Conformational analysis, Part 31.[1] A theoretical and lanthanide induced shift (LIS) investigation of the conformations of some epoxides

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Received (in Cambridge) 10th August 1998, Accepted 4th November 1998

An improved LIS technique, using $Yb(fod)_3$ to obtain the paramagnetic induced shifts of all the spin $\frac{1}{2}$ nuclei in the molecule, together with complexation shifts obtained by the use of $Lu(fod)_3$, has been used to investigate the conformations of a group of epoxides. These are *cis* (**1**) and *trans* (**2**) stilbene oxide, cyclopentene oxide (**3**), cyclohexene oxide (**4**), cycloheptene oxide (**5**), propene oxide (**6**) and styrene oxide (**7**).

The LIRAS3 complexation model involving two symmetric lone pairs on the oxygen atom was used for the symmetric compounds but, for the unsymmetric compounds, a more complex unsymmetric complexation model (HARDER) was found to be necessary. The calculated LIS for styrene oxide and *cis*- and *trans*-stilbene oxide were in excellent agreement with the observed data for both the molecular mechanics (MM) and the *ab initio* geometries with the phenyl ring dihedral angles optimised.

In styrene oxide and *trans*-stilbene oxide the phenyl rings are approximately perpendicular to the oxirane ring, in agreement with the conformation in the solid state and with the theoretical calculations. In *cis*-stilbene oxide steric repulsions between the phenyl rings splay them apart so that they are now *exo* to the oxirane ring. Again the LIS analysis is in good agreement with the theoretical calculations.

Both the LIS data and the modelling studies agree that cyclopentene oxide is in a boat conformation with an angle of pucker of *ca.* 30° and that cyclohexene oxide is in a half-chair conformation with C4 and C5 displaced from the ring plane.

The LIS analysis of cycloheptene oxide gave good agreement for two equilibrating chair conformations with an *endo*/*exo* ratio of 70 : 30, in excellent agreement with low temperature NMR data.

The accurate reproduction of the LIS data provides an unambiguous method of assigning the proton chemical shifts of the individual methylene protons in the cyclic epoxides, which are not easily available by any other technique.

Introduction

Epoxides are some of the most versatile intermediates in synthetic chemistry, the Sharpless asymmetric epoxidation being a noteable recent example.[2a] They are also both commercially important compounds and reactive agents and intermediates in many natural processes and include both carcinogens and anti-tumour agents.[2b] Despite this commercial and chemical importance the conformational analysis of epoxides has received comparatively little attention. This is even more surprising when one considers that the epoxide system provides an ideal opportunity to study the steric and polar interactions between the oxygen atom, which is precisely located in the carbon framework, and any substituent atom.

A number of NMR studies of simple epoxides were reported some time ago.[3a–d] The analysis of the proton spectra was complicated by the existence of long range couplings of either sign between the side-chain protons and the protons on the epoxide ring.[3b] For example, the proton couplings (Hz) in propene oxide are $^3J_{HH}$ 3.88 (*cis*), 2.57 (*trans*) and 5.15 (Me) and $^4J_{HH}$ −0.36 (*cis*) and +0.52 (*trans*).[3b] This, plus the large solvent effects due to the polar oxygen atom made the determination of the conformer populations of epoxides such as the epihalohydrins not an easy task and it was only solved by the combined use of NMR plus solvation theory.[3d]

These complexities also mean that the complete analysis of the proton NMR spectra of any cyclic epoxide is a non-trivial task and it is perhaps for this reason that most of the conformational investigations of cyclic epoxides have been carried out by other physical techniques.

We now report a lanthanide induced shift (LIS) and theoretical analysis of a group of basic epoxides, *cis*-(**1**) and *trans*-(**2**) stilbene oxide, cyclopentene (**3**), cyclohexene (**4**) and cycloheptene (**5**) oxides, propene oxide (**6**) and styrene oxide (**7**) of which **1**–**5** and **7** may exhibit conformational flexibility.

The rigid planar epoxide ring with the consequent eclipsed CHCH fragment will behave in an analogous fashion to a double bond when part of a cyclic system, with of course the added complication of a non-symmetric environment about the eclipsed CC fragment. Thus cyclopentene oxide is considered to have two possible puckered conformations, the boat and chair forms (see later). The stable form in the gas phase was found to be the boat conformer by microwave[4] (MW) and electron diffraction[5,6] (ED) investigations and this is in agreement with NMR[7] and dipole moment[8] measurements on substituted cyclopentene oxides. Cyclohexene oxide may exist in two boat and a half-chair conformation but ED[6,9,10] and MW[11] investigations found that the only populated conformer is the half-chair form. There are a number of possible conformers of cycloheptene oxide but a low temperature NMR study found only two populated conformers in the ratio of 71 : 29 at −146 °C, which were assigned to the two chair forms.[12] A subsequent ED study[6] confirmed these results and found that the two chair conformers were present in a ratio of *ca.* 2 : 1 (*endo*/*exo*).

Previous LIS investigations in our laboratories have demon-

strated the importance and utility of the LIS method in determining the structures and conformations of a variety of molecules in solution [1,13–18] and the essential conditions necessary for successful LIS studies have been given. Amongst these are the determination of only one or two molecular parameters (*e.g.* a torsional angle or conformer ratio) and both the quality and the comprehensiveness of the experimental data. In particular, (i) $Yb(fod)_3$-induced shifts (ΔM_i) are collected for all the ^1H and ^{13}C nuclei of the substrate, (ii) $Lu(fod)_3$ is used [1,13] to evaluate diamagnetic complexation contributions (ΔD_i), (iii) pseudocontact contributions $(\Delta M - \Delta D)_i$ are simulated according to the McConnell–Robertson equation [19] and a chemically reasonable complexation model is used.[17] This technique gave excellent results with agreement factors (AF) < 0.5% for unhindered aromatic ketones when reliable starting geometries were available.[13] It was also shown [14] that the LIS can be used to refine *ab initio* optimised geometries. Thus the refined LIS method given in preceding parts of this series is now a sensitive method of testing molecular structures in solution.

