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Conformational analysis, Part 41. A modelling and LIS/NMR investigation of the conformations of α,β-unsaturated carbonyl compounds

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ABSTRACT: A novel Lanthanide Induced Shift Analysis (LISA) is presented. In this analysis both the paramagnetic and the diamagnetic lanthanide induced chemical shifts are normalised separately in contrast to previous techniques in which only the paramagnetic shifts were normalised. This procedure is used together with molecular mechanics (MMFF94) and *ab initio* (RHF/6-31G, RHF/6-311G** and B3LYP/6-311G**) calculations to investigate *s-cis*/*s-trans* isomerism in some *α*,*β*-unsaturated aldehydes, ketones and esters. In tiglic aldehyde **1** and *trans*-cinnamaldehyde **4** the *s-trans* conformer predominates with energy differences ΔE (*s-cis*–*s-trans*) of 1.64 and 1.76 kcal/mol. In methyl vinyl ketone **2** and *trans*-cinnamyl methyl ketone **5** the populations of the *s-cis* and *s-trans* isomers are almost equal (ΔE 0.24 and 0.0 kcal/mol) and in methyl crotonate **3** and methyl *trans*-cinnamate **6** the *s-cis* conformer is more stable (ΔE −0.72 and −0.41 kcal/mol). These results are in agreement with both the MMFF94 and *ab initio* calculated energies for the compounds except tiglic aldehyde **1** in which all the calculated values are too large and cinnamyl ketone **5**. In this compound the *ab initio* calculations predict the *s-cis* form to be more stable than the *s-trans* in contrast to both the MM calculations and the observed result which give both forms of equal energy. Also in both the MM and *ab initio* calculations phenyl substitution in the ketone (**2** vs. **5**) considerably stabilises the *s-cis* form. This is not observed in practise. In phenyl acetate **7** the B3LYP calculations give two equally stable structures, one planar one non-planar. The MMFF94 and MP2 calculations and the LIS analysis support the existence of only the *non*-planar conformer in solution, which is also the conformation of phenyl acetate in the crystal.
Supplementary electronic material for this paper is available in Wiley Interscience at http://www.interscience.wiley.com/jpages/0894-3230/suppmat/17/v17.html

KEYWORDS: ^{1}H; ^{13}C; LIS; NMR; conformations; *α*,*β*-unsaturated carbonyl compounds; modelling; *ab initio* theory

INTRODUCTION

Although many chemists consider that the conjugative stabilisation of *α*,*β*-unsaturated carbonyl compounds gives only the *s-trans* conformer (Fig. 1) there is little evidence to justify this. An early molecular mechanics investigation[2] calculated the energy difference (*s-cis*–*s-trans*) in a number of aldehydes and ketones. For acrolein (Fig. 1, X, $R_1, R_2, R_3 = H$) this was 1.6 kcal/mol.[3] In **1** this increased to 3.3 kcal/mol but in **2** the difference was only 0.56 kcal/mol and in *cis* 1-methyl-1-buten-3-one (Fig. 1, X, $R_3 = Me$, R_1, $R_2 = H$,) the energy difference was −1.7 kcal/mol. There was little experimental evidence to confirm these predictions at that time.

More recently there has been evidence both for and against the predominance of the *s-trans* form. *Ab initio* calculations on acrolein[4] gave the trans form as ca 2 kcal/mol more stable than the *cis*. A LIS analysis[5] using only Eu(fod)$_3$ ^{1}H LIS values gave 10% *s-cis* for **1** and 27% *s-cis* for **2** in solution. An IR and Raman study[6] of **2** in the vapour gave ΔE 0.80 kcal/mol. The IR spectrum of the *s-cis* form could not be detected in the solid[7] and the rotational spectrum of the *s-cis* form could not be detected in the vapour.[8] A recent theoretical study[9] suggested that the *s-cis* form was destabilised by steric interactions between the C=O and the *cis* ethylene proton. An IR investigation on methyl acrylate[10] gave ΔE 0.33 kcal/mol in CS_2 solution assuming the *s-trans* form as the more stable form. However, a more recent electron diffraction study[11] using *ab initio* geometries gave the ratio of *s-cis–to-trans* as 2:1. This agrees with the earlier value of the energy difference but the conformer stabilities are reversed.

There are few investigations of the *s-cis*/*s-trans* ratio in the phenyl compounds. IR studies[12,13] suggested that

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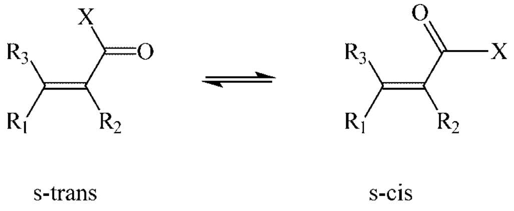


1: Tiglic aldehyde.	X, R_3=H; R_1, R_2=Me
2: Methyl vinyl ketone.	X=Me; R_1, R_2, R_3=H
3: Methyl crotonate.	X=OMe; R_1=Me; R_2, R_3=H
4: trans cinnamaldehyde.	X, R_2, R_3=H; R_1=Ph
5: trans cinnamyl methyl ketone.	X=Me; R_1=Ph; R_2, R_3=H
6: methyl trans cinnamate.	X=OMe; R_1=Ph; R_2, R_3=H

Figure 1. Conformational isomerism in α,β-unsaturated carbonyl compounds

4 exists almost entirely in the *s-trans* form but in **5** the *s-cis*/*s-trans* ratio was ca 43:57%. An NMR/NOE study of **6** concluded that the *s-cis* form is slightly favoured over the *s-trans* form.[14]

