Conformational Analysis. Part 11.[1] A Theoretical and Nuclear Magnetic Resonance Lanthanide-induced Shift (LIS) Study of the Conformation of α-Tetralone

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The conformational behaviour in solution of α-tetralone [3,4-dihydronaphthalen-1(2*H*)-one] has been studied through a combination of theoretical methods and LIS analysis. The force-field method MMPI predicts the *envelope* conformation as more stable (*ca.* 0.94 kcal mol^{-1}), in accordance with previous results, whilst the semi-empirical MNDO method gives equal energies for the *envelope* and *half-chair* conformations due possibly to the under-evaluation of the π-conjugation energy. The LIS analysis cannot differentiate between the two possible conformations because, in both cases, well defined minima with good agreement factors (%*Rx*: *ca.* 1.4 and 1.6) are obtained. The complexation geometry found for the lanthanide ion in α-tetralone has been used to analyse the cyclohex-2-en-1-one LIS in order to resolve the under-determination for this system found in the previous LIS analysis, giving in this way better defined minima in the correlation coefficients.

In a recent paper,[1] the conformational behaviour of cyclohexenone in solution was investigated by a combination of theoretical methods and the lanthanide-induced shift n.m.r. technique (LIS). In this investigation the theoretical methods used predicted the *envelope* conformation as more stable than the *half-chair* (see Figure 1) by *ca.* 0.5—1.0 kcal mol^{-1}, in agreement with microwave[2] and Raman[3] experimental studies, which indicated a predominant *envelope* conformation in the vapour phase.

The two conformers could not be distinguished by the LIS analysis, because both gave an excellent agreement factor in the minimum (lower than 1.2%). This could have been because the system was not very well determined. There were only eleven LIS ΔM values (six carbons and five hydrogens) to determine eight unknowns. [Two sets of polar co-ordinates for the lanthanide position, one per each complexing site (see Figure 2), plus the % population between these positions and the normalisation constant for the McConnell–Robertson equation.]

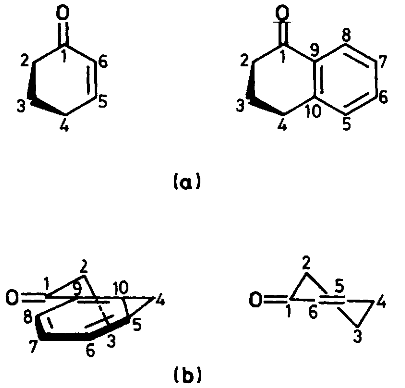

Figure 1. Conformations of cyclohexenone and α-tetralone (a) *envelope*; (b) *half-chair* †

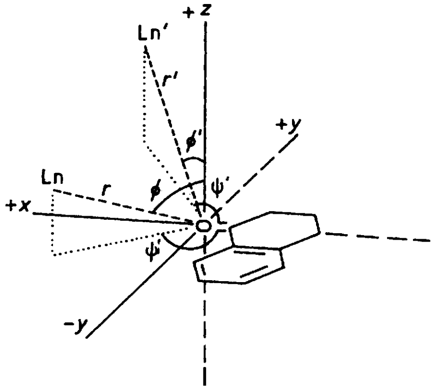

Figure 2. Lanthanide complexation geometry and spatial orientation in HARDER program for two complexation sites

In order to overcome this problem we investigate here α-tetralone [3,4-dihydronaphthalen-1(2*H*)-one], a molecule with a similar structure but with considerably more data, in which one ring is analogous to the cyclohexenone ring (see Figure 1). This molecule can be used in two different ways. Firstly as a cyclohexenone ring analogue with more shifted centres (it has seventeen) in which the predominant conformation (*envelope* or *half-chair*) could be determined more precisely. Secondly α-tetralone may be used as a model for the lanthanide complexation on the side of the carbonyl group away from the aromatic ring (the '+*y*' side, Figure 2) as this could be expected to very similar to cyclohexenone. This lanthanide position can then be used in the cyclohexenone analysis to ensure an over-determined system. There will be only five unknowns (a set of polar co-ordinates, for the '−*y*' site, plus the population between the '+*y*' and '−*y*' sites and the normalisation constant) with eleven LIS data points.

