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ARTICLE TYPE

Phenolic oxime based receptors for selective detection of fluoride

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The possibilities to employ phenol and oxime functionalities as the fluoride recognition motif are investigated. In this regard, two new phenolic oximes **H1** and **H2** were prepared where the two units are linked via different aliphatic spacers. Among them, **H1** exhibits intense and instantaneous colour change upon addition of fluoride ion which is clearly discernible by "naked eye". Optical, ^{1}H NMR and CV analysis establishes that **H1** is a highly selective receptor for fluoride ion as compared to other anions tested during this investigation.

Introduction

Anions are ubiquitous in nature and many of them play important roles in biology, medicine, agriculture, catalysis and environmental sciences. Therefore the selective recognition, sensing and extraction of anions has evolved as a fevered area of research during the last decade.[1]In this context, the rational design and synthesis of new abiotic receptor molecules which can bind anions of interest with high affinity and selectivity has remained one the most pressing challenges in supramolecular chemistry.[2] Among various anions, the selective recognition and sensing of fluoride ion has been the subject of intensive research due to its relevance in environment and health sectors.[3] Fluoride has many industrial applications and used as an essential additive in toothpaste to prevent corrosion of teeth by acids. Fluoride is also used as an ingredient in drugs to treat the brittle-bone disease called Osteoporosis. The main source of fluoride in water is basically geogenic. United States Environmental Protection Agency (EPA) puts the maximum contamination level goal (MCLG) for fluoride in drinking water as 4 ppm.[3] 0.7-1.2 ppm level of fluoride in drinking water is sufficient to maintain public health dental benefits of caries prevention while also minimizing the incidence of enamel fluorosis. Excessive intake of fluoride has many severe health implications *viz.* fluorosis and osteofluorosis.[3] Thus accurate determination of the amount of fluoride in drinking water and living organs is important. Generally, ion selective electrodes, ion chromatography, Willard-Winter methods are used for quantitative detection of fluoride ion but the very high cost and difficulty in handling as well as transportation limits their utility.[4] Thus, development of a simple, economical, highly selective, sensitive and rapid fluoride detection method for practical purpose is worthwhile. In this regard, colorimetric and fluorometric sensors for fluoride recognition with high selectivity and sensitivity have received considerable attention. A plethora of abiotic receptors exploiting the diversity of non-covalent interactions which feature cationic sites, Lewis acidic sites, electron-deficient π-systems and H-bond donor motifs have been designed and their anion binding behaviour explored.[5] Conventional hydrogen bonded F^- binding receptors rely on either adjacent reporter (*i.e.* chromogenic and fluorogenic) units or deprotonation followed by electron delocalization to display a colorimetric response. Therefore, most of the receptors cannot differentiate F^- from other anions with same or more basicity.

Fluoride exhibits unique physico-chemical properties due to its smaller size and high electronegativity. Moreover, due to its high hydration enthalpy, fluoride is not willing to bind with (or recognize) other molecules in presence of water. Therefore the receptor has to compete with water for fluoride *i.e.* with O-H…F^- interaction of F^- and water.[6] Hence the design of receptors capable of binding fluoride ion efficiently and selectively in water *i.e.* for real-life applications is consequently a meaningful, however challenging task.[5] In order to achieve enhanced selectivity towards fluoride, fine tuning of interaction sites are required, which in turn needs appropriate functionalization, such that the complementarity of interacting sites, size and shape between the receptor and the guest has to be achieved.[7] It is envisaged that fine tuning of the acidity of the hydrogen bond donor sites is crucial for designing H-bonding neutral receptors capable of binding fluoride ion in aqueous environment.[8] In principle, more acidic the binding sites, the probability of the receptor to bind fluoride in aqueous environment would be higher. Therefore, it is presumed that incorporation of hydroxyl group in a flexible scaffold suitable for fluoride size may be a

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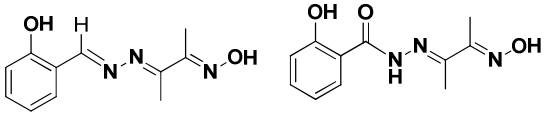
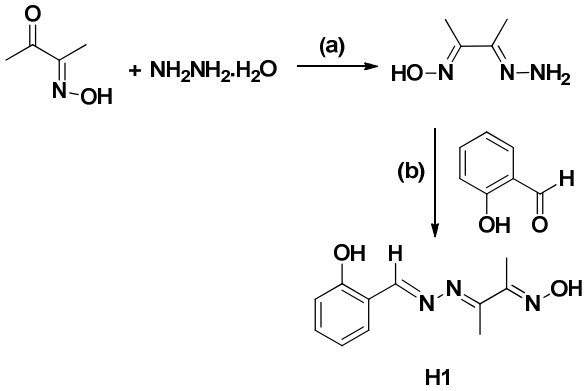
practical strategy for fluoride discrimination in aqueous medium. In addition, the use of highly acidic hydrogen bond donor sites may favour deprotonation which can subsequently alter the electronic structure of the receptor and consequently a remarkable change in colour of the solution with a large bathochromic shift is expected which provides naked eye visualization of the recognition event. Towards this, a number of receptors with hydroxyl group as binding motif were reported and their anion binding properties were bstudied.[9]



H1 H2

Figure 1 Structure of receptor **H1** and **H2**.

