SUPPORTING INFORMATION

Intramolecular Hydrogen Bond Involving Organic Fluorine in the Derivatives of Hydrazides: An NMR Investigation substantiated by DFT based theoretical calculations

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Contents

1. **Scheme. 1S:** Chemical structures of 2-X-N-(2-X')benzohydrazides 1-10 ................. 4

2. **Fig.1S.** (a) $^{13}$C and (b) Two dimensional $^1$H-$^{13}$C HSQC NMR spectra of the molecule 1 ........................................... 4-5

3. **Fig.2S.** (a) $^1$H and (b) $^{13}$C NMR spectra of molecule 2 ................................. 5-6

4. **Fig.3S.** 2D $^1$H-$^{15}$N HSQC NMR spectrum of molecule 2. ........................................... 6

5. **Fig.4S.** (a) $^1$H and (b) $^{13}$C NMR spectra of the molecule 3 ................................. 7-8

6. **Fig.5S.** 2D $^1$H-$^{13}$C HSQC NMR spectrum of molecule 3 ................................. 8

7. **Fig.6S.** 2D $^1$H-$^{15}$N HSQC NMR spectrum of molecule 3 ................................. 9

8. **Fig.7S.** (a) $^1$H and (b) $^1$H{$^{19}$F} NMR spectra of the molecule 4 ................................. 10

9. **Fig.8S.** $^1$H NMR spectrum of the molecule 4 in solvent DMSO-d$_6$ ................................. 11

10. **Fig.9S.** (a) 1D $^{13}$C NMR and (b) 2D $^1$H-$^{13}$C HSQC NMR spectrum of the molecule 4 ........................................................................................................... 11-12

11. **Fig.10S.** 2D $^1$H-$^{15}$N HSQC NMR spectrum of molecule 4 ................................. 13-14

12. **Fig.11S.** (a) 1D $^{19}$F (b) 2D heteronuclear correlation

    $^1$H-$^{19}$F HOESY$^{[5]}$ NMR spectra of the molecule 4 ........................................... 14-15

13. **Fig.12S.** (a) $^1$H and (b) $^1$H{$^{19}$F} NMR spectrum in CDCl$_3$

    (c) $^1$H NMR spectra of the molecule 5 in the solvent DMSO-d$_6$ ...................................... 16-17

14. **Fig.13S.** (a) $^{13}$C and (b) 2D $^1$H-$^{13}$C HSQC spectrum of the molecule 5 ................. 17-18

15. **Fig.14S.** (a) 1D $^{19}$F and (b) 2D heteronuclear correlated

    $^1$H-$^{19}$F HOESY$^{[5]}$ NMR spectra of the molecule 5 ........................................... 18-19

16. **Fig.15S.** (A) $^1$H-$^{15}$N HSQC NMR spectrum of the molecule 5 ...................................... 20-21

17. **Fig.16S.** (a) $^1$H and (b) $^1$H{$^{19}$F} NMR spectra of the molecule 6 ................................. 22-23

18. **Fig.17S.** (a) $^{13}$C and (b) $^1$H-$^{13}$C HSQC NMR spectra of the molecule 6 ................................. 23-24
19. **Fig.18S.** (a) 1D $^{19}$F and (b) 2D $^1$H-$^{19}$F HOESY at 298K;
   (c) 2D $^1$H-$^{19}$F HOESY at 220K NMR spectra of molecule 6 ................................24-26
20. **Fig.19S.** (A) $^1$H-$^{15}$N HSQC NMR spectrum of the molecule 6 .........................27-28
21. **Fig.20S.** (a) $^1$H (b) $^1$H-$^{15}$N HSQC NMR spectra of the molecule 7 .................29-30
22. **Fig.21S.** (a) $^{13}$C and (b) $^1$H-$^{13}$C HSQC NMR spectra of the molecule 7 ....30-31
23. **Fig.22S.** (a) $^1$H NMR (b) $^1$H{$^{19}$F} NMR spectra of the molecule 8......................31-32
24. **Fig.23S.** (a) $^{13}$C and (b) $^1$H-$^{13}$C HSQC NMR spectra of the molecule 8 ..........33
25. **Fig.24S.** (a) 1D $^{19}$F NMR (b) 2D $^1$H-$^{19}$F HOESY at 298K
   (c) 2D $^1$H-$^{19}$F HOESY NMR spectra at 220K of the molecule 8 ......................34-35
26. **Fig.25S.** 2D $^1$H-$^{15}$N HSQC NMR spectrum of molecule 8 .................................36
27. **Fig.26S.** $^1$H NMR spectrum of molecule 9 .................................................................37
28. **Fig.27S.** (a) $^{13}$C and (b) 2D $^1$H-$^{13}$C HSQC NMR spectra of the molecule 9 ....37-38
29. **Fig.28S.** (a) $^1$H and (b) 2D $^1$H-$^{15}$N HSQC NMR spectra of the molecule 9 ....38-39
30. **Fig.29S.** The plot of $\text{sign} (\lambda_2(r))^*p(r)$ as function 1 V/s The reduced density gradient (RDG) as function 2 of molecules 2-9, .................................................39-40
31. **Fig.30S.** Coloured Isosurface plot (green colour denotes weak H-bond and red colour stands for steric effect) of molecules 2-9 ...............................................................40-41
32. **Fig.31S.** The optimized structures with (3, -1) bond critical points (BCP) for the molecules 1-9........................................................................................................42
33. References .................................................................................................................43-44
General structure of the investigated molecules

