Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

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

General structure of the investigated molecules

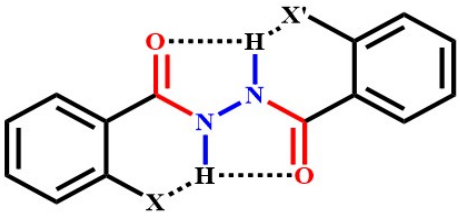
a

1. X=X'=F

2. X=X'=Cl

3. X=X'=OMe

10. X=X'=H



b

4. X=F and X'=Cl,

5. X=F and X'=OH,

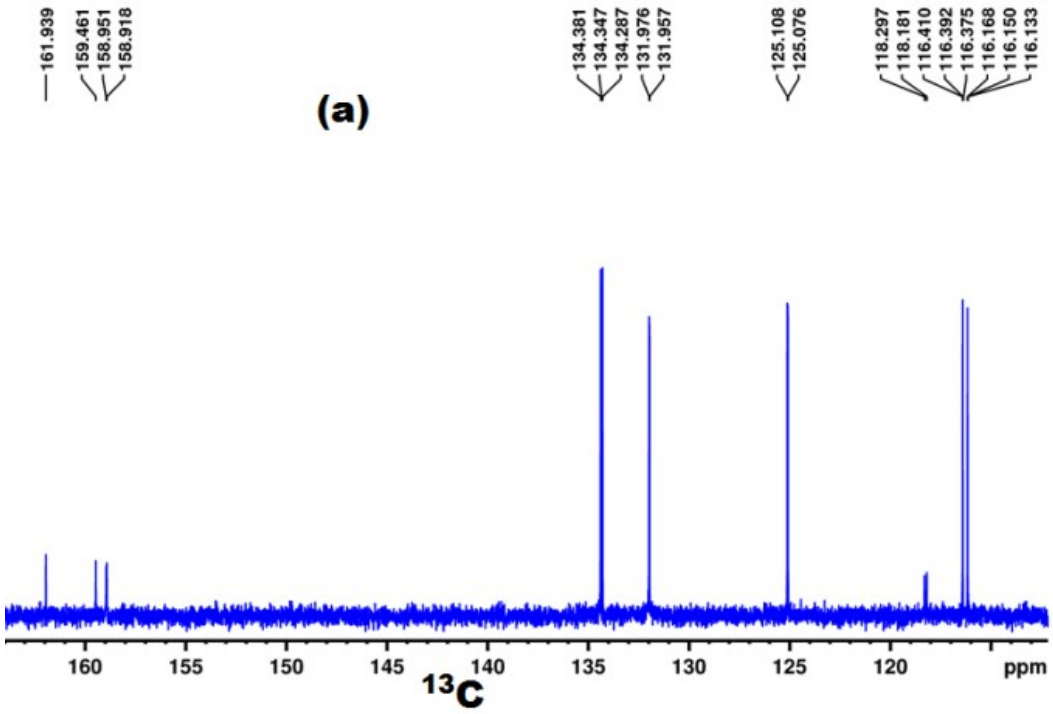
6. X=F and X'=CF_3,

7. X=Cl and X'=OMe,

8. X=CF_3 and X'= OMe,

9. X=OH and X'=OMe

Scheme. 1S: Chemical structures of 2-X-N-(2-X')benzohydrazides[1] (a) symmetrically substituted molecules, where X = X') (b) asymmetrically substituted molecules (substituent X ≠ X').



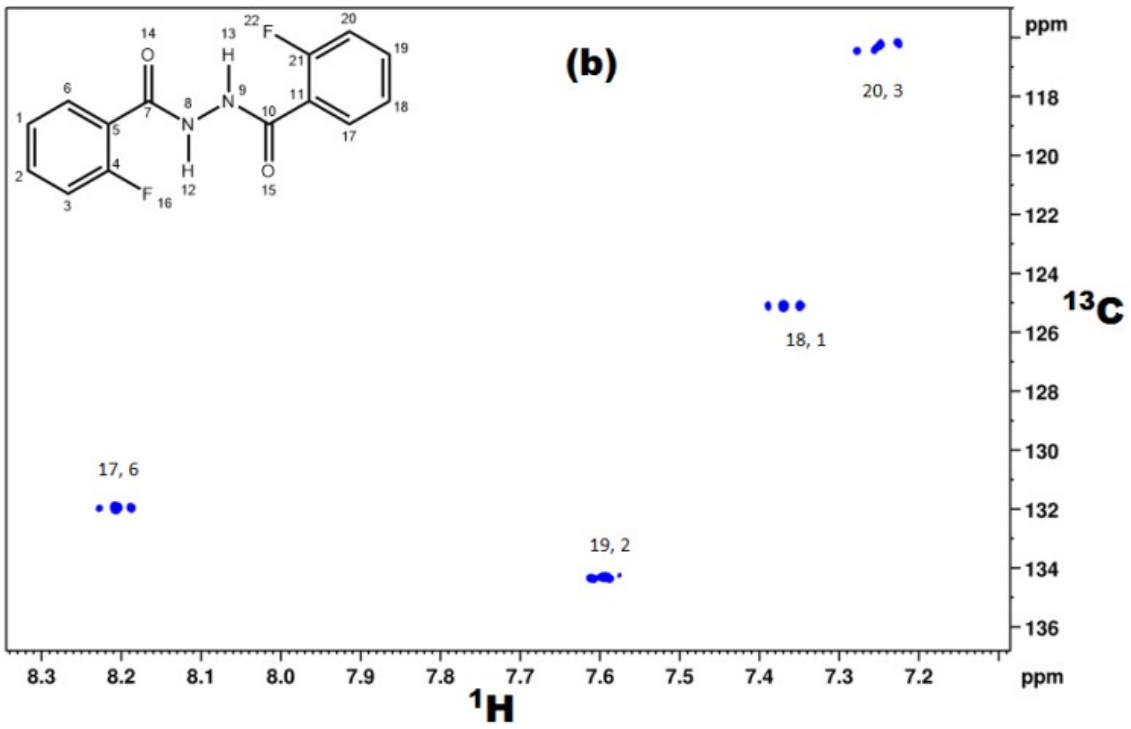
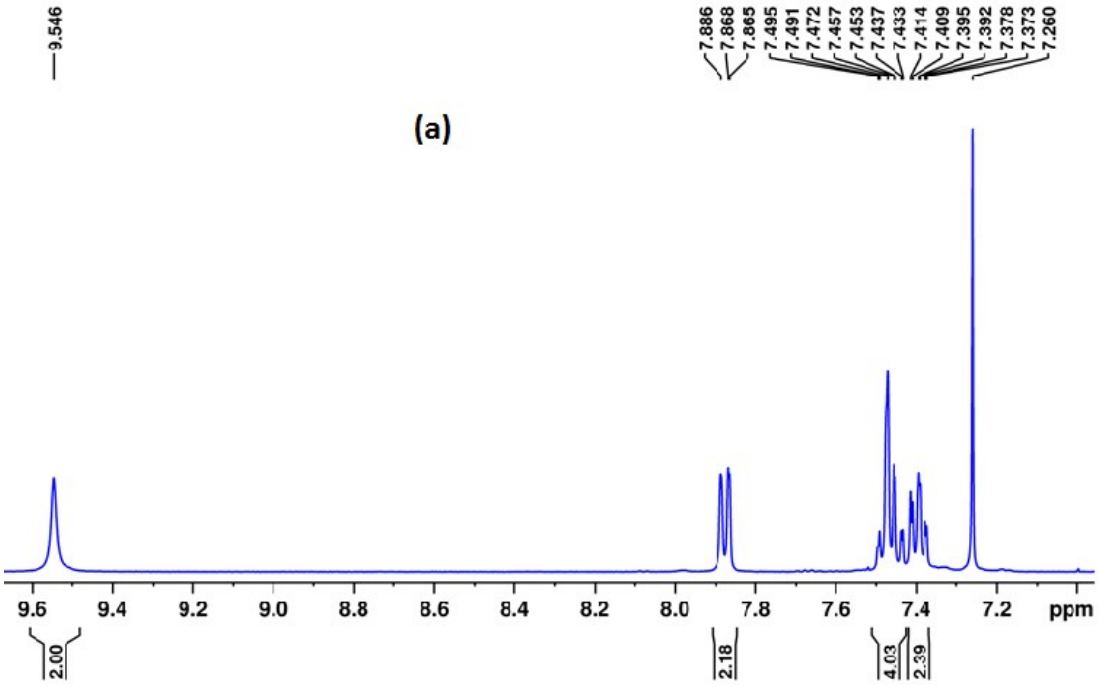


Fig.1S. (a) ^{13}C and (b) Two dimensional ^{1}H-^{13}C HSQC (with peak assignments) NMR spectra of the molecule **1** in the solvent $CDCl_3$ acquired on a 400 MHz NMR spectrometer.



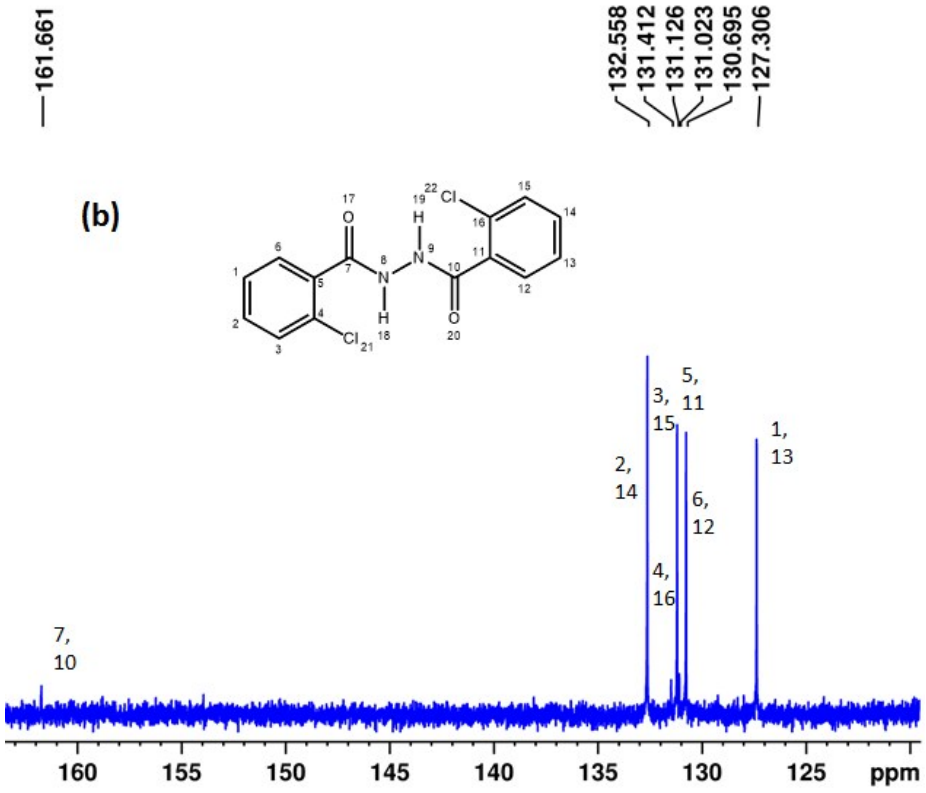


Fig.2S. (a) ^{1}H and (b) ^{13}C (with peak assignments) NMR spectra of molecule **2** in the solvent $CDCl_3$ acquired on a 500 MHz NMR spectrometer.

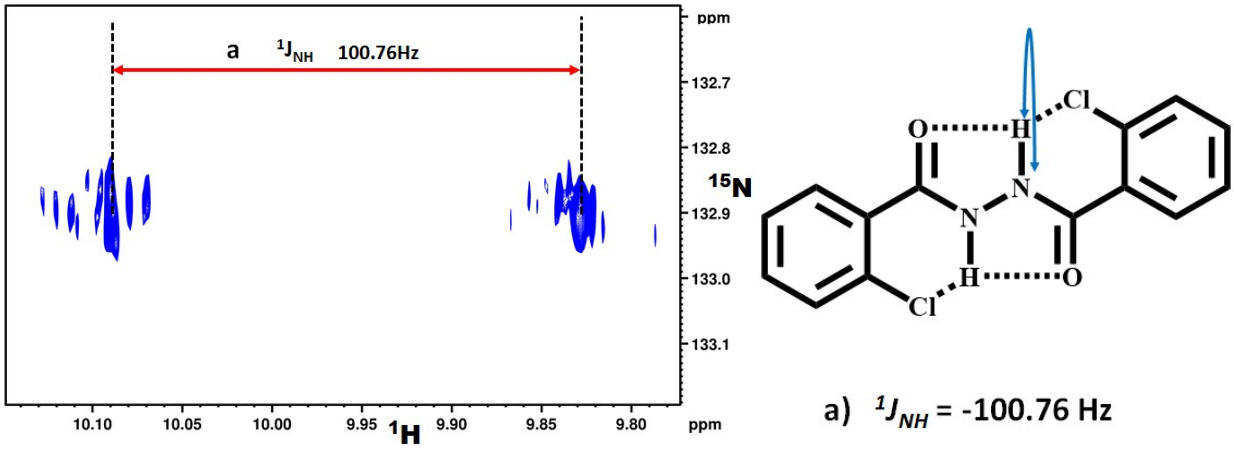
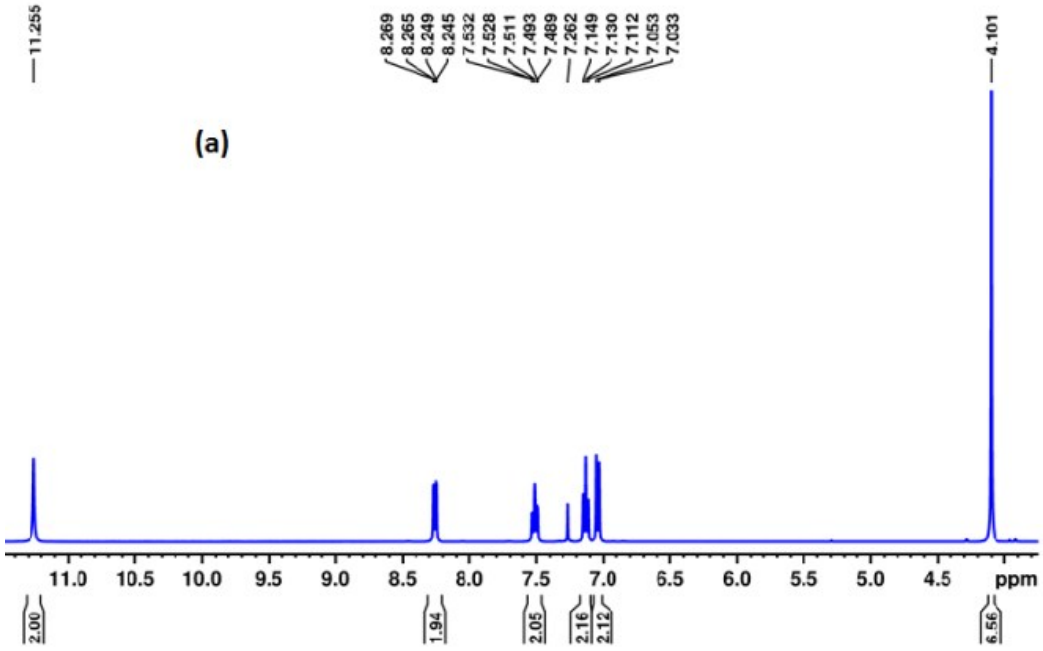


Fig.3S. Two dimensional ^{1}H-^{15}N HSQC NMR spectrum of molecule **2** in the solvent $CDCl_3$ acquired on 400 MHz NMR spectrometer. The separation providing the magnitudes of the couplings[2-4] are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling 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 $^{3}J_{HH}$ couplings of different strengths are seen in the ^{1}H-^{15}N HSQC spectrum (Fig.3S).



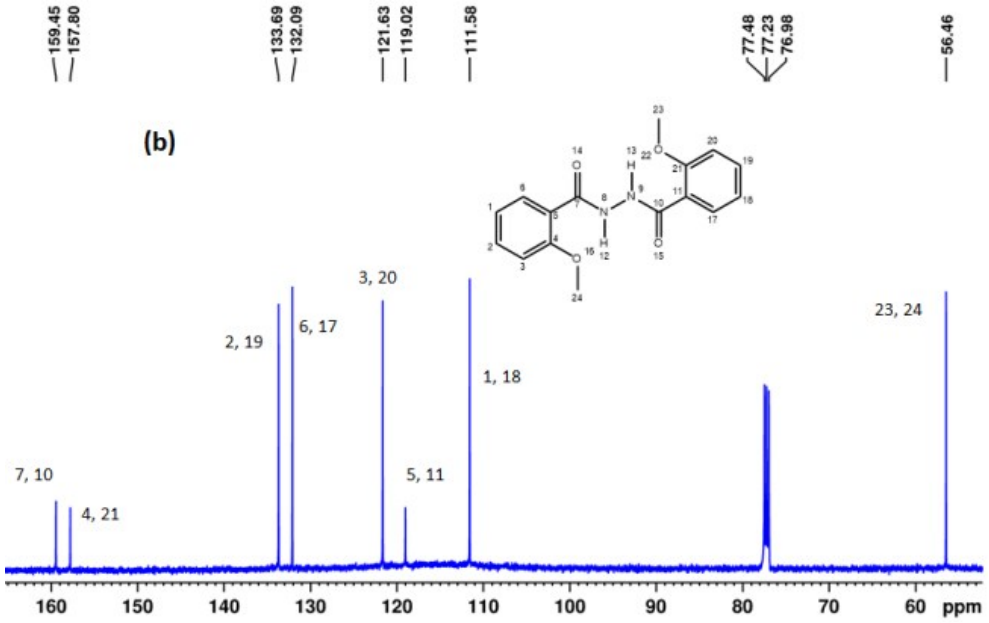


Fig.4S. (a) ^{1}H (acquired on 400 MHz NMR spectrometer) and (b) ^{13}C (peaks assigned) NMR spectra of the molecule **3** in the solvent $CDCl_3$ acquired on 500 MHz NMR spectrometer.