α-Tetralone has been previously investigated. LISs have been used by Epsztajn *et al.*,[4] together with theoretical calculations and u.v. spectroscopy to determine the torsional angle between the carbonyl group and the aromatic ring in relation to the number of carbons in the ketone ring, for some related benzocycloalkanones. In α-tetralone they found that this angle has a small value, near to a planar form. These results are from a geometry obtained *via* the MNDO semi-empirical method which gave a conformation close to a *half-chair* conformation, in agreement with the results obtained from force-field calculations in the related *exo*-methylene benzoalkenones.[5]

The assignment of the ^{13}C spectrum of α-tetralone is controversial. The assignment given for α-tetralone in reference

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† Numbering of cyclohex-2-en-1-one does not follow IUPAC recommendations but is used for direct comparison with the analogous structure α-tetralone.

6 does not accord with reference 7 for the resonance lines of carbons C-5 and C-8. The first assignment was obtained from the lanthanide-induced shifts produced for a single addition of Yb(dpm)$_3$.[6] The other assignment was carried out using the Chemically Induced Dynamic Nuclear Polarisation technique (CIDNP)[7] which used the alternating sign of the spin density in the aromatic portion of a π-radical to assist in the assignment of the ^{13}C n.m.r. lines.

Our assignment of the ^{13}C spectra is in agreement with reference 7. The diamagnetic shifts (see Table 4) show that the atoms in the *ortho* and *para* positions with respect to the complexing group have a larger value than the others in the aromatic ring, due to the fact that this shift is a π-transmitted effect in aromatic compounds.[8] The pseudo-contact shifts further support this assignment as they are related to the proximity to the complexation centre. This interpretation of the LIS is in opposition to the assignment made in the former work using shift reagents.[6]

The conformation of the six-membered alicyclic ring in α-tetralone had been studied previously using the coupling constants between the aliphatic protons.[9] The determination of the *R*-values for the two ethanic fragments in the ring gave for the C(2)–C(3) fragment a dihedral angle of 57° and for the C(3)–C(4) fragment a dihedral angle of 56°. These results were based on the assumption of sp^3 hybridisation, and the results are in agreement with an *envelope* conformation in α-tetralone. But it is possible to obtain the same *R*-value in the C(3)–C(4) fragment from a *half-chair* conformation if the C–C–H bond angles are deformed due to steric effects between C(5) and H-4 (see Figure 1). For these reasons and in view of results obtained previously in cyclohexenone it is not possible to reject '*a priori*' the *half-chair* conformation in this ring.

In the present work we have analysed α-tetralone by calculating the primary structure (bond lengths and bond angles) through theoretical methods, and the secondary structure (pucker or twist angles) from the analysis of the experimental LIS data.

Experimental

^{1}H and ^{13}C n.m.r. spectra were all obtained on a Bruker WM 250 MHz spectrometer at approximately 25 °C. All solutions were in CDCl$_3$, previously stored over molecular sieves and passed through a dried Al$_2$O$_3$ column immediately before use. Lanthanide shift reagents were used as commercial samples dried *in vacuo* over P$_4$O$_{10}$ for 24 h. A commercial sample of α-tetralone was used without further purification.

The assignment of ^{13}C and ^{1}H shifts was carried out according to the results found in the literature.[7,9] LIS experiments used the incremental weighing method, using molar ratios, ρ, in the range 0.0—0.20 from four additions of lanthanide shifts reagents ($\rho = [L]/[S]_0$).

Computer calculations were performed by the University of Liverpool VAX 11/780 and IBM 3083 computer.

Theoretical Calculations

The geometries used to determine the conformations in solution were obtained from two different theoretical methods: semi-empirical *via* the computer program MNDO[10] and Allinger's force-field through the MMPI[11] program.