Scheme. 1S: Chemical structures of 2-X-N-(2-X')benzohydrazides\textsuperscript{[1]} (a) symmetrically substituted molecules, where $X = X'$) (b) asymmetrically substituted molecules (substituent $X \neq X'$).
Fig. 1S. (a) $^{13}$C and (b) Two dimensional $^1$H-$^{13}$C HSQC (with peak assignments) NMR spectra of the molecule 1 in the solvent CDCl$_3$ acquired on a 400 MHz NMR spectrometer.
Fig. 2S. (a) $^1$H and (b) $^{13}$C (with peak assignments) NMR spectra of molecule 2 in the solvent CDCl$_3$ acquired on a 500 MHz NMR spectrometer.

Fig. 3S. Two dimensional $^1$H-$^{15}$N HSQC NMR spectrum of molecule 2 in the solvent CDCl$_3$ acquired on 400 MHz NMR spectrometer. The separation providing the magnitudes of the couplings are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.
The HB between Chlorine and NH proton is relatively weak. Hence the molecular structure is dynamic resulting in several conformers in solution. Due to presence of more than one conformer with different dihedral angles between two NH protons, several $^3J_{HH}$ couplings of different strengths are seen in the $^1H$-$^{15}N$ HSQC spectrum (Fig.3S).
Fig. 4S. (a) $^1$H (acquired on 400 MHz NMR spectrometer) and (b) $^{13}$C (peaks assigned) NMR spectra of the molecule 3 in the solvent CDCl$_3$ acquired on 500 MHz NMR spectrometer.

Fig. 5S. 2D $^1$H-$^{13}$C HSQC NMR spectrum of molecule 3 in solvent CDCl$_3$ acquired on a 500 MHz NMR spectrometer.
Fig. 6S. 2D $^1$H-$^{15}$N HSQC NMR spectrum of molecule 3 in the solvent CDCl$_3$ acquired on 400 MHz NMR spectrometer. The separation providing the magnitudes of the couplings are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.
Fig. 7S. (a) $^1$H and (b) $^1$H($^{19}$F) NMR spectra of the molecule 4 in the solvent CDCl$_3$ acquired on 500 MHz NMR spectrometer.
Fig. 8S. $^1$H NMR spectrum of the molecule 4 acquired in solvent DMSO-d$_6$ obtained on a 400 MHz NMR spectrometer.
Fig. 9S. (a) $^{13}$C NMR spectrum of the molecule 4 acquired on 400 MHz NMR spectrometer and (b) 2D $^1$H-$^{13}$C HSQC (with peak assignments) spectrum acquired on a 500 MHz NMR spectrometer in solvent CDCl$_3$. 
Fig. 10S. 2D $^1$H-$^{15}$N HSQC NMR spectrum of molecule 4 acquired on a 400 MHz NMR spectrometer in the solvent CDCl$_3$. The separation providing the magnitudes of the couplings$^{[2-4]}$ are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.

