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Conformational impact of pentafluorosulfanylation on acyclic aliphatic molecules

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ABSTRACT

The diastereotopic nature of geminal protons γ to the pentafluorosulfanyl (SF_5) group was investigated by computational modeling and experimental methods. 1D and 2D NMR techniques were employed to determine the vicinal coupling constants used in the estimation of H–C–C–H dihedral angles required for the approximation of the average solution conformation of SF_5-substituted alkyl chains. Rotational energy barriers were calculated at the B3LYP/6-31++G (d,p) level in an effort to assess the relative steric demand of the SF_5 group relative to a trifluoromethyl or *tert*-butyl group. The observed diastereotopicity is likely a result of hindered molecular rotation where one of the γ protons is trapped between two equatorial fluorines of the SF_5 group.

1. Introduction

Fluorine and fluorinated substituents can significantly influence molecular conformation. Individual fluorine atoms influence conformation primarily through electrostatic or dipolar interactions [1,2]. Hydrogen bonding interactions are however frequently of less importance in organofluorine compounds [3–5] where fluorine is a poor hydrogen bond acceptor as consequence of the high electronegativity and lower polarizability of fluorine.

Molecular conformation can be profoundly influenced by the interactions of fluorinated groups. Even though the van der Waals radius of fluorine is only 1.47 Å [6], as the extent of fluorination increases, the steric demand of fluorinated groups also increases. For example, the trifluoromethyl group has nearly the same steric demand as an ethyl group [7,8]. Conceptually an analog of a trifluoromethyl (CF_3) group, the pentafluorosulfanyl (SF_5) group, with five fluorine atoms arranged in a square pyramid about sulfur, may impart unique properties to molecules into which it has been substituted. The electronegativity of the SF_5 group has been proposed to be slightly higher than that of the CF_3 group, 3.62 in comparison to a value of 3.36 [9]. However the Hammett σ_p value for SF_5 was determined to be 0.68 in contrast to σ_p value for CF_3 of 0.54 [10]. This has been further refined to a σ_I value for SF_5 of 0.55 and a σ_R value of 0.11 [10] in contrast to σ_I value for CF_3 of 0.39 and a σ_R value of 0.12 [11,12]. The diminished resonance and increased inductive contributions are consistent with the calculated dipole moments [13,14] of 2.5896 D and 3.556 D for the C–CF_3 and C–SF_5 bonds, respectively. This combination of effects likely amplifies dipolar and electrostatic interactions in pentafluorosulfanylated compounds. Occupying only slightly smaller volume than a *tert*-butyl group ($C(CH_3)_3$) [15], the SF_5 group is sterically demanding and may therefore restrict molecular conformation by occupied volume considerations.

Conformational analysis is central to understanding the impact of substituents on molecular structure and also affords a comparative framework within which the relative effects of various substituents can be compared. The spatial orientation of substituents can affect not only the physical and spectroscopic properties of a molecule but also the reactivity of a substance. With fluorinated compounds with a long liquid range, the principal tools available to examine the conformational influence of fluorinated groups are spectroscopic. Of particular utility are the NMR methods first described in the 1960s that establish a relationship between vicinal proton coupling constants and torsional angles. Karplus [16,17] successfully correlated vicinal proton-proton coupling constants ^3J with the torsional angle φ between the two spins, according to the parameterized equation

$$^3J = A + B\cos\varphi + C\cos 2\varphi. \quad (1)$$

While the incorporation of inductive effects on the polarization of the C–H bonds [18,19] into Eq. (1) indicated that the contribution of those effects to the correlation was relatively small, it was observed that substituent-induced hybridization changes at carbon did modulate vicinal coupling [16,17,20,21].

More recently the influence of substituent electronegativity and orientation on ^3J values was recognized. In 1980, Haasnoot et al. [22] reported a generalized version of Eq. (1) based on empirical

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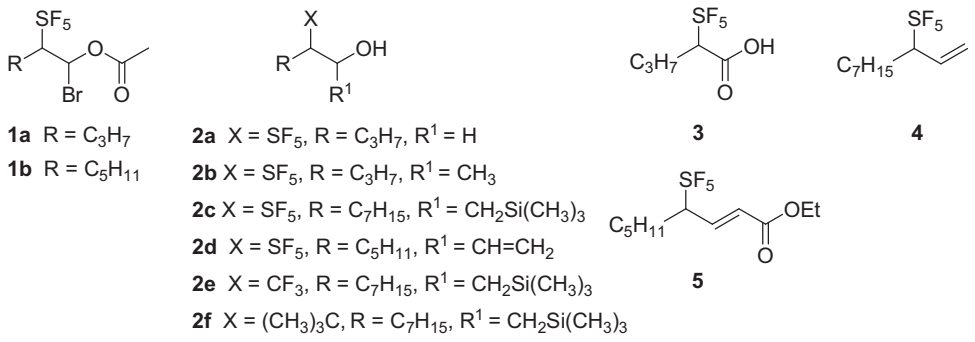