In the geometry optimisation a similar procedure was used as previously[1] in that the molecule was assumed planar apart from the carbon atoms which define the pucker or dihedral angle. This is an approximation to avoid the tendency of theoretical methods to give a final conformation that could be neither an *envelope* nor a *half-chair* but an intermediate one of lower symmetry. However this approximation would appear reasonable in view of previous results[4] in which the carbonyl group was found to be essentially coplanar with the aromatic ring in α-tetralone.

Table 1. (a) Heats of formation and (b) steric energies for α-tetralone (in kcal mol^{-1})

Half-chair θ(34109) (°)[b]	(a) MNDO	(b) MMPI
0	−20.96	8.77
2	−21.11	8.21
6	−22.13	7.40
10	−23.52	3.12
14	−23.83	1.67
18	−21.63	2.08
22	−14.48	5.00
26	−1.11	10.90
30	17.11	c
34	37.48	c

Envelope θ(34109) (°)[a]	(a) MNDO	(b) MMPI
0	−20.96	8.77
2	−21.00	8.58
6	−21.31	7.38
10	−21.92	5.77
14	−22.68	4.10
18	−23.37	2.60
22	−23.77	1.45
26	−23.67	0.79
30	−22.65	0.76
34	−20.18	1.51
38	−16.16	3.12
42	−10.04	5.68
46	−2.03	9.25

[a] Atoms 1, 9, 10, 4, and 2 in the plane. [b] θ(21 910) = θ(34 109). [c] SCF calculations do not converge.

In Table 1 the MNDO-calculated heat of formation and the steric energies from the MMPI calculations are shown as functions of the angle of pucker for the *envelope* and *half-chair* forms. For the *half-chair* conformer both methods give the minimum at the same dihedral of 14°, while for the *envelope* form the MNDO calculations give a minimum at a dihedral of 22°, and MMPI gives a minimum at 30°. These results are very close to those obtained for cyclohexenone in which the *half-chair* conformation had a dihedral angle 10—14° and the *envelope* form a pucker angle of 22—26°.

The energy difference between the conformers, in α-tetralone, is very similar to that in cyclohexenone. The MNDO calculations give a similar energy for both conformers, with the *half-chair* conformations slightly more stable than the *envelope* (0.06 kcal mol^{-1}) (see Table 1). We attribute this to the known under-evaluation of the π-conjugation energy in the MNDO program. The MMPI calculations give the *envelope* conformation as more stable than the *half-chair* (0.94 kcal mol^{-1}), similar to the results obtained for cyclohexenone (0.68 kcal mol^{-1}).

The minimum-energy geometries obtained from both theoretical methods are summarised in Tables 2 and 3. It can be seen that both theoretical methods afford very similar structures, except for those atoms involved in the variation of pucker and twist angles.

The C(2)–C(3) ethanic fragment is staggered, and the value of the dihedral calculated from the theoretical methods (Table 3) agrees well with the value estimated from the vicinal proton coupling constants,[9] which was 57°. On the other hand, in the C(2)–C(3)–C(4)–C(10) fragment, only the *envelope* conformation is in agreement with the dihedral angle estimated from the coupling constants (56°), the value for this dihedral in the *half-chair* conformation is 40—42°. The calculations thus favour the *envelope* conformation, but in view of the approximations of the *R*-value analysis, it is not possible to reject entirely the *half-chair* conformation.

