



Investigation of 2-Hydroxyacetophenone Nicotinic Acid Hydrazone as a Fluoride Sensor

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Abstract: In the present work, we studied the selective chemosensing behavior of 2- hydroxyacetophenone nicotinic acid hydrazone (H_2L) with fluoride anion. Theoretical and experimental tools were deployed to understand the mechanism of sensing. Experimentally, upon the addition of fluoride to H_2L , a change in colour was observed. The 1H NMR spectral studies showed a change in electronic environment around the N-H and O-H bonding sites of the receptor. UV visible spectrum confirmed the formation of a new complex and IR spectrum showed the absence of the hydrogen bond donor peaks. Density Functional Theory (DFT) calculations were carried out in ground state and they were found to be in accordance with the experimental results.

Keywords: Colorimetric Sensor, IR Sensing, Fluoride Anion Recognition, Hydrogen Bonding, DFT Calculations, Acetyl Hydrazones

1. Introduction

Recognition of anions has become a formidable area of research, of which fluoride anion is a vital component [1, 2]. Fluoride, the smallest and the most electronegative anion, has clinched a lot of attention due to its involvement in biomedical, environmental and chemical processes [3–5]. Regulated use of fluoride can be a potential cure for osteoporosis [6, 7] and hence artificial fluorination of water has helped to serve several bone and teeth related problems. But fluoride consumptions above 20-100 mg on a daily basis could cause severe medical disorders like abnormal increase in skeletal mass, sclerosis, etc. Further, fluoride level in water and environment greatly influences the animal and plant growth [8]. Thus, the indication of fluoride level in food and beverage industry has become increasingly important in order to make sure the level of consumption of fluoride is monitored [9]. ^{19}F NMR or electrode sensors are very sensitive but require expensive instrumentation and maintenance [10]. Therefore, the quest

for a good sensor is increasingly important [11]. Some of the desirable properties of sensors are easy operation, sensitivity and cost efficiency [12]. Study of the mechanism of sensing becomes vital for the construction of better chemosensors. Several mechanisms have been proposed to understand the mechanism of sensing; popular ones being photo induced electron transfer (PET), internal charge transfer (ICT), and hydrogen bonding between the anion and the receptor. Particularly in the case of fluoride, the mechanism of hydrogen bonding is highly accepted due to its high electronegativity [13 - 17].

Our current work deals with the chemosensing behaviour of 2-hydroxyacetophenone nicotinic acid hydrazone (H_2L) towards fluoride anion. Similar hydrazides have been synthesized and studied [18, 19]. The presence of hydrogen bond donors in acid hydrazone derivatives strongly suggest the presence of hydrogen bonding between H_2L and the anion which gave rise to a colored complex.

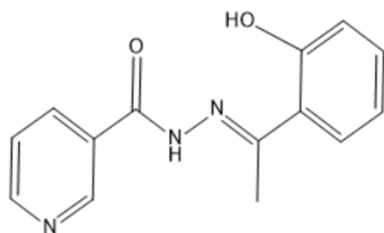


Figure 1. Structure of the receptor - H_2L .

2. Experimentation

All computational calculations were carried out using Gaussian 16 software package. Ground state geometry optimization was performed using hybrid exchange-correlation density functional with B3LYP method using 6-311G+(d,p) as basis set. Both receptor and receptor with

fluoride were geometrically optimized and their NMR and IR spectra were recorded. The 1H NMR spectra was carried out using the gauge-invariant atomic orbital method (SCF GIAO magnetic shielding) where TMS B3LYP/6-311+G(2d,p) GIAO was used as a reference. The fundamental vibrations involving the prominent N atom has been analyzed in corresponding bandwidth and the variation in fundamental frequencies have been noted. The solvent acetonitrile was incorporated using Polarizable Continuum Model (PCM) using the integral equation formalism variant (IEFPCM).

Synthesis scheme of H_2L

The substituted acid hydrazone receptor, 2-hydroxyacetophenone nicotinic acid hydrazone (H_2L) was synthesized from an equimolar ratio of hydroxyacetophenone and nicotinic acid hydrazide [20]. This was refluxed for 7 hours with methanol as a solvent. The product obtained was crystallized and confirmed using 1H NMR.

