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PII: S0040-4039(13)01342-7
DOI: http://dx.doi.org/10.1016/j.tetlet.2013.08.005
Reference: TETL 43362

To appear in: *Tetrahedron Letters*

Received Date: 18 June 2013
Revised Date: 29 July 2013
Accepted Date: 1 August 2013

Please cite this article as: Vinithra, G., Suganya, S., Velmathi, S., Naked eye sensing of anions using thiourea based chemosensors with real time application, *Tetrahedron Letters* (2013), doi: http://dx.doi.org/10.1016/j.tetlet.2013.08.005

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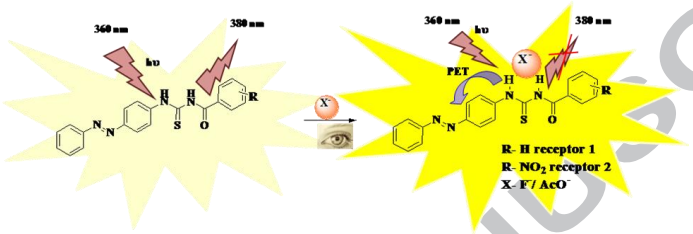

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Naked eye sensing of anions using thiourea based chemosensors with real time application

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Azo linked thiourea
F^- and AcO^- ions
Naked eye sensing
Real sample analysis
Fluorescence quenching

ABSTRACT

Novel chromogenic sensors with thiourea moiety as receptor unit were synthesized and characterized using IR and NMR spectroscopic techniques. The receptors **1** and **2** bearing hydrogen bonding site demonstrate visually striking colour change, UV-Vis, and fluorescence responses for F^-, AcO^- and OH^- over other anions such as Cl^-, Br^-, $H_2PO_4^-$ and HSO_4^-. Both the receptors **1** and **2** demonstrate detection limit at micro molar level. Further insight to the nature of interaction between receptors and anions was studied using ^{1}H NMR titration experiment. In particular, the fluoride of tooth paste and mouthwash in water phase can be detected by receptor **2**.

Chemosensors provide a powerful method for studying molecular recognition and thus they have wide application in biological, environmental, clinical as well as industrial, chemical processes.[1-3] The development of chromogenic receptors for anion sensing is a relatively new area of research in supramolecular chemistry.[4-5] Indeed, designing a colorimetric anion sensor is a challenging one as it allows 'naked eye' detection without the aid of sophisticated probes. Fluoride is attracting huge interest, as it is a biologically important anion that shows beneficial effect in human physiology such as prevention of dental caries, treatment of osteoporosis[6] etc. Similarly acetate also plays a major role in daily life because carboxylates are critical components in numerous metabolic processes[7] and is present in living system as acetyl coenzyme and also used as a food additive. Initially, anion recognition was mainly achieved by using charged host molecules, such as protonated polyamines or azamacrocycles[8] guanadinium[9] or transition metal or lanthanide ion based complexes[10]. More recently, neutral receptors such as amides,[11] carbamides[12], urea and thioureas[13], amidoureas[14] as well as pyrroles[15], indoles[16], calixpyrroles[17] and catechols[18] have been employed as recognition moieties for anions. The use of such versatile synthetic functionalities has enabled the design and construction of more refined anion receptors, which facilitates a more effective targeting approach to anion sensing using arrays of hydrogen bonding sites, where both the selectivity and the sensitivity of the recognition process can be achieved[19]. The motive of choosing sensor studies with receptor possessing thiourea as binding site is to establish the fact that small synthetic molecule could act as efficient chemosensors. Moreover, thiourea moiety is often chosen as anion binding site as it is a good hydrogen bond donor and forms quite stable complexes with anions like fluoride and acetate. Therefore, a large number of anion receptors containing the thiourea subunits have been designed, synthesized and tested for anion recognition and sensing during the past decades[20]. But simple thiourea does not act as a visual sensor, in order to make them do so some signaling unit or chromophore bearing group which imparts colour change has to be tailored with thiourea moiety on either side. Sensitivity at lower equivalent can be achieved only by integrating thiourea moiety with bulkier group which in turn require multistep synthesis which is very cumbersome.[14,21-22] Thiourea moiety linked with simple signaling unit are also known,[23-25] however sensitivity and selectivity is achieved only at higher equivalent. Accordingly development of simple, small, synthetic molecule which is sensitive enough to anions at lower amount is still a challenge. Here we have introduced thiourea based chemosensor prepared in a one- pot synthesis method, which can be efficiently used for sensing anions at low concentration and further use in real sample analysis.