Herein we have designed and reported the synthesis and anion binding properties of a new class of receptor, **H (H1** and **H2)** containing oxime and phenol hydroxyl groups as the H- bonding recognition unit (Figure 1). In case of **H1** the recognition units are separated by the conjugated aliphatic spacer containing imine moiety while in **H2** conjugation breaks due to the presence of the amide moiety. Phenolic and oxime hydroxyl groups have different acidities, and therefore have different H-bonding affinities.[10] In addition, these two OH moieties have higher acidities compared to water. Therefore, it is envisaged that these two hydroxyl moieties can compete with water to bind fluoride ion in aqueous medium.[10]



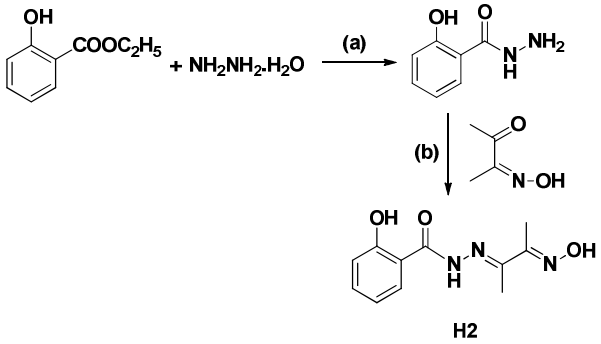
H1

Scheme 1 Synthesis of **H1**: (a) CH_3OH, RT, 2h (b) CH_3CH_2OH, reflux, overnight

Results and discussion

Synthesis and characterization

Receptor **H1** was conveniently synthesized by a two-step reaction scheme from 2,3-butanedionemonoxime. The synthesis involves the preparation of monoximehydrazone from 2,3-butanedione monoxime followed by its Schiff base condensation reaction with salicylaldehyde (Scheme 1) which yield compound **H1** as yellow crystalline solid.[11] Receptor **H2** was synthesised conveniently from ethyl-2-hydroxybenzoate by following scheme 2 as a light yellow colour solid.[12]



H2

Scheme 2 Synthesis of receptor **H2**: (a) CH_3CH_2OH, RT, 4h (b) CH_3CH_2OH, reflux, overnight.

Both the compounds were characterized by using standard spectroscopic techniques such as ^{1}H NMR, ^{13}C NMR spectroscopy and elemental analysis. Further, solid state structures of compound **H1** was unequivocally elucidated by single crystal X-ray diffraction method with a crystal grown by slow evaporation of ethanol solution. ^{1}H NMR spectrum of **H1** in DMSO-d_6 shows two hydroxyl ^{1}H peaks at 11.92 and 11.28 ppm which clearly reveals the highly acidic nature of the hydroxyl protons. Further, it is observed that the compound isomerizes on keeping the sample for longer time as DMSO solution. ^{1}H NMR spectra of the aforementioned solution shows the emergence of new peaks slightly downfield to the prevailing hydroxyl peaks and this can probably be attributed to the emergence of new isomers in the solution (Figure 2).

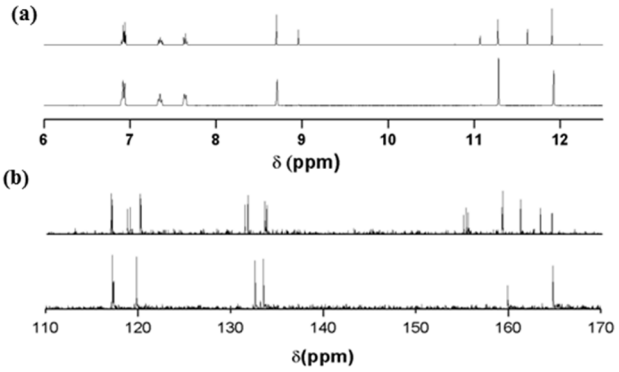
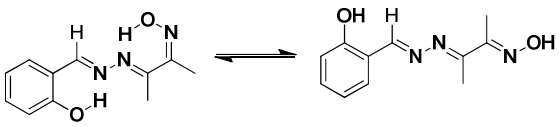


Figure 2 Change in NMR spectra of **H1** in DMSO-d6 while isomerization. (a) ^{1}H- NMR spectra- bottom: pure isomer, top: isomeric mixture; (b) ^{13}C- NMR spectra- bottom: pure isomer, top: isomeric mixture.

