Conformational and electronic interaction studies of 2-fluoro-substituted N,N-dimethylacetamides

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Abstract

The $\nu_{\text{CO}}$ IR analysis of the 2-fluoro-substituted N,N-dimethylacetamides RC(O)NMe\textsubscript{2} [R=FCH\textsubscript{2} (1), F\textsubscript{2}CH (2) and F\textsubscript{3}C (3)] and of the parent N,N-dimethylacetamide [R=CH\textsubscript{3} (4)] in solvents of increasing polarity suggests the occurrence of Fermi resonance for 2, 3 and 4 and of cis–gauche rotational isomerism for 1. The 1st overtone analysis along with \textit{ab initio} calculations at MP2/6 – 31 + G(d,p) level are in agreement with the existence of the cis and gauche conformers for 1 and indicate the occurrence of cis–gauche and gauche–gauche conformers for 2 and of a single cis–gauche–gauche rotamer for 3.

The stabilisation of the gauche rotamer with respect to the cis rotamer for 1 and of the gauche–gauche rotamer over the cis–gauche rotamer for 2, along with the unique cis–gauche–gauche rotamer for 3 is discussed in terms of a -1 inductive effect of the CF\textsubscript{3} group, a Repulsive Field Effect between the C=O and C – F dipoles and the orbital interaction between one or two fluorine 2p lone pairs (in the gauche conformation) and the $\pi^*_{\text{CO}}$ orbital. Eigenvector analysis shows that the fluorine 2p orbital coefficient at the LUMO increases progressively, going from the cis–gauche–gauche rotamer of 3 to the cis–gauche rotamer of 2, to the gauche–gauche rotamer of 2 and to the gauche rotamer of 1. Carbonyl frequency gauche shifts (\Delta$\nu$) are in line with this trend and support the $\pi^*_{\text{CO}}$ orbital increases in the same direction.

Keywords: 2-Fluoro-substituted N,N-dimethylacetamides; Electronic interactions; Conformational analysis; Infrared spectroscopy; Theoretical calculations

1. Introduction

Previous IR studies on some $\alpha$-heterosubstituted carbonyl compounds XCH\textsubscript{2}C(O)Y (X=F, OMe, NR\textsubscript{2}, Cl, Br, SEt and I; and Y=Me [1], Ph [2], SR [3], OMe [4] and NEt\textsubscript{2} [5,6], together with theoretical calculations indicated the existence of the cis–gauche rotational isomerism. The progressive increase in the gauche rotamer population in each series, on going from $\alpha$-fluoro to $\alpha$-iodo derivatives, has been mainly ascribed to the increasing contribution of $\pi^*_{\text{CO}}/\sigma_{\text{C–X}}$ and $\pi^*_{\text{CO}}/\pi_{\text{X}}$ orbital interactions.

In general, due to stereo-electronic effects, the $\alpha$-fluorine atom adopts a gauche conformation in the title compounds [2–4,6], excepting in the case of $\alpha$-fluorooacetone [1,7] for which the trans geometry is the preferred one. In fact, it has been observed [8] that for N,N-dimethylfluoroacetamide and N,N-dimethylfluoroopropionamide the gauche conformer is more stable only in the vapour phase and in nonpolar solvents; in solvents of medium and high polarity the cis conformer becomes more stable.
2. Experimental

2.1. Theoretical calculations

The more stable conformers were obtained from the potential energy surfaces (PES) through ab initio calculations with the HF method using the 6–31G(d,p) basis set of the Gaussian 98 program [12]. Their energies, geometries, relevant Molecular Orbitals (LUMO), and electron charge distribution at the various atoms of the 2-fluorosubstituted N,N-dimethylacetamide were optimised at MP2/6–31 + G(d,p).

2.2. Infrared measurements

The spectrograde solvents for IR measurements were used without further purification. The compounds 2-fluoro- (1), 2,2-difluoro- (2) and 2,2,2-trifluoro-N,N-dimethylacetamide (3) were prepared from reactions between corresponding methyl fluorocetates and dimethylamine [8]. The parent N,N-dimethylacetamide is available from Aldrich and was used after distillation.