Scheme 1. Pentafluorosulfanyl, trifluoromethyl and *tert*-butyl compounds **1–5**.

studies. The equation corrects for the differences in the electronegativity of the substituent relative to hydrogen ($\Delta\chi_i$) and in the orientation of the substituent relative to the coupled protons (ξ_i) (Eq. (2))

$$^3J_{HH} = P_1\cos^2\varphi + P_2\cos\varphi + P_3 + \Sigma\Delta\chi_i\{P_4 + P_5\cos^2(\xi_i\varphi + P_6 \cdot |\Delta\chi_i)\} \quad (2)$$

It is this most contemporary approach to the correlation of coupling constants and dihedral angles that was used in this work.

During the synthesis and reactions of α-SF_5 carbonyl compounds (See Scheme 1) [23], ^{1}H NMR resonances with unanticipated coupling constants, as well as diastereotopic geminal proton resonances were observed (Fig. 1).

For example, from the spectrum of a single diastereomer of **1a**, the presence of two broad multiplets at δ 1.78 ppm and δ 1.58 ppm, resonances assigned to the geminal protons γ to the SF_5 group, strongly suggested that those protons were diastereotopic. Other diastereotopic resonances were also observed for SF_5-containing alcohols **2a–d**, carboxylic acid **3**, alkene **4** and α,β-unsaturated ester **5**. To the best of our knowledge the analogous CF_3-containing compounds did not exhibit any diastereotopicity for the corresponding γ protons. In a 2009 report by MacMillan et al. [24], on the preparation of 2-(trifluoromethyl)octan-1-ol, 5-(benzyloxy)-2-(trifluoromethyl)-pentan-1-ol or ethyl 6,6,6-trifluoro-5-(hydroxymethyl)hexanoate, resonances corresponding to the protons γ to a CF_3 group were not obviously diastereotopic.

2. Results and discussion

2.1. Determination of average conformations of *1a*, *2c*, *2d* and *4a* by $J_{H,X}$ coupling analyses

By a combination of selective decoupling, COSY and 2D *J*-resolved spectroscopic techniques it was possible to definitively assign the proton resonances and the coupling relationships for four molecules, **1a**, **2c**, **2d** and **4a** that are illustrative of the influence of the pentafluorosulfanyl group on the conformation of an alkyl chain. Translation of the coupling constants to the dihedral angles φ using Eq. (2) (Table 1) enabled determination of a conformation for each molecule consistent with those coupling constants.

The structures of **2c** and **2d** derived from coupling constant analyses share structural features that are in close agreement with those predicted by the modeling calculations (Fig. 2). In both compounds, the small $J_{5,6}$ coupling constants observed for the protons α to the SF_5 and OH groups correspond to a nearly orthogonal orientation for those protons (Fig. 2B) resulting in S–C–C–O dihedral angles of ±85° (Fig. 2C) the predicted torsional angle in 2-(pentafluorosulfanyl)propan-1-ol when dipolar interactions were investigated [25].

Also found in the conformational modeling of each compound are deformations of the SF_5 group geometry. In both alcohols, two of the C–S–F_{eq} bond angles, averaging 93.5°, deviate significantly from the optimal 90° predicted by the square pyramidal geometry of the SF_5 group. In addition the equatorial fluorines deviate from the normal equatorial plane approximately 0.052 Å (Fig. 3).

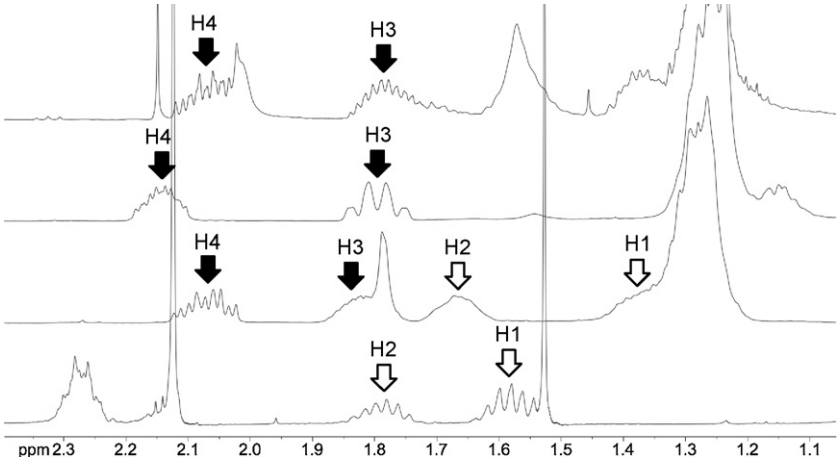
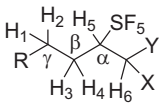


Fig. 1. NMR spectra of compounds **4**, **2d**, **2c**, and **1a** (top to bottom). Diastereotopic proton resonances are indicated by the arrows.