This study infers the presence of a dynamic equilibrium between two conformational isomers of compound H**1** in DMSO (Scheme 3) and the integration of the corresponding signal established the ratio of the two isomer as 2:1 showing 30 % isomeric conversion. UV-visible spectra of **H1** in DMSO reveal two absorption maxima (λ_{max}) at 294 and 338 nm. Single crystal X-ray diffraction analysis reveals the *trans*-orientation of the oxime double bond w.r.t. the N-N single bond in the solid state (Figure 2). Solid state packing pattern reveals the occurrence of



Scheme 3 Plausible isomeric structure of **H1** in DMSO.

intramolecular O-H….N hydrogen bond (with 2.597Å distance, <O-H..N=147.7˚) between phenolic OH and hydrazine nitrogen atom and intermolecular O-H….N hydrogen bond (with 2.855 Å distance, <O-H..N=175.8˚) between oxime OH and oxime N of a nearby molecule (Figure 4, inset). Further, careful analysis of the packing pattern reveals the presence of the herringbone packing mode which is facilitated by slip stacked π-π stacking interaction between the phenyl rings (Figure 4). Further, Hirshfeld surface analysis of the crystal structure also confirms the same (ESI).[13]

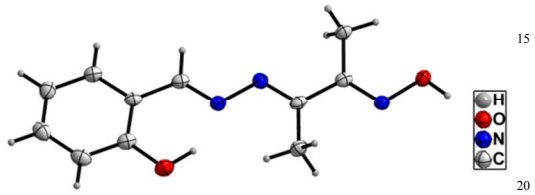


Figure 3 ORTEP diagram of **H1**, with the displacement ellipsoid drawn at the 35% probability level. Crystal data: C11H13N3O2, a = 19.7074 (7) Å, b = 4.4839(5) Å, c = 12.7541 (5) Å, α = γ = 90˚, β = 107.994˚ (2), V = 1071.91 (8), T = 296 K, Monoclinic, Space group P2(1)/n, z = 4. Colour code: red: O, blue: N, grey ellipsoid: C, grey sphere: H.

^{1}H NMR spectra of receptor **H2** features three singlets at 11.29, 11.49 and 11.60 ppm which corresponds to the two hydroxyl protons and the amide NH proton. This large down field shift of the aforesaid protons indicates their highly acidic character. However, unlike **H1**, **H2** does not show any noticeable conformational isomerisation in DMSO-d_6. Unfortunately, even after repeated attempts we could not obtain any good quality crystal to determine the solid state structure of **H2**.

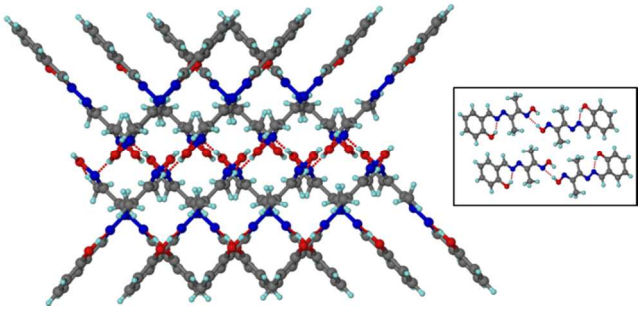


Figure 4 Herringbone packing pattern of H in the solid state showing. Inset: H-bonding structure in the solid state packing.

Anion binding study

Preliminary solution phase anion binding studies were carried out using UV-visible spectroscopy in dimethyl sulfoxide with various anions (F^-, Cl^-, Br^-, I^-, CN^-, CH_3COO^-, $H_2PO_4^-$, HSO_4^-, ClO_4^-) as their tetrabutylammonium salts. Further, the mechanistic study of binding was also performed with the help of ^{1}H NMR spectroscopy in DMSO-d_6.

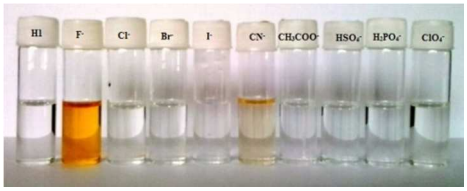


Figure 5 Change in colour of **H1** (20 μM) in dry DMSO after the addition of 10 equivalents of tetrabutylammonium salt of anions.

It is presumed that the two preorganized O-H H-bond donor moiety interact with anionic guest which are principally H-bond acceptors and exhibit certain change in spectroscopic properties upon interaction with anions which make visualization of the anion binding events meaningful. It is observed that the solution changes its colour from colourless to dark yellow upon addition of fluoride to **H1** solution in DMSO which can be easily detected by naked eye whereas the change with cyanide was less prominent. However, no colour change was observed upon addition of other anions (Figure 5). However, receptor **H2** does not show any naked eye detectable colour change upon addition of the tested anions.

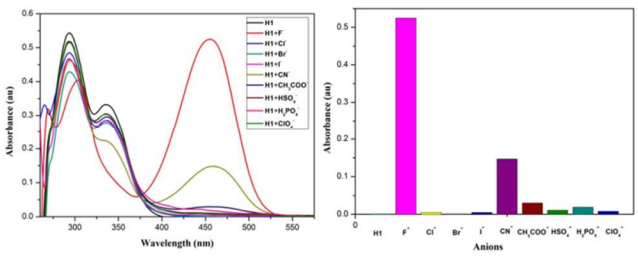


Figure 6 Left: UV-Vis absorption spectra of **H1** in dry DMSO (20 μM) after addition of 10 equiv. of different anions in the form of TBA salts. Right: Intensity of the new 445 nm peak after addition of 10 equiv. of different anions in the form of TBA salts.