The IR spectra were obtained on a FTIR Nicolet Magna 550 spectrometer, with 1.0 cm⁻¹ resolution. The carbonyl region (1800–1600 cm⁻¹) was recorded at a concentration of 2.0 × 10⁻² mol · dm⁻³ in carbon tetrachloride, toluene, chloroform and acetonitrile.

Table 1

<table>
<thead>
<tr>
<th>Comp.</th>
<th>R</th>
<th>n-C₃H₈</th>
<th>H₂C-φ</th>
<th>CHCl₃</th>
<th>CH₃CN</th>
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<tr>
<td></td>
<td>v/cm⁻¹</td>
<td>α</td>
<td>α/αₗ</td>
<td>v/cm⁻¹</td>
<td>α</td>
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<tr>
<td>1</td>
<td>FCH₂</td>
<td>1704.1</td>
<td>0.081</td>
<td>0.21</td>
<td>1688.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1672.2</td>
<td>(0.39)</td>
<td></td>
<td>1663.1</td>
</tr>
<tr>
<td>2</td>
<td>F₂CH</td>
<td>1705.6</td>
<td>0.037</td>
<td>0.08²</td>
<td>1695.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1689.0</td>
<td>(0.44)</td>
<td></td>
<td>1682.4</td>
</tr>
<tr>
<td></td>
<td>F₂C</td>
<td>1677.6</td>
<td>(0.04)</td>
<td></td>
<td>1674.7</td>
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<tr>
<td>3</td>
<td>F₃C</td>
<td>1711.8</td>
<td>(1.00)</td>
<td>-</td>
<td>1704.3</td>
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<td></td>
<td></td>
<td>1691.6</td>
<td>(0.07)</td>
<td></td>
<td>1688.9</td>
</tr>
<tr>
<td>4</td>
<td>H₃C</td>
<td>1673.8</td>
<td>0.71</td>
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<td>1662.0</td>
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<tr>
<td></td>
<td></td>
<td>1657.4</td>
<td>(0.02)</td>
<td></td>
<td>1651.5</td>
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</table>

a Intensity expressed as absorbance.

b Absorbance ratio from the higher and the lower frequency components of the analytically resolved carbonyl band.

c Absorbance ratio between the higher frequency component and the summing up of the two lower frequency components of the carbonyl triplet.
Table 2: Frequencies and intensity ratios of carbonyl stretching bands in the IR spectra of 2-fluoro-substituted N,N-dimethylacetamides (1–3) and the N,N-dimethylacetamide (4). RC(=O)NMe₂, in CCl₄

<table>
<thead>
<tr>
<th>Comp.</th>
<th>R</th>
<th>Fundamental ν/cm⁻¹</th>
<th>α</th>
<th>α₁/α₆⁺</th>
<th>1st overtone ν/cm⁻¹</th>
<th>α</th>
<th>α₁/α₆⁺</th>
<th>Δνᵣ(cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FCH₂</td>
<td>1691.4</td>
<td>(0.14)</td>
<td>0.23</td>
<td>3363.4</td>
<td>(0.035)</td>
<td>0.32</td>
<td>19.4</td>
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<td></td>
<td></td>
<td>1661.8</td>
<td>(0.60)</td>
<td></td>
<td>3309.3</td>
<td>(0.11)</td>
<td></td>
<td>14.3</td>
</tr>
<tr>
<td>2</td>
<td>F₆CH</td>
<td>1696.2</td>
<td>(0.13)</td>
<td>0.15⁺</td>
<td>3376.6</td>
<td>(0.024)</td>
<td>0.20</td>
<td>16.0</td>
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<td></td>
<td></td>
<td>1683.6</td>
<td>(0.53)</td>
<td></td>
<td>3344.7</td>
<td>(0.12)</td>
<td></td>
<td>15.0⁺</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1674.9</td>
<td>(0.35)</td>
<td></td>
<td>–</td>
<td></td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>F₆C</td>
<td>1706.1 (1705.2)</td>
<td>(1.30)</td>
<td>9.21</td>
<td>3392.7</td>
<td>(0.18)</td>
<td>–</td>
<td>19.4 (17.7)⁺</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1696.4 (1697.4)</td>
<td>(0.14)</td>
<td></td>
<td>–</td>
<td></td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>H₂C</td>
<td>1662.5 (1659.4)</td>
<td>(0.81)</td>
<td>1.55</td>
<td>3300.4</td>
<td>(0.09)</td>
<td>–</td>
<td>24.6 (18.4)⁺</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1651.5 (1654.6)</td>
<td>(0.52)</td>
<td></td>
<td>–</td>
<td></td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

