

NMR Studies of Complexes of Fluorides of Triethylamine

N. Ilayaraja¹, S. Radha Krishnan^{1,*}, G. Ravindran² and N. G. Renganathan²

¹CSIR-Central Electrochemical Research Institute, Karaikudi, 630 006, India

²Vel Tech Dr.RR & Dr.SR.University, Avadi, Chennai, 600 062, India

Abstract: Different mole ratio of triethylamine HF (Et_3nHF , n = 3, 4 and 5) adducts were prepared and ^1H and ^{19}F NMR spin-lattice relaxation was measured at various temperatures for these three adducts. From this data the bond length and dipole properties of these three adducts were studied. These three adducts can be readily identified by ^{19}F NMR chemical shifts.

Keywords: Hydrogen fluorides, adducts, NMR, spin-lattice relaxation.

INTRODUCTION

Fluorine atom in a molecule is going to have significant influence on the biological and physical properties of compounds. The compounds thus synthesized will have increase of membrane permeability, hydrophobic binding and stability against metabolic oxidation and these are due to the presence of fluorine compounds, being bioactive compounds, are expected to play a vital role in medicinal chemistry. In view of high rate of growth in the medicinal field the synthesis of organo fluorine compounds gains importance [1-4]. Despite the availability of multi step chemical routes, attempts have been made in this laboratory to synthesize fluorination of amine through single step electrochemical fluorination. For partial fluorination of aromatic compounds the electrochemical method, in fluoride containing solvent free electrolyte systems, has been extensively studied in this laboratory and reviewed [5-8]. These studies are mainly aimed at to fluorinate active methylene group attached to sulfur atom. In continuation of the electrochemical fluorination work in this laboratory efforts are made to fluorinate nitrogen containing aliphatic compounds and in this series electro-fluorination of triethylamine has been done and the resulting products have been analyzed from the spectroscopic angle, especially using NMR and the results are presented in this paper.

In aprotic solvents or amine complexes, acids AH and bases B can form a number of different hydrogen bonded complexes. In aqueous solutions AH and B are separated. Hydrogen bonded to water molecules can have only two protonation states [9]. Several complexes of pyridine are formed with number of HF complexes, like $(\text{AH})_n\text{B}$ [10] with a varying number of HF molecules. In the present study three types of HF adducts with triethylamine complexes as indicated in the Fig. (1) can be considered.

These may be $(\text{C}_2\text{H}_5)_3\text{N}\cdot 3\text{HF}$, $(\text{C}_2\text{H}_5)_3\text{N}\cdot 4\text{HF}$ and $(\text{C}_2\text{H}_5)_3\text{N}\cdot 5\text{HF}$. In these studies the addition of HF reduces

the F-N distances as we move from triethylamine 5HF adduct to triethylamine to 3HF adduct [11]. The present study aims to understand the addition of HF molecules to the parent triethylamine electrolyte when electro-fluorination is undertaken.

EXPERIMENTAL

Chemicals

High pure (>99%) triethylamine was purchased from Sisco Research Laboratory, India. Anhydrous hydrogen fluoride (AHF) >99.9% was obtained from M/s TANFAC, Cudalore, Tamilnadu, India.

Equipment

^1H NMR spectra were recorded with 400 MHz Bruker NMR Spectrometer with CDCl_3 and TMS as solvent and reference, respectively. ^{19}F NMR (376.5 MHz) of the products was recorded using CFCl_3 as internal reference.

Preparation of $\text{Et}_3\text{N}\cdot\text{nHF}$

$\text{Et}_3\text{N}\cdot 3\text{HF}$ is a well-known conventional electrolyte medium for selective electrochemical fluorination. The following procedure was adopted for the preparation of $\text{Et}_3\text{N}\cdot 3\text{HF}$. A long jar of high-density polypropylene was cooled with ice salt mixture in a well-ventilated fume chamber. Slightly excess quantity of (>4 mole) anhydrous hydrogen fluoride (AHF) was taken to account for possible loss due to volatility of AHF. The reaction vessel was provided with magnetic stirrer and closed with a lid containing a provision for inlet and an outlet tube for the release of AHF vapors during the reaction. One mole of pre-cooled triethylamine was added drop wise using separating funnel. After the completion of addition of each drop, sufficient time was given to ensure cooling of the reactant mixture. The overall addition was completed in 3 h. The HF content was determined by acid-base titration. Excess of AHF if any beyond 1:3 mole ratio of $\text{Et}_3\text{N}\cdot\text{nHF}$ in the mixture was appropriately compensated by the addition of triethylamine. The same procedure was

*Address correspondence to this author at the Central Electrochemical Research Institute, Karaikudi, 630 006, India; Tel: 04565 - 227550; Fax: 04565 - 227205; E-mail: radha_1965@yahoo.com

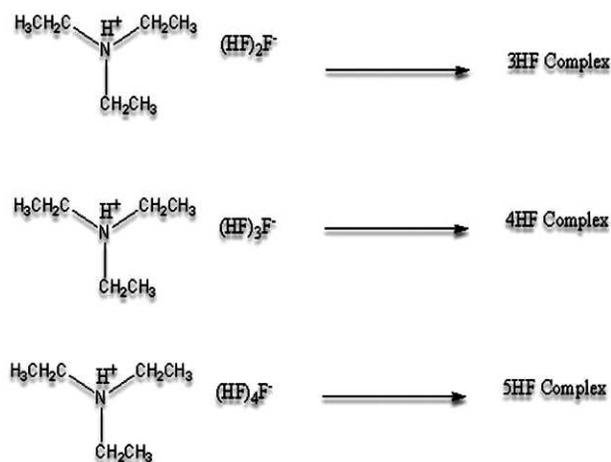


Fig. (1). Structure of Triethylamine HF adducts.

repeated for the preparation of Et₃N.4HF and Et₃N.5HF mixture.

RESULTS AND DISCUSSION

Fig. (1) shows the structures of the various complexes that are likely to be formed in the present study. Figs. (2, 3 & 4) gives the temperature variations of ¹H NMR spectra of solutions of triethylamine and HF where the HF ratio to triethylamine is 5, 4, and 3:1. The spectra show major spectral changes arising from the formation of various complexes assigned to structures as depicted in Fig. (1).

The Fig. (2) shows the effect of temperature on the adduct of fluorine complex with triethyl amine. As

temperature increases the downfield shift takes place. Normally these chemical shifts take place due to dipole dipole interactions in hydrocarbon and fluorocarbon groups. But in this case when adducts are formed the chemical shift may occur due to relaxation caused by interaction between nuclei and unpaired electron spins.

