

## Solid state and theoretical evaluation of $\beta$ -fluoroethyl esters indicate a fluorine-ester *gauche* effect

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### Abstract

Single crystal X-ray diffraction studies and a theoretical analysis indicate a preferred conformation for *O*- $\beta$ -fluoroethyl esters, where the C–F and C–O(CO) bonds are *gauche* rather than *anti* to each other. The O–C–F dihedral angles for three compounds and five independent structures indicate a range of only 63.4–69.6°. Evaluation of a rotational energy profile around this bond in a model system ( $\beta$ -fluoroethyl acetate) predicted a similar dihedral angle and the *gauche* conformation to be the minimum on the rotational energy profile. High level ab initio calculations measured the *gauche* conformer to be 0.95 kcal mol<sup>-1</sup> lower in energy than the *anti* conformer and application of a solvation model further increased this differential to 1.6 kcal mol<sup>-1</sup>, consistent with a previous solution state (NMR) evaluation of this system. © 2003 Elsevier B.V. All rights reserved.

**Keywords:** *Gauche* effect;  $\beta$ -Fluoroethyl ester; Stereoelectronic effects; X-ray crystal structure; Ab initio calculations

### 1. Introduction

The preference of 1,2-difluoroethane **1** to adopt a *gauche* in favour of an *anti* conformation has been widely reported and is acknowledged as the classical example of the fluorine-*gauche* effect [1–3]. The magnitude of this preference (*anti*–*gauche*) has been calculated in the range of 0.5–1.0 kcal mol<sup>-1</sup> [4,5]. This contra intuitive preference appears to originate from vicinal interactions possible between the polar C–F bond and other polar covalent bonds. In a related example, we recently demonstrated a fluorine-amide *gauche* effect [6,7] in which the C–F bond is vicinal to the C–N(CO) bond of an *N*- $\beta$ -fluoroethylamide **2** as shown in Fig. 1. There was no evidence that this effect benefited from an intramolecular F...H bond and its origin was attributed to a stereoelectronic *gauche* preference.

Like 1,2-difluoroethane **1** which has two polar vicinal C–F bonds, the C–N bond in **2** is vicinal to a C–F bond and is significantly polarised by the electron withdrawing nature of the amide carbonyl. A theoretical analysis of this system revealed a difference in the *anti*–*gauche* energies of ~1.7 kcal mol<sup>-1</sup> [6]. The *gauche* effect has also been evaluated for

2-fluoroethanol **3**, however in this case, although there is a measurable *gauche* preference, this has been attributed to weak intramolecular hydrogen bonding between F and H, and not to any particular stereoelectronic effect [8]. In this context, we have now explored further the *gauche* effect of *O*- $\beta$ -fluoroethylesters. This study reports such *gauche* effects in the solid state and evaluates the magnitude of the effect by a calculation.

The general *O*- $\beta$ -fluoroethyl ester structure **4** (Fig. 1) can be compared to 2-fluoroethanol **3** and that of *N*- $\beta$ -fluoroethylamide **2**, which displays a strong *gauche* preference [6,7]. It has already been shown that such esters adopt a *gauche* preference in solution. In 1972, Abraham and Monasterios studied the solution conformation of 2-fluoroethyl acetate **4a** and 2-fluoroethyl trichloroacetate **4b** [9]. This study revealed a large *gauche* preference for these molecules in solution with *anti*–*gauche* values calculated to be around 1.5–1.7 kcal mol<sup>-1</sup> in favour of the *gauche* conformation. This is a relatively large value in the context of other accepted *gauche* preferences, for example, 1,2-difluoroethane [4,5]. Amos et al. have carried out ab initio calculations on the ester of fluoroethyl formate **5** and determined a *gauche* preference of 0.66 kcal mol<sup>-1</sup> [2]. In order to examine further the fluorine-*gauche* effect in esters, we have prepared three crystalline *O*- $\beta$ -fluoroethylesters **4c–e** and examined the solid state conformations of these molecules by X-ray crystallographic analyses. In addition, ab initio calculations were

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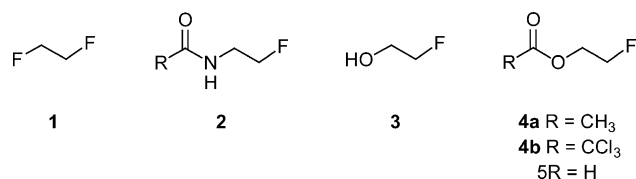


Fig. 1.

conducted to measure relative energies of the *anti* and *gauche* conformers for both gas phase and solvation models using **4a** as a model system.

## 2. Results and discussion

### 2.1. Synthesis and X-ray structures of compounds **4c–e**

Compounds **4c–e** were prepared [10] straightforwardly by reaction of their corresponding acid chlorides with 2-fluoroethanol in the presence of pyridine at 4 °C. On crystallization, the *O*- $\beta$ -fluoroesters **4c–e** afforded crystals suitable for X-ray structural analysis.