Figure 5 depicts the change in colour of receptor **H1** upon addition of 10 equivalents of the respective anions which clearly reveals that the receptor shows highest optical change towards fluoride ion, somewhat lesser extent toward cyanide ion and little to none towards other anions. To verify the change in electronic structure and selective fluoride binding, the changes in UV-Vis absorption of the receptors were recorded in dry DMSO (20 μM solution), after adding 10 equivalent of the respective tetrabutylammonium salts. As depicted in figure 6, only F^- ion and CN^- ion induces instantaneous bathochromic shift in the absorption maxima and all other anions did not induce any perceptible change in the UV-Vis spectrum. In case of F^- and CN^- ion, UV-Vis study shows the emergence of a new peak at ~445 nm which could be the reason behind the observed colour. The bar diagram clearly reveals that the intensity of the newly emerged peak is maximum in case of fluoride (Figure 6). The observed colour change might be due the alteration of the

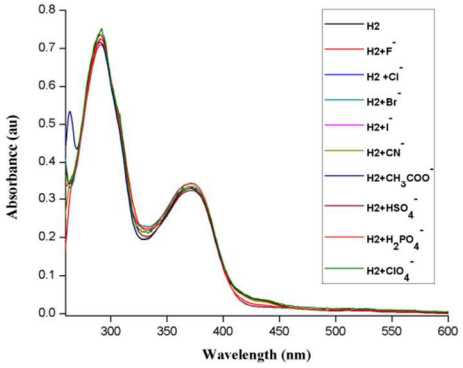


Figure 7 Change in colour of **H2** (20 μM) in dry DMSO after the addition of 10 equivalents of tetrabutylammonium salt of anions.

electronic environment of **H1** as a result of charge transfer due to deprotonation upon fluoride binding. However, in case of receptor **H2** the absorption spectra retain its identity even after addition of large excess of anions (Figure 7). This clearly reveals that the binding of anion to receptor **H2** does not induce any significant modification in the electronic structure of the receptor. To verify the binding selectivity of receptor **H2**, we have studied the interaction between receptor **H2** and anions with ^{1}H NMR spectroscopy in DMSO-d_6. The study shows the disappearance of the ^{1}H NMR signal corresponding to the –OH proton after addition of F^- and CN^- but other ions did not show any significant change. However, it is observed that the amide protons did not participate in the recognition event. This observation reveals that like **H1**, **H2** also shows selective binding towards F^- and CN^- (Figure 8).

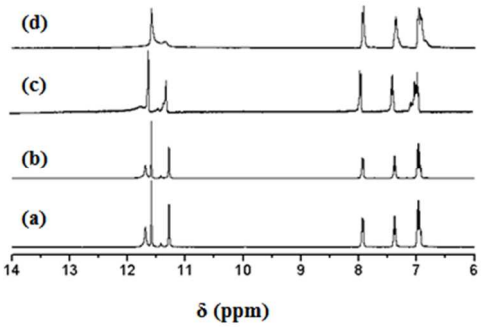


Figure 8 A portion of ^{1}H NMR spectra in DMSO-d_6 of (a) **H2** (b) **H2** in presence of Cl^-, Br^-, I^-, CH_3COO^-, $H_2PO_4^-$, HSO_4^-, ClO_4^- (c) **H2** in presence of CN^- (d) **H2** in presence of F^-.

The fluoride recognition event of receptor **H** was further studied with cyclic voltammetry in DMSO which provides evidence of an anion-dependent electrochemical response with fluoride ions. Analysis of the CV of **H1** with $TBAClO_4$ as supporting electrolytes reveals a single oxidation at Ep,a = 0.92 V while on the negative scan, two reduction peaks occurred at Ep,c = -0.48 V and -0.98 V. The appearance of two cathodic peaks may be due to the reduction of two phenol oxidation product *i.e.* orthoquinone to orthophenol and paraquinone to paraphenol.[14] However, CV of **H1** does not provide any information regarding the redox behaviour of the oxime moiety. Whereas

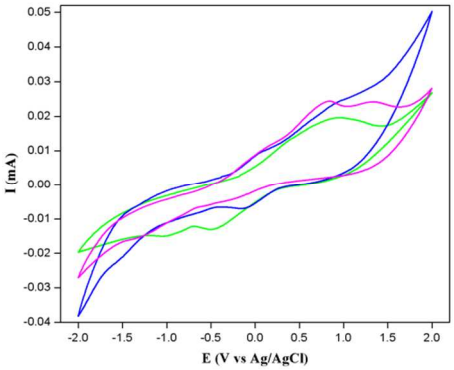


Figure 9 CVs recorded in *n*-Bu_4NClO_4/DMSO. Green: **H1** with $TBAClO_4$ as electrolyte; Pink: **H1** with TBAF as electrolyte; Blue: **H1.F**$^-$ with $TBAClO_4$ as electrolyte.