Fig. (3) shows the adduct of HF with triethylamine with 4HF. As temperature increases the shift takes place towards more positive and as temperature goes down they try to come closer and negative shift occurs. This clearly indicates the formation of NH bond and deviates from HF bond. Since fluorine being more electronegative compared to nitrogen, which contains lone pair of electrons, is beneficial for the formation of absorbing proton the downfield shift occurs. This is more predominant in the case of 4HF compared to 3HF where the shift is of more or less having equal magnitude.

Fig. (4) shows the chemical shift of the adduct 5HF with tri ethyl amine. Here the effect is due to lone pair electrons in the nitrogen. There is a transition at the temperature 0⁰ C where the shift is appreciable. This indicates that there is a preferential formation of N-H bond compared to the detachment of hydrogen bond from HF and thus enables the formation of adduct of HF with triethylamine.

Figs. (5, 6 & 7) imply that as the temperature decreases downfield shift takes place from 173 to 168 ppm. This clearly gives an idea of change in the bond distance of HF as the temperature goes down. In 4HF down filed shift takes place from 183 to 173 ppm as temperature decreases. In 5HF again down field shift takes place from 186 to 176 ppm. It is seen that from up field shift as it gets fluorinated in aprotic environments, due to competition with the solvent, weak hydrogen bonding is expected and is generally found. It has

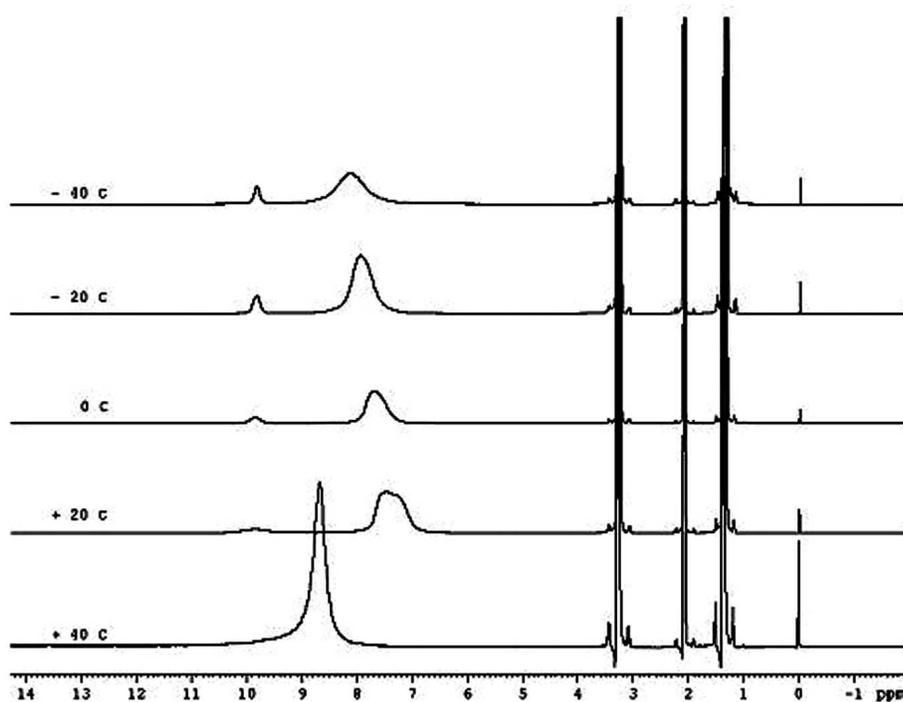


Fig. (2). ¹H NMR spectra of triethylamine 3HF adduct recorded at various temperatures.

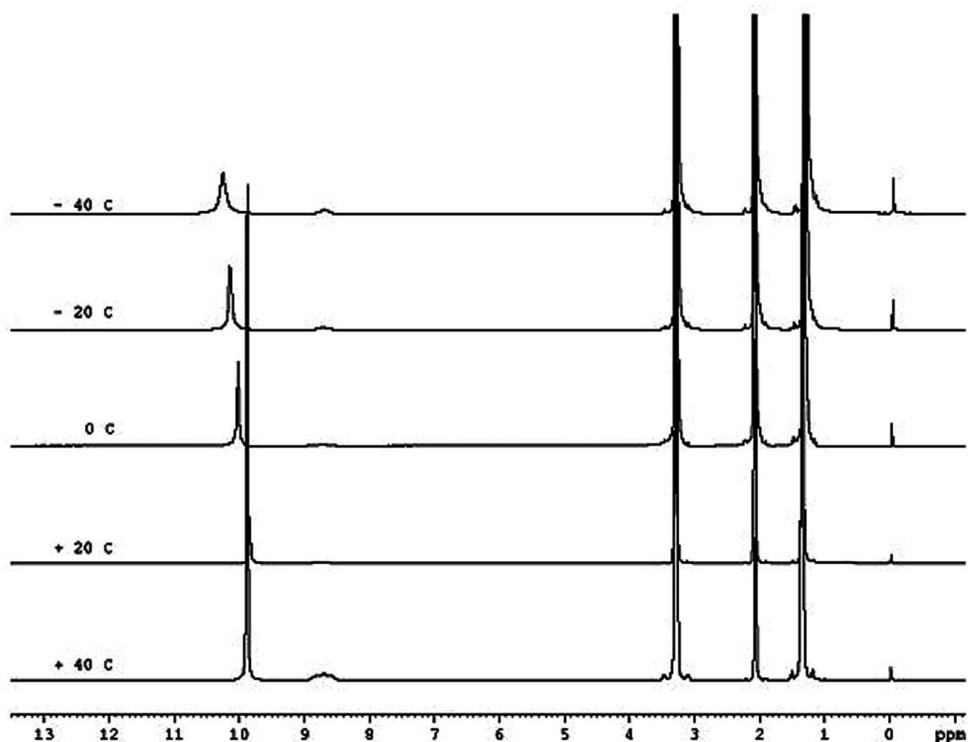


Fig. (3). ^1H NMR spectra of triethylamine 4HF adduct recorded at various temperatures.