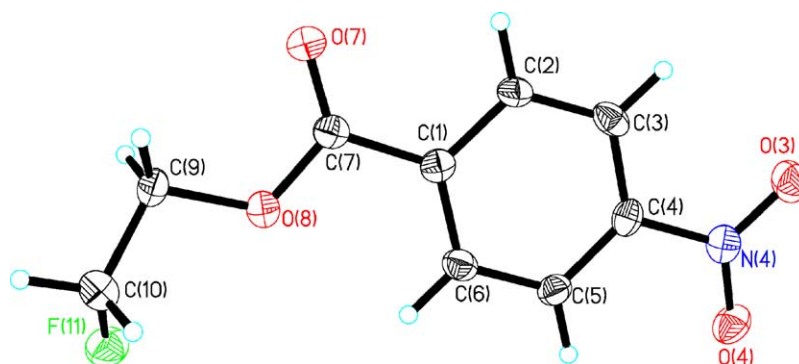
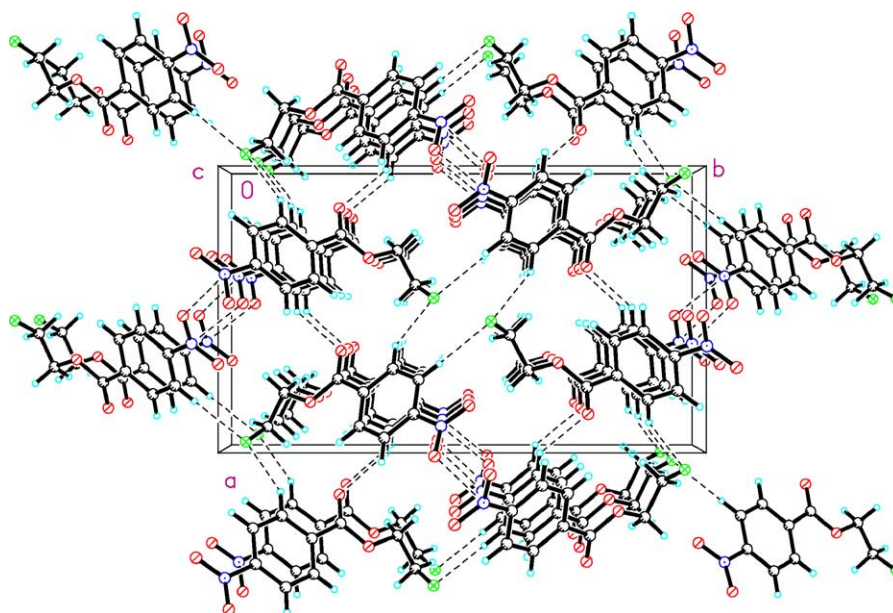
#### 2.1.1. Structure **4c**

Analysis of the X-ray crystal structure of **4c** (Fig. 2) clearly shows the C–F and C–O bonds in the  $\beta$ -fluoroethyl-ester moiety adopt a near optimal *gauche* arrangement relative to each other with a O(8)–C(9)–C(10)–F(11) dihedral angle of  $-66.7(3)^\circ$ .

The unit cell image of X-ray structure **4c** is viewed along the *c*-axis in Fig. 3 and the molecules in the crystal are linked together in chains in the *a/b*-plane by O<sub>2</sub>N(4)  $\cdots$  O<sub>2</sub>N(4) (2.809(3) Å, 130.7°) interactions. In the packing diagram, F(11) can be seen to participate in two intermolecular interactions between H(C3) (2.43(1) Å) and H(C2) (2.50(1) Å). These distances indicate weak F  $\cdots$  H hydrogen bonding interactions between adjacent units. An interaction between carbonyl O(7)  $\cdots$  H(C5) (2.46(1) Å) is also apparent.

#### 2.1.2. Structure **4d**

Analysis of the X-ray crystal structure of **4d** (Fig. 4) shows two chemically identical but crystallographically distinct species related by a non-crystallographic (approximate)

Fig. 2. The X-ray structure of **4c** showing the *gauche* relationship between C(10)–F(11) and C(7)–O(7) bonds in the  $\beta$ -fluoroethyl-ester moiety.Fig. 3. Crystal packing diagram of **4c**.

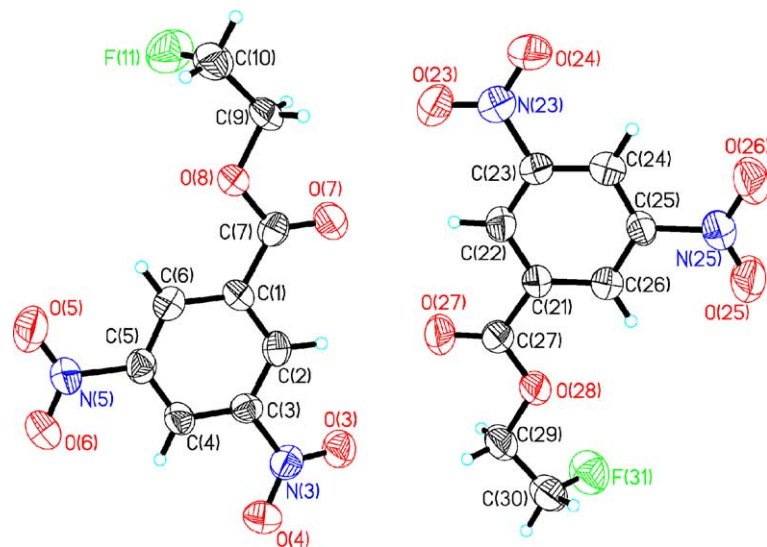


Fig. 4. The X-ray structure of ester **4d** showing the *gauche* relationships between C(10)–F(11) and C(7)–O(7) and C(30)–F(31) and C(27)–O(27) bonds in the  $\beta$ -fluoroethylester moiety.