Table 1
Experimentally determined torsional angles from coupling constant data.



Cmpd.	R	X	Y	$J_{1,3}$[a]	$\varphi_{1,3}$[b]	$J_{1,4}$[a]	$\varphi_{1,4}$[b]	$J_{2,3}$[a]	$\varphi_{2,3}$[b]	$J_{3,5}$[a]	$\varphi_{3,5}$[b]	$J_{4,5}$[a]	$\varphi_{4,5}$[b]	$J_{5,6}$[a]	$\varphi_{5,6}$[b]
1a	CH_3	Br	OAc	2.5	62	–[c]	–[c]	7.8	137	8.9	−26	–[c]	–[c]	1.0	88
2c	C_5H_{11}	OH	CH_2TMS	5.1	50	10.3	145	10.4	145	2.8	−51	9.9	156	0.4	85
2d	C_3H_8	OH	$CH{=}CH_2$	5.0	50	9.8	143	–[c]	–[c]	8.4	−36	4.3	43	0[c]	90
4a	C_5H_{11}	–	$=CH_2$	3.0	60	12.0	153	10.0	144	3.1	−50	12.0	176	–[d]	–[d]

[a] In Hz.
[b] Torsional angle φ (in degrees) corresponding to measured coupling constant. The sign of φ is defined as positive assuming a clockwise rotation to describe the angle between the vectors assigned to each of the interacting protons. The intervening C–C bond vector is assumed to be pointing from the carbon bearing the protons with the lower numerical value to the carbon with the protons having a higher numerical value. Angles greater than 180° are negative and reported as the difference from 180°.
[c] Coupling was not sufficiently resolvable to obtain φ.
[d] Haasnoot eq applies only to sp^3 hybridized centers.

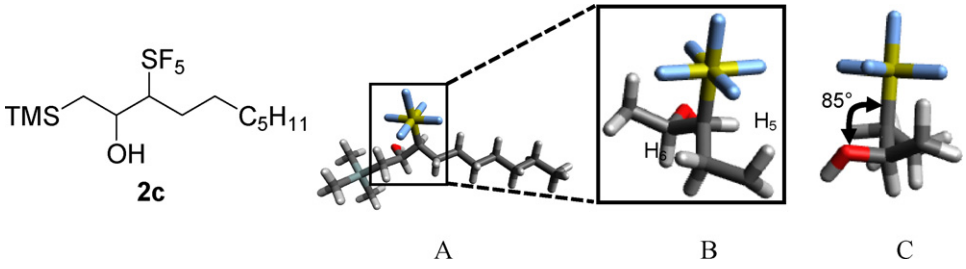


Fig. 2. (A) Average conformation of **2c** derived from coupling constant analyses; (B) the approximate 90° dihedral angle between H5 and H6; (C) the corresponding S–C–C–O dihedral angle.

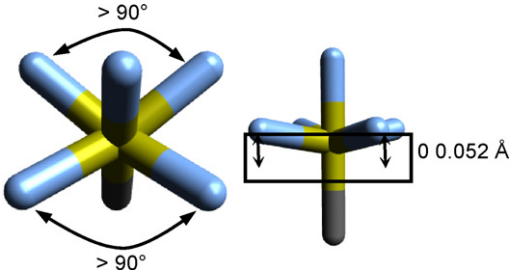


Fig. 3. Deformation of the pentafluorosulfanyl group as predicted by computational experiments.

Between the two affected equatorial fluorines, the fluorine interacting with the hydroxyl group has the more open C–S–F_{eq} bond angle. The remaining affected fluorine atom is dislocated upward by the carbon atom in the β position. A second deformation occurs in the equatorial plane of the SF_5 group between equatorial fluorine atoms, where there is an increase in the F_{eq}–S–F_{eq} bond angle in the vicinity of the γ methylene group. Computations previously performed by Kirsch [26] showed the same widening of the F_{eq}–S–F_{eq} bond angle in the presence of steric stress.

In adduct **1a**, a smaller S–C–C–O torsional angle (−49°) is found than in the **2c** or **2d**. Despite this difference, similar deformations of the SF_5 equatorial plane are observed. In the vicinity of the γ methylene hydrogen, the F_{eq}–S–F_{eq} bond angle is approximately 92°, while the other three F_{eq}–S–F_{eq} angles correspondingly diminish to 89° to compensate. Additionally, all four equatorial fluorine atoms have C–S–F_{eq} bond angles that are greater than 90°, with the result that the equatorial plane defined by the fluorines moves closer toward the axial fluorine.

