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A selective indole based chemosensor for fluoride ion detection

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The selective detection of anions via chemosensors have recently emerged as an important area of research due to their vital role in biological, chemical and environmental sciences. An efficient indole based chemosensor C**1** exhibiting selective detection of fluoride ions has been synthesized by condensation reaction of substituted indole derived Carbohydrazide **1** with substituted ethenone **2** and characterized by ^{1}H NMR and ^{13}C NMR spectroscopy. Chemosensor shows notable colorimetric changes from light yellow to greenish yellow, upon addition of fluoride ions. The absorption studies shows red shift in the absorption spectra upon titration with fluoride ions. The receptor–anion interaction occurs through hydrogen bonding followed by deprotonation of –OH proton. Chemosensor shows 2:1 stoichiometry as calculated from the Job's plot.

Keywords: Chemosensor, Colorimetric sensor, Fluoride detection, Indole, Schiff base condensation

Introduction

The selective detection of anions via chemosensors have recently emerged as an important area of research due to their vital role in biological, chemical and environmental sciences[1,2]. Amongst various strategy of anion detection, there exists an increasing interest in the synthesis of chemosensors with colorimetric response. A wide variety of chemosensors have been designed utilising various building blocks such as amide, carbazole, dipyrrolyl derivatives, thiazole, urea, thiourea, sulfonamide etc.[3-9]. Among various anions, the recognition of fluoride ions is of significant interest due to its long association with a diverse array of biological, medical, and technological processes[1]. Fluoride is required for our body in optimum concentration to prevent dental cavities and osteoporosis. Excess amount of fluoride can cause fluorosis, gastric and kidney problems[2]. Commonly used fluoride-detecting methods are the colorimetric (UV) and fluorimetric sensing, the electrode method and ^{19}F NMR analysis.[1]

Indole, an aromatic building block, contains benzenoid nucleus with 10 π-electrons which makes indole based scaffolds significant for various medicinal, material and sensing applications[10-14]. Indole derivatives have been reported to detect various anions through H-bonding or deprotonation,[14,15] which encouraged us to develop a low cost indole based chemosensor for fluoride ion detection with high senstivity and selectivity.

In this work, we report the synthesis, and properties of the indole-based chemosensor **C1** (*E*)-*N*-(1-(2-hydroxy-5-methylphenyl)ethylidene)-5-methyl-3-phen yl-1*H*-indole-2-carbohydrazide. The chemosensor **C1** was synthesized via condensation reaction of 5-methyl-3-phenyl-1*H*-indole-2-carbohydrazide **1** with 1-(2-hydroxy-5-methylphenyl) ethenone **2**. The chemosensor **C1** acts as colorimetric sensor for fluoride ions with high selectivity and sensitivity.

Experimental Section

General information

Chemicals were procured from Sigma-Aldrich and used as such. HPLC grade solvents were procured from Spectrochem, India and used as such. The NMR spectra were recorded using Bruker, Avance II (400 MHz) spectrometer. Multiplicities of resonance are reported as s (singlet), d (doublet), and m (multiplet). Perkin Elmer UV-visible absorption spectrometer (Lambda 365) was used to record the absorption spectra.

