

## Conformational Analysis. Part 6.<sup>1</sup> A Lanthanide-induced Shift Nuclear Magnetic Resonance Investigation of Steric Effects in Mesitaldehyde and 2,4,6-Trimethylacetophenone

Raymond J. Abraham,\* Helen A. Bergen, and Derek J. Chadwick  
The Robert Robinson Laboratories, Liverpool University, P.O. Box 147, Liverpool L69 3BX

A lanthanide-induced shift (L.I.S.) n.m.r. investigation of the structures in solution of mesitaldehyde (1) and 2,4,6-trimethylacetophenone (2) has been performed. The use of the crystal structure geometry of the mesitaldehyde-perchloric acid complex was unsatisfactory and no reasonable fit to the L.I.S. data was achieved. In contrast, use of a model geometry in which steric relaxation (of the methyl groups) was allowed gave good agreement. The formyl group is co-planar with the benzene ring, but the CCC angles to the adjacent methyl groups are increased (to 126°) to relieve steric interactions. In contrast, in (2) the acetyl group has a dihedral of 60–90° with the aromatic ring whilst the methyl CCC angles are unaffected. The lanthanum(III) diamagnetic complexation shifts further illustrate the lack of conjugation of the carbonyl group with the aromatic ring in (2) compared with (1).

In previous parts of this series,<sup>1,2</sup> we have shown that by the simultaneous use of <sup>1</sup>H and <sup>13</sup>C L.I.S.s, with the <sup>13</sup>C diamagnetic complexation shifts removed by use of La(fod)<sub>3</sub> and a chemically appropriate model for the lanthanide ion binding, the L.I.S. technique can be quantitatively applied to the determination of conformer isomerism and structures in aromatic aldehydes and ketones. This includes 2- and 3-formyl-furan and -thiophene, benzaldehyde and a substituted derivative, and acetophenone.

In all of these molecules steric effects between the carbonyl moiety and the remainder of the molecule are minimal, and thus the carbonyl group and the aromatic rings are co-planar. It was thought of some interest to extend this technique to related sterically crowded compounds to see whether the L.I.S. technique could determine their structures in solution, and to this end we report here the analyses of the L.I.S. of mesitaldehyde (1) and 2,4,6-trimethylacetophenone (2).

In these compounds the repulsive interactions between the *ortho*-methyl groups and the formyl (or acetyl) substituent may be relieved either by rotation of the carbonyl group out of the aromatic plane and/or by relaxing the CCC bond angles at the methyl groups. However, there has been little quantitative study of such interactions to date. The only crystal structures available for comparable compounds are those of the mesitaldehyde-perchloric acid complex<sup>3</sup> and of mesitoic acid.<sup>4</sup> In the former the aldehyde group is presumably co-planar with the aromatic ring (this is not stated explicitly in the paper), but the methyl CCC angles are considerably relaxed (126°). This analysis is complicated by the presence of two crystallographically non-equivalent molecules in the unit cell, with apparently very different bond lengths and bond angles.

Mesitoic acid in the crystal has a dihedral angle of 48° between the mesityl and carbonyl groups with less deformation of the adjacent methyl groups (CCC angles 123°).

2-Methylbenzaldehyde has been shown to have two almost equally populated conformers by low-temperature n.m.r.,<sup>5,6</sup> and Benassi *et al.*,<sup>7</sup> from L.I.S. studies and *ab initio* calculations concluded that in both conformers the formyl group is co-planar to the aromatic ring. These investigations used Eu(fod)<sub>3</sub> and thus only the <sup>1</sup>H L.I.S. could be used in their calculations; the system was in consequence not very well determined. Perhaps for this reason in the more critical case of anthracene-9-carbaldehyde they could not distinguish between two (identical) co-planar conformers and the orthogonal one.

In the *ortho*-substituted compounds, there is some discrepancy between the results of <sup>13</sup>C studies that indicate considerable out-of-plane twisting of the acetyl group in 2-methyl- and 2-methoxy-acetophenone,<sup>8</sup> and <sup>17</sup>O n.m.r.<sup>9</sup> results and crystallographic<sup>10</sup> data on *ortho*-substituted benzoic acids, which suggest much smaller angles of twist (<10° in the solid). A recent <sup>13</sup>C investigation of substituent effects in 2-methyl-, 2-methoxy-, and 2,6-dimethyl-acetophenone<sup>11</sup> shows clearly the very different effects in the 2,6-dimethyl compound, indicating essentially no conjugation in the last case, but variable effects in the former. In a preliminary communication<sup>12</sup> we have suggested the use of diamagnetic lanthanum shifts ( $\Delta D$  values) as a sensitive probe of  $\pi$ -electron delocalisation in these molecules and the  $\Delta D$  values also indicate much less conjugation in the ketone (2) than the aldehyde (1) (*vide infra*).