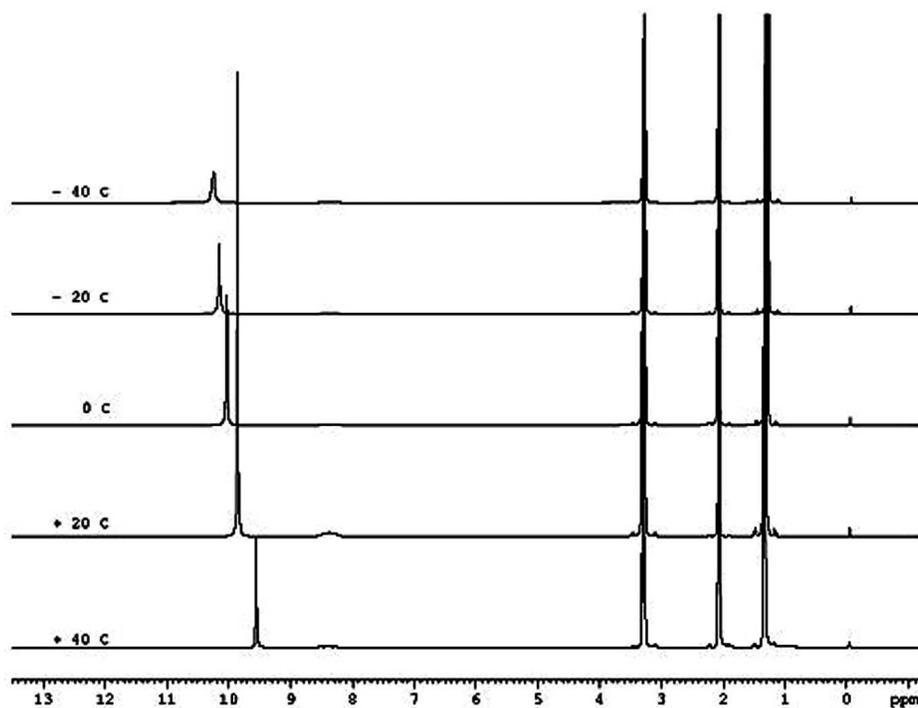


Fig. (4). ^1H NMR spectra of triethylamine 5HF adduct recorded at various temperatures.

been shown in [12] in that hydrogen bond lengths measured by X-ray diffraction correlates with the chemical shift of the proton [12]. Further it has been reported in the aforementioned reference that hydrogen bonds decrease in length from 3.0\AA to 2.45\AA . This indicates the trend of strength of hydrogen bond. The trend proceeds from weak to strong. Then the proton becomes more de-shielded and this is the reason for resonance shift towards the downfield as in the present case

approaching a value of 18 ppm (from 3HF to 5HF) against 21 ppm reported in the aforementioned reference. The reason for de-shielding is the increasing the length of the covalent bond N-H moiety of the N-H-F hydrogen bond as the overall hydrogen bond length decreases. This lengthening attenuates the major shielding provided by the sigma bonding electron pair.

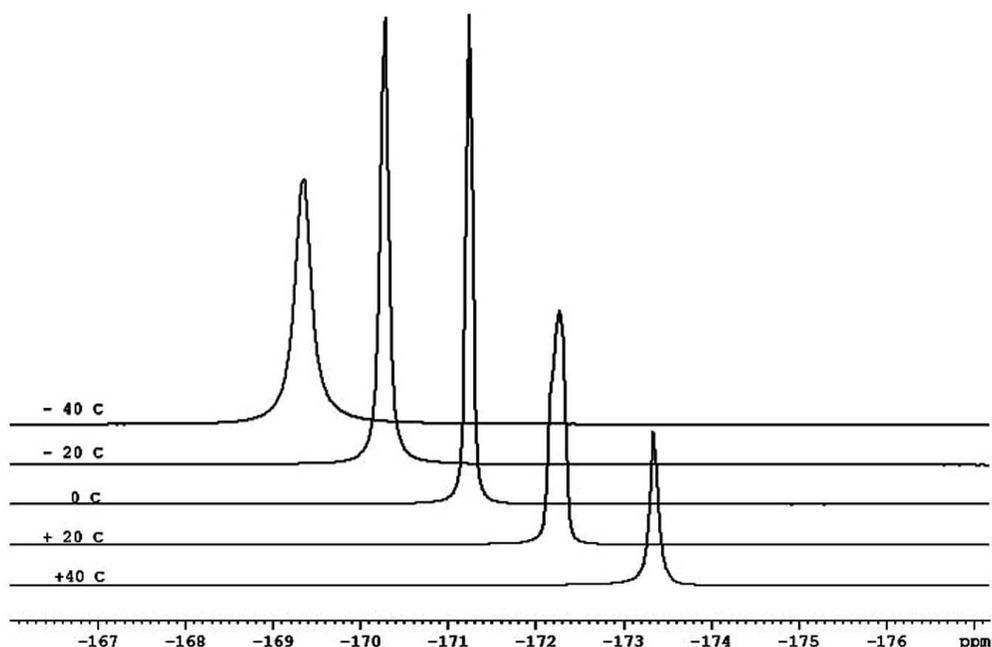


Fig. (5). ^{19}F NMR spectra of triethylamine 3HF adduct recorded at various temperatures.

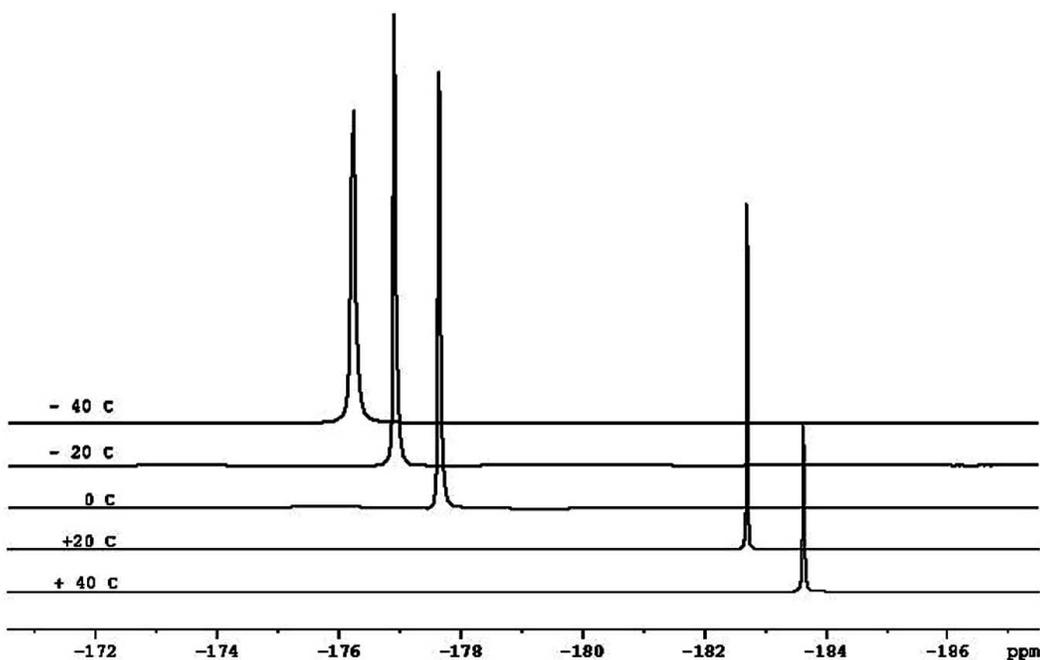


Fig. (6). ^{19}F NMR spectra of triethylamine 4HF adduct recorded at various temperatures.

A rigorous highly useful correlation of N-H-F hydrogen bond lengths D , measured by small molecule high resolution X-ray crystallography, with chemical shifts δ , determined by solid state NMR, is reported in [13]. It is justifiable to have long weak hydrogen bonds with an empirical equation provided in [14]. To get the value of D from chemical shift data the equation used in is $D = 5.04 - 1.16 \ln(\delta) + 0.0447(\delta)$ [14]. And using this equation the chemical shift data were inserted in the equation and bond lengths in Angstrom unit have been calculated and Fig. (16) shows the exponential decrease of bond length *versus* increase of chemical shifts. From the figures it is seen that bond lengths decrease as chemical shift value increases. This indicates the trend of strength of

hydrogen bond which proceeds from weak to strong and the proton becomes more de-shielded. The resonance is shifted downfield.

Hydrogen bridge, the parameter characterizing the geometry, denotes the distances between nitrogen and hydrogen and hydrogen and fluorine. With increase of temperature the broader peak becomes sharper and the intensity also gets increased to a certain temperature, viz, 0°C and then it becomes broader and also lesser as temperature is higher. In general, the peaks shift to downfield. Spin lattice relaxation is low at lower temperature 350 ms compared to 908 ms at higher temperature $+40^{\circ}\text{C}$.

Fig. (5) further elucidates the formation of NH bond and eliminates the interaction of hydrocarbon with HF. This is clearly evident from the stationary peaks of methyl and methylene compared to NH and HF bonds. At 40^o C the HF bond is clearly seen whereas it slowly reduces and diminishes as temperature goes down and slight formation of NH interaction is indicated from the downfield shift.

Fig. (6) shows the interaction of HF with triethylamine as more of HF is coming into contact with parent molecule and here the clear diminishing of the peak HF compared to the NH as temperature goes down. Fig. (7) further clearly indicates the aforementioned behavior and confirms the lone pair of nitrogen role in the formation of complexes with HF. Figs. (8, 9, 10, 11 & 12) clearly demonstrated the aforementioned discussion. An increase in the interaction between neighboring fluorine is responsible for the lower field reso-

nance and this fact is true in increasing the de-shielding and increasing the coupling constants due to the interaction of fluorine. Each downfield shift is greater than 5 to 10 ppm. Nuclear spin lattice relaxation measurements are known to be an effective tool in studying complexes formed with HF by triethylamine. The interpretation of spin lattice relaxation is usually based on the analysis of fluctuations of dipole-dipole interactions in hydrocarbon and fluorocarbon groups and of anisotropic electron–nuclear interactions responsible for chemical shielding anisotropy. These fluctuations are caused by molecular mobility. In the complexes of triethylamine with fluorine complexes there is an origin of paramagnetic defects and these arise from unpaired electrons. Such defects are usually created during the sample preparation process. The interaction between nuclear and electron spins is known to strongly influence the nuclear spin lattice

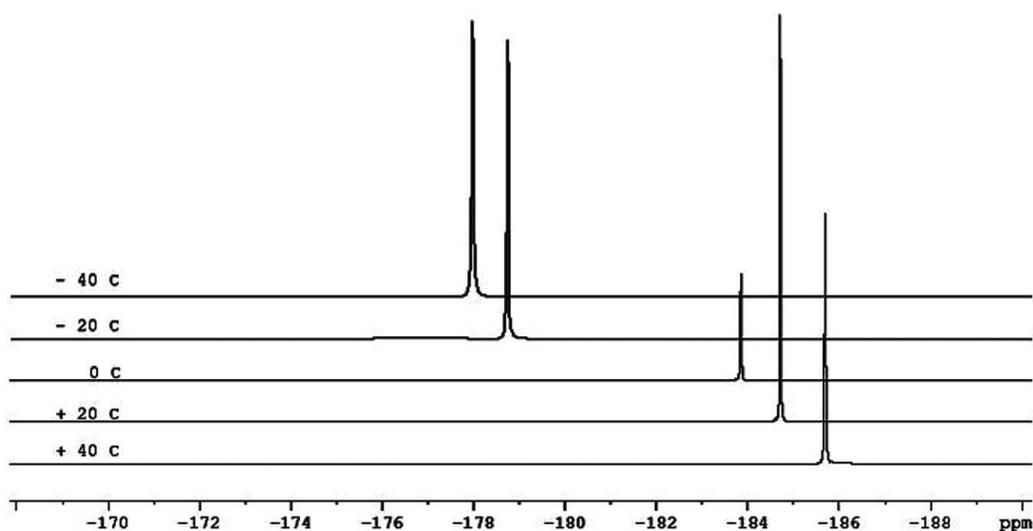


Fig. (7). ¹⁹F NMR spectra of triethylamine 5HF adduct recorded at various temperatures.

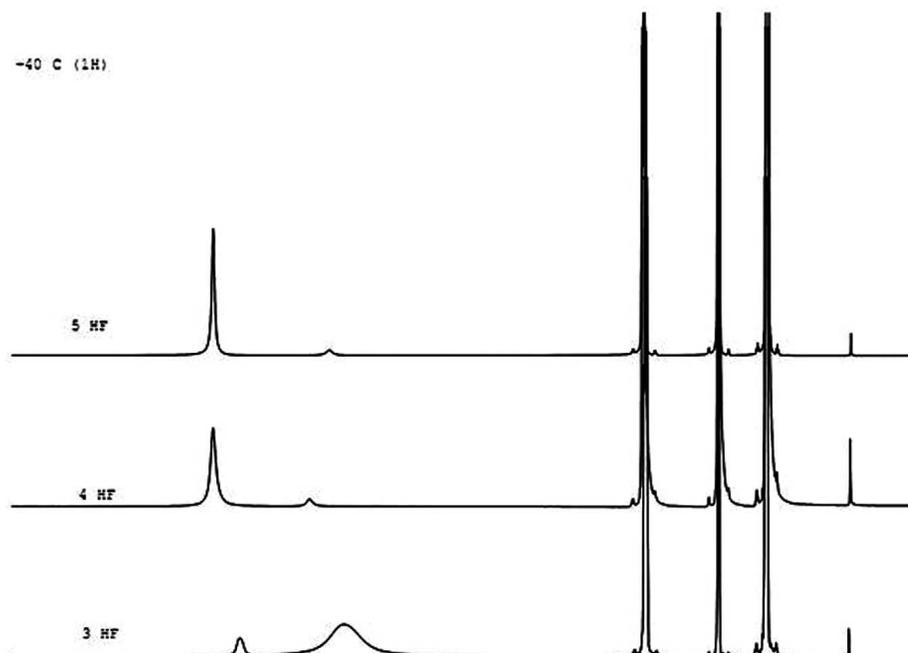


Fig. (8). ¹H NMR spectra of triethylamine nHF adduct recorded at -40 c.

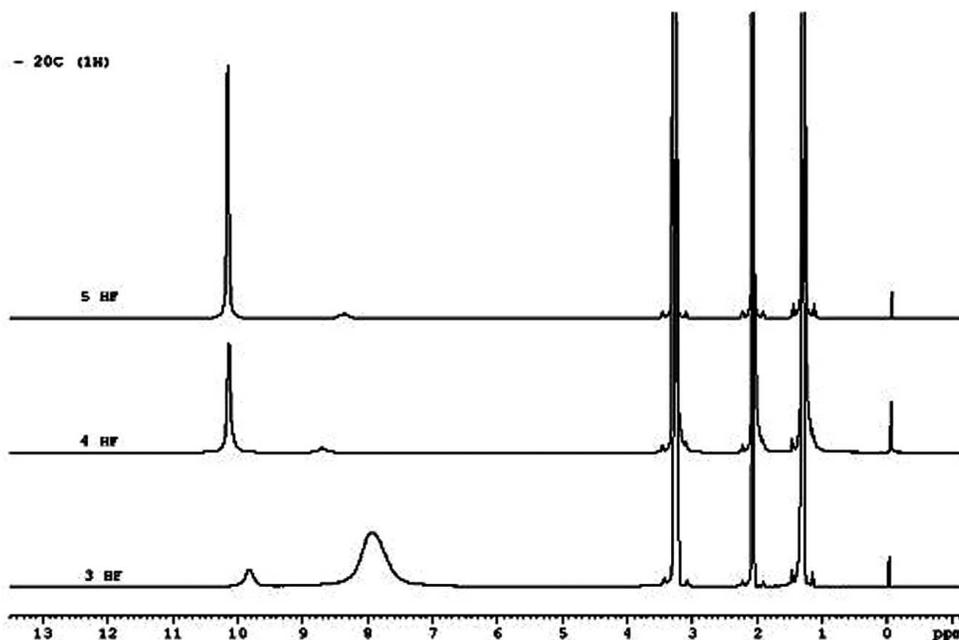


Fig. (9). ¹H NMR spectra of triethylamine nHF adduct recorded at -20 c.

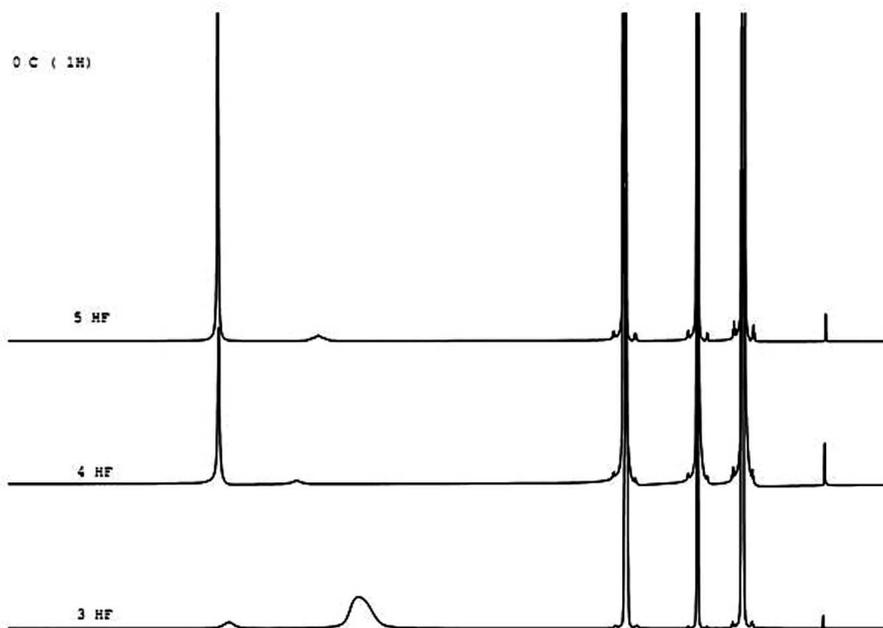


Fig. (10). ¹H NMR spectra of triethylamine nHF adduct recorded at 0 c.

relaxation. Another contribution might come from the interaction of nuclear spins with adsorbed para magnetic nitrogen molecules.

Temperature dependence of spin-lattice relaxation rate: Nuclear spin lattice relaxation rate $R_1 = T_1^{-1}$ is determined by the expression [15, 16].

$$R_1 = R_{1F} + R_{1F-X}$$

where $R_{1F} = T_{1F}^{-1}$ is the contribution to the spin lattice relaxation caused by dipole-dipole coupling between spins of magnetic nuclei in rotating complexes and $R_{1F-X} = T_{1F-X}^{-1}$ is the contribution caused by the dipole-dipole interaction of fluorine spins and magnetic moments of paramagnetic

defects. The first contribution is known to be described by the Bloemergen-Purcell-Pound (BPP) theory and is given by the expression [17].

$$R_{1F} = T_{1F}^{-1} = \frac{2}{3} \{ \frac{2\Delta M_{2F}}{3w_0} \} \{ \frac{x}{1+x^2} + \frac{4x}{1+4x^2} \} \quad (1)$$

where w_0 is the Larmor frequency and τ_c is the correlation time of the molecular rotation and $x = w_0 \tau_c$.

Spin lattice relaxation (T_1 measurement) versus temperature values for 3HF, 4HF and 5HF given in the Table 1, also plotted as graph which is shown in the Fig. (13) for 3HF. From this figure the minimum point is noted. From the minimum value symmetrical V shaped curves were drawn and this is shown as extended curves in the figures (The

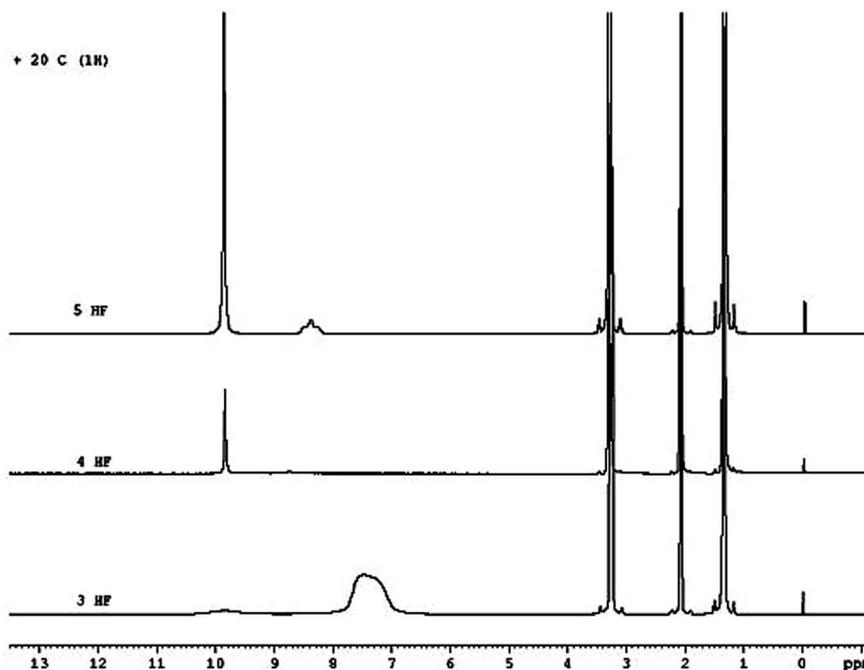


Fig. (11). ^1H NMR spectra of triethylamine nHF adduct recorded at +20 c.

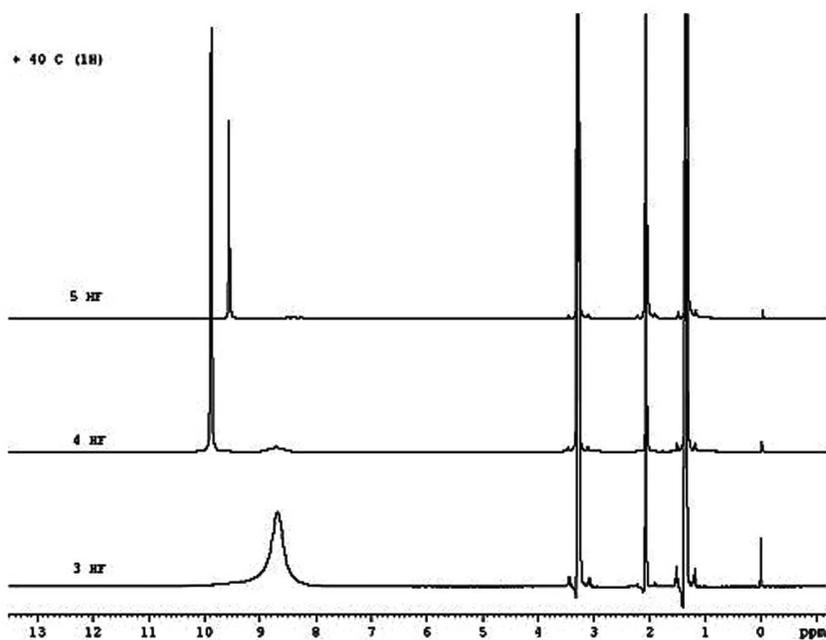


Fig. (12). ^1H NMR spectra of triethylamine nHF adduct recorded at +40 c.

values are extrapolated outside the range of experiments). This is shown in the Figs. (13-15) and consolidated results are shown in Fig. (16). This figure is a semi logarithmic plot of spin lattice relaxation at different temperature at the larmour frequency of ω_F . The extended curve corresponds to a higher frequency than ω_F .

The corresponding ^{19}F T_1 minimum value in the Fig. (16) decreases with increasing the fluorination of the complex and increasing with temperature and these data are given in the Table 3. This also suggests that location of T_1 minima on the variable temperature relaxation curves directly depends on molecular mobility. This suggests that molecular motions are fast as the triethylamine is added with more HF. This

Table 1. T_1 Measurements for the Nuclii ^{19}F is Provided

Temperature	T_1 in Milli Seconds		
	3HF	4HF	5HF
40°C	909.8	210.7	260.2
20°C	525.5	393.8	407.7
0°C	556.5	823.3	810.6
-20°C	464.1	923.9	773.2
-40°C	351.8	707	489.9

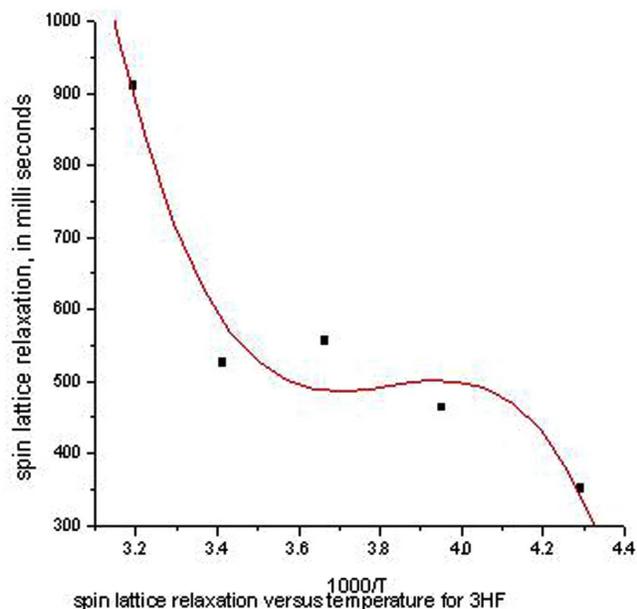


Fig. (13). Spin lattice relaxation *versus* temperature for 3 HF.

Table 2. Bond Length Versus Chemical Shifts

δ	D
2	4.288418
4	3.580699
6	3.199759
8	2.955448
10	2.786001
12	2.663908
14	2.574493
16	2.508997
18	2.461769

also suggests that the tri ethyl complex with 3HF is different from 4HF and 5HF, where in 3HF there is still a link of hydrogen bonding with nitrogen is expected and in 4HF and 5 HF this has shifted to hydrogen fluorine bonding rather nitrogen hydrogen link.

When HF interacted with a strong proton acceptor, namely, nitrogen which has a lone pair of electrons in tri ethyl amine, the conventional hydrogen bonding will be the dominant interaction. The strength of this interaction will increase upon the addition of HF to triethylamine. Thus as the main goal of the present work in this investigation is to use ^1H and ^{19}F NMR to understand the formation of HF bridges in aprotic environments and this is partly fulfilled in the sense that ^{19}F NMR is able to give a clue of the formation of HF bond as HF molecules are added to triethylamine.

The terms r_{AH} and r_{BH} denote the distance between N-H and H-F. There is a fast exchange between the hydrogen bond and bulk HF tri ethyl anion. When the exchange is suppressed spectrum displays two signals and there is no such

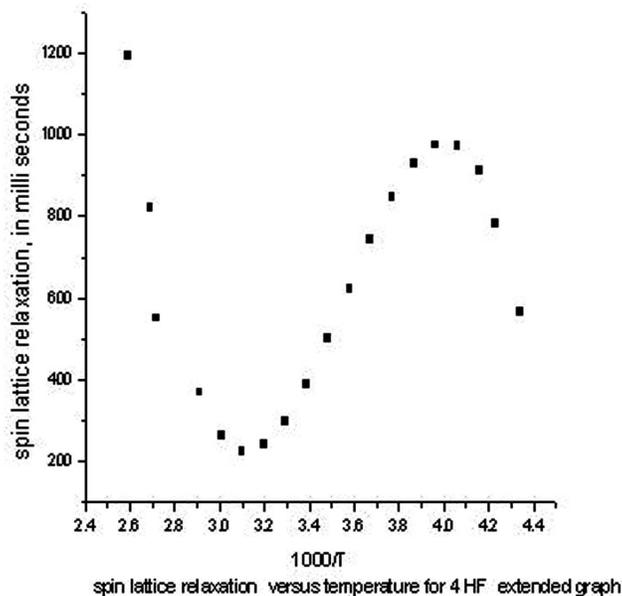


Fig. (14). Spin lattice relaxation *versus* temperature for 4HF extended graph.

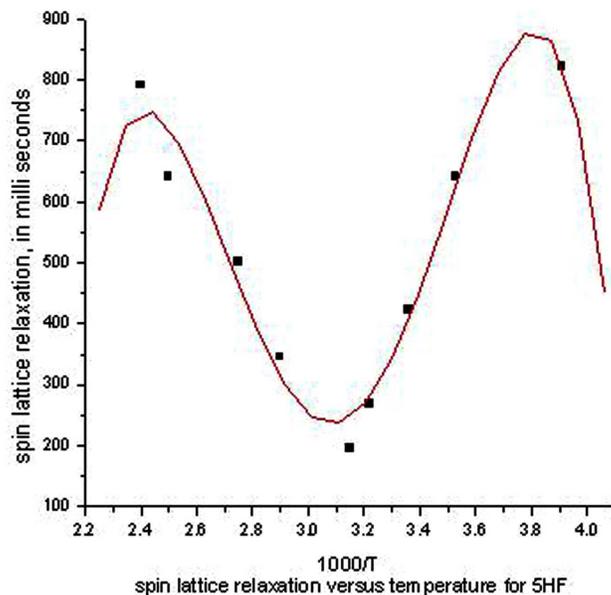


Fig. (15). Spin lattice relaxation *versus* temperature for 5HF extended graph.

splitting occurs in the present study and this indicates two kinds of interactions viz either N-H bond or H-F bond formation.

Upon increase of H-F content the signal at >180 ppm becomes dominant. While the intensity of the signal at 170 ppm triethylamine is strongly reduced. When HF is in excess, the spectrum displays only signal at 186 ppm whose chemical shift does not depend on the HF content. As long as triethylamine to HF content is 3 or 4 the spectra contain exclusively 3HF or 4HF species. In contrast, when this ratio is below 4 the corresponding spectra displays the only signal at 170 to 180 ppm.

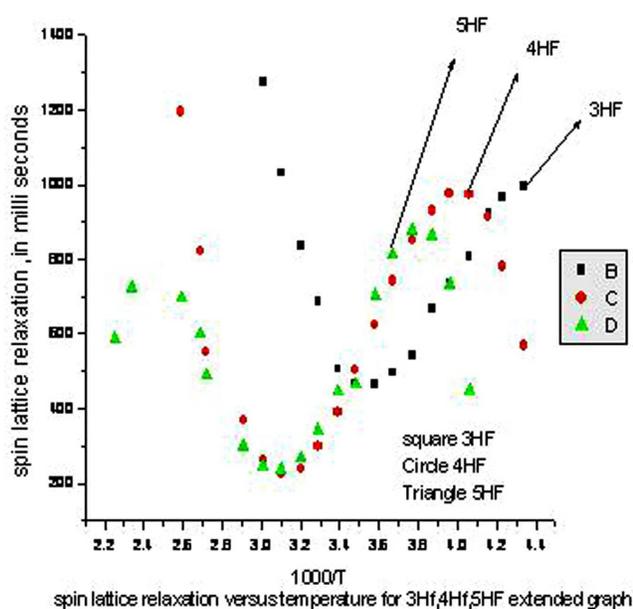


Fig. (16). Spin lattice relaxation versus temperature for 3 HF, 4HF and 5 HF as extended graph.

In aprotic environment protons of solitary HF molecules resonate around 170 to 186 ppm while HF micro drops give rise to a peak at 176 ppm typical for HF. Water molecules involving stronger hydrogen bonds are characterized by higher values of ^1H chemical shift. Generally the protons and hydrogen bonds exchange between different acid base complexes in solution is very fast on the NMR time scale. At room temperature it is not possible to identify their structure and properties.

The position and intensity of the peak depend strongly on temperature. At room temperature HF molecules become involved in more or less stable hydrogen bonded complexes with each other and triethylamine. The exchange between different structures is still too fast to suppress on averaging but the peak intensity becomes broader. The line broadening is accompanied by a dramatic reduction of the signal and

this is due to HF precipitation from the complex with base. The chemical shift asymptotically approach to a value of 18 to 21 ppm.