Experimental

All samples were obtained commercially (Aldrich and Fluka), purified by distillation and stored in a refrigerator prior to use. The solutions were made up as 0.5 M in deuteriochloroform which had been stored for at least 24 hours over molecular sieves prior to use. The shift reagent $Yb(fod)_3$ is available commercially and $Lu(fod)_3$ was prepared following Springer *et al.*[20] The shift reagents were dried *in vacuo* over P_2O_5 at *ca.* 35 °C for 24 hours, and maintained *in vacuo* over P_2O_5 between successive additions to the sample. Three additions of shift reagent (*ca.* 15–20 mg, *i.e.* 0.01 M) were weighed directly in the NMR tube. The plots of chemical shift *vs.* ρ the ligand : substrate ratio were checked for linearity (all correlation coefficients > 0.999) and for the intercept at the origin (a good test for any impurities interacting with the shift reagent). The slopes obtained are the ΔM values recorded. The diamagnetic shifts (ΔD) were obtained from identical experiments using $Lu(fod)_3$.

The LIS measurements were recorded on a Varian Gemini 200 spectrometer operating on ^1H and ^{13}C at 22 °C. Digital resolution was better than 0.09 Hz for the proton spectra and 0.36 Hz for the carbon spectra. A 4 second pulse delay was used for the accumulation of the carbon spectra.

The $Lu(fod)_3$ experiment with **1** and both LIS experiments for compounds **6** and **8** were recorded on a Bruker AMX-400 spectrometer. Typical proton spectral widths were 6000 Hz with 128 K transform, carbon spectral widths were typically 23 000 Hz with 128 K transform using a line broadening of 2.0 Hz.

Spectral assignments

The spectral assignments for the carbon spectra of all the compounds were straightforward utilising previous literature assignments for **1**,[21,22,23] **2**,[21,23,24] **3**,[23,25] **4**,[23,24,25] **6**[23,24,26] and **7**,[23] additive substituent chemical shifts [26] and the size of the ΔM values obtained. The assignments for the proton spectra were not so obvious, particularly the assignment of the protons on each methylene group in the cycloalkene oxides. In cyclopentene oxide the assignment of the C_β and C_γ methylene protons was facilitated by the 2 : 1 intensity ratio of the C_β/C_γ protons. In cyclohexene and cycloheptene oxide COSY and HETCOR correlations were used to assign the protons on each methylene group from the assigned carbon spectra. The assignment of the *cis* and *trans* protons in **3** and **4** was made on the basis that the *cis* protons would be expected to have the larger value of the pseudo contact shift than the corresponding *trans* protons and this assignment was subsequently confirmed by the detailed LIS analysis. However the assignment of the *cis* and *trans* protons on each methylene group in cycloheptene oxide was less obvious and is considered later. Full details of all the spectral assignments are given elsewhere.[27] The observed chemical shifts (δ), diamagnetic shifts (ΔD), LIS values (ΔM) and pseudocontact shifts ($\Delta M - \Delta D$) are given in Tables 1 and 2 for the compounds measured here. It is more convenient to use a simple nomenclature rather than the systematic numbering, so the following has been used. For the symmetric compounds α,β,γ refer to the position of the atom with respect to the epoxide oxygen and for the substituted epoxides the protons are designated gem, *cis* and *trans* with respect to the substituent.

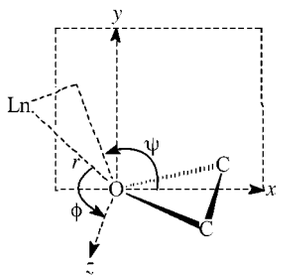


Fig. 1 Coordinate geometry for lanthanide–epoxide complexation.

The initial molecular geometries were taken from either experimental (*i.e.* X ray, microwave or electron diffraction) data or molecular mechanics (PCMODEL [28]) and *ab initio* optimisations (GAUSSIAN92 [29] at the recommended RHF(MP2)/6-31G* basis set level [30]) and a selection of the parameters for the ring geometries for the stable conformers of all the compounds studied are given in Tables 3–7. Further details of all these geometries are given in ref. 27.

Results

The lanthanide complexation model

It is first necessary to determine the most appropriate complexation model for the epoxides. The LIRAS3 complexation model [15] was first used for the epoxides. In this the complexing lone pairs on the oxygen atom are considered to be above and below the ring plane of the epoxide. Thus for the two-site option this would result in a pseudo tetrahedral configuration of the oxygen atom. The lanthanide position is given in polar coordinates (r, φ, ψ) which are symmetrical with respect to the epoxide ring plane, any asymmetry being reflected solely in the lanthanide populations. As the two-site LIRAS programme reflects the lanthanide position in the *xz* plane it is necessary for this model to place the epoxide ring plane in the *xz* coordinate plane (Fig. 1). There is also a four-site option in LIRAS3, in which reflection is performed in both the *xz* and *xy* planes and this takes some account of the spread of the oxygen atom electron density around the "classical" lone pairs. In this option the lanthanide populations can be varied about the *xz* plane as before, but not about the *xy* plane. Both options were used for the symmetric epoxides.