In Fig. 4, from the structures determined by coupling constant analyses, it is clear that one of the γ hydrogens, H_2, in **1a**, **2c**, **2d** or **4a** is located between the fluorines. Accommodation of the proton by deformation of the SF_5 group geometry appears to trap that proton between the two fluorines and hence lead to the observed diastereotopic signals in the NMR spectra.

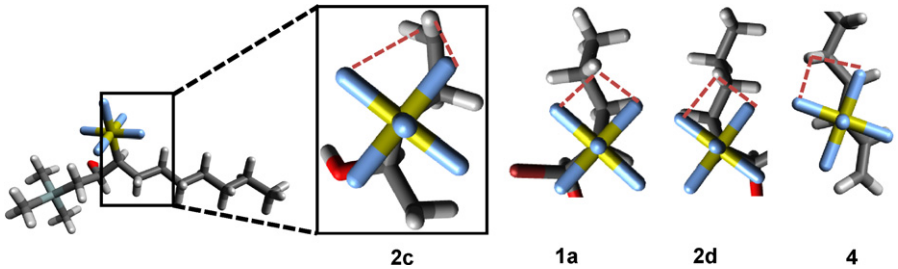


Fig. 4. The relationship of the SF_5 group with the alkyl chains of **2c**, **1a**, **2d** and **4** as derived from coupling constant analyses. In the enlarged images, the dotted lines show the relationship between equatorial fluorines and γ proton.

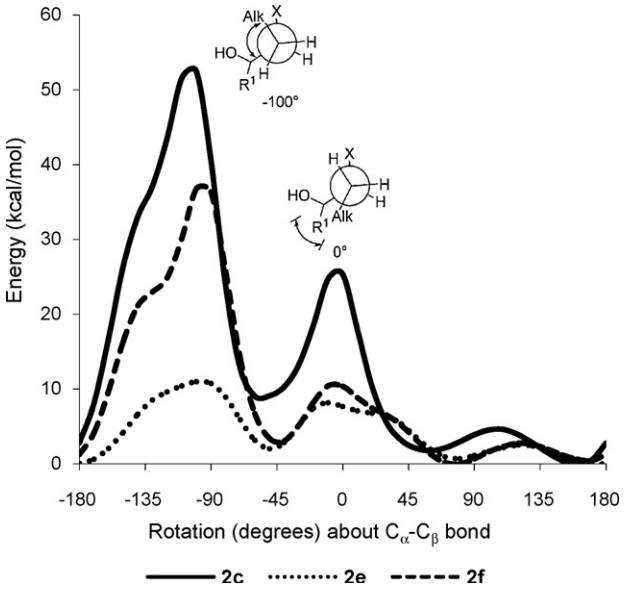


Fig. 5. Barriers to rotation about the torsional angle φ for the C_α–C_β bond. φ is defined as 0° for the fully eclipsed conformation where the alkyl and hydroxymethylene groups are synperiplanar.

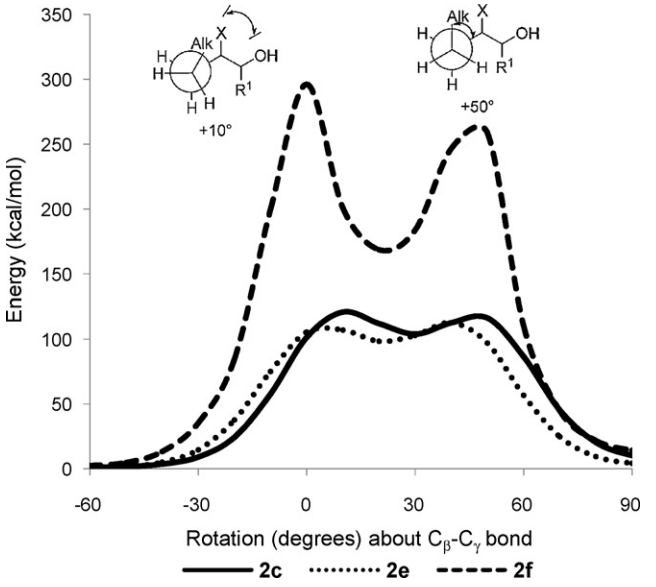


Fig. 6. Barriers to rotation about the torsional angle φ for the C_β–C_γ bond. φ is defined as 0° for the fully eclipsed conformation where the alkyl groups are synperiplanar.