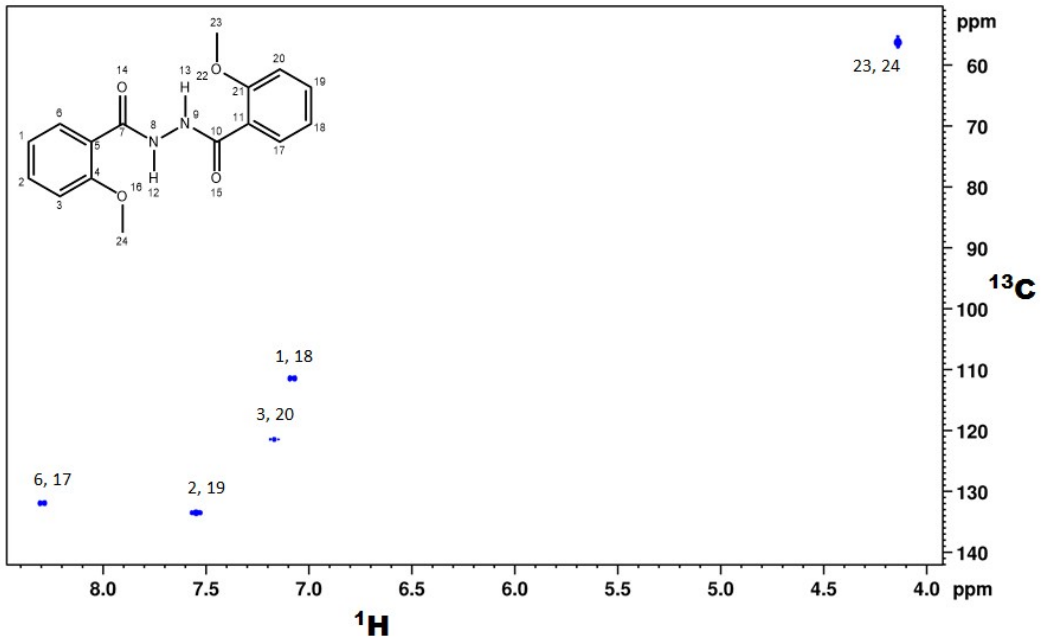
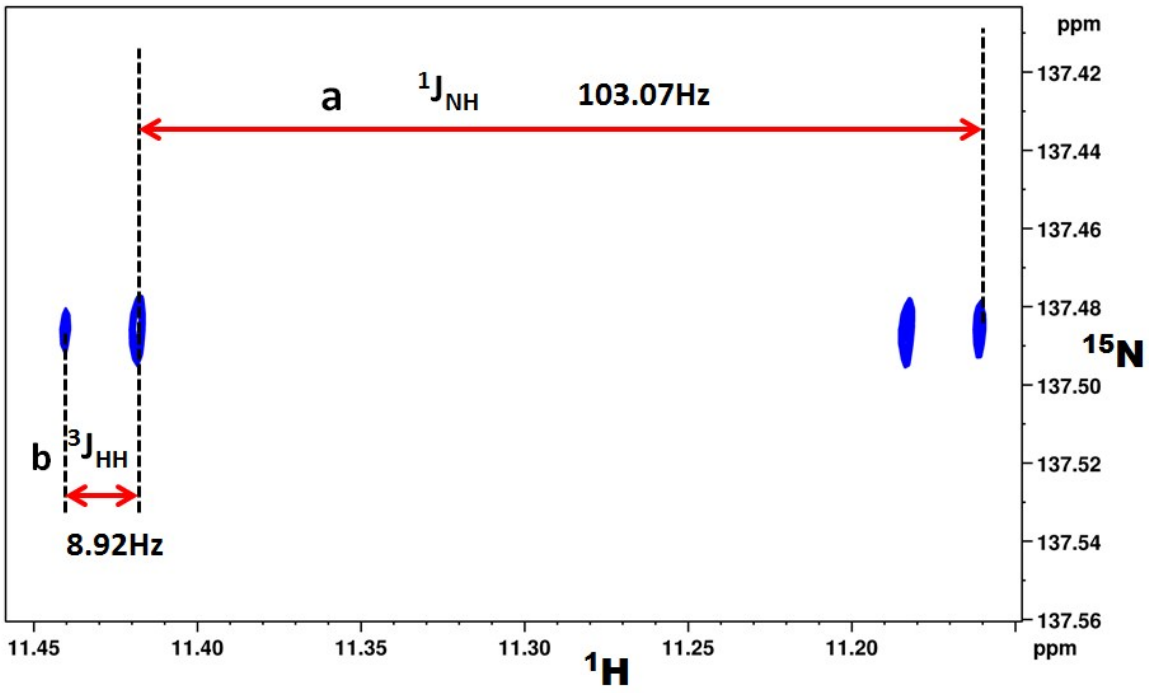


Fig.5S. 2D ^{1}H-^{13}C HSQC NMR spectrum of molecule **3** in solvent $CDCl_3$ acquired on a 500 MHz NMR spectrometer.



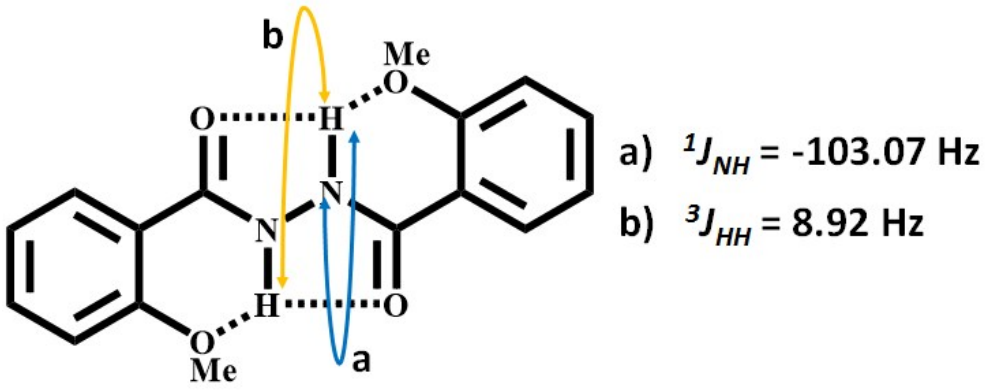


Fig.6S. 2D ^{1}H-^{15}N HSQC NMR spectrum of molecule **3** in the solvent $CDCl_3$ acquired on 400 MHz NMR spectrometer. The separation providing the magnitudes of the couplings[2-4] are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.

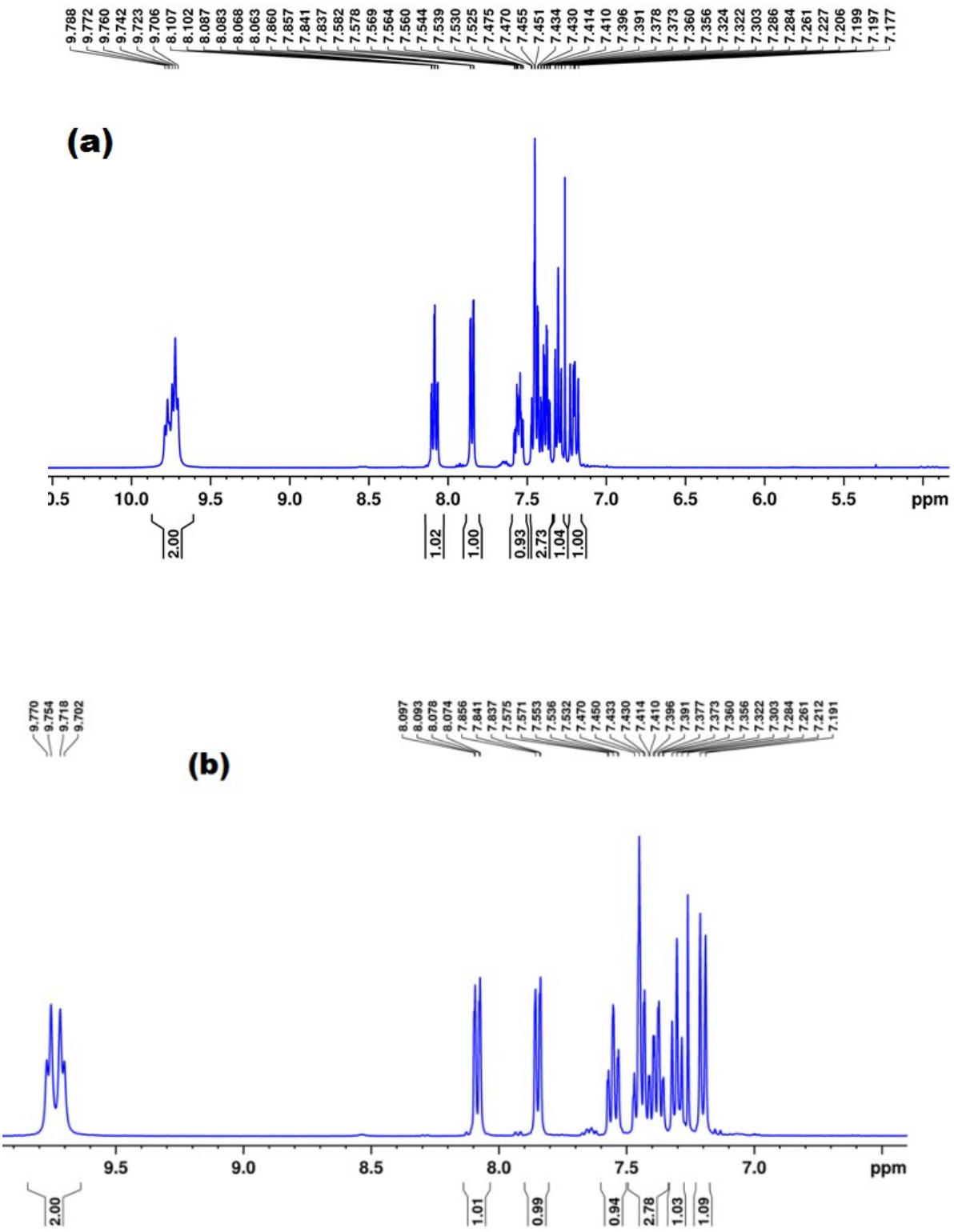


Fig.7S. (a) ^{1}H and **(b)** $^{1}H\{^{19}F\}$ NMR spectra of the molecule **4** in the solvent $CDCl_3$ acquired on 500 MHz NMR spectrometer.

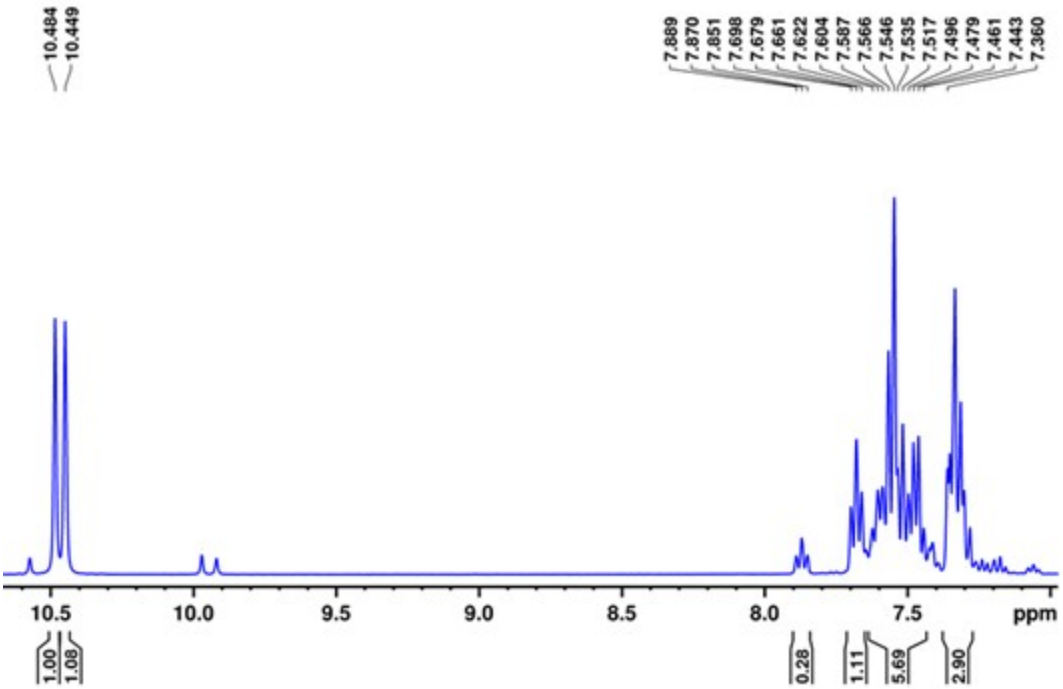
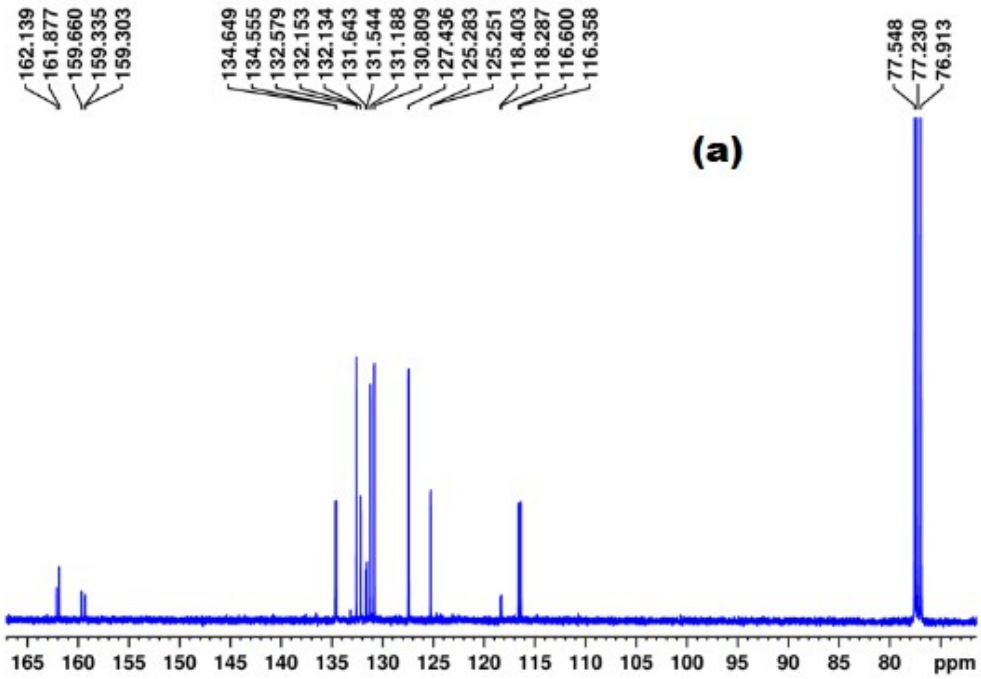


Fig.8S. ^{1}H NMR spectrum of the molecule **4** acquired in solvent DMSO-d_6 obtained on a 400 MHz NMR spectrometer.


162.139
161.877
159.660
159.335
159.303
134.649
134.555
132.579
132.153
132.134
131.643
131.544
131.188
130.809
127.436
125.283
125.251
118.403
118.287
116.600
116.358
77.548
77.230
76.913
(a)
165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 ppm

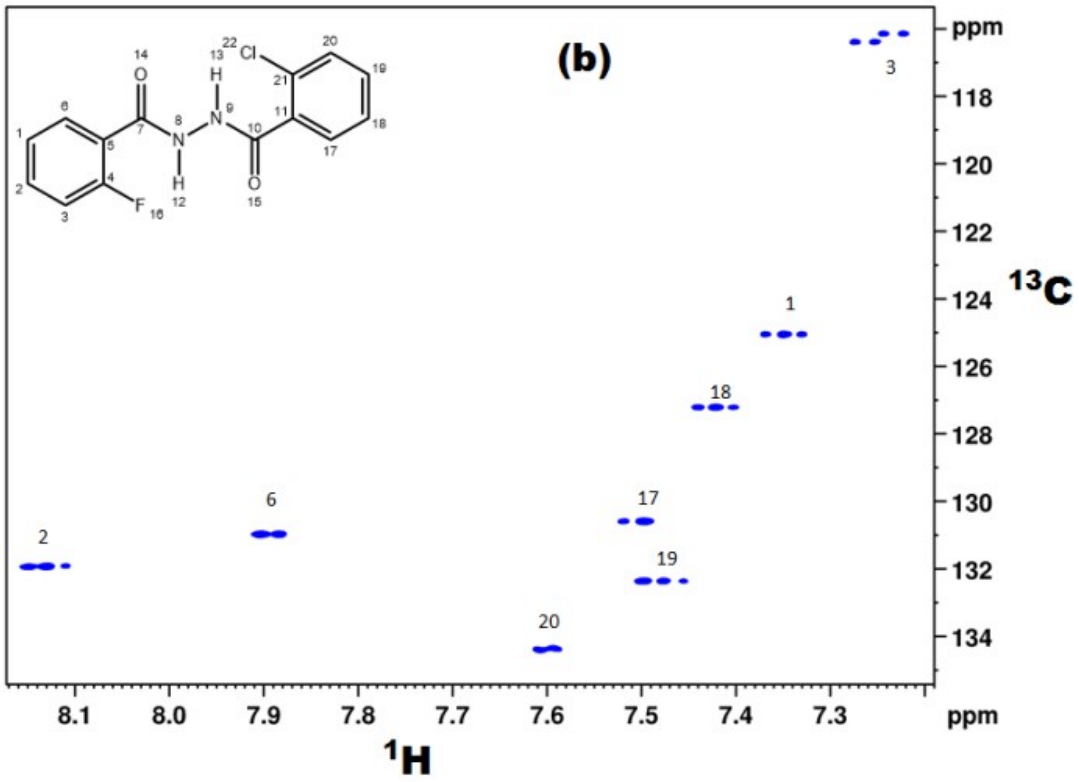
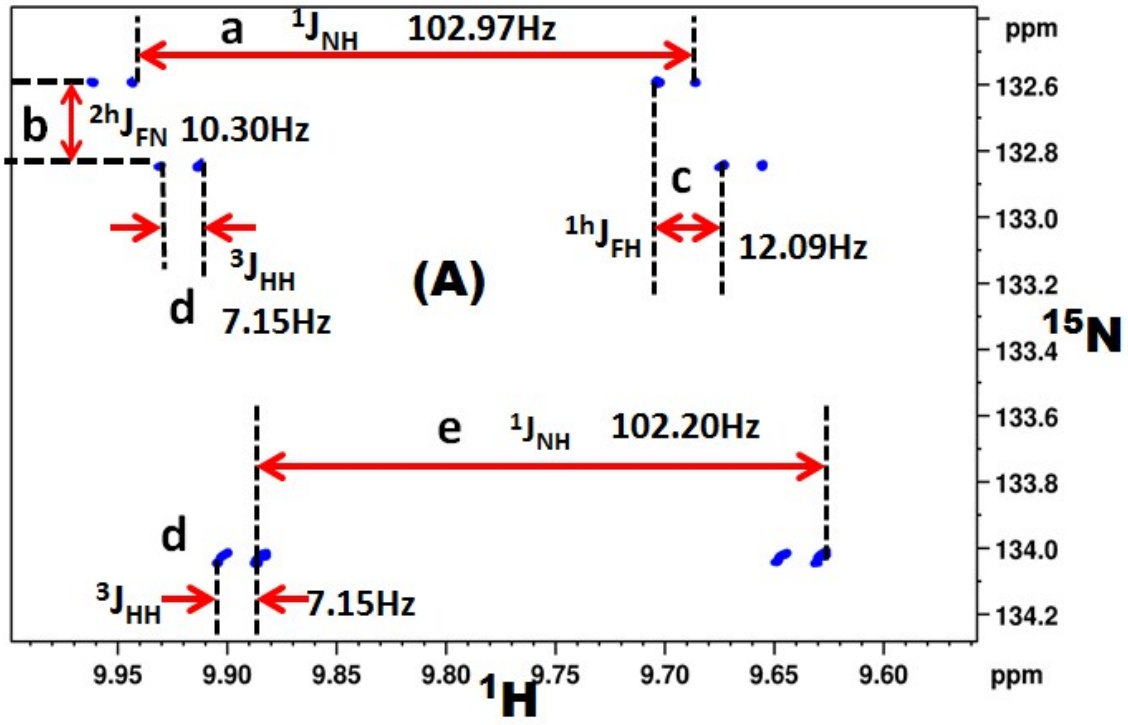

(b)
ppm
118
120
122
124
126
128
130
132
134
13C
1
2
3
6
17
18
19
20
8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 ppm
1H

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 $CDCl_3$.