The chromogenic receptors **1** and **2** were prepared by simple two-step, one- pot synthesis method and the structure was confirmed using FTIR and NMR spectroscopy. The formation of thiourea was confirmed from the singlet peak formed in the region 12.8 and 9.4 ppm in ^{1}H NMR spectrum and a band at 3394 cm^{-1} in IR spectrum. (For details see supporting information).

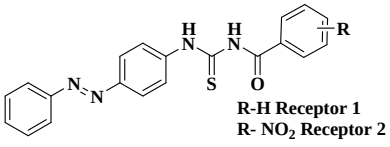

Figure 1. Structure of **1** and **2**

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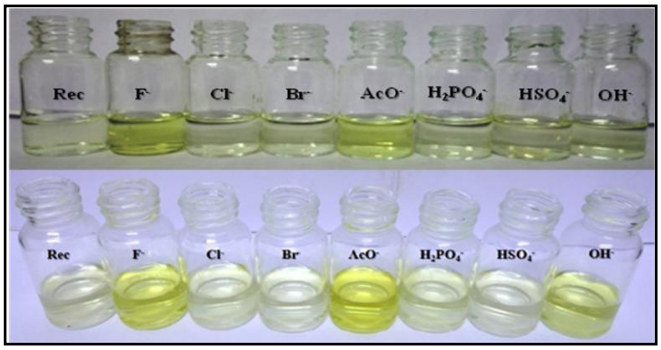

Figure 2. Color changes of receptor **1** (top) receptor **2** (bottom) in ACN (2.5 x 10^{-5} M) before and after the addition of four equivalents of respective anions.

To inquest the recognition behavior of the receptors, naked eye detection experiment was carried out by addition of acetonitrile (ACN) solution of 1.5x10^{-3} M of various anions such as F^-, Cl^-, Br^-, AcO^-, HSO_4^-, $H_2PO_4^-$, OH^- (tetrabutyl ammonium was used as the counter cation) to the solution of receptors (2.5x 10^{-5} M). The dramatic color change of receptor **1** from pale yellow to intense yellow upon the addition of F^- and AcO^- ion solution was clearly observed visually even on addition of four equivalents. Similar color changes were also observed upon introducing F^-, AcO^- and OH^- to ACN solution of receptor **2**. Both the receptors were found to be insensitive to large excess addition of other anions (Figure 2). The color change clearly suggests the formation of anion complexes of receptors via hydrogen bonding. The color change is more visible to receptor **2** than receptor **1**, which specifies the presence of NO_2 group as chromogenic signaling subunit[26].

The anion binding ability of receptors (2.5 x 10^{-5} M) in ACN with tetrabutyl ammonium salts of various anions (1.5 x 10^{-3} M) were investigated using UV-Vis titration experiment. The electronic spectra in the absence of anions was dominated by two bands, one at 283nm (receptor **1**) and 289nm (receptor **2**) which is assigned to the excitation of π electron in the aromatic system and another band at 350nm. Upon addition of only F^- and AcO^- ions to receptor **1** resulted in the intensity of the absorbance band at 283 nm decrease gradually with concomitant increase with red shift in the absorbance band at 350nm(Figure 3).