addition of TBAF led to two oxidations at Ep,a = 0.05 and 0.92 V while in the negative scan, two reduction peaks at Ep,c = -1.5 V and 0.12V were observed. This may be due to the oxidation of both phenolic as well as oxime moiety in presence of fluoride ion. To verify the contribution of fluoride ion in the change in electrochemical behaviour of **H1**, we have recorded the CV with TBAF as the supporting electrolyte which clearly shows a different pattern compared to that of the CV recorded with tetrabutylammonium perchlorate as electrolyte. This study clearly reveals that upon addition of fluoride, the integrity of **H1** has lost which may be due to deprotonation of the hydroxyl groups and subsequently led to a different electrochemical behaviour. However, addition of fluoride to **H2** does not affect its electrochemical properties significantly as compared to **H1** (ESI).

Furthermore, to examine the binding selectivity and sensitivity of **H1** in a complex environment of potentially competing anions,

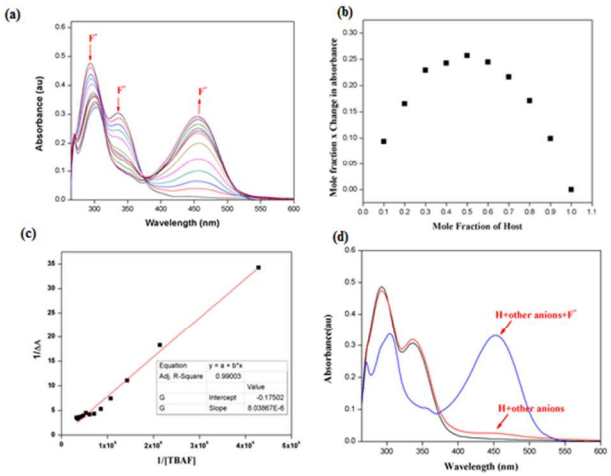


Figure 10 (a) Evolution of UV-Vis spectra of **H1** in DMSO upon gradual addition of TBAF (b) Job's plot of **H1** vs. TBAF in DMSO (C) Benesi-Hildebrand plot of titration data of **H1** vs. TBAF (d) UV-Vis spectra: Red: **H1**; Gray: **H1** and TBA salts of other anions and Blue: addition of TBAF in **H1** combined with other anions.

the screening is investigated in presence of other anions tested in the solution. The experiment is performed by adding fluoride to a solution containing receptor **H1** along with other anions. Interestingly, it is observed that only the presence of CN^- ion can interfere with the detection of F^- ion but to a very small extent, while other anions did not show any remarkable interference with the detection process (Figure 10d). In order to evaluate the binding affinity of receptor **H1** towards fluoride, systematic spectrophotometric titration was carried out in DMSO with varying concentration of fluoride ion, which indicated a strong binding event, accompanied by gradual emergence of a new peak at 445 nm. Job's plot analysis shows the maximum at 0.5 which dictates the formation of a 1:1 complex (Figure 10b). From the titration data the association constant K_a for fluoride anion was calculated by using Connor equation where the linear fitting is achieved by following Benesi-Hildebrand method.[15] The calculated binding constant is found to be $2.17 \times 10^4\ M^{-1}$.

To check the versatility of our synthesized receptor **H1** we have checked the binding in aqueous medium. Although it is observed that receptor **H1** shows prominent colour change upon TBAF in DMSO-water mixture, unfortunately it fails to detect fluoride ion when added as sodium fluoride.

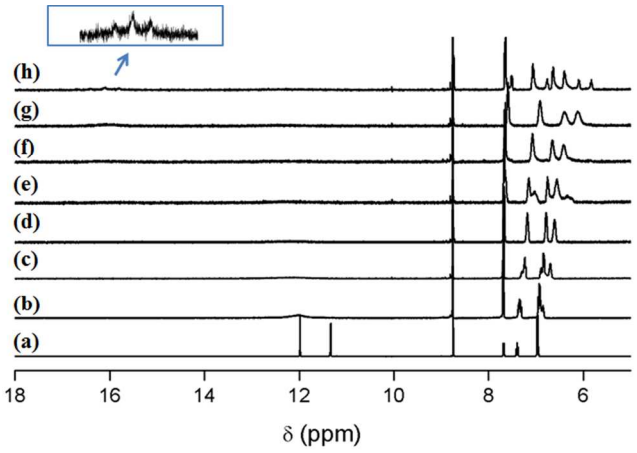


Figure 11 Selected portions of ^{1}H NMR indicating changes in the ^{1}H NMR spectra of **H1** (10 mM) upon gradual addition of TBAF in DMSO-d_6: (a) Free **H1** (b) **H1**+ 0.2 equiv. TBAF (c) **H1**+ 0.4 equiv. TBAF (d) **H1**+ 0.6 equiv. TBAF (e) **H1**+ 1.0 equiv. TBAF (f) **H1**+ 1.5 equiv. TBAF (g) **H1**+ 2.0 equiv. TBAF (h) **H1**+ 3.0 equiv. TBAF.