2.2. The flexibility of the alkyl chain

Comparison of the electronic influences of pentafluorosulfanylation and trifluoromethylation is relatively straightforward especially considering the availability of group electronegativities, σ_p values and calculated values for the dipole moments of the C–CF_3 and C–SF_5 bonds. However the relative effect of SF_5-, CF_3-, and $C(CH_3)_3$-substitution on conformation is not easily quantified. To advance the comparison of the three substituents, the flexibility of the substituted alkyl chain was determined by computing the energy of the barrier to rotation about the C_α–C_β and C_β–C_γ bonds in SF_5-, CF_3-, and $C(CH_3)_3$-substituted trimethylsilylated alkanols **2c**, **2e** and **2f**, respectively.

2.2.1. The C_α–C_β bond

The barrier to rotation about the C_α–C_β bond very clearly allows a comparison of the influence of SF_5-, CF_3-, and $C(CH_3)_3$-group eclipsing interactions with both protons and alkyl chains. As expected, the most stable conformer about the C_α–C_β bond places the alkyl chain *anti* to the hydroxymethylene substituent, minimizing steric interactions. However the barrier to rotation between the low energy conformations at 60° and −60° illustrates a clear difference of the effect of SF_5-substitution. The barrier between the corresponding minima for **2e** and **2f**, is only 6.1 kcal/mol and 7.3 kcal/mol, respectively, but the barrier for the SF_5-substituted compound **2c** is significantly higher,16.4 kcal/mol (Fig. 5 and Table 2).

Table 2
Conformer energy dependence upon C_α–C_β torsional angle φ.

R	φ[a]	Energy in kcal/mol
SF_5	+60	1.76
SF_5	0	25.4
SF_5	−60	9.04
SF_5	−100	52.5
CF_3	+80	0.69
CF_3	−10	8.16
CF_3	−50	2.01
CF_3	−100	11.0
$C(CH_3)_3$	+80	0
$C(CH_3)_3$	−10	10.4
$C(CH_3)_3$	−40	3.07
$C(CH_3)_3$	−100	36.8

[a] In degrees. See Table 1 footnote b.

The 9 kcal/mol difference in eclipsing interaction of hydrogen with SF_5 relative to the nominally larger *tert*-butyl group when $\varphi = 0°$ was unanticipated. A similar phenomenon was observed for the highest energy conformation where the alkyl chain is gauche to both the hydroxymethylene group and either SF_5-, CF_3-, and $C(CH_3)_3$-groups. The energy of **2c** is 52 kcal/mol, 41 kcal/mol more destabilized than **2e** and 16 kcal/mol more than **2f** (Table 2). In both of these interactions the greater influence of the SF_5 group is unanticipated, as the SF_5 and $C(CH_3)_3$ groups have nearly an equivalent occupied volume, with the SF_5 group being the smaller group [15].

When $\varphi = -100°$, the distance between H_2 bonded to the β-carbon and the fluorines of either the SF_5- or CF_3-groups, and the hydrogen bonded to the β-carbon and a hydrogen of the $C(CH_3)_3$ group is also informative. The distance between the atoms for **2c** is 1.27 Å, for **2e** 2.06 Å and **2f** 1.06 Å. These values are significantly less than the combined van der Waals radius of hydrogen and fluorine, 2.67 Å and of hydrogen and hydrogen 2.4 Å. From these findings it is clear that functional group volume considerations underestimate the influence of the pentafluorosulfanyl group gauche interactions.

2.2.2. The C_β–C_γ bond

The barrier to rotation about the C_β–C_γ bond enables a comparison of the influence of the remote substituent on eclipsing interactions of two alkyl chains. In the eclipsed conformation where the alkyl chains are nearly synperiplanar, as expected the conformations are dramatically higher in energy for **2c**, **2e** and **2f** (Fig. 6). In this analysis the eclipsed conformation of *tert*-butyl substituted **2f** is dramatically higher in energy, approximately 180 kcal/mol higher, than the corresponding conformations of **2c** or **2e**. The source of the destabilization is evident in this high energy, computed conformation, in that the distance between a hydrogen bound to the δ-carbon and a hydrogen of the *tert*-butyl

group would be an unreasonable 0.44 Å. In contrast to the interactions described for the C_α–C_β bond, the pentafluorosulfanyl group of **2c** affects the rotation of the C_β–C_γ bond in a manner consistent with the smaller occupied volume of the group relative to *tert*-butyl (Fig. 6). In this analysis the comparable energies between **2c** and **2e** might suggest that the pentafluorosulfanyl group has an impact on conformation quite comparable to the much smaller trifluoromethyl group.

3. Conclusion

An investigation of the influence of the pentafluorosulfanyl group on the conformation of aliphatic molecules by both NMR and computational methods that were in good agreement has shown that this group to be very effective at constraining the geometry of substituted molecules. Of particular note is the profound interaction of the pentafluorosulfanyl group with hydrogens located on the γ-carbon. The SF_5 group constrains the freedom of rotation about the C_α–C_β bond so that the protons of that carbon are in intimate contact with the SF_5 group, with one proton bisecting the F-S-F angle. The additional 15 kcal/mol barrier to rotation, relative to the larger *tert*-butyl group was not predictable based on estimates of occupied volume. However, the influence of the SF_5 group on rotation of the C_β–C_γ bond was completely consistent with occupied volume arguments. These effects indicate that a pentafluorosulfanyl group can dramatically constrain the energetically accessible conformations of side chains up to C_7 suggesting that the pentafluorosulfanyl group may find utility in the design of compounds where conformational control is important.

4. Experimental methods

4.1. NMR methods

Determination of the three-dimensional structures of compounds **1a**, **2c–d**, and **4a** were performed using NMR coupling constant data. ^{1}H spectra were recorded on a Bruker Avance-400 MHz NMR spectrometer at 400 MHz. Chemical shifts were recorded relative to the residual signal of $CDCl_3$. For the 2D COSY and *J*-resolved experiments, 2048 × 128 data points were collected. The number of transients collected for each experiment were 8 (with 8 dummy scans) for COSY and 16 for 2D *J*-resolved. The spectral widths for the COSY and 2D *J*-resolved experiments were 10 ppm and 10 ppm × 0.07 ppm, respectively. Coupling constants were determined from 1D spectra, with selective decoupling as needed, and 2D *J*-resolved spectra. The coupling constants were then used in the Haasnoot equation to arrive at a series of torsional angles to produce a three-dimensional structure of each compound. The parameters used for the equation were obtained from the original report by Haasnoot et al. [22] group electronegativities (see Table 1) were obtained from reports by Huheey [27,28], except for the SF_5 group, which was reported by Lal and Minnich [29] (Table 3).

Table 3
χ and $\Delta\chi$ values for use in Eq. (2).

Substituent	χ	$\Delta\chi$
H	2.20	0.00
CH_3	2.27	0.07
$Si(CH_3)_3$	2.27	0.07
CH_2CH_3	2.28	0.08
CH_2–CH=CH_2	2.37	0.17
CH=CH_2	2.41	0.21
$OC(O)CH_3$	2.95	0.75
Br	2.96	0.76
OH	3.51	1.31
SF_5	3.62	1.42

4.2. 1-Bromo-2-pentafluorosulfanylpentyl acetate (1a)

4.2.1. Mixture of two diastereoisomers, 3.4:1

^{1}H, isomer 1 (major, 400 MHz, $CDCl_3$): δ_H (ppm) = 7.27 (d, $J_{5,6}$ = 1.0 Hz, 1H, H6), 4.17 (m, $J_{5,3}$ = 8.9 Hz, $J_{5,6}$ = 1.0 Hz 1H, H5), 2.27 (m, $J_{3,5}$ = 8.9 Hz, $J_{3,2}$ = 7.8 Hz, $J_{3,1}$ = 2.5 Hz, 2H, H3 and H4), 2.12 (s, 3H, acyl CH_3), 1.79 (m, $J_{1,3}$ = 2.5 Hz, 1H, H1), 1.59 (m, $J_{2,3}$ = 7.8 Hz, 1H, H2), 1.02 (t, *J* = 7.4 Hz, 3H, alkyl CH_3). ^{1}H, isomer 2 (minor, 400 MHz, $CDCl_3$): 7.11 (d, $J_{6,5}$ = 3.2 Hz, 1H, H6), 4.01 (dtt, $J_{5,3}$ = 9.2 Hz, 6.1 Hz, $J_{5,6}$ = 3.2 Hz, 1H, H5), 2.27 (m, $J_{3,5}$ = 8.9 Hz, $J_{3,2}$ = 7.8 Hz, $J_{3,1}$ = 2.5 Hz, 2H, H3 and H4), 2.12 (s, 3H, acyl CH_3), 1.79 (m, $J_{1,3}$ = 2.5 Hz, 1H, H1), 1.59 (m, $J_{2,3}$ = 7.8 Hz, 1H, H2), 1.02 (t, *J* = 7.4 Hz, 3H, alkyl CH_3). ^{13}C, isomer 1 (major, 100 MHz, $CDCl_3$): δ_C (ppm) = 167.2 ($C_{Carbonyl}$), 90.3 (C2, qn, $J_{C,F}$ = 8.1 Hz), 71.8 (C1, qn, $J_{C,F}$ = 5.4 Hz), 29.7 (m, C3), 21.1 (bs, C4), 20.5 (C_{methyl}), 13.6 (C5). ^{13}C, isomer 2 (minor, 100 MHz, $CDCl_3$): δ_C (ppm) = 167.1 ($C_{Carbonyl}$), 87.9 (C2, m), 73.4 (C1, m), 33.4 (m, C3), 20.8 (C_{methyl}), 20.2 (bs, C4), 13.8 (C5). ^{19}F, isomer 1 (major, 376 MHz, $CDCl_3$): δ_F (ppm) = 83.3 (qn, $J_{ax,eq}$ = 142.7 Hz, 1F, F_{ax}), 58.8 (d, $J_{eq,ax}$ = 143.1 Hz, 4F, F_{eq}). ^{19}F, isomer 2 (minor, 376 MHz, $CDCl_3$): δ_F (ppm) = 83.4 (qn, $J_{ax,eq}$ = 144.3 Hz, 1F, F_{ax}), 59.7 (dd, $J_{eq,ax}$ = 144.3 Hz, $J_{eq,H}$ = 5.6 Hz, 4F, F_{eq}).