Synthesis of target chemosensor C1 and characterization

The ethanolic solution of 1-(2-hydroxy-5-methylphenyl)ethenone **2** (1.2 mmol) was added to the ethanolic solution of 5-methyl-3-phenyl-1*H*-indole-2-carbohydrazide **1** (1.2 mmol) with subsequent addition of sodium polyacrylate and 2-3 drops of H_2SO_4. The solution was refluxed for 3 h. The reaction mixture was cooled to room temperature, filtered and the precipitate was dried and recrystallized from ethanol to afford **C1** as pale yellow crystalline solid (Scheme 1). Yield 82%; ^{1}H NMR (DMSO-d6, 400 MHz) δ 12.78 (s, 1H), δ 11.94 (s, 1H), δ 10.15 (s, 1H), δ 7.54-7.52 (m, 4H), δ7.43-7.41 (m, 2H), δ7.34-7.30 (m, 1H), δ 7.28 (s, 1H), δ 7.13 (d, 1H), δ 7.08 (d, 1H), δ 6.77 (d, 1H) , δ 2.37 (s, 3H), δ 2.23 (s, 3H), δ 1.90 (s, 3H); ^{13}C NMR (DMSO-d6, 100 MHz): δ 12.49, 20.11, 21.16, 112.15, 116.99, 118.75, 119.18, 126.27, 127.01, 127.18, 128.38, 128.72, 129.21, 130.21, 131.85, 133.77, 134.32, 155.84, 156.17.

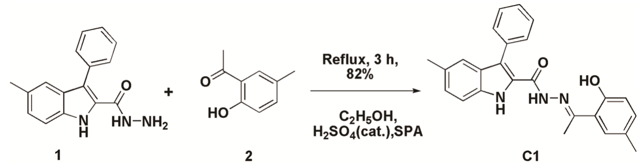
Results and Discussion

The synthesis of indole-derived chemosensor **C1** is shown in Scheme 1. Intermediate **1** was prepared using reported procedure[17-18]. The Schiff base reaction of compound **1** with 1-(2-hydroxy-5-methylphenyl) ethanone **2** resulted chemosensor **C1** in 82% yield. The chemosensor **C1** was characterized by ^{1}H and ^{13}C NMR. The chemosensor **C1** showed good solubility in common organic solvents.

The colorimetric detection of anions by chemosensor **C1** has been explored by addition of various anion to a fixed concentration of the **C1** in DMF. The addition of fluoride ion (10^{-3} M) to the stock solution of chemosensor **C1** resulted in naked-eye detectable colour change from colourless to yellow. However, no detectable colour change was observed upon addition of other anions (F^-, Br^-, Cl^-, I^-, ClO_4^-, NO_3^-, HSO_4^- and PF_6^-) under similar experimental condition. The naked eye colour change for chemosensor **C1** upon addition of fluoride ions at various concentration is shown in Fig. 1.

The absorption spectra of chemosensor **C1** in DMF shows two bands at 317 and 344 nm. The binding affinities of chemosensor **C1** were investigated in the presence of TBA salts of various anions (F^-, Br^-, Cl^-, I^-, ClO_4^-, NO_3^-, HSO_4^- and PF_6^-) by using UV-visible absorption spectroscopy in DMF.

Upon titration of chemosensor **C1** with increasing concentration of fluoride ions, a regular decrease in intensity was observed for the absorption bands at 344 nm and 317 nm and a new red shifted band at 393 nm gradually appears (Fig. 2). An isosbestic point at 368 nm was observed which indicates the formation of complex between chemosensor **C1** and F^- ion, and the presence of equilibrium between the reactants and the product complex.



Scheme 1 — Synthesis of chemosensor **C1**

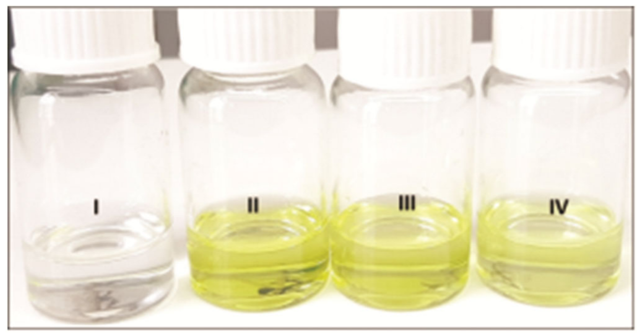


Fig. 1 — Colour changes of chemosensor **C1**(66 µM in DMF): (I) Blank (II) 10^{-2} M (III) 10^{-3} M, and (IV)10^{-4} M solution of F^- ions in DMF

