

# Hyperconjugation is the source of helicity in perfluorinated *n*-alkanes

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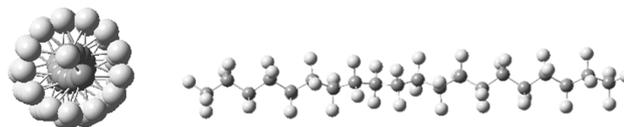
**Abstract:** Hyperconjugative, steric and electrostatic effects were evaluated as possible sources of the helicity in linear perfluorinated alkanes through analysis of natural bond orbitals and classical electrostatics. Contrary to previous rationalisations, which indicate dominating steric or electrostatic effects, this analysis indicates that hyperconjugative stabilisation through  $\sigma_{CC} \rightarrow \sigma_{CF}^*$  interactions are the underlying driving force for the origin of the observed helicity in perfluoroalkanes.

The particular properties of perfluorocarbons, with their high chemical and thermal stability and low surface energy (poor affinity for hydrophobic and hydrophilic materials) have found their use in a wide range of applications such as gas dissolution (eg. artificial blood), as lubricants, textile finishes, liquid crystals, propellants, anaesthetics, solvents and materials for eye surgery and cosmetics.<sup>1</sup> The properties originate in the high electronegativity of fluorine which results in both the strongest bond to carbon in organic chemistry due to significant ionic character ( $\delta^+C-\delta^-F$ ), very compact lone pairs with poor donor and acceptor affinity, and low energy  $\sigma_{CF}^*$  antibonding orbitals.<sup>2</sup>

A notable structural difference between linear perfluoroalkanes and hydrocarbons is the preference for a helical geometry along the perfluoroalkane chain [eg. (poly)tetrafluoroethylene - PTFE], instead of the familiar all-*trans* (*anti* zig-zag) conformation associated with hydrocarbon alkanes (Figure 1), geometries which impact on the different physicochemical properties of these molecular classes.<sup>3</sup>

The first rationale as to why perfluoroalkanes prefer helical geometries argued an origin in 1,3-fluorine-fluorine steric repulsion, proposed by Bunn and Howells in the 1950's when discussing their analysis of the crystal structure of PTFE.<sup>4</sup> This was supported by several theoretical and experimental papers in the literature over the following years carried out on smaller perfluorinated alkanes<sup>5</sup> and reproduced in textbooks.<sup>6</sup> However, as pointed out by Fournier *et al.*,<sup>7</sup> perfluoropropane (**3**) does not prefer a helical geometry even though there are 1,3-fluorine-fluorine repulsive interactions in this molecule,

suggesting that other forces may contribute to the helical preference in longer perfluoroalkane chains. On the other hand, in a much-cited study, Goddard *et al.*,<sup>8</sup> developed a force field to reproduce the helical structure and energy difference between zig-zag and helical perfluorohexane, and suggested that simple, classical electrostatic effects are responsible for the helicity in the extended perfluoroalkane geometry.



**Figure 1:** Calculated helical geometry for perfluoroicosane (**20**) at the B3LYP/6-31G\*\* level (frontal and side view).

The fluorine *gauche* effect describes a stereoelectronic phenomenon of organofluorine compounds<sup>9</sup> where the more electron rich C-H sigma bonds align antiparallel to the C-F bond to accommodate stabilising  $\sigma_{CH} \rightarrow \sigma_{CF}^*$  hyperconjugative interactions. This quantum mechanical (QM) effect helps rationalise why 2-fluoroethanol and 2-fluoroethanolamine prefer *gauche* conformations and is supported by QM analysis.<sup>10</sup> Although there have been some efforts to reproduce theoretically the observed properties and helical structures of short perfluoroalkanes and longer chains extending to an infinite PTFE chain, to the best of our knowledge, there have been no efforts to explain the helicity of perfluorocarbons based on QM analyses.<sup>11</sup>

We have now applied modern QM tools to elucidate the preference of the helical geometry of perfluoroalkanes, namely Natural Bond Orbital (NBO) analysis,<sup>12</sup> Quantum Theory of Atoms in Molecules (QTAIM),<sup>13</sup> and the Non Covalent Interactions (NCI)<sup>14</sup> method, using DFT wave functions. This new approach indicates the importance of  $\sigma_{CC} \rightarrow \sigma_{CF}^*$  hyperconjugation in dictating the helical conformation of extended perfluorocarbon chains, a rationale that has not previously been considered.

