Conformation of ω-fluoroacetophenone: an NMR study using a liquid crystalline solvent

Donata Catalano,[a] Giorgio Celebre,[b] James W. Emsley,*[,c] Marcello Longeri,[b] Giuseppina De Luca[b] and Carlo A. Veracini[a]

[a] *Dipartimento di Chimica, Universita di Pisa, 56100 Pisa, Italy*
[b] *Dipartimento di Chimica, Universita di Calabria, 87030 Arcavacata di Rende (Cs), Italy*
[c] *Department of Chemistry, University of Southampton, Southampton, UK SO17 1BJ*

The proton NMR spectrum of a sample of ω-fluoroacetophenone dissolved in a nematic liquid crystalline solvent has been obtained and analysed to yield a set of 10 independent dipolar couplings. These have been used to obtain a conformational distribution, $P_{LC}(\varphi,\psi)$, for the bond rotational angles φ, which is for the C–CF bond, and ψ, which is for the ring–C bond. The distribution has a maximum at $\varphi = 0°$, which corresponds to a *cis* arrangement of the C–F and C=O bonds, and $\psi = 0$ or 180°, which refer to the C=O bond being in the plane of the phenyl ring. There is a smaller peak in the distribution at $\varphi = 180°$, corresponding to the *trans* arrangement of the C–F and C=O bonds, and $\psi = 0$ or 180°. The barrier to rotation about the C–CF bond through φ depends strongly on ψ, and *vice versa*.

Introduction

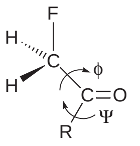
Studies of compounds of the type CH_2F–COR find that the shape of the potential $V(\varphi)$ for rotation about the C–C bond depends on the nature of R. Thus, when R = CH_3 or H the lowest energy is when $\varphi = 180°$, which is the *trans* form,[1] whereas when R is the bulkier phenyl group it was concluded by Olivato *et al.*[2] from an infrared study, that the minimum energy has $\varphi = 0°$, the *cis* form. Olivato *et al.* also report that molecular mechanics calculations for fluoroacetophenone support this conclusion, and also predict that there is a secondary minimum when $\varphi = 130°$, a *gauche* form. The reason for this change in shape of $V(\varphi)$ is most probably a repulsion between the fluorine atom and the protons in the *ortho* positions of the ring. However, this is an incomplete picture of the bond rotational motion in fluoroacetophenone, since there is also restricted rotation about the ring–carbon bond through an angle ψ. Steric strain when $\varphi = 180°$ can be relieved either by rotation through φ, or through ψ. This suggests that rotation about these two bonds could be correlated. To investigate this possibility we have recorded and analysed the proton NMR spectrum of a sample of fluoroacetophenone dissolved in a liquid crystalline solvent.[3] The dipolar couplings, D_{ij}, obtained from this analysis are averages over the motion of the molecule in the mesophase relative to the magnetic field direction, specified by the polar angles, β and γ, as well as over the two bond rotations. Thus D_{ij} is given by eqn. (1), where $P_{LC}(\beta,\gamma,\psi,\varphi)$ is the probability

$$D_{ij} = \int D_{ij}(\beta,\gamma,\psi,\varphi)P_{LC}(\beta,\gamma,\psi,\varphi)\sin\beta\, d\beta\, d\gamma\, d\psi\, d\varphi \qquad (1)$$