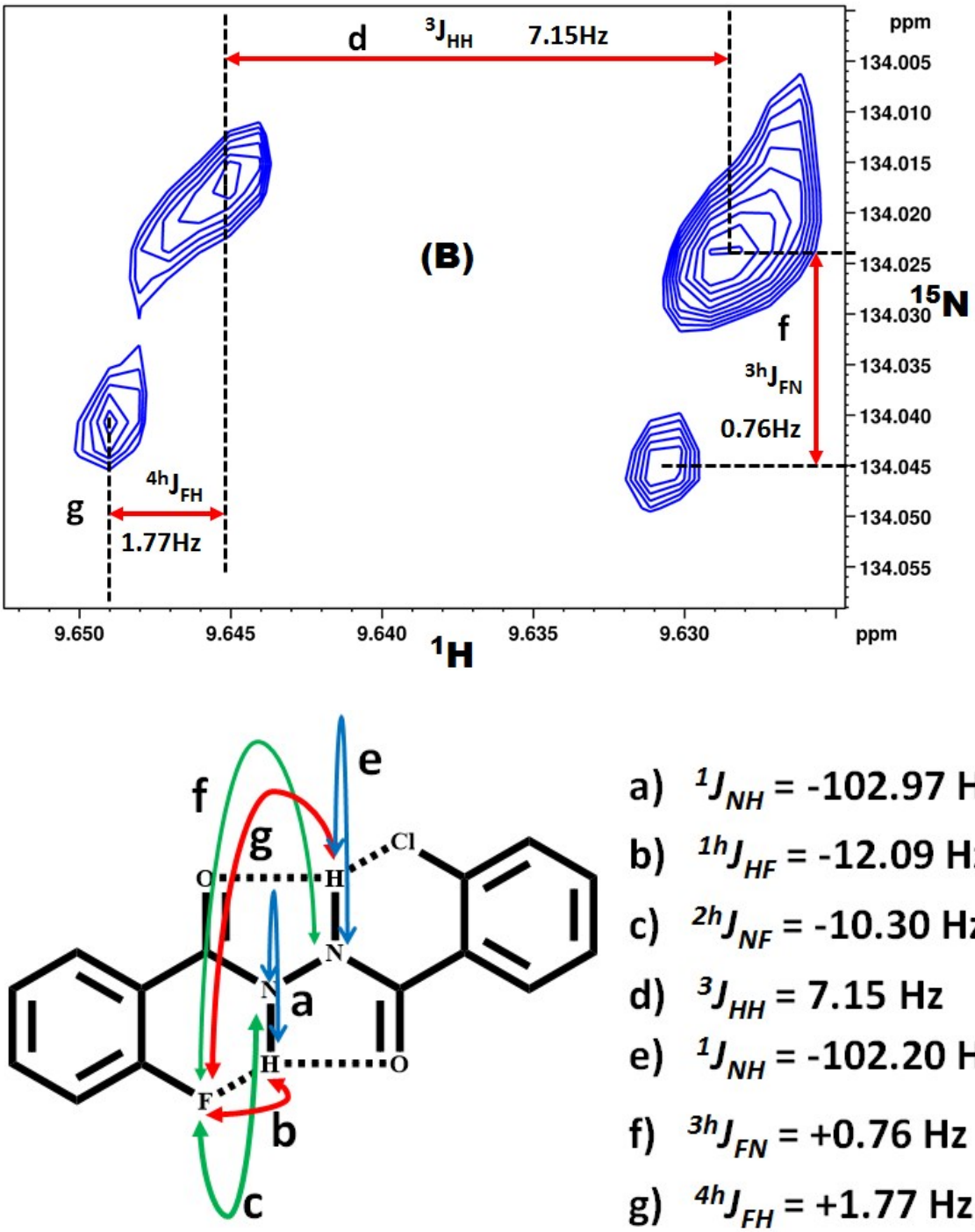


Fig.10S. 2D ^{1}H-^{15}N HSQC NMR spectrum of molecule **4** acquired on a 400 MHz NMR spectrometer in the solvent $CDCl_3$. The separation providing the magnitudes of the couplings[2-4] are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.

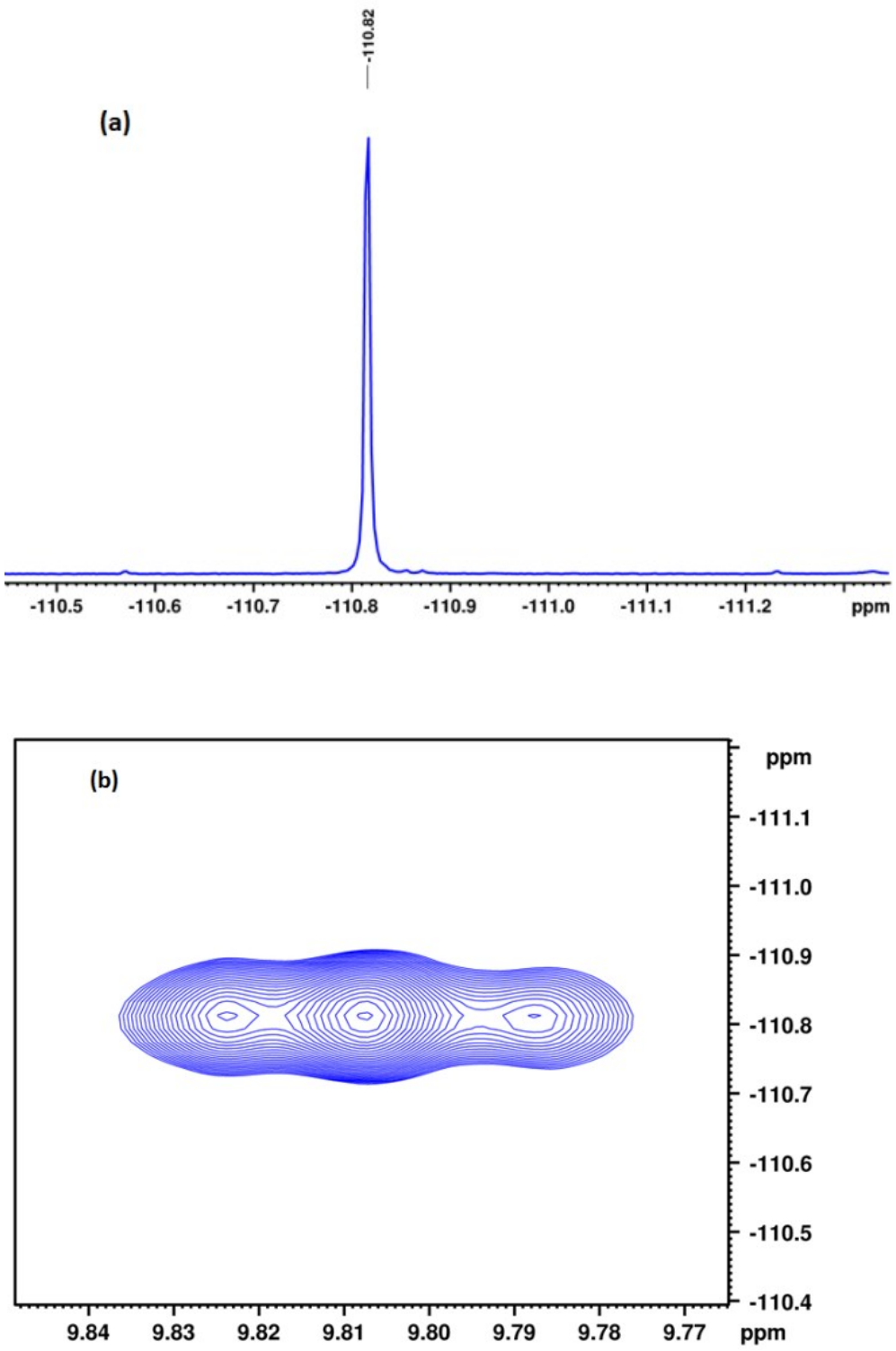
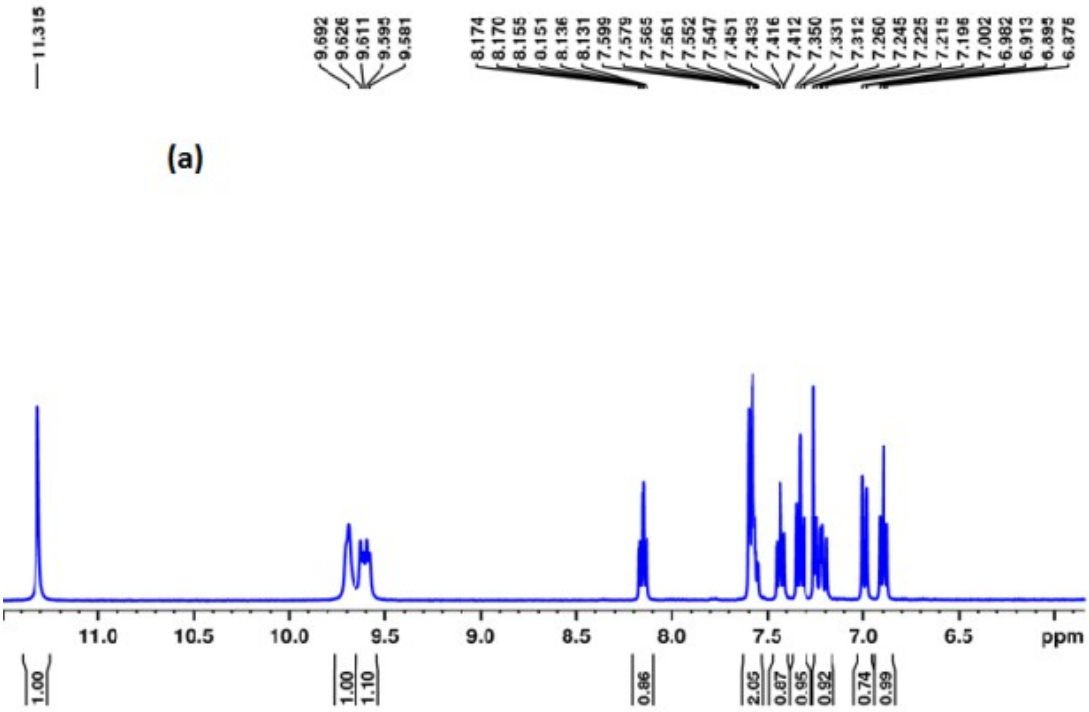


Fig.11S. (a) 1D ^{19}F (b) 2D heteronuclear correlation ^{1}H-^{19}F HOESY[5] NMR spectra of the molecule **4** in the solvent $CDCl_3$ acquired on a 400 MHz NMR spectrometer.

^{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.



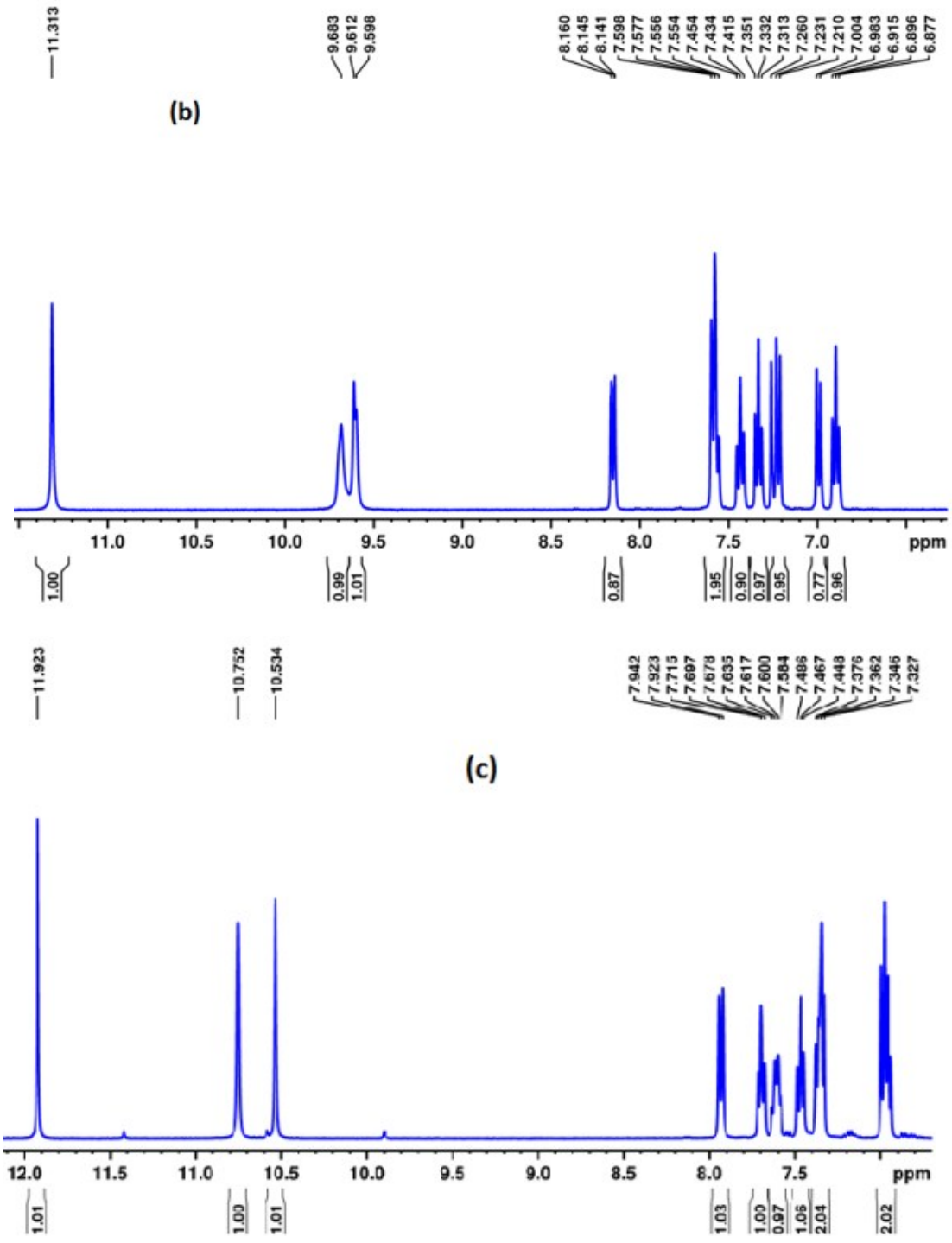


Fig.12S. (a) ^{1}H and **(b)** $^{1}H\{^{19}F\}$ NMR spectra of the molecule **5** in the solvent $CDCl_3$ (c) ^{1}H NMR spectrum of the same molecule in the solvent DMSO-d_6. Both the spectra were acquired on 400 MHz NMR spectrometer.

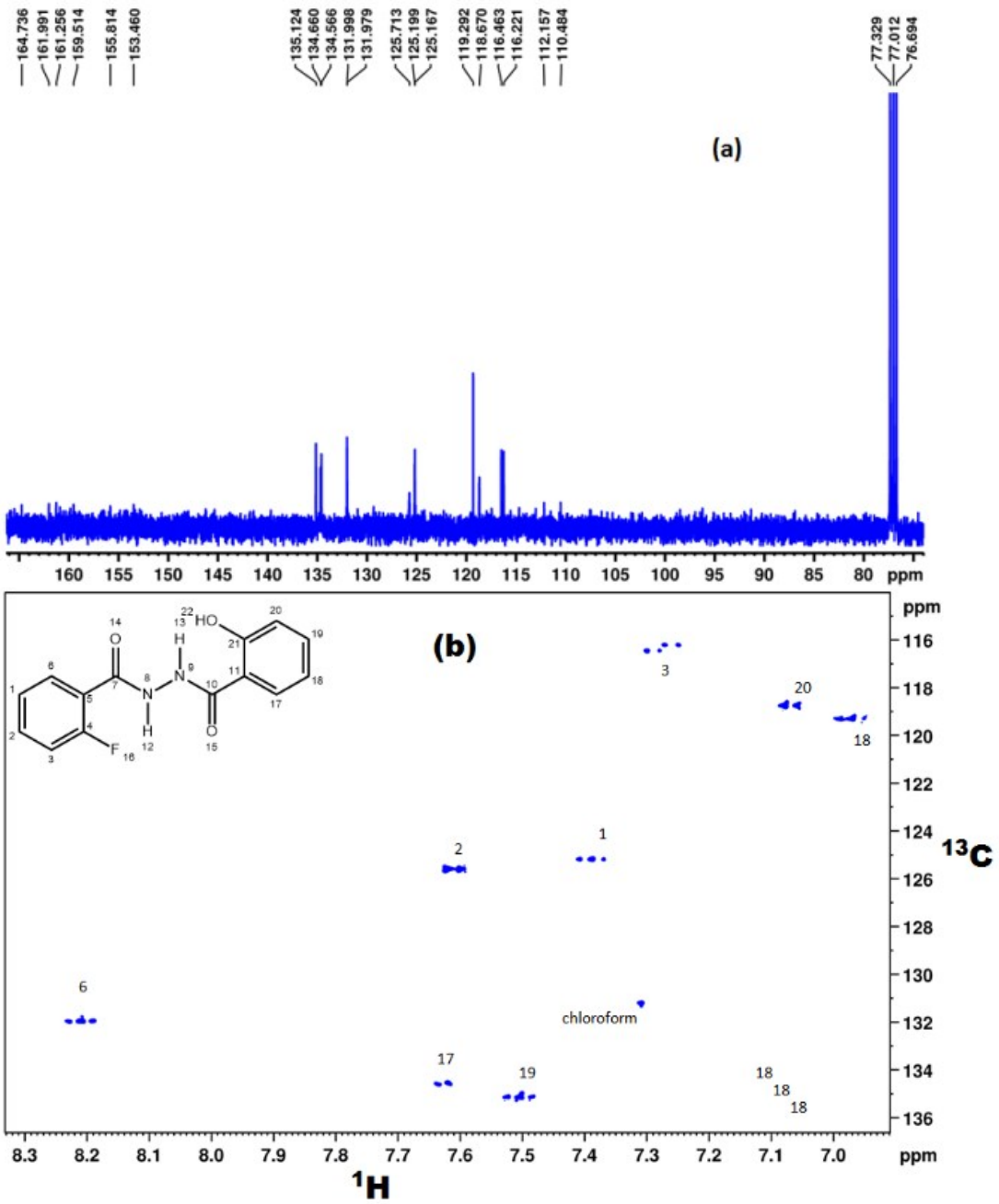


Fig.13S. (a) ^{13}C spectrum of the molecule **5** acquired on 400 MHz NMR spectrometer in solvent $CDCl_3$; and (b) 500 MHz ^{1}H-^{13}C HSQC (with peak assignments) spectrum acquired on a 500 MHz NMR spectrometer.