Further the mode of binding was studied with the help of ^{1}H NMR spectroscopy titration in DMSO-d_6. Addition of 0.2 equivalents of TBAF to **H1** solution results a broad peak at ~ 12 ppm. However it is not clear whether the disappearance of the peak at 11.28 ppm is due to deprotonation or due to the merging of the two peaks at 11.98 and 11.28 ppm due to the formation of **H1: F**$^-$ complex since aromatic CH signals does not indicate any significant change in the electronic ring current upon fluoride addition (Figure 11). However addition of another 0.2 equiv. of TBAF results broadening and downfield shift of the O-H signal with concomitant up field shift indicating H-bonding interaction between the two moiety (Figure S20-S21, ESI). Further increase in anion concentration results in the disappearance of the OH signal due to broadening, up field shift of the aromatic C-H protons and concomitant splitting of the phenyl CH peaks into multiple signals. Finally after addition of ~ 2 equiv. of TBAF the peak due to HF_2^- appears at ~ 16 ppm which clearly indicates the deprotonation of the hydroxyl proton. Also the up field shift of the phenyl CH protons clearly indicates the increase in electron density in the phenyl ring which again supports the deprotonation of the acidic protons. Furthermore the ^{1}H NMR titration experiment in acetonitrile-d_3 also reveals the same phenomena with complete resolution of the phenyl CH peaks into four signals with equal intensity (Figure S22, ESI). This indicates that deprotonation restricts the conformational dynamics of **H1** and as a result all the phenyl protons appear as chemically different protons. It can be concluded that the restriction of conformational dynamics may favour facile delocalization and hence favours dissipation of the excess electron density via the conjugated imine spacer leading to the observed colour change. For further confirmation of the deprotonation process, we have recorded the ^{1}H NMR spectra of **H1** in presence of hydroxide ion which has comparatively higher basicity than fluoride. Like fluoride, addition of hydroxide ion to **H1** solution results the change in colour of the solution towards red and ^{1}H NMR spectra reveals the complete disappearance of the hydroxyl proton signals and a significant up field shift of the aromatic CH signals (ESI). This unequivocally concludes that **H1** recognizes fluoride via deprotonation of the hydroxyl proton atleast at higher concentration of fluoride. As expected, the quantitative ^{1}H NMR titration study of receptor **H2** with TBAF also shows broadening and gradual downfield shift of the hydroxyl proton signal along with concomitant up field shift of the phenyl CH proton and emergence of the HF_2^- signal at ~ 16 ppm after addition of approximately 2 equivalent of TBAF. However, as observed in the anion screening experiment, ^{1}H NMR titration

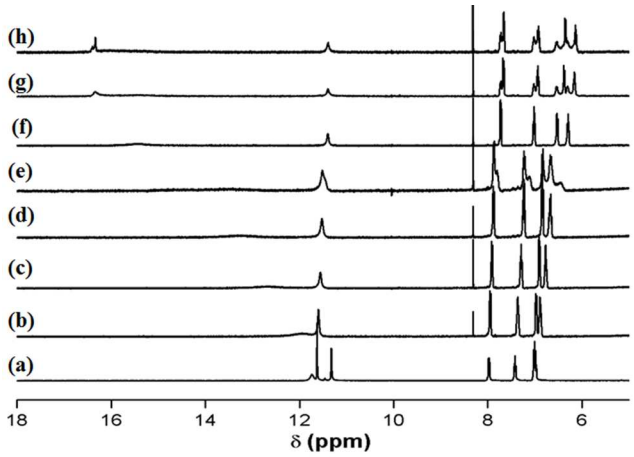


Figure 12 Selected portions of ^{1}H NMR indicating changes in the ^{1}H NMR spectra of **H2** (10 mM) upon gradual addition of TBAF in DMSO-d_6: (a) Free **H2** (b) **H2**+ 0.2 equiv. TBAF (c) **H2**+ 0.4 equiv. TBAF (d) **H2**+ 0.6 equiv. TBAF (e) **H2**+ 1.0 equiv. TBAF (f) **H2**+ 1.5 equiv. TBAF (g) **H2**+ 2.0 equiv. TBAF (h) **H2**+ 3.0 equiv. TBAF.

experiment also does not infer any involvement of the amide protons in the recognition process. This indicates that in these receptors binding is controlled by acidity of the H-bond donors. ^{1}H NMR experiments finally concludes that the fluoride recognition by receptor H involves interaction via O-H…F-hydrogen bonding followed by deprotonation of both the phenolic and oxime protons indicating the involvement of the two hydroxyl protons in the recognition and a possible 1:2 recognition event. However, UV-Vis Job's plot analysis reveals 1:1 complexation in contrast to the 1:2 binding evident from NMR experiments. This surprising anomaly may be due to the occurrence of two step recognition event where first step is the binding of fluoride ions through H-bond followed by deprotonation of the hydroxyl protons. At low fluoride concentration *i.e.* the concentration range (20 μM) at which the UV-Vis Job's experiment was performed, the first process may control the event while at comparatively higher concentration of fluoride (*i.e.* > 1mM) both the process may be functional. Further the shift of the isobestic point during gradual addition of TBAF also suggest the presence of more than one stoichiometric species in solution indicating the presence of a complex process.[16] We have tried to determine the stoichiometry by ^{1}H NMR experiments. But unfortunately due to the large broadening and splitting of the concerned signals, the experiments did not give any conclusive result.