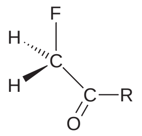
that a molecule is at an orientation (β,γ) to B_0, and in the conformation specified by φ and ψ. The magnitude of the dipolar coupling, $D_{ij}(\beta,\gamma,\varphi,\psi)$, for this orientation and conformation depends also on the relative positions of the interacting nuclei, i and j. In the present case these can be taken to be calculated from standard bond lengths and angles without introducing an appreciable error. The probability, $P_{LC}(\psi,\varphi)$, that the molecule is in a particular conformation irrespective of its orientation with respect to the magnetic field, can be obtained from $P_{LC}(\beta,\gamma,\psi,\varphi)$ by integration as shown in eqn. (2). These two

$$P_{LC}(\psi,\varphi) = \int P_{LC}(\beta,\gamma,\psi,\varphi)\sin\beta\, d\beta\, d\gamma \qquad (2)$$

probability densities have been obtained from the D_{ij} by the maximum entropy (ME) method, which was proposed first by Di Bari *et al.*,[4] and which has been demonstrated to be an effective way of obtaining the shape of these distributions.[5,6] The advantage of the ME method is that it does not make assumptions about the shape of the potential $V(\psi,\varphi)$, and provides the least biased estimate for $P_{LC}(\beta,\gamma,\psi,\varphi)$ and hence for $P_{LC}(\psi,\varphi)$.



cis



trans

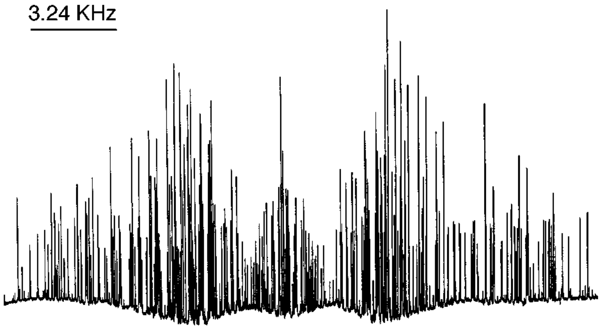


Fig. 1 300 MHz spectrum of the protons in a sample of ω-fluoroacetophenone dissolved in the nematic solvent ZLI 1132 at 300 K

Experimental

The proton spectrum of an approximately 10% by weight solution of ω-fluoroacetophenone dissolved in the nematic liquid crystalline solvent ZLI 1132 (Merck) was recorded on a Bruker AM 300 spectrometer, and is shown in Fig. 1. The solvent is a mixture of compounds of the general formula **1**, with

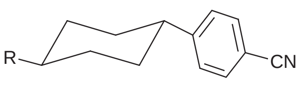


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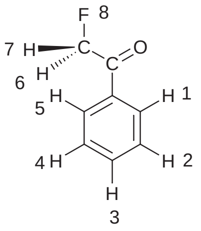
Table 1 Dipolar couplings, D_{ij}, and chemical shifts, δ_i, obtained from the 300 MHz NMR spectrum of the protons in a sample of ω-fluoroacetophenone dissolved in the nematic solvent ZLI 1132 at 300 K



i,j	D_{ij}/Hz	J_{ij}/Hz[a]
1,2	−2303.43 ± 0.04	7.9
1,3	−333.59 ± 0.08	1.3
1,4	−74.4 ± 0.04	0.6
1,5[b]	−4.3 ± 0.1	1.8
1,6	−866.36 ± 0.06	
1,8	−397.71 ± 0.01	
2,3	−575.71 ± 0.08	7.5
2,4[b]	−4.3 ± 0.1	1.3
2,6	−195.11 ± 0.06	
2,8	−122.78 ± 0.1	
3,6	−142.99 ± 0.05	
3,8	−93.52 ± 0.09	
6,7	4833.66 ± 0.04	
6,8	−638.8 ± 0.2	46.89

i	δ_i/Hz
1	564.93 ± 0.16
2	497.85 ± 0.16
3	698.65 ± 0.15
6	0.00

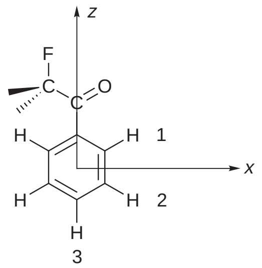
[a] Taken from W. Brügel, *NMR Spectra and Chemical Structure*, Academic Press, 1967, and kept fixed in the analysis. [b] $(D_{1,5} + D_{2,4})$ is obtained and not their separate values. The value given is $\frac{1}{2}(D_{15} + D_{24})$.