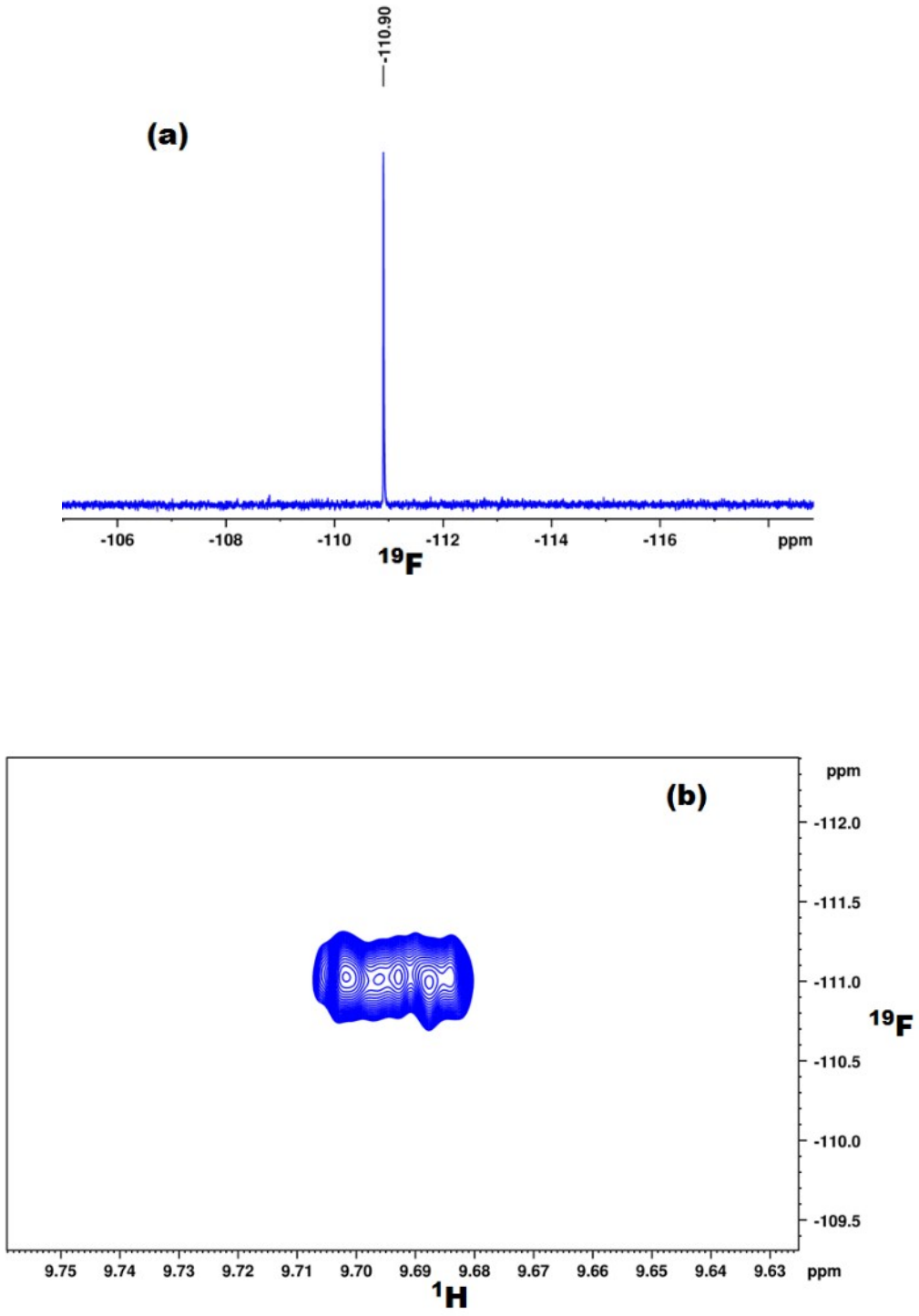
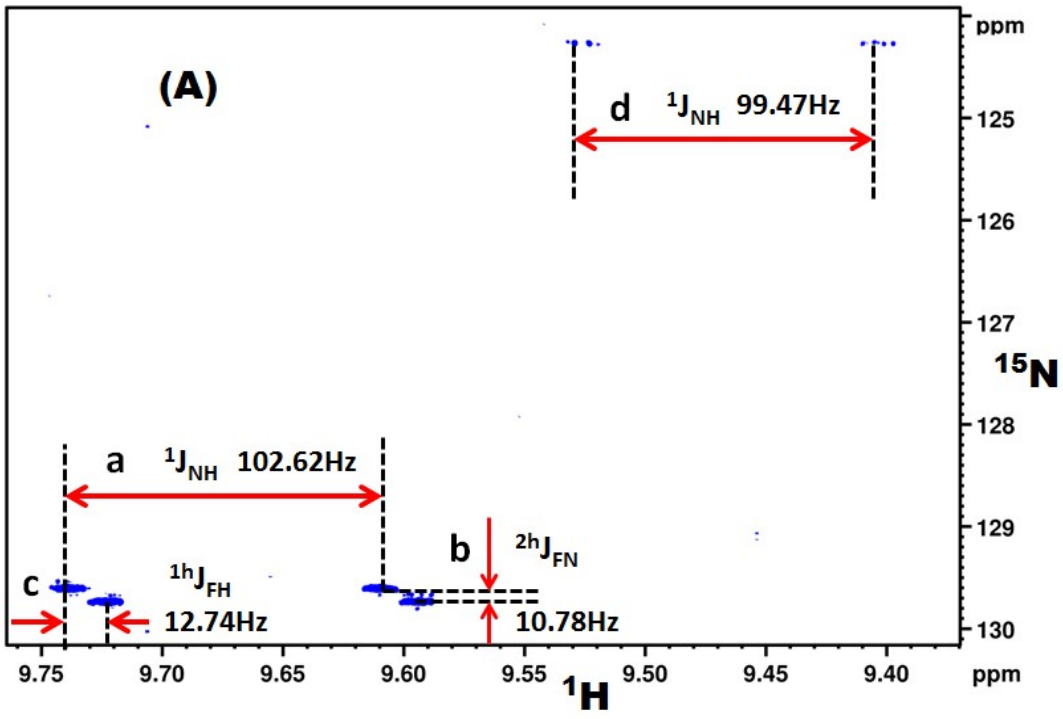
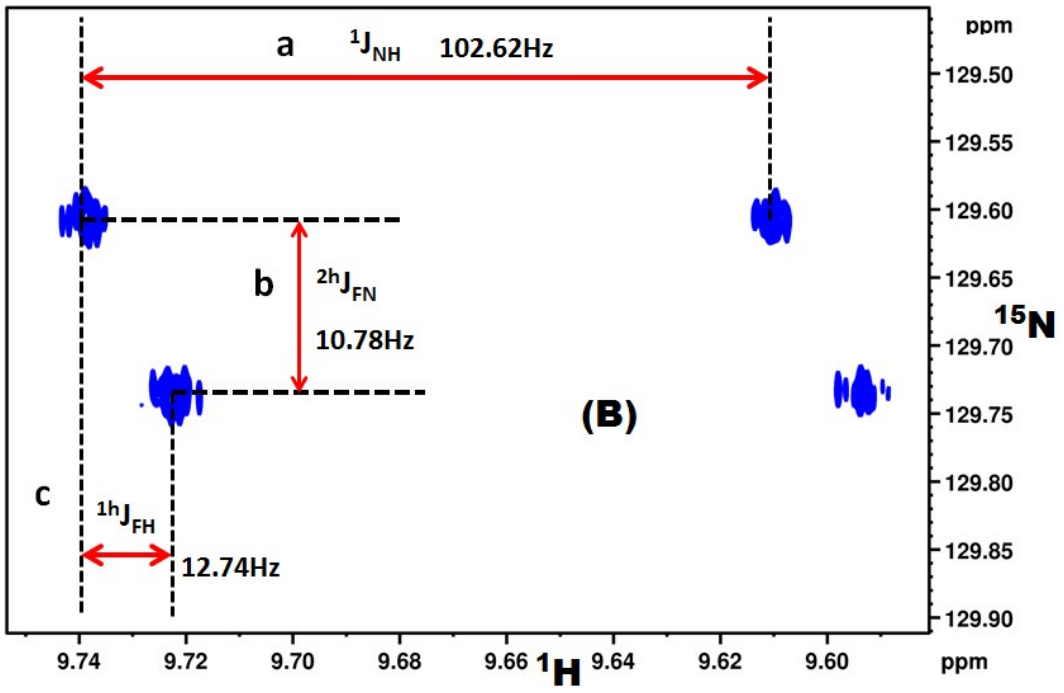
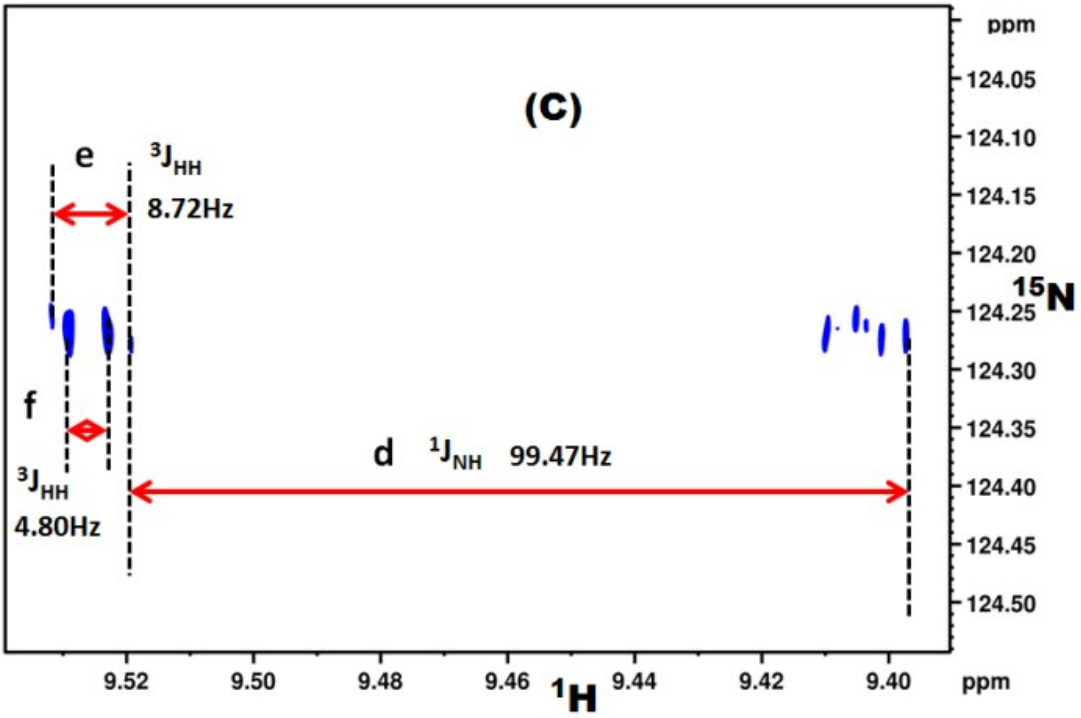


Fig.14S. (a) 1D ^{19}F and (b) 2D heteronuclear correlated ^{1}H-^{19}F HOESY[5] NMR spectra of the molecule **5** in the solvent $CDCl_3$ acquired on 400 MHz NMR spectrometer.

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.




a
$^{1}J_{NH}$ 102.62Hz
b
$^{2h}J_{FN}$
10.78Hz
c
$^{1h}J_{FH}$
12.74Hz
(B)
ppm
129.50
129.55
129.60
129.65
129.70
129.75
129.80
129.85
129.90
^{15}N
9.74
9.72
9.70
9.68
9.66
9.64
9.62
9.60
ppm
^{1}H


(C)
e
$^{3}J_{HH}$
8.72Hz
f
$^{3}J_{HH}$
4.80Hz
d
$^{1}J_{NH}$ 99.47Hz
ppm
124.05
124.10
124.15
124.20
124.25
124.30
124.35
124.40
124.45
124.50
^{15}N
9.52
9.50
9.48
9.46
9.44
9.42
9.40
ppm
^{1}H

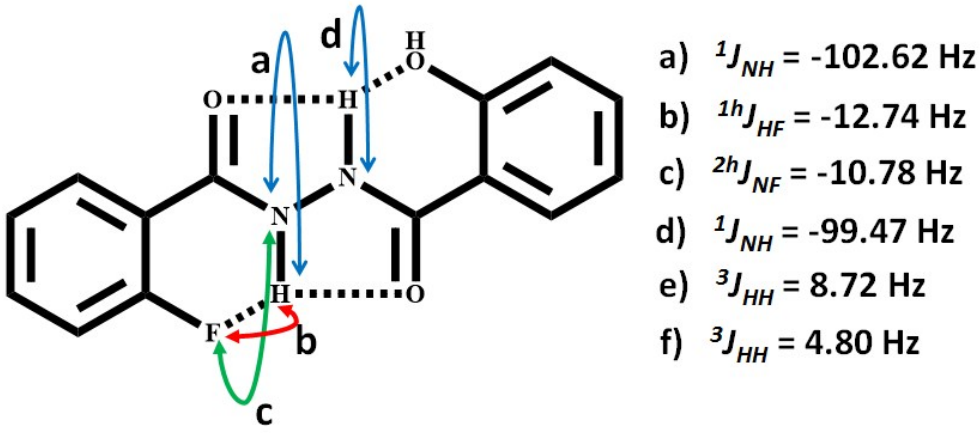


Fig.15S. (A) ^{1}H-^{15}N HSQC NMR spectrum of the molecule **5** acquired on 800 MHz NMR spectrometer in the solvent $CDCl_3$. B) and C) are zoomed regions of the spectrum. The separation providing the magnitudes of the couplings[2-4] are identified by double headed arrows. The chemical structure of 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 $^{3}J_{HH}$ 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.

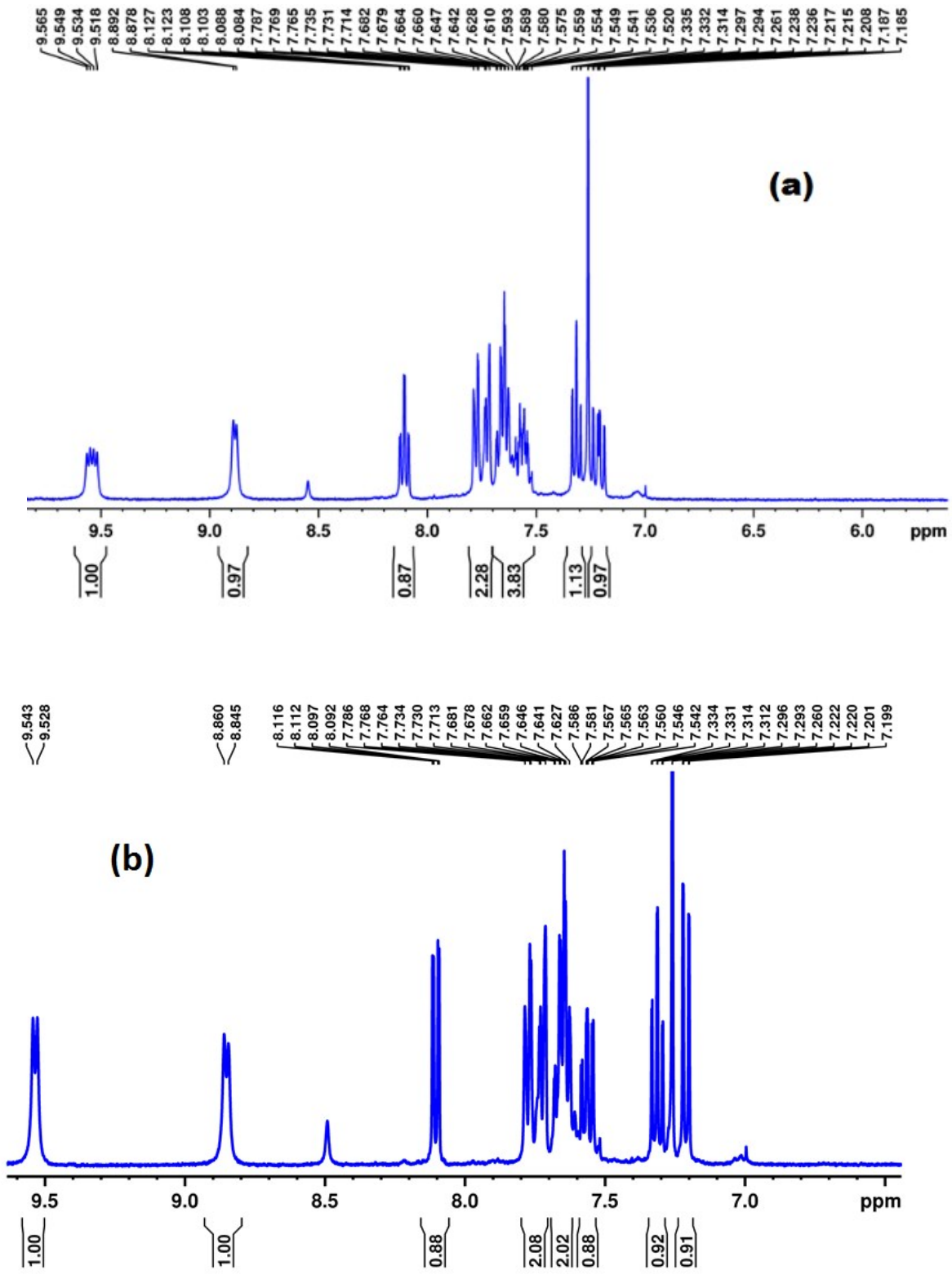


Fig.16S. 400 MHz (a) ^{1}H and **(b)** $^{1}H\{^{19}F\}$ NMR spectra of the molecule **6** in the solvent $CDCl_3$.