For  $C_nF_{2n+2}$  ( $n = 2, \dots, 10$ , compounds **2-10**), the linear zig-zag ( $C_{2h}$  and  $C_{2v}$  symmetry for even and odd numbers of C atoms, respectively) and helical structures ( $C_2$  symmetry) were optimised at a variety of QM levels. We used B3LYP and B3LYP-D3 with 6-31G\*\* basis and HF, MP2 and SCS-MP2 using aug-cc-pVDZ basis. In accord with previous findings,<sup>8</sup> the energetic preference for helical over linear zig-zag structures increases monotonically with the chain length  $n$ , up to ca. 3-5 kcal mol<sup>-1</sup> for perfluorodecane **10** (Table S1). The optimised geometry of perfluorohexane **6** at the B3LYP/6-31G\*\* level is also in good agreement with the experimental X-ray structure (Table S2). Thus the simple B3LYP/6-31G\*\* level was chosen for all further calculations.<sup>15</sup>

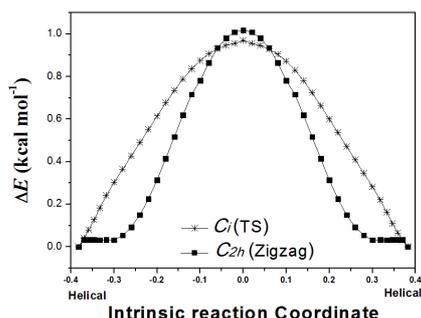
We note in passing that the linear zig-zag geometries are a minimum for perfluoropropane **3**, true transition states for perfluorobutane **4** and -pentane **5**, and higher-order saddle points from perfluorohexane **6** onwards. The true transition states connecting the two enantiomeric helical geometries of compounds **6-10** have quasi-helical  $C_i$  symmetry ( $C1-C2-C3-C4 = 172^\circ$ ). However, as shown for perfluorohexane **6** in Figure 2, the inversion barriers through the linear zig-zag ( $C_{2h}$  symmetry) and the true transition state ( $C_i$  symmetry) are very similar. To assess

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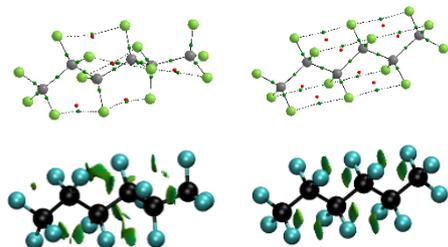
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**Figure 2:** Intrinsic reaction coordinate (IRC) calculated at the B3LYP/6-31G\*\* level for **6** starting from stationary points with  $C_{2h}$  (zig-zag, second-order saddle point) and  $C_1$  (TS) symmetries.

The lowest minima for perfluoroalkanes **4-10** are helical, with C-C-C-C dihedral angle values of  $\sim 167^\circ$  for **4** and ca.  $164^\circ$ - $162^\circ$  for **5-10** (Tables S3-S6 in the ESI). Because the QTAI between 3 and



**6 helical**

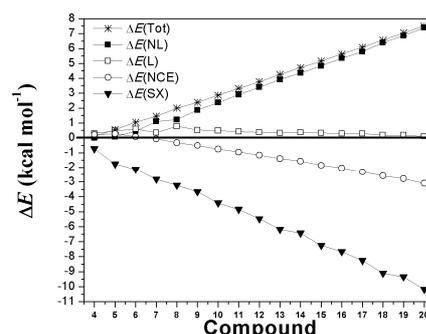
**6 zigzag**

**Figure 3:** QTAI (upper) and NCI (lower) plots for helical and zigzag geometries of compound **6** obtained from B3LYP/6-31G\*\* electron densities.

Previously we studied 1,3-CF...FC interactions using topological, spectroscopic and energetic criteria and it was demonstrated, across a variety of different organofluorine compounds, that the fluorine-fluorine interactions are not stabilising. Stabilising 1,3-CF...FC interactions would favour zig-zag geometries as suggested by QTAI and NCI methods.<sup>16</sup> There are numerous such interactions with higher electron densities at QTAI bond critical points (BCP) and NCI isosurfaces for the zig-zag geometries. If these interactions were stabilising, there should be a clear overall preference for a zig-zag structure in case this effect dominated for **4-10**. (Table S7).