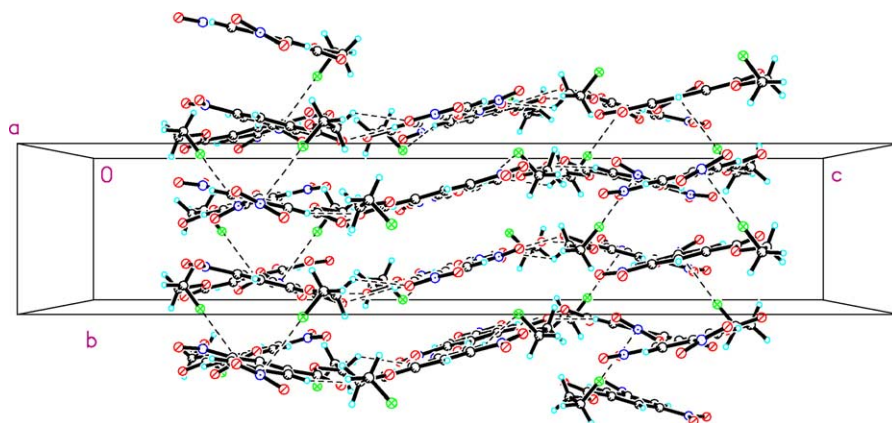


Fig. 5. Crystal packing of **4d** as viewed along the *a*-axis.

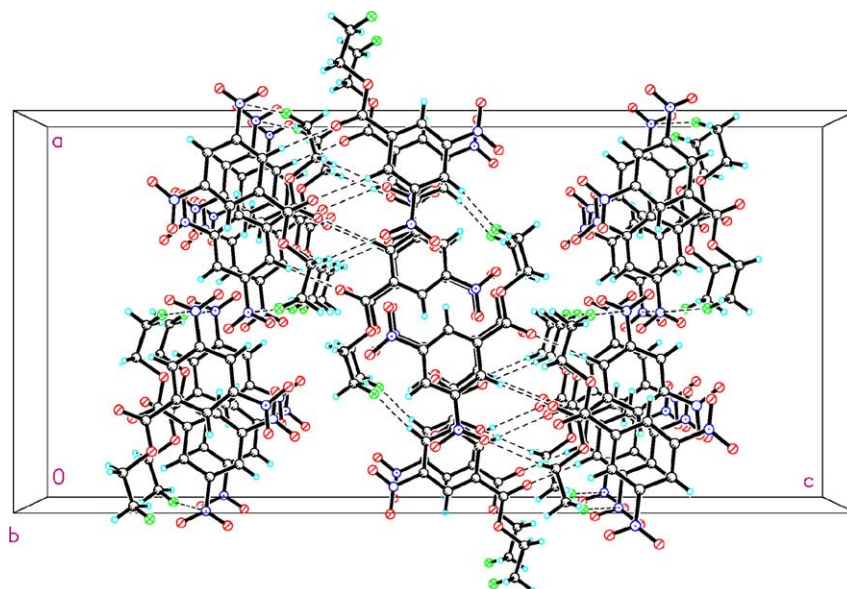


Fig. 6. Crystal packing of **4d** as viewed along the *b*-axis.



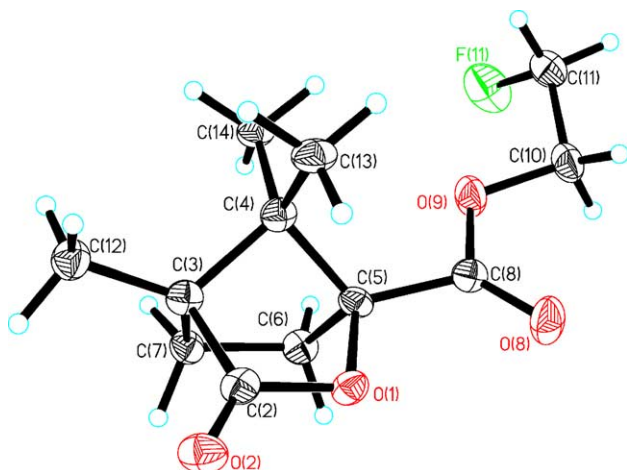


Fig. 7. The X-ray structure of one crystallographic species in the structure of **4e** showing the *gauche* relationship between C–F and C–O bonds in the  $\beta$ -fluoroethyl-ester moiety.

two-fold axis. The C–F and C–O bonds in the  $\beta$ -fluoroethyl-ester moiety clearly adopt a near optimal *gauche* arrangement relative to each other with observed dihedral angles of O(8)–C(9)–C(10)–F(11)  $-69.7(4)^\circ$  and O(28)–C(29)–C(30)–F(31)  $-67.0(4)^\circ$ . The observed dihedral angles are

almost identical to the optimal angle calculated theoretically (vide infra).