⁺ Twice the mechanical anharmonicity (2Xₑνₑ) (from Ref. [18]) estimated by the difference: 2 × νᵣ(CO(fund) − νᵣ(CO(1st overtone)).

⁻ In absorbance.

⁺⁺ Absorbance ratio from the higher and the lower frequency components of the analytically resolved carbonyl band.

⁺⁺⁺ Absorbance ratio between the higher frequency component and the summing up of the middle and the lower frequency components of the carbonyl triplet.

⁻⁻ Anharmonicity estimated by the difference: 2 × the mean value of the middle and the lowest carbonyl triplet frequency components, in the fundamental transition, and the lowest carbonyl doublet frequency component in the 1st overtone.

⁻⁻⁻ Corrected frequency for the shift caused by Fermi Resonance (see Section 2).

⁻⁻⁻⁻ Anharmonicity estimated by the difference: 2 × the corrected highest frequency doublet component for the Fermi Resonance and the frequency of the single symmetrical carbonyl band of the 1st overtone.

solutions and at ca. 10⁻³ mol · dm⁻³ in n-hexane solution, using a 0.519 mm sodium chloride cell. For the carbonyl first overtone region (3600–3100 cm⁻¹) the spectra were obtained at 3.0 × 10⁻² mol · dm⁻³ in carbon tetrachloride solution using a 1.00 cm quartz cell. The overlapped carbonyl stretching bands were deconvoluted by means of the Grams/32 curve fitting program version 4.04 Level II [13]. The relative concentrations of the cis–gauche rotamers for 1 and 2 were estimated from the absorbance ratio at the maxima (αₑ/α₆⁻) of the carbonyl band components, assuming equal molar absorptivity coefficients for the cis and gauche rotamers.

The frequencies of the observed carbonyl band components for the doublet of compounds 3 and 4, in CCl₄, were corrected [14] for the shift caused by Fermi resonance through the equation:

\[ ν = [(ν₁ + ν₂)/2 ± (ν₁ - ν₂)/2][(ρ - 1)/(ρ + 1)] \]

where ν is the corrected frequency, ν₁ and ν₂ are observed frequencies and ρ is the ratio of the observed absorption intensities of the two bands. It should be pointed out that the above equation does not apply for the Fermi resonance in the triplet of 2.

3. Results and discussion

Table 1 presents the stretching frequencies and the absorbance ratios of the analytically resolved carbonyl bands for some 2-fluoro substituted N,N-dimethyl acetamides (1–3) and for the parent N,N-dimethyl acetamide (4) in n-hexane, toluene, chloroform and acetonitrile. The corresponding data for the title compounds in carbon tetrachloride (fundamental and 1st overtone transitions) are presented in Table 2.

Inspection of Tables 1 and 2 shows that in the fundamental region 1, 3 and 4 exhibit a doublet in all solvents, excepting compound 3, for which a single symmetrical band is observed in n-hexane.

It should be noted for 1 that, with the increase of the solvent polarity (from n-hexane to acetonitrile), there is a progressive increase of the intensity of the higher doublet frequency component in relation to the lower
one, while for \( \text{3 and 4} \) a reverse trend is observed, i.e. there is a progressive increase of the intensity of the lower doublet frequency component with respect to the higher one. Figs. 1, 3 and 4 illustrate this behaviour.