Goddard *et al.*<sup>8</sup> used force fields to separate classical energy components and calculated that electrostatic repulsion in the zig-zag conformation would be more disfavoured than that in the helical conformation, thus identifying electrostatics as the source of helicity in perfluoroalkanes. In order to evaluate Coulomb repulsions in a QM framework, we applied the Natural Coulomb Energy (NCE)<sup>12</sup> analysis, which provides the potential Coulomb electrostatic energy by using natural charges in the classical Coulomb equation [ $E(\text{NCE}) = \sum_{A,B} Q_A Q_B / R_{AB}$ ] for compounds **4-20** as shown in Table S8 and Figure 4.

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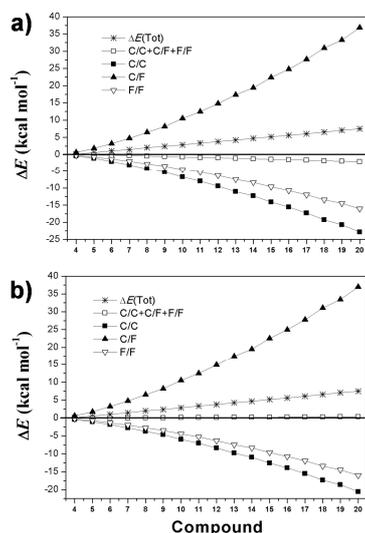
**Figure 4:** Changes in  $\Delta E(\text{Tot})$ ,  $\Delta E(\text{L})$ , and  $\Delta E(\text{NL})$ ,  $\Delta E(\text{NCE})$  and  $\Delta E(\text{SX})$  values between the zig-zag and helical conformations for compounds **4-20** in  $\text{kcal mol}^{-1}$  (see Table S8 for numerical data).

Surprisingly the NCE analysis indicates that electrostatic repulsion has a very small stabilising effect for the helical structures of the short compounds **4-6** only, whereas it actually disfavours all other helical conformations from **7-20** (Figure 4 and Table S10). Also, Natural Steric Analysis (NSA)<sup>17</sup> indicates that there are more steric interactions in the helical than in the zig-zag conformations (Figure 4 and Table S10). Thus, both the NCE and the NSA analysis indicate that neither electrostatic nor steric interactions lead to the helicity of perfluoroalkanes. By using the NBO method to obtain the relative Natural Lewis energy [ $\Delta E(\text{L})$ ], which takes only steric/electrostatic interactions into account but not hyperconjugation, and the Natural Non-Lewis relative energies [ $\Delta E(\text{NL})$ ], which takes only hyperconjugation into account, it is clear that hyperconjugation has a decisive role in stabilising the helical in comparison to the zig-zag geometry, especially for the longer perfluoroalkanes. Indeed,  $\Delta E(\text{NL})$  increases with the carbon chain length (Figure 4 and Table S10), because the zig-zag structures are less stabilised by hyperconjugation. For the longer chains,  $\Delta E(\text{NL})$  closely follows the energy difference between the zig-zag and the helical geometries, e.g. for **20**, which has  $\Delta E(\text{NL})$  of  $7.40 \text{ kcal mol}^{-1}$  and a total barrier of  $7.50 \text{ kcal mol}^{-1}$ .

Thus, NBO analysis indicates that steric plus electrostatic interactions are the most important only for the smallest perfluoroalkanes and become progressively less important as the carbon chain grows, until hyperconjugation accounts for almost all of the stabilization of the helical geometry. This finding is in apparent disagreement with Goddard *et al.* which concluded a definitive role for electrostatic effects.<sup>8</sup> For a direct comparison with those results we evaluated the classical Coulomb energies [cf. the formula for  $E(\text{NCE})$  above] using Mulliken charges and dissected them into contributions from C/C, C/F and F/F pairs. The resulting energy differences between zig-zag and helical structures are plotted in Figure 5a, with the  $\Delta E(\text{Tot})$  values closely following the  $\Delta E(\text{L})$  values in Figure 4 (which are based on charges from natural population analysis, cf. Table S12 in the ESI). This classical electrostatic analysis is not very sensitive to the actual charges that are used and clearly shows that electrostatics cannot be the source of helicity in perfluoroalkanes.