From the unit cell image of the X-ray structure of **4d** (Figs. 5 and 6), it can be seen that the molecules in the crystal are linked together in units of *aa*- and *bb*- type interactions in the *b/c*-plane. There are no significantly short intramolecular or intermolecular contacts between fluorine and hydrogen in the solid state structure of **4d**.

### 2.1.3. Structure **4e**

Ester **4e** was prepared from (*S*)-camphanic acid chloride. Analysis of the X-ray crystal structure of **4e** (Fig. 7) also shows two chemically identical but crystallographically distinct species (only one drawn). Of course, the absolute stereochemistry could not be determined by this method but that shown in Fig. 7 follows from the starting material. The C–F and C–O bonds in the  $\beta$ -fluoroethyl-ester moiety clearly adopt a near optimal *gauche* arrangement relative to each other with observed dihedral angles of O(9)–C(10)–C(11)–F(11)  $-63.4(3)^\circ$  and O(29)–C(30)–C(31)–F(31)  $-69.6(3)^\circ$ .

The independent molecules in the X-ray structure of **4e** (Fig. 8) are linked together in units of *ab*-type interactions. There are no significant intermolecular interactions in the crystal packing which is reflected in the absence of dashed lines in the unit cell diagram.

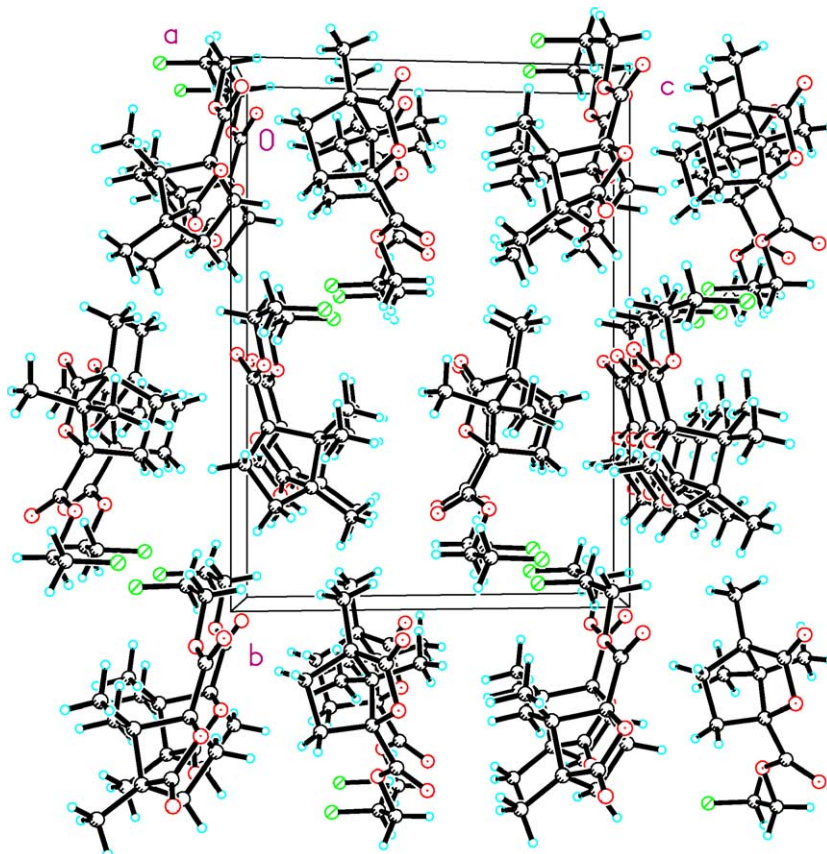


Fig. 8. Crystal packing diagram of **4e** as viewed along the *a*-axis.