Conclusion

To summarize, we have synthesized a new class of receptor **H** with two competing hydroxyl binding domain for instantaneous and selective detection of fluoride in organic as well as in aqueous medium. This study infers that strategic modulation of the aliphatic spacer led to a remarkable change in the reporting property (*i.e.* optical, electrochemical *etc.*) of the host-guest recognition event. **H1** shows solvent induced isomerization which was unequivocally confirmed by ^{1}H NMR. Anion binding studies reveals that both **H1** and **H2** are selective towards fluoride ion and among them **H1** shows a sharp colour change. Competition experiments also confirms the fluoride induced color change in presence of other tested anions. ^{1}H NMR titration analysis concludes that fluoride recognition involves binding of fluoride via O-H...F^- hydrogen bonding followed by deprotonation. Finally, we have shown that the simple aromatic hydroxy-aldoxime conjugates can act as a binding domain for fluoride discrimination. Fluoride binding was found to act through binding followed by deprotonation of the hydroxyl protons which led to large bathochromic shift in the absorption spectroscopy and as a consequence a naked eye optical readout (colourless to dark yellow) is observed. Electrochemical study further demonstrates phenolic oximes as potential fluoride binding motif for electrochemical fluoride sensor. Unfortunately this receptor cannot recognize inorganic fluoride salts such as metal fluorides in aqueous medium which is the main objective of our research. This observation limits the utility of our receptor for field application. Presently, further study is going on to modulate the system in order to enhance its host-fluoride response in aqueous medium.

Experimental Section

Materials and methods

Melting points were recorded on a JSCW melting point apparatus. Elemental analysis was done by using Perkin Elmer PR 2400 series analyzer. Infrared spectra were recorded with a Nicolet Impact I-410 FT-IR spectrometer as KBr diluted discs. The ^{1}H NMR spectra (400 MHz) and ^{13}C NMR spectra (100 MHz) were recorded on a 'JEOL' NMR spectrophotometer in DMSO-d_6 at room temperature. In NMR spectra, chemical shifts are reported in parts per million downfield of Me_4Si (TMS) as internal standard. The diffraction data was obtained with a Bruker Smart APEX- II diffractometer with Mo-K_α rotating anode generator, and Smart CCD detector. Structures were solved and refined using SHELXL-97 with anisotropic displacement parameters for non-H atoms. The hydrogen atoms on O and N atoms were located from the Fourier map in all of the crystal structures. All C–H atoms were fixed geometrically. Empirical absorption correction was done using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm. A check of the final CIF file using PLATONS3 did not show any missed symmetry. UV-visible data were recorded with a Shimadzu UV2450 spectrophotometer. ^{1}H NMR spectroscopy based titration studies were carried out on a Bruker Avance-400 MHz NMR spectrometer in acetonitrile-d_3. UV-visible titrations were carried out in dimethylsulphoxide solution. All tetrabutylammonium salts for NMR andUV-Vis titration were purchased from Sigma-Aldrich® and used as such. All anions were used in the form of their tetrabutyl ammonium salts (fluoride as its trihydrate). The receptor solutions were titrated by adding known quantities of concentrated solution of the anions in question. The anion solutions used to effect the titrations contained the receptor at the same concentration as the receptor solutions into which they were being titrated so as to nullify the dilution effect.

*1.1. Synthesis of **H1***

A mixture of salicylaldehyde (122 mg, 1 mmol) and diacetyl monoxime hydrazone (115 mg, 1 mmol) was taken in a round bottom flask and dissolved in 50 mL ethanol. The solution was refluxed for 4 h with continuous stirring. The resultant solution was cooled to room temperature and filtered. The yellow coloured filtrate was kept undisturbed in a beaker for crystallization at room temperature. Yellow block shaped crystals were observed after 2 days at the bottom of the beaker. The solvent was decanted and the solid was dried in air which yield 127 mg of **H1** as light yellow solid.