### Results

The pseudo-contact shifts given in Tables 1 and 2, corrected for the effects of complex formation ( $\Delta M - \Delta D$ ), have been used along with the program LIRAS-3 (described previously)<sup>2</sup> to obtain the required conformational information. As we have repeatedly stressed, in all such studies the major problem is the necessity for an overdetermined set of equations. We use the model derived previously<sup>2</sup> of four-site lanthanide ion complexation in which the lanthanide position is reflected in the *xy* and *yz* planes. (This is equivalent, of course, to the two-site model for a planar substrate.) Furthermore, the percentage population of the lanthanide ion *cis* and *trans* to the phenyl group is allowed to vary. Thus, five unknowns need to be determined to fix the lanthanide complexation (one normalisation factor, three lanthanide ion co-ordinates, and the percentage population).

The additional information required is the substituent torsional angle ( $\theta$ ) and the CCC bond angles ( $\alpha_{2,6}$ ) of the abutting methyl groups, making a total of seven unknowns in each case. (In mesitaldehyde this could be reduced to six unknowns, as all previous studies have shown that the lanthanide atom is exclusively *exo*, *i.e.*, towards the aldehyde proton.) In each molecule sufficient  $\Delta M - \Delta D$  values have been obtained to make the system overdetermined (11 and 12, respectively). However, as a number of the nuclei measured lie along the symmetry axis of the benzene ring, and thus their pseudo-contact shifts are unaffected by variations of either

**Table 1.** Observed shifts ( $\delta$ ), L.I.S. ( $\Delta M$ ), diamagnetic shifts ( $\Delta D$ ), and pseudo-contact shifts ( $\Delta M - \Delta D$ ) (p.p.m.) for mesitaldehyde

$\rho$	C=O	C(1)	C(2),(6)	C(3),(5)	C(4)	2-,6-Me	4-Me
0.0	193.10	130.20	141.62	130.68	143.97	20.65	21.60
0.0707	203.55	133.78	144.23	131.93	145.26	22.66	22.17
0.1219	210.75	136.34	146.05	132.83	146.05	24.06	22.54
0.1631	216.63	138.35	147.44	133.48	146.82	25.16	22.83
0.2058	222.59	140.38	148.91	134.17	147.52	26.26	23.14
Intercept	193.23	130.24	141.67	130.71	143.99	20.69	21.62
$\Delta M^a$	143.15	49.53	35.40	16.97	17.20	27.28	7.45
$\Delta D^b$	7.94	-2.45	4.80	0.44	4.39	0.0	0.24
$\Delta M - \Delta D$	135.21	51.98	30.60	16.53	12.81	27.28	7.21

$\rho$	CHO	3-,5-H	2-,6-Me	4-Me
0.0	9.857	6.883	2.566	2.305
0.0707	16.157	7.763	4.405	2.816
0.1219	20.099	8.376	5.685	3.174
0.1631	23.333	8.864	6.711	3.457
0.2058	26.568	9.356	7.745	3.742
Intercept	10.11	6.90	2.59	2.31
$\Delta M$	80.88	12.02	25.17	6.99

<sup>a</sup>  $S_0 = 0.720 \text{ ml}^{-1}$ , all correlation coefficients  $> 0.9994$ . <sup>b</sup>  $S_0 = 0.646 \text{ ml}^{-1}$  from four additions of  $\text{La}(\text{fod})_3$ ,  $\rho$  7.44, 14.37, 19.67, and 25.98  $\times 10^{-2}$ .

**Table 2.** Observed shifts ( $\delta$ ), L.I.S. ( $\Delta M$ ), diamagnetic shifts ( $\Delta D$ ), and pseudo-contact shifts ( $\Delta M - \Delta D$ ) (p.p.m.) for 2,4,6-trimethylacetophenone

$\rho$	C=O	C(1)	C(2),(6)	C(3),(5)	C(4)	2-,6-Me	4-Me	$\text{COCH}_3$
0.0	208.69	140.13	132.46	128.70	138.50	19.26	21.19	32.37
0.0372	212.85	141.77	133.54	129.24	138.97	20.10	21.38	34.02
0.0912	218.34	143.89	134.94	129.97	139.59	21.16	21.66	36.25
0.1410	222.83	145.66	136.11	130.53	140.13	22.05	21.90	38.04
0.1878	226.84	147.28	137.19	131.07	140.60	22.83	22.08	39.67
Intercept	209.11	140.29	132.56	128.76	138.54	19.35	21.20	32.53
$\Delta M^a$	96.28	37.84	25.03	12.54	11.15	18.90	4.79	38.74
$\Delta D^b$	11.09	-2.25	1.19	0.0	1.05	-0.47	-0.40	-0.26
$\Delta M - \Delta D$	85.19	40.09	23.84	12.54	10.10	19.37	5.19	39.0

$\rho$	$\text{COCH}_3$	4-H	2-,6-Me	4-Me
0.0	2.445	6.826	2.209	2.265
0.0372	3.471	7.191	2.933	2.468
0.0912	4.844	7.679	3.903	2.734
0.1410	5.993	8.090	4.717	2.958
0.1878	7.008	8.452	5.437	3.154
Intercept	2.54	6.86	2.27	2.28
$\Delta M$	24.24	8.64	17.15	4.72

<sup>a</sup>  $S_0 = 0.741 \text{ ml}^{-1}$ , all correlation coefficients  $> 0.9985$ . <sup>b</sup>  $S_0 = 0.815 \text{ ml}^{-1}$  from four additions of  $\text{La}(\text{fod})_3$ ,  $\rho$  6.39, 11.29, 16.36, and 22.06  $\times 10^{-2}$ .

$\theta$  or  $\alpha_{2,6}$ , the data set for both molecules is not very overdetermined. This presented some difficulties in our analyses.

**Mesitaldehyde.**—Initially the geometry of the mesitaldehyde-perchloric acid crystal structure<sup>3</sup> was used. However, both the geometries of the different molecules comprising the unit cell gave unsatisfactory results and this approach was abandoned. Instead the benzaldehyde geometry described earlier<sup>2</sup> was used with the addition of standard methyl groups (C-C 1.51 Å, C-H 1.09 Å, CCH 109.47°).

The analysis proceeded by varying continuously both the CCC bond angles ( $\alpha_{2,6}$ ) and the dihedral angle ( $\theta$ ) between the carbonyl and the ring plane until the agreement factor ( $R_x$ ) was at a minimum value for both the variables. The global

minimum was obtained for values of  $\alpha_{2,6}$  equal to 126° and  $\theta$  of 0–20° and Figure 1 illustrates the separate dependence of  $R_x$  on these parameters at the global minimum. When only one bond angle ( $\alpha_2$  *cis* to the carbonyl oxygen) was varied, the results were similar to those shown in Figure 1,  $\alpha_2$  minimised at 126° with  $\alpha_6$  at 120°. This apparent anomaly is resolved when it is realised that owing to rapid rotation of the formyl group about the C(1)–CHO bond, the observed pseudo-contact shifts of the nuclei in the 2,6- and 3,5-positions on the benzene ring are the averages over the two separate positions. Essentially the agreement factor is not sensitive to variations of  $\alpha_6$ , as this methyl is both well removed from the lanthanide atom and also the C–C bond is almost orthogonal to the lanthanum-nuclei vector. The averaging process merely tends

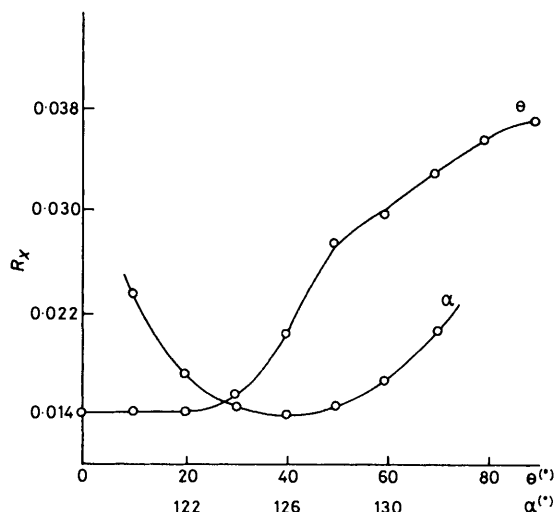
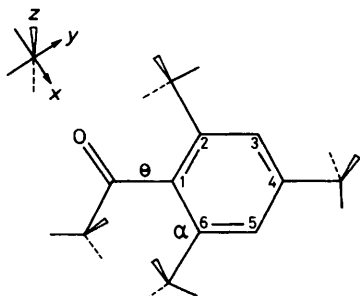


Figure 1. The agreement factor ( $R_x$ ) versus the carbonyl dihedral angle ( $\theta$ ) and the C(2),(6) CCC angles ( $\alpha$ ) in mesitaldehyde



Scheme. Conformations of mesitaldehyde (1) and 2,4,6-trimethylacetophenone (2) used in the L.I.S. analysis

to obscure the separate dependencies of the 2- and 6-methyl groups.

The plots of Figure 1 are given for the methyl-group orientations in which one CH hydrogen on the 2-methyl eclipses the carbonyl group and the 6-methyl is staggered with respect to the formyl hydrogen (Scheme). Two other possible orientations of the methyl groups were considered, one in which both methyl groups were staggered with respect to the formyl substituent and the other in which one hydrogen in each methyl was orthogonal to the aromatic ring. In the first case the results were similar to those of Figure 1. However, in the second case no reasonable minimum with respect to either  $\alpha$  or  $\theta$  could be obtained. This illustrates the sensitivity of the L.I.S. technique to the precise conformation of groups near to the complexing site.

The lanthanide positions at the minimum ( $r$  2.65 Å,  $\phi$  70°,  $\psi$  120°, population 100%) are unremarkable and very similar to those obtained previously for aromatic aldehydes.<sup>1,2</sup>

**2,4,6-Trimethylacetophenone.**—Initially the geometry used was adapted from the crystal structure of mesitoic acid.<sup>4</sup> However, this also gave anomalous results and instead the acetophenone geometry described previously<sup>1</sup> was used with again the addition of standard methyl groups at the 2-, 4-, and 6-positions. The analysis proceeded similarly by first varying the dihedral angle ( $\theta$ ) between the acetyl and the benzene ring with the methyl groups oriented as shown in the Scheme, *i.e.*, the acetyl methyl has a hydrogen eclipsed by the carbonyl

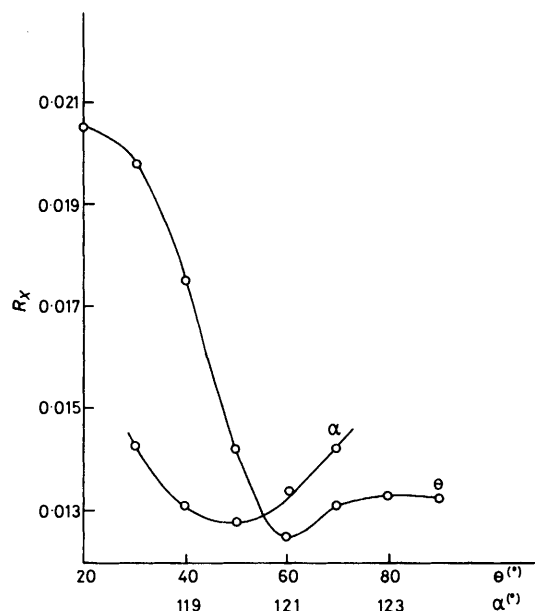


Figure 2. The agreement factor ( $R_x$ ) versus the carbonyl dihedral angle ( $\theta$ ) and the C(2),(6) CCC angles ( $\alpha$ ) in 2,4,6-trimethylacetophenone

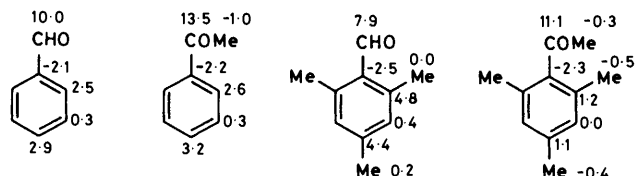


Figure 3.  $\Delta D$  values (p.p.m.) of  $\text{La}(\text{fod})_3$  induced shifts for benzaldehyde, acetophenone, and the mesityl analogues

group (the minimum-energy position in acetone), and the 2- and 6-aromatic methyl groups are staggered with respect to the acetyl group. This analysis converged to a good solution ( $R_x$  0.013) with a minimum at  $\theta$  *ca.* 60°. However, the agreement factor does not significantly increase between 60 and 90° (Figure 2). Thus, the L.I.S. data are consistent with an orthogonal conformation of the acetyl group. Variation of the bond angles  $\alpha_{2,6}$  of the 2- and 6-methyl groups at the minimum value of  $\theta$  (60°) showed (Figure 2) that in this case there was no deformation of these angles and that the global minimum in the agreement factor occurs at  $\theta$  60° and  $\alpha_{2,6}$  120°.