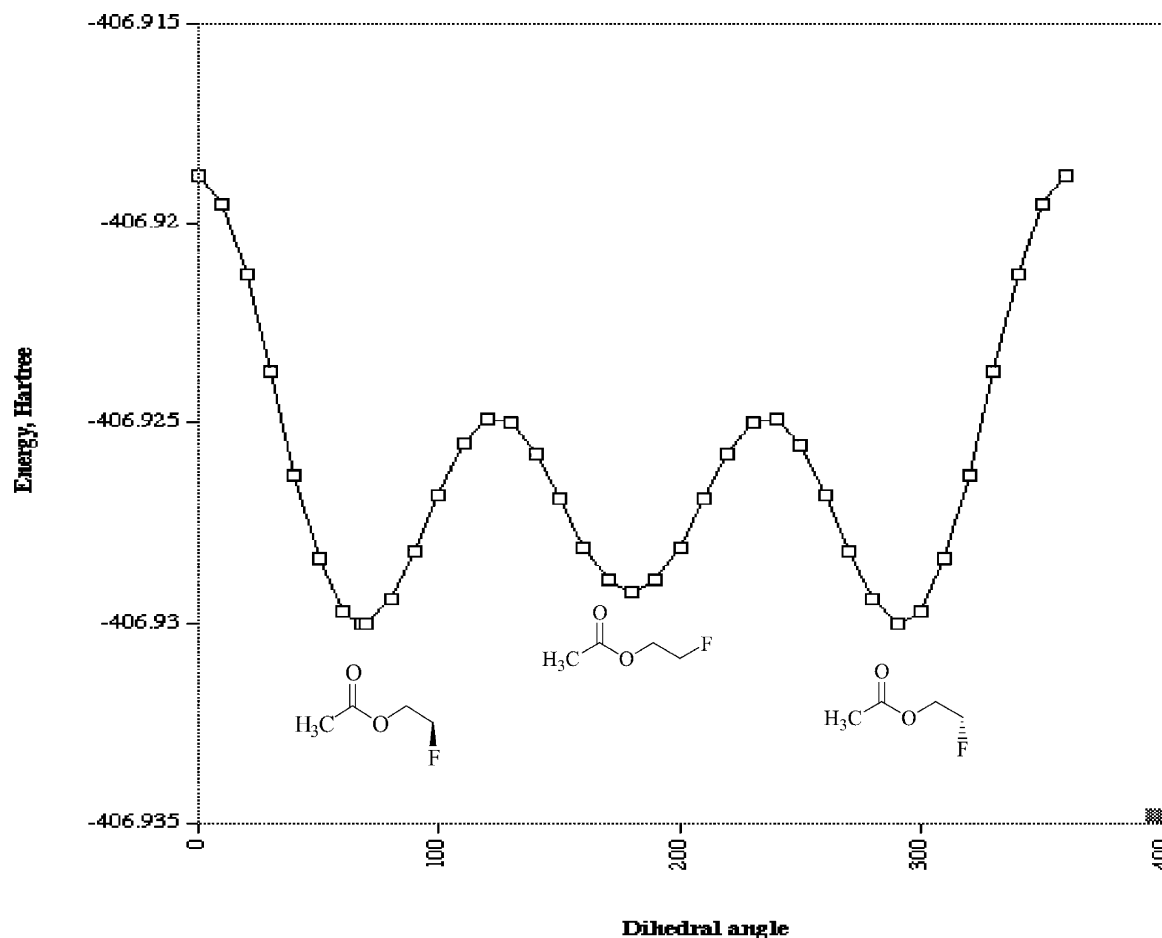


Fig. 9. Rotational energy profile of fluoroethyl acetate monitoring rotation around the C–CF bond. Ab initio calculations were carried out at the B3LYP/6–31G(d) level.

## 2.2. Calculations

In order to quantify the magnitude of this fluorine-ester *gauche* effect, an ab initio analysis of fluoroethyl acetate **4a** as a model system was carried out at both the B3LYP/6–31G(d) and B3LYP/6–311(3d, p) levels using the GAUSSIAN98 program [11]. A rotational energy profile monitoring rotation around the C–F bond of fluoroethyl acetate **4a** was computed at the smaller basis set level in order to quantify the dependence of the  $\beta$ -fluoroethyl ester conformation on the F–C–C–O torsion angle ( $\tau$ ). Only the dominant (*z*) ester conformation was considered [12]. The calculated rotational energy profile (Fig. 9) revealed two minima, the *gauche* (F–C–C–O, 68.2°), and *trans* (F–C–C–O, ~180°) rotamers. The maxima at 0°/360° and 130°/250° are due to eclipsing interactions.

The calculated energy difference between the *gauche* and *trans* conformers at this level emerged at 0.5 kcal mol<sup>-1</sup> (for the total energy) and 0.4 kcal mol<sup>-1</sup> (for the energy corrected for zero-point and entropy contributions) in favour of the *gauche* conformation in the gas phase. At the superior 6–311(3d, p) level, the total energy difference becomes -0.95 kcal mol<sup>-1</sup> (-407.0685/-407.0700 Hartree).

This value is lower than that previously calculated for the *gauche* preference observed in chloroform solution for 2-fluoroethyl acetate (-1.5 kcal mol<sup>-1</sup>) [8]. This difference can most probably be attributed to solvation effects which act to lower further the energy of the *gauche* conformer relative to the *anti*, by relaxation of electrostatic repulsion between the fluorine and oxygen atoms. Application of the self-consistent conductor reaction field solvation model [13] (SCRF = CPCM keyword, 6-311G(3d, p) basis) increased the computed (free energy) difference to -1.3 and -1.6 kcal mol<sup>-1</sup> for chloroform and water, respectively, in reasonable agreement with experiment.

## 3. Conclusions

In conclusion, it is shown that *O*- $\beta$ -fluoroesters adopt a preferred conformation where the C–F and C–O(CO) bonds are *gauche* in the solid state and it is noteworthy that the theoretically calculated F–C–C–O dihedral angle of 6° was very close to the observed angles in four out of five of the X-ray structures. The theoretical calculations at the B3LYP/6–311G(3d, p) level performed on the model system

