mass spectrum: 278 (M$^+$). Found: C, 68.71; H, 7.91%. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97%.

*Diethyl 1,4-Phenylenediacetate (**3**),* mp 58.0—59.0 °C(lit,$^{15)}$ mp 59 °C), was obtained similarly.

Measurement of Spectra. NMR spectra were recorded on a Hitachi R-20B spectrometer operating at 60 MHz. Shift reagents stocked over P_2O_5 were used.

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* n is the number of the members of the ansa chain.