4.3. 3-Pentafluorosulfanyl-1-trimethylsilyldecan-2-ol (2c)

^{1}H (400 MHz, $CDCl_3$): δ_H (ppm) = 4.65 (dd, $J_{6,8}$ = 10.0 Hz, $J_{6,7}$ = 4.7 Hz, $J_{6,5}$ = 0.4 Hz, 1H, H6), 3.77 (m, $J_{5,4}$ = 9.9 Hz, $J_{5,3}$ = 2.8 Hz, $J_{5,6}$ = 0.4 Hz, 1H, H5), 2.10 (m, $J_{4,1}$ = $J_{4,3}$ = 10.3 Hz, $J_{4,5}$ = 9.9 Hz, $J_{4,2}$ = 5.0 Hz, 1H, H4), 1.86 (m, $J_{3,2}$ = 10.4 Hz, $J_{3,4}$ = 10.3 Hz, $J_{3,1}$ = 5.1 Hz, $J_{3,5}$ = 2.8 Hz 1H, H3), 1.82 (bs, 1H, OH), 1.69 (m, $J_{2,3}$ = 10.4 Hz, $J_{2,4}$ = 5.0 Hz, H2), 1.41 (m, $J_{1,4}$ = 10.4 Hz, $J_{1,3}$ = 5.0 Hz, H1), 1.32 (m, 8H, C_4H_8), 1.00 (dd, $J_{8,7}$ = 14.5 Hz, $J_{8,6}$ = 10.0 Hz, 1H, H8), 0.90 (t, *J* = 6.7 Hz, 3H, alkyl CH_3), 0.70 (dd, $J_{7,8}$ = 14.5 Hz, $J_{7,6}$ = 4.7 Hz, 1H, H7), 0.10 (s, 9H, $Si(CH_3)_3$). ^{13}C (100 MHz, $CDCl_3$): δ_C (ppm) = 97.1 (m, C3), 69.6 (t, $J_{C,F}$ = 4.0 Hz, C2), 31.8 (C8), 29.5 (C7), 29.0 (C6), 28.4 (bs, C5), 26.6 (t, $J_{C,F}$ = 3.2 Hz, C4), 24.3 (C1), 22.7 (C9), 14.1 (C10), −1.0 (C_{TMS}). ^{19}F (376 MHz, $CDCl_3$): δ_F (ppm) = 88.2 (qn, $J_{ax,eq}$ = 140.7 Hz, 1F, F_{ax}), 57.6 (d, $J_{eq,ax}$ = 140.6 Hz, 4F, F_{eq}).

4.4. 4-Pentafluorosulfanylhept-1-en-3-ol (2d)

^{1}H (400 MHz, $CDCl_3$): δ_H (ppm) = 5.82 (ddd, $J_{7,9}$ = 17.1 Hz, $J_{7,8}$ = 10.6 Hz, $J_{7,6}$ = 4.6 Hz, 1H, H7), 5.46 (dt, $J_{9,7}$ = 17.1 Hz, $J_{9,8}$ = 1.5 Hz, 1H, H9, *trans* to H7), 5.30 (dt, $J_{8,7}$ = 10.5 Hz, $J_{8,9}$ = 1.5 Hz, 1H, H8, *cis* to H7), 5.01 (bs, 1H, H6), 3.86 (m, $J_{5,3}$ = 8.4 Hz, $J_{5,4}$ = 4.3 Hz, 1H, H5), 2.10 (m, $J_{3,5}$ = 8.4 Hz, $J_{3,1}$ = 5.0 Hz, 1H, H3), 1.84 (m, $J_{4,1}$ = 9.8 Hz, $J_{4,5}$ = 4.3 Hz, 1H, H4), 1.6 (bs, 2H, OH and H2), 1.42 (m, $J_{1,4}$ = 9.8 Hz, $J_{1,3}$ = 5.0 Hz, 1H, H1) 1.32 (m, 4H, C_2H_4), 0.89 (t, *J* = 6.9 Hz, CH_3). ^{13}C (100 MHz, $CDCl_3$): δ_C (ppm) = 136.8 (C2), 117.1 (C1), 92.8 (qn, $J_{C,F}$ = 4.9 Hz, C4), 71.8 (qn, $J_{C,F}$ = 4.0 Hz, C3), 28.7 (qn, *J* = 3.2 Hz, C5), 21.3 (bs, C6), 13.8 (C7). ^{19}F (376 MHz, $CDCl_3$): δ_F (ppm) = 87.3 (9 peaks, $J_{ax,eq}$ = 142 Hz, 1F, F_{ax}), 58.0 (td, $J_{eq,ax}$ = 142 Hz, $J_{eq,H}$ = 5.0 Hz, 4F, F_{eq}).