As already reported [15] the solvent effect on the intensities of the doublet components for \( \text{1} \) strongly suggests the existence of rotational isomerism, the higher frequency component corresponding to the more polar \( \text{cis} \) rotamer (I) and the lower one to the less polar \( \text{gauche} \) rotamer (II) (Scheme 2). On the other hand the solvent effect on the doublet components intensities for \( \text{3 and 4} \) suggests the occurrence of Fermi resonance [15,17]. Moreover, the occurrence for \( \text{1} \) of two resolved bands in the 1st overtone region at frequencies twice those in the fundamental, minus 14 and 19 cm\(^{-1}\) of anharmonicity \(^1\), and with approximately the same

\(^1\) The term anharmonicity used throughout the text and in Table 2, means the value of the mechanical anharmonicity \( \chi, \nu_3 \) (from Ref. [18]).
Fig. 2. IR spectra of \(N,N\)-dimethyl-2,2-difluoroacetamide (2) showing the analytically resolved carbonyl stretching bands, in \(n\)-hexane (a), carbon tetrachloride [fundamental (b) and 1st overtone (c)], toluene (d), chloroform (e) and acetonitrile (f).
Fig. 3. IR spectra of N,N-dimethyl-2,2,2-trifluoroacetamide (3) showing the analytically resolved carbonyl stretching bands, in n-hexane (a), carbon tetrachloride [fundamental (b) and 1st overtone (c)], toluene (d), chloroform (e) and acetonitrile (f).

Contrary to 1, the existence of a single symmetrical carbonyl band for 3 and 4 in the 1st overtone region, whose frequency is twice that of the corrected value (for the Fermi resonance; see Section 2) of the highest doublet frequency component, in the fundamental, minus ca. 18 cm⁻¹ of anharmonicity, strongly suggests the occurrence of Fermi resonance [17] in the fundamental transition for the referred compound. Thus, the 1st overtone analysis indicates that 3 and 4 should exist as single rotamers (Structure V) in solution (Scheme 2).

As for 2, a resolved triplet is observed in solvents of low relative permittivity [19] (n-hexane, ε = 1.9; carbon tetrachloride, ε = 2.2 and toluene, ε = 2.4). However, the lowest triplet frequency component vanishes in solvents of high relative permittivity such chloroform (ε = 4.7) and acetonitrile (ε = 38). Fig. 2 illustrates this behaviour.

Although this solvent effect on the intensities of the
triplet components of 2 suggests Fermi resonance, the occurrence of two resolved bands in the 1st overtone region at frequencies twice that of the highest triplet frequency component and twice the mean value of the middle and the lowest frequency components, minus ca. 15 cm$^{-1}$ of anharmonicity, strongly suggests the existence of rotational isomerism in 2. The highest frequency component of the overtone should correspond to the more polar cis–gauche rotamer (III) and the lowest one to the less polar gauche–gauche rotamer (IV) (Scheme 2).

The occurrence of Fermi resonance in the amides (2)–(4) can be justified as follows. The low symmetry conformers III–V of the amides (2)–(4) belong to the Point Groups [18] $C_1$ or $C_s$. Therefore, it seems probable that some combination band or 1st overtone band of low lying vibrational modes of the referred molecules may belong to the same symmetry species (A or $A'$) and, having a frequency close to that of the fundamental $\nu_{CO}$ mode, thus originating the Fermi resonance.

Table 1 shows that the intensity of the lowest carbonyl frequency component for 2 and 4, in n-hexane, is very low, while it is absent for 3. Therefore, it may be assumed that, in this solvent, the middle component for 2, the single band for 3 and the highest frequency component for 4 should correspond practically to the unperturbed frequencies of conformer IV.
doublet frequency components for 1, the highest and the middle frequency components for 2, the single frequency for 3 and the highest frequency component for 4, in n-hexane, and the corresponding frequencies for 1–4 in the 1st overtone region, in CC14.

As expected for 3 and 4, going from n-hexane to the more polar solvents there is a progressive decrease of the unperturbed carbonyl frequency (in the fundamental) which corresponds to conformer (V), giving rise to an increasing interaction with the low lying combination or 1st overtone mode (s) (Fermi resonance) which, in turn, is responsible for the progressive increase of the lower frequency component intensity with respect to the higher one.

On the other hand, for 2 the disappearance of the lowest triplet frequency component in more polar solvents (CHCl3 and CH3CN) indicates the suppression of the Fermi resonance and, unusually, suggests that the frequency of the low lying combination or 1st overtone mode decreases to a larger extent than the unperturbed fundamental νCO frequency of the highest and the middle triplet components, which correspond to the conformers III and IV, respectively.

Aiming to confirm the IR conformer attribution for the 2-fluoro substituted amides (1–3) and of the parent compound 4 and to have precise geometries of the different conformers, ab initio calculations at the MP2/6–31 + G(d,p) level have been performed on the title compounds (Table 3).

These computations are in agreement with the IR

Table 3

<table>
<thead>
<tr>
<th>Comp.</th>
<th>R</th>
<th>Conf. a</th>
<th>Relative energy/KJ mol⁻¹</th>
<th>P1(%)</th>
<th>μ(D)</th>
<th>Dihedral anglesb,c</th>
<th>(\phi)</th>
<th>(\theta_1)</th>
<th>(\theta_2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FCH₂</td>
<td>(I)</td>
<td>9.53</td>
<td>1.1</td>
<td>5.79</td>
<td>0.0</td>
<td>0.0</td>
<td>180.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(II)</td>
<td>0.00</td>
<td>98.9</td>
<td>3.21</td>
<td>135.7</td>
<td>-4.6</td>
<td>170.9</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>F₂CH₂</td>
<td>(III)</td>
<td>7.82</td>
<td>8.0</td>
<td>5.22</td>
<td>2.3, -115.6</td>
<td>3.8</td>
<td>175.6</td>
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<tr>
<td></td>
<td></td>
<td>(IV)</td>
<td>0.00</td>
<td>92.0</td>
<td>3.08</td>
<td>120.0, -120.0</td>
<td>0.0</td>
<td>180.0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>F₂C</td>
<td>(V)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>H₂C</td>
<td>(VI)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

a Conformer attribution (Scheme 2), where the fluorine atom occupies the cis or gauche position.
b Molar fraction of each rotamer in percentage.
c \(\phi = F-\text{C}-\text{C}=\text{O}, \theta_1 = \text{H}(\text{syn})-\text{N}-\text{C}=\text{O}, \theta_2 = \text{H}(\text{anti})-\text{N}-\text{C}=\text{O}.\)
d The meaning of syn and anti geometries is shown in Structure VI (Scheme 3).
e Parent compound.
f Rotamer V (Scheme 2) replacing F₁, F₂, F₃ by H₁, H₂, H₃, respectively.
data in solution, showing that in the vapour phase 1 exists in the cis (I) and gauche (II) conformations, 2 in the cis–gauche (III) and gauche–gauche (IV) conformations, 3 and 4 in the (single) cis–gauche–gauche (V) conformation (Scheme 2).

The extraordinary stabilisation of the gauche rotamer (conc. ≈ 99%) for 1 with respect to the cis rotamer is slightly higher in comparison to the gauche–gauche rotamer (conc. ≈ 92%) for 2 with respect to its cis–gauche rotamer. In general the N,N-dimethylcarboxyamide group C(O)NMe₂ is planar (θ₁ = 0°; θ₂ = 180°) for the conformers: cis of 1; gauche–gauche of 2 and cis–gauche–gauche of 3 and 4, but it deviates slightly from planarity for the conformers: gauche of 1 and cis–gauche of 2.

The higher dipole moment of the cis rotamer of 1, ca. 0.57 D, with respect to the cis–gauche rotamer of 2 seems to be at first sight the main factor which determines the higher population of cis–gauche rotamer of 2 (ca. 8%) with respect to that of the cis rotamer of 1 (ca. 1%). In fact the larger negative charges at the carbonyl oxygen and fluorine atoms for the cis rotamer of 1, in comparison with those of the corresponding atoms for the cis–gauche rotamer of 2 (Table 4), originates a stronger repulsive Field Effect [16,20] (F) between the Cδ+ = Oδ− and Cδ+ = Fδ− dipoles for the cis conformer of 1 than for the cis–gauche conformer of 2, leading to a more stable cis–gauche rotamer of 2 than the cis rotamer of 1, in the vapour phase.

However, in n-hexane solution, a reverse trend is observed (Table 1), i.e. the cis conformer of 1 becomes more stable than the cis–gauche conformer of 2. This behaviour may be ascribed to the dipole–induced dipole interaction which should be more effective in the more polar cis conformer of 1 than in the less polar cis–gauche conformer of 2.

The large stability of the gauche conformer of 1, the gauche–gauche conformer of 2 and the unique cis–gauche–gauche conformer of 3 may be explained on the grounds of the πC(O)NMe₂/nF superjacent orbital interaction [21].

In spite of the large energy gap between the unper- turbed energy levels of the fluorine 2p orbital nF (I.E.² = 12.5 eV for CH₃F) [22], and the πC(O)NMe₂ orbital (A.E. = 2.26 eV for H₃C = C(O)NMe₂) [9], the dihedral angle φ between the C–F and C=O bonds in the gauche geometry for compounds (1)–(3) is in the range 116°–136° and brings the fluorine

Table 4
Charges at selected atoms (e) for N,N-dimethylacetamides (1–4), RC(O)NMe₂, obtained by ab-initio MP2/6-31 + G(d,p) calculations (a minus sign indicates an excess of negative charge)

<table>
<thead>
<tr>
<th>Comp.</th>
<th>R</th>
<th>Conf.a</th>
<th>N</th>
<th>C(CO)</th>
<th>O(CO)</th>
<th>F</th>
<th>LUMO (C₈)b</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>FCH₂</td>
<td>(I)</td>
<td>-0.1032</td>
<td>0.0836</td>
<td>-0.3448</td>
<td>-0.1845</td>
<td>~0</td>
</tr>
<tr>
<td>2</td>
<td>F₁F₁CH</td>
<td>(III)</td>
<td>-0.1028</td>
<td>0.1294</td>
<td>-0.3550</td>
<td>-0.1684</td>
<td>~0.493</td>
</tr>
<tr>
<td>3</td>
<td>F₁F₁F₁C</td>
<td>(V)</td>
<td>-0.1121</td>
<td>0.0770</td>
<td>-0.3366</td>
<td>-0.1423 (F₁)</td>
<td>-0.169</td>
</tr>
<tr>
<td>4</td>
<td>H₃C</td>
<td>(V)</td>
<td>-0.1656</td>
<td>0.0633</td>
<td>-0.3042</td>
<td>-0.1087 (F₁)</td>
<td>-0.114</td>
</tr>
</tbody>
</table>

a Refers to structures (I–V) (see text).
b Refers to the eigenvector of the fluorine atom at the LUMO of each conformer for the title compounds.

2 I.E. and A.E. means ionization and attachment energy, respectively (see Ref. [9]).
2p lone pair very close to the $\pi_{C(O)ONMe_2}^*$ orbital (structure VII) (Scheme 3) leading to a significant orbital interaction and, thus, stabilising any conformation which has one or two fluorine atoms in the gauche conformation.

Table 4 shows that, with the increasing number of the fluorine atoms on going from 1 to 3, there is a progressive decrease of the mean value of the negative charge at the fluorine atoms [(-0.17e for 1; -0.14e for 2; -0.12e for 3). This behaviour may be ascribed to the reciprocal action of the -1 effect of each fluorine atom, which increases progressively on going from one to two and to three fluorine atoms.

Moreover, on going from 1 to 3 there is an increasing -1 effect of the CF$_n$ group, i.e. CH$_2$F ($\sigma_1 = +0.12$) [23], CHF$_2$ ($\sigma_1 = +0.29$) [23], and CF$_3$ ($\sigma_1 = +0.40$) [23], which leads to a progressive decrease of the carbonyl oxygen negative charge mean value (-0.35e for 1; -0.33e for 2 and -0.30e for 3).

Additionally, with the increasing number of the fluorine atoms at the $\alpha$-carbon, on going from 1 to 3, there is a progressive stabilisation of their unperturbed lone pair 2p orbital energy level and also stabilisation of the $\pi_{CO}^*$ orbital energy level but to a lesser extent. Fig. 5 illustrates well this behaviour for the gauche conformation of 1, for the cis–gauche and the gauche–gauche conformer of 2 and for the cis–gauche–gauche conformer of 3. Therefore, the energy gap ($\Delta E$) between the $n_F$ and $\pi_{CO}^*$ orbital unperturbed energy levels should increase from CH$_2$F to CHF$_2$ and to CF$_3$ groups, leading to a progressive decrease of the stabilising $\pi_{CO}^*/n_F$ orbital interaction ($\delta E$) [24] in this direction. However, when two fluorine atoms are in the gauche conformation (gauche–gauche) as in 2 and 3 there is a splitting between the two unperturbed $n_F$ lone pair energy levels leading to a higher energy out-of-phase combination and to a lower energy in-phase combination. Therefore, for 2 the antibonding combination of the gauche–gauche conformer should have higher energy than that of the cis–gauche conformer, leading to a stronger $\pi_{CO}^*/n_F$ orbital interaction ($\delta E_2$) in the gauche–gauche conformer than in
the cis–gauche conformer (δE₁), which has only one fluorine atom in the gauche geometry.

In the case of the cis–gauche–gauche conformer of 3, the larger stabilisation of the n_F energy level due to the stronger −1 effect of the CF₃ group, in relation to that of the CHF₂ group of 2, makes the out-of-phase combination of the two gauche n_F lone pair energy levels of 3 further from the π*_{CO} energy level, in comparison to that between the n_F energy level of the cis–gauche conformer of 2 and the π*_{CO} energy level. Consequently, the π*_{CO}/n_F interaction in the cis–gauche–gauche conformer of 3 (δE₃) is weaker than that in the cis–gauche conformer of 2. Fig. 6 shows schematically the stronger stabilising orbital interaction between the out-of-phase combination of the 2p fluorine orbitals (F₁ and F₂) having the gauche–gauche geometries for 2 and 3 and the π*_{CO} orbital (structure VIIIa), in comparison with the weaker interaction between the in-phase combination of the 2p fluorine orbital and the π*_{CO} orbital (structure VIIIb).

It should be pointed out that in the case of the gauche rotamer of 1 (structure VII) the energy gap between the n_F and π*_{CO} orbital energy levels is the smallest in the whole series and thus gives the largest π*_{CO}/n_F orbital interaction (δE₀). Therefore, the π*_{CO}/n_F orbital interaction which acts to stabilise the gauche conformations of the title compounds follows the order: δE₀ [for gauche conformer of 1] > δE₂ [for gauche–gauche conformer of 2] > δE₁ [for cis–gauche conformer of 2] > δE₃ [for cis–gauche–gauche conformer of 3].

It is worth noting that these qualitative predictions are fully supported by eigenvector analysis. In fact, Table 4 shows that the absolute coefficient value of the fluorine 2p orbital (C₉) in the LUMO (which is mainly π*_{C(O)NMe₂} orbital) in the gauche rotamer of 1 is 0.493; in the gauche–gauche rotamer of 2 is 0.425 and in its cis–gauche rotamer is 0.302; and in the cis–gauche–gauche rotamer of 3 is only 0.268.

As expected, the C₉ absolute value in the LUMO when the fluorine atom (F₁) has a cis geometry is very low and varies from ~0 to 0.169 in the series 1–3.

Table 5 shows the carbonyl frequency shifts for the conformations where at least one fluorine atom has the cis (Δν₁) or the gauche (Δν₂) geometry for the 2-fluoro-substituted amides (1)–(3), in comparison to the unsubstituted amide (4), in n-hexane. It may be seen that Δν₁ values are positive and vary from +30.0 to +38.0 cm⁻¹ on going from 1 to 3.
It has been shown that the positive cis shifts for the cis rotamer of the α-monosubstituted carbonyl compounds may be attributed to the Repulsive Field Effect (F) [11] between the C=O and C–X dipoles, combined with the inductive effect (–I) of the α-substituent. Table 5 shows that Δν1 frequency shift on going from 1 to 2 presents almost the same value. This behaviour can be explained considering that the 2nd fluorine gauche atom, which increases the (–1) inductive effect on the carbonyl group, is counterbalanced by the ππ*CO/nπ orbital interaction which leads to the almost invariability of the Δν1 frequency shift.

As for 3, the 2nd and 3rd fluorine atoms which are in the gauche–gauche conformation, the absolute coefficient value of the fluorine lone pair at the LUMO (C = 0.268) is smaller than that of the 2nd fluorine atom, which is in the gauche conformation of 2 whose value is 0.302. Therefore, in 3, the summing up of the inductive (–1) and Field (F) effects should prevail over the ππ*CO/nπ orbital interaction and increase the Δν1 frequency shift of 3 by ca. 6 cm⁻¹ with respect to 2.

The gauche shifts (Δν2) [which includes the (Δν1) frequency shift for the cis–gauche rotamer of 2] show values that vary from ca. –2 cm⁻¹ for the gauche rotamer of 1, to ca. +15 cm⁻¹ for the gauche–gauche rotamer of 2, to ca. +32 cm⁻¹ for the cis–gauche rotamer of 2 and to +38 cm⁻¹ for the cis–gauche–gauche rotamer of 3 (Table 5). It is worth of noting that these gauche shifts correlate well with the absolute values of the 2p fluorine orbital coefficients (C_F) in the LUMO (r = 0.992) and with the carbonyl oxygen negative charge (r = 0.956).

These trends give further support to the successive increase of the ππ*CO/nπ orbital interactions on going from the cis–gauche–gauche conformer of 3, to the cis–gauche conformer of 2, to the gauche–gauche conformer of 2 and to the gauche conformer of 1, which leads to a progressive decrease of the carbonyl bond order which, in turn, shows a progressive decrease of the νCO frequency and a progressive increase of the carbonyl oxygen negative charge.

4. Conclusions

IR νCO analysis of the 2-fluoro-substituted N,N-dimethylacetamides RC(O)NMe₂ [R=FCH₂ (1), F₂CH (2) and F₃C (3)] and of the parent N,N-dimethylacacetamide [R=CH₂ (4)] in solvents of increasing polarity (in the fundamental transition) suggests the occurrence of Fermi resonance for 2, 3 and 4 and of cis–gauche rotational isomerism for 1. The 1st overtone analysis (in CCl₄) along with ab-initio MP2/6–31 + G(d,p) indicate the existence of the cis and gauche conformers for 1, of the cis–gauche and gauche–gauche conformers for 2 and of the single cis–gauche–gauche conformer for 3.

The large stabilisation of the gauche rotamer with respect to the cis rotamer for 1 and of the gauche–gauche rotamer over the cis–gauche rotamer for 2, along with the unique cis–gauche–gauche rotamer for 3, in the vapour phase and in n-hexane solution, is discussed in terms of: (a) –I inductive effect of CF₃ group which better stabilises the nπ energy level than the ππ*CO orbital; (b) Repulsive Field Effect between the C=O and C–F dipoles, which act to destabilise the cis conformation; and (c) the orbital interaction between one or two fluorine 2p lone pairs, which are in the gauche conformation and the ππ*CO orbital which stabilises this conformation.

Carbonyl frequency gauche shifts (Δν), which correlate well with the absolute value of the 2p fluorine orbital coefficients (C_F) at the LUMO (which is mainly the ππ*CO/NMe₂ orbital) (r = 0.992) and with the carbonyl oxygen negative charge (r = 0.956) are in line with the increase of the ππ*CO/nπ orbital interactions which operate to progressively stabilise the gauche geometry on going from the cis–gauche–gauche conformer of 3 to the cis–gauche conformer of 2 to the gauche–gauche conformer of 2 and to the gauche conformer of 1. Moreover there is a synergism of the Repulsive Field Effect between the C=O and C–F dipoles which destabilises the cis rotamer of 1 and the cis–gauche rotamer of 2 and the ππ*CO/nπ orbital interaction which stabilises the gauche rotamer of 1 and the gauche–gauche rotamer of 2. This behaviour is responsible for the large predominance of the gauche conformer of 1 and of the gauche–gauche conformer of 2, with respect to their corresponding cis and cis–gauche conformers, respectively.

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