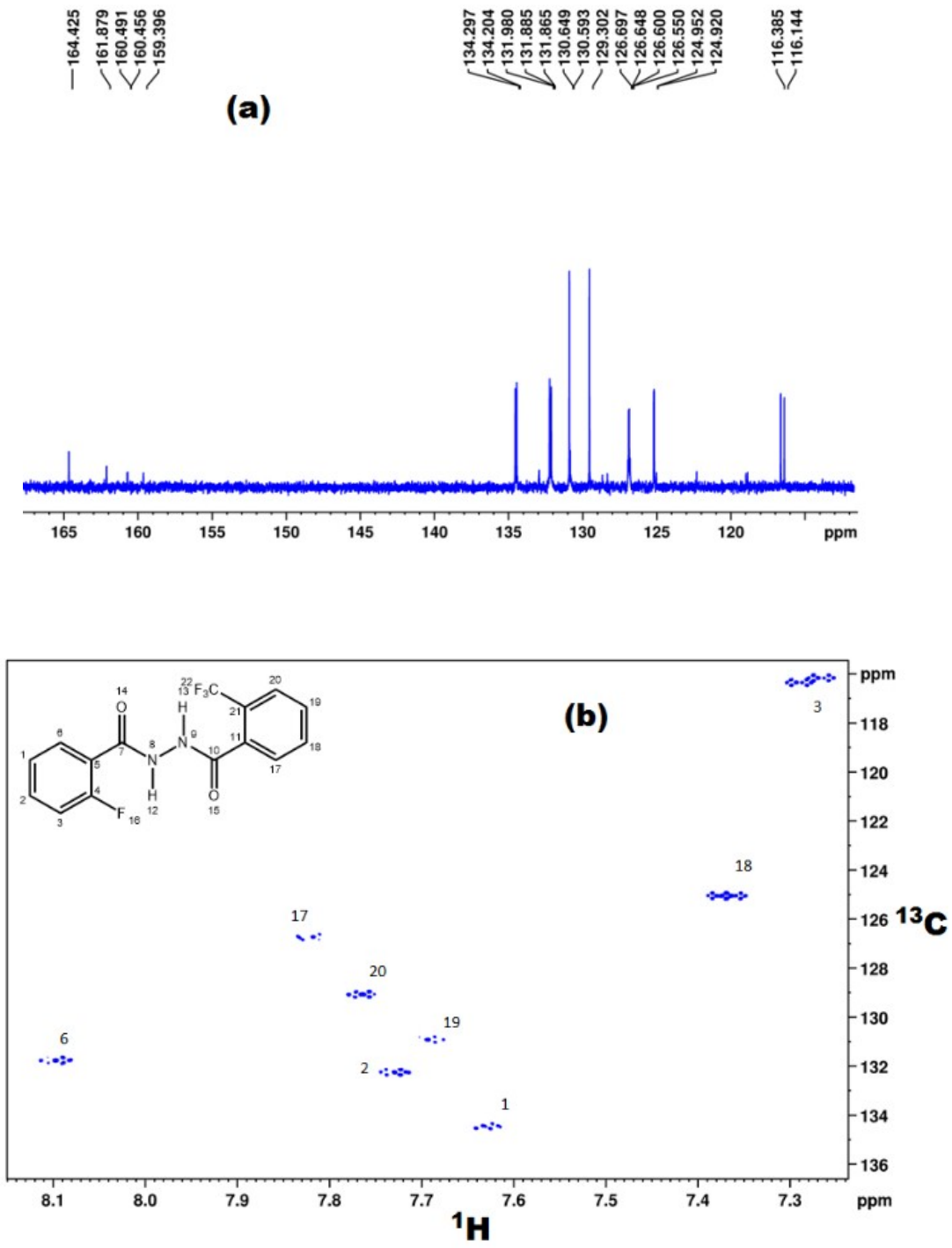
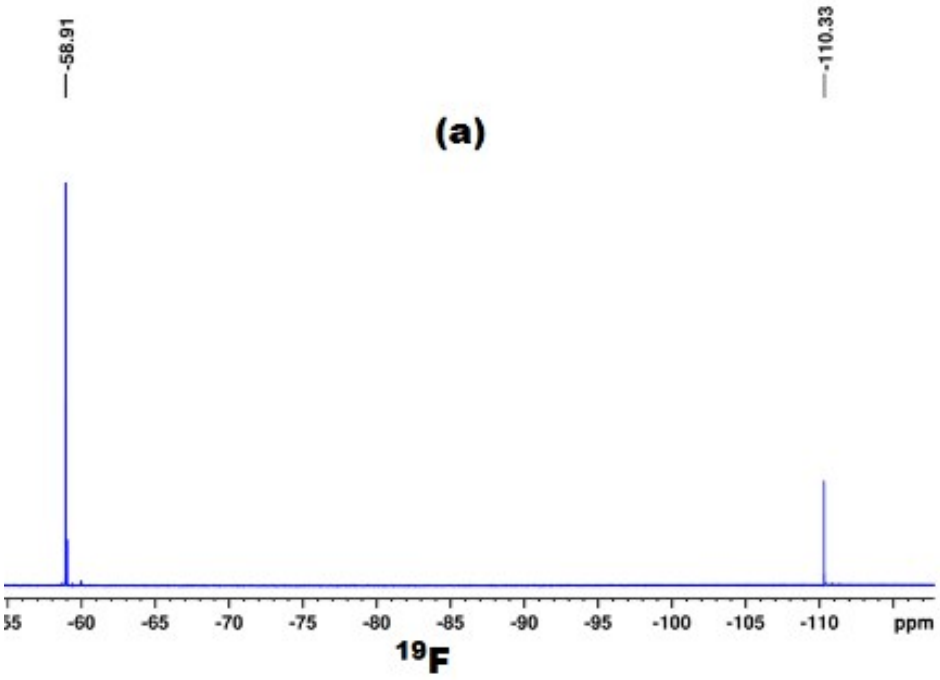
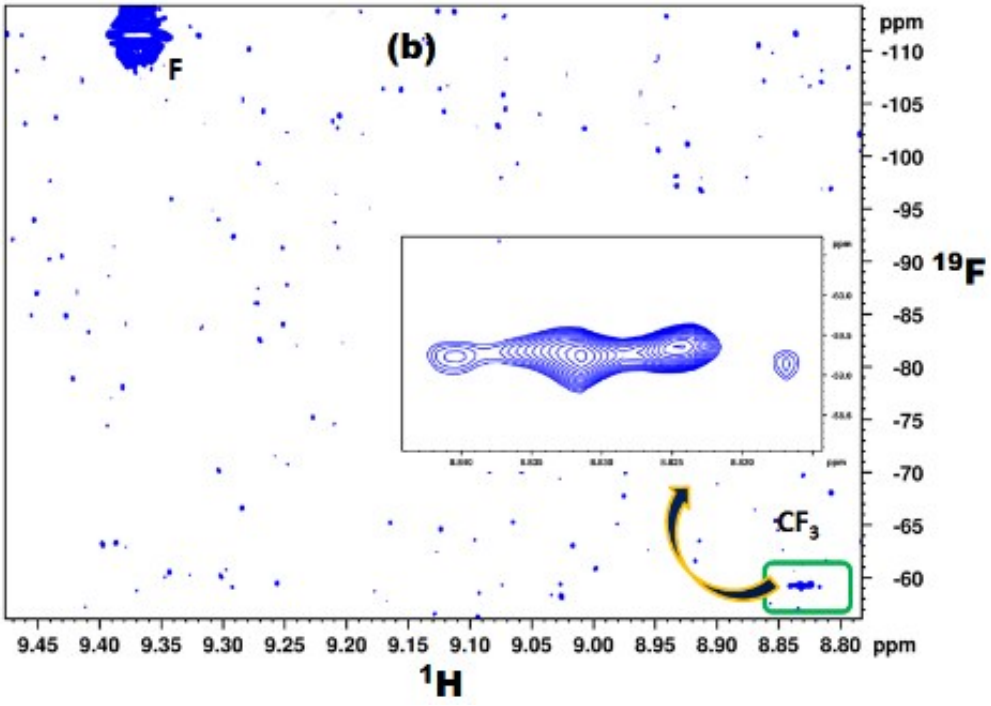


Fig.17S. (a) ^{13}C and (b) ^{1}H-^{13}C HSQC (with peak assignments) NMR spectra of the molecule **6** in solvent $CDCl_3$ acquired on 500 MHz NMR spectrometer.


-58.91
-110.33
(a)
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
ppm
19F


(b)
F
ppm
-110
-105
-100
-95
-90
-85
-80
-75
-70
-65
-60
19F
CF3
9.45
9.40
9.35
9.30
9.25
9.20
9.15
9.10
9.05
9.00
8.95
8.90
8.85
8.80
ppm
1H

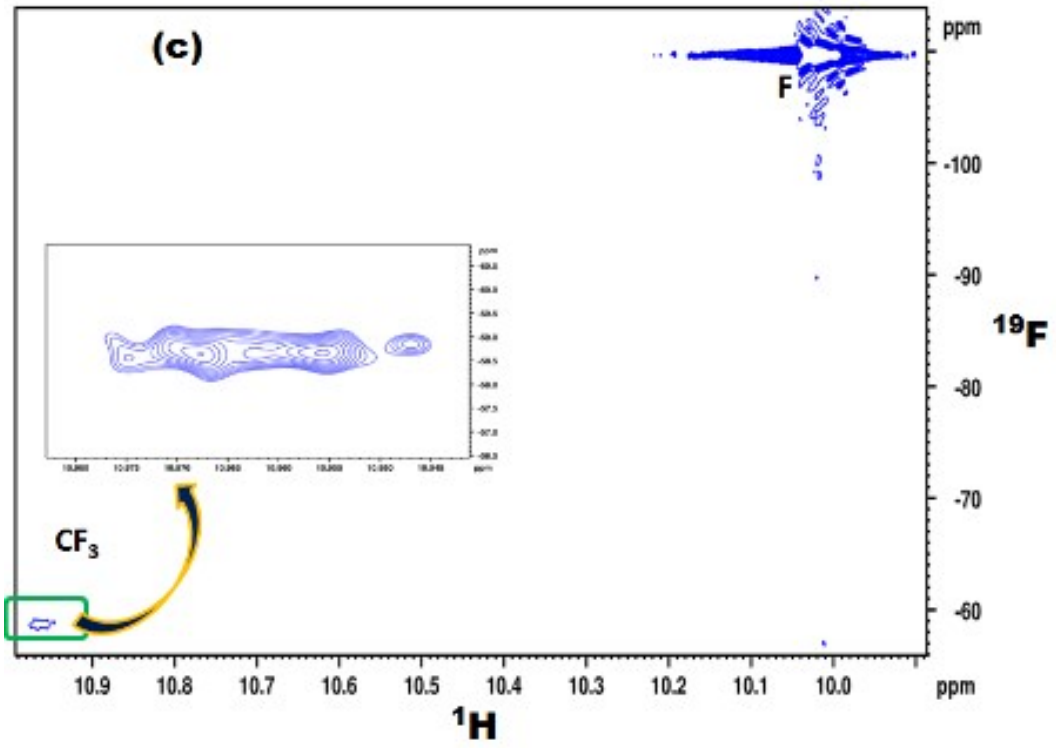
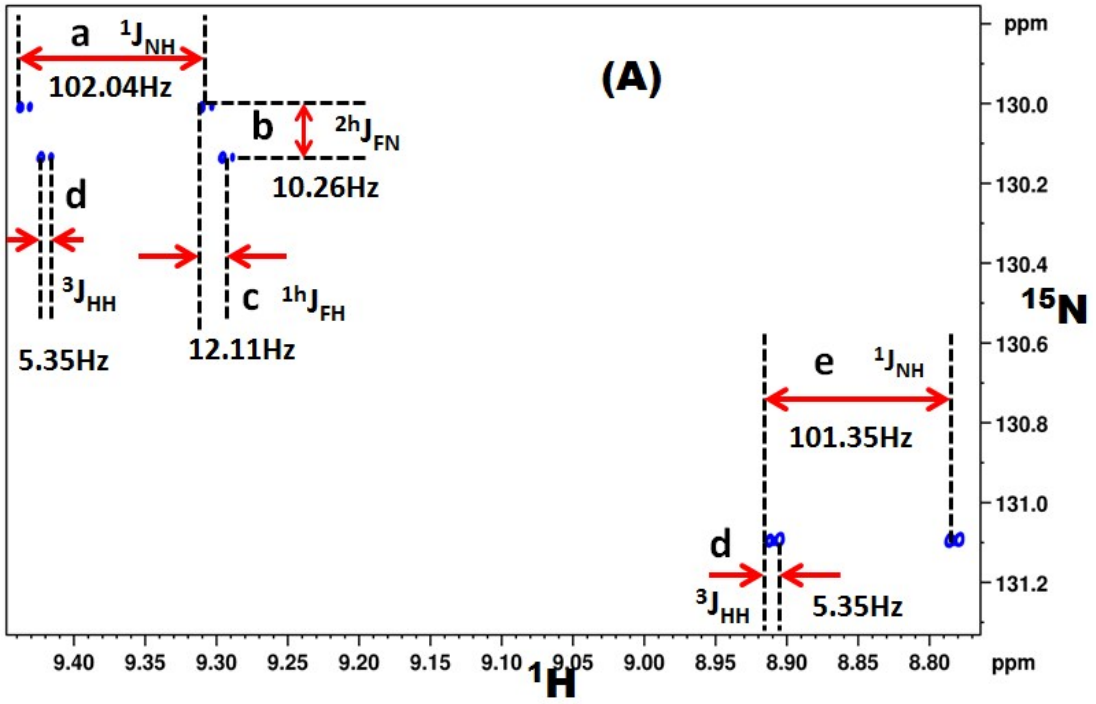
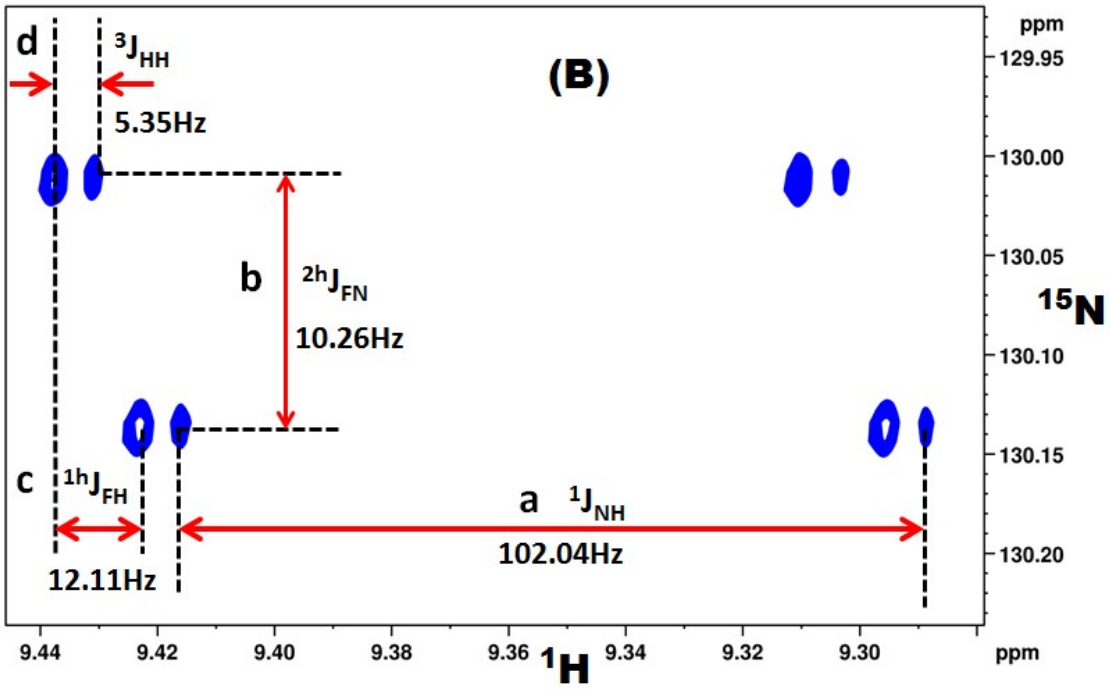


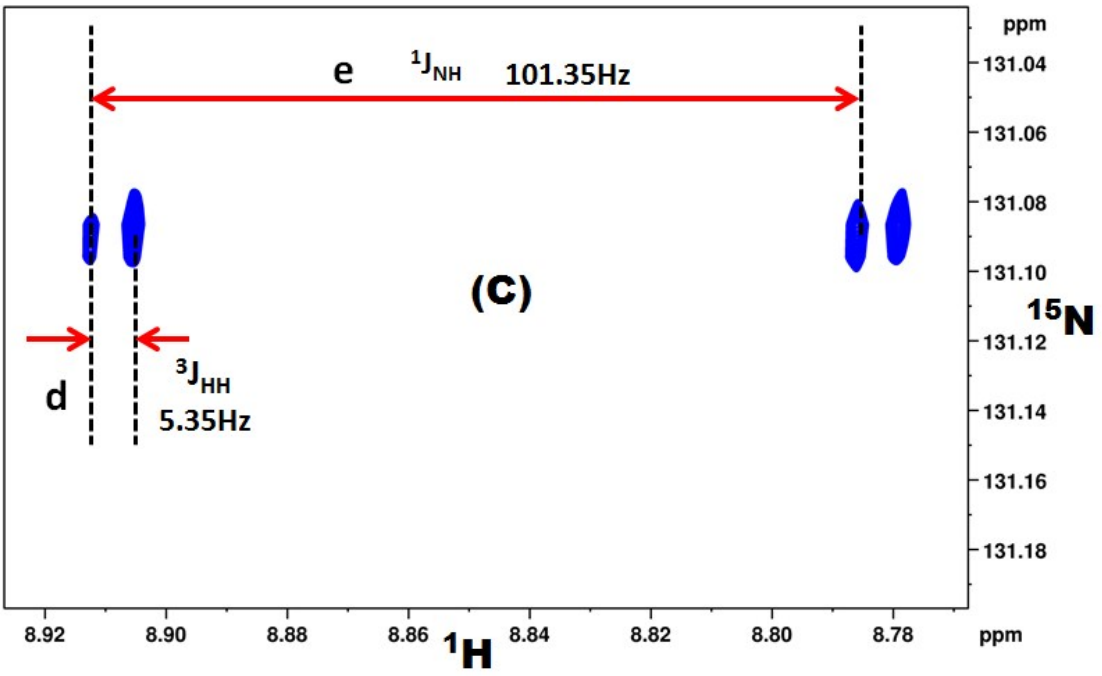
Fig.18S. (a) 1D ^{19}F and **(b)** 2D heteronuclear correlation ^{1}H-^{19}F HOESY NMR spectra of the molecule **6** at 298K; **(c)** 2D heteronuclear correlation ^{1}H-^{19}F HOESY NMR spectra of molecule **6** 220K. Both the spectra were acquired in the solvent $CDCl_3$ on a 400 MHz NMR spectrometer.