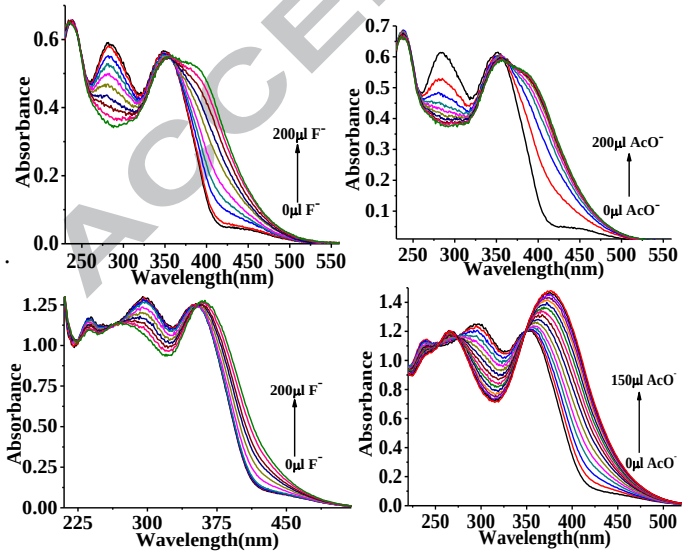

Figure 3. The UV-Vis absorption spectrum of receptor **1** (top) **2** (bottom) (2.5 x 10^{-5} M in ACN, 3ml) on incremental addition of F^-(left) and AcO^-(right).

The binding constant of the anion complexes of receptor **1** and **2** were calculated using Benesi- Hildebrand (B-H) plot from the variation in the absorbance in the region around 390-420nm. The binding constants for F^- and AcO^- complexes of receptor **1** were determined to be 1.22x10^4 and 2.59x10^4 respectively, whereas for F^-, AcO^- and OH^- complexes of receptor **2** were found to be 9.58x10^3, 1.96x10^3 and 3.02x10^3 respectively. The binding constant of receptor **1** is higher than that of receptor **2**, and this indicates that nitro group in receptor **2** does not show any influence on binding constant. Job's plot study revealed that receptor **1** and **2** forms complex in the ratio 1:1 with respective anions. Detection limits were calculated using the absorbance obtained on incremental addition of individual anions with fixed concentration of receptors at 2.5 x 10^{-5} M (Table 1).

	Detection limit (in M)		
Receptor	**F^-**	**AcO^-**	**OH^-**
1	5.36x10^{-7}	2.94 x 10^{-5}	-
2	3.43x10^{-6}	6.58 x 10^{-6}	5.92 x10^{-7}

Table 1. Detection limit of various anions with receptor **1** and **2**

This shows that the receptors are sensitive enough to monitor quantity of F^-, AcO^- and OH^- in micro molar level.

The emission properties of these receptors were explored to establish if the changes in absorbance spectra could be observed through the emission spectra, Figure 4 shows the fluorescence spectra recorded from solutions of receptor **1** and **2** (2.5 x 10^{-5} M) in ACN in the presence and absence of various anions. The free receptor **1** exhibited a band centered at 412nm (λ_{ex} = 360nm) on introducing only four equivalents of F^- and AcO^- ions, which resulted in the noticeable quenching of the fluorescence emission. In the case of receptor **2** fluorescence band with emission maxima at 416nm quenched dramatically on addition of F^-,AcO^- and OH^-. The quenching is endorsed to photo induced electron transfer (PET) mechanism[27]. The excited state of the fluorophore was not quenched by electron transfer from the receptor (thiourea group) to the fluorophore (azophenyl group), prior to the receptor–anion interactions. However, upon interaction with anions, electron transfer from the electron-rich thiourea moiety bonded with the anion to the electron deficient azophenyl signaling unit became more feasible. Upon further addition of F^- and AcO^- the deprotonated species, which was more electron-rich than the hydrogen-bonded complex with anion, activated the PET process more efficiently and supported more quenching. The possible mechanism is shown in Scheme 2 (supporting information). The quenching constant was calculated from the measurement of fluorescence intensity of the receptors both in presence and absence of F-, AcO^- and OH^- ions. (Table 2).

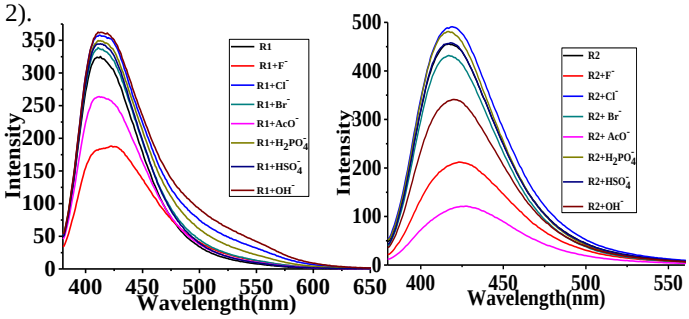

Figure 4. The fluorescence change of receptor **1** (left) and **2** (right) (2.5 x 10^{-5} M in ACN) upon addition of four equivalents of respective anions (1.5 x10^{-3}M in ACN).