2-fluoroethyl acetate **4a** have revealed a preference for the *gauche* conformation over the *anti* by 0.95 kcal mol<sup>-1</sup> in the gas phase. This is smaller than that previously described for the *gauche* conformational preferences in *N*- $\beta$ -fluoroethylamides (1.8 kcal mol<sup>-1</sup>) [5] and in 1,2-difluoroethane (0.5–1 kcal mol<sup>-1</sup>) [3,4]. However, the *gauche* conformation is retained in the solid state and it is not overridden by crystal packing effects in any of the systems studied. These observations can be compared to a previous solution analysis of 2-fluoroethyl acetate [8]. Interestingly, in that case, this *gauche* conformational preference becomes measurably greater in solution (-1.5 kcal mol<sup>-1</sup> in CHCl<sub>3</sub>) than that calculated in the gas phase. This arises as a consequence of solvation effects which further stabilise the *gauche* relative to the *anti* conformer by attenuating electrostatic repulsion between the electronegative atoms. It is interesting that the observed *gauche* effect in these  $\beta$ -fluoroethyl esters persists in the solid state and further that it is maximal in solution. Clearly there is the potential to use the C–F bond as a design tool in influencing the conformation of small organic esters for materials and bio-organic applications.

## 4. Experimental

### 4.1. General

All Chemicals were purchased from Acros Organics Ltd. Pyridine was dried and distilled prior to use using standard procedures. The solvents used in reactions were dried, distilled using standard literature procedures and stored under nitrogen prior to use. Reactions were carried out under nitrogen atmosphere. FT-IR spectra were recorded using a Perkin-Elmer 2000 FT-IR as Nujol mulls, NMR Spectra were recorded on a Bruker Advance 300 MHz (<sup>1</sup>H at 300.06 MHz, <sup>13</sup>C at 74.45 MHz, <sup>19</sup>F at 282.34 MHz) spectrometer in CDCl<sub>3</sub>. Mass spectroscopy data were recorded on a VG Autospec instrument. Elemental (C, H and N) analyses were obtained using a CE Instrument EA 1110 CHNS analyser.

#### 4.1.1. Selected analytical and spectroscopic data for **2**, **3** and **4**

For **4c**; mp 67–68 °C; (Found: C, 50.71; H, 3.77; N, 6.58. C<sub>9</sub>H<sub>8</sub>FNO<sub>4</sub> requires: C, 50.71; H, 3.78; N, 6.57%);  $\nu_{\max}$  (Nujol)/cm<sup>-1</sup> 2923, 1716 (C=O), 1611, 1541, 1413, 1349, 1271, 1128, 1050;  $\delta_{\text{H}}$  (300 MHz, CDCl<sub>3</sub>) 4.62 (2H, dt, <sup>2</sup>J<sub>H–F</sub> = 3.8 Hz and <sup>3</sup>J<sub>H–F</sub> = 28.9 Hz, –H<sub>2</sub>CH<sub>2</sub>F), 4.76 (2H, dt, <sup>2</sup>J<sub>H–F</sub> = 4.1 Hz and <sup>2</sup>J<sub>H–F</sub> = 46.9 Hz, –CH<sub>2</sub>F), 8.30 (4H, m, Ar–H);  $\delta_{\text{F}}$  (282 MHz, CDCl<sub>3</sub>) –225.1 (1F, tt, <sup>2</sup>J<sub>F–H</sub> = 47.4 Hz and <sup>3</sup>J<sub>F–H</sub> = 28.9 Hz, –CH<sub>2</sub>F);  $\delta_{\text{C}}$  (75 MHz, CDCl<sub>3</sub>) 64.6 (d, <sup>2</sup>J<sub>C–F</sub> = 20.5 Hz, –CH<sub>2</sub>CH<sub>2</sub>F), 81.0 (d, <sup>1</sup>J<sub>C–F</sub> = 171.4 Hz, –CH<sub>2</sub>F), 123.6 (s, 2 × Ar–CH), 131.0 (s, 2 × Ar–CH), 135.0 (s, Ar–CCO), 150.8 (s, Ar–CNO<sub>2</sub>), 164.4 (s, Ar–CO); *m/z* (CI): 214 (MH<sup>+</sup>, 100%), 168 (MH<sup>+</sup>–NO<sub>2</sub>, 28).

For **4d**; mp 78–79 °C; (Found: C, 41.88; H, 2.75; N, 10.86. C<sub>9</sub>H<sub>7</sub>FN<sub>2</sub>O<sub>6</sub> requires: C, 41.87; H, 2.73; N, 10.85%);  $\nu_{\max}$  (Nujol)/cm<sup>-1</sup> 3082, 2923, 1731 (C=O), 1628, 1538, 1459, 1348, 1286, 1175, 1050, 938, 877, 855, 723;  $\delta_{\text{H}}$  (300 MHz, CDCl<sub>3</sub>) 4.70 (2H, dt, <sup>2</sup>J<sub>H–F</sub> = 4.9 Hz and <sup>3</sup>J<sub>H–F</sub> = 28.2 Hz, –CH<sub>2</sub>CH<sub>2</sub>F), 4.79 (2H, dt, <sup>2</sup>J<sub>H–F</sub> = 4.4 Hz and <sup>2</sup>J<sub>H–F</sub> = 47.6 Hz, –CH<sub>2</sub>F), 9.17 (2H, d, J<sub>H–H</sub> = 2.3 Hz, 2 × Ar–H), 9.21 (1H, t, J<sub>H–H</sub> = 2.1 Hz, Ar–H);  $\delta_{\text{F}}$  (282 MHz, CDCl<sub>3</sub>) –225.1 (1F, tt, <sup>2</sup>J<sub>F–H</sub> = 47.4 Hz and <sup>3</sup>J<sub>F–H</sub> = 28.9 Hz, –CH<sub>2</sub>CH<sub>2</sub>F);  $\delta_{\text{C}}$  (75 MHz, CDCl<sub>3</sub>) 65.4 (d, <sup>2</sup>J<sub>C–F</sub> = 19.9 Hz, –CH<sub>2</sub>CH<sub>2</sub>F), 80.8 (d, <sup>1</sup>J<sub>C–F</sub> = 171.9 Hz, –CH<sub>2</sub>F), 122.5 (s, Ar–CH), 129.5 (s, 2 × Ar=CH), 133.2 (s, Ar–CCO), 148.6 (s, 2 × Ar–CNO<sub>2</sub>), 162.3 (s, Ar–CO); *m/z* (CI): 259 (MH<sup>+</sup>, 100%).