The unsymmetric epoxides **6** and **7** did not however give a satisfactory solution with either of the LIRAS3 options whatever the starting geometry. Even the experimental geometry of propene oxide did not give a good solution and this suggested that the problem was due to the dichotomy between the implicitly symmetric complexation of LIRAS3 and the chiral epoxide. Therefore a more complex LIS programme (HARDER),[16] which was written to take account of the unsymmetric complexing environment in chiral ketones (*e.g.* norbornanone), was applied to these compounds. This programme considers two complexing sites with independant geometries and varying populations. Thus two more parameters are needed to define the lanthanide geometries (three coordinates for each site and the % populations) than in the LIRAS3 model. In HARDER the epoxide may be in any orientation but for these calculations the epoxide ring was also placed in the *xz* plane (Fig. 1).

We shall show that the application of this programme does

Table 1 Observed carbon and proton chemical shifts (δ), LIS values (ΔM), diamagnetic shifts (ΔD) and pseudo-contact shifts ($\Delta M - \Delta D$) for *cis*-(**1**) and *trans*-(**2**) stilbene oxides and cyclopentene (**3**), cyclohexene (**4**) and cycloheptene (**5**) oxides

Compound		C_α	C_i	C_o	C_m	C_p	H_o	H_m	H_p	H_α
1	δ	59.67	134.26	126.75	127.65	127.38	7.154	7.154	7.154	4.343
	ΔM	129.39	52.31	32.19	15.30	12.69	34.57	9.62	7.20	77.11
	ΔD	6.15	−2.70	0.22	0.09	0.79	—	—	—	0.75
	$\Delta M - \Delta D$	123.24	55.01	31.97	15.21	11.90	34.57	9.62	7.20	76.36
2	δ	62.75	137.01	125.39	128.44	128.19	7.344	7.344	7.344	3.850
	ΔM	131.93	55.64	29.79	9.52	7.08	30.27	3.11	2.13	79.15
	ΔD	5.94	−2.91	0.80	0.39	1.14	—	—	—	0.55
	$\Delta M - \Delta D$	125.99	58.55	28.99	9.13	5.94	30.27	3.11	2.13	78.60

		C_α	C_β	C_γ	H_α	$H_{\beta cis}$	$H_{\beta trans}$	$H_{\gamma cis}$	$H_{\gamma trans}$
3	δ	57.16	27.17	18.26	3.462	2.017	1.547	1.361	1.547
	ΔM	145.03	60.99	52.45	85.64	44.97	36.38	52.13	29.90
	ΔD	9.05	−0.53	−0.15	0.77	—	—	—	—
	$\Delta M - \Delta D$	135.98	61.52	52.60	84.87	44.97	36.38	52.13	29.90
4	δ	52.08	24.47	19.46	3.126	1.991	1.847	1.414	1.255
	ΔM	136.25	55.57	39.64	81.70	45.98	32.25	37.16	26.42
	ΔD	8.36	−0.94	−0.45	0.76	—	—	—	—
	$\Delta M - \Delta D$	127.89	56.51	40.09	80.94	45.98	32.25	37.16	26.42

		C_α	C_β	C_γ	C_δ	H_α
5	δ	56.02	29.08	24.50	31.09	3.076
	ΔM	143.32	56.71	38.73	30.71	85.85
	ΔD	7.65	−1.12	−0.45	−0.28	0.76
	$\Delta M - \Delta D$	135.68	57.83	39.18	30.99	85.09

		$H_{\beta cis}$	$H_{\beta trans}$	$H_{\gamma cis}$	$H_{\gamma trans}$	$H_{\delta trans}$	$H_{\delta cis}$
5	δ	1.928	1.928	1.479	1.479	1.189	1.479
	ΔM	42.40	34.98	40.47	23.26	23.85	23.26
	ΔD	0.05	0.05	−0.03	−0.03	−0.11	−0.03
	$\Delta M - \Delta D$	42.35	34.93	40.50	23.39	23.96	23.29

Table 2 Carbon and proton chemical shifts (δ), LIS values (ΔM), diamagnetic shifts (ΔD), and pseudo-contact shifts ($\Delta M - \Delta D$) for propene (**6**) and styrene (**7**) oxides

Compound		C_1	C_2	C(Me)	H_{gem}	H_{cis}	H_{trans}	Me
6	δ	47.97	48.17	17.95	2.995	2.438	2.758	1.323
	ΔM	130.78	129.2	52.43	74.69	76.03	76.89	39.01
	ΔD	5.36	7.43	−1.30	0.62	0.39	0.61	—
	$\Delta M - \Delta D$	125.42	121.77	53.73	74.07	75.64	76.28	39.01

		C_1	C_2	C_i	C_o	C_m	C_p
7	δ	51.16	52.34	137.65	125.51	128.50	128.18
	ΔM	132.29	126.27	50.57	31.59	14.90	12.32
	ΔD	5.06	6.13	−2.86	0.54	0.22	1.07
	$\Delta M - \Delta D$	127.23	120.15	53.43	33.81	14.68	11.25

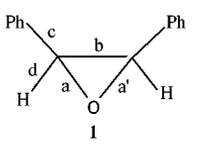
		H_{gem}	H_{trans}	H_{cis}	H_o	H_m	H_p
7	δ	3.844	3.126	2.783	7.287	7.311	7.311
	ΔM	75.97	81.93	76.74	33.81	9.65	7.18
	ΔD	0.62	0.69	0.36	—	—	—
	$\Delta M - \Delta D$	75.35	81.24	76.38	33.81	9.65	7.18

give good results for the unsymmetric compounds. It should be noted here that the HARDER programme reduces to the LIRAS3 solutions for the symmetric compounds but it is much less convenient and far more time consuming to use.