However, Goddard *et al.*<sup>8</sup> deleted all 1-2 and 1-3 electrostatic interactions in their analysis. Deleting the 1,2 and 1,3 electrostatic interactions makes sense in Goddard's force-field framework, because they are implicitly included in the stretching and bending terms, respectively. This is not the case in our QM framework, where all electrostatic interactions require to be accounted for. As it turns out, it is

this deletion that is responsible for the different conclusions, because it clearly inverts the result. As shown in Figure 5b (and Figure S7 and Tables S12 and S13 in the ESI), when these interactions are deleted, electrostatic interactions favour the helical more than the zig-zag geometries. Thus, when all electrostatic interactions are taken into account, the Coulomb analysis is in agreement with our NCE results and both indicate that electrostatic effects do not dictate the observed helicity.



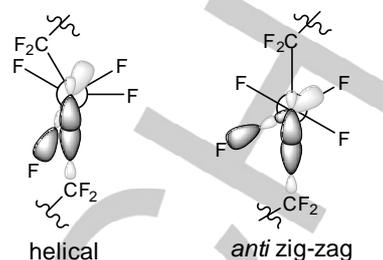
**Figure 5:** Graphs comparing  $\Delta E(\text{Tot})$ ,  $\Delta E(\text{CC}+\text{CF}+\text{FF})$ ,  $\Delta E(\text{C/C})$ ,  $\Delta E(\text{C/F})$  and  $\Delta E(\text{F/F})$  relative energy values for 4-20 in kcal mol<sup>-1</sup>; **a)** all interactions included; **b)** all 1-2 and 1-3 electrostatic interactions deleted. Mulliken charges used were C(CF<sub>3</sub>) = + 0.72 au, C(CF<sub>2</sub>) = +0.52 au, F(CF<sub>3</sub>) = -0.24 au and F(CF<sub>2</sub>) = -0.26 au

Similar NBO, NCE, NSA and classical Coulomb analysis were carried out for compounds **6** and **20**, tracing the individual components along IRC paths connecting zig-zag and helical structures. For perfluorohexane **6**, where the total energy barrier  $\Delta E(\text{Tot})$  is rather small, the potential energy curve is closely followed by  $\Delta E(\text{L})$ , indicating that steric/electrostatic interactions are decisive. For **20** with its much larger barrier, it is  $\Delta E(\text{NL})$  that determines the overall energy profile (cf Figure S8), reinforcing our conclusion that it is hyperconjugation that rules the helicity in longer perfluoroalkanes such as **20**.

Which are these hyperconjugative interactions that stabilize the helical geometries? According to second-order perturbation theory analysis, the donations from the 2p lone pairs on the F atoms into the antibonding C-F and C-C orbitals [LP2(F) →  $\sigma_{\text{CF}}^*$  and LP3(F) →  $\sigma_{\text{CC}}^*$ ] are the most important ones, but their contributions are quite similar in magnitude between the helical and zigzag geometries. On the other hand, there are notable  $\sigma_{\text{CC}} \rightarrow \sigma_{\text{CF}}^*$  hyperconjugative interactions that exist in the helices that are all but absent in the zig-zags conformation.<sup>18</sup>

Helicity attenuates the  $\sigma_{\text{CC}} \rightarrow \sigma_{\text{CC}}^*$  and  $\sigma_{\text{CF}} \rightarrow \sigma_{\text{CF}}^*$  orbital overlaps in comparison to the all-*trans* zig-zag geometry, where they are optimised to overlap geometry. However the creation of multiple  $\sigma_{\text{CC}} \rightarrow \sigma_{\text{CF}}^*$  (and consequently low energy  $\sigma_{\text{CF}} \rightarrow \sigma_{\text{CC}}^*$ ) interactions in the helical conformation more than outweighs this attenuation, since the  $\sigma_{\text{CF}}^*$  orbital is a much better acceptor orbital than that of  $\sigma_{\text{CC}}^*$ . The number of  $\sigma_{\text{CC}} \rightarrow \sigma_{\text{CF}}^*$  interactions

increase with the number of CF<sub>2</sub> groups, consistent with the observed hyperconjugative contributions in longer rather than shorter perfluoroalkanes (Table S13), and an increased tendency to helicity, as indicated by the NBO method.