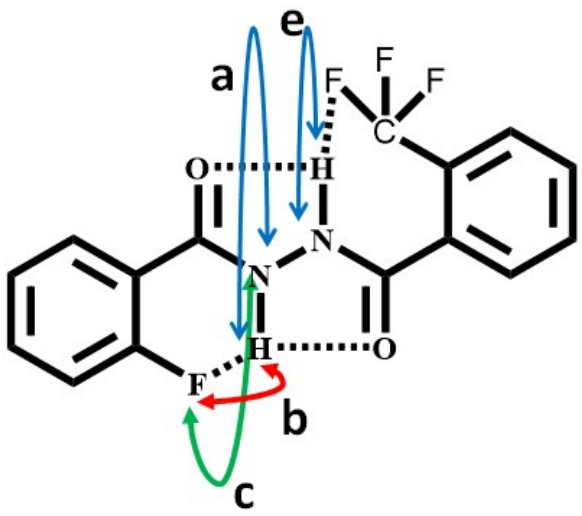
Discussion:

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^{o} 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).


(A)
a $^{1}J_{NH}$
102.04Hz
b $^{2h}J_{FN}$
10.26Hz
d
$^{3}J_{HH}$
5.35Hz
c $^{1h}J_{FH}$
12.11Hz
e $^{1}J_{NH}$
101.35Hz
d
$^{3}J_{HH}$
5.35Hz
ppm
130.0
130.2
130.4
^{15}N
130.6
130.8
131.0
131.2
9.40 9.35 9.30 9.25 9.20 9.15 9.10 9.05 9.00 8.95 8.90 8.85 8.80
ppm
^{1}H


(B)
d
$^{3}J_{HH}$
5.35Hz
b $^{2h}J_{FN}$
10.26Hz
c $^{1h}J_{FH}$
12.11Hz
a $^{1}J_{NH}$
102.04Hz
ppm
129.95
130.00
130.05
^{15}N
130.10
130.15
130.20
9.44 9.42 9.40 9.38 9.36 9.34 9.32 9.30
ppm
^{1}H





a) $^1J_{NH}$ = -102.04 Hz

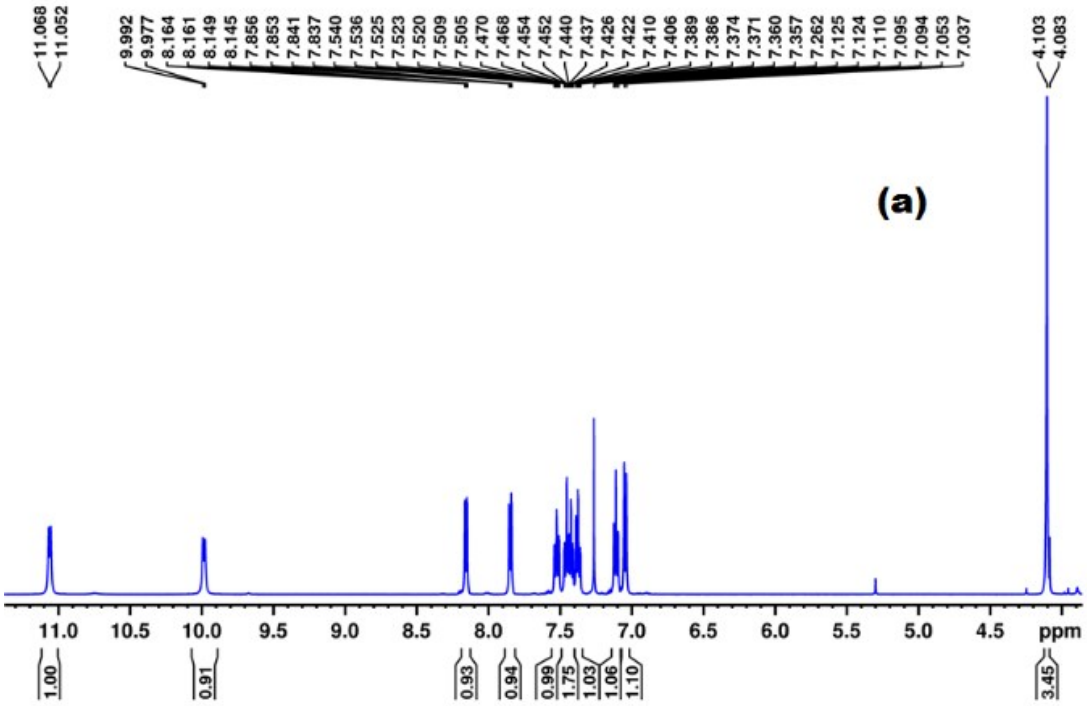
b) $^{1h}J_{FH}$ = -12.11 Hz

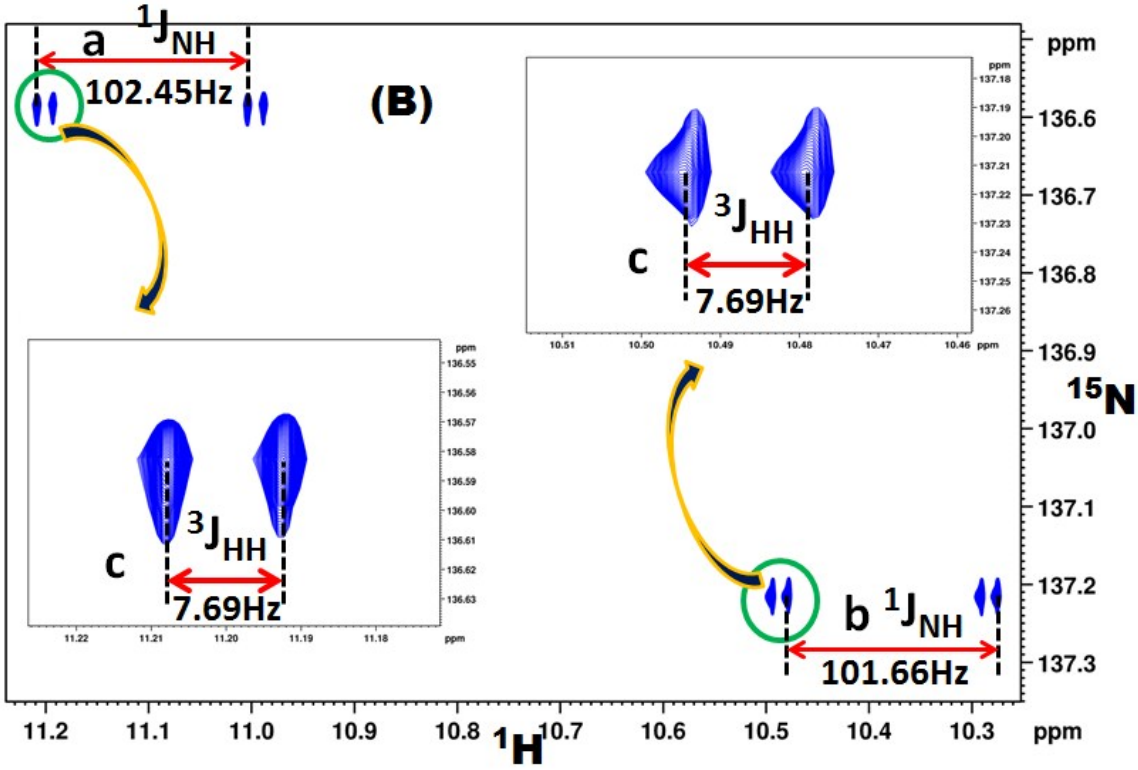
c) $^{2h}J_{FN}$ = -10.26 Hz

d) $^3J_{HH}$ = 5.35 Hz

e) $^1J_{NH}$ = 101.35 Hz

Fig.19S. (A) ^{1}H-^{15}N HSQC NMR spectrum of the molecule **6** acquired on an 800 MHz NMR spectrometer in the solvent $CDCl_3$. 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.


(a)
11.068
11.052
9.992
9.977
8.164
8.161
8.149
8.145
7.856
7.853
7.841
7.837
7.540
7.536
7.525
7.523
7.520
7.509
7.505
7.470
7.468
7.454
7.452
7.440
7.437
7.426
7.422
7.410
7.406
7.389
7.386
7.374
7.371
7.360
7.357
7.262
7.125
7.124
7.110
7.095
7.094
7.053
7.037
4.103
4.083
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 ppm
1.00
0.91
0.93
0.94
0.99
1.75
1.03
1.06
1.10
3.45


(B)
a
$^{1}J_{NH}$
102.45Hz
c
$^{3}J_{HH}$
7.69Hz
c
$^{3}J_{HH}$
7.69Hz
b $^{1}J_{NH}$
101.66Hz
ppm
136.6
136.7
136.8
136.9
^{15}N
137.0
137.1
137.2
137.3
11.2 11.1 11.0 10.9 10.8 ^{1}H 10.7 10.6 10.5 10.4 10.3 ppm

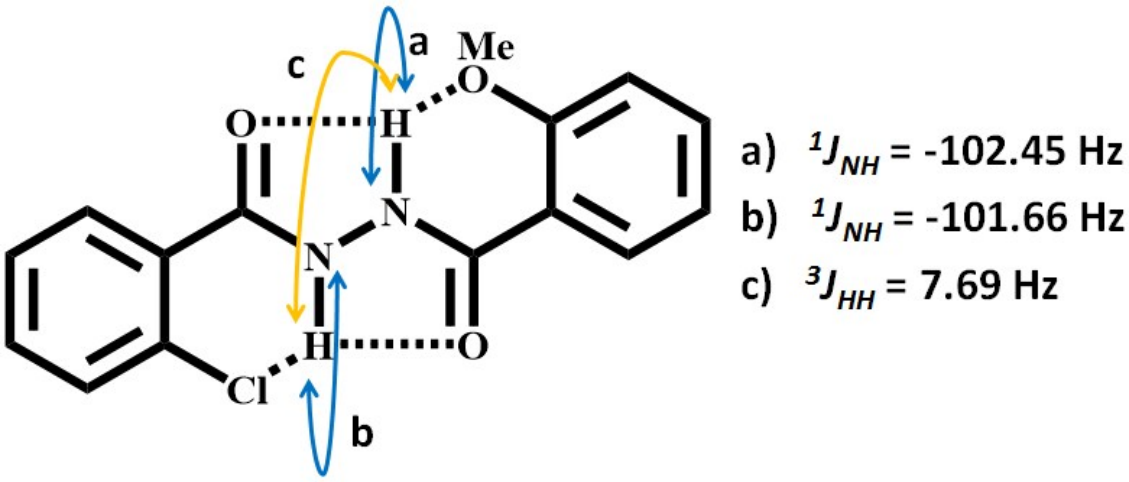
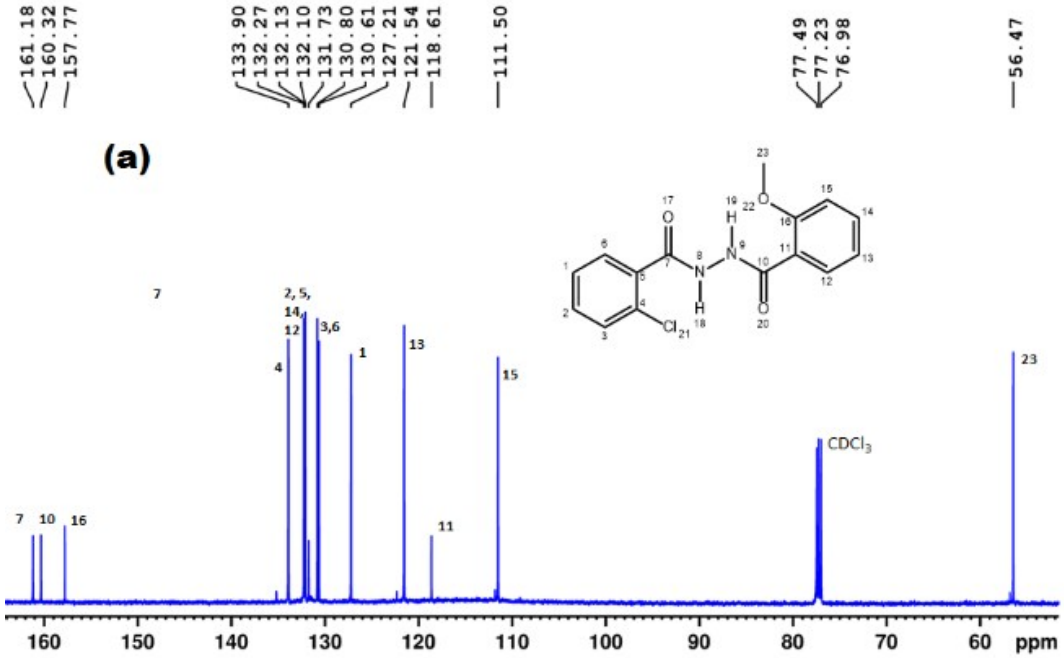


Fig.20S. (a) ^{1}H (b) ^{1}H-^{15}N HSQC NMR spectra of the molecule **7** acquired on a 400 MHz NMR spectrometer in the solvent $CDCl_3$. The separation providing the magnitudes[2-4] of the couplings are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.



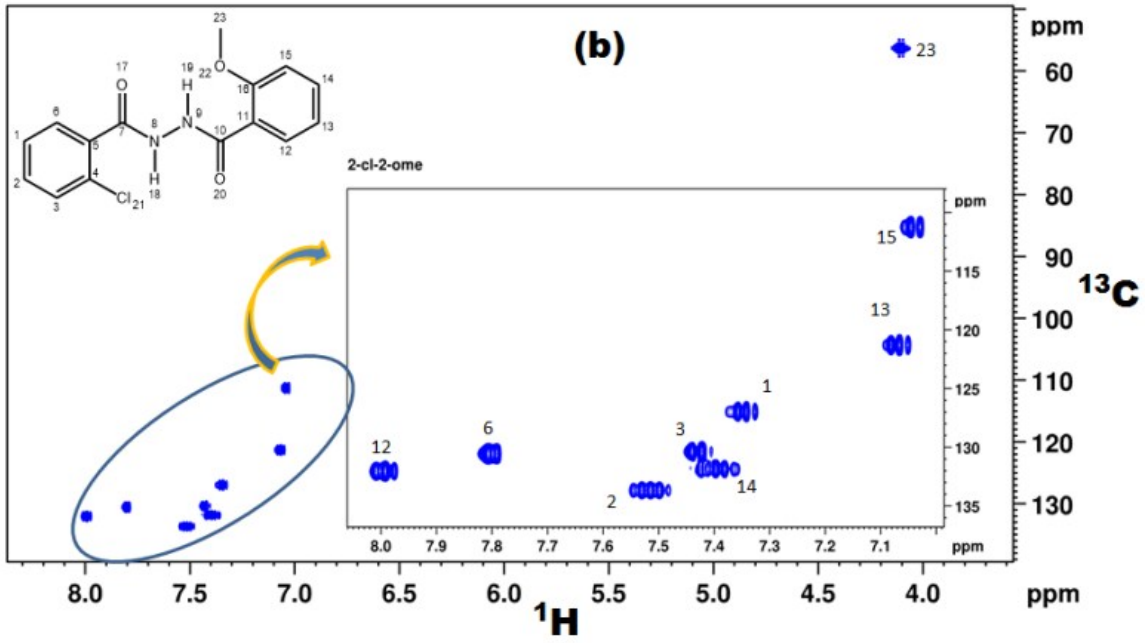
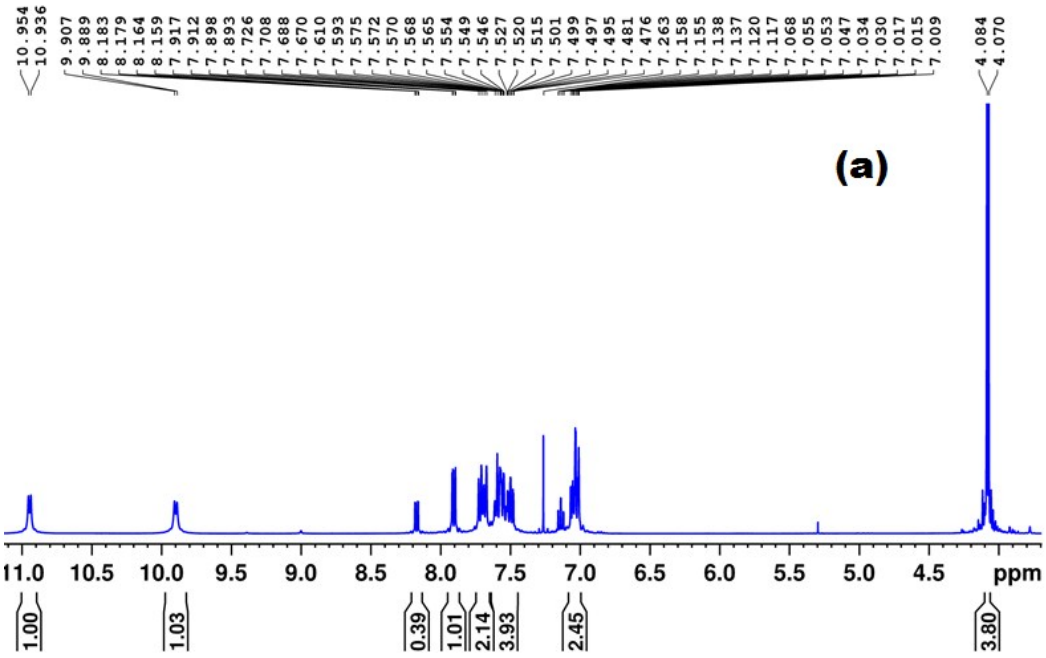


Fig.21S. (a) ^{13}C (with peak assignments) and (b) ^{1}H-^{13}C HSQC (with peak assignments) NMR spectra of the molecule **7** acquired on 500 MHz NMR spectrometer in the solvent $CDCl_3$. The zoomed region of the spectrum is given in the inset.



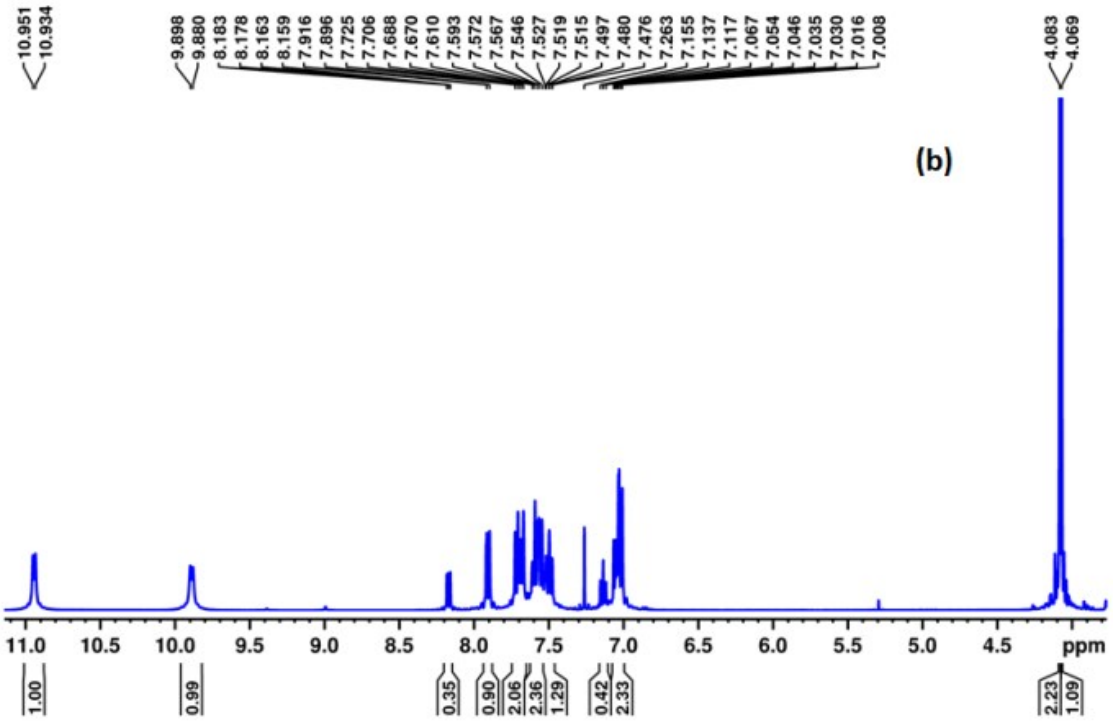


Fig.22S. (a) ^{1}H NMR **(b)** $^{1}H\{^{19}F\}$ NMR spectra of the molecule **8** acquired on 400 MHz NMR spectrometer in the solvent $CDCl_3$.