$R = C_3H_7$, C_5H_{11} and C_7H_{15}. The sample was contained in a normal 5 mm tube, and the spectrum obtained using a normal high resolution probe. The analysis of this complex spectrum proceeded in two stages, the first being to synthesise a sample containing two deuterium atoms in the fluorinated methyl group, that is ω-fluoro-ω,ω-dideuterioacetophenone, and to record a deuterium decoupled proton spectrum of a sample dissolved in ZLI 1132 at the same conditions of concentration and temperature. This spectrum was recorded on a Bruker MSL 200 spectrometer with the sample contained in a 5 mm sample tube, mounted horizontally in a probe with a solenoid coil double tuned to the proton and deuterium frequencies. Deuterium decoupling was achieved by single pulses of radiation at the centre of the deuterium spectrum. The analysis of the six spin AA′BB′CX spectrum was carried out with the aid of an iterative computer program ARCANA.[7] The second stage was to use the parameters obtained from this analysis as starting parameters in the analysis of the AA′BB′C$_2$X spectrum of the undeuteriated sample to give the parameters in Table 1.

Synthesis of ω-fluoroacetophenone and ω-fluoro-ω,ω-dideuterioacetophenone

A mixture of 1-phenyl-2-fluoroethanone (1.020 g), water or deuterium oxide (9 ml, 99.8% from BDH) and potassium carbonate (20 mg) was refluxed under nitrogen for 13 h, cooled and extracted with diethyl ether. The combined organic phase was dried over anhydrous sodium sulfate, the solvent removed and the residue distilled to give the desired product in either undeuteriated or deuteriated form. The purity of the compounds was checked by proton NMR to be >99%. The isotopic purity of the deuteriated compound was determined to be >90%.

Table 2 The positions of the protons, and the local order parameters, S_{zz}^{R} and $S_{xx}^{R} - S_{yy}^{R}$, obtained for the phenyl ring of a sample of ω-fluoroacetophenone dissolved in the nematic solvent ZLI 1132



i	x_i/Å	z_i/Å
1	2.1245 ± 0.0016	1.2420 ± 0.0007
2	2.1800	−1.2420
3	0.0000	−2.5186 ± 0.0014
S_{zz}^{R}	0.2944 ± 0.0002	
$S_{xx}^{R} - S_{yy}^{R}$	0.3001 ± 0.0004	

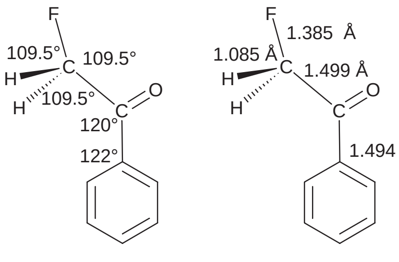


Fig. 2 The bond lengths and angles adopted for ω-fluoroacetophenone

Results and discussion

Structures of the rigid molecular fragments

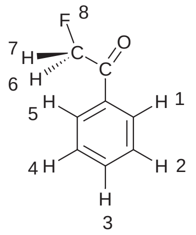
The model adopted for the conformations is that of rigid molecular sub-units which move relative to one another without changing their structures. The bond lengths and angles in each rigid sub-unit are based on standard values for similar compounds, and are given in Fig. 2. In the case of the phenyl ring it is possible to obtain the relative positions of the five protons from the NMR data. Thus, the six dipolar couplings between the five aromatic protons are related to local order parameters, S_{zz}^{R} and $S_{xx}^{R} - S_{yy}^{R}$, by eqn. (3) where θ_{ijz} is the

$$D_{ij}/\text{Hz} = -120\,067[S_{zz}^{R}(3\cos^2\theta_{ijz} - 1) + (S_{xx}^{R} - S_{yy}^{R})(\cos^2\theta_{ijx} - \cos^2\theta_{ijy})]/(r_{ij}/\text{Å})^3 \quad (3)$$

angle made with the z axis by the internuclear vector $\boldsymbol{r}_{ij}$. Note that the sum $D_{15} + D_{24}$ is obtained from the spectral analysis rather than their separate values, and so the number of independent couplings reduces to five. Fixing $r_{24} = 4.36$ Å then allows the order parameters and the coordinates of the aromatic protons to be obtained and these are shown in Table 2. These coordinates are then used in the conformational analysis.