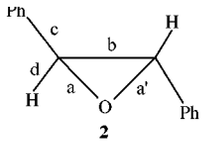
Conformational analysis

The LIS data in Tables 1 and 2 may now be used to investigate the conformational equilibria in these compounds. It is important to restate the caveat mentioned earlier, that due to the small number of LIS only one or two unknowns can be investigated in any given system. Here we will attempt to determine the conformations and conformational equilibria in these compounds and also one key geometric parameter, which is usually a torsional angle. As mentioned earlier the analysis of the observed LIS for the symmetric compounds **1** to **5** was carried out using the LIRAS3 programme with the two-site and four-site options and we will first consider these analyses. Following ref. 1 we may regard any solution (observed minus calculated shifts) with an agreement factor (AF) < 1.0% (*i.e.* 0.01) and

Table 3 Optimised geometries for *cis*- (**1**) and *trans*- (**2**) stilbene oxides[a,b,c]



1



2

Compound		a	b	c	d	ab	bc	bd	dba′	cba′
1	G92	1.402	1.468	1.495	1.079	58.4	124.4	116.2	107.4	−104.7
	PCM	1.436	1.517	1.456	1.095	58.1	118.5	116.7	106.5	−110.5
2	G92	1.402	1.467	1.494	1.070	58.4	124.1	116.6	102.8	−104.5
	PCM	1.435	1.513	1.459	1.094	58.1	118.2	120.8	101.7	−107.4

[a] Bond lengths in Å and bond and dihedral angles in degrees. [b] Other bond lengths and bond angles: PhCC 1.387 (G92), 1.40 (PCM); CH 1.075 (G92), 1.103 (PCM). Standard bond angles. [c] Torsional angle θ: (**1**) 10.5 (G92), 15.0 (PCM); (**2**) −8.0 (G92), −61.3 (PCM).

with all calculated LIS within 1.0 ppm of the observed shifts as an acceptable solution.

***Cis* and *trans*-stilbene oxide (1) and (2).** In the absence of an experimental structure for these molecules we used optimised geometries. Both PCMODEL and GAUSSIAN gave optimised geometries (Table 3) in reasonable agreement. The only conformational variable is the torsional angle of the two phenyl rings with respect to the epoxide ring, which may be defined by the C_oC_iCO dihedral angle (θ). The optimised geometry for **1** from PCMODEL was unsymmetric with values of θ of 9 and 23° for the two phenyl rings. In contrast the G92 optimisation was symmetric with θ equal to 10° even when the starting geometry was unsymmetric. A similar result was obtained for the *trans* compound. As the phenyl rings are equivalent on the NMR time scale and for the *trans* compound in particular there is no obvious reason why the molecule is not symmetric, the PCMODEL iteration for both compounds was symmetrised, *i.e.* averaged over the two phenyl rings. The symmetrised geometry for *cis*-stilbene oxide gave a value of θ of 15°, in excellent agreement with the G92 geometry, but for *trans*-stilbene oxide there is still a large disagreement, the G92 value of −8.0° being very different from the PCM value of −61.3°. In this nomenclature a positive value of θ means that the phenyl rings are *exo* to the oxirane ring, which is to be expected in *cis*-stilbene oxide due to steric interactions.

It was therefore of interest to see whether the LIS method can determine the value of these torsional angles. These geometries were input with the observed pseudo-contact shifts into LIRAS3 and the torsional angles searched for the best solution. The four-site model gave better agreement factors for these epoxides and more reasonable complexation geometries and only these results will be given here. For *cis*-stilbene oxide **1** and for the *cis* compounds **3**–**5**, the C_2 molecular symmetry is accurately reflected by the LIRAS3 option, thus the torsional angle was the only variable to deduce. A well defined minimum in the plot of the AF *vs.* θ was found with excellent AFs of 0.60 (G92) and 0.41 (PCM) with values of θ of 20 and 10° respectively. In these iterations the C_2 symmetry of the molecule was preserved so that the actual values of θ are +20 and −20° for the two phenyl rings *etc*. Thus the values of θ obtained from the LIS are in excellent agreement with those of the optimised geometries.

For *trans*-stilbene oxide the molecular symmetry is a two-fold axis of symmetry and not a mirror plane, as in the *cis* compound. Thus the LIRAS3 option with reflection about the epoxide ring plane needed to be modified to accurately reflect the molecular symmetry. This was simply achieved by rotating the epoxide ring plane an angle (ω) about the x axis from the vertical xz plane (Fig. 1). In **1**, ω is of course 0°. The LIRAS3 search proceeded in exactly analogous fashion as for **1** but now both the phenyl ring dihedral angle θ and the "effective symmetry angle" ω were varied, searching for the best AF. In this case the correct molecular symmetry was maintained by the phenyl ring torsional angle θ having the same value for the two phenyl rings. Again both geometries gave excellent AFs of 0.50 (PCM) and 0.54 (G92) with values of θ and ω of −39 and 18° (PCM) and −42 and 4° (G92).

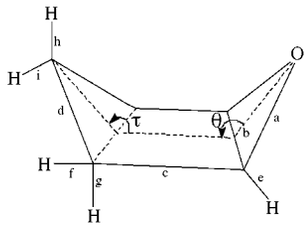
These results are of some interest. The two values of θ found for the two geometries are in excellent agreement, which is strong support for both the appropriateness of the model used and the determination of this angle by the LIS method. The value of θ obtained by the LIS method of −40 is inbetween the two optimised values of θ of −8 and −61° but in better agreement with the G92 value (see later). The values of ω found are also in reasonable agreement for the two geometries as the AF is not very sensitive to the value of ω. Thus in the LIS search with the G92 geometry the AF only changed from 0.50 to 0.60 for a variation in ω from −12 to +20°. The other parameters determining the lanthanide geometry are given in Table 8 and will be discussed later.

