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^{19}F NMR of linear *N*,*N*-difluoroaminoalkanes

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ABSTRACT

Whereas most *N*,*N*-difluoroaminoalkanes exhibit a single ^{19}F resonance at about +50 ppm, the tri-component mixtures of both *N*,*N*-difluoroaminopentanes and *N*,*N*-difluoroaminohexanes exhibited a more complex pattern. The individual 1-*N*,*N*-difluoroamino-, 2-*N*,*N*-difluoroamino- and 3-*N*,*N*-difluoroaminopentanes have been synthesized and their separated resonances are reported.

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1. Introduction

1.1. ^{19}F spectra of N,N-difluoroaminoalkanes

We have previously shown that Nitrogen Trifluoride (NF_3) can be reacted in a controlled manner with alkanes, cycloalkanes and ethers in a 400 °C vapor phase reactor to generate *N*,*N*-difluoroaminoalkanes, -cycloalkanes and -ethers [1]. In most cases, a singular resonance was observed in each ^{19}F spectrum between +25 and +55 ppm vs. $CFCl_3$ (see Table 1). In the cases of *n*-pentane + NF_3 and *n*-hexane + NF_3, three isomeric products were generated. However, rather than three individual singlets, a pattern of five equidistant peaks at about +39 ppm was observed for both the *N*,*N*-difluoroaminopentanes mixture and the *N*,*N*-difluoroaminohexanes mixture (see Fig. 1). In addition, a nearby singlet at +56 ppm added more uncertainty to the assignment of resonances to individual isomers.

To positively assign resonances and coupling values to each individual isomer, and thus interpret the spectra of the mixed isomers, we undertook to prepare each isomer of *N*,*N*-difluoroaminopentane and *N*,*N*-difluoroaminohexane independently and to observe the individual ^{19}F spectra. The individual *N*,*N*-difluoroaminopentanes and -hexanes were prepared by reaction of the appropriate Grignard reagent with NF_3 (see Section 4).

2. Results and discussion

2.1. ^{19}F spectra of N,N-difluoroaminopentane isomers

2.1.1. ^{19}F spectra of 1-N,N-difluoroaminopentane

1-*N*,*N*-difluoroaminopentane, **1**, was prepared by the reaction of NF_3 with 1-bromomagnesiopentane. The ^{19}F NMR spectrum of **1** shows that this compound is responsible for the single resonance observed at +55.8 ppm in the mixed spectra. NMR literature for 1-*N*,*N*-difluoroaminobutane [2] indicates a single resonance at +54.6 ppm (sign inverted from Φ), supportive of our result.

2.1.2. ^{19}F spectra of 2-N,N-difluoroaminopentane

2-*N*,*N*-difluoroaminopentane, **2**, was prepared by the reaction of NF_3 with 2-bromomagnesiopentane. The ^{19}F NMR spectrum of **2** is observed to be an AB pattern of two doublets, one for each fluorine, at +43.1 ppm and +35.7 ppm. They are coupled J_{F-F} = 566 Hz.

Reference [3] reports that the spectrum of 2-*N*,*N*-difluoramino-3-fluorobutane "had bands centered about +39.1" (again, sign inverted from Φ and CF_3CO_2H standard), consistent with our result.

2.1.3. ^{19}F spectra of 3-N,N-difluoroaminopentane

3-*N*,*N*-difluoroaminopentane, **3**, was prepared by the reaction of NF_3 with 3-bromomagnesiopentane. The ^{19}F NMR spectrum of **3** is observed to be a single resonance at +39.4 ppm. In light of the widely separated doublets observed for 2-*N*,*N*-difluororamino-pentane, we had expected a more complex pattern from **3**, superimposed upon the pattern of **2** in the mixed spectra. Such is

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Table 1
Representative ^{19}F resonances.

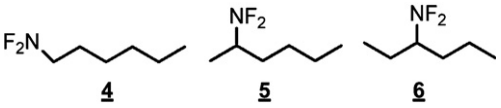
2-*N*,*N*-difluoroamino-2-methylpropane	δ +28.3 (s)
α-*N*,*N*-difluoroaminotetrahydrofuran	δ +31.9 (d, J = 66.5 Hz) (a relatively small splitting)
N,*N*-difluoroaminocyclohexane	δ +42.3 (s)
N,*N*-difluoroaminocyclopentane	δ +52.9 (s)
N,*N*-difluoroaminobenzene	δ −63.2 (s)

not the case. However, the resonance of **3** is precisely positioned at the center point of the 2-*N*,*N*-difluororaminopentane pattern! The simplicity of the resonance for **3** can be attributed to the symmetry of the molecule, where each F is in equivalent magnetic environments.