- $^1J_{NH} = -102.97$ Hz
- $^1hJ_{HF} = -12.09$ Hz
- $^2hJ_{NF} = -10.30$ Hz
- $^3J_{HH} = 7.15$ Hz
- $^1J_{NH} = -102.20$ Hz
- $^3hJ_{FN} = +0.76$ Hz
- $^4hJ_{FH} = +1.77$ Hz
Fig. 11S. (a) 1D $^{19}$F (b) 2D heteronuclear correlation $^1$H-$^{19}$F HOESY$^2$ NMR spectra of the molecule 4 in the solvent CDCl$_3$ acquired on a 400 MHz NMR spectrometer.
$^1$H-$^{19}$F HOESY$^5$ spectrum of molecule 4 shows a triplet (Fig.11S(b)) in the $^1$H dimension due to the presence of more than one conformers. The presence of more than one conformers is also confirmed by $^1$H NMR spectrum (both $^{19}$F-coupled and decoupled) showing several peaks for NH proton because of multiple conformers.
Fig. 12S. (a) $^1$H and (b) $^1$H$^{[19]F}$ NMR spectra of the molecule 5 in the solvent CDCl$_3$ (c) $^1$H NMR spectrum of the same molecule in the solvent DMSO-d$_6$. Both the spectra were acquired on 400 MHz NMR spectrometer.
**Fig. 13S.** (a) $^{13}\text{C}$ spectrum of the molecule 5 acquired on 400 MHz NMR spectrometer in solvent CDCl$_3$; and (b) 500 MHz $^1\text{H}-^{13}\text{C}$ HSQC (with peak assignments) spectrum acquired on a 500 MHz NMR spectrometer.
Fig. 14S. (a) 1D $^{19}\text{F}$ and (b) 2D heteronuclear correlated $^{1}\text{H}-^{19}\text{F}$ HOESY$^{[5]}$ NMR spectra of the molecule 5 in the solvent CDCl$_3$ acquired on 400 MHz NMR spectrometer.
The $^1$H-$^{19}$F HOESY spectrum of molecule 5 (Fig. 14S(b)) exhibits several correlations in the $^1$H dimension with $^{19}$F confirming that this molecule exists in more than one conformers at the room temperature. This was also observed in the temperature perturbation study.
Fig. 15S. (A) $^1$H-$^{15}$N HSQC NMR spectrum of the molecule 5 acquired on 800 MHz NMR spectrometer in the solvent CDCl$_3$. B) and C) are zoomed regions of the spectrum. The separation providing the magnitudes of the couplings\textsuperscript{[2-4]} are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.

**Discussion:**

The $^1$H-$^{15}$N HSQC spectrum of the molecule 5 (Fig. 14S) exhibited $^3J_{HH}$ couplings of different values further strengthening the evidence for existence of more than one conformers in the solution. The strength of coupling varies with the change in dihedral angle.

\begin{itemize}
  \item a) $^1J_{NH} = -102.62$ Hz
  \item b) $^1J_{HF} = -12.74$ Hz
  \item c) $^2J_{NF} = -10.78$ Hz
  \item d) $^1J_{NH} = -99.47$ Hz
  \item e) $^3J_{HH} = 8.72$ Hz
  \item f) $^3J_{HH} = 4.80$ Hz
\end{itemize}
Fig. 16S. 400 MHz (a) $^1$H and (b) $^1$H-$^{19}$F NMR spectra of the molecule 6 in the solvent CDCl$_3$. 

23
Fig. 17S. (a) $^{13}$C and (b) $^1$H-$^{13}$C HSQC (with peak assignments) NMR spectra of the molecule 6 in solvent CDCl$_3$ acquired on 500 MHz NMR spectrometer.
Fig.18S. (a) 1D $^{19}$F and (b) 2D heteronuclear correlation $^1$H-$^{19}$F HOESY NMR spectra of the molecule 6 at 298K; (c) 2D heteronuclear correlation $^1$H-$^{19}$F HOESY NMR spectra of molecule 6 220K. Both the spectra were acquired in the solvent CDCl$_3$ on a 400 MHz NMR spectrometer.

Discussion:

For the molecule 8, the quartet in $^1$H-$^{19}$F HOESY spectra (Fig.18S(b)) is due to the fast rotation of CF$_3$ group. Due to the 180° flipping of CF$_3$ substituted phenyl ring a correlation with other NH peak is also seen in the HOESY spectrum. The correlated peak with the fluorine of CF$_3$ is shifted towards the downfield at lower temperature (Fig.18S(c)) due to the deshielding of NH proton and the strengthening of H...F interaction. Due to the strong interaction between F(CF$_3$)...H the enhancement of S/N ratio is in Fig.18S(c).
Fig. 19S. (A) $^1$H-$^{15}$N HSQC NMR spectrum of the molecule 6 acquired on an 800 MHz NMR spectrometer in the solvent CDCl₃. B) and C) are the zoomed portions belonging to different NH protons. The separation providing the magnitudes$^{[2-4]}$ of the couplings are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.
Fig. 20. (a) $^1$H (b) $^1$H-15N HSQC NMR spectra of the molecule 7 acquired on a 400 MHz NMR spectrometer in the solvent CDCl$_3$. The separation providing the magnitudes\(^{2,4}\) of the couplings are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.
Fig. 21S. (a) $^{13}$C (with peak assignments) and (b) $^1$H-$^{13}$C HSQC (with peak assignments) NMR spectra of the molecule 7 acquired on 500 MHz NMR spectrometer in the solvent CDCl$_3$. The zoomed region of the spectrum is given in the inset.
Fig. 22S. (a) $^1$H NMR (b) $^1$H-$^{19}$F NMR spectra of the molecule 8 acquired on 400 MHz NMR spectrometer in the solvent CDCl$_3$. 
**Fig. 23S.** (a) $^{13}\text{C}$ and (b) $^1\text{H}-^{13}\text{C}$ HSQC (with peak assignments) NMR spectra of the molecule 8 acquired on 500 MHz NMR spectrometer in the solvent CDCl$_3$. The zoomed region of the spectrum is given in the inset.