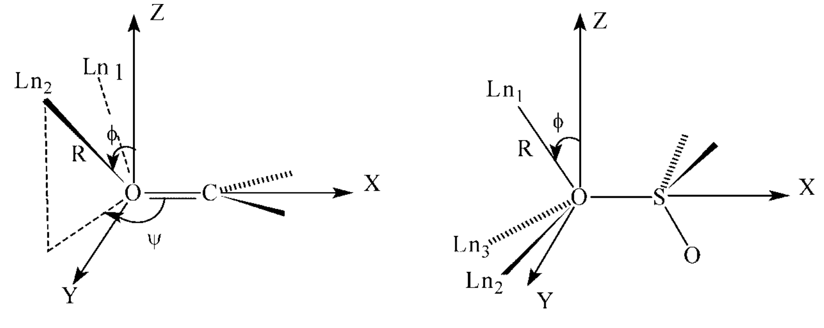
These somewhat conflicting results suggested that it would be useful to examine the *s-cis*/*s-trans* isomerism of different α,β-unsaturated carbonyl compounds with the same technique and we present the results of an investigation on simple aldehydes, ketones and esters and similar phenyl compounds (Fig. 1) using LIS together with theoretical calculations. In order to increase the definition in the LIS experiments (as discussed below) methyl and phenyl derivatives were used. All the compounds examined may exhibit conformational flexibility. In addition a corresponding investigation of the conformation of phenyl acetate **7** in solution is given. The structure in solution of **7** is unknown but the crystal structure is non-planar with the phenyl ring at an angle of 42° with the ester group.[15]

THEORY

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[1,16–21] 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) $La(fod)_3$ or preferably $Lu(fod)_3$ is used to evaluate diamagnetic complexation contributions (ΔD_i), (iii) pseudocontact contributions $(\Delta M\text{–}\Delta D)_i$ are simulated according to the McConnell–Robertson equation and a chemically reasonable multi-site complexation model is used.[16] Recent very accurate *ab initio* calculations[22] on carbonyl complexes in which the C═O..M (M═H,B etc.) angle is *ca.* 120° strongly support the use of multi-site models for such weak interactions.

The lanthanide coordination models used for the carbonyl group in our previous LIS investigations are the two-site and four-site models of LIRAS3 and the three-site model of LIRAS4. 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 *x-z* 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 populations. In the more diffuse four-site model (not shown in Fig. 2) the lanthanide position is reflected about both the *x-z* and *x-y* planes. The population of the two couples of sites reflected about the *x-z* plane may be varied as in the two-site model but the population of those reflected about the *x-y* plane is kept constant at 50:50. Note that the two-site model becomes a one-site model when the lanthanide populations are 0 or 100% and for a planar substrate molecule the two-site and four-site 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 sulphone[21] or sulphoxide[22] group. The S—O bond is more appropriately considered



(a) (b)

Figure 2. The LIRAS3 (a) and LIRAS4 (b) Lanthanide coordination models

as a single bond rather than as a double bond and the model was modified accordingly. In this model there are three possible coordination sites separated by 120° dihedral angles from the three lone pairs on the sp^3 hybridised oxygen atom. These may be rotated an angle β about the S—O bond and their populations may be varied from 0 to 100%. This coordination model has the same number of variables as LIRAS3. Full details of these programmes have been given.[16]

There are, however, some deficiencies in this treatment. Lutetium is more similar to Ytterbium than Lanthanum (the atomic radii are 85.0, 85.8 and 101.6 pm respectively) and is therefore a better model than lanthanum for the diamagnetic effects of Ytterbium. There are, however, still differences between Lutetium and Ytterbium ions and this could affect the weighting of the diamagnetic contribution. In the LIS calculations the agreement factor (R_x) is obtained by normalising the experimental and calculated shifts.[16] This is necessary as the equilibrium constants for the Yb Substrate (and Lu Substrate) equilibria are not known. In our previous work these were assumed to be identical. This assumption may be removed by normalising the diamagnetic contribution as in Eqn (1) where f is a normalising factor to be determined (=1 if $Lu(fod)_3$ was identical to $Yb(fod)_3$).

$$\Delta M^{PC} = \Delta M - f\Delta D \qquad (1)$$

Also errors can be introduced into the LIS analysis by small amounts of impurity in the commercial $Yb(fod)_3$.[23] This would not affect the calculations if only the paramagnetic shifts were considered but this is not the case when the diamagnetic shifts are included as the normalised values of ΔM^{PC} will be affected by these factors. Again these errors can be reduced by using the diamagnetic normalising factor. The LIRAS3 and LIRAS4 programs have now been rewritten to include this new treatment and are termed LISA3 and LISA4. In the new treatment there are now six unknown parameters, four to define the lanthanide-substrate coordination geometry and the site populations and the two normalizing factors. Thus six equations are required to define the system. The least well-defined compound considered is **2** in which eight LIS are measured. Compounds **1,3,7** have nine LIS and **4,5,6** >12 LIS, thus all the systems are overdetermined.

COMPUTATIONAL

As has been mentioned previously, *ab initio* theory at various levels of sophistication has been used to deduce the geometries and energies of these molecules. Wiberg *et al.*[4] used geometries minimised at the MP2/6-31G** level with single point energies calculated at the higher MP3/6-311++G** level to obtain the *s-cis/s-trans* energies of acrolein. Garcia *et al.*[9] stated that geometries minimised at the RHF/6-31G* level were adequate provided that single point energies were calculated at high levels. They used the same level as Wiberg[4] to calculate *s-cis/s-trans* energies in **2** and methyl acrylate. Egawa *et al.*[11] used geometries minimised at the RHF/4-31G* level to provide structural constraints for their analysis of the electron diffraction pattern of methyl acrylate. Recently a systematic study of *ab initio* methods for small molecules was given and the B3LYP calculation with a reasonably large basis set such as 6-311G** was shown to give good general agreement with experiment for small molecule geometries and energies.[33]

In order to differentiate the effects of the method of calculation and the basis set, we have used first the RHF method with the 6-31G basis set, then the RHF method with an extended basis set (6/311G**) and finally the B3LYP calculation with the same extended basis set to calculate the molecular geometries and energies. Comparison of these different methods with both the molecular mechanics energies and the observed data is of some interest (as discussed below).

