Conformational Analysis. Part 7.[1] A Lanthanide Induced Shift (L.I.S.) Nuclear Magnetic Resonance Investigation of Conformational Isomerism in *ortho*- and *meta*-Substituted Benzaldehydes

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A lanthanide induced shift n.m.r. investigation of conformational isomerism in *o*- and *m*-methyl- and -chloro-benzaldehydes and *m*-methoxybenzaldehyde has been carried out. With the ^{13}C diamagnetic complexation shifts removed by use of La(fod)$_3$ and the application of a previously described lanthanide ion complexing model, the pseudo-contact shifts have been used to obtain precise conformational preferences of the aldehydes. The *m*-methyl-, -chloro-, and -methoxy-benzaldehydes are 44, 42, and 32%, respectively in the *O-trans* conformation, whereas the *o*-methyl is 59% in the *O-trans* form and the *o*-chloro 100% in the *O-trans* form. Possible structural deformations in the *ortho*-substituted compounds have been considered. The technique is a sensitive probe of the methyl torsional angle for the *O-cis* conformer, the methyl being staggered with respect to the aldehyde group. The *o*-methylbenzaldehyde geometry is not appreciably distorted and the aldehyde group is coplanar with the aromatic ring. In *o*-chlorobenzaldehyde the structural changes are small and are interpreted as arising from the attractive Cl $\cdots$ HCO interaction.

In previous Parts,[1-3] we have shown that by the simultaneous use of ^{1}H and ^{13}C lanthanide induced shifts (L.I.S.s), with the ^{13}C diamagnetic complexation shifts removed by the use of La(fod)$_3$ 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.

Benzaldehyde and two substituted benzaldehydes have been examined in this way. In *m*-nitrobenzaldehyde[2] the molecule is 45% in the *O-trans* form, the non-equal conformer populations being presumably due to electrostatic interactions as there are negligible steric interactions between the substituents.

In mesitaldehyde, in contrast,[1] no possibility of conformational isomerism exists; however, an acceptable level of agreement between observed and calculated L.I.S.s was only obtained after relaxation of the CCC angles of the abutting 2- and 6-methyl groups. These relax to 126°, but the aldehyde group is still coplanar with the phenyl ring.

In order to examine further the complex pattern of substituent and steric effects in these molecules, we report here the L.I.S. analyses of *o*- and *m*-chloro- and -methyl-benzaldehydes and *m*-methoxybenzaldehyde.

There have been a number of determinations of the conformational isomerism in these molecules with varying success and not always very good agreement. Dipole moment measurements have been used extensively to obtain the conformer ratios in the *m*-chloro-, *m*-methyl-, and *o*-chloro-compounds,[4-7] assuming additive group moments. I.r. measurements, both alone[8-10] and in conjunction with dipole moment data[7] have also been used, though doubts have been expressed as to the validity of the earlier work.[5] An interesting study by Braude and Sondheimer[11] showed that the steric effects of abutting *o*-methyl groups in benzaldehyde could be monitored by the electronic spectrum, and they derived torsion angles for the CHO group (with respect to phenyl) for a number of methyl-substituted benzaldehydes. However, the major technique used to study this conformational isomerism has been n.m.r. spectroscopy. The pioneering investigations of Karabatsos and Vane[12] utilised the stereospecific $^5J_{HH}$ long range coupling between the aldehyde and *anti*-oriented *meta*-

protons to obtain conformer populations, and this was also the technique used by Schaefer *et al.*,[13] for *o*-methylbenzaldehyde. L.I.S. investigations have also been performed on the *m*-chloro- and the *o*- and *m*-methyl compounds,[14] but the use of Eu(fod)$_3$ precluded the inclusion of the ^{13}C shifts in the analyses, giving poorly determined systems of equations. The most unambiguous n.m.r. method, however, is the direct integration of the resonances due to the separate conformers, at a temperature sufficiently low for the rate of their interconversion to be slow on the n.m.r. time scale. Both Lunazzi *et al.*[15] and Drakenberg *et al.*[16] have obtained the 'slow exchange' n.m.r. spectra of these molecules. Lunazzi *et al.* obtained the ^{1}H n.m.r. spectrum of *o*-methylbenzaldehyde at *ca.* -145 °C, in which the formyl peak appears as a doublet of intensity 3:2. Drakenberg *et al.* observed the ^{13}C spectra of the *o*- and *m*-methyl- and -chloro-benzaldehydes at -150 °C, in which separate signals for the *cis*- and *trans*-forms were detected, apart from the *o*-chloro-compound which was all in one form (presumably *trans*). These low temperature studies cover a very narrow temperature range (*e.g.*, from the coalescence temperature of *ca.* -133 to *ca.* -150 °C), too narrow to permit the determination of accurate thermodynamic parameters (except ΔG° at low temperature). We have recently combined the measurement of ΔG° at room temperature by L.I.S. with that of ΔG° at low temperatures from coalescence measurements to derive the enthalpy of the steroid to non-steroid conformational equilibrium in *cis*-2-decalone,[17] and it was felt to be of some interest to examine the generality of this approach.

Results

The observed L.I.S.s (ΔMs) with Yb(fod)$_3$ are given in Tables 1—5, together with the unperturbed chemical shifts (δ), the extrapolated values (intercepts) from the linear regression analyses of the data, and the ^{13}C diamagnetic complexation shifts (ΔD) from the corresponding experiments with La(fod)$_3$. Both the intercepts (which are identical with the original δs) and the correlation coefficients (all >0.998) demonstrate accurate linearity of these plots.

The pseudo-contact contributions ($\Delta M - \Delta D$) were analysed

Table 1. Observed shifts (δ), L.I.S.s (ΔM), diamagnetic shifts (ΔD), and pseudo-contact shifts ($\Delta M - \Delta D$) p.p.m. for m-chlorobenzaldehyde

	C_{CO}	C-1	C-2	C-3	C-4	C-5	C-6
δ^a	190.67	137.92	129.26	135.49	134.33	130.37	127.94
ΔM^b	103.31	35.87	24.84	13.06	11.46	11.94	23.99
Int.	190.84	137.97	129.31	135.50	134.36	130.40	127.99
ΔD^c	10.30	−1.36	1.83	0.83	3.12	0.83	3.19
$\Delta M - \Delta D$	93.01	37.23	23.01	12.23	8.34	11.11	20.80

	H_F	H-2	H-6	H-4, -5
δ^a	9.97	7.83	7.71	7.55
ΔM^b	56.03	25.31	22.83	6.84
Int.	10.04	7.87	7.75	7.55

^{a} [S]$_0$ 1.0165M in CDCl$_3$. ^{b} From three additions of Yb(fod)$_3$, ρ 3.95, 7.25, 10.60 × 10^{-2}, all correlation coefficients >0.998. ^{c} From three additions of La(fod)$_3$, [S]$_0$ 0.9913M, ρ 4.41, 8.05, 12.47 × 10^{-2}.

Table 2. Observed shifts (δ), L.I.S.s (ΔM), diamagnetic shifts (ΔD), and pseudo-contact shifts ($\Delta M - \Delta D$) p.p.m. for m-methylbenzaldehyde

	C_{CO}	C-1	C-2	C-3	C-4	C-5	C-6	CH$_3$
δ^a	192.48	136.57	130.04	138.91	135.28	128.89	127.23	21.17
ΔM^b	123.17	43.35	29.72	15.37	13.79	14.72	29.13	7.89
Int.	192.56	136.61	130.05	138.90	135.29	128.90	127.22	21.16
ΔD^c	10.63	−1.89	1.76	0.74	3.19	0.32	3.24	
$\Delta M - \Delta D$	112.54	45.24	27.96	14.63	10.60	14.40	25.89	

	H_F	H-2	H-6	H-5	H-4	CH$_3$
δ^a	9.97	7.66	7.66	7.40	7.40	2.41
ΔM^b	65.82	29.76	27.55	9.65	7.56	6.66
Int.	10.00	7.67	7.67	7.40	7.43	2.42

^{a} [S]$_0$ 0.9945M. ^{b} From three additions of Yb(fod)$_3$, ρ 3.24, 8.87, and 11.69 × 10^{-2}, all correlation coefficients >0.999. ^{c} From three additions of La(fod)$_3$, [S]$_0$ 0.9683M, ρ 3.84, 8.21, and 12.15 × 10^{-2}.

Table 3. Observed shifts (δ), L.I.S.s (ΔM), diamagnetic shifts (ΔD), and pseudo-contact shifts ($\Delta M - \Delta D$) p.p.m. for m-methoxybenzaldehyde

	C_{CO}	C-1	C-2	C-3	C-4	C-5	C-6	CH$_3$
δ^a	191.96	138.02	112.39	160.34	121.42	130.08	123.39	55.48
ΔM^b	130.77	45.11	32.15	17.10	16.18	15.19	30.07	8.09
Int.	192.04	138.04	112.39	160.34	121.42	130.07	123.41	55.49
ΔD^c	11.53	−2.11	1.29	0.45	4.15	0.53	3.79	
$\Delta M - \Delta D$	119.24	47.22	30.38	16.65	12.03	14.66	26.28	

	H_F	H-2	H-4	H-5	H-6	CH$_3$
δ^a	9.96	7.41	7.20	7.41	7.41	3.84
ΔM^b	71.93	35.73	8.99	10.35	26.84	7.74

^{a} [S]$_0$1.0396M. ^{b} From three additions of Yb(fod)$_3$, ρ 3.66, 6.99, 10.04 × 10^{-2}, all correlation coefficients >0.999. ^{c} From three additions of La(fod)$_3$, [S]$_0$1.080M, ρ 3.66, 6.63, 11.32 × 10^{-2}.

with the program LIRAS-3 (described previously[3]) to obtain the required conformational information. As we have stressed repeatedly, in these studies a major problem is the provision of an over-determined set of equations. The general model derived previously is of four-site lanthanide ion complexation in which the lanthanide position is reflected in the xy and xz planes (this being equivalent, of course, to the two-site model for a planar substrate) and in which the percentage population of the lanthanide ion *exo* and *endo* to the carbonyl is allowed to vary. However, as all our previous studies with aromatic aldehydes have yielded 100% *exo*-populations, there is little point in varying this parameter, unless the aldehyde group becomes non-planar with respect to the aromatic ring. Thus, four parameters are required to fix the lanthanide complexation (one normalisation factor and three lanthanide ion co-ordinates). The additional information required is the conformer population in the *meta*-substituted aldehydes, and the conformer population plus any geometrical distortion in

the *ortho*-substituted aldehydes. The *meta*-substituted benz-aldehydes will be discussed first.

meta-*Substituted Benzaldehydes* (X = Cl, Me, OMe).—In these systems there are 12 pseudo-contact shifts for the aromatic and aldehyde carbons and protons, plus the substituent nuclei for the methyl and methoxy compounds (Tables 1—3): the systems are thus well determined. As previously, we give the analyses both with and without the carbonyl carbon shift, as there is some doubt as to whether this carbon experiences a contact shift contribution. The benz-aldehyde geometry of ref. 3 was used with the addition of standard bond lengths and angles for the m-methyl (C–C 1.505 Å, C–H 1.09 Å, CCH tetrahedral) and m-methoxy (C–O 1.36 Å, COC 120.9°)[18] substituents. The m-methoxy-substituent was considered as flipping between two equally populated planar conformers. The program searched for the minimum

Table 4. Observed shifts (δ), L.I.S.s (ΔM), diamagnetic shifts (ΔD), and pseudo-contact shifts ($\Delta M - \Delta D$) p.p.m. for m-methylbenzaldehyde