Cyclopentene oxide (3). The conformational analysis of the five membered ring of cyclopentene oxide is simplified by the coplanarity of the epoxy ring substituents thus only C_γ projects out of the plane of the other four carbon atoms. The interactions in this molecule are such that, although two possible non-planar conformations—the boat and chair forms—are often shown, it is very probable that there is no appreciable energy barrier between these forms. In the formally similar compound bicyclo[3.1.0]hexan-5-one *ab initio* calculations showed that the energy profile was a smooth function of the flap angle with only one minimum at the boat conformer.[18] Thus it is preferable to consider the conformational analysis simply in terms of the torsional angle (τ) between the $C_\beta C_\gamma$ flap and the plane of the $C_\alpha C_\beta$ atoms (Table 4). The MW[4] and ED[5,6] investigations obtained a value for this angle of 150 to 155°, which corresponds to the boat conformer. The geometries considered are given in Table 4. The results of the most recent ED investigation are given in the Table. The geometry obtained is very similar to the earlier MW study.

These geometries were input into the LIRAS3 programme with the observed pseudocontact shifts (Table 1). Using the ED geometry and varying the torsional angle gave a minimum at 150° but a poor AF of 1.30 (Table 8). However the same procedure using the optimised geometries from G92 and PCMODEL gave much better AF of 0.441 and 0.871 for values of τ of 151 and 145° respectively. These values are in complete agreement with the MW and ED results They are also in good agreement with the corresponding values obtained directly from the geometry optimisations of 152.2 (G92) and 150.5° (PCM). Thus both the LIS analysis and the modelling calculations fully confirm the earlier results. The lanthanide geometries are given in Table 8 and will be considered later.

Cyclohexene oxide (4). The conformational analysis of cyclohexene oxide proceeded along similar lines to that of cyclopen-

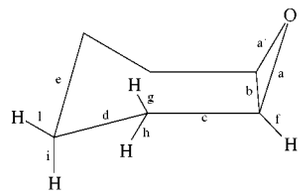
Table 4 Experimental and optimised geometries for cyclopentene oxide[a]



	ED[b]	PCM	G92
a	1.439	1.437	1.410
b	1.467	1.505	1.451
c	1.530	1.522	1.512
d	1.530	1.542	1.544
e	1.106	1.100	1.076
ring C-H	1.106	1.110	1.084
ab	59.35	58.4	59.03
bc	108.3	107.8	109.5
cd	105.6	105.6	103.74
be	125	138.9	123.2
ce	115.9	101.0	121.03
cf	*c*	111.3	112.65
cg	*c*	111.3	108.89
df	*c*	111.9	112.41
dg	*c*	111.9	111.41
dh	*c*	112.0	109.56
di	*c*	112.0	112.25
θ	104.3	109.0	105.96
τ	153.6	150.5	152.20

[a] Bond distance in Å, bond and interplanar angles θ and τ in °. [b] From ref. 6. [c] Assumed tetrahedral.

Table 5 Experimental and optimised geometries for cyclohexene oxide[a]



	ED	PCM	G92
a	1.445	1.440	1.405
b	1.474	1.511	1.458
c	1.530	1.522	1.510
d	1.530	1.535	1.531
e	1.530	1.532	1.530
f	1.118	1.095	1.079
g	1.118	1.116	1.086
ab	59.35	58.0	61.43
ac	115.8	113.9	116.08
cd	112.4	115.8	112.06
de	110.4	110.8	110.75
bf	116.0	120.8	118.39
ch	*b*	108.5	109.11
cg	*b*	107.9	108.16
di	*b*	109.8	109.56
dl	*b*	110.8	109.39
bcd	−17.7	−15.9	−20.5
cde	48.8	45.0	50.6
el	*b*	110.0	109.9
ei	*b*	110.2	110.1
a′bc	103.6	101.1	103.7

[a] Bond distances in Å, bond and dihedral angles in degrees. [b] Assumed tetrahedral.

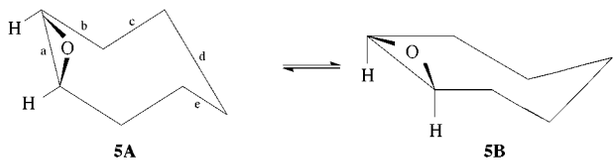
tene oxide. Both ED[6,9,10] and MW[11] investigations concluded that the only detectable conformer was the half-chair form. This conformer on the NMR time scale exists as two rapidly interconverting mirror-image conformers. The most recent ED geometry together with those obtained by molecular modelling are shown in Table 5 and there are significant differences between them. The central question is, therefore, whether any or all of these geometries agree with the LIS data and if not, whether a refined geometry would give a better fit. The above geometries were therefore input, together with the observed data, into the LIRAS programme using both the two-site and four-site models. It was found that the two-site model gave slightly better AFs and those with the resulting lanthanide complexation geometries are given in Table 8. It is immediately seen that the AF for the ED geometry is above the acceptable limit (1.0%), but those for the optimised geometries are both acceptable, if not particularly good. It was therefore decided to slightly modify these geometries to attempt to obtain better solutions. The parameter most likely to be uncertain is the angle of pucker of the half chair. This can be described either in terms of the deviation of the C*y* atoms (C4 and C5) from the plane of the other ring atoms or by the torsional angle C2C3C4C5 (cde in Table 5). It is a feasible geometric problem to displace C4 and C5 in equal and opposite directions without altering the positions of any of the other atoms or any of the CC bond lengths (see ref. 27 for full details of these calculations). When these atoms were displaced a marked improvement in the AF for all the geometries was found. The optimum values of the torsional angle cde and the AFs for the optimised geometries are given in Table 8. The ED and optimised geometries gave similar values of this angle (48.8, 45.0 and 50.6, Table 5). The optimised values of this angle from the LIS data were also consistent but somewhat less in all the cases considered (39.4, 43.8 and 43.8, Table 8). This small decrease in the ring puckering could be due to solvation effects (which are not included in the modelling calculations). Alternatively, atomic displacements in this rapidly interconverting system could lead to a "time-averaged" value of the ring puckering, which is slightly less than calculated. However we may conclude that the LIS analysis is fully consistent with a half-chair conformation for cyclohexane oxide with a torsional angle of 44 (±2)°.