Yield: 127 mg, 58 %; m.p.:122-124 °C; FT-IR (ν_{max}/cm^{-1},KBr): 3201(br), 3052(w), 1964(w), 1612(s), 1543(w), 1492(w), 1359(m), 1267(m), 1202(m), 1147(m), 1011(m), 941(m), 796(w), 750(m), 702(m), 649(w); ^{1}H NMR (DMSO-d_6, 400 MHz, δ in ppm): 11.92 (s, 1H), 11.28 (s, 1H), 8.71 (s, 1H) 7.64 (d, J=7.32 Hz, 1H), 7.35 (t, J=7.76 Hz, 1H), 6.9 (m, 2H), 2.18 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz, δ in ppm): 162.16, 156.78, 155.15, 131.33, 120.33, 40.22, 40.02, 39.81, 11.70, 9.85

164.60, 161.23, 159.25, 155.24, 133.55, 131.71, 120.07, 118.96, 116.94, 13.48, 9.89. Elemental analysis: Found: C, 59.93; H, 5.99; N, 15.10. Calc. for $C_{11}H_{13}N_3O_2$: C, 60.27; H, 5.98; N, 19.16%; UV-Vis: λ_{max} (DMSO)/ nm: 294, 338.

*1.2. Synthesis of **H2**:*

Diacetylmonoxime (200 mg, 2 mmol) was dissolved in 30 mL of ethanol in a 100 mL round bottom flask. To the solution, 2-hydroxybenzohydrazide (300 mg, 2 mmol) was added and the solution was refluxed overnight with continuous stirring. The resultant solution was evaporated in vacuum which yield 367 mg **H2** as white solid.

Yield: 78 %; m.p.: 276-279 ºC; FT-IR (ν_{max}/cm^{-1},KBr): 3283 (w), 3104 (br), 2717(m), 2575(m), 1927(w), 1811(w), 1651(s), 1547(s), 1495(w), 1452(s), 1373(s), 1299(s), 1227(s), 1150(s), 1101(w), 1023(m), 985(w), 944(s), 828(w), 745(s), 619(s), 565(m), 503(m), 456(m), 414(w); ^{1}H NMR (DMSO-d_6, 400 MHz, δ in ppm): 11.69(s, 1H) , 11.59(s, 1H), 11.28(s, 1H), 7.94-7.92 (d, J = 7.96 Hz, 1H), 7.73(s, 1H), 7.38-7.36 (d, J = 7.16 Hz, 1H), 6.98-6.92 (m, 1H), 2.22-2.12(d, J =39.68, 3H), 2.09-1.99 (d, J = 36.52, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz, δ in ppm) : 162.16, 156.78, 155.15, 131.33, 120.33, 40.22, 40.02, 39.81, 11.70, 9.85; Elemental analysis:Found: C, 56.28; H, 5.22; N, 17.77% Calc. for $C_{11}H_{13}N_3O_3$: C, 59.15; H, 5.87; N, 18.83%; UV-Vis: λ_{max}(DMSO)/ nm280, 375.

1.3. Anion binding study:

The quantitative anion binding study was performed with the help of UV-Vis spectroscopy as DMSO solution. The receptor **H** solutions were titrated by adding known quantities of concentrated solution of the anions in question. The anion solutions used to effect the titrations contained the receptor at the same concentration as the receptor solutions into which they were being titrated so as to nullify the dilution effect. After getting the absorption data, the binding constant is evaluated by using Connor equation:

$$\frac{[A-A_0]}{b} = \frac{S_t K_a \Delta\varepsilon [L]}{1+K_a[L]}$$

where $A_\circ$, A: Measured absorbance of the substrate in absence and in presence of guest; S_t: Total host concentration (M); $[L]$: Guest concentration (M); K_a: Binding constant (M^{-1}); $\Delta\varepsilon$: Molar absorptivity of the host-guest solution, b: Path length.

The corresponding Benesi-Hildebrand plot is

$$\frac{1}{[A-A_0]} = \frac{1}{S_t K_a b \Delta\varepsilon [L]} + \frac{1}{S_t b \Delta\varepsilon}$$

From the ratio of the slope and intercept of the Benesi-Hildebrand plot the binding constant K_a can be evaluated.[15]

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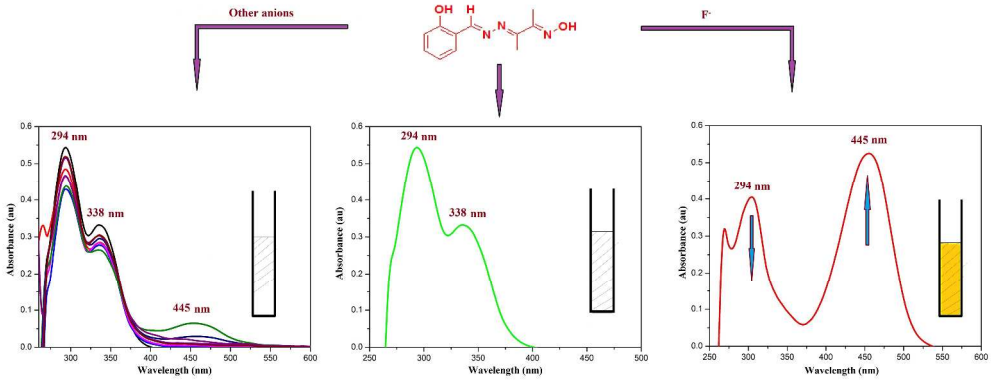

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