For **4e**; mp 68–69 °C; (Found: C, 59.38; H, 7.01. C<sub>12</sub>H<sub>17</sub>FO<sub>4</sub> requires: C, 59.01; H, 7.02%);  $\nu_{\max}$  (Nujol)/cm<sup>-1</sup> 1775 (C=O), 1747, 1447, 1336, 1305, 1274, 1233, 1173, 1107, 1049, 1020;  $\delta_{\text{H}}$  (300 MHz, CDCl<sub>3</sub>) 0.88 (1H, s, –CH<sub>3</sub>), 0.99 (1H, s, –CH<sub>3</sub>), 1.04 (1H, s, –CH<sub>3</sub>), 1.61–2.37 (4H, m, 2 × CH<sub>2</sub>), 4.41 (2H, dt, <sup>2</sup>J<sub>H–H</sub> = 3.6 Hz and <sup>3</sup>J<sub>H–F</sub> = 28.2 Hz, –CH<sub>2</sub>CH<sub>2</sub>F), 4.58 (2H, dt, <sup>2</sup>J<sub>H–H</sub> = 3.8 Hz and <sup>2</sup>J<sub>H–F</sub> = 47.1 Hz, –CH<sub>2</sub>CH<sub>2</sub>F);  $\delta_{\text{F}}$  (282 MHz, CDCl<sub>3</sub>) –225.6 (1F, tt, <sup>2</sup>J<sub>F–H</sub> = 46.4 Hz and <sup>3</sup>J<sub>F–H</sub> = 28.9 Hz, –CH<sub>2</sub>CH<sub>2</sub>F);  $\delta_{\text{C}}$  (75 MHz, CDCl<sub>3</sub>) 10.0 (s, –CH<sub>3</sub>), 16.9 (s, –CH<sub>3</sub>), 17.0 (s, –CH<sub>3</sub>), 29.2 (s, –CH<sub>2</sub>), 30.9 (s, –CH<sub>3</sub>), 54.6 (s, –CCH<sub>3</sub>), 55.0 (s, –C(CH<sub>3</sub>)<sub>2</sub>), 64.5 (d, <sup>2</sup>J<sub>C–F</sub> = 19.9 Hz, –CH<sub>2</sub>CH<sub>2</sub>F), 81.2 (d, <sup>1</sup>J<sub>C–F</sub> = 170.8 Hz, –CH<sub>2</sub>F), 91.4 (s, –C(O)CO), 167.5 (s, CO), 178.3 (s, CO); *m/z* (CI): 245 (MH<sup>+</sup>, 100%); 181 (MH<sup>+</sup>–OCH<sub>2</sub>CH<sub>2</sub>F, 10).

### 4.2. Crystal data

#### 4.2.1. General

Data were corrected for Lorentz, polarization and absorption. The structures were solved by direct methods and refined by full-matrix least squares on *F*<sup>2</sup> for all data using SHELXTL software. All non-hydrogen atoms were refined with anisotropic thermal parameters; all hydrogen atoms were assigned riding isotropic thermal parameters and constrained to idealised geometries.

**4c**: C<sub>9</sub>H<sub>8</sub>FNO<sub>4</sub>, *M* = 213.16, orthorhombic, space group *Pna*2<sub>1</sub>, *a* = 10.648(3), *b* = 18.092(4), *c* = 4.7347(11) Å, *U* = 912.1(4) Å<sup>3</sup>, *F*(000) = 440, *Z* = 4, *D*<sub>c</sub> = 1.552 Mg m<sup>-3</sup>,  $\mu$  = 0.136 mm<sup>-1</sup> (Mo K $\alpha$ ,  $\lambda$  = 0.71073 Å). The data were collected at *T* = 125(2) K, 3805 reflections (2.22 ≤  $\theta$  ≤ 23.31°) measured on a Bruker SMART CCD diffractometer equipped with Oxford Cryostream low-temperature device ( $\omega$ -scan, 0.3°/frame) yielding 1293 unique data (*R*<sub>merge</sub> = 0.0425). Conventional *R* = 0.0333 for 1125 reflections with *I* ≥ 2 $\sigma$ , GOF = 1.046. Final *wR*<sub>2</sub> = 0.0759 for all data (137 refined parameters). The largest peak in the residual map is 0.150 eÅ<sup>-3</sup>. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication 212513.