**Discussion:**

There are three peaks for the methoxy group in the $^{13}\text{C}$ NMR spectrum (Fig. 23S(a)) for molecule 8 indicating the presence of three different conformers in the solution.
Discussion:

The $^1$H-$^{19}$F HOESY spectrum (Fig.24S(b)) of the molecule 8 at 298 K provides clear evidence for the existence of more than one conformers in the solution. In the Fig. 22S(b) in the $^1$H-$^{19}$F HOESY spectrum both the NH protons gave correlation with the fluorine of CF$_3$ group (Fig. 22S(b)). This is observed due to the rotation of CF$_3$ substituted phenyl ring through the single bond. In the Fig. 22S(b) the heteronuclear multiple correlation peaks are detected because due to ring flipping and the free rotation of CF$_3$ group at ambient temperature, creating the possibility of several conformers.
Fig.24S. (a) 1D $^{19}$F NMR (b) 2D heteronuclear correlated $^1$H-$^{19}$F HOESY$^{[5]}$ NMR spectra at 298K (c) 2D heteronuclear correlation $^1$H-$^{19}$F HOESY$^{[5]}$ NMR spectra at 220K of the molecule 8 acquired on 400 MHz NMR spectrometer in the solvent CDCl$_3$. Two different conformers are given with the plot.

Discussion:

For further investigation the $^1$H-$^{19}$F HOESY spectrum of the molecule 8 was recorded at 220K (Fig. 24S(c)). In the Fig. 24S(c) there is only one doublet for each NH proton at 220K. This confirms the existence of only two conformers at 220K. The comparison of the intensities of the peaks gives the qualitative idea the conformer (1) is more stable than the conformer (2). The conformer 2 arises due to 180° flip of CF$_3$ containing phenyl ring at lower temperature.
Fig. 25S. Two dimensional $^1$H-$^{15}$N HSQC NMR spectrum of molecule 8 acquired on 400 MHz NMR spectrometer in the solvent CDCl$_3$. The separation providing the magnitudes of the couplings are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.
**Fig. 26S.** $^1$H NMR spectrum of molecule 9 acquired on 400 MHz NMR spectrometer in the solvent CDCl$_3$. 
Fig.27S. (a) $^{13}$C (with peak assignments) and (b) 2D $^1$H-$^{13}$C HSQC (with peak assignments) NMR spectra of the molecule 9 acquired on 500 MHz NMR spectrometer in solvent CDCl$_3$. 
**Fig. 28** (a) $^1$H and (b) 2D $^1$H-$^{15}$N HSQC NMR spectra of the molecule 9 acquired on 400 MHz NMR spectrometer in the solvent CDCl$_3$. The separation providing the magnitudes of the couplings$^{[2-4]}$ are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.

**Discussion:**

The molecules 5 contain OH group at ortho position of a phenyl ring. The molecule has two possible conformations. One is where oxygen of OH group is Hydrogen bonded to the proton of NH group and other is where proton of OH group gets H-bonded to the oxygen of CO group. For molecule 5 this was clearly evident from the temperature dependent study.
Fig.29S. The plot of \( \text{sign}(\lambda_2(r)) \cdot p(r) \) as function 1 V/s The reduced density gradient (RDG) as function 2 of molecules 2-9, plotted using multiwfn\(^6\) programme by utilizing wavefunction (.wfn) files. The Wavefunction files were generated by Gaussian09 \(^7\) programme during DFT\(^8\) structure optimization.
There are three spikes on the left hand side (i.e. sign($\lambda_2(r)$)*$r(r)$ is negative) in the Fig.29S(2) which denote three H-bonds namely N-H---Cl, N-H---O and C-H---O. These three non-covalent interactions can be seen in the Fig. 30S(2) as green coloured isosurface. The steric hindrance arising from phenyl ring and other rings formed by H-bond can be seen as the four type of spikes on right hand side (i.e. sign($\lambda_2(r)$)*$r(r)$ is positive) in Fig.29S(2) and red isosurface in Fig. 30S(2). Similarly for all other molecules the H-bonds as spikes on left hand side and steric hindrance as spikes on right hand side in fig. 29S(3-9) can be seen. In the coloured Isosurface plots Fig. 30S(3-9) the H-bonds as green isosurface and steric hindrance as red isosurface are visible.
Fig. 31S. The optimized structures with (3, -1) bond critical points (BCP) for the molecules 1-9.

References:


