

Naked Eye Detection of Fluoride Ions using Simple Dihydroxy Chalcone Sensor

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Abstract

Design and development of a novel dihydroxy chalcone-based receptor (R) for selective identification of fluoride ions is the primary focus of this study. With absorption and emission maxima at 394 nm and 454 nm, respectively, the novel chalcone demonstrated good optical properties. When this receptor interacted with fluoride ions, the absorption peak shifted to 450 nm. It was discovered that the receptor and fluoride ions interacted at a ratio of 1:1 after UV titration, and Job plots were used to identify the interactions. To further understand how fluoride and its receptors interact, computational modelling was performed. The results of the computational modelling and experimental results were in good agreement. The findings showed that the new receptor works well as a sensor for fluoride ions in the naked eye.

Keywords: Fluoride ion sensing, receptor, dihydroxy chalcone, UV-Titration.

1.0 Introduction

Over the past decade, the detection and quantification of anions in various environmental, clinical, biological, industrial, and chemical systems have increased significantly. Fluoride ions, which have the smallest ionic radius, highest charge density, and a hard Lewis basic nature, have been of great interest to the scientific community for their recognition and quantification [1-2] because of their vital role in treating osteoporosis, orthodontics [3], and dental health, and approximately 99% of total body fluoride is contained in bones and teeth [4]. However, fluoride can also be toxic to the human body if it is not present at the right concentrations [5]. Fluoride is a potent inhibitor of many enzymes [6] and can easily be absorbed by the human body; however, it is excreted

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slowly, resulting in variations in its concentration, leading to acute gastric and kidney problems[7], tooth decay, destruction of the chemosphere, skeletal deformity, and dental caries. This functional diversity of fluorides necessitates the development of novel methods for selectively sensing Fluoride ions. Accordingly, numerous techniques have evolved to sense Fluoride ions, including the ion selective electrode method, Nuclear Magnetic Resonance spectroscopic (NMR) analysis, and colorimetric sensing[8], and colorimetric chemo sensors have gained more attention due to their cost effectiveness, high selectivity, and sensitivity, which are inherent in this method. Its general structure includes a host molecule that, when interacting with anions, changes its electronic and spectral properties, allowing naked-eye detection of Fluoride ions. Colorimetric sensing of fluoride ions was achieved through one of the following viz. Lewis acid-base interaction, H-bond interaction and Fluoride ion-induced chemical reaction. Considerable attempts have been made to formulate H-bond interactions, implementing various signalling mechanisms to develop colorimetric anion sensors, including Intramolecular Charge Transfer (ICT), Photoinduced Electron Transfer (PET), Metal-to-ligand Charge Transfer (MLCT), and Excited-state intra/intermolecular Proton Transfer (ESPT). A large number of reports have been published on chemo sensors based on proton transfer mechanisms, including urea[9], thiourea[10], amide, imidazole[11], pyrrole[12], acridinium, and phenol[13]-based receptors with N-H or O-H groups as binding sites[14]. However, the complexity of the receptor molecule, its synthesis, and the selectivity of the system remain challenging.

In recent years, chalcone derivatives have emerged as potential candidates for anion sensing because of their ability to donate protons in hydrogen-bonding interactions and their conjugation system through phenol rings and en-1-one groups [15]. They enable various electron-donating or electron-accepting groups to be substituted to tune the intramolecular hydrogen bond, thereby enhancing the responsivity towards selective anions. In particular, hydroxychalcones show high antioxidant activity and are efficient radical scavengers[16]. Recently, Adita et al.[17] reported a methoxy-substituted chalcone receptor as a colorimetric sensor based on proton transfer, which changed its colour from yellow to red/orange upon addition of fluoride and also senses various other anions. Guan et al. [18] reported a chalcone armed with coumarin and naphthol, which showed fluorescent turn-on properties in the presence of Fluoride ions. However, the selectivity of chalcone-based receptors is still challenging, and a literature study suggests that chalcone

derivatives are extensively used as receptors for detecting cyanide ions and many other metal ions; however, their Fluoride ion-sensing capabilities have not been extensively explored.

Herein, we report a new fluoride receptor, 2',2-dihydroxychalcone (1) shown in Fig. 1, for the selective detection of Fluoride ions by the naked eye. Here, the 2-OH group substituted in the benzene ring of the structure behaves as a binding site for Fluoride ions through H-bonds, followed by deprotonation. As the receptor has no urea/thiourea moieties, it avoids the problem of multianion sensitivity. The anion recognition properties of the receptor towards Fluoride ions were studied experimentally using the naked eye, UV-visible, and Jobs plot methods. The receptor showed selectivity towards fluoride among the tested anions by changing the colour from green to fluorescent red. Further, theoretical studies using density functional theory and time-dependent density functional theory (DFT/TDDFT) calculations were carried out on 1 and 1-F⁻ to optimize their geometry, explain the anion-analyte interaction mechanism, and study their electronic transitions. The experimental and calculated data were compared, and their agreement was briefly discussed.

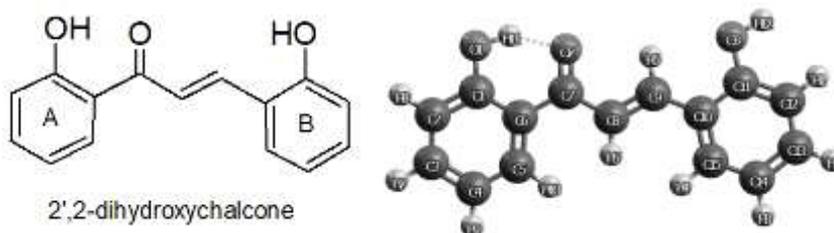


Fig. 1. Structure of hydroxychalcone

2.0 Materials and methods

2.1 Materials

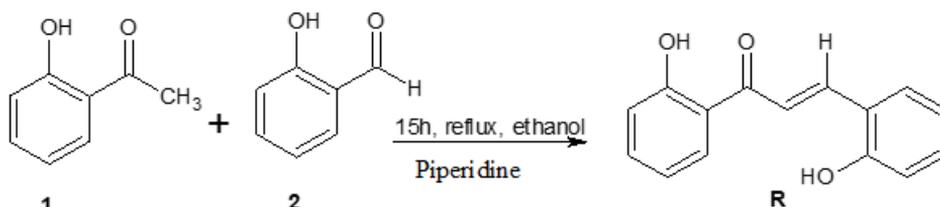
All chemicals and solvents required for the present research work were procured from Sigma Aldrich and used without further purification.

2.2 Methods

2.2.1.1 Synthesis of receptor (2E)-1,3-bis(2-hydroxyphenyl) prop-2-en-1-one (R)

First, 5 g (0.0367 mol) of 2 hydroxy acetophenone (1) was dissolved in 30 ml of ethanol. Piperidine (0.2 ml of Piperidine was then added dropwise to the flask. Then 4.48g(0.0367 mol) of 2 hydroxybenzaldehyde (2) was dissolved in 10 ml of ethanol and slowly added to the flask, and the

reaction mixture was refluxed for 15h. The completion of the reaction was monitored by TLC. The solvent was then stripped off and poured into water to obtain the gummy mass. The crude product was purified by column chromatography using hexane/ethyl acetate as the eluent to obtain the target receptor R as a yellowish fluffy solid. Yield: 78%. Melting point: 86 °C. (Scheme 1) FTIR spectral data (in cm^{-1}): 3032 (Aromatic -C-H) stretching and 3604-3202 (O-H) stretching, 1645 (C=O) stretching, and 1492 (C=C) stretching.



Scheme 1. Synthesis of chalcone receptor

3.0 Results and Discussion

The 2 hydroxy acetophenone and 2 hydroxy benzaldehyde were used to produce chalcone-based receptors. To create a chalcone with two hydroxy groups and one keto functionality, the reaction was conducted. This receptor contains two phenolic proton molecules that can be readily removed. As a result, this is the principal group that might bind to fluoride ions, aiding their detection by the naked eye. Different ions, including iodide, chloride, bromide, and acetate anions, were investigated using their tetrabutyl ammonium salts in extremely low quantities to determine the selective detection of fluoride ions. The fluoride ion, however, displayed a heightened red colour coupled with when it responded to the receptor in the naked eye itself, while all other ions showed negligible changes in intensity as well as colour when they interacted with ions. The results of the comparison of the fluoride ion intensities with those of other ions (Fig.2). Fig.3 also shows the receptor and its complex colour under daylight and UV light conditions.

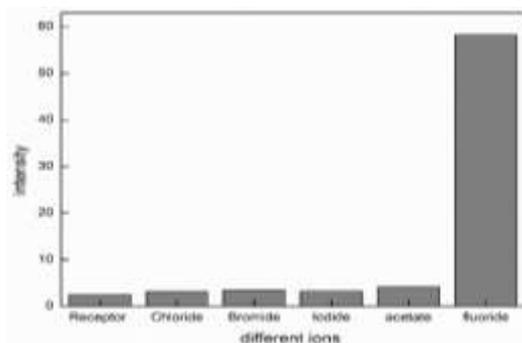


Fig. 2. Intensity of absorption when receptor is reacted with various ions

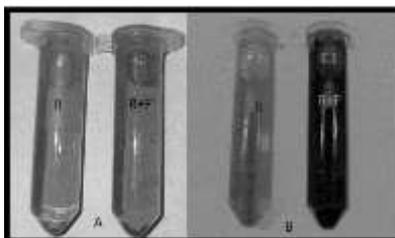


Fig. 3. Photograph of receptor and acceptor fluoride complex under (a) day light and (b) UV light

The optical properties of the receptor are essential for determining its sensing ability. Hence, the absorption spectra of the receptor were recorded in acetonitrile and showed a broad absorption curve with absorption maxima at 395 nm and a small kink at 512 nm. The peak at 395 nm is due to $\pi-\pi^*$ transition. The peak at 512 nm may be due to $n-\pi^*$ transitions. In addition, the chalcone receptor showed very good fluorescence behaviour with an emission maximum of 454 nm along with a Stokes shift of 60 nm. The UV-visible absorption and fluorescence emission spectra of the receptors are shown in Fig. 4 and 5, respectively.

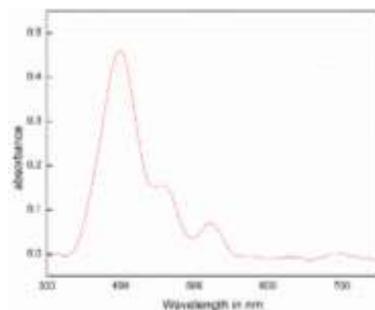


Fig.4. UV-Visible absorption spectra of chalcone receptor in Acetonitrile solvent

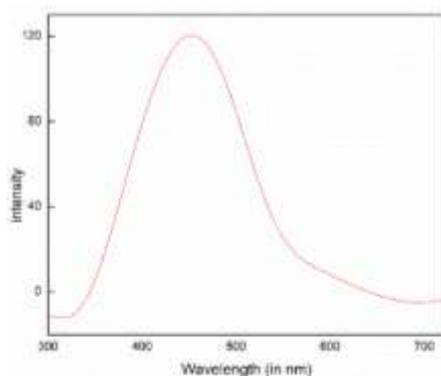


Fig.5. Fluorescence emission spectra of the receptor in acetonitrile when excited at 395 nm.

The chalcone receptor showed a very good response to fluoride ions, even with the naked eye. To investigate the sensing behaviour of the receptor, UV-visible titrations were carried out in acetonitrile solvent using tetrabutyl ammonium fluoride as the fluoride source. For each fluoride addition, the spectra were recorded and plotted against the optical density. During this titration, it was observed that upon the addition of fluoride ions, the intensity of the π to π^* transition peak of the receptor at 394 nm continuously decreased, with the formation of a new peak at 450 nm with increasing intensity. The UV-visible titration results are shown in Fig. 6. This indicates the binding of fluoride ions to the receptors. To investigate binding ability, job plots were plotted with various ratios of chalcone receptor and fluoride ion concentrations ($0-5 \times 10^{-5}$ M). Fluoride and receptors were prepared at various concentrations, and the absorption of each component was separately measured and plotted. The results of this study showed that these fluoride ions and the receptor react in a 1:1 ratio. The job plot of the same is shown in Fig. 7.

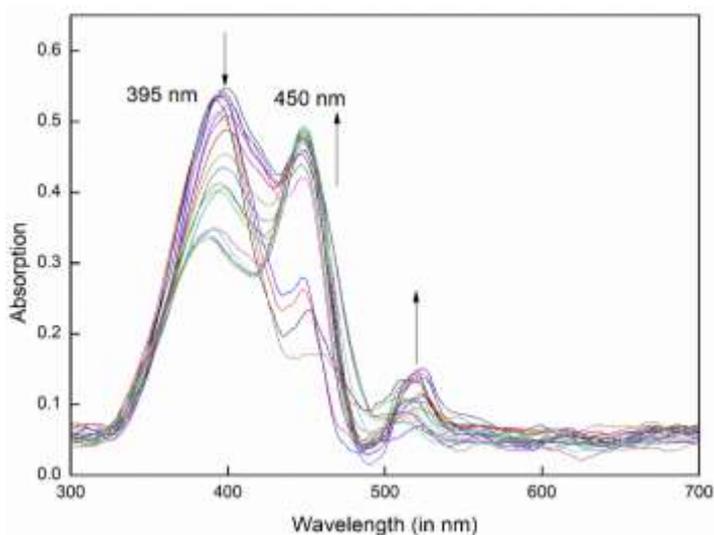


Fig. 6. UV-Visible titration of chalcone receptor (1×10^{-5} M) with acetone nitrile solution of tetrabutylammonium fluoride (0 to 4×10^{-5} M)

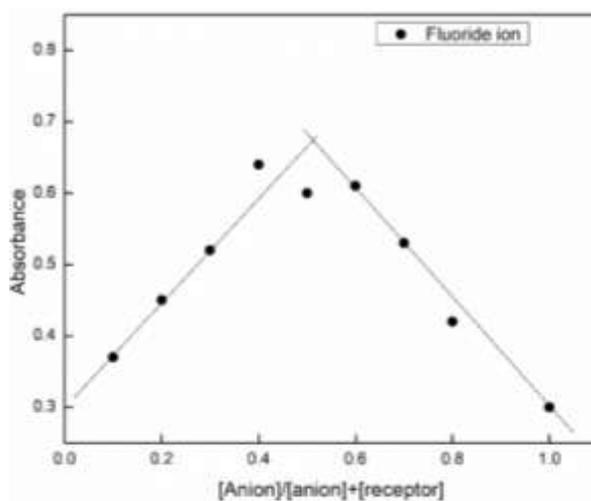


Fig.7. Jobs plot of chalcone receptor with various concentration of fluoride ions

The results of these studies showed that chalcone-based compounds are excellent compounds for naked-eye detection of fluoride in order to substantiate the results of computational modelling studies. In this study, properties such as the binding energy, highest occupied molecular orbital (HOMO), lowest unoccupied molecular orbital (LUMO), theoretical UV spectra, and binding interactions were calculated.

4.0 Computational Methods

The structural properties of receptor (1) were determined at the molecular level employing Density Functional Theory (DFT)[19]. The ground-state geometry of 1 and its complex (1-F⁻) were optimized using Becke's three-parameter hybrid functional[20] combined with the Lee, Yang, and Parr correlation functional (B3LYP) using the Pople basis set, that is, 6-31G(d)[21], in the gas phase. The vibrational frequencies calculated at the same level of theory showed no imaginary frequencies, indicating that the optimized geometries were global minima. Time-dependent DFT (TD-DFT) calculations were performed at the B3LYP level using the Dunning correlation-consistent polarized split-valence triple- ζ basis set (cc-pVTZ)[22] to investigate the optical and electronic properties of the ground and excited states. DFT/B3LYP/6-31G(d) optimized structures were used for TDDFT calculations. The solvents effects were included for the TDDFT calculations using Conductor-like Polarizable Continuum Model (CPCM)[23] for ACN solvent ($\epsilon=36.6$). All the DFT and TDDFT calculations were performed using the ORCA 4.0.1 program[24].

4.1 Quantum Chemical Calculations

To confirm the anion-analyte interaction mechanism through hydrogen bonding between 1 and F⁻ followed by proton abstraction from the hydroxyl group (-OH) of 1 to the fluoride ion, theoretical calculations were performed using DFT. Optimization was performed using 1:1 receptor-additive forms (1-F⁻), as indicated by the experimental results. There are two acidic protons in the 2-OH and 2'-OH receptors. The Bond dissociation Energy (BDE) of 2'-OH is increased due to formation of intra-molecular hydrogen bond (IHB) with the carbonylic oxygen[25], this suggests that the 2-OH moiety acts as an active binding site[26]. Hence, the geometries were optimized following the same procedure. The geometries of 1 and 1-F⁻ were optimized using DFT at the B3LYP/6-31G(d) level of theory (Fig.8a). Analytical vibrational frequencies were calculated at the same level of theory to ensure that the optimized structures corresponded to global minima. According to the calculation results, the O-H bond distance in compound 1 was 0.970 Å, which lengthened to 1.505 Å upon the addition of fluoride ions to the 1-F⁻ complex (Fig.8b).

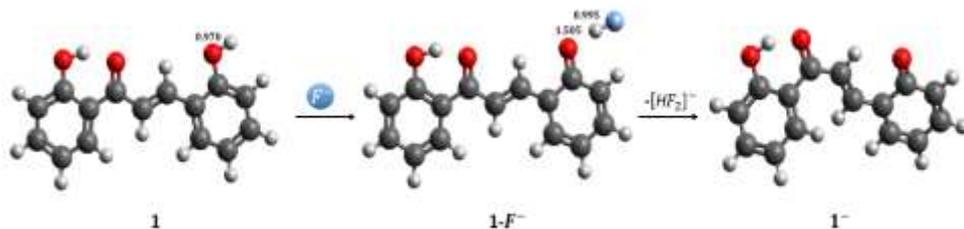


Fig.8a. Proposed mechanism with optimized structures calculated at B3LYP/6-31G(d) in gas phase.

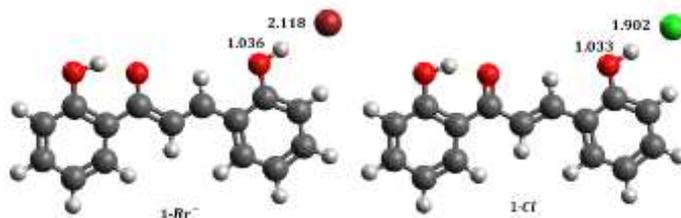


Fig.8b. Optimized structure of 1-anion complex

The H-F bond distance was found to be 0.995 Å, whereas a normal H-F bond distance is around 0.93 Å [27] and a typical H...F hydrogen bond distance range from 1.73 to 1.77 Å. This attributes for the colorimetric sensing of Fluoride ion by 2',2-dihydroxychalcone (1) through formation of O-H...F hydrogen bond and subsequent deprotonation of hydroxyl group in receptor 1 resulting in intermolecular proton transfer (IPT). However, for Cl⁻ and Br⁻ anions, the O-H bond length was less elongated (Fig.8b), which suggests that these anions failed to deprotonate the receptor molecule, which can be inferred from the selectivity of the receptor towards Fluoride ions. Additionally, the structure of neutral receptor molecule (1) maintained its coplanarity at the complex state (1-F⁻) and the phenoxy radical formed by hydrogen abstraction was well stabilized by the aromatic resonance in structure 1⁻.

Table1. Photophysical properties of receptors.

	Major Transitions*	Energy (cm ⁻¹)	Osc. Strength(<i>f</i>)	λ_{max} (nm)	Symmetry	λ_{abs} Exp.
1	H→L (75%) H-1→L (20%)	25371.4	0.4061	394.1	Singlet	
1-F ⁻	H→L (92%)	20492.7	0.5805	488	Singlet	-
1 ⁻	H→L (90%)	20332.4	0.4059	491.8	Singlet	

*H denotes HOMO and L denotes LUMO

To gain further insight into the optical and electronic properties of the neutral receptor (**1**) and the corresponding receptor anion ($1-F^-$) complex, they were studied using TDDFT at the B3LYP/cc-pVTZ level of theory in ACN solvent using the optimized geometry. The dispersion interactions effects were also included using Grimme's DFT-D3(BJ) method[28]. The frontier molecular orbital (FMO) density distribution of receptor **1**, $1-F^-$ and 1^- and their major electronic transitions are shown in Fig.9a which demonstrates a $\pi \rightarrow \pi^*$ excitation. The bathochromic red shift in the absorption maximum of **1** is clearly indicated by the decrease in the excitation energy gap of HOMO-LUMO (from $\Delta E=3.708$ eV to $\Delta E=2.84$ eV) upon binding with the Fluoride ion.

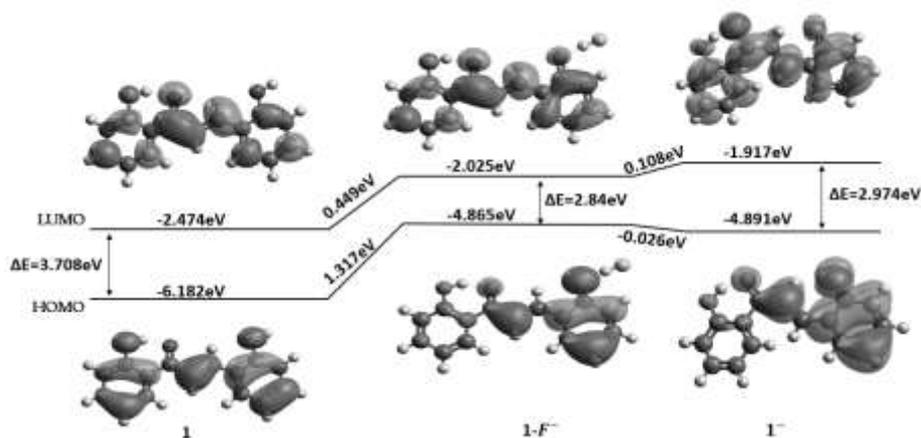


Fig.9a. The orbital distribution and HOMO-LUMO energy of **1**, 1^- , and $1-F^-$ at the B3LYP/cc-pVTZ level of theory in the ACN solvent (isovalue=0.02).

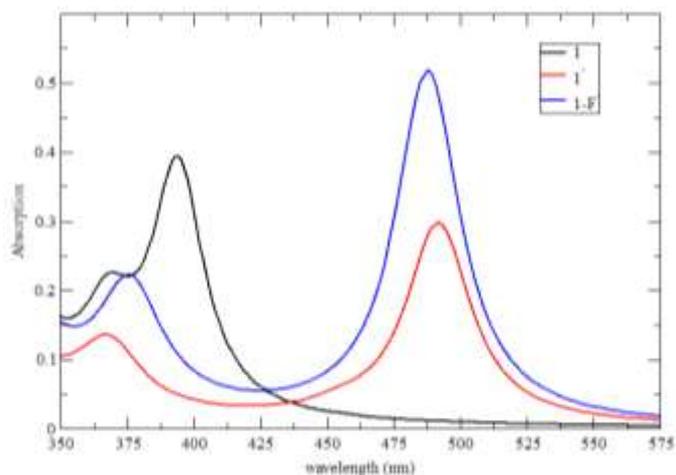


Fig. 9b. Theoretical absorption spectra of **1**, $1-F^-$ and 1^- in ACN solvent

For receptor 1 as shown in the Fig. 9a a strong delocalization is present in LUMO whereas the HOMO shows more localization of iso-surfaces of the wave functions on the substituted phenyl rings. For the deprotonated state, the HOMO was predominantly distributed on phenyl ring B, while the LUMO was delocalized over entire molecule illustrating the intramolecular charge transfer (ICT) through the system[29]. The excitation of receptor 1 (HOMO \rightarrow LUMO) causes the redistribution of electron density which increases the acidity of hydroxyl group in the excited state (1-F⁻) leading to deprotonation. Further, as the LUMO is associated with the electron accepting ability of a molecule, the Fluoride ion would prefer LUMO of 1 more than the HOMO. This is indicated by the lesser increase in the potential energy of the LUMO compared to that of the HOMO. The absorption wavelengths, oscillator strengths, and major orbital contributions are presented in Table 1. The calculated absorption spectra were in good agreement with the experimental data. Furthermore, the first absorption peak of 1 was observed at 394 nm (Fig.9b) (experimental 395 nm), which was assigned to the HOMO \rightarrow LUMO transition (75%) and HOMO-1 \rightarrow LUMO (20%), with an oscillator strength of $f = 0.4061$. When receptor 1 formed a complex with F⁻, the absorption peak at 394 nm decreased, and a new peak was observed at 488 nm [Fig.9(b)], corresponding to the transition from HOMO \rightarrow LUMO (92%) with an oscillator strength $f = 0.5805$. The deprotonation of 1 causes a bathochromic red shift of 94nm in ACN solvent. In experimental study it showed a bathochromic shift of 55 nm. In both the case bathochromic shifts are observed hence both results are well matching.

5.0 Conclusion

In this study, a chalcone-based fluoride ion sensor was designed and synthesized. The sensor was able to recognize fluoride ions with the naked eye even at the lowest concentrations. UV titrations were performed to study the behaviour of the receptor. This shows the interaction between the phenolic hydrogen and fluoride ions. Further, job plots confirmed this interaction by forming a 1:1 complex. Furthermore, this interaction was proved by a computational study. In this study, the theoretical and practical wavelengths are in good agreement, which confirms the interaction. Hence This chalcone based receptor may be a potential candidate for the naked eye detection of fluoride ions.

6.0 Acknowledgement

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