**4d**: C<sub>9</sub>H<sub>7</sub>FN<sub>2</sub>O<sub>6</sub>, *M* = 258.17, orthorhombic, space group *Pbca*, *a* = 17.103(8), *b* = 6.936(4), *c* = 35.802(17) Å,

$U = 4247(4) \text{ \AA}^3$ ,  $F(000) = 2112$ ,  $Z = 16$ ,  $D_c = 1.615 \text{ Mg m}^{-3}$ ,  $\mu = 0.148 \text{ mm}^{-1}$  (Mo  $K\alpha$ ,  $\lambda = 0.71073 \text{ \AA}$ ). The data was collected at  $T = 293(2) \text{ K}$ , 13152 reflections ( $2.28 \leq \theta < 24.71^\circ$ ) measured on a Mercury diffractometer ( $\omega$ -scan,  $0.5^\circ/\text{frame}$ ) yielding 3357 unique data ( $R_{\text{merg}} = 0.0684$ ). Conventional  $R = 0.0591$  for 1604 reflections with  $I \geq 2\sigma$ , GOF = 0.992. Final  $wR2 = 0.1234$  for all data (326 refined parameters). The largest difference in the residual map is  $-0.168 \text{ e\AA}^{-3}$ . Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication 212514.

**4e:**  $\text{C}_{12}\text{H}_{17}\text{FO}_4$ ,  $M = 244.26$ , monoclinic, space group  $P2_1$ ,  $a = 6.7416(12)$ ,  $b = 15.681(3)$ ,  $c = 11.545(2) \text{ \AA}$ ,  $\beta = 99.688(3)^\circ$ ,  $U = 1203.1(4) \text{ \AA}^3$ ,  $F(000) = 520$ ,  $Z = 4$ ,  $D_c = 1.348 \text{ Mg m}^{-3}$ ,  $\mu = 0.110 \text{ mm}^{-1}$  (Mo  $K\alpha$ ,  $\lambda = 0.71073 \text{ \AA}$ ). The data were collected at  $T = 125(2) \text{ K}$ , 5187 reflections ( $1.79 \leq \theta \leq 23.29^\circ$ ) measured on a Bruker SMART CCD diffractometer equipped with Oxford Cryostream low-temperature device ( $\omega$ -scan,  $0.3^\circ/\text{frame}$ ) yielding 3150 unique data ( $R_{\text{merg}} = 0.0390$ ). Conventional  $R = 0.0391$  for 3101 reflections with  $I \geq 2\sigma$ , GOF = 1.041. Final  $wR2 = 0.1042$  for all data (308 refined parameters). The largest difference in the residual map is  $-0.224 \text{ e\AA}^{-3}$ . The Flack parameter refined to 0.2(7). Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication 212515.

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### References

- [1] N.C. Craig, A. Chen, K.H. Suh, S. Klee, G.C. Mellau, B.P. Winniewisser, M. Winniewisser, *J. Am. Chem. Soc.* 119 (1997) 4789–4790.
- [2] R.D. Amos, N.C. Handy, P.G. Jones, A.J. Kirby, J.K. Parker, J.M. Percy, M.D. Su, *J. Chem. Soc., Perkin Trans. 2* (1992) 549–558.
- [3] K.B. Wiberg, *Acc. Chem. Res.* 29 (1996) 229–234.
- [4] J.R. Durig, J. Liu, T.S. Little, V.F. Kalasinsky, *J. Phys. Chem.* 96 (1992) 8224–8233.
- [5] P. Huber-Wälchli, Hs.H. Günthard, *Spectrochim. Acta* 37A (1981) 285.
- [6] D. O'Hagan, C. Bilton, J.A.K. Howard, L. Knight, D.J. Tozer, *J. Chem. Soc., Perkin Trans. 2* (2000) 605–607.
- [7] C.R.S. Briggs, D. O'Hagan, J.A.K. Howard, D.S. Yufit, *J. Fluorine Chem.* 119 (2003) 9–13.
- [8] D.A. Dixon, B.E. Smart, *J. Phys. Chem.* 95 (1991) 1609–1612.
- [9] R.J. Abraham, J.R. Monasterios, *Org. Magn. Reson.* 5 (1973) 305–310.
- [10] W.L.F. Armarego, D.D. Perrin, *Purification of Laboratory Chemicals*, fourth ed., Butterworth. Heinemann.
- [11] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, V.G. Zakrzewski, J.A. Montgomery, Jr., R.E. Stratmann, J.C. Burant, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G.A. Petersson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J. Cioslowski, J.V. Ortiz, A.G. Baboul, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P.M.W. Gill, B.G. Johnson, W. Chen, M.W. Wong, J.L. Andres, M. Head-Gordon, E.S. Replogle, J.A. Pople, *Gaussian, Inc.*, Pittsburgh PA, 1998, Gaussian 98, Revision A. 11.
- [12] K.B. Wiberg, K.E. Laidig, *J. Am. Chem. Soc.* 109 (1987) 5935–5943.
- [13] F. Eckert, A. Klamt, *AIChE J.* 48 (2002) 369–385.