Cycloheptene oxide (5). The conformational analysis of cycloheptene oxide has been investigated by both low temperature NMR[12] and electron diffraction.[6] The low temperature NMR studies observed two populated conformers at −146 °C in the ratio of 71 : 29, which were attributed to the two chair forms **5A** and **5B** though the authors were not certain as to which form was the more populated.

The later ED study confirmed these results and assigned the more populated conformer as the *endo* conformer **5A**. Thus we shall consider the conformational analysis solely in terms of the two forms **5A** and **5B**. Selected geometrical parameters for these two forms are given in Table 6. The experimental and optimised geometries for the epoxide ring in **5** are essentially identical to those for **4** and are not given in Table 6. Also the ED investigation assumed the same geometry for conformers **5A** and **5B** apart from the dihedral angle Oab which has the opposite sign in conformer **5B**.

As the ED geometry is only a partial one the PCM geometry was input into the LIRAS3 programme together with the observed LIS (Table 1). In this input it is necessary to include both the conformers **5A** and **5B** and this was performed by constructing a joint Z-matrix of both conformers. The populations of the two forms may be varied in the input and thus it is possible to manually search for the population ratio with the best AF. The assignments of the protons in each methylene group were made on the same basis as previously, *i.e.* that the proton *cis* to the epoxide would have the larger LIS, and these assignments for the β and γ protons were confirmed by the good agreement factor (*e.g.* on interconverting γ*cis* and γ*trans* the AF was >10%). The δ protons have the same LIS and thus the AF is independant of their assignment. The provisional

Table 6 Selected geometrical parameters for cycloheptene oxide (**5**)[a,b]

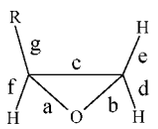


5A **5B**

Conformer		ab	bc	cd	de	abc	bcd	cde	Oab
5A	ED[c]	121.6	117.5	113.9	114.5	68.9	−83.7	61.7	106.7
	PCM	122.4	120.7	114.3	113.8	51.1	−73.8	71.1	100.9
5B	PCM	118.4	112.6	113.6	116.1	68.9	−83.6	61.7	−101.3

[a] Bond lengths in Å and bond and dihedral angles in degrees. [b] Other parameters: CO 1.445 (ED), 1.435 (PCM); CC (ED) a 1.474, b, c, d 1.530; (PCM) a 1.504, b 1.518, c, d 1.534. [c] ED geometry is averaged over **5A** and **5B**.

Table 7 Experimental and optimised geometries for propene oxide (**6**) and styrene oxide (**7**)[a,b,c]



6 R = Me, **7** R = Ph

Compound		a,b	c	g	ac/bc	ag	cg	af	bd	be
6	MW	1.438	1.470	1.505	59.2	116.1	121.7	114.8	114.8	114.8
	PCM	1.435	1.508	1.518	58.3	114.5	117.7	117.1	118.0	118.0
	G92	1.443	1.466	1.502	59.5	116.6	122.0	113.4	115.2	115.2
7	X ray	1.432	1.448	1.487	59.6	116.5	121.7	114.0	115.0	114.0
	PCM	1.434	1.509	1.457	58.2	118.4	117.6	115.4	117.3	117.8
	G92	1.391	1.459	1.495	58.8	117.5	122.2	113.8	115.2	115.2

[a] Bond lengths in Å and bond and dihedral angles in degrees. [b] Other bond lengths and bond angles: CH 1.090 (G92, MW, PCM), 1.077 (X ray); Ph group, CC 1.387 (G92), 1.40 (PCM); CH 1.077 (G92), 1.103 (PCM). Standard bond angles. [c] Torsional angle θ (C_oC_iCO) for (**7**) −24.7 (X ray), −17.7 (PCM), −9.4 (G92).

assignment for these protons given in Table 2 was made on the basis that the *trans* (axial) proton in the dominant conformer **5A** would be to high field.[26] The results of the LIS search gave the optimum population ratio of 70 : 30 in favour of conformer **A** in excellent agreement with the previous investigations. The AF was 1.1%, which is slightly larger than the limit previously considered acceptable (1%). On inspection of the data it is seen that $H_{\gamma trans}$ and $H_{\delta cis}$ are overlapping multiplets with the same chemical shift and LIS (Table 1). The observed LIS for these protons are in error by +0.8 and −0.9 ppm respectively and clearly these errors are due to this accidental degeneracy. Removing these protons gave the same solution with an AF of 0.94%, now well within the acceptable limit.

The complete agreement between the LIS results and the ED and low-temperature NMR results for the populations of the two conformers serves to reinforce one basic assumption in the LIS method, that the complexation of the ligand by the lanthanum atom has little effect on the conformation of the ligand. This has been found repeatedly in our previous investigations.[15–18] A probable reason is that the mono-dentate Ln–substrate complexes formed are of very low energy with, in consequence, a long Ln–X bond (the Ln–O bond is *ca.* 2.5–3 Å, see Table 8). Thus even the bulky $Ln(fod)_3$ group has negligible steric effect on the substrate. This is in contrast to the Ln complexes formed with bidentate ligands, in which the ligand geometry will be affected by the complexation.

Propene oxide (6). There is no conformational isomerism in propene oxide but it was decided to investigate this molecule by the LIS technique as it was the simplest unsymmetric epoxide. The failure of the LIRAS3 complexation model to reproduce the LIS data for styrene oxide (see later) when the same model was successful for the analogous *cis*- and *trans*-stilbene oxides, suggested that the problem was related to the dichotomy between the symmetric LIRAS3 complexation model and the unsymmetric molecules. This was confirmed when propene oxide was examined by the LIS technique.

There is a well determined microwave geometry for propene oxide and in addition the small number of atoms in this molecule allowed us to optimise the molecular geometry at the 6-31G*/MP2 level. These geometries and the PCMODEL geometry are given in Table 7.

When any of these geometries were input together with the observed LIS (Table 2) into the LIRAS3 programme poor agreement factors were obtained even though the comparatively small number of atoms meant that the LIS determination was not very over determined. There are seven LIS data points for the five unknown parameters of the lanthanum coordinates and populations (Fig. 1) and the normalisation factor. The three geometries of Table 7 all gave similar agreement factors (1.2–1.4%), much larger than those for the comparable molecules given earlier. Rotation of the lanthanide coordinates about the *xz* plane (*cf. trans*-stilbene oxide) did not significantly affect the AF nor did the use of either the two-site or four-site models.

It was therefore decided to attempt the analysis of these shifts using the unsymmetric complexation model given by the HARDER programme. In this programme the coordinates of both the lanthanide complexation sites, and also the relative populations of the two sites, may be varied independently. This complexation model gave excellent AFs for all the molecular geometries of 0.1–0.2% (Table 8). Although this iteration is even less well determined than the LIRAS3 analysis the excellent agreement does strongly support the hypothesis that in the unsymmetric epoxides an unsymmetric complexation with the lanthanide occurs. The lanthanide complexation geometries are

Table 8 LIRAS3/HARDER analysis of *cis*-(**1**) and *trans*-(**2**) stilbene oxide, cyclopentene oxide (**3**), cyclohexene oxide (**4**), cycloheptene oxide (**5**), propene oxide (**6**) and styrene oxide (**7**)

Compound	Geometry	R_{cryst}(%)	*r*/Å	*φ*/°	*ψ*/°	Pop(%)[a]
1[b]	G92	0.604	2.56	90	149	0
	PCM	0.408	2.84	65	146	3
2[c]	G92	0.540	2.64	87	161	50
	PCM	0.502	2.97	133	177	50
3[d]	ED	1.300	2.98	60	134	96
	G92	0.441	2.70	73	142	100
	PCM	0.871	3.40	60	126	97
4[e]	ED/	1.708	3.05	63	135	100
	opt	0.398	3.07	63	132	99
	G92/	0.797	2.67	83	140	100
	opt	0.254	2.67	92	141	93
	PCM/	0.712	2.83	76	133	100
	opt	0.195	2.84	75	132	99
5[f]	PCM	1.11	2.94	74	122	0
6[g]	MW	0.105	2.78	84	118	62/
			3.28	118	137	38
	G92	0.119	2.62	84	130	68/
			3.48	128	152	32
	PCM	0.120	2.84	86	116	64/
			3.26	118	152	36
7[g,h]	X-ray	0.494	3.22	30	180	34/
			2.74	108	136	66
	PCM	0.487	3.48	8	168	18/
			2.86	106	140	82
	G92	0.319	1.62	120	170	5/
			2.86	80	162	95

[a] The % population is in the positive *y* axis (Fig. 1). [b] θ (C_oC_iCO) 20° (G92), 10° (PCM), see text. [c] θ −39° (G92), −42° (PCM), see text. [d] τ 150° (ED), 151° (G92), 145° (PCM), see text. [e] cde 48.8° (ED), 39.4° (opt); 50.6° (G92), 43.8° (opt); 45.0° (PCM), 43.8° (opt), see text. [f] 70% *endo* chair/30% *exo* chair. [g] The complexation geometry along the negative *y* axis is given for each solution. [h] θ −20° (X ray), −30° (G92), 0° (PCM), see text.

given in Table 8 and it can immediately be seen that the two geometries on either side of the *xz* plane are very different, again supporting the use of the HARDER programme. These will be discussed later.

Styrene oxide (7). The conformational analysis of styrene oxide proceeded in a similar manner to that of propene oxide, though in this case there is one geometric parameter to determine *i.e.* the torsional angle of the phenyl group with respect to the epoxide ring. This is conveniently expressed in terms of the dihedral angle θ between the C_oC_iCO atoms. This angle varied considerably in the different geometries available (Table 7) from −24.0 in the X-ray geometry of *para*-nitrostyrene oxide to −17.7 (PCMODEL) to −9.4 (G92).

When these geometries were input together with the LIS (Table 2) into the LIRAS3 programme as in the propene oxide case no reasonable agreement was obtained, with AFs always >2%. Varying the torsional angle of the phenyl ring gave slightly better agreement for the X-ray and G92 geometries but for the PCMODEL geometry the AF was always >2%. For the X-ray geometry the best AF was 1.67% for $\theta = -30$ and for the G92 geometry the corresponding values were 1.57% and −30. Rotating the axis of rotation of the lanthanide about the *xz* plane (*cf. trans*-stilbene oxide) gave no better agreement.