Recent advances in *ab initio* methods have included solvation in the calculations. A well known example is the polarisable continuum model (PCM) of Tomasi *et al.*[34] It has been noted[35] that this model is the quantum mechanical version of the classical Onsager solvation model and as such the energy difference between two conformers with similar dipole moments will not be affected by the solvent. In the molecules investigated here there is no evidence and no expectation of any appreciable change in the conformer energy with solvent. This is in direct contrast to conformer energies of molecules with two polar functional groups, such as 2-halocycohexanones or furfural, which are strongly dependant on the solvent.[36]

EXPERIMENTAL

All samples were obtained commercially (Aldrich). Compounds **1–4** were distilled before use, all the others used directly for the LIS experiments. The solutions were made up as 0.5 M in $CDCl_3$ which had been stored for at least 24 h over molecular sieves prior to use. The shift reagent $Yb(fod)_3$ is available commercially while $Lu(fod)_3$ was prepared following Springer *et al.*[24] The shift reagents were dried in vacuo over P_2O_5 at *ca.* 35 °C for 24 h, and maintained in vacuo over P_2O_5 between successive additions to the sample. Three additions of $Yb(fod)_3$ (*ca.* 15–20 mg each) were weighed directly in the NMR tube. The plots of chemical shift *vs.* ρ (the ligand/substrate molar ratio) were checked for linearity (all correlation coefficients >0.9992) and for the intercept at the origin (a good test for any impurities). The slopes obtained are the ΔM values recorded. The diamagnetic shifts (ΔD) were obtained from identical experiments using $Lu(fod)_3$. The LIS measurements for compounds **1** and **2** were performed on a Varian Gemini 200 spectrometer operating on ^{1}H 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 sec pulse delay was used for the accumulation of the carbon spectra. The measurements for compounds **3**–**7** were recorded on a Bruker AMX-400 spectrometer at 20 °C. Typical spectral widths were ^{1}H, 6000 Hz with 128 K transform, C-13 23,000 Hz with 128 K transform using a line broadening of 2.0 Hz.

RESULTS

Spectral assignments

The spectral assignments were straightforward and agreed with previous literature assignments.[12,14,25] The observed chemical shifts (δ_i), LIS values (ΔM_i) and diamagnetic shifts (ΔD_i) are given in Tables 1 and 2. The nomenclature used follows Fig. 1.

The molecular geometries

The initial molecular geometries were taken from molecular mechanics (PCMODEL with the MMFF94 force field)[26] and *ab initio* optimisations (GAUSSIAN98 at the RHF/6-31G, RHF/6-311G** and B3LYP/6-311G** levels and basis sets).[27]

A selection of the more important bond lengths (Å) and bond and dihedral angles (degrees) for **1**, **2** and **3** is given in the supplementary material. In both conformers of these compounds all the calculations give a planar carbon skeleton and the heavy atom dihedral angles are all 0 and 180°. In **1** in both conformers the methyl groups are oriented such that a proton of each methyl is coplanar (eclipsed) to the double bond. The distance between these protons is calculated as 2.10 Å (PCMODEL) or 2.19 Å (RHF/6-311G**). All the calculations give the *s-trans* form of **1** as much more stable than the *s-cis* form, the *s-trans* form of **2** as more stable but with a much smaller energy difference and the *s-cis* form of **3** more stable than the *s-trans*.

The geometries of the phenyl compounds **4**–**6** are very comparable to those of the corresponding **1**–**3** except for the phenyl group. The phenyl group is a regular hexagon; the C_3—$C_{1'}$ bond length is 1.470 ± 0.005 Å and the C_2—C_3—$C_{1'}$ angle equals $127.5 \pm 0.5°$. The phenyl group is also coplanar with the double bond in the *ab initio* geometries but makes a dihedral angle (C_2—C_3—$C_{1'}$—$C_{2'}$) of 36° with the C=C bond in the PCMODEL geometry. More complete data are given in Refs. [28] and [29]. NOE work[14] on **6** suggested the existence of conformations with the OMe anti to the CO group so we also took this possibility into account. However, these forms were found to be much less stable than the corresponding syn ones in all the calculations, (e.g. B3LYP/6-311G**: $\Delta E(\text{syn-anti})_{s\text{-}cis} = 9.0$ kcal/mol, $\Delta E(\text{syn-anti})_{s\text{-}trans} = 12.4$ kcal/mol) or even did not correspond to an energy minimum, as in the case of the *s-trans* form in the PCModel or RHF/6-31G calculations.

For **7** all the theoretical calculations gave the ester group in the favoured *cis* conformation with the C—O—C=O dihedral equal 0°. This leaves only the phenyl ring conformation to be obtained. The crystal structure was not planar with the phenyl dihedral angle of 45° and the C—O—C angle of 119°. The PCMODEL and MP2 geometries are similar with the corresponding angles

Table 1. ^{13}C and ^{1}H chemical shifts (δ), LIS values (ΔM) and diamagnetic shifts (ΔD) for compounds **1**, **2** and **3**