Proton bonding ability of HF molecule bonded to the base increases due to the mutual cooperative ability with other HF molecules and is associated with clusters. A shortening of nHF bond results in the length of the other. This can be explained by stronger basicity. The chemical shift changes of individual hydrogen atoms. High field shift as already discussed, indicates an increased electron density of the hydrogen atoms and this weakens of the hydrogen bonding interaction. It is also clear that 3HF tends to form N-H bond and in the case of 4HF and 5HF it is clear that there is a deviation from bond formation and this tends to wards H-F and N-H-F bond slowly leans towards fluorine and this is clearly indicated from the fig. by the formation of minimum occurs at a particular temperature.

Towards this argument an attempt has been made to calculate the bond distance from the NMR data. Using the equation (1), as provided in [18]. Homo nuclear coupling corresponds to interactions of nuclei of the same sort, when two coupled nuclei are identical,

For example, the strength of the protons in homo nuclear dipolar coupling $DC_{\text{H-H}}$ is written as

$$DC_{\text{H-H}} = 0.3 (\mu_0/4\pi)^2 \gamma_{\text{H}}^4 \hbar^2 r(\text{H-H})^{-6} \quad (1)$$

and if the magnetic dipole of one nucleus, for example, a proton, can interact with the magnetic dipole of nucleus F, other than proton then the strength of this hetero nuclear dipolar coupling $DC_{\text{H-F}}$ is written as

$$DC_{\text{H-F}} = 4/30 (\mu_0/4\pi)^2 \gamma_{\text{H}}^2 \gamma_{\text{F}}^2 \hbar^2 I_{\text{B}}(I_{\text{B}} + 1) r(\text{H-F})^{-6} \quad (2)$$

In these, the values used for the calculations are given in Table 4

Bond distance in 3HF is calculated and the value is = 2.6 Å

Bond distance in 4HF is calculated and the value is = 5.6 Å

Bond distance in 5HF is calculated and the value is = 5.66 Å

Table 3. $1/T_1$ Values at Minimum Temperature

Complex	Minimum Temp 1000/T	Minimum Temp in K	$1/T_1$ in Milli Seconds
3HF	3.58	279	465
4HF	3.2	312	240
5HF	3.1	322	224

Table 4. Values Used in the Calculation for Bond Distances

Nucleus	Spin	NMR Frequency ν (MHz) at B_0 2.4388T	γ ($10^7 \text{ radT}^{-1} \text{ s}^{-1}$)
^1H	1/2	100	26.752
^{14}N	1	7.22	1.934
^{19}F	1/2	94.08	25.18

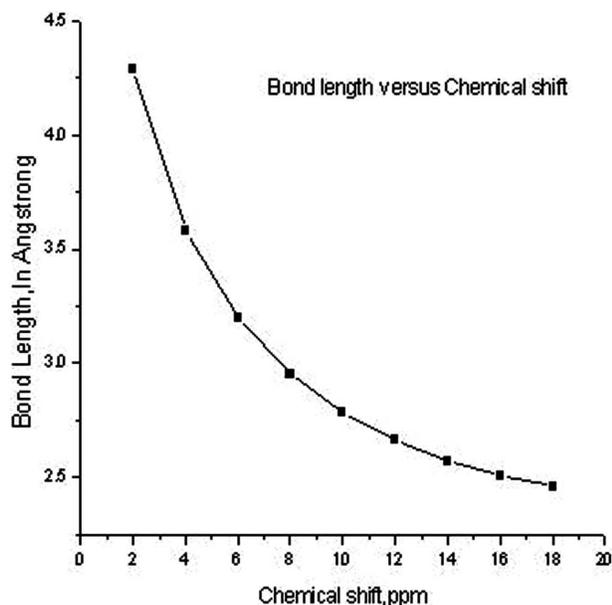


Fig. (17). Plot of Bond length *versus* chemical shifts.

This bond distance is compared with the chemical shift calculations provided in the Fig. (17), and these data are given in Table 2. The bond distance of 2.6 Å corresponds to 3HF whereas the bond distance for 4HF and 5HF is slightly higher 5.6 Å compared to 4.2 Å for 4HF and 5HF from chemical shift data. This higher value is due to experimental and calculation error and the magnitude should not be matter in this type and only the trend is to be taken and hence the assumption that fluorination of tri ethyl amine leads to different adducts of HF and higher adducts HF bond is predominant compared to lower adducts of HF where N-H-F bond is expected.

CONCLUSIONS

Fluorination takes place as HF adducts and not as C-F bond. From NMR data it is possible to identify three different adducts to triethylamine. From chemical shift values it is possible to distinguish the three adducts. From NMR data it is possible to calculate bond distance of homo nuclear and hetero nuclear nuclei. ¹H NMR chemical shift data of three adducts were measured at five different temperatures are given below:

3 HF

- 0°C = 1.32 (t, 3H), 3.26 (d, 2H), -171.2 (s, HF)
 20°C = 1.34 (t, 3H), 3.25 (m, 2H), -172.2 (s, HF)
 40°C = 1.36 (t, 3H), 3.26 (m, 2H), -173.3 (s, HF)
 -20°C = 1.31 (t, 3H), 3.25 (m, 2H), -170.2 (s, HF)
 -40°C = 1.30 (t, 3H), 3.24 (m, 2H), -169.3 (s, HF)

4 HF

- 0°C = 1.32 (t, 3H), 3.28 (m, 2H), -177.6 (s, HF)
 20°C = 1.33 (t, 3H), 3.28 (m, 2H), -178.4 (s, HF)

- 40°C = 1.34 (t, 3H), 3.28 (m, 2H), 9.8 (s, NH), -178.9 (s, HF),
 -20°C = 1.30 (t, 3H), 3.27 (m, 2H), -176.8 (s, HF)
 -40°C = 1.29 (t, 3H), 3.27 (m, 2H), -176.2 (s, HF)

5 HF

- 0°C = 1.30 (t, 3H), 3.27 (m, 2H), 10.03 (s, NH), -183.8 (s, HF)
 20°C = 1.32 (t, 3H), 3.28 (m, 2H), 9.8 (s, NH), -184.7 (s, HF)
 40°C = 1.33 (t, 3H), 3.28 (m, 2H), 9.7 (s, NH), -185.6 (s, HF),
 -20°C = 1.29 (t, 3H), 3.27 (m, 2H), -178.7 (s, HF)
 -40°C = 1.28 (t, 3H), 3.20 (d, 2H), -177.9 (s, HF)

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CONFLICT OF INTEREST

None declared.

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