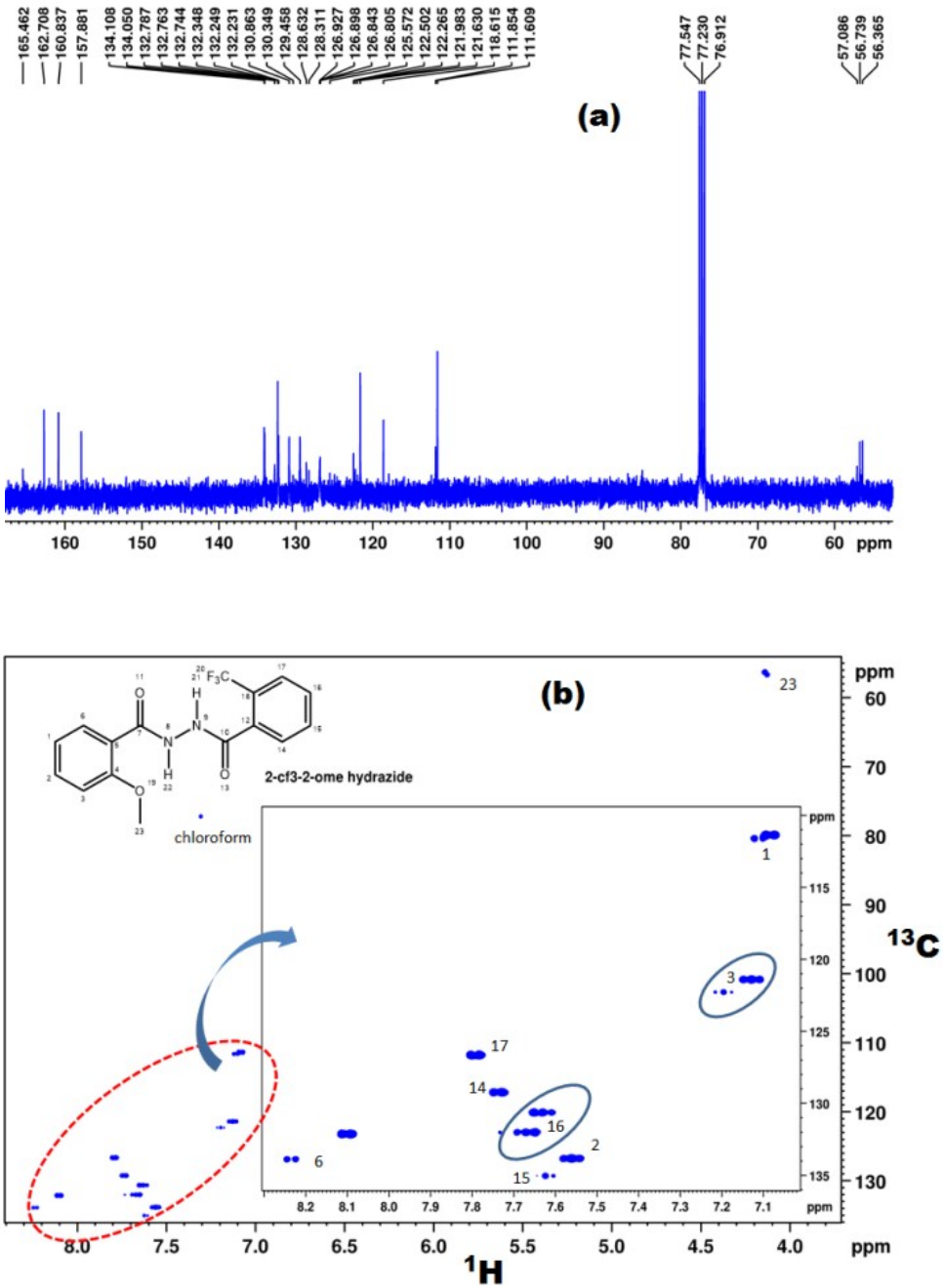
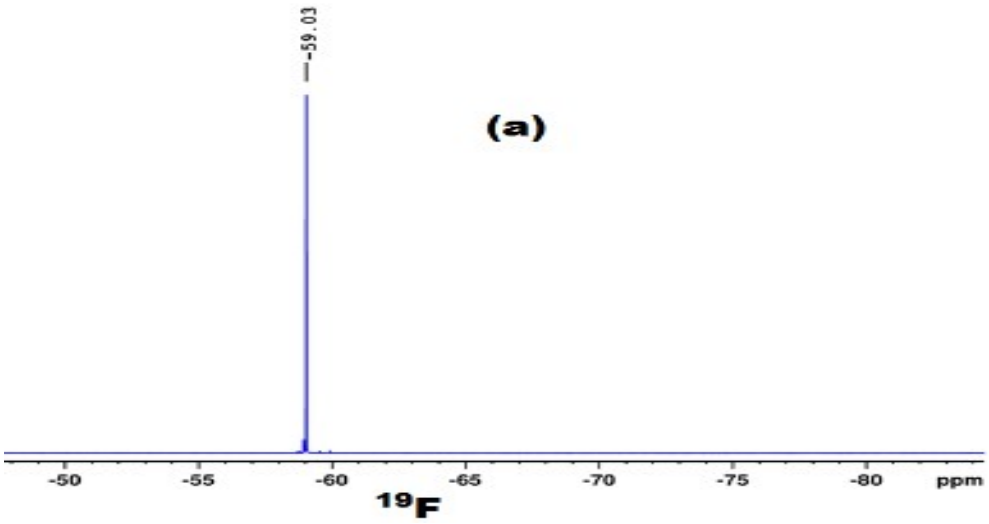
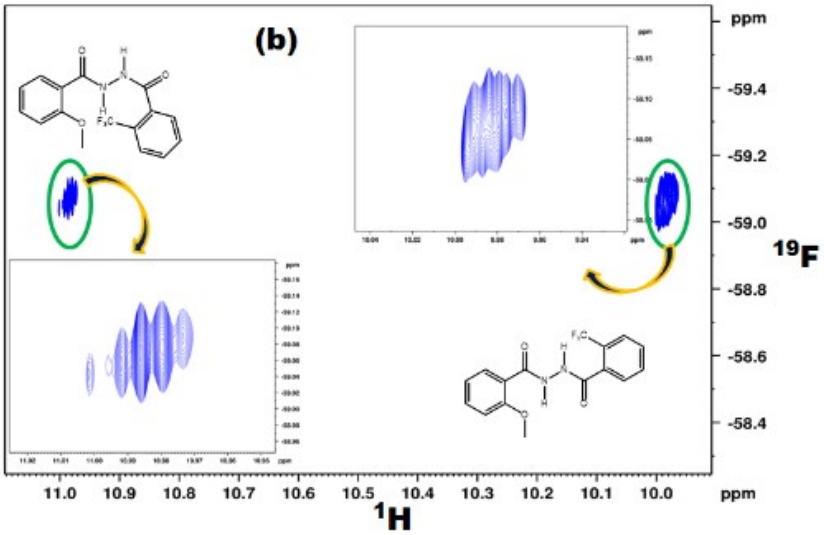


Fig.23S. (a) ^{13}C and (b) ^{1}H-^{13}C HSQC (with peak assignments) NMR spectra of the molecule **8** acquired on 500 MHz NMR spectrometer in the solvent $CDCl_3$. The zoomed region of the spectrum is given in the inset.

Discussion:

There are three peaks for the methoxy group in the ^{13}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.

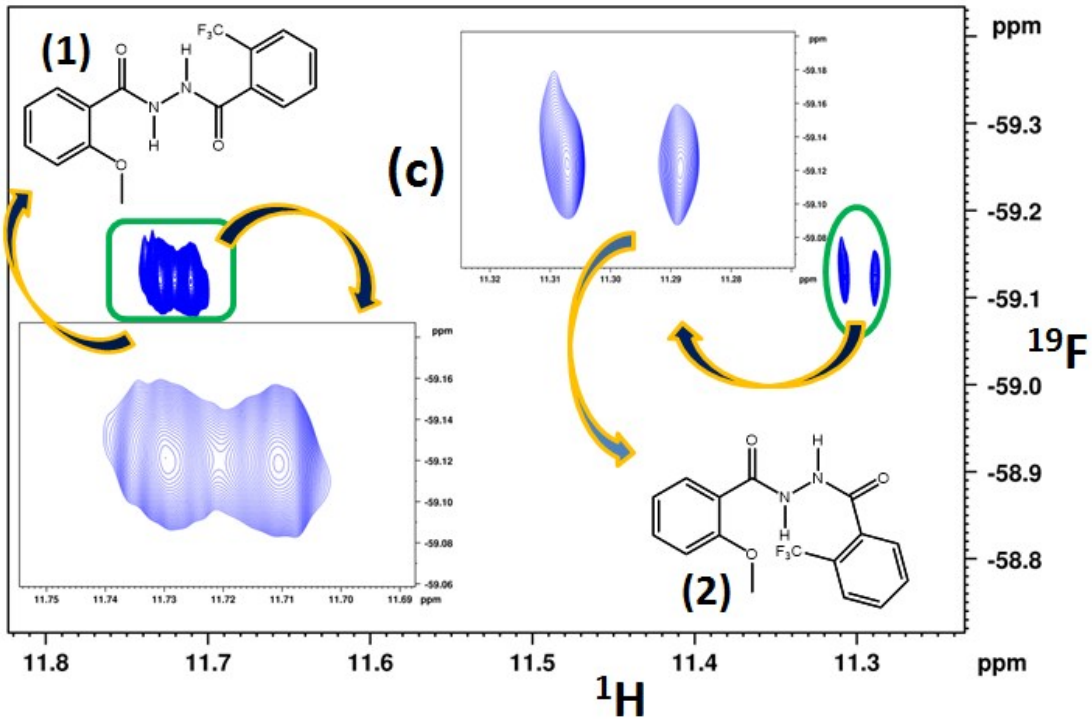


Fig.24S. (a) 1D ^{19}F NMR **(b)** 2D heteronuclear correlated ^{1}H-^{19}F HOESY[5] NMR spectra at 298K **(c)** 2D heteronuclear correlation ^{1}H-^{19}F HOESY[5] NMR spectra at 220K of the molecule **8** acquired on 400 MHz NMR spectrometer in the solvent $CDCl_3$. Two different conformers are given 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^{o} flip of CF_3 containing phenyl ring at lower temperature.

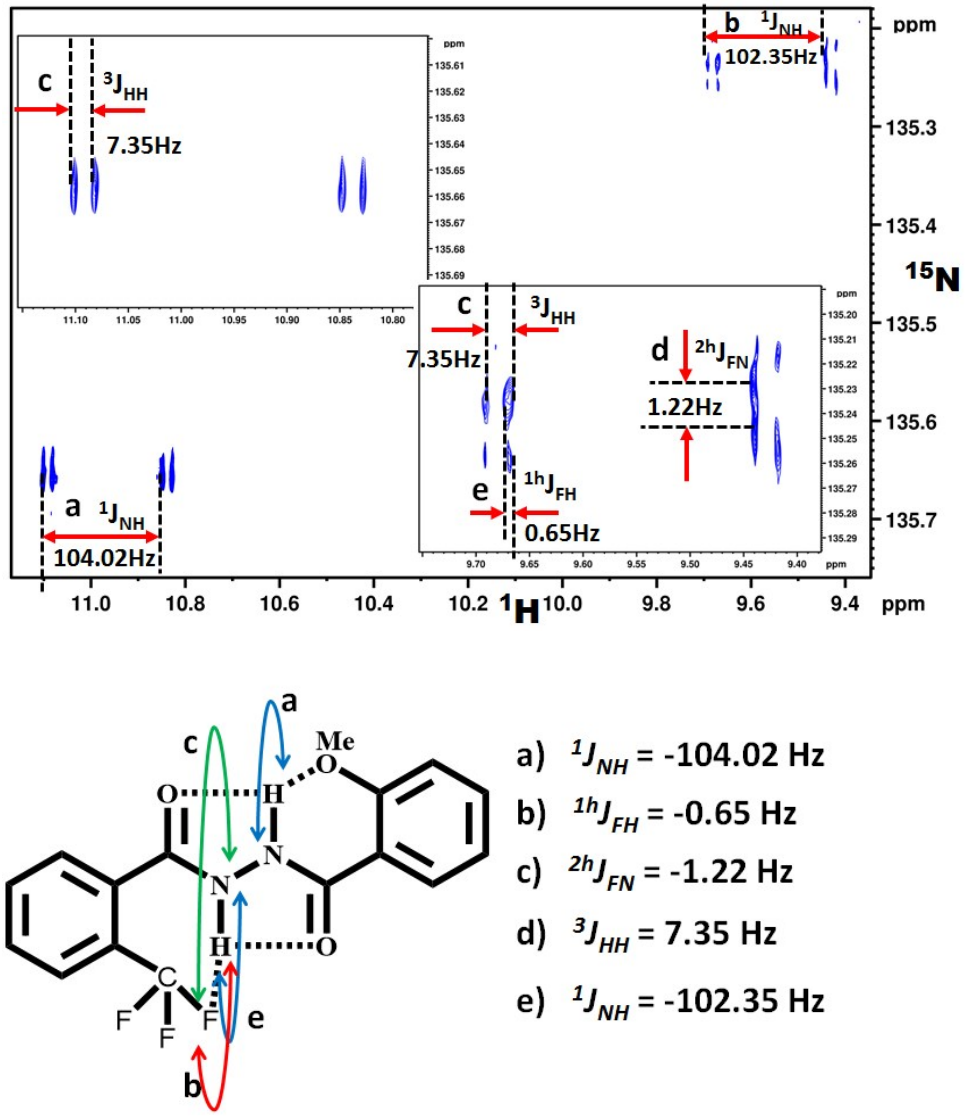


Fig.25S. Two dimensional ^{1}H-^{15}N HSQC NMR spectrum of molecule **8** acquired on 400 MHz NMR spectrometer in the solvent $CDCl_3$. The separation providing the magnitudes of the couplings are identified by double headed arrows. The chemical structure of the molecule and the sign of the coupling is also given.

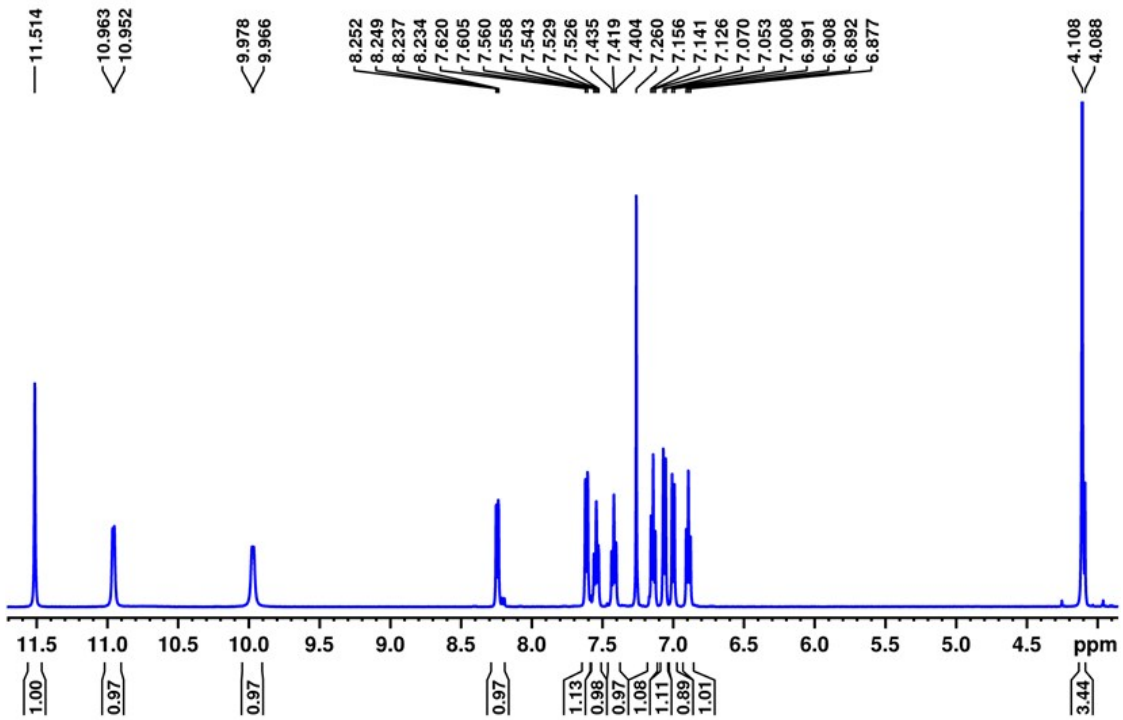


Fig.26S. ^{1}H NMR spectrum of molecule **9** acquired on 400 MHz NMR spectrometer in the solvent $CDCl_3$.