The effect of vibrational motion on the dipolar couplings has not been taken into account. Small amplitude vibrational motion averages the dipolar couplings, and the magnitude of this effect can be calculated for a molecule which is otherwise rigid. However, a procedure for allowing for such motion when there are also bond rotations has yet to be devised, and is indeed a formidable task. The effect of vibrational motion on interproton couplings is usually of the order of 1%, and so its neglect here is estimated to produce a similar error on the local order parameters and proton coordinates.

Table 3 The fitting parameters, λ_{ij}, and the differences, $\Delta D_{ij} = D_{ij}$(observed) − D_{ij}(calculated), obtained by the maximum entropy method from the dipolar couplings measured for a sample of ω-fluoroacetophenone dissolved in the nematic solvent ZLI 1132



i,j	ΔD_{ij}/Hz	$\lambda_{ij}/10^{-4}$
1,2	0.00	1.846 ± 0.008
1,3	0.00	−23.50 ± 0.04
1,4	0.00	
1,5[a]	−0.01	
1,6	0.00	−0.15 ± 0.01
1,8	0.00	−0.862 ± 0.005
2,3	0.00	
2,4[a]	−0.01	
2,6	−0.11	−13.4 ± 0.3
2,8	0.75	18.36 ± 0.09
3,6	0.04	20.5 ± 0.6
3,8	−0.69	
6,7	0.00	0.778 ± 0.002
6,8	0.00	0.208 ± 0.003

[a] $\Delta_{ij} = \frac{1}{2}(\Delta D_{15} + \Delta D_{24})$.

Conformational analysis

In the ME analysis the probability $P_{LC}(\beta,\gamma,\psi,\varphi)$ is expressed as eqn. (4), where $[D_{ij}(\psi,\varphi)]_{2,m}$ is an irreducible component of the

$$P_{LC}(\beta,\gamma,\psi,\varphi) = Z^{-1}\exp\{\Sigma_{i,j,m}\lambda_{ij}[D_{ij}(\psi,\varphi)]_{2,m}C_{2,m}(\beta,\gamma)\} \quad (4)$$

dipolar coupling tensor in a molecule-fixed reference frame, and Z is a normalisation factor. The λ_{ij} are undetermined Lagrangian multipliers, which are varied so as to bring observed and calculated dipolar couplings into the best, least-squares, agreement. The maximum entropy method for analysing data, and specifically dipolar couplings, has been described in detail elsewhere,[3–6,8] but some general comments on this approach are in order here. An important advantage of this method is that a model for the bond rotational potentials is not required. This is particularly useful for molecules for which there is doubt about the nature of the rotational potentials, and this is the main reason why the method has been used for fluoroacetophenone. Perhaps of equal importance is that the probability distribution determined by the maximum entropy method reflects directly the information content of the experimental data. For this reason it is often described as being the *least biased* approach to data analysis. Finally, it should be noted that, unlike methods of analysing data which depend on models for the bond rotational motion,[3] it is necessary to include couplings within the rigid molecular fragments as well as between these groups in the set of D_{ij} used to determine $P_{LC}(\beta,\gamma,\psi,\varphi)$.

For a fixed geometry the six intra-ring couplings are fixed by two local order parameters. This means that only two intra-ring λ_{ij} values should be used as variables. These were chosen to be λ_{12} and λ_{23}, which correspond with the largest intra-ring D_{ij} values. There are eight D_{ij} in addition to those between ring protons, so that there are 10 couplings which can be used in the conformational analysis. However, it is preferable to reduce the number of fitting parameters to being less than 10, so that there is a check, through comparing calculated with observed couplings that the model is correct.