**Figure 6:** Illustration of the key  $\sigma_{\text{CC}} \rightarrow \sigma_{\text{CF}}^*$  interaction, which has increased orbital overlap in the helical versus anti zig-zag conformation.

Energy values and illustrative plots of MOs involved in these hyperconjugative donor-acceptor interactions are shown in the ESI Table S13 and Figures S5 and S6 (see Figure 6 for schematic plots). The importance of  $\sigma_{\text{CC}} \rightarrow \sigma_{\text{CF}}^*$  hyperconjugation is manifest in the C-F and C-C bond lengths. As this hyperconjugative interaction moves electrons out of a bonding orbital ( $\sigma_{\text{CC}}$ ) to an antibonding orbital ( $\sigma_{\text{CF}}^*$ ), both the C-C and C-F bond lengths should increase. Indeed the average C-F and C-C bond lengths increase from 1.339 Å and 1.547 Å, respectively, for perfluoropropane **3** to 1.353 Å and 1.561 Å, respectively, for **20** in its helical geometry.<sup>19</sup> Thus, the hyperconjugative interactions under scrutiny may also affect the geometrical parameters of perfluoroalkanes. This analysis also nicely explains why hydrocarbons prefer linear zig-zag over helical structures, because the  $\sigma_{\text{CH}}^*$  antibonding orbitals are much poorer acceptors than  $\sigma_{\text{CF}}^*$  antibonding orbitals. Therefore the weaker  $\sigma_{\text{CC}} \rightarrow \sigma_{\text{CH}}^*$  hyperconjugative interactions do not dominate the steric and electrostatic interactions in the hypothetical helical geometry for hydrocarbons.<sup>20</sup>

In summary, detailed QM analysis indicates that hyperconjugation dictates the preference for the helical over the linear zig-zag conformation observed in perfluoroalkanes, rather than previously and variously proposed steric or electrostatic effects. In particular  $\sigma_{\text{CC}} \rightarrow \sigma_{\text{CF}}^*$  hyperconjugative interactions along the alkyl chain are responsible for a distortion to helicity, an effect that becomes increasingly stabilising for longer chain lengths.

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**Keywords:** perfluoroalkane helical geometries • stereoelectronic effects • hyperconjugation • steric and electrostatic effects • conformational analysis

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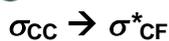
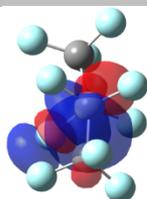
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- [17] J. K. Badenhop, F. Weinhold, *J. Chem. Phys.* **1997**, *107*, 5406.
- [18] For canonical MOs, orbitals with predominantly  $\sigma_{CC}$  and  $\sigma_{CF}^*$  character are strictly orthogonal in linear zig-zags, and apparently only weak overlap arises upon transformation to localised MOs.
- [19] When comparing linear zigzag and helical structures, directly, the effects are smaller (e.g. in **20** the mean CF and CC distances increase from 1.325 Å and 1.561 Å, respectively, in the zigzag to 1.328 Å and 1.565 Å, respectively, in the helix) but are still noticeable and go in the same direction.
- [20] Perchlorinated *n*-alkanes also prefer helical over zig-zag structures (see e.g. Tables S16-S17 in the ESI for molecules containing 3-10 carbon atoms), which would be expected from the larger 1,3 repulsions between the chlorines in the linear zig-zag structures. The helical preference for perchloroalkanes is even more pronounced than in perfluoroalkanes (e.g. by up to 30.1 kcal mol<sup>-1</sup> for perchlorodecane). Detailed NBO analyses were inconclusive, (see Table S17 and Figure S9 in the ESI), but that substantial steric repulsions between the Cl atoms are present is indicated by the atomic charges, which are very small and actually positive for Cl (e.g. up to +0.10e on average for C<sub>10</sub>Cl<sub>22</sub>).

**Entry for the Table of Contents** (Please choose one layout)

Layout 1:

## COMMUNICATION

It is hyperconjugation (i.e. quantum mechanics), not simple electrostatics, that dictates the helical shape of perfluoroalkanes

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Layout 2:

## COMMUNICATION

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