The lanthanide position at the minimum ( $r$  2.60 Å,  $\phi$  70°,  $\psi$  147°, population 100%) is similar to that obtained for acetophenone,<sup>1</sup> except that in this case there is 100% population *exo*, *i.e.*, towards the carbonyl methyl group, compared with 85% for acetophenone. Steric hindrance between the 2- and 6-methyl groups and the bulky lanthanide complex provides the obvious rationalisation for this.

**The Diamagnetic Complexation Shifts.**—The diamagnetic complexation shifts ( $\Delta D$ ) measured for these compounds further support the above L.I.S. results in confirming the presence of considerable conjugation of the carbonyl group with the benzene  $\pi$ -orbitals in (1) but not in (2). This is best illustrated in the comparison of the  $\Delta D$  values of (1) and (2), with those of the parent compounds benzaldehyde and acetophenone (Figure 3). The  $\Delta D$  values reflect the  $\pi$ -transmitted interactions in these systems. Thus, in benzaldehyde

and acetophenone there are the expected large shifts at the carbonyl carbons and apart from a characteristic small negative shift at C(1) only the *ortho*- and *para*-carbons are affected. In mesitaldehyde the  $\Delta D$  values are precisely what would be expected from the presence of electron-donating methyl groups, *i.e.*, they have the same overall pattern as for benzaldehyde, but are substantially increased. In complete contrast the  $\Delta D$  values for (2) are much reduced from those of the parent compound, presumably owing to the decreased conjugation of the carbonyl group and the aromatic  $\pi$ -electrons as a result of the essentially orthogonal conformation found.

### Experimental

The proton and  $^{13}\text{C}$  spectra were obtained with a Bruker WM-250 spectrometer on solutions in  $\text{CDCl}_3$  previously stored over molecular sieves, with  $\text{Me}_4\text{Si}$  as internal standard. Commercial samples of (1) and (2) were used without further purification.  $\text{Yb}(\text{fod})_3$  and  $\text{La}(\text{fod})_3$ , dried *in vacuo* over  $\text{P}_4\text{O}_{10}$  for 24 h prior to use, were added in incremental quantities to the substrate solution. The observed and bound shifts are given in Tables 1 and 2. All computations were performed on the University ICL 1906S and IBM 4341 computers.

Assignment of the  $^{13}\text{C}$  resonances was carried out by inspection of the chemical shifts, intensities (quaternary carbons), and use of additive substituent chemical shift calculations. For C(4), C(2), and C(6) of (2), the assignments are based on the observed  $\Delta M$  values, not on the calculated substituent chemical shifts. The proton resonances were assigned by inspection of the chemical shifts, splitting patterns

and integrals. The  $\Delta M$  values obtained in the Yb shift experiment confirmed these assignments.

### Acknowledgements

We acknowledge S.E.R.C. grants towards the purchase of the Bruker WM-250 spectrometer and for a research assistantship (H. A. B.) and the University of Liverpool Computer Department for computational facilities.

### References

- 1 Part 5, R. J. Abraham, D. J. Chadwick, and F. Sancassan, *Tetrahedron*, 1982, **38**, 3245.
- 2 R. J. Abraham, D. J. Chadwick, and F. Sancassan, *Tetrahedron*, 1982, **38**, 1485.
- 3 C. D. Fisher, L. H. Jensen, and W. M. Schubert, *J. Am. Chem. Soc.*, 1965, **87**, 33.
- 4 V. Benghiat and L. Leiserowitz, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1778.
- 5 L. Lunazzi, M. Tiecco, D. Macciantelli, and G. Spunta, *J. Chem. Soc., Perkin Trans. 2*, 1976, 1121.
- 6 T. Drakenberg, R. Jost, and J. M. Sommer, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1682.
- 7 R. Benassi, D. Larossi, U. Folli, L. Schenetti, and F. Taddei, *J. Chem. Soc., Perkin Trans. 2*, 1981, 228.
- 8 K. S. Dhami and J. B. Stothers, *Can. J. Chem.*, 1965, **43**, 479.
- 9 D. W. Beistel and W. D. Edwards, *J. Phys. Chem.*, 1976, **80**, 2023.
- 10 M. Charton, *Prog. Phys. Org. Chem.*, 1971, **8**, 235.
- 11 G. Goethals, R. Uzan, L. Nadjo, and J. P. Doucet, *J. Chem. Soc., Perkin Trans. 2*, 1982, 885.
- 12 R. J. Abraham, H. A. Bergen, D. J. Chadwick, and F. Sancassan, *J. Chem. Soc., Chem. Commun.*, 1982, 998.

Received 2nd December 1982; Paper 2/2017