Conformational analysis. Part 39.† A theoretical and lanthanide induced shift (LIS) investigation of the conformations of cyclopentanol and *cis*- and *trans*-cyclopentane-1,2-diol

Raymond J. Abraham,*[a] Rodothea Koniotou[a] and Fernando Sancassan*[b]

[a] *Department of Chemistry, The University of Liverpool, PO Box 147, Liverpool, UK L69 3BX*
[b] *Departimento di Chimica e Chimica Industriale, Via Dodecaneso 31, I-16146 Genova, Italy*

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The conformations of cyclopentanol and *cis*- and *trans*-cyclopentane-1,2-diol have been studied by *ab initio* and molecular mechanics (MM) calculations and by the LIS technique, using $Yb(fod)_3$ to obtain the induced shifts of all ^1H and ^{13}C nuclei in the molecule, together with complexation shifts obtained by the use of $La(fod)_3$. The MM calculations gave two optimised geometries for cyclopentanol. These were envelope conformations with the hydroxyl group equatorial (**1A**) and axial (**1B**) at the flap of the envelope. In contrast Gaussian 98 at the B3LYP level with the 6-31G** basis set gave an optimised geometry (**1C**) which was an envelope conformation with the hydroxyl group in an axial position at the fold of the envelope. ΔE(**1A** − **1B**) = 0.47 kcal mol^{-1} (MM) and 0.93 kcal mol^{-1} (*ab initio*) and ΔE (**1B** − **1C**) = 0.15 kcal mol^{-1} (*ab initio*). The MM and *ab initio* calculations for *cis*-1,2-cyclopentanediol gave different envelope conformations (**2A**) and (**2B**), both with one equatorial and one axial hydroxyl group. For *trans*-1,2-cyclopentanediol both calculations gave the same geometries, an envelope conformation with two axial hydroxyls (**3A**) and a half chair conformer with diequatorial hydroxyls (**3B**). ΔE (**3A** − **3B**) = 2.9 kcal mol^{-1} (MM) and 0.70 kcal mol^{-1} (*ab initio*). The LIRAS4 model involving an sp^3 hybridised oxygen atom with two symmetric lone pairs was used for these compounds. The calculated LIS for cyclopentanol gave poor agreement with the observed data for **1A**, moderate agreement for **1B** but good agreement for **1C**. A LIS analysis combining **1B** and **1C** suggests that the population of **1C** was >80% in $CHCl_3$ solution. The *ab initio* calculations and the LIS analysis agree that the unsymmetric conformer **1C** is the major form in solution. The similarity between this conformer of cyclopentanol and that of the furanose sugars suggests that the anomeric effect may be more fundamental than hitherto realised. In *cis*-cyclopentane-1,2-diol the observed data were in good agreement with the calculated LIS for both **2A** and **2B**. In *trans*-cyclopentane-1,2-diol the observed data were in good agreement with the calculated LIS for **3B** but in poor agreement for **3A**. The LIS allowed the assignment of the proton chemical shifts of the individual methylene protons in these molecules which had not been given previously.

Introduction

The conformational analysis of cyclohexanes is an important part of organic chemistry, but that of cyclopentanes has been largely neglected. In Eliel and Wilen's comprehensive text on stereochemistry six-membered ring conformations take up 60 pages and five membered rings four pages.[2] Yet compounds with five-membered rings are some of the most common natural products and include many steroids, prostaglandins, sugars and nucleotides. The reasons for this comparative neglect are well known. The rigidity of the cyclohexane ring allows a variety of chemical and spectroscopic experiments whereas the flexibility of the cyclopentane ring with rapid interconversion amongst many conformers often precludes detailed analysis and leads directly to the concept of pseudorotation.

There are two symmetrical puckered conformations of cyclopentane, the envelope C_s and the half-chair C_2 (Fig. 1). The energy barrier between the conformations is very small and Eliel and Wilen[2] describe the cyclopentane ring as 'in a conformational flux between the two conformations above and also among other in-between structures'. The puckered atom gives the impression that it successively rotates from one position to the other around the ring and this is termed pseudorotation.[3]

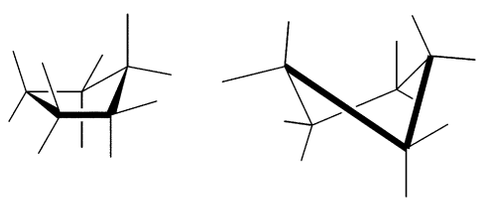

Fig. 1 The envelope (C_s) and the half-chair (C_2) conformation of cyclopentane.

A number of studies of substituted cyclopentanes have been reported.[4–7] IR,[4] microwave[5] and electron diffraction[6] studies on chlorocyclopentane agreed that the chlorine prefers the axial position at the flap of an envelope conformation and this result was in accord with molecular mechanics calculations. In methyl cyclopentane molecular mechanics calculations gave the envelope conformation with an equatorial methyl group at the flap of the envelope, but subsequent calculations gave different results.[7] An investigation of the ^{13}C chemical shifts in methylcyclopentanes suggested that the most stable conformation has an axial methyl group.[8] Similar controversy exists in the dimethyl derivatives. Eliel[2] notes prophetically that "oversimplifications may have been made in the literature by assuming that the ring is either an envelope or half chair".

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IR and NMR studies on cyclopentanol have been reported. Ekejiuba and Hallam[9] observed "an ill-resolved doublet" for the free hydroxyl stretching band at 3612cm^{-1} in the IR spectrum of cyclopentanol in CCl_4 and a similar doublet for the CD stretch in α-deuterocyclopentanol. They interpreted this as evidence of an equilibrium between axial and equatorial conformers. LIS studies of cyclopentanol using Eu reagents to resolve the cyclopentanol protons have been reported.[10,11] Neither of these studies assigned the proton chemical shifts of cyclopentanol itself. Roberts *et al.*[8] used a shift reagent to assign the ^{13}C-chemical shifts of *cis*- and *trans*-3-methyl- and 1,3-dimethylcyclopentanols and hence determined the configuration of these compounds.

Previous LIS investigations in our laboratories have demonstrated the importance and utility of the LIS method in determining the structures and conformations of a variety of molecules in solution[12–17] 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 ^{1}H and ^{13}C nuclei of the substrate, (ii) La(fod)$_3$ or preferably Lu(fod)$_3$ is used[12] to evaluate diamagnetic complexation contributions (ΔD_i), (iii) pseudocontact contributions ($\Delta M - \Delta D)_i$ are simulated according to the McConnell–Robertson equation[18] and a chemically reasonable complexation model is used.[17] The McConnell–Robertson equation used assumes axial symmetry along the O ··· Ln bond. The question of axial vs non-axial symmetry was examined in detail by several investigations in the evolution of the LIS technique,[17] one of the most authoritative being that of Hawkes *et al.*[19] Since that time there has been general acceptance that the assumption of axial symmetry along the O ··· Ln bond is justified. This technique gave excellent results with agreement factors (AF) < 0.5 % for unhindered aromatic ketones when reliable starting geometries were available.[12] It was also shown[13] 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.

We report here a theoretical and LIS investigation of cyclopentanol (**1**) and *cis* (**2**) and *trans* (**3**) cyclopentane-1,2-diol. We shall show that the conformation of cyclopentanol in solution is not symmetrical but is a non-symmetric conformation. Similar results are obtained for the two diols.

The lanthanide complexation model[19]

It is first necessary to determine the most appropriate complexation model for the compounds investigated. Due to the necessity to obtain an over-determined solution the complexation model is a compromise between the minimum number of parameters required to define the lanthanide-substrate complex and chemically reasonable binding models. The LIRAS (lanthanide induced relaxations and shifts) suite of complexation models used here has been described and applied to a number of different substrates. There are three different variations of this programme, LIRAS3, LIRAS4 and HARDER. For our analysis we used only the LIRAS3 and LIRAS4 coordination models. The complexation parameters for LIRAS3 and LIRAS4 are shown in Fig. 2.

The LIRAS3 coordination model was designed originally for the very common case of carbonyl complexation. In the two-site model, the lanthanide is assumed to complex along the C=O lone pairs and the complexation coordinates are given by r, ϕ, ψ (Fig. 2a). In order to take account of the two C=O lone pairs without doubling the number of parameters the lanthanide position is reflected in the xz plane (Fig. 2a) but the populations of the two sites may be varied from 0 to 100%. Thus four parameters are required to fix the lanthanide coordinates and

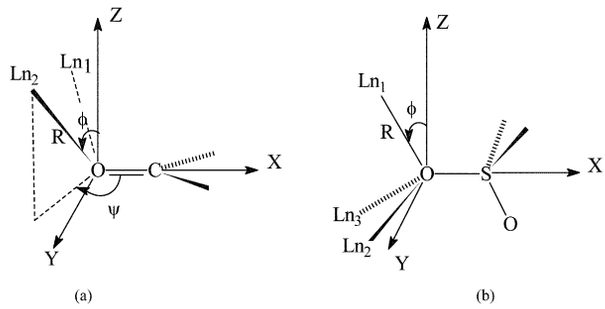


Fig. 2 The LIRAS3 (a) and LIRAS4 (b) lanthanide coordination models.

populations. Note that the two-site model becomes a one-site model when the lanthanide populations are 0 or 100%. In the more diffuse four-site model the lanthanide position is reflected about both the xz and xy planes and this takes some account of the spread of oxygen atom electron density around the lone pairs. The population of the two sites reflected about the xz plane may be varied as in the two-site model but the population of the sites reflected about the xy plane is kept constant at 50 : 50. These options thus provide a range of possible coordination geometries for the lanthanide–substrate complex. For a planar substrate molecule these two models are identical.

The LIRAS4 model of Fig. 2b was constructed to take account of the very different coordination geometry when a lanthanide complexes to a sulfone or sulfoxide group.[14] The S–O bond is more appropriately considered as a single bond rather than as a double bond and the complexation model was modified accordingly. In this model there are three possible coordination sites reflecting the three lone pairs on the sp^3 hybridised oxygen atom. These are separated by 120° dihedral angles but they may all be rotated a variable angle β about the S–O bond. Also each of their populations may be varied from 0 to 100%. For $\beta = 0$, site 1 is along the z-axis. This coordination model has the same number of variable parameters as LIRAS3. This model may be applied to any sp^3 hybridised coordinating group such as alcohols (ROH) and primary amines (RNH_2). It has been used in a LIS study of norbornanol.[15]

Experimental

The cyclopentanols, Yb(fod)$_3$ and La(fod)$_3$ were obtained commercially (Aldrich). The solutions were made up to 0.5 M in deuteriochloroform, which was obtained from a sealed 1 ml capsule. The chemical shifts in D_2O solvent are also recorded from TSP internal reference, as part of an ongoing investigation of the ^{1}H shifts of hydroxyl compounds in D_2O solvent. The substrates and 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. Five additions of shift reagent (*ca.* 5–20mg, *i.e.* 0.01M) were weighed directly into the NMR tube. The plots of chemical shift *vs.* ρ the ligand: substrate ratio were checked for linearity (all correlation coefficients >0.99) 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 La(fod)$_3$.

The LIS measurements were recorded on a Bruker Avance 400 MHz spectrometer operating on ^{1}H and ^{13}C at 22 °C. Typical running conditions of the spectrometer were, ^{1}H experiments 128 transients, spectral width 6000 Hz and 32000 data points to give an acquisition time of 5s. The FIDs were zero filled to128k to give a digital resolution of 0.1 Hz. The ^{13}C spectral widths were typically 23000 Hz with 128K transform using a line broadening of 2.0 Hz to give digital resolution of 0.36 Hz. The 2D experiments were conducted using the Bruker Avance COSY and HMQC pulse sequences.[20]

Table 1 Observed carbon and proton chemical shifts (δ), LIS (ΔM), diamagnetic shifts (ΔD) and pseudo-contact shifts ($\Delta M - \Delta D$) for cyclopentanol (**1**)

1	C_1	$C_{2,5}$	$C_{3,4}$	H_1	H2,5 *cis*	H2,5 *trans*	H3,4 *cis*	H3,4 *trans*
δ ($CDCl_3$)	74.39	35.80	23.45	4.319	1.560	1.764	1.764	1.560
δ (D_2O)	74.43	34.81	23.92	4.302	1.557	1.787	1.787	1.557
ΔM	144.31	67.48	43.37	85.56	64.48	38.46	38.46	25.20
ΔD	5.00	−0.93	−0.83	—	—	—	—	—
$\Delta M - \Delta D$	139.31	68.41	44.20	85.56	64.48	38.46	38.46	25.20

The molecular geometries were taken from molecular mechanics (PCModel7[21] using the MMF94 force field) and *ab initio* optimisations (Gaussian98 at the recommended B3LYP/6-31G** basis set level[22]).

Spectral assignments

The spectral assignments for all the ^{13}C spectra were straightforward and were from previous literature assignments.[23]

Cyclopentanol

The ^1H spectrum of cyclopentanol at 400MHz consists of two single intensity peaks at 4.32 and 1.28δ due to the α CH and OH respectively and two unresolved multiplets at 1.56 and 1.76δ both of intensity 4. The assignment of the protons in these multiplets is not obvious. An HMQC plot showed that both peaks gave correlations with both the C2,5 and C3,4 carbons, thus they both contain the 2,5 and 3,4 protons. An obvious assumption is that one peak contains the protons *cis* to the hydroxyl group and the other the *trans* protons, but this is not the only possibility. In order to resolve these assignments we proceeded to the LIS experiment. On the addition of shift reagent the peak at 1.56δ separates into two equal intensity peaks. An HMQC plot of the solution after the final addition of shift reagent showed that the low-field more shifted peak correlated with C2,5 and the upfield less shifted with C3,4. The peak of intensity 4 at 1.76δ moved on addition of shift reagent but was not resolved further. On the basis that the protons *cis* to the hydroxyl will have larger ΔM values than the corresponding trans protons these results together with the actual ΔM values gave the assignments of Table 1.

cis-Cyclopentane-1,2-diol

The symmetry of this compound results in five separate signals for the ring protons but the 400 MHz spectra showed only four separate resonances. The only obvious assignments were H-1,2 (the a protons) at 4.00δ, the OH protons at 2.6δ and a single intensity peak at 1.5δ which can only be due to one of the C4 protons. HMQC correlations then assigned the protons at 1.86 and 1.66δ to the H-3,5 methylene protons and one at 1.80δ to the remaining H4 proton. Again it was not possible to identify the *cis* and *trans* protons in the methylene groups and the LIS technique was used to assign them on the basis that the *cis* protons would be expected to have larger ΔM values than the *trans* protons.

trans-Cyclopentane-1,2-diol

The symmetry of this compound gives four resonances for the ring protons as the H4 protons are chemically equivalent and in this case four separate resonances were observed. An HMQC plot gave the complete assignment except for the *cis* and *trans* H3,5 protons and these were assigned again on the basis that the protons *cis* to the near hydroxy group have larger ΔM values than the corresponding *trans* proton.

The assignments for all the compounds were subsequently confirmed by the detailed LIS analysis (see later). The observed chemical shifts (δ), diamagnetic shifts (ΔD), LIS values (ΔM) and pseudo-contact shifts ($\Delta M - \Delta D$) are given in Table 1 for cyclopentanol. The diamagnetic shifts are negligible for the protons (<0.1ppm) and small with respect to the ΔM values for the carbon atoms. Thus it was not considered necessary to obtain the diamagnetic shifts for the *cis* and *trans* diols and only the ΔM values are given in Table 2. We note that the assignment of the ^1H spectrum of cyclopentanol is a question in the A-level examination. However the official answer, that one peak contains H2,5 and the other H3,4 is unfortunately incorrect.

Results

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 conformer preferences in these compounds.

Cyclopentanol (1). In the absence of an experimental structure for these molecules we used optimised geometries. The molecular mechanics PCModel programme gave two optimised geometries for cyclopentanol. These were both envelope conformations with the hydroxyl group in an equatorial (**1A**) and axial (**1B**) position in the flap of the ring (Fig. 3) .The axial

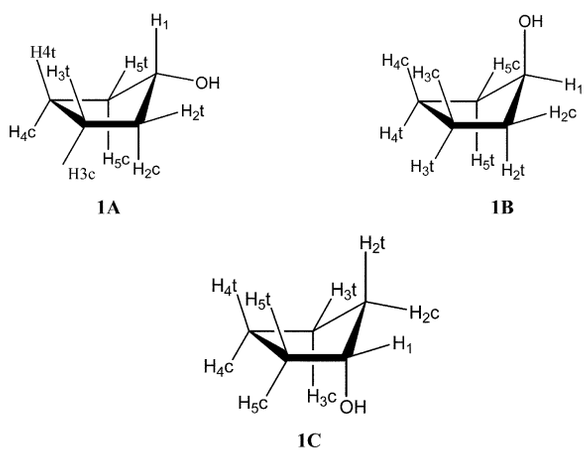


Fig. 3 Envelope conformations of cyclopentanol

conformer **(1B)** was calculated to be more stable by 0.47 kcal mol^{-1}. However, the *ab initio* Gaussian98 programme gave a different optimised geometry. This was an envelope conformation with the hydroxyl group in axial position at the fold of the envelope (**1C**) (Fig. 3).

Conformers **1A** and **1B** could be obtained by quantum mechanics by starting with the PCMODEL geometries. The Gaussian98 iteration then retained the same conformation. The calculated conformer energies were **1B**–**1C** = 0.15 kcal mol^{-1}. and **1A**–**1B** = 0.93kcal mol^{-1}. As **1C** has a statistical weight of two the ab initio results give the populations of **1C**:**1B**:**1A** as 70:25:5% at room temperature. The ring and oxygen dihedrals for the conformers are given in Table 3 where $\theta_{1,2}$ is the dihedral angle for C_5,C_1,C_2,C_3 etc. It can be seen that all the conformations are of the envelope form with *ca.* the same ring buckle but the position of the hydroxyl substituent is very different in the

Table 2 Observed carbon and proton chemical shifts (δ) and LIS (ΔM) for cis (**2**) and trans (**3**) cyclopentane-1,2-diol

		$C_{1,2}$	$C_{3,5}$	C_4	$H_{1,2}$	$H_{3,5cis}$	$H_{3,5tr}$	H_{4cis}	H_{4tr}
2	δ ($CDCl_3$)	74.28	31.39	20.11	4.009	1.659	1.860	1.805	1.505
	δ (D_2O)	74.10	29.55	18.93	4.003	1.640	1.840	1.769	1.525
	ΔM	106.06	51.50	36.70	50.98	43.83	29.19	26.22	21.86
3	δ ($CDCl_3$)	79.57	31.59	19.94	4.000	1.529	2.007	1.711	1.711
	δ (D_2O)	78.88	31.02	20.07	4.004	1.548	2.004	1.720	1.720
	ΔM	153.37	66.29	46.61	108.6	57.01	45.90	33.53	33.53

Table 3 Ring and oxygen dihedral angles (θ) for optimised geometries of cyclopentanol (**1**)

Conformer	$\theta_{1,2}$	$\theta_{2,3}$	$\theta_{3,4}$	$\theta_{4,5}$	$\theta_{5,1}$	$\theta_{3,2,1}$,O	$\theta_{4,5,1}$,O
1A	−40.2	24.9	0.3	−25.4	40.5	−158.8	159.6
1B[a]	34.9	−20.1	−2.5	24.6	−38.0	−79.7	79.7
1B[b]	39.5	−24.4	0.0	24.3	−39.5	−78.2	74.7
1C	40.1	−40.1	24.6	0.0	−24.6	−74.5	93.0

[a] PCMODEL geometry. [b] G98 geometry.

Table 4 LIRAS4 analysis of cyclopentanol (**1**) and cis (**2**) and trans (**3**) cyclopentane-1,2-diol

Conformer	R_x (%)	r/Å	ϕ/°	β/°	Population (%)		
					Site 1	Site 2	Site 3
1A	10.3	2.46	66	−2	100	0	0
1B[a]	3.71	2.52	70	18	84	16	0
1B[b]	3.49	2.56	72	34	0	24	76
1C	2.34	2.46	70	82	90	10	0
2A	2.75	2.32	32	56	92	0	8
2B[c]	2.19	2.00	46	54	88	2	10
2B[d]	7.26	2.16	48	124	100	0	0
3A[b]	1.42	2.84	2	−6	0	0	100
3B[b]	0.093	2.75	45	−22	0	0	100

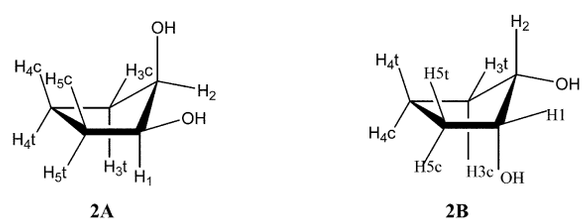
[a] PCMODEL geometry. [b] GAUSSIAN geometry. [c] OH axial. [d] OH equatorial.

three cases. Further details of all these geometries are given in ref. 24.

It was of considerable interest to see whether the LIS method can determine which conformation is the most populated in solution. For cyclopentanol (**1**) the four-site LIRAS3 model was initially used. This gave much poorer solutions (not shown) than LIRAS4 and the LIRAS4 model was then applied to all the compounds. This analysis gives a total of eight LIS with six unknowns (the lanthanide coordinates and populations and the normalisation factor) thus the calculations are over determined. The geometries were input with the observed pseudo-contact shifts into LIRAS4 and the complexation parameters searched for the best solution. In the search process the complexation parameters R, ϕ, β, and the percentage population of the lanthanide in the three sites (Pop) were optimised and the optimised values and the agreement factors (R_x) are given in Table 4. The results are of some interest. The equatorial conformation **1A** gives a totally unacceptable R_x value of 10.3% (In previous similar LIS studies[12,13] it has been stated that an acceptable solution is one in which the agreement factor should be less than *ca.* 0.02, *i.e.* 2%). The axial conformer **1B** also gave a poor agreement factor. The PCMODEL geometry of **1B** gave a slightly worse agreement factor than the Gaussian geometry with R_x 3.71 *vs.* 3.49%. However the unsymmetric geometry **1C** gave an acceptable agreement factor (2.34%). There is a possibility that atom C_1 being only two bonds from the lanthanide, could have some contact shift contribution. Thus the analyses were repeated but omitting C_1. The agreement factors for **1B** (PCMOD), **1B** (G98) and **1C** were 2.15, 2.47 and 0.37 confirming the above analysis. These results suggest that the major conformer of cyclopentanol in solution is conformer **1C** and that the equatorial conformer **1A** is not present in any significant amount. To investigate further the percentage of conformer **1C** in solution the Z matrices of the two favoured geometries of cyclopentanol (**1B** and **1C**) were combined and the populations of each geometry optimised for the best solution.

The agreement factor for this combined geometry gradually increased as more **1B** was included from the 100% conformer **1C** value (2.34) to the value for 100% conformer **1B** of 3.71%. There was no minimum in this plot. This suggests that **1C** is the predominant conformer with >80% population in chloroform solution. The observed *vs.* calculated pseudo-contact shifts for **1C** are given in Table 6 and it can be seen that there is generally very good agreement with the possible exception of H1 and $H2,5_{CIS}$, both of which have large pseudo-contact shifts. Thus in conclusion the LIS study supports the *ab initio* calculations that there are two populated conformers of cyclopentanol in solution, **1C** and **1B** and that conformer **1C** predominates.

***cis*-Cyclopentane-1,2-diol (2).** As in the case of cyclopentanol PCModel and Gaussian did not give the same optimised geometries. The PCModel geometry was a slightly distorted envelope conformation with an axial OH at the flap of the envelope and an equatorial OH at the fold of the envelope (**2A**, Fig. 4 and Table 5). The G98 geometry was an envelope



2A **2B**

Fig. 4 Envelope geometries for *cis*-1,2-cyclopentanediol (**2**).

conformation but this geometry had the equatorial OH at the flap and axial OH at the fold of the envelope, as in cyclopentanol (**2B**, Fig. 4 and Table 5). The relative energies of the conformers were obtained by minimising **2A** in G98 keeping the oxygen dihedral angles constant. This gave **2A** 0.56 kcal mol^{-1} higher energy than **2B**.

It was of interest to check these results with the LIS method and these geometries were input into LIRAS4 with the observed pseudo-contact shifts (Table 2). There is an additional complexity in this case as the two OH groups are non-equivalent, thus the lanthanide may complex with either (or

Table 5 Ring and oxygen dihedral angles for the optimised geometries of *cis* (**2**) and *trans* (**3**) cyclopentane-1,2-diol

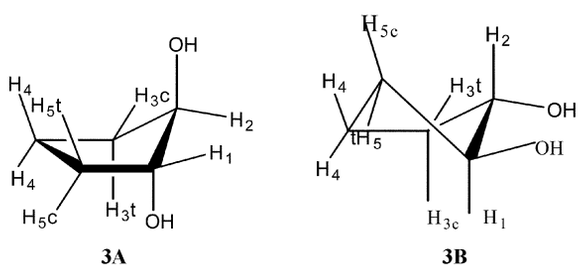
Conformer	$\theta_{1,2}$	$\theta_{2,3}$	$\theta_{3,4}$	$\theta_{4,5}$	$\theta_{5,1}$	$O_{1,2,3}$	$O_{1,5,4}$	$O_{2,1,5}$	$O_{2,3,4}$	$O_{1,2,}O$
2A (PCM)	−40.9	35.3	−16.6	−8.8	30.6	−160.6	150.6	76.0	−80.9	−43.74
2B (G98)	−40.4	41.2	−26.0	1.0	24.3	−75.3	92.0	163.3	−159.1	−47.54
3A (G98)	−39.8	40.6	−25.8	1.2	23.8	75.3	−93.4	−78.43	−73.09	−166.46
3A (PCM)	−38.3	36.8	−21.3	−2.5	25.2	78.7	−93.0	79.63	−81.07	−163.46
3B (G98)	−43.6	33.5	−10.9	−15.6	36.3	−167.4	155.1	−164.82	156.20	71.40
3B (PCM)	−43.0	34.7	−13.4	−13.3	34.7	−163.1	153.8	−163.09	153.81	76.75

Table 6 Observed *vs.* calculated LIS for cyclopentanol (**1**) and *cis* (**2**) and *trans* (**3**) cyclopentane-1,2-diols

Nucleus	(**1**)		Nucleus	(**2**)		(**3**)	
	Obs.	Calc.		Obs.	Calc.	Obs.	Calc.
C1	139.3	138.2	C1,2	106.1	106.0	153.4	151.8
C2,5	68.4	68.9	C3,5	51.5	51.8	66.3	66.2
C3,4	44.2	44.8	C4	36.7	37.4	46.6	46.6
H1	85.6	88.9	H1,2	51.0	51.5	108.6	108.6
H2,5c	64.5	61.2	H3,5c	43.8	44.1	57.0	57.1
H2,5t	38.5	39.6	H3,5t	29.2	26.1	45.9	45.9
H3,4c	38.5	38.1	H4c	26.2	26.1	33.5	33.5
H3,4t	25.2	25.3	H4t	21.9	22.1	33.5	33.5

both) of the OH groups. The LIRAS optimisation for the case of two non-identical coordinating groups is both too complex and too under-determined for any proper evaluation and the same applies to a bidentate coordination. Thus we assumed a complexation model in which the lanthanide complexes with only one of the two hydroxyl groups. With the lanthanide complexing with the axial OH group the LIRAS4 search gave reasonable solutions for both the geometries (Table 4). Both the coordination geometries and agreement factors are similar for **2A** and **2B** which is not unexpected in view of the similarity between the two forms. However, the agreement factor for **2B** (2.2%) is better than that of **2A** (2.75%). The alternative model with the lanthanide complexing the equatorial hydroxyl group gave a very poor agreement factor (7.3%, Table 4) and this shows clearly that the lanthanide binds predominantly to the axial hydroxyl group.

***trans*-Cyclopentane-1,2-diol (3).** For the *trans*-cyclopentane-1,2-diol PCModel and G98 gave the same minimised conformations, one an envelope conformer with both hydroxy groups axial (**3A**, Fig. 5 and Table 5), the other a half-chair



3A **3B**

Fig. 5 The stable conformations of *trans*-1,2-cyclopentanediol (**3**)

conformation with both hydroxy groups equatorial (**3B**). The diequatorial conformer was calculated to be more stable by 2.9 kcal mol^{-1} (PCModel) and 0.70 kcal mol^{-1} (G98).

On examining these geometries by LIRAS, again both geometries have two different OH groups and therefore on our model two different complexing sites. However both geometries gave acceptable solutions (Table 4). The diaxial geometry **3A** with complexation at the fold of the envelope gave a reasonable agreement factor of 1.4% but complexation at the other OH gave a very poor agreement factor of 5.7%. The diequatorial geometry **3B** with complexation at the fold gave an excellent agreement factor of 0.09%, but it must be noted that this compound has one fewer pseudo-contact shift than the other compounds and therefore the analysis is less overdetermined.

The observed *vs.* calculated LIS shifts for **1**, **2** and **3** are given in Table 6. The agreement is such that this confirms unequivocally the assignments of the *cis* and *trans* 2,5 and 3,4 protons in (**1**), the *cis* and *trans* 3,5 and 4 protons in (**2**) and the *cis* and *trans* 3,5 protons in (**3**). Invariably the protons *cis* to the hydroxyl groups have larger LIS than the *trans* protons.

Discussion

All the previous investigations of the conformations of monosubstituted cyclopentanes have assumed a symmetric envelope conformation with the substituent at the flap of the envelope. Both the theoretical and LIS results presented here show clearly that the major conformation of cyclopentanol in solution is an unsymmetric envelope conformation with the axial hydroxyl substituent at the fold of the envelope. The symmetric conformation with an axial hydroxyl at the flap of the envelope is present but is of higher energy than the unsymmetric conformer. The symmetric equatorial conformer is a minor component in solution. It is of interest to consider whether the earlier investigations could be reinterpreted on the basis of the present results. Certainly the IR data of Ekejiuba and Hallam[9] are consistent with the present results as one would expect the OH stretching frequency in **1B** and **1C** to differ and therefore two free OH bands would be observed in dilute solutions. However it is not clear whether the electron diffraction studies of Hildebrandt and Shen on chlorocyclopentane[6] could be reinterpreted on this basis.

The stable conformation **1C** of cyclopentanol is of particular interest in the relationship it has with the preferred conformer of 2-methoxytetrahydrofuran and of the furanose sugars. In both cases the axial OR substituent is strongly preferred and this gave rise to the concept of the anomeric effect involving interaction between the ring oxygen and the axial oxygen.[25,26] The present results indicate that this conformation is preferred even in cyclopentane and therefore the origin of the anomeric effect may be more fundamental than the interaction of the two oxygen atoms. The proof of this fascinating speculation is outside the range of this investigation.

The results for the 1,2-diols support this hypothesis in that the conformer with an axial hydroxyl group at the fold of the envelope is also the more stable conformer in the *cis* diol.

However in the *trans* diol the attractive *gauche* interaction[27] of the two vicinal oxygens would appear to be greater than this orientation effect and the diequatorial conformer **3B** is the more stable form in solution.

The parameters for the different lanthanide complexation geometries and the agreement factors R_x for the best solutions for the compounds studied are given in Table 4 and it is of interest to see whether the coordination geometries give any information on the complexing behaviour of the compounds. The coordination geometries with **1C** are as expected from previous studies[15] with the lanthanide away from the ring in a direction *ca. trans* (*anti*) to C_2. The complexation geometries of the diols **2B** and **3B** are similar to **1C**. However these are less definitive as the problems of under-determined solutions meant that it was not feasible to include two conformers in the *Z* matrix. We cannot however exclude bidentate complexation in these complexes. There may be a different type of complex than in **1** but one would need further evidence before any conclusions could be made.

Although due to limitations in the LIRAS model the LIS results for the diols are not as definitive as those for cyclopentanol both the modelling calculations and the LIS analysis give a consistent picture of the conformational equilibria in the compounds studied.

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