4.5. 3-Pentafluorosulfanyldec-1-ene (4)

^{1}H (400 MHz, $CDCl_3$): δ_H (ppm) = 5.83 (m, $J_{6,8}$ = 16.9 Hz, $J_{6,7}$ = 10.0 Hz, $J_{6,5}$ = 9.0 Hz, 1H, H6), 5.43 (dd, $J_{7,6}$ = 10.0 Hz, $J_{7,8}$ = 0.9 Hz, 1H, H7, cis to H6), 5.37 (dd, $J_{8,6}$ = 16.9 Hz, $J_{8,7}$ = 0.9 Hz, 1H, H8, trans to H6), 4.25 (m, $J_{5,4}$ = 12.0 Hz,

$J_{5,6}$ = 9.0 Hz, $J_{5,3}$ = 3.1 Hz, 1H, H5), 2.17 (m, $J_{3,4}$ = 12.0 Hz, $J_{3,2}$ = 10.0 Hz, $J_{3,5}$ = 3.1 Hz, $J_{3,1}$ = 3.0 Hz, 1H, H3), 1.83 (m, $J_{4,1}$ = $J_{4,3}$ = $J_{4,5}$ = 12.0 Hz, $J_{4,2}$ = 3.0 Hz, 1H, H4), 1.30 (m, 9H, C_4H_8 and H2), 1.18 (m, $J_{1,3}$ = 3.0 Hz, $J_{1,4}$ = 12.0 Hz, 1H, H1), 0.89 (t, J = 6.9 Hz, 3H, alkyl CH_3). ^{13}C (100 MHz, $CDCl_3$): δ_C (ppm) = 133.3 (q, J = 3.4 Hz, C1), 122.7 (C2), 90.8 (qn, $J_{C,F}$ = 9.0 Hz, C3), 31.9 (qn, $J_{C,F}$ = 3.7 Hz, C4), 31.7 (C8), 29.0 (C7), 28.9 (C6), 27.0 (m, C5), 22.6 (C9), 14.1 (C10). ^{19}F (376 MHz, $CDCl_3$): δ_F (ppm) = 84.5 (qn, $J_{ax,eq}$ = 141.7 Hz, 1F, F_{ax}), 54.2 (dd, $J_{eq,ax}$ = 141.6 Hz, $J_{eq,H}$ = 5.8 Hz, 4F, F_{eq}).

4.6. Computational studies

Calculations were performed using Firefly QC package [30], which is partially based on the GAMESS (US) [31] source code, Gaussian 98, and Titan. The input matrix was created using MacMolPlt or Avogadro for computations performed using Firefly; Titan was used to create the input matrix for calculations performed in Gaussian 98. Structure optimization was performed using standard convergence criteria. Frequency calculations were performed for all optimized structures to confirm the stationary points were energy minima, and not transition structures or higher-order loci on the potential energy surface. All structures were computed for isolated molecules in the gas phase, without solvation models. Partial charges were calculated using Mulliken, Lowdin, or Natural Bond Orbital methods.

The influence of R and R^1 on the conformation of **2** was examined using computational methods. Alkyl chain flexibilities for **2c**, **2e** and **2f** (R = SF_5, CF_3, and $(H_3C)_3C$, respectively) were investigated by determining the substituent effects on rotational barriers of the alkyl chain using the B3LYP/6-31 + G(d) level of theory. Calculations were performed from −180° to +180° in 10° increments; unrelaxed calculations were utilized to significantly reduce computation times. The 1-hydroxy-2-(trimethylsilyl)ethyl group was constrained during torsional angle scans. One of the methylene protons was fixed to bisect the equatorial F-S-equatorial F angle, a previously established minimum energy conformation for this portion of the molecule. To investigate the distortions of the SF_5 group geometry, the energies of the structures were minimized at the same level of theory but with select torsional angles constrained to be in agreement with the spectroscopic data.

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