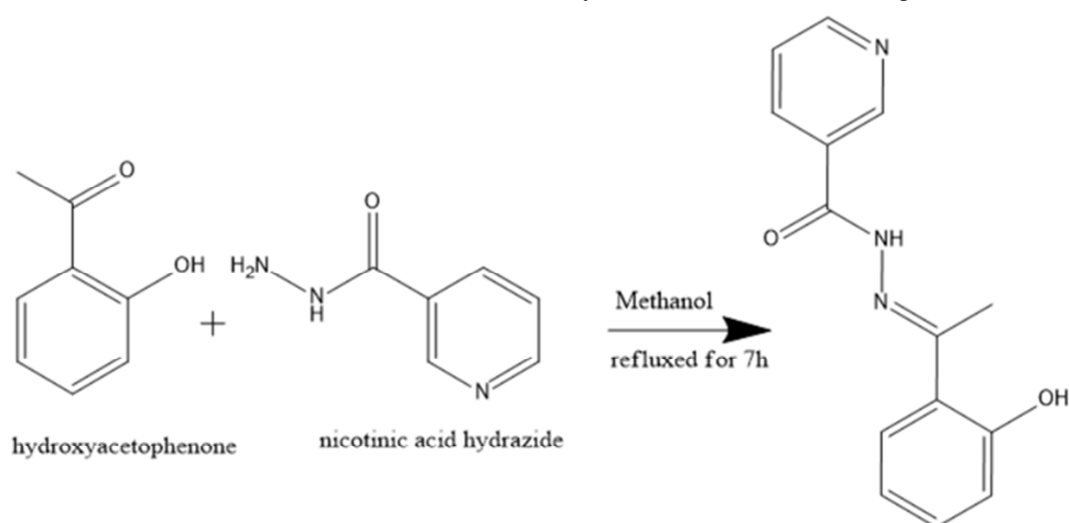


Figure 1. Synthetic scheme of H_2L .

3. Results and Discussions

The receptor synthesized using the above procedure was tested with the TBA salt of fluoride and the solution turned yellow. The observation was the same for other fluoride sources while it remained colourless with non-fluoride substances.

3.1. UV-Visible Spectral Studies

The color obtained on adding fluoride can be explained using electronic spectroscopy. The UV-vis spectra of H_2L and H_2L with fluoride (H_2L-F) were recorded using acetonitrile as the solvent (Figure 3). An absorption maximum was observed at 281 nm for H_2L . On addition of fluoride, a decrease in the intensity of the peak corresponding to H_2L was observed while a new peak was formed at 374 nm. This peak could be attributed to the deprotonated form of the receptor. Although, the hydrogen bonded species is formed,

the color developed is prominently due to the deprotonated form.

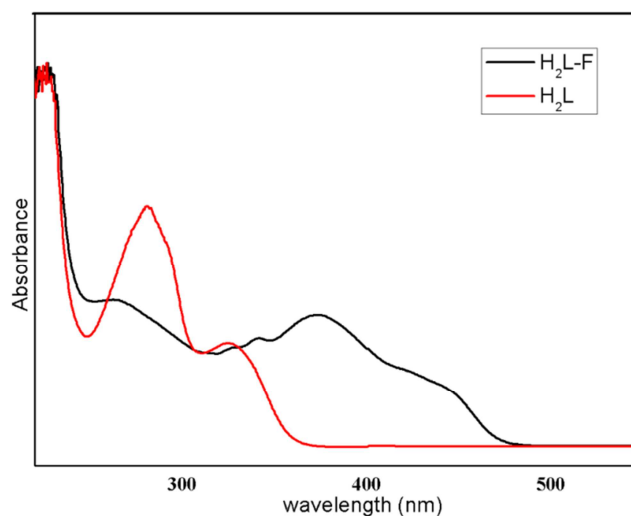


Figure 2. UV-vis spectrum.

3.2. Geometry Optimization

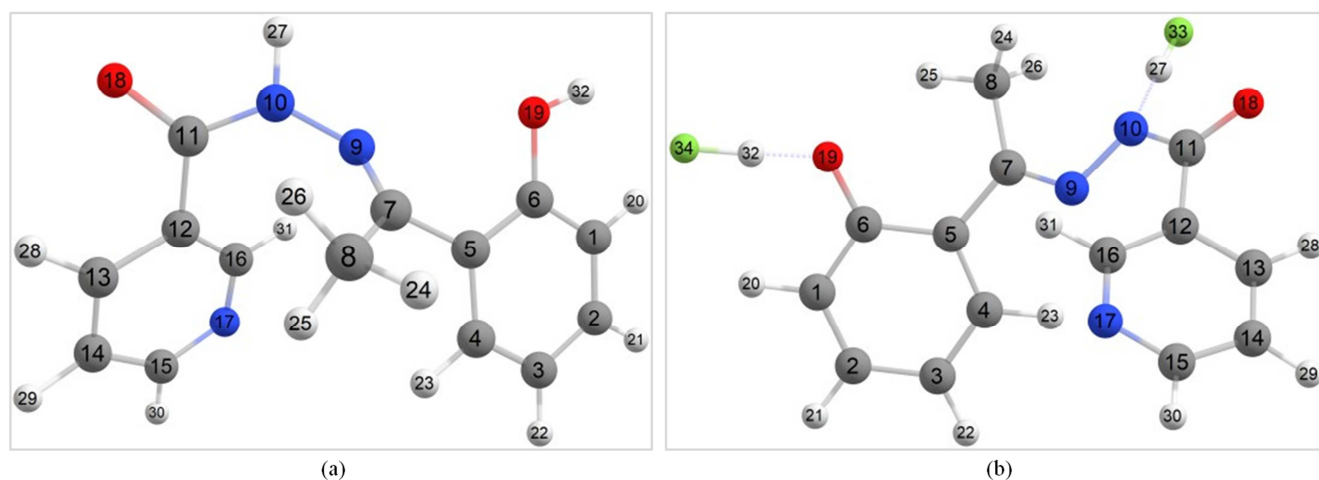


Figure 3. Geometry optimized structure of (a) H_2L (b) H_2L-F (grey - C, white - H, blue - N, green - F, red - O).

The geometry optimization suggested that the N-H and O-H protons have higher affinity towards the highly basic fluoride (Figure 4). The N-H bond distance was observed to increase from 1.01313 Å to 1.49251 Å and O-H bond distance was observed to increase from 0.964996 Å to 1.26251 Å for H_2L and H_2L-F complex respectively. A new bond with fluoride with bond distances 1.026 Å and 1.09962 Å for N-H and O-H protons were observed respectively. It can therefore

be inferred that there exists a hydrogen bond in H_2L-F complex [13, 21, 22].

3.3. 1H NMR Spectral Analysis

The receptor H_2L was studied before and after the addition of fluoride using theoretical and experimental methods.

3.3.1. Theoretical Calculations

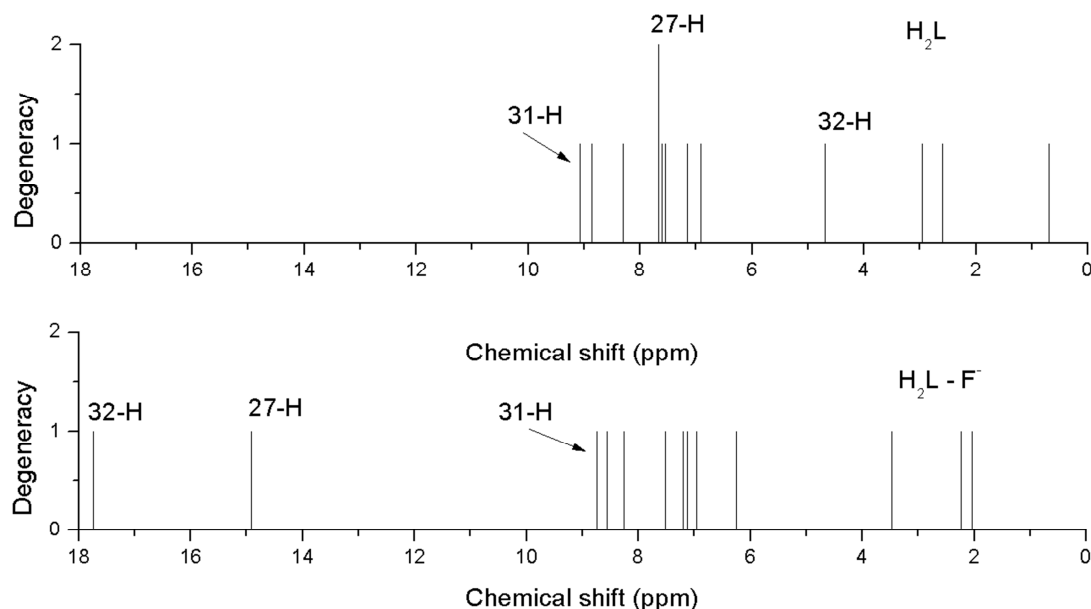


Figure 4. 1H NMR of H_2L and H_2L-F using GIAO method.

The theoretical calculations were carried out by using B3LYP density functional using 6311g+ (d, p) as the basis set using GIAO method with acetonitrile as solvent where TMS B3LYP/6311+G (2d, p) was taken as reference. The 1H NMR for the receptor showed peaks at 7.67 and 4.60 ppm for N-H and O-H protons respectively. After the addition of fluoride, the N-H and O-H peaks were observed at 14.9091 and 17.7368 ppm respectively (Figure 5). This suggested the increased de-shielding around N-H and O-H protons after the addition of fluoride indicating the movement of protons towards the highly basic fluoride anion. This can be visualized as a hydrogen bonded complex.

3.3.2. Experimental Results

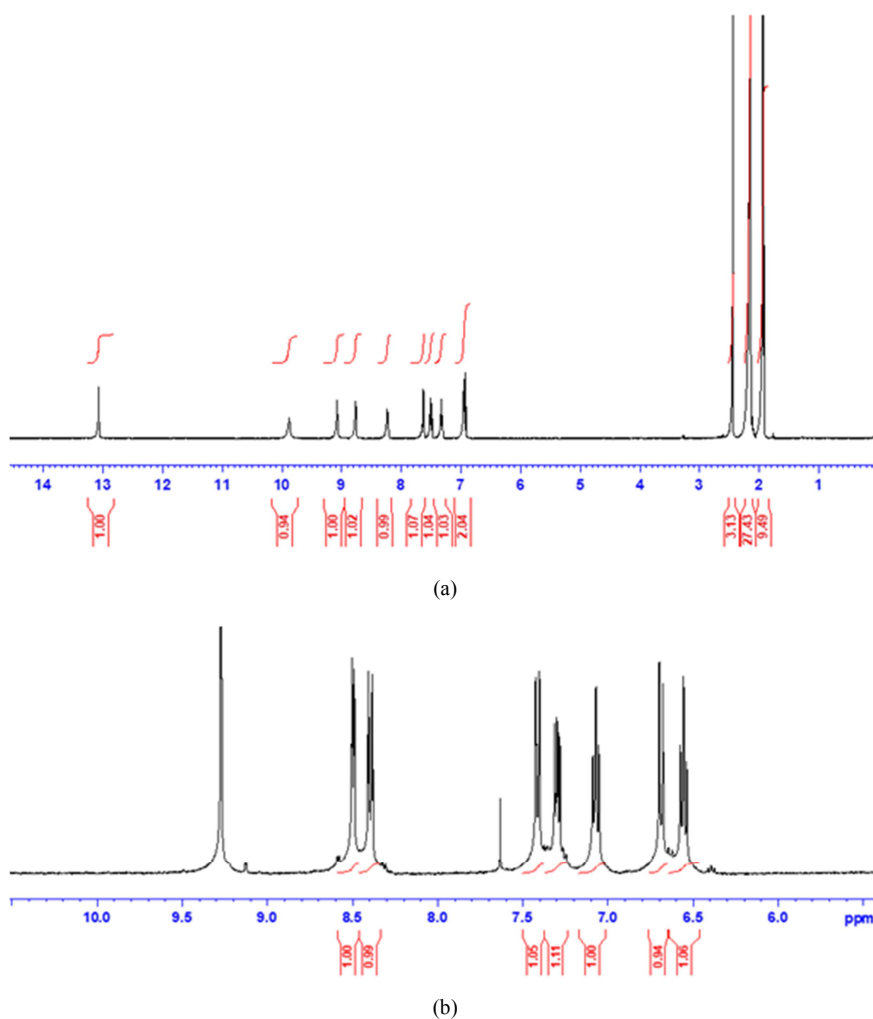
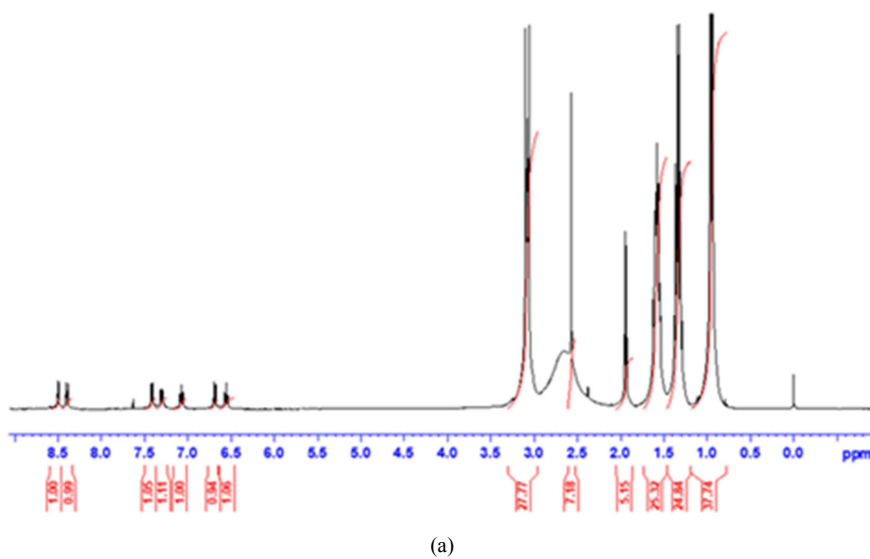


Figure 5. (a) ¹H NMR spectrum of H₂L (b) enlarged view.

Experimentally the N-H and O-H protons for the receptor were observed at 9.880 ppm and 13.074 ppm (Figure 6). Upon addition of considerable amount of fluoride, the peaks were found to disappear indicating the deprotonated state of the receptor (Figure 7).



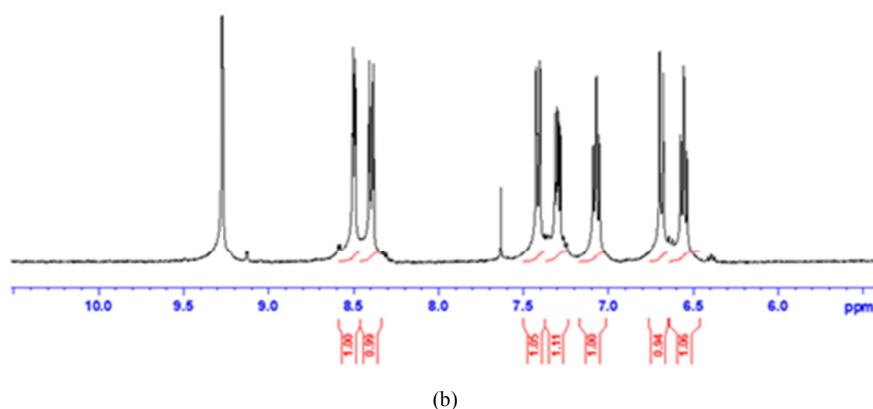


Figure 6. (a) ^1H NMR spectrum of $\text{H}_2\text{L-F}$ (b) enlarged view.

Table 1. Comparison of ^1H NMR peaks (in ppm).

Proton No.	Theoretical		Experimental	
	H_2L	$\text{H}_2\text{L-F}$	H_2L	$\text{H}_2\text{L-F}$
32-H	4.6964	17.7368	9.880	-
27-H	7.6719	14.9091	13.074	-

3.4. IR Spectral Analysis

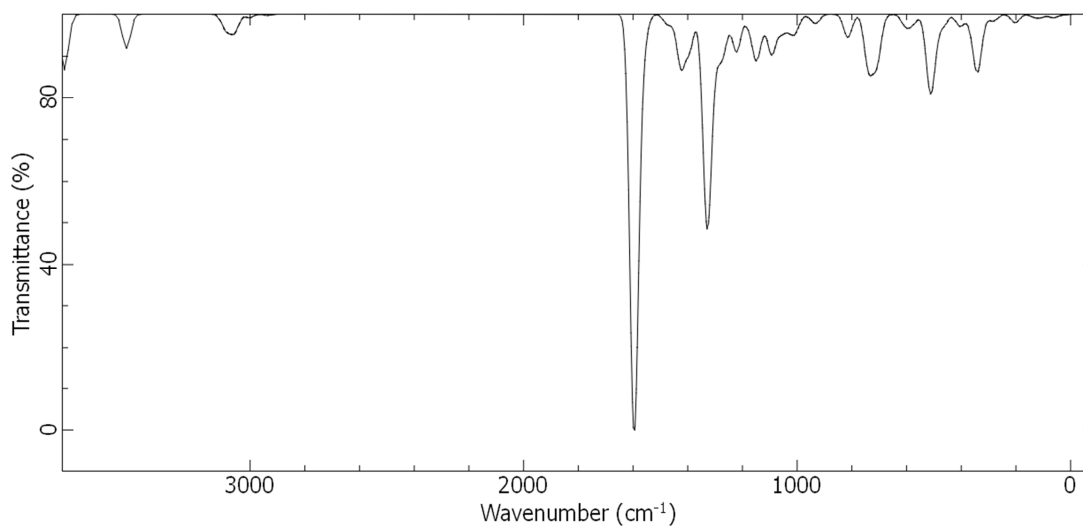


Figure 7. Vibrational spectrum of H_2L using 6-311G B3LYP.

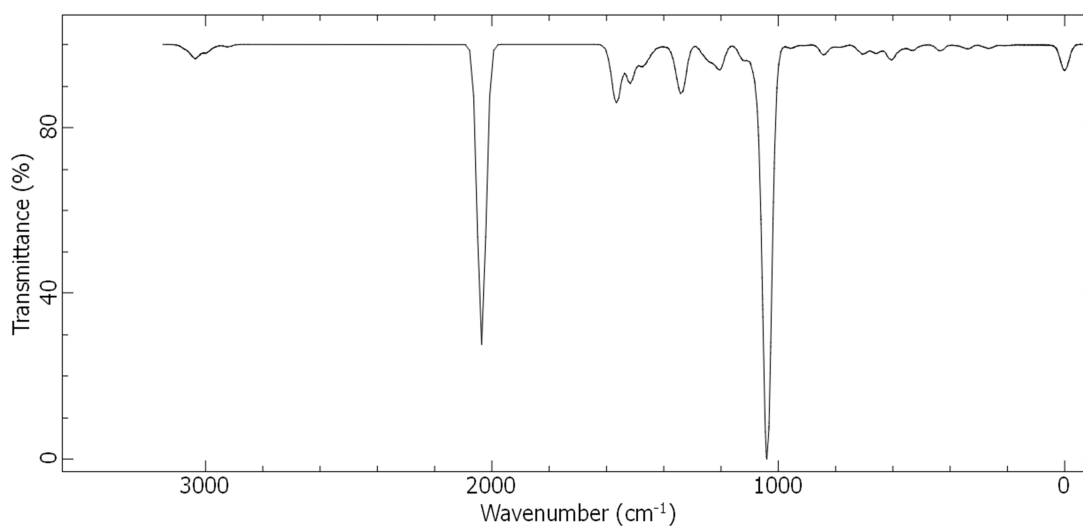


Figure 8. Vibrational spectrum of $\text{H}_2\text{L-F}$ using 6-311G B3LYP.

To monitor the changes occurring at the N-H and O-H sites on adding fluoride, experimental and computational IR spectra were recorded for both H_2L and H_2L-F . The experimental IR spectra for the receptor H_2L gave rise to N-H and O-H peaks at 3020 cm^{-1} and 3300 cm^{-1} respectively. On addition of fluoride the N-H and O-H peaks were not observed, this suggests the abstraction of the protons by the highly basic fluoride anion (Figure 10).

Geometry optimized structures of H_2L and H_2L-F were

used to calculate the IR absorption intensities using B3LYP method and 6-311+G(d,p) as the basis set. The calculated frequencies were scaled by a scaling factor of 0.964 to reduce the deviation between theoretical and experimental results. The computational IR spectra results were in accordance with the experimental data (Figure 8).

On adding fluoride anion, the O-H peak was not observed, and the huge red shift of the N-H peaks suggested deprotonation (Figure 9).