	C_{CO}	C-1	C-2	C-3	C-4	C-5	C-6	CH_3
δ^a	192.72	134.25	140.59	131.78	133.64	126.34	132.06	19.54
ΔM^b	137.33	47.86	33.04	16.73	15.97	16.80	33.43	26.12
Int.	192.95	134.31	140.64	131.81	133.65	126.36	132.11	19.58
ΔD^c	11.76	−1.82	4.78	0.90	3.69	0.82	3.55	
$\Delta M - \Delta D$	125.57	49.68	28.26	15.83	12.28	15.98	29.88	26.12

	H_F	H-3, -4, -5	H-6	CH_3
δ^a	10.24	7.34	7.77	2.65
ΔM^b	73.08	10.27	33.22	23.62
Int.	10.34	7.36	7.82	2.68

^{a} [S]$_0$ 0.9622M. ^{b} From three additions of Yb(fod)$_3$, ρ 5.06, 9.59, and 13.42 × 10^{-2}, all correlation coefficients >0.999. ^{c} From three additions of La(fod)$_3$, [S]$_0$ 0.8933M, ρ 3.77, 8.63, and 14.00 × 10^{-2}.

Table 5. Observed shifts (δ), L.I.S.s (ΔM), diamagnetic shifts (ΔD), and pseudo-contact shifts ($\Delta M - \Delta D$) p.p.m. for o-chlorobenzaldehyde

	C_{CO}	C-1	C-2	C-3	C-4	C-5	C-6	H_F	H-6
δ^a	189.63	132.59	137.92	130.62	135.07	127.31	129.40	10.46	7.91
ΔM^b	131.08	47.81	26.46	14.57	14.79	17.25	38.03	76.49	46.73
Int.	189.82	132.69	137.96	130.65	135.08	127.34	129.48	10.50	7.92
ΔD^c	10.27	−1.03	3.26	0.77	3.29	0.36	2.28		
$\Delta M - \Delta D$	120.81	48.84	23.20	13.80	11.50	16.89	35.75		

	H_F	H-3	H-4	H-5
δ	10.47	7.44	7.53	7.38
ΔM^d_{norm}	76.49	10.40	9.32	12.89
Int.	10.55	7.46	7.54	7.39

^{a} [S]$_0$ 1.0289M. ^{b} From three additions of Yb(fod)$_3$, ρ 3.27, 7.11, 12.01 × 10^{-2}, all correlation coefficients >0.999. ^{c} From three additions of La(fod)$_3$, [S]$_0$ 1.000M, ρ 3.57, 7.84, 11.56 × 10^{-2}. ^{d} From three additions of Yb(fod)$_3$, [S]$_0$, 1.3095M, ρ 5.37, 9.37, 16.55 × 10^{-2}, normalised on H_F.
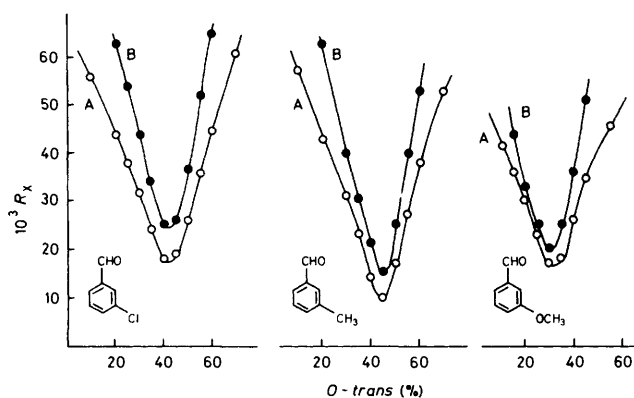

Figure 1. The agreement factor (R_X) versus the percentage O-trans conformer for m-chloro-, -methyl-, and -methoxy-benzaldehyde (A) with and (B) without the inclusion of the carbonyl carbon