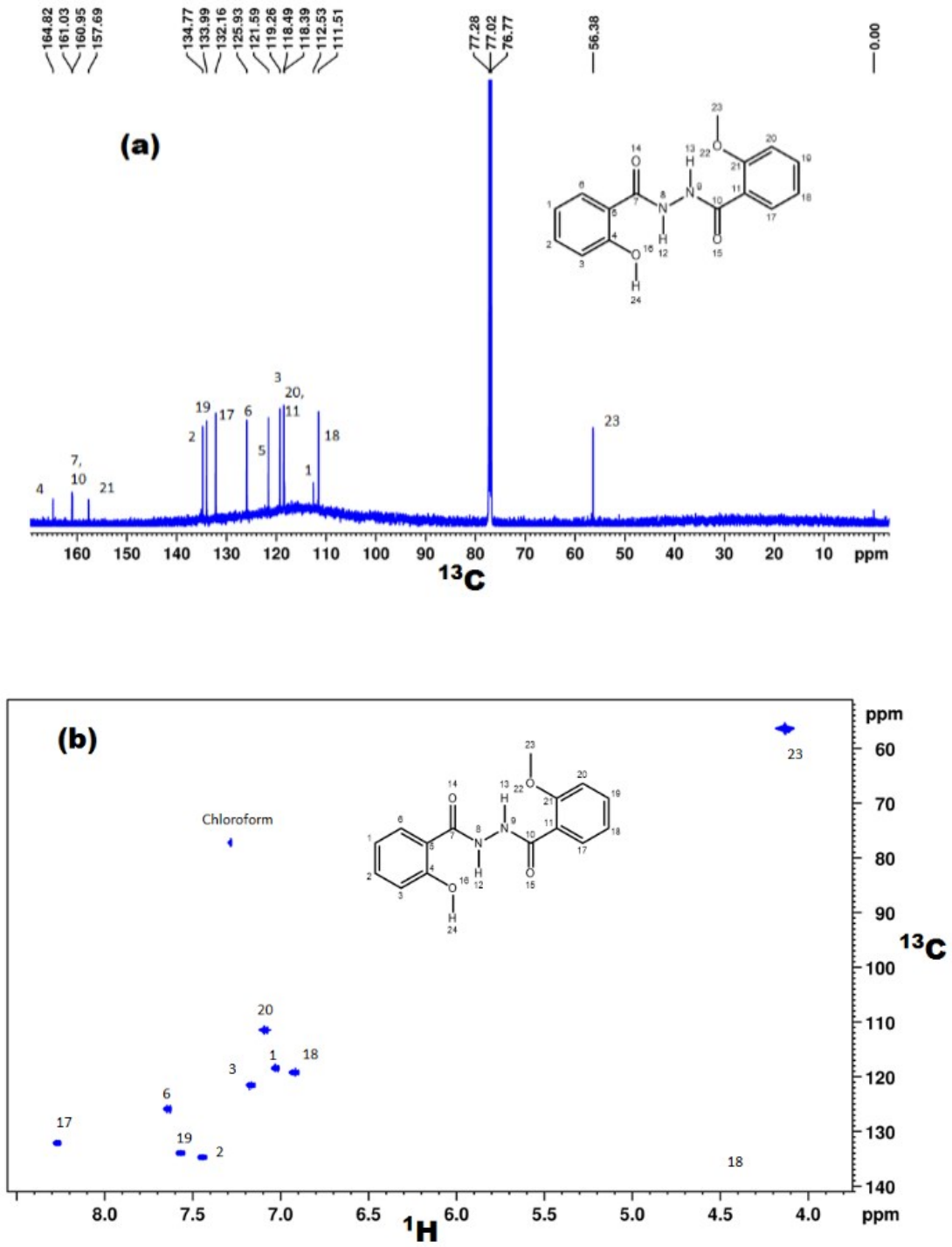
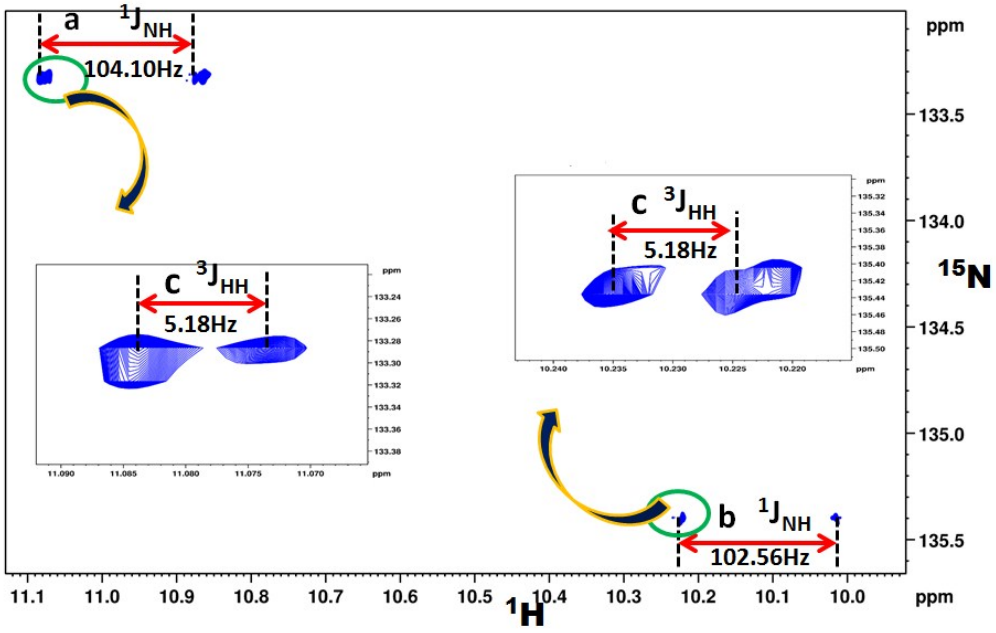
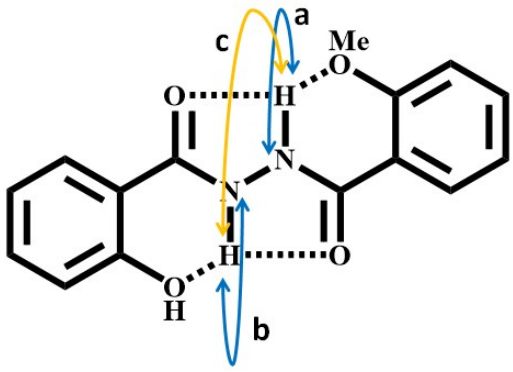


Fig.27S. (a) ^{13}C (with peak assignments) and (b) 2D ^{1}H-^{13}C HSQC (with peak assignments) NMR spectra of the molecule **9** acquired on 500 MHz NMR spectrometer in solvent $CDCl_3$.





a) $^1J_{NH}$ = -104.10 Hz

b) $^1J_{NH}$ = -102.56 Hz

c) $^3J_{HH}$ = 5.18 Hz

Fig.28S.(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.

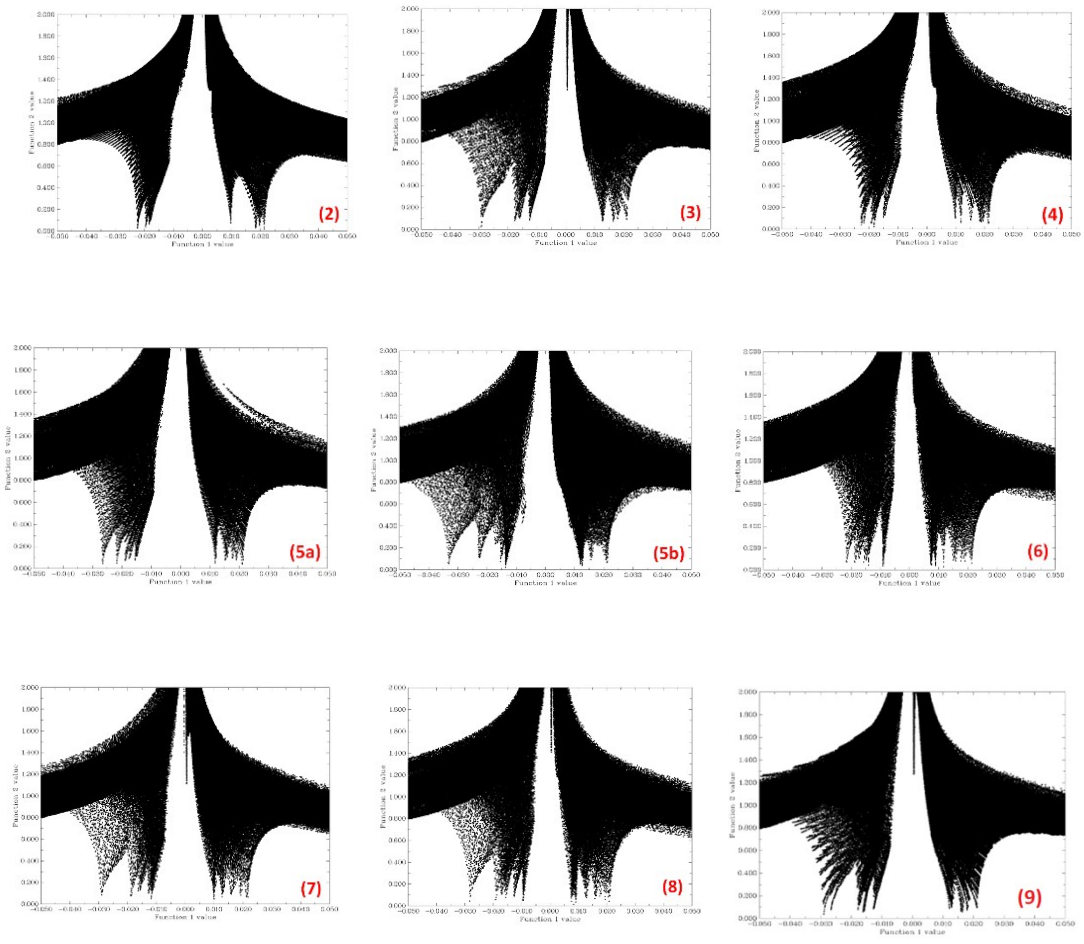
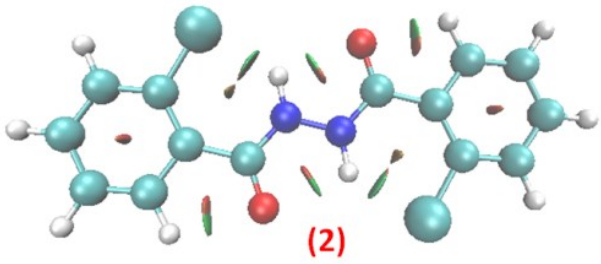
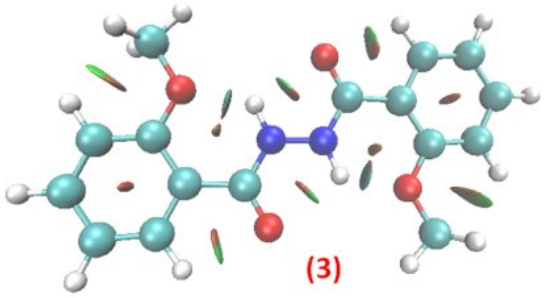


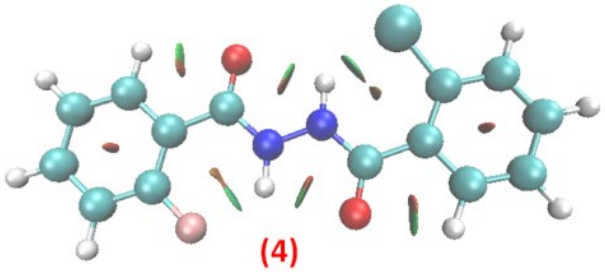
Fig.29S. The plot of sign(λ_2(r))*ρ(r) as function 1 V/s The reduced density gradient (RDG) as function 2 of molecules **2-9,** plotted using multiwfn[6] programme by utilizing wavefunction (.wfn) files. The Wavefunction files were generated by Gaussian09 [7] programme during DFT[8] structure optimization.



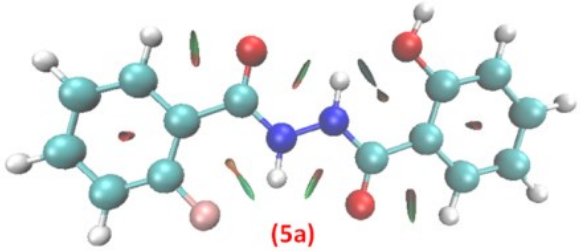
(2)



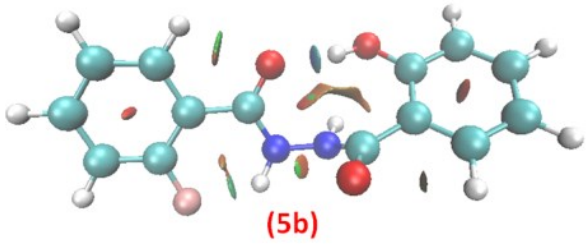
(3)



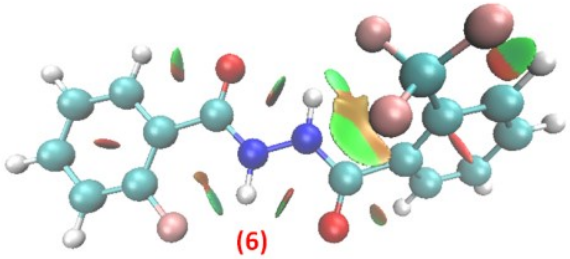
(4)



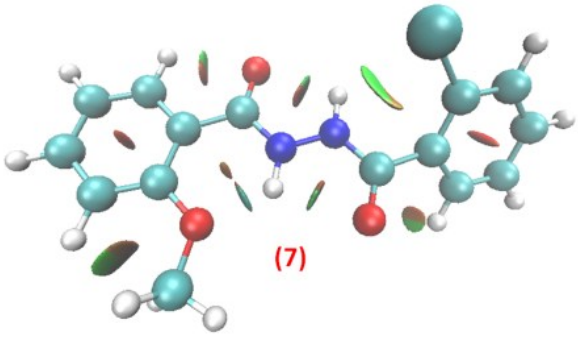
(5a)



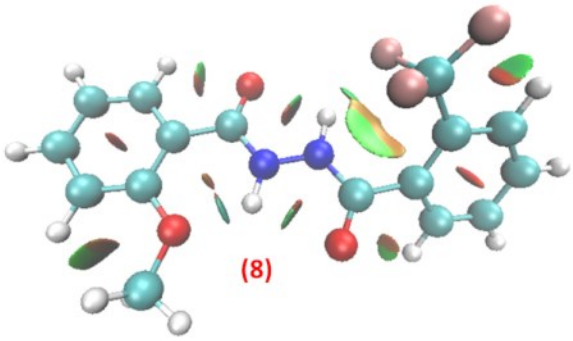
(5b)



(6)



(7)



(8)

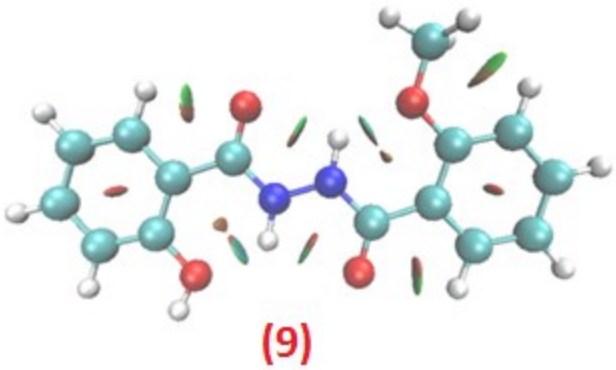
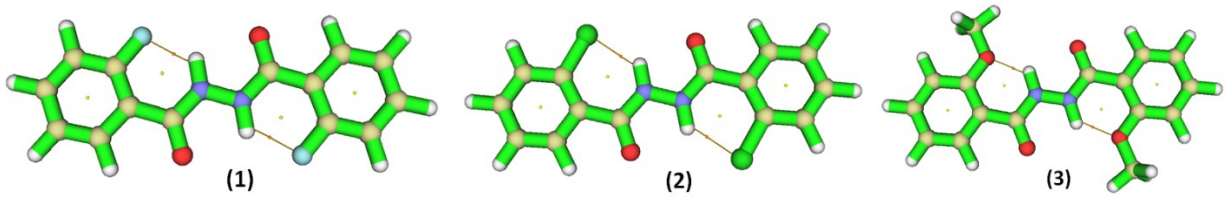


Fig.30S. Coloured Isosurface plot (green colour denotes weak H-bond and red colour stands for steric effect) of molecules **2-9**, ploted using VMD[9] programe.

There are three spikes on the left hand side (i.e. sign(λ_2(r))*ρ(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(λ_2(r))*ρ(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.



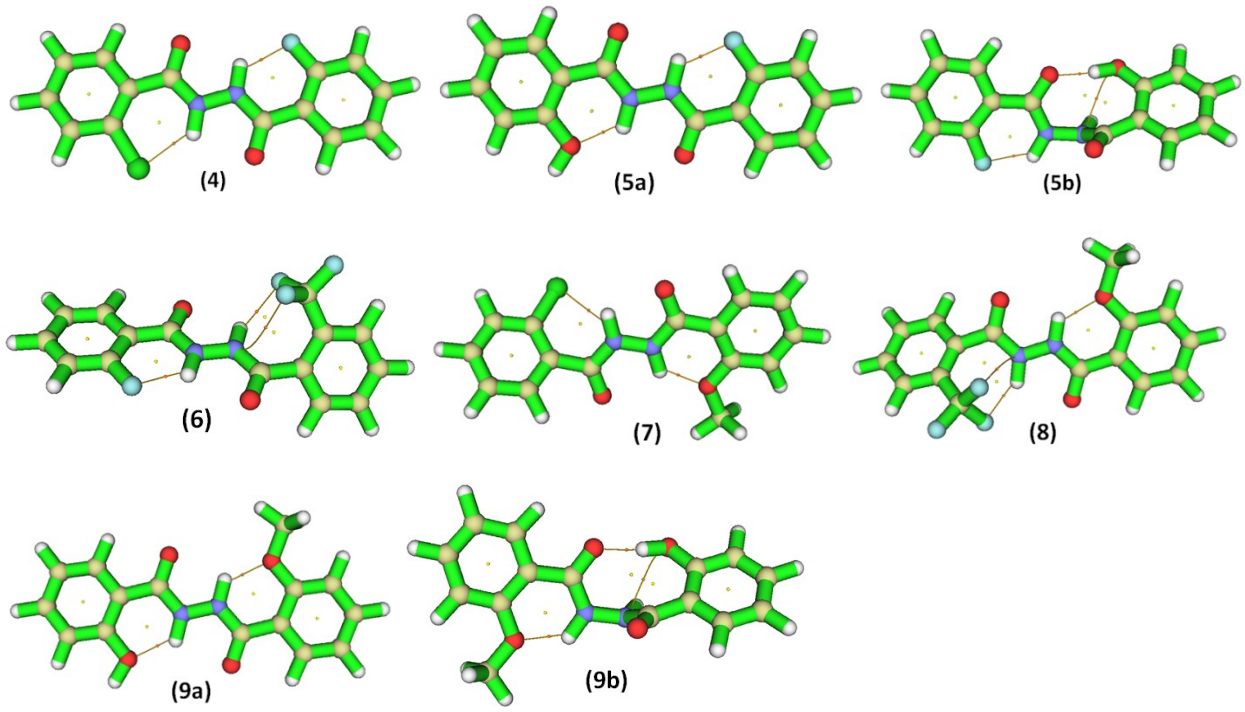


Fig.31S. The optimized structures with (3, -1) bond critical points (BCP) for the molecules **1-9**.

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