Table 2. Bond lengths (Å) and bond angles (°) in α-tetralone from MNDO and MMPI calculations

	MNDO[a]	MM2[a]		MNDO[a]	MM2[a]
O–C(1)	1.23	1.22	C(3)–C(4)	1.53	1.53
C(1)–C(9)	1.51	1.49	C(2)–C(3)	1.54	1.54
C(1)–C(2)	1.54	1.52	C(8)–C(7)	1.40	1.40
C(9)–C(10)	1.43	1.41	C(7)–C(6)	1.40	1.40
C(9)–C(8)	1.41	1.41	C(6)–C(5)	1.41	1.40
C(10)–C(4)	1.51	1.51	C(Al)–H	1.11	1.11
C(10)–C(5)	1.41	1.40	C(Ar)–H	1.09	1.10

	Envelope		Half-chair	
	MNDO	MM2	MNDO	MM2
O–C(1)–C(9)	122.32	123.18	122.18	123.56
C(1)–C(9)–C(10)	120.38	120.05	118.86	120.66
C(1)–C(9)–C(8)	120.60	119.68	121.04	118.97
C(9)–C(10)–C(4)	119.98	120.10	122.78	122.61
C(10)–C(4)–C(3)	112.31	110.15	115.38	113.41
C(10)–C(4)–H(4)	110.25	109.72	109.61	110.46
C(10)–C(4)–H(4′)	109.17	109.35	108.22	106.73
H(4)–C(4)–H(4′)	105.65	107.16	105.63	107.49
C(4)–C(3)–H(3)	110.17	110.35	109.15	110.28
H(2)–C(2)–H(2′)	106.26	107.44	105.52	107.54
C(8)–C(7)–H(7)	119.97	120.10	119.82	120.21
C(4)–C(3)–C(2)	108.38	105.03	112.05	112.53
C(4)–C(3)–H(3′)	111.21	111.81	109.94	108.49
H(3)–C(3)–H(3′)	106.19	108.17	106.13	106.70
C(3)–C(2)–C(1)	111.56	110.56	101.83	103.19
C(3)–C(2)–H(2)	109.25	108.69	109.17	109.86
C(3)–C(2)–H(2′)	110.79	112.12	111.45	110.23
C(9)–C(8)–H(8)	120.89	120.93	121.13	120.85
C(8)–C(7)–C(6)	119.77	119.90	119.93	119.70
C(7)–C(6)–C(5)	119.68	120.04	120.14	119.88
C(7)–C(6)–H(6)	120.37	119.95	120.17	120.01
C(6)–C(5)–C(10)	121.22	120.84	121.06	121.36
C(6)–C(5)–H(5)	118.55	119.20	118.71	118.99

[a] Identical values in both conformations.

Table 3. Dihedral angles (°) in α-tetralone from MNDO and MMPI calculations[a]

	Envelope		Half-chair	
	MNDO	MM2	MNDO	MM2
O–C(1)–C(9)–C(10)	−180.00	180.00	−166.82	−169.16
C(9)–C(10)–C(4)–C(3)	30.00	33.27	14.00	14.34
C(10)–C(4)–C(3)–C(2)	−58.41	−63.73	−40.76	−42.03
C(4)–C(3)–C(2)–C(1)	57.94	64.00	53.61	55.96
C(2)–C(1)–C(9)–C(10)	0.00	0.00	14.00	14.04
C(3)–C(4)–C(10)–C(9)	151.38	152.67	136.99	138.02
H(4′)–C(4)–C(10)–C(9)	−92.99	−90.06	−108.27	−105.42
H(3)–C(3)–C(4)–C(10)	63.71	57.38	82.24	77.25
H(3′)–C(3)–C(4)–C(10)	−178.82	177.82	−161.74	−166.22
H(2)–C(2)–C(3)–C(4)	180.01	−176.71	175.61	177.66
H(2′)–C(2)–C(3)–C(4)	−63.26	−58.09	−68.21	−64.01

[a] The aromatic ring and carbon atoms 1 and 4 are co-planar.

Results

The pseudo-contact shifts given in Table 4, corrected for the effects of complex formation ($\Delta M - \Delta D$), have been used along with the program HARDER described previously,[12] to obtain the required conformational information. This program assumes a co-ordination geometry shown in Figure 2, where the co-ordination centre is placed at the origin.

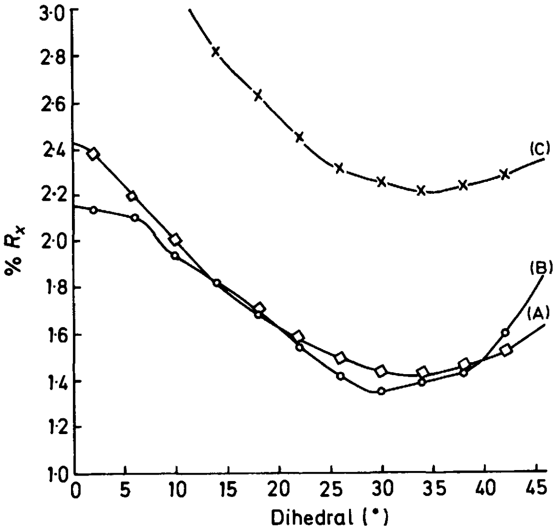

Figure 3. *Rx* (%) *versus* pucker angle in α-tetralone, *envelope* conformation: (A) MMPI geometry; (B) MNDO geometry; (C) MMPI averaged geometry

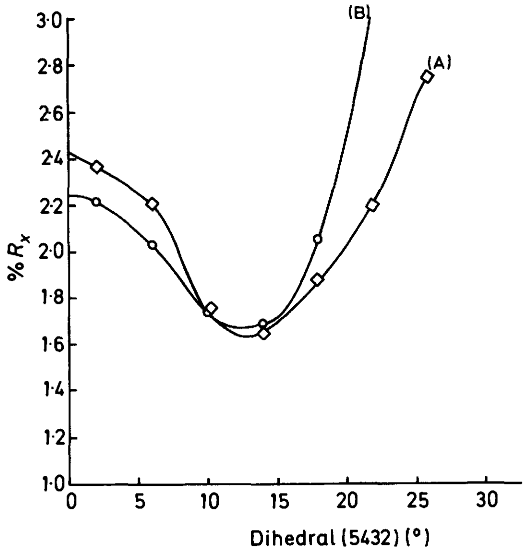

Figure 4. *Rx* (%) *versus* twist angle in α-tetralone, half-chair conformation: (A) MMPI geometry; (B) MNDO geometry

We use the model of four-site lanthanide complexation in which the lanthanide position is reflected through the '*xy*' plane from the two independent sites, on the '$+y$' and '$-y$' sides. The lanthanide ion position is allowed to vary over a chemically acceptable range,[13] according to the spatial disposition of the lone pairs in the carbonylic oxygen, of: r = 2.50—3.50 Å, φ = 0—90°, and ψ = 120—160°. The geometries obtained from the different theoretical methods were analysed using the LIS results through the HARDER program in a similar way to that for cyclohexenone.[1] Figures 3 and 4 show the agreement factor (%*Rx*) *versus* the angle of pucker and twist respectively for the *half-chair* and *envelope* conformations.

The *half-chair* conformation shows a minimum at *ca.* 10—14° for both the MMPI and MNDO geometries, with a good agreement factor (%*Rx* 1.6). In the *envelope* form the minimum is predicted at a pucker angle of 30—34°, with an agreement factor of *ca.* 1.4% (Figure 3); this pucker angle is similar to that

Table 4. Observed shift (δ), LISs (Δ*M*), diamagnetic shifts (Δ*D*), and pseudo-contact shifts (Δ*M* − Δ*D*) for α-tetralone

	C=O	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
δ[a]	198.59	39.97	23.45	29.89	128.97	133.61	126.80	127.34	132.78	144.73
Δ*M*[b]	145.41	61.05	25.23	20.51	15.83	15.36	17.45	44.02	57.94	29.71
Interc.	198.94	39.50	23.53	29.94	129.01	133.64	126.84	127.45	132.93	144.79
Δ*D*[c]	12.51	−1.31	−0.56	−0.43	−0.10	3.24	0.34	3.30	−1.86	3.20
Δ*M* − Δ*D*	132.90	62.36	25.79	20.94	15.93	12.12	17.11	40.72	59.90	26.51

	2-H	3-H	4-H	5-H	6-H	7-H	8-H
δ[a]	2.65	2.13	2.96	7.25	7.46	7.29	8.03
Δ*M*[b]	44.64	18.10	15.44	11.14	8.58	9.66	51.00
Interc.	2.73	2.17	2.97	7.27	7.48	7.33	8.13

[a] $[S]_0$ 1.0M in Cl_3CD. [b] From four additions of $Yb(fod)_3$, ρ = 5.34, 9.73, 13.71, and 19.65 × 10^{-2}. All correlation coefficients >0.998. [c] From three additions of $La(fod)_3$ ρ = 1.15, 4.67, and 11.67 × 10^{-2}.

Table 5. Results of LIS analyses of α-tetralone

	θ(5432)			Lanthanide co-ord			pop.
Half-chair	(°)	*Rx*(%)		*r* (Å)	φ (°)	ψ (°)	(% +*y*)
MNDO	14	1.685	−*y*	3.35	30	120	
			+*y*	2.95	90	144	83
MMPI	14	1.652	−*y*	3.16	36	120	
			+*y*	2.92	90	144	86
Envelope							
MNDO	30	1.349	−*y*	3.16	30	120	
			+*y*	2.94	80	146	86
MMPI	34	1.415	−*y*	3.12	33	120	
			+*y*	2.91	86	144	86

obtained when we fix the lanthanide position for an averaged geometry of all the shifted centres, except C-5, 5-H, 4-H, and 6-H, which change their co-ordinates according to the pucker angle [curve (C) in Figure 3]. We can deduce from these results that these are the atoms which determine the changes in the agreement factor value with the angle of pucker.

In α-tetralone, in contrast to the results obtained in cyclohexenone, the minimum of the LIS curves in the *envelope* conformation from the MMPI and MNDO geometries is reasonably well defined, as are those obtained for the *half-chair* form. This is very probably due to the fact that the system in α-tetralone is more over-determined than in cyclohexenone. In both molecules the variation due to the spatial disposition takes place with an identical number of atoms and in a similar amount, but in cyclohexenone there are only eleven shifted centres to resolve eight unknowns and the agreement factor did not vary significantly between very different pucker angles.[1]

In the *half-chair* conformation, as in cyclohexenone, we obtain a well-defined minimum for both geometries because in this conformer the orientation of the carbonyl oxygen changes slightly with the torsional angle and thus a small change in the torsional angle causes a significant change in the %*Rx* value. Furthermore the torsional angle change affects more atoms than in the *envelope* conformation (see Figure 1).

The LIS parameters for the minima in both conformations are displayed in Table 5. For α-tetralone and cyclohexenone the %*Rx* values obtained for the *envelope* conformation are always lower than those for the *half-chair*, from the same kind of geometry (*ca.* 0.2 %*Rx*), and the MNDO geometries always give a slightly better %*Rx* value that the MMPI.

The lanthanide ion geometry is very similar in all the minima, with an alternated disposition with respect to the nearby groups (see Figure 2). In the '+*y*' side, the lanthanide is essentially in

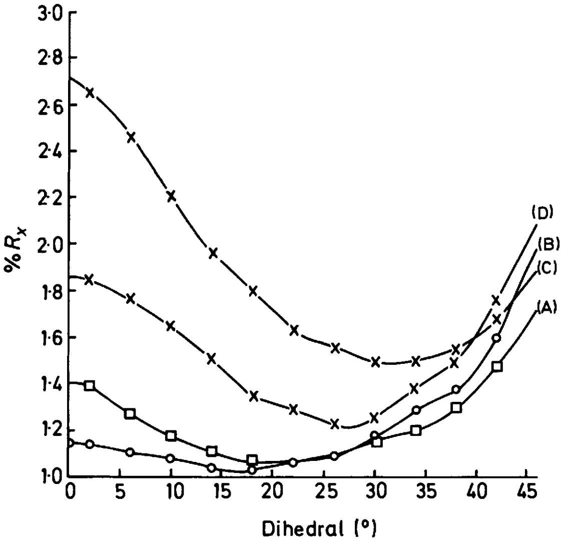

Figure 5. *Rx* (%) *versus* pucker angle in cyclohexenone, *envelope* conformation: (A) MMPI geometry; (B) MNDO geometry; (C) MMPI geometry with '+*y*' lanthanide geometry; (D) MNDO geometry with '+*y*' lanthanide geometry

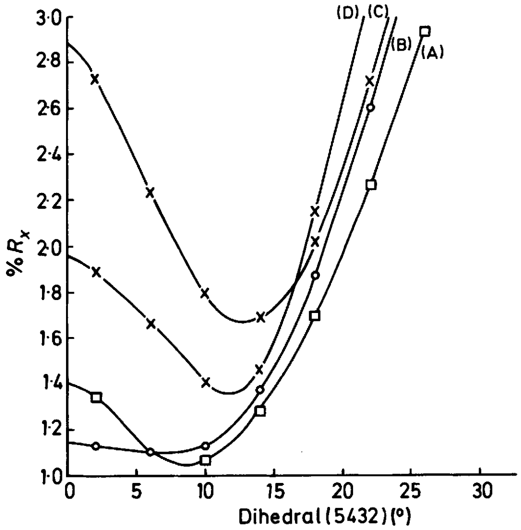

Figure 6. *Rx* (%) *versus* twist angle in cyclohexenone, *half-chair* conformation: (A) MMPI geometry; (B) MNDO geometry; (C) MMPI geometry with '+*y*' lanthanide geometry; (D) MNDO geometry with '+*y*' lanthanide geometry

the *xy* plane in order to avoid the steric hindrance of the 2-H atoms. In the '$-y$' side the lanthanide ion is placed above and below the *xy* plane to avoid the aromatic ring atoms.

The '$+y$' lanthanide geometries found in the minima for each theoretical method may now be used to fix the '$+y$' lanthanide geometry in cyclohexenone thus allowing only the polar coordinates for the '$-y$' side and the population of both sides to vary. The results obtained are shown in Figures 5 and 6 together with the previous %*Rx* values obtained when the '$+y$' lanthanide geometries was allowed to vary[1] [curves (A) and (B)]. In all the geometries, the minima have been shifted to higher pucker and twist angles (26—30° for the *envelope* conformers *versus* 18—22°, and 14—18° *versus* 6—10° for the *half-chair*), and as in α-tetralone, the curves show well defined minima with acceptable agreement factors (%*Rx*) of 1.2 and 1.7.

These results point to the successful use of α-tetralone as a model for the '$+y$' lanthanide position so as to ensure the over-determination of the LIS analysis for cyclohexenone, since through this method better defined minima were obtained. However, this modified LIS analysis, as is the case for the corresponding LIS analysis of α-tetralone, still cannot differentiate unequivocally between the two possible conformers.

Conclusions

The theoretical calculations for α-tetralone are very similar to those for cyclohexenone and both methods (MMPI and MNDO) afford very similar geometries. The force-field MMPI calculations we believe give more realistic energies for the two conformers than the MNDO programme, with the *envelope* conformer *ca.* 0.9 kcal mol^{-1} more stable than the *half-chair*.

The LIS analysis of α-tetralone does not resolve, in an unequivical way, the predominance of one conformation, because the analysis gave a well defined minimum for both conformers with a very good agreement factor (%*Rx* 1.6 in *half-chair* with a twist angle of 10—14° and %*Rx* 1.4 in *envelope* conformation at a pucker angle 30—34°). It is possible to use the results obtained in α-tetralone as a model to reduce the number of unknowns in order to resolve the LIS analysis of cyclohexenone, giving much better defined minima in the agreement factors. But as in the case of α-tetralone, these agreement factors do not permit the rejection of one of the two possible conformations as not present in solution.

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