However when the same input geometries and LIS were used with the HARDER programme excellent AFs were obtained. Again the phenyl/epoxide torsional angle θ was varied for the best solution and the values of the AF and θ obtained for the X-ray and G92 geometries were 0.49 and 0.32% and −20 and −30°. The PCMODEL geometry gave a good AF (0.49%) but a value of θ of 0°. This was not a very well defined value as any value of θ from +30 to −30° for this geometry gave an AF < 1.0%. This is probably due to small errors in the PCMODEL geometry, which differs considerably from the other geometries in some parameters (*cf.* the HCC angles in Table 7), combined with a not very over-determined analysis. The values of θ obtained from the more accurate geometries are very similar to those found using LIRAS3 but the AFs are significantly better even when it is considered that HARDER uses two more variables than LIRAS3. The value of θ obtained (−25 ± 5°) is in very good agreement with that obtained from the X-ray data and also with the values from the optimised geometries (see later). The complexation geometries are also of some interest and are given in Table 8. These will be considered further in the discussion.

Discussion

The bent-bond model of cyclopropane[31] when applied to the oxirane ring predicts that the maximum conjugation between the oxirane ring and an adjacent π system occurs when the plane of the oxirane ring is perpendicular to the plane of the π system. When this occurs the C_oC_iCO dihedral angle (θ) in the convention used here equals −30°. Thus it is of some interest to consider the theoretical and experimental results obtained here for styrene oxide (**7**) and the stilbene oxides. For **7** the LIS analysis for the two most accurate geometries gave θ equals −25 (± 5)° in complete agreement with the value found in the crystal (−24°) and in fair agreement with the modelling studies, −17.7° (PCM) and −9.4° (G92). Thus the solution conformation of styrene oxide appears to be essentially the same as in the solid state and in agreement with that predicted by theory.

trans-Stilbene oxide (**2**) would be expected to have a similar conformation to styrene oxide and the LIS analysis confirms this with θ equal to −40 (±5)° for the two geometries used. The

modelling calculations gave rather different values of θ of -8.0 (G92) and $-61°$ (PCM). The G92 calculations give similar values of θ for these compounds but the values from the PCM calculations are very different. This could be due to approximations in the optimisation or to too large steric interactions between the phenyl groups in the PCM force-field.

In *cis*-stilbene oxide it would be expected that there are appreciable steric interactions between the phenyl groups and this is shown in the LIS analysis, which obtains a value of θ of $+15°$, *i.e.* the phenyl ring is *exo* to the oxirane ring. This is confirmed by the modelling calculations which give values of $+10°$ (G92) and $+16°$ (averaged, PCM).

In conclusion both the modelling calculations and the LIS analysis give a consistent picture of the orientation of the phenyl rings in the compounds studied.

The parameters for the different lanthanide complexation geometries and the agreement factors R_{cryst} for the best solutions for the compounds studied are given in Table 8 and it is of interest to consider these results. The lanthanide geometries obtained from the LIRAS3 routine are as expected from previous studies.[1] In **3** and **4** the geometric axes are such that the ring carbon atoms lie in the negative y axis (Fig. 1) and the lanthanum complexes predominantly in the positive y axis as expected. In **5** the Z-matrix was constructed with the ring carbon atoms in the positive y axis and as a result the lanthanum complexes now entirely in the negative y axis.

The lanthanide complexation geometries found for the unsymmetric compounds from the HARDER calculations are also of interest, though it must be emphasised that, as these are not very well determined systems, the actual values of the parameters will also be less definitive than those from the LIRAS3 analysis. In propene oxide the parameters are very similar for all three geometries considered, which is encouraging. In this molecule the coordinate axes for the calculation are such that the methyl group is in the $+x,+y,+z$ quadrant (Fig. 1) , thus it would be expected that the lanthanide would coordinate preferentially along the negative y direction and this is observed. The lanthanide complex geometry for the negative y axis is normal with the lanthanide essentially along the oxygen lone pair. In the positive y axis there is an increase in the Ln–O distance and φ is *ca.* 120°, which again places the lanthanide away from the methyl group. Thus these appear to be chemically reasonable complexation geometries.

In styrene oxide the phenyl ring is now in the $+x,-y,-z$ quadrant (Fig. 1) and the preferred orientation of the lanthanide will be along the $+y$ axis. This is clearly seen in Table 8 and the population of the lanthanide in this direction is >90% for the G92 geometry. The coordination geometry in the positive y axis is again normal, *i.e.* along the oxygen lone pair, but that in the negative y axis is unusual with the metal atom along the negative x axis (Fig. 1), *i.e.* bisecting the COC angle. It should be noted, however, that the large weighting of the lanthanide in the positive y axis means that the definition of the geometry in the negative y axis will not be very precise. This is particularly noticeable for the G92 solution where the coordinates in the positive y axis are very indeterminate (*e.g.* if the radius for the positive y complexation is fixed at a more reasonable figure of 2.50 Å the AF is still only 0.456 for the same value of θ).

Acknowledgements

We acknowledge ERASMUS/SOCRATES travel grants to R. J. A., I. C., F. S. and T. A. D. S. and also a Chemical Society travel grant (F. S.), which were indispensable for the successful conclusion of this work. It is a pleasure to acknowledge the continuous support and assistance of Professor Carlo Dell'Erba and the technical assistance of Mr Mark A. Warne.

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Paper 8/06284F