2.2. ^{19}F spectra of N,N-difluoroaminohexane isomers

2.2.1. Analogous interpretation of the spectral pattern of mixed N,N-difluoroaminohexane isomers

The ^{19}F spectrum of the mixed *N*,*N*-difluoroaminohexane isomers is identical to that of the pentane isomers (completely superimposable!). By direct analogy, we can interpret the singlet observed at +55.9 ppm to be the resonance of 1-*N*,*N*-difluoroaminohexane, **4**. The spectrum of 2-*N*,*N*-difluoroaminohexane, **5**, can be extracted as two coupled AB doublets at +46.7 and +35.7 ppm, J_{F-F} = 566 Hz. The presumed spectrum of 3-*N*,*N*-difluoroaminohexane, **6**, gives us pause. As this molecule is NOT symmetrical like **3**, we would predict two resonances, one for each fluorine, as in **2** and **5**. Since the mixed spectra has a central peak, we could explain this by predicting the spectra of **6** to be two overlapping coupled doublets at +40.6 and +38.1 ppm, J_{F-F} = 566 Hz, but integration of various fractions of the mixed isomers did not support this idea. To be confident, we had no choice but independently prepare **5** and **6** and observe their spectra.



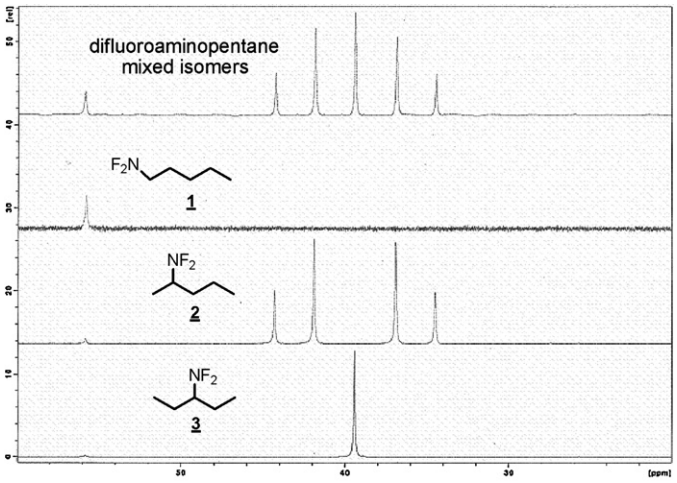


Fig. 1. ^{19}F NMR of difluoroaminopentanes.

2.2.2. ^{19}F spectra of 2-N,N-difluoroaminohexane

2-*N*,*N*-difluoroaminohexane, **5**, was prepared by the reaction of NF_3 with 2-chloromagnesiohexane. As predicted, the ^{19}F NMR spectrum of **5** is observed to be two doublets, one for each fluorine, at +43.1 ppm and +35.7 ppm. They are coupled J_{F-F} = 566 Hz.

2.2.3. ^{19}F spectra of 3-N,N-difluoroaminohexane

3-*N*,*N*-difluoroaminohexane, **6**, was prepared by the reaction of NF_3 with 2-chloromagnesiohexane. The ^{19}F NMR spectrum of **6** is observed to be a single resonance at +39.3 ppm. Despite a formal lack of symmetry in the molecule, the two fluorines of **6** are apparently in identical environments. How the molecule is attaining a symmetric configuration, at this point, we do not know. None-the-less, the resonance of **6** is precisely positioned at the center point of the 2-*N*,*N*-difluororaminopentane, **5**, pattern just as the resonance of **3** is centered on that of **2**!