An attempt was made first to fit the data with motion about the ring–C bond, through ψ, restricted to being jumps from 0 to 180°, but with a continuous rotation about the C–C bond through φ. It was decided to exclude $\lambda_{3,8}$ from the fitting process, on the grounds that $D_{3,8}$ is the least sensitive of the inter-fragment couplings to the bond rotational motion. This means that 9 parameters were varied to fit the 10 experimental couplings, which gave a very good fit to the data, but the distribution obtained, $P_{LC}(\varphi)$, is not credible. It has a sharp maximum at $\varphi = 15°$ and unphysical undulations away from this value. It was concluded that it is necessary to explore the whole of the range of ψ as well as φ. Doing this, again with $\lambda_{3,8}$ excluded, gives an excellent fit to the data, and now the distribution obtained, $P_{LC}(\varphi,\psi)$ does not have any non-credible features. The results of the fitting process are given in Table 3, and the probability distribution, $P_{LC}(\varphi,\psi)$ produced is shown in Fig. 3. We have verified that the quality of the fit, and the form of the derived $P_{LC}(\varphi,\psi)$, do not change when the geometry of the rigid fragments is changed within acceptable limits. Excluding $\lambda_{3,6}$, or $\lambda_{3,6}$ and $\lambda_{6,8}$, in addition to $\lambda_{3,8}$ from the fitting process leads to a significantly worse agreement between observed and calculated dipolar couplings, and shows that these parameters have to be included in the fitting process in order to obtain the correct probability distribution.

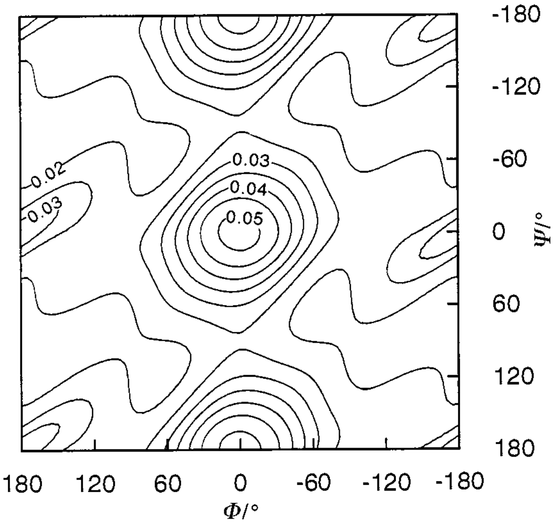


Fig. 3 The probability distribution, $P_{LC}(\varphi,\psi)$, obtained by the maximum entropy method for a sample of ω-fluoroacetophenone dissolved in the nematic solvent ZLI 1132 at 300 K

The $P_{LC}(\varphi,\psi)$ obtained has the most probable conformation at $\varphi = \psi = 0°$, which is in agreement with the conclusion drawn by Olivato *et al.*[2] However, in contrast to the prediction of the molecular mechanics calculation, the secondary maximum is at $\varphi = 180°$, $\psi = 0°$, rather than at $\varphi = 130°$.

Fig. 3 also shows that the potential to rotation about the ring–C bond is strongly correlated with the potential for rotation about C–C(FH$_2$). Thus, Fig. 4 shows sections $P_{LC}(\varphi, 0°)$ and $P_{LC}(\varphi, 90°)$. These demonstrate that there is almost free rotation about the C–C(H$_2$F) bond when ψ is 90°. Sections $P_{LC}(0°, \psi)$ and $P_{LC}(180°, \psi)$ are shown in Fig. 5, and these show very large changes in the distributions about ψ as φ is changed.