		CHO	C_2	C_3	C_4	2-CH_3	CHO	H_3	H_4	2-CH_3
1	δ^a	195.20	140.49	149.56	14.83	8.88	9.40	6.61	1.99	1.75
	ΔM^b	140.32	50.18	32.46	13.78	37.36	76.70	21.43	11.15	32.67
	ΔD^c	6.35	0.14	7.43	0.77	−0.46	−0.11	0.19	0.05	−0.05
		C_1	CO	C_3	C_4	H_1	H_3	H_{4n}	H_{4x}	
2	δ^a	26.27	198.95	137.38	128.97	2.26	6.31	6.16	5.88	
	ΔM^d	54.93	131.00	54.14	33.25	37.01	40.80	28.51	15.87	
	ΔD^e	−1.20	8.39	−1.23	5.04	0.19	0.27	0.32	0.24	
		CO	C_2	C_3	C_4	O$\underline{C}$H$_3$	H_2	H_3	H_4	OC$\underline{H}_3$
3	δ^a	167.23	122.76	144.96	18.21	51.60	5.85	6.98	1.88	3.72
	ΔM^f	138.57	58.52	37.94	9.94	47.98	36.57	33.62	6.12	35.75
	ΔD^g	5.14	−1.16	5.83	0.00	2.18	0.19	0.32	−0.09	0.16

[a] $[S]_0$ 0.5 M l^{-1}

[b] Yb(fod)$_3$ experiment: $\rho \times 10^{-2}$ 0.00, 1.87, 4.31, 9.64, corresponding coefficients > 0.9993.

[c] Lu(fod)$_3$ experiment: $\rho \times 10^{-2}$ 0.00, 4.02, 7.13, 10.49, corresponding coefficients > 0.9988.

[d] Yb(fod)$_3$ experiment: $\rho \times 10^{-2}$ 0.00, 4.39, 7.49, 13.74, corresponding coefficients > 0.9993.

[e] Lu(fod)$_3$ experiment: $\rho \times 10^{-2}$ 0.00, 3.79, 5.48, 8.88, corresponding coefficients > 0.9950.

[f] Yb(fod)$_3$ experiment: $\rho \times 10^{-2}$ 0.00, 2.65, 5.45, 8.13, 11.00, corresponding coefficients > 0.9998.

[g] Lu(fod)$_3$ experiment: $\rho \times 10^{-2}$ 0.00, 1.37, 2.72, 4.20, 5.72, corresponding coefficients > 0.9989.

Table 2. ^{13}C and ^{1}H chemical shifts (δ), LIS values (ΔM) and diamagnetic shifts (ΔD) for compounds **4**, **5**, **6** and **7**

		CO	C_2	C_3	$C_{1'}$	$C_{2'.6'}$	$C_{3'.5'}$	$C_{4'}$	$C\underline{H}O$	H_2	H_3	$H_{2'.6'}$	$H_{3'.5'}$	$H_{4'}$	
4	δ^a	193.66	128.59	152.75	133.99	128.49	129.10	131.27	9.70	6.71	7.48	7.56	7.44	7.44	
	ΔM^b	171.59	62.88	37.70	15.27	12.07	6.93	7.29	87.06	53.02	26.20	11.19	4.89	3.87	
	ΔD^c	6.71	−1.02	6.47	0.0	1.12	0.51	1.66	0.0	0.0	0.0	0.0	0.0	0.0	
		C_1	CO	C_3	C_4	$C_{1'}$	$C_{2'.6'}$	$C_{3'.5'}$	$C_{4'}$	H_1	H_3	H_4	$H_{2'.6'}$	$H_{3'.5'}$	$H_{4'}$
5	δ^a	27.50	198.29	127.16	143.39	134.44	128.25	128.97	130.50	2.38	6.71	7.51	7.54	7.39	7.39
	ΔM^d	71.61	170.92	69.99	47.25	16.61	11.72	6.25	6.51	47.24	50.60	42.52	10.01	3.70	3.01
	ΔD^e	−0.31	8.29	−1.21	6.27	−0.44	1.12	0.42	1.63	0.0	0.0	0.25	0.0	0.0	0.0
		CO	C_2	C_3	$C_{1'}$	$C_{2'.6'}$	$C_{3'.5'}$	$C_{4'}$	$O\underline{C}H_3$	H_2	H_3	$H_{2'.6'}$	$H_{3'.5'}$	$H_{4'}$	$OC\underline{H}_3$
6	δ^a	167.31	117.81	144.78	134.38	128.00	128.83	130.21	51.58	6.44	7.69	7.51	7.37	7.37	3.80
	ΔM^f	135.69	56.26	34.52	9.21	4.97	1.63	2.08	48.20	36.00	31.55	3.48	0.67	0.67	36.06
	ΔD^g	4.90	−1.59	4.10	−0.49	0.56	0.10	0.96	2.18	0.14	0.15	0.0	0.0	0.0	0.17
		$\underline{C}H_3$	CO	C_1	$C_{2,6}$	$C_{3,5}$	C_4	$C\underline{H}_3$	$H_{2,6}$	$H_{3,5}$	H_4				
7	δ^a	21.10	169.45	150.77	121.57	129.42	125.82	2.27	7.08	7.36	7.21				
	ΔM^h	59.28	144.55	44.82	27.34	11.05	8.28	36.16	26.62	4.19	2.62				
	ΔD^i	−0.31	6.00	−0.31	−0.42	0.12	0.71	0.0	0.0	0.0	0.0				

[a] $[S]_0$ 0.5 Ml^{-1}.
[b] $Yb(fod)_3$ experiment: $\rho \times 10^{-2}$ 0.00, 4.18, 7.17, 10.84, corresponding coefficients > 0.9996.
[c] $Lu(fod)_3$ experiment: $\rho \times 10^{-2}$ 0.00, 2.90, 5.30, 11.85, corresponding coefficients > 0.9975.
[d] $Yb(fod)_3$ experiment: $\rho \times 10^{-2}$ 0.00, 1.85, 5.39, 10.33, corresponding coefficients > 0.9996.
[e] $Lu(fod)_3$ experiment: $\rho \times 10^{-2}$ 0.00, 3.80, 5.84, 9.84, corresponding coefficients > 0.9966.
[f] $Yb(fod)_3$ experiment: $\rho \times 10^{-2}$ 0.00, 5.46, 8.85, 13.77; corresponding coefficients > 0.9995.
[g] $Lu(fod)_3$ experiment: $\rho \times 10^{-2}$ 0.00, 3.65, 7.53, 11.93, corresponding coefficients > 0.9990.
[h] $Yb(fod)_3$ experiment: $\rho \times 10^{-2}$ 0.00, 1.66, 3.33, 4.77; corresponding coefficients > 0.9996.
[i] $Lu(fod)_3$ experiment: $\rho \times 10^{-2}$ 0.00, 1.42, 3.09, 4.49, corresponding coefficients > 0.9990.

58° and 116° (PCMODEL) and 42° and 117° (MP2). The B3LYP minimisation produced two geometries. The higher energy one was a flat geometry having the ester group in the plane of the phenyl ring. The lower energy conformer has the ester group out of the plane by 64° and a C—O—C angle of 120°. The energy difference between the two conformers was only 0.16 kcal/mol.

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 conformational equilibria, that is the ratio of the *s-cis* and *s-trans* forms in these compounds. For the ketones studied previously any solution (observed minus calculated shifts) with an agreement factor (R_x) ≤ 1.0% (i.e. 0.01) and with all calculated LIS within 1.0 ppm of the observed shifts was regarded as an acceptable solution.[16] The compounds considered here have similar LIS thus this limit may be adopted here.

Tiglic aldehyde 1

The analysis of the observed LIS was carried out using the LISA3 program incorporating the two-site or four-site coordination model. These give the same answer for a planar molecule thus as all the heavy atoms are in one plane and the out-of-plane hydrogens are rapidly interconverting their positions they give identical answers here. None of the geometries gives an acceptable answer for the *s-cis* form ($R_x > 10.0$) and only one of the *ab initio* geometries a barely acceptable answer for the *s-trans* form. However, when a combined *z*-matrix is constructed involving proportions of both forms the answers are very different. In every case excellent agreement was obtained for a large majority of the *s-trans* form (Table 3). The percentage of *s-trans* for the best agreement is 89% (PCMODEL) and 92, 95 and 95% for the three *ab initio* geometries. We conclude that **1** is largely in the *s-trans* form in solution with 6 ± 1.5% of the *s-cis* form, which corresponds to an energy difference of 1.64 ± 0.1 kcal/mol.

Methyl vinyl ketone 2

For **2** as for **1** the two-site and four-site models of LISA3 give identical answers. Analysis of the LIS with LISA3 showed again that no geometry gave an acceptable solution for either the *s-cis* or *s-trans* form. When they were combined the answers were much better. The LIS analysis is illustrated in Fig. 3a. All the geometries gave excellent agreement for 59–60% *s-trans* (Table 3), corresponding to an energy difference (*s-cis*–*s-trans*) of 0.24 kcal/mol.

Table 3. LISA3 analysis of compounds **1**, **2** and **3**

Compound	Method	Percentage of *s-trans*	R_x(%)	R (Å)	ϕ (°)	ψ (°)[a]	Population (%)[b]	f[c]
1	PCMODEL	89	0.465	2.70	72	121	100	0.85
	RHF/6-31G	92	0.448	2.60	80	123	100	0.90
	RHF/6-311G**	95	0.399	2.61	83	125	100	0.85
	B3LYP/6-311G**	95	0.485	2.70	70	124	100	0.95
2	PCMODEL	60	0.508	2.89	61	140	25	0.65
	RHF/6-31G	59	0.326	2.84	62	142	26	0.65
	RHF/6-311G**	59	0.113	2.84	67	142	26	0.60
	B3LYP/6-311G**	59	0.552	2.83	69	143	29	0.65
3	PCMODEL	24	0.320	2.58	66	167	15	0.60
	RHF/6-31G	21	0.443	2.51	80	168	1	0.65
	RHF/6-311G**	23	0.429	2.57	88	161	28	0.60
	B3LYP/6-311G**	23	0.400	2.60	79	160	29	0.65

[a] two-site model.
[b] Percentage of population anti to the C=C bond.
[c] Diamagnetic normalising factor.

Methyl crotonate 3

In this case there are in principle four possible conformers as the ester methyl group can be either *cis* or *anti* to the carbonyl group. We have shown earlier that all the calculations give the *cis* orientation to be much more stable than the *anti*. This is observed experimentally unless there are large steric interactions involved (e.g. *t*-butyl acetate).[30] We will therefore not consider the *anti* methyl conformer henceforth. With this resolved the conformational analysis of this compound was virtually identical to that of **2** above, with a planar heavy atom skeleton for both conformers and the hydrogens symmetrical about this plane. Analysis of the LIS with LISA3 showed again that no geometry gave an acceptable solution for either the *s-cis* or *s-trans* form. When they were combined the solutions were much better. The best agreement was for 24% *s-trans* (PCMODEL) and 21, 23 and 23% for the *ab initio* geometries all with excellent R_x (Table 3 and Fig. 3b). The results are consistent with 23% of the *s-trans* form corresponding to an energy difference (*s-cis–s-trans*) of −0.72 kcal/mol. Noteworthy in Fig. 3a,b is the sharp definition of the minima, giving very accurate results.

trans Cinnamaldehyde 4

The *s-trans* form gave an unacceptable agreement for the PCMODEL geometry ($R_x = 1.189$) but acceptable values of 0.642 and 0.440 and 0.678 for the *ab initio* geometries. Much better agreement was obtained when small amounts of the *s-cis* conformer were included in the *z*-matrix. The agreement factors and lanthanide coordination

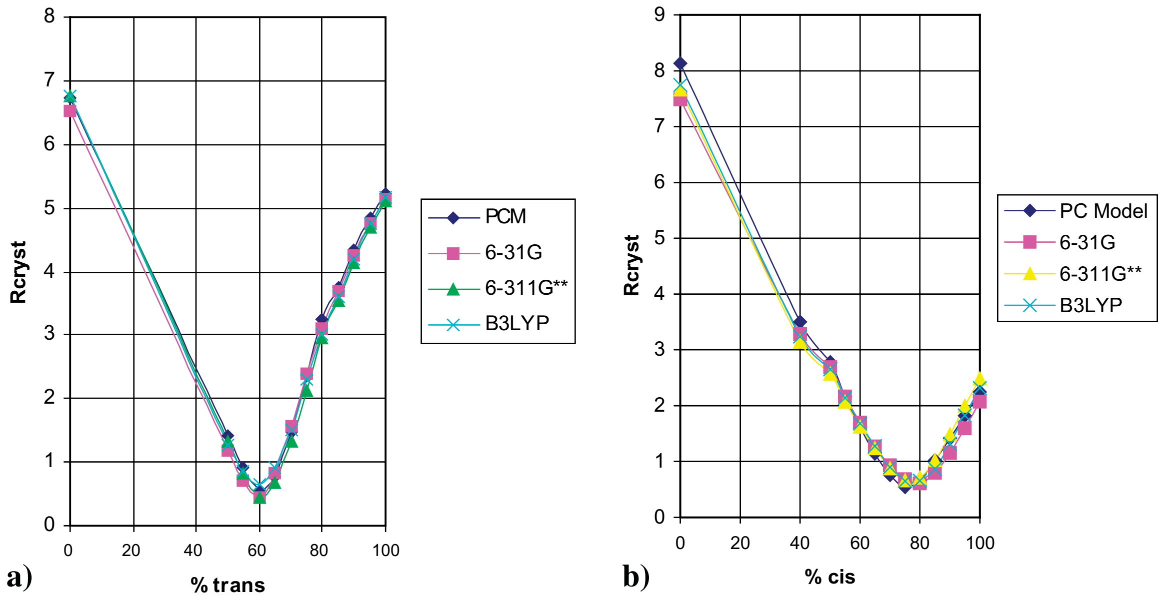


Figure 3. (a) R_x vs. percentage of the *s-trans* form in **2** and (b) R_x vs. percentage of the *s-cis* form in **3**. [This figure is available in colour online at www.interscience.wiley.com]

Table 4. LISA3 analysis of compounds **4**, **5**, **6** and **7**

Compound	Method	Percentage of *trans*	R_x (%)	R (Å)	ϕ (°)	ψ (°)[a]	Population (%)[b]	f[c]
4	PCMODEL	90	0.452	2.56	50	139	100	1.00
	RHF/6-31G	94	0.375	2.37	55	149	100	1.00
	RHF/6-311G**	98	0.376	2.40	55	154	100	1.00
	B3LYP/6-311G**	94	0.436	2.50	53	145	100	1.00
5	PCMODEL	50	0.558	2.87	60	141	20	0.95
	RHF/6-31G	50	0.862	2.73	70	145	22	1.00
	RHF/6-311G**	51	0.826	2.65	78	150	24	0.95
	B3LYP/6-311G**	51	1.011	2.61	82	151	25	0.95
6	PCMODEL	29	0.559	2.56	63	164	28	0.55
	RHF/6-31G	30	0.642	2.43	77	168	13	0.55
	RHF/6-311G**	36	0.913	2.47	76	167	16	0.65
	B3LYP/6-311G**	30	0.697	2.45	101	168	13	0.60
		GEOM					Population (%)[g]	
7	Crystal	54[d], 121[e]	0.427	3.30	24	134	100	0.45
	PCMODEL	54[d], 118[e]	0.740	2.78	50	145	96	0.15
	MP2/6-31G**	56[d], 117[e]	0.748	3.22	26	134	100	0.50
	B3LYP/6-311G**[f]	59[d], 117[e]	0.728	3.24	26	136	100	0.80

[a] two-site model.
[b] Percentage of population anti to the C=C bond.
[c] Diamagnetic normalising factor.
[d] Phenyl dihedral angle.
[e] C–O–C angle.
[f] On-planar geometry.
[g] The percentage of population is anti to the ester oxygen.

geometries for these solutions are given in Table 4. The best agreement was for 10% *s-cis* (PCMODEL) and 6, 2 and 6% for the *ab initio* geometries. Thus **4** is mainly in the *s-trans* form in solution with ca 6% of the *s-cis* form, corresponding to an energy difference of 1.76 kcal/mol.

trans-Cinnamyl methyl ketone 5

Neither of the pure conformers gave acceptable agreement in the analysis with R_x values of ca 6% in all cases. Again a combined *z*-matrix gave much better results. The best agreement for all the geometries considered was for 50:50% of the two conformers. The agreement factors (R_x) and lanthanide coordination geometries are given in Table 4.

trans Methyl cinnamate 6

The LISA analysis of **6** proceeded in similar fashion to that of methyl crotonate **3**. The conformers with the O-methyl *anti* to the carbonyl group may be ignored for the same reasons as in **3**. Using only the *s-cis* and *s-trans* geometries gives again poor agreement in the LISA analysis for all the geometries considered. Varying the *s-trans*/*s-cis* ratio gave better agreement with the best agreement for 61–65% *s-cis* form but the R_x values were still *ca*. 1.3–2.4% well above the recommended limit (1%). In previous LIS investigations on esters[19] the ether oxygen bond angle (C—O—C) was observed to be very flexible. In the calculated geometries the angle varies from 114° (PCMODEL) to 121° (6-31G) (also see **7** below) and an attempt was made to see if changing this angle would give any better agreement. Reducing the angle to 110° (PCMODEL) and 113° (*ab initio*) gave better agreement, but this was still not good enough for the *ab initio* geometries. When the methyl and phenyl orientation in the *ab initio* geometries were altered to agree with the PCMODEL geometry (methyl staggered to CO and phenyl 34° out of the molecular plane) all the geometries gave good agreement (Table 4). From the values in Table 4 the percentage of *s-trans* is 32 ± 2% which corresponds to an energy difference (*s-cis*–*s-trans*) of −0.41 ± 0.05 kcal/mol.