2.3. Analysis of the 2-NF_2 vs. 3-NF_2 spectral difference

In seeking an explanation for the stark difference in the ^{19}F resonances of 2-difluoroamino- and 3-difluoroaminoalkanes

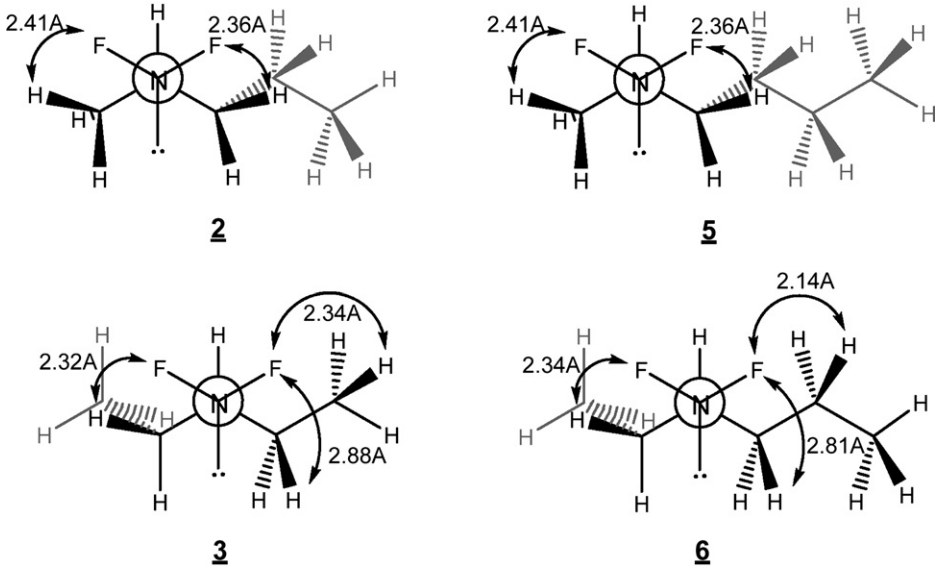


Fig. 2. Calculated F–H distances of difluoroaminopentanes and difluoroaminohexanes.

(particularly the lack of an AB pattern in **6**), we evaluated each molecule for differentiated interaction between the fluorine atoms and nearby hydrogen atoms. This was first attempted theoretically by availing ourselves of a configurational model for each isomer as determined by Gaussian *ab initio* calculations [4]. Fig. 2 shows Newman projections of the four molecules in question based on the Gaussian results. It can be seen that for both 2-substituted compounds, **2** and **5**, each F atom is nearly equidistant and of equal dihedrals to their respective vicinal protons. One would not expect differentiation in the ^{19}F signals from the slight differences. Conversely, both 3-substituted compounds, **3** and **6**, have distinctly different distances between the F atoms and their vicinal neighbors (2.3A vs. 2.8A). However, a proton on the 5 position of each is nearly equidistant with the proton at the 2 position, thus possibly affording a magnetically symmetrical environment to each F atom and equalizing their signals. As it is, then, theoretical analysis of the vicinal F–H interactions does not explain the observed resonance patterns.

We sought to circumvent theoretical analysis by repeating the ^{19}F NMR spectra of compounds **2**, **3**, **5** and **6** in non-decoupled mode (H–F coupled) and observing for tell-tale F–H couplings. As it were, the only couplings observed at 235 MHz were the $^{3}J_{F-H}$ coupling to the respective geminal protons. The ^{19}F NMR signals of **2** exhibited a doublet $^{3}J_{F-H}$ = 18.0 for the upfield F and a doublet $^{3}J_{F-H}$ = 27.7 for the downfield F and **5** similarly exhibited doublets $^{3}J_{F-H}$ = 19.8 and $^{3}J_{F-H}$ = 27.6. This suggests a variation from the perfectly staggered configuration calculated and shown in Fig. 2 and is in excess of that which could be attributed to the electronic effect of the extended sidechain [5]. This vicinal coupling information is otherwise uninformative. The ^{19}F signal for **3** exhibited a doublet $^{3}J_{F-H}$ = 24.6 and for **6** exhibited a doublet $^{3}J_{F-H}$ = 21.6, with no other couplings observable. This (along with the original fact that there is only one F resonance), indicates that both F's in both molecules are symmetrically disposed in the staggered conformation and that distances to neighboring protons are more or less equivalent or are too distant to couple.

One final and slightly more fruitful look into the possible causes for the lack of differentiation of the F signal in **6** was an evaluation of the F interactions with neighboring C atoms. Fig. 3 shows C_α–C_β and C_α–$C_{\beta'}$ bond distances as well as the dihedral angles to the rest of the carbon chains, again as calculated by Gaussian. In each case, all C–C bond lengths are 1.53–1.54 A. No differentiation in signals could be expected from such identical distances. Evaluation of the dihedral angle of the C3–C4 bonds of **2** and of **4** show each to be ~176° and nearly optimal for orbital interaction with the N–F bond. The C1 side obviously has no such possibility for interaction. Again, however, we are disappointed when we evaluate the interactions of **3** and **6**. We see almost no potential for interaction with the C4–C5 bond as the dihedral angles with the nearest F are close to the minimally interactive 90° (89° and 92°). However, this time, there is the strong potential for interaction with the C1–C2 bond with the nearest F with dihedral angles of ~166° for both **3** and **6**. Of course, the C1–C2 and C4–C5 interactions are inversed for the more distant F's, but the expectation of interaction is the same. From the calculated dihedral angles, compounds **3** and **6** should have differentiated ^{19}F signals as well as compounds **2** and **3**. Again, this is not the case and our modeling is not helpful.

Table 2
F–C coupling constants from ^{13}C spectra (α carbon in bold).

Compound	J_{F-C1}	J_{F-C2}	J_{F-C3}	J_{F-C4}	J_{F-C5}	J_{F-C6}
2	9.8	**6.1**	6.5	0	0	–
3	10.0	8.2	**5.3**	8.2	10.0	–
5	9.8	**6.2**	6.7	0	0	0
6	0	8.6	**5.5**	7.8	0	0

A follow-up to this theoretical analysis of the F-sidechain interactions is an evaluation of the observed F–C couplings for each molecule. Table 2 displays those coupling constants as measured from the ^{13}C spectra. One observes, as expected, that the clearly unsymmetrical compounds **2** and **5** show distinctly different coupling constants to the β and β′ carbons (ΔJ = 3.2 Hz) and thus evidence of unsymmetrical interactions with the F atoms. Likewise, completely symmetrical compound **3** shows equal F interactions with the β and β′ carbons, as expected. However, the anomalous compound **6**, with its single F resonance, exhibits much more similar couplings (ΔJ = 0.8 Hz) than its five carbon analog **5**. In this small difference from one side of the molecule to the other, we finally find supporting evidence for a magnetically symmetric environment around the NF_2 group of an otherwise unsymmetric molecule.

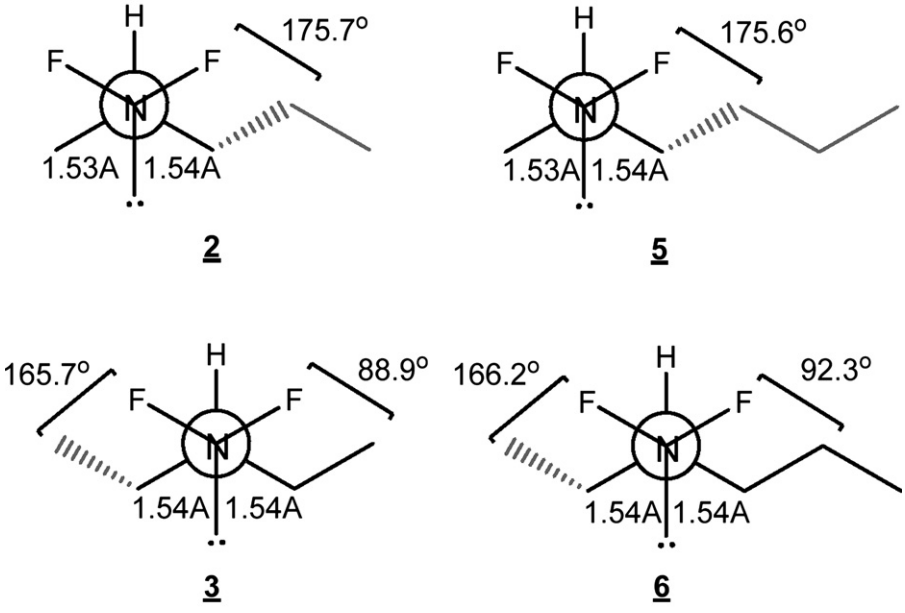


Fig. 3. C–C bond lengths and dihedral angles for 2- and 3-difluoroaminoalkanes.

3. Conclusion

At 400 °C, NF_3 reacts in the vapor phase with *n*-pentane and *n*-hexane to generate a mixture of *N*,*N*-difluoroaminopentanes and *N*,*N*-difluoroaminohexanes, respectively. By generating each individual isomer of *N*,*N*-difluoroaminopentane and -hexane by solution chemistry, we have recorded the individual ^{19}F spectra of 1-*N*,*N*-difluoroaminopentane, 2-*N*,*N*-difluoroaminopentane, 3-*N*,*N*-difluoroaminopentane, 2-*N*,*N*-difluoroaminohexane and 3-*N*,*N*-difluoroaminohexane. The separate ^{19}F spectra clarify the interpretation of the spectral pattern observed for the mixed *N*,*N*-difluoroaminopentanes and mixed *N*,*N*-difluoroaminohexanes isomers generated by the high temperature vapor phase reaction.

The 1-substituted difluoroaminoalkanes have an associated resonance frequency of ~ + 56 ppm which clearly distinguishes this substitution from the others.

The 2-substituted and 3-substitute difluoroaminoalkanes share identical resonance "centers of gravity" at +39.4 ppm. However, 2-substituted compounds exhibit an AB pattern of doublets whereas the 3-substituted compounds exhibit a single resonance. This makes differentiation of the isomers by NMR easy.

It is logical that the unsymmetrical 2-substituted difluoroaminoalkanes should exhibit individual resonances for each of the two fluorine atoms. It is equally logical that the symmetric 3-substituted difluoroaminopentane should exhibit a single resonance for the two equivalent fluorine atoms. However, the observation of a single resonance for the unsymmetrical 2-difluoroaminohexane is not immediately logical and insinuates a somehow magnetically symmetrical conformation of the molecule around the NF_2-group. Gaussian conformational analysis resulted in the modeling of such a conformation, but it also resulted in similar models for the other asymmetric isomers. Evaluation of the actual F–C coupling constants gives supporting evidence of a magnetic symmetry within 3-difluoroaminohexane. It is apparent that to the extent that it is observable by ^{19}F NMR, an excess of at least two carbon atoms to one side of the – NF_2 attachment point is necessary to put the – NF_2 group in an unsymmetrical environment.

4. Experimental

4.1. General

The generation of the individual isomers of *N*,*N*-difluoroaminopentane and *N*,*N*-difluoroaminohexane also allowed us to generate individual ^1H and ^{13}C NMR spectra. These were in agreement with the partial assignments given in reference [1] and are repeated here complete. Products were identified by ^1H and ^{13}C and ^{19}F NMR performed on a Bruker DPX-250. Older literature ^{19}F values reported in Φ have had their signs inverted (− for +) and values relative to external CF_3CO_2H were converted to relative to internal $CFCl_3$ by addition of 78 ppm [6].

The difluoroaminopentanes were prepared from the reaction of the appropriate pentanomagnesium bromides with NF_3 as described below. The prerequisite bromopentanes were acquired from Aldrich. The difluoroaminohexanes were prepared from the reaction of the appropriate hexanomagnesium chlorides with NF_3 as described below. The prerequisite chloropentanes were prepared from the reaction of $SOCl_2$ with the appropriate hexanol which was acquired from Aldrich. Magnesium turnings were Aldrich 98%. Diethyl ether was distilled from benzophenone/sodium ketyl.

4.2. General procedure for the synthesis of N,N-difluoroanimoalkanes

5 g of magnesium turnings were suspended with stirring in 200 ml diethyl ether at 0 °C. The requisite haloalkane (0.2 mol) was added dropwise. The reaction was stirred a further 1–2 h. Stirring was ceased and the solution allowed to settle. The clear solution was transferred via non-metallic cannula to a 250 ml pressure-rated glass round bottomed flask and held at 0 °C.

A 500 ml pressure-rated glass round bottomed flask, with Teflon coated magnetic stir bar was charged with 200 ml diethyl ether. This solution was cooled to 0 °C and sparged with NF_3. The solution was cooled to −25 °C and pressurized with NF_3 to 140 psi.

The Grignard solution in the 250 ml flask was slowly transferred under pressure of N_2 to the NF_3 solution in the 500 ml flask. The transfer cannula was non-metallic and positioned with the outlet end below the surface of the NF_3 solution. The solution was stirred 1 hour, then vented and quenched with sat. aq. NH_4Cl solution. After warming to room temperature, the phases were separated. The ether layer was dried with $MgSO_4$ and filtered. Excess ether was removed by fractional distillation through a glass ring packed column at ~18 °C under slight vacuum (400 mmHg). The difluoroaminoalkane product was isolated in various fractions at about 20 °C (~1 mmHg) without concern for yield. The purest fraction as per GC was analyzed by NMR.

4.3. Spectral details

1-*N*,*N*-difluoroaminopentane, **1** ^{13}C NMR (62 MHz $CDCl_3$): δ 13.7 (s, C-5), 22.5 (s, C-4), 23.8 (t, *J* = 7.8 Hz, C-2), 29.1 (s, C-3), 66.2 (t, *J* = 6.3 Hz, C-1); ^{19}F NMR (235 MHz $CDCl_3$): δ +55.8 (s).

2-*N*,*N*-difluoroaminopentane, **2** ^1H NMR (250 MHz $CDCl_3$/TMS): δ 0.95 (t, 3H, *J* = 7.2), 1.26 (d, 3H, *J* = 6.2 Hz), 1.43 (m, 2H), 1.73 (mm, 2H), 3.48 (tp, 1H, *J* = 22.4, 6.5 Hz); ^{13}C NMR (62 MHz $CDCl_3$): δ 13.1 (t, *J* = 9.8 =Hz, C-1), 14.0 (s, C-5), 18.8 (s, C-4), 33.0 (t, *J* = 6.5 Hz, C-3), 70.0 (t, *J* = 6.1 Hz, C-2); ^{19}F NMR (235 MHz $CDCl_3$): δ +35.7 (d, *J* = 565.7 Hz), +43.1 (d, *J* = 565.7 Hz).

3-*N*,*N*-difluoroaminopentane, **3** ^1H NMR (250 MHz $CDCl_3$/TMS): δ 0.96 (sext, 6H, *J* = 7.5 Hz), 1.64 (sept, 2H, *J* = 7.2 Hz), 1.72 (m, 2H), 3.17 (tp, 1, *J* = 26.3, 6.0 Hz); ^{13}C NMR (62 MHz $CDCl_3$): δ 10.0 (s, C-1), 20.9 (t, *J* = 8.2 Hz, C-2), 76.7 (t, *J* = 5.3 Hz, C-3); ^{19}F NMR (235 MHz $CDCl_3$): δ +39.4 (s); ^{19}F NMR (235 MHz $CDCl_3$): δ +55.9 (s), δ +39.2 (p, *J* = 579.3 Hz); IR 2958, 2875, 1462, 1370, 953, 860, 844, 810; GC/MS 70 eV, m/z (rel. int.): 71(100), 55(40).

1-*N*,*N*-difluoroaminohexane, **4** by subtraction ^{13}C NMR (62 MHz $CDCl_3$): δ 14.1 (s, C-6), 22.6 (s, C-5), 24.1 (t, *J* = 7.7 Hz, C-2), 26.6 (s, C-4), 31.6 (s, C-3), 66.2 (t, *J* = 6.3 Hz, C-1); ^{19}F NMR (235 MHz $CDCl_3$): δ +55.9 (s).

2-*N*,*N*-difluoroaminohexane, **5** ^1H NMR (250 MHz $CDCl_3$/TMS): δ 0.92 (brs, 3H), 1.26 (d, 3H, *J* = 5.6 Hz), 1.36 (brm, 4H), 1.43 (m, 1H), 1.73 (mm, 1H), 3.41 (tp, 1H, *J* = 21.6, 6.5 Hz); ^{13}C NMR (62 MHz $CDCl_3$): δ 12.9 (t, *J* = 9.8 Hz, C-1), 13.5 (s, C-6), 22.3 (s, C-5), 27.5 (s, C-4), 30.4 (t, *J* = 6.7 Hz, C-3), 70.0 (t, *J* = 6.2 Hz, C-2); ^{19}F NMR (235 MHz $CDCl_3$): δ +35.7 (d, *J* = 565.8 Hz), +43.1 (d, *J* = 565.8 Hz).

3-*N*,*N*-difluoroaminohexane, **6** ^1H NMR (250 MHz $CDCl_3$/TMS): δ 0.95 (t, 3H, *J* = 7.1 Hz), 1.00 (t, 3H, *J* = 7.1 Hz), 1.43 (sext, 2H, *J* = 7.4 Hz), 1.67 (mm, 4H), 3.28 (tp, 1, *J* = 26.4, 5.8 Hz); ^{13}C NMR (62 MHz $CDCl_3$): δ 10.1 (s, C-1), 14.0 (s, C-6), 19.1 (s, C-5), 21.5 (t, *J* = 8.6 Hz, C-2), 30.0 (t, *J* = 7.8 Hz, C-4), 75.4 (t, *J* = 5.5 Hz, C-3); ^{19}F NMR (235 MHz $CDCl_3$): δ +39.3 (s).

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