Note that the distribution $P_{LC}(\varphi,\psi)$ is relatively flat, with appreciable intensity at the least favourable angle combinations. This is a characteristic result produced by the maximum entropy method, and stems from the unbiased nature of this procedure for obtaining a distribution function. Thus, if all the D_{ij} were zero, as in the isotropic phase, the ME method would produce a totally uniform, flat distribution. This is clearly not the true distribution, for the internal rotation potentials do not vanish in the isotropic phase. Introducing non-zero D_{ij} into the ME analysis produces peaks in $P_{LC}(\Phi,\psi)$, and these grow as the

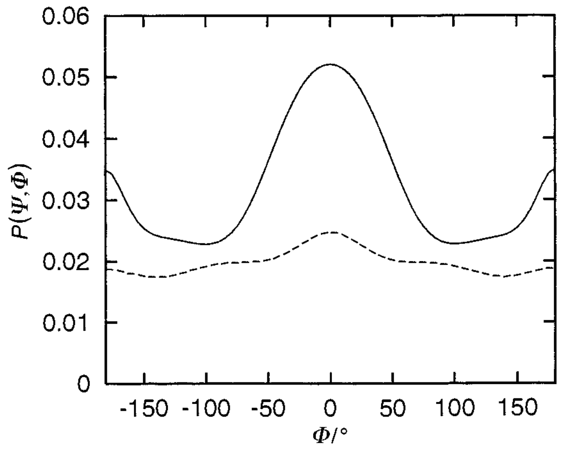


Fig. 4 Sections $P_{LC}(\varphi,0)$, continuous, and $P_{LC}(\varphi,90)$, broken line, through Fig. 3 at constant values of $\psi = 0$ and 90°

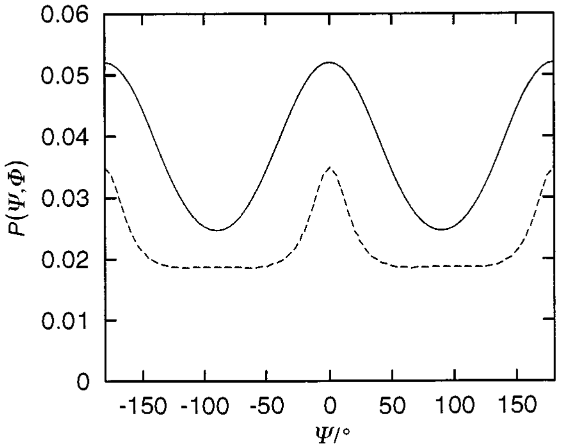


Fig. 5 Sections $P_{LC}(0,\psi)$, continuous, and $P_{LC}(180,\psi)$, broken line, through Fig. 3 at constant values of $\varphi = 0$ and 180°

orientation order in the liquid crystal phase increases, as measured by the orientational order parameters S_{zz}, $S_{xx} - S_{yy}$ and S_{xz}. The studies of internal bond rotational motion by maximum entropy analyses of dipolar couplings carried out so far have shown that increasing the orientational order enhances the maxima in the probability distribution, but does not substantially displace their positions. The strongest conclusion, therefore, to be drawn from the data in Fig. 3 is that the molecules reside for most of the time in the $\varphi = 0°$, $\psi = 0°$ conformation.

Conclusion

The conclusions reached by a maximum entropy analysis of experimental data do not extend beyond the limits of that data. In the present case this means that the conformational distribution refers only to the molecule in the liquid crystalline phase of the particular solvent used. The dipolar couplings are all zero in the isotropic phase, and so no information on this phase can be obtained by these experiments. However, computer simulations of flexible molecules in liquid crystalline and isotropic phases suggest that the presence of the orientational order in the liquid crystalline phase has only a small effect on the conformational distributions for small molecules which have order parameters similar to those found for fluoroacetophenone.[8,9] The polar character of the solvent molecules may, however, be having an effect on the distribution, as noted by Abraham *et al.* for fluoroacetone.[10]

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