Figure 2. The agreement factor (R_X) versus the percentage O-trans conformer for o-methyl- and -chloro-benzaldehyde (A) with and (B) without the inclusion of the carbonyl carbon

disagreement between the observed and calculated shifts over a range of conformer populations. The results are shown in Figure 1. The curves show well defined minima with acceptable agreement factors (R_X) of 0.01—0.02 at 44, 42, and 32% O-trans conformer for X = Me, Cl, and OMe, respectively. The well defined minima suggest that the random errors in the analyses could lead to, at most, percentage errors of ±5%. The inclusion of the substituent carbon and proton nuclei for the m-methyl and -methoxy-groups makes little difference to the final solutions, not surprisingly in view of the comparatively small shifts observed for these nuclei. Comparison of these results with those of previous investigations will be deferred to the Discussion section.
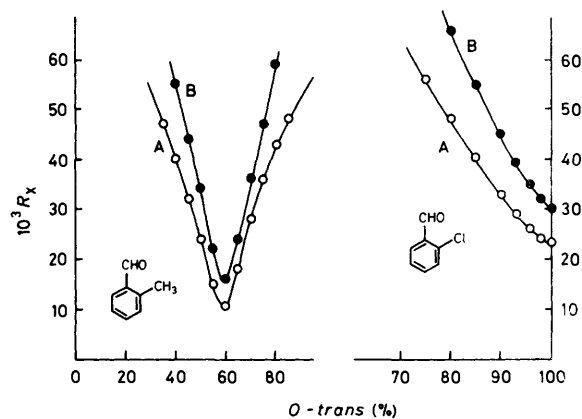
o-*Methylbenzaldehyde.*—The analysis of the data proceeded along similar lines to the above. The signals due to H-3, -4, and -5 on the benzene ring appear as one broad resonance in all the spectra. As the L.I.S.s of H-3 and -5 will be very similar (they are identical by symmetry for a 50:50 ratio of the O-trans and O-cis forms), these observed pseudo-contact shifts are retained in the analysis, but the value for H-4 has been discarded as containing possibly unacceptably large errors. (Owing to the necessary extrapolation procedure used to obtain the ΔM values, the possible error in the L.I.S. of H-4 is $ca.$ 1—2 p.p.m.) Neglecting also, for the moment, the 2-methyl protons (see later) still gives 12 pseudo-contact shifts for the analysis. The geometry used was again the basic benzaldehyde geometry as previously and

Table 6. Results of the analyses of the L.I.S. shifts[a] of substituted benzaldehydes

Substituent	No. of nuclei	R_X	R.m.s.[b]	Lanthanide co-ordinates $R(\text{Å})$	φ (°)	ψ (°)	Population (%)	O-trans (%)
m-chloro	12	0.018	0.7	2.80—2.85	50—55	135—140	100	42
m-methyl	13	0.010	0.4	2.65	60	140	100	44
m-methoxy	14	0.017	0.75	2.70	70—75	130—135	100	32
o-chloro	12	0.023	1.1	2.90—3.00	50—55	135—140	100	100
o-methyl	12	0.011	0.5	2.65	60	135	100	60

[a] All nuclei included. [b] R.m.s. error, observed *versus* calculated shifts.

Table 7. Percentage population of the O-trans conformer in substituted benzaldehydes

Method Solvent Substituent	Dipole moment CCl_4	C_6H_6	I.r. Liquid	U.v. Hexane	$^5J_{HH}$/Hz CCl_4 etc.	N.m.r. Low temperature CHF_2Cl	L.I.S. CCl_4	$CDCl_3$
m-NO₂	65, 63	66			60—70			44
m-Cl	58, 55	56	50	50	60—70	35	46	42
m-Me		50	50		30	45	48	44
m-OMe					10—20			32
o-Cl	100	100	100	50, 100	80—100	100		100
o-Me		50	25		45	50, 64	50	57, 59
Reference	5, 7	6	8, 9	20, 21	12, 13	15, 16	14	22, this work

the 2-methyl substituent was added using the standard bond lengths and angles given earlier.

The computational search procedure converged to a very good solution (R_X 0.011 with the carbonyl carbon shift included, see Figure 2) at 60% of the O-trans form. This was the global minimum both for variations of the conformer populations (as shown), and also for variations in the aldehyde torsional angle (not shown), i.e. the best agreement is obtained for a planar heavy atom structure. All the calculated pseudo-contact shifts are within ca. 0.5 p.p.m. of the observed values which is roughly what is expected to be the experimental error in the derived pseudo-contact shifts. Thus the analysis of o-methyl-benzaldehyde suggests that, within the limits of precision of the L.I.S. technique, the molecule is not significantly deformed in either conformer. This contrasts with the situation in 2,6-dimethylbenzaldehyde[1] in which at least one of the $\overset{\frown}{CCCH_3}$ angles is deformed to 126°. (The analysis in this latter case cannot distinguish between both the $\overset{\frown}{CCC}$ angles opening together and the one cis to the carbonyl oxygen opening.)

The precise conformation of the o-methyl group is of some interest, in view of the possible mechanisms for the 'ortho effect'.[11] This was examined in the present work by the inclusion of the methyl hydrogens, at the best solution of Figure 2, and subsequent rotation of the methyl group to obtain the best R_X. The value of R_X is very sensitive to the precise conformation of the methyl group when it is cis to the carbonyl oxygen, varying from 0.011 for a staggered methyl orientation to 0.018 for an eclipsed geometry. (In this latter solution the error on the methyl proton pseudo-contact shift is > 2 p.p.m., well outside acceptable error limits.) Thus, in this case the L.I.S. technique can define the rotational conformation of the substituent adjacent to the aldehyde. However, the value of R_X is invariant with respect to the orientation of the methyl group when it is trans to the carbonyl oxygen. This situation is precisely that found in mesitaldehyde[1] and presumably for the same reason: the L.I.S. is, of course, much more sensitive to the orientation of the hydrogens cis to the C=O as they are much nearer to the site of complexation.

The level of disagreement between observed and calculated

L.I.S.s at minimum R_X is still within the experimental error of the pseudo-contact shifts, even when the methyl hydrogens are included, and this further reinforces our contention that the molecule is not significantly distorted from the standard geometry used.

o-*Chlorobenzaldehyde.*—In this molecule all the 12 possible carbon and proton pseudo-contact shifts were measured and have been included in the LIRAS-3 analysis. In the first instance, the basic benzaldehyde geometry was used whereupon the search procedure converged to a reasonable minimum (R_X 0.023) at 100% of the O-trans form (Figure 2). Attempts were then made to achieve better agreement by relaxation of the bond angles around the aldehyde group, in particular the ring–aldehyde angle. (In a recent electron diffraction investigation of this molecule Chiu et al.[19] analyse their data in terms of a quinonoid structure with a deformed benzene ring. As there would seem to be no good reason to invoke a quinonoid structure in this molecule, as distinct from the other benzaldehydes investigated, we have not considered this possibility.)

The value of R_X reduces to 0.020 for a ring–CHO angle of 116° (compared with the unstrained value of 120°). Furthermore, at this geometry, there is some indication that R_X decreases further, slightly, on the inclusion of small (ca. 2%) amounts of the O-cis conformer. Thus, whilst the analysis of the pseudo-contact shifts gives a reasonable solution at 100% O-trans with an unstrained geometry, we cannot exclude both small distortions of the basic geometry used and the possibility of small amounts (< 2%) of the O-cis conformer.

The results of the above analyses of the L.I.S.s are collected in Table 6. These are in complete agreement with our earlier studies of aromatic aldehydes,[2,3] confirming the general applicability of the procedure used.

Discussion

The percentages of the O-trans conformer found in the above L.I.S. studies are compared with the results of previous

investigations in Table 7, which also includes the corresponding data for m-nitrobenzaldehyde obtained previously.[2]

The percentages of the O-trans conformer found for the m-chloro- and m-methyl compounds compare well with both the results from low temperature n.m.r. studies,[15,16] and also with Grimaud and Pfister-Guillouzo's results from Eu(fod)$_3$ determinations.[14] The comparison with the low temperature n.m.r. results is informative because the agreement for the four compounds studied by both techniques is well within the experimental error of the measurements and this demonstrates the negligible entropy effects occurring (as would be expected) in this conformational equilibrium. The poorest agreement is for the m-chloro-case (35 versus 42%) and this is solely a consequence of the different temperatures used: the values of $\Delta G°$ obtained are 0.15 and 0.19 kcal mol^{-1} at 123 and 300 K, respectively. This good general agreement excludes the possibility of systematic temperature and solvent effects cancelling for each of the four compounds.

The agreement between the results obtained in the present work and the conformer populations obtained from measurements of the $^5J_{HH}$ coupling is not so good: we have previously discussed possible reasons for this for the case of m-nitrobenzaldehyde.[2] At the low applied magnetic fields used in the early investigations, the aromatic protons comprise a strongly coupled spin system in nearly all the molecules. The observed splittings of the aldehyde proton do not in this case equal the couplings. We suggested that the value of the $^5J_{HH}$ coupling for a fixed pathway was ca. 0.8 Hz, i.e. twice the coupling found in benzaldehyde, rather than the value of 0.6—0.7 Hz used. This is further supported by the value of the coupling observed at high field in o-chlorobenzaldehyde (0.82 Hz), which compares with the value of 0.6 Hz quoted in ref. 11, from a much more strongly coupled spectrum. Assuming, as previously, that there is no $^5J_{HH}$ coupling to the cis-orientated m-proton, the observed couplings of 0.47[2] and 0.40—0.45 Hz[11] for the m-nitro- and m-chloro-compounds, respectively, give populations of the O-trans conformer of 55 and 49%, much more in line with the values found in our studies. The splittings recorded for the m-methyl and m-methoxy-cases may also be subject to similar errors, thus affecting the calculated percentages.

The extensive dipole moment studies, though consistent in themselves, also do not agree with the n.m.r. determinations, apart from the o-chloro-compound which is consistently observed to be 100% O-trans. The discrepancy between the two sets of data is probably systematic: a key factor may be the assumption in the dipole moment determinations that there is no interaction between the substituents. This central assumption has been criticised for the p-substituted benzaldehyde derivatives,[23] and the observed values of the dipole moments of the ortho compounds are often below the limits of the O-cis and O-trans conformers, again suggesting small, but significant, substituent interactions.

In conclusion, the L.I.S. method would appear to be of equal reliability and accuracy as any other method for the determination of conformer populations in these systems, with the possible exception of the low temperature n.m.r. method. The combination of these two n.m.r. methods would appear to be of special interest wherever there is the possibility of a sizeable entropy difference between the conformers. In the molecules studied here the combination of these two methods shows that the entropy difference between the conformers is very small.

Experimental

The ^1H and ^{13}C spectra for L.I.S. analysis were recorded at 80 and 20 MHz respectively on the same samples with a Varian FT-80 spectrometer, at a probe temperature of ca. 25 °C. Some spectra were also run on a Bruker WM 250 spectrometer. All spectra were measured on solutions in CDCl$_3$ which had been stored over molecular sieves and passed through a dried Al$_2$O$_3$ column immediately before use. Commercial lanthanide shift reagents were dried in vacuo over P$_4$O$_{10}$ for 24 h. Commercial substrates were distilled in vacuo the day before their use.

The results of the L.I.S. experiments with Yb(fod)$_3$ (incremental weighing method) are given in Tables 1—5. The proton and carbon assignments follow from additive substituent effects.[24] The experimental points were all obtained with a molar ratio $\rho = [L]/[S]$ (L = shift reagent, S = substrate), in the range between 0.00 and 0.17. Both the correlation coefficients (> 0.998) and the intercepts (which are identical to the unshifted spectra) demonstrate the accurate linearity of these plots.

La(fod)$_3$-induced shifts on carbon signals are reported in Tables 1—5 (protons did not display any meaningful shifts). Obviously agreement factors are good only when variations in chemical shifts are not too small. However, even in such cases, the intercepts are identical to the unshifted spectra, thus demonstrating the linearity of these plots.

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