Phenyl acetate 7

The conformation of this compound was required for an investigation of the effect of the ester group on ^{1}H NMR chemical shifts.[31] The conformation is unknown in solution and the theoretical calculations did not give an unambiguous geometry. The only unknown parameters are the conformation of the ester group and the dihedral angle made with the phenyl group. Thus two dihedral angles need to be determined, the C—O—C=O and C_{ortho}—C_1—O—C angles.

Some of the geometries of phenyl acetate produced were not planar. For example carbons C1 and C4 of the phenyl ring are not exactly in the plane of the ester group. For this reason the four-site model of LISA3 was preferred to the two-site model. It is also chemically more reasonable and also gave much better and more consistent results. The LISA3 analysis with the observed LIS gave very different results for the different geometries used. R_x varied from *ca*. 1.0 for the crystal, PCMODEL and MP2 geometries to 1.46 for the non-planar B3LYP geometry and a quite unacceptable value of 8.7 for the flat B3LYP geometry. An iterative search was then performed varying both the phenyl dihedral angle and the C—O—C bond angle (see above) for the calculated geometries. These results are given in Table 4 together with the coordination geometries.

All the LIS analyses iterated to give good agreement except for the flat B3LYP geometry which even after optimising the C—O—C angle still gave a totally unacceptable agreement factor. This shows conclusively that the flat geometry is unacceptable. Note also that the final geometries when optimised through LISA give consistent values of both the C—O—C angle (*ca*. 118°) and the phenyl dihedral angle (55°). The optimised structures are also very similar to the crystal structure except that the phenyl ring dihedral angle increases from 45° in the crystal to *ca*. 55° in solution. This difference could well be due to crystal packing forces. These results show clearly that the conformation of phenyl acetate in solution is similar to the conformation in the crystal with the ester group out of the phenyl ring plane. The lanthanide coordination geometries given in Table 4 are of interest in that the coordinates for the PCMODEL geometry are quite different from those of the other geometries. This may be due to the very different geometry of the ester group in the PCMODEL structure. The O═C—O angle is 127° cf 122° in the crystal and this may be the reason.

DISCUSSION

The observed and calculated conformer energies are given in Table 5 and are of some interest. Wiberg *et al.*[32] examined the source of the conjugation in butadiene and acrolein and concluded that the description of π-electron system given by the simple Huckel approach is essentially correct. They did not consider conformer energies as there was insufficient data available at that time to compare with the theoretical calculations. The conformer energies obtained here are in good agreement with those reported earlier for **1**,**2**,**3** and **5**. The conformer energies calculated by PCMODEL are also in good agreement with those obtained here, the only exception being (**1**) in which the calculated value is rather high and this is also the case for the *ab initio* calculated energies for (**1**). The *ab initio* calculated energies are also in good agreement with the observed data for all the compounds except methyl cinnamyl ketone (**5**) in which the calculations give the *s-cis* form as more stable than the *s-trans* form by 0.9–1.3 kcal/mol whereas PCMODEL gives equal energies for the two forms in agreement with the observed data. Thus for this set of molecules the MM program PCMODEL gives as reliable conformer energies as any of the three *ab initio* calculations used. An intriguing trend in the MM and *ab initio* calculations is that the introduction of the phenyl group in the ketone (**2** vs. **5**) stabilises the *s-cis* form by *ca*. 1–2 kcal/mol. but this does not occur in the ester (**3** vs. **6**). This is not shown in the observed data, in which the introduction of the phenyl group in both molecules has very little effect on the conformer energies.

The lanthanide complexation geometries and crystallographic agreement factors R_x for the best solutions for compounds (**1**)–(**4**) are given in Tables 3 and 4. We note that the lanthanide population is as expected almost entirely anti to the double bond in the aldehydes and ketones but anti to the ester oxygen in all the esters. In phenyl acetate the lanthanide population is also anti to the

Table 5. Observed versus calculated energy differences (*s-cis–s-trans*) for the compounds investigated

	Energy differences (*s-cis–s-trans*), kcal/mol					
					Experimental	
Compound	PCMODEL	RHF/6-31G	RHF/6-311G**	B3LYP/6-311G**	LISA	Other
1	3.10	2.54	3.25	3.07	1.64	1.31[a]
2	0.64	0.58	0.31	0.85	0.24	0.59[a], 0.80[b]
3	−0.64	−0.65	−0.70	−0.85	−0.72	−0.33[c], −0.41[d]
4	1.80	0.85	1.40	1.21	1.76	
5	−0.11	−1.34	−0.92	−1.00	0.0	0.17[e]
6	−0.88	−0.75	−0.81	−0.97	−0.41	

[a] Ref. 5,
[b] Ref. 6,
[c] Ref. 10,
[d] Ref. 11,
[e] Ref. 13.

ester oxygen but the y-axis has been reversed in this analysis.

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REFERENCES

1. part 40, Abraham RJ, Koniotou R, *Magn. Reson. Chem.*, 2003; **41**: 1000.
2. Liljefors T, Allinger N. *J. Am. Chem. Soc*. 1976; **98**: 2745.
3. Carreira LA. Personal comm., quoted in Ref 2.
4. Wiberg KB, Rosenberg RE, Rablen PR. *J. Am. Chem. Soc*. 1991; **113**: 2890.
5. Montaudo G, Librando V, Caccamese S, Maravigna P. *J. Am. Chem Soc*. 1973; **95**: 6365.
6. Durig JR, Little TS. *J. Chem. Phys*. 1981; **75**: 3660.
7. Olelichmann HJ, Bougeard D, Schrader B, *J. Mol. Struct*. 1981; **77**: 179.
8. Foster PD, Rao VM, Curl RF, Jr. *J. Chem. Phys*. 1965; **43**: 1064.
9. Garcia JI, Mayeral JA, Salvatina AL, Assfeld X, Ruiz-Lopez MF, *J. Mol. Sruct. (theochem)* 1996; **362**: 187.
10. George WO, Hassid DV, Maddams WF. *J. Chem. Soc., Perkin Trans. 2* 1972; 400.
11. Egawa T, Maekawa S, Fujiwara HF, Takeuchi H, Konaka S. *J. Mol. Struct*. 1995; **353**: 193.
12. (a) Savin VI, Temyachev ID, Kitaev YP. *J. Org. Chem. USSR (Eng. Transl)*. 1974; **10**: 1605; (b) Savin VI, Kitaev YP, Saidashev II. *Izv. Acad. Nauk. SSSR, Ser. Khim*. 1972; 851.
13. Hayes WP, Timmons CJ. *Spect. Acta, Pt A* 1968; **24**: 323.
14. Shida N, Kabuto C, Niwa T, Ebata T, Yamamoto Y. *J. Org. Chem*. 1994; **59**: 4068.
15. Gavuzzo E, Mazza EF, Giglio E. *Acta Cryst., Sect B* 1974; **30**: 1351.
16. Abraham RJ, Sancassan F. *Encyclopedia of NMR* **vol. 9**, Grant DM, & Harris RK (eds). J. Wiley & Sons: NY. 2002; 578–588.
17. Abraham RJ, Castellazzi I, Sancassan F, Smith TAD. *J. Chem. Soc. Perkin Trans 2* 1999; 99.
18. Abraham RJ, Ghersi A, Petrillo G, Sancassan F. *J. Chem. Soc. Perkin Trans 2* 1997; 1279.
19. Abraham RJ, Angiolini S, Edgar M, Sancassan F. *J. Chem. Soc. Perkin Trans 2* 1995; 1973.
20. Sancassan F, Petrillo G, Abraham RJ. *J. Chem. Soc. Perkin Trans 2* 1995; 1965.
21. (a) Abraham RJ, Pollock L, Sancassan F. *J. Chem. Soc. Perkin Trans 2* 1994; 2329; (b) Abraham RJ, Haworth IS. *Magn. Reson. Chem*. 1988; **26**: 252.
22. Wiberg KB, Marquez M, Castejon H. *J. Org. Chem*. 1994; **59**: 6817.
23. Peters JA, Schuyl PJW, Knol-Kalkman AR. *Tet Lett*. 1982; **23**: 4497.
24. Springer CS, Jr., Meek DW, Sievers RE. *Inorg. Chem*. 1967; **6**: 1105.
25. (a) Iwata M, Emoto S. *Bull. Chem. Soc. Japan* 1976; **49**: 1369; (b) Miyata O, Shimada T, Ninomiya I, Naito T. *Synthesis* 1990; 1123; (c) Lewis FD, Oxman JD, Gibson LL, Hampsch HL, Quillen SL. *J. Am. Chem. Soc*. 1986; **108**: 3005.
26. PC Model Version 7.0 Serena Software, Box 3076, Bloomington, In, USA, 1998.
27. GAUSSIAN 98, Revision.A9, Gaussian Inc., Pittsburgh PA, 1998. Frisch MJ, Trucks CW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Zakrzewski VG, Montgomery JA, Stratmann RE, Burant JC, Dapprich S, Millam JM, Daniels AD, Kudin KN, Strain MC, Farkas O, Tomasi J, Barone V, Cossi M, Cammi R, Mennucci B, Pomelli C, Adamo C, Clifford S, Ochterski J, Petersson GA, Ayala PY, Cui Q, Morokuma K, Malick DK, Rabuck AD, Raghavachavi K, Foresman JB, Ciolowski J, Ortiz JV, Baboul AG, Stefanov BB, Liu G, Liashenko A, Piskorz P, Komaromi I, Gomperts R, Martin RL, Fox DJ, Keith T, Al-Laham MA, Peng CY, Nanayakkara A, Gonzalez C, Challacombe M, Gill PMW, Johnson BG, Chen W, Wong MW, Andres JL, Head-Gordon M, Replogle ES, Pople JA.
28. Ratti J, Tesi di Laurea, University of Genova, 2004.
29. Smith TAD. Ph.D. Thesis, University of Liverpool, 1997.
30. Pawar DM, Khalil AA, Hooks DR, Collins K, Elliott T, Stafford J, Smith L, Noe EA. *J. Am. Chem. Soc*. 1998; **120**: 2108.
31. Abraham RJ, Bardsley B, Mobli M, Smith RJ. *Magn. Reson. Chem*. 2005; **43**: 3.
32. Wiberg KB, Rosenberg RE, Rablen PR. *J. Am. Chem. Soc*. 1991; **113**: 2890.
33. Foresman JB, Frisch A. *Exploring Chemistry with Electronic Structure Methods*, (2nd edn). Gaussian inc.: Pittsburgh, 2003.
34. (a) Tomasi J, Persico M. *Chem. Rev*. 1994; **94**: 2027; (b) Tomasi J, Mennucci B, Cammi R. *Chem. Rev*. 2005; **105**: 1999.
35. Abraham RJ, Byrne JJ, Griffiths L, Perez M. *Magn. Reson. Chem*. 2006; **44**: 491–509.
36. Yoshinaga F, Tormena CF, Freitas MP, Rittner R, Abraham RJ. *J. Chem. Soc., Perkin Trans 2* 2002; 1494.