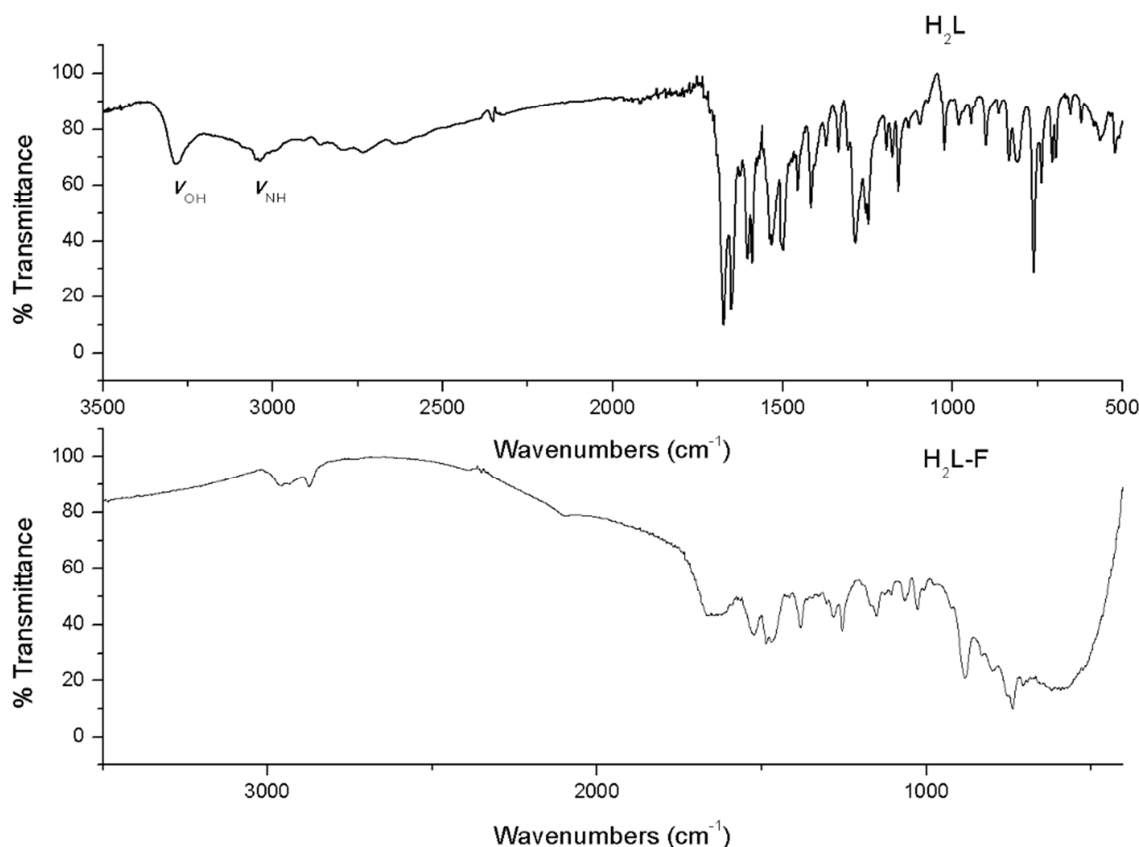


Figure 9. IR spectra of H_2L and H_2L-F .

Table 2. Comparison of IR spectra.

	Theoretical		Experimental	
	H_2L	H_2L-F	H_2L	H_2L-F
ν_{NH}	3056	2010	3020	-
ν_{OH}	3442	-	3300	-

4. Conclusion

The receptor was found to be a very effective fluoride sensor in acetonitrile. This was proved using UV-Vis, IR and 1H NMR experiments. The computational studies provided a useful insight on the mechanism of sensing. The mechanism is shown to involve a hydrogen bonded complex which was deprotonated at appreciable concentrations of fluoride. Selectivity of the receptor towards fluoride over other anions was tested. It could be a potential sensor for heavy metals like lead, copper, etc.

The hydrophobic nature of the receptor limits its use to

organic aprotic solvents. More work must be done on increasing the hydrophilic nature of the receptor, so that fluoride anion in aqueous environment can be sensed and quantitatively detected. Increasing the polar groups on the receptor might improve the solubility in aqueous medium but the proton donation ability of water is much better compared to the receptor in aqueous medium and hence the receptor must be designed in a way that the hydrogen bond donors of the receptors competes with water molecules to abstract the protons to act as a sensor in aqueous medium.

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