	Quenching constant		
Receptor	**F^-**	**AcO^-**	**OH^-**
1	6.1x10^3	2.120x10^3	-
2	1.5941x10^4	2.4503x10^4	2.379x10^3

Table 2. Quenching constant of various anions with receptors **1** and **2**

To get the insight into the binding mode of receptor **2** with F^- and AcO^- ,^{1}H NMR titration experiments were then performed in DMSO-d_6. It was found that the intensity of thiourea N–H signal at 12.5 and 12 ppm broadens on addition till one equivalent and disappears entirely on further addition and slight shielding in the

aromatic protons is also observed. These observations indicate that the deprotonation process of thiourea N–H segments is involved in the receptor's interaction with F^-/AcO^- through hydrogen bonding (Figure 5). With the output of all the spectroscopic titrations, mechanism was proposed behind the anion sensing nature of both receptors **1, 2** (Figure 6).

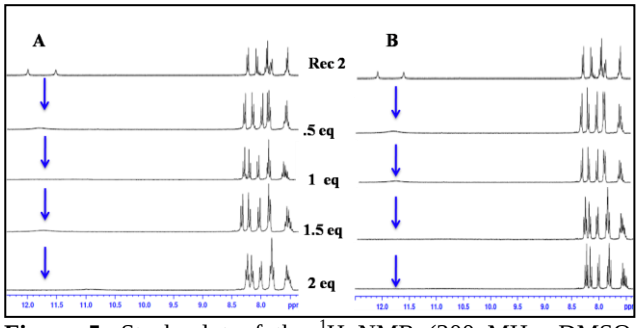

Figure 5. Stack plot of the ^{1}H NMR (300 MHz, DMSO-d_6) spectra of receptor **2** upon addition of 0.5, 1, 1.5 and 2 equivalents of F^- (A) and AcO^- (B).

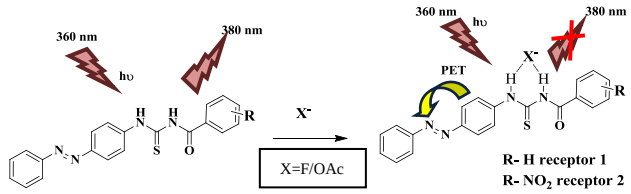

Figure 6. Proposed mechanism of receptors **1**, **2** with F^-/AcO^- ions.

Commercially available toothpaste and mouthwash which contain fluoride was used to investigate the efficiency of receptor **2** as real time sensor. 100mg of tooth paste was made into solution with 5ml H_2O and used for colorimetric analysis[28] and mouth wash was used as such. To our surprise on adding only 50µl of toothpaste solution and mouthwash into the receptor **2** resulted in an excellent colour change (Figure 7), which was further proved from the quenching of fluorescence and changes in absorption spectrum (supporting information).

Figure 7. Colorimetric changes of receptor **2** with toothpaste (A) and mouthwash (B).

Mostly, thiourea based receptors consisting of electron withdrawing substituents such as $–NO_2$, -Cl, -Br, are used as anion sensor to enhance the acidity of NH unit.[29] The additional importance of azo group is that it can give positive response even in the absence of any electron withdrawing substituent since azo phenyl itself can act as signaling unit and enhance the acidity of thiourea moiety. The newly developed small and azo linked thio urea compounds fortunately showed positive response in the real sample analysis.

To sum up, we have presented new colorimetric chemosensors **1-2**, which allow "naked-eye" detection in a straightforward and inexpensive manner. Further the anion recognition via hydrogen-bonding interactions was easily monitored by anion-complexation induced changes in UV–Vis fluorescence and NMR spectroscopic studies. In particular, the sensor has detected successfully fluoride of toothpaste and mouth wash and is expected to provide useful opportunities in detection of anions in real-life owing to the simplicity in the synthesis and sensitivity towards analytes.

Acknowledgments

Authors express their thanks to DRDO (ERIP/ER/1006004/M/01/1333 dated 23-05-2011) for financial assistance in the form of a major sponsored project

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Supplementary Material

General materials, methods, details for UV-Vis and fluorescent titrations spectroscopic data are available.