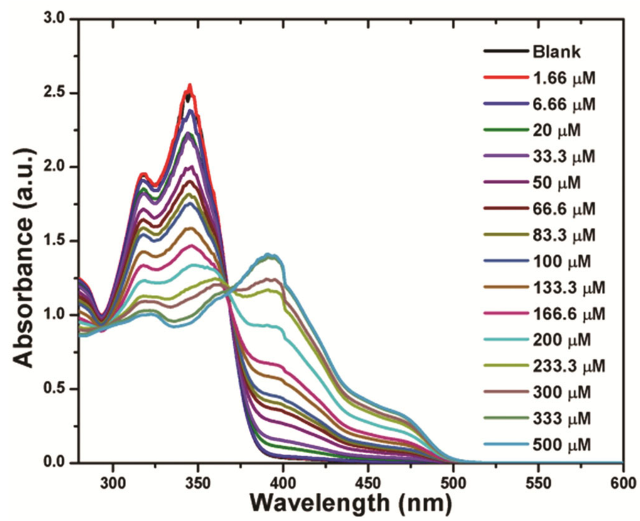


Fig. 2 — UV–visible absorption spectra of chemosensor **C1** (66 µM) upon titration with F^- ion in DMF

The calibration curve was constructed by plotting absorbance at 393 nm against concentration of fluoride ions (Fig. 3). A good linearity was observed from 1.66 µM to 200 µM concentration of fluoride ions with a limit of detection (LOD) value of 1.02 µM. The LOD values was calculated using the

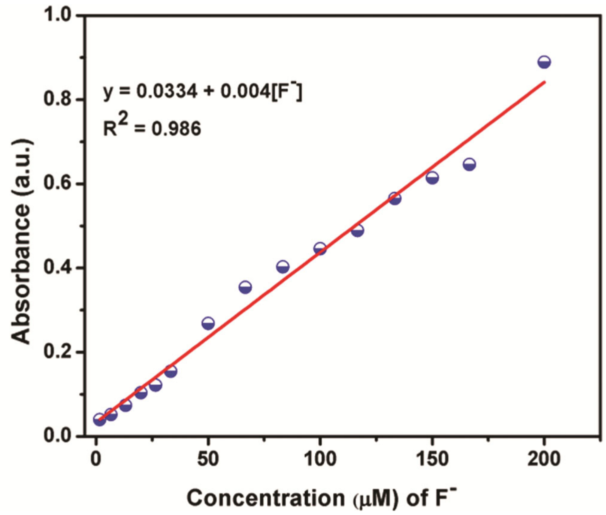


Fig 3 — Calibration curve as constructed from UV-visible absorption studies by plotting absorbance at 393 nm vs concentration of F^- ions

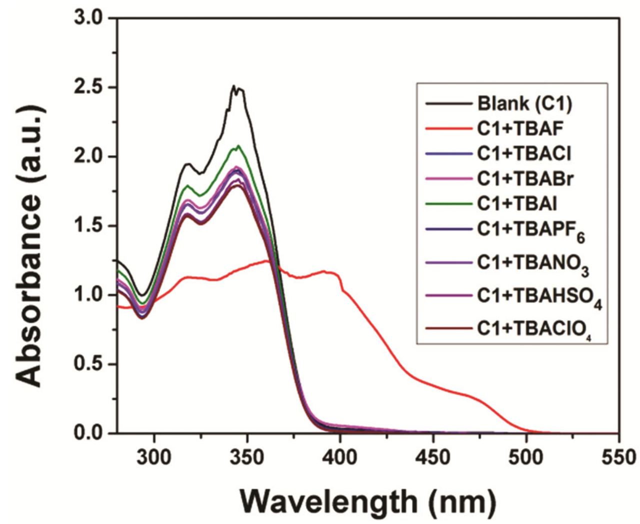


Fig. 4 — UV-visible spectra of chemosensor **C1** in presence of 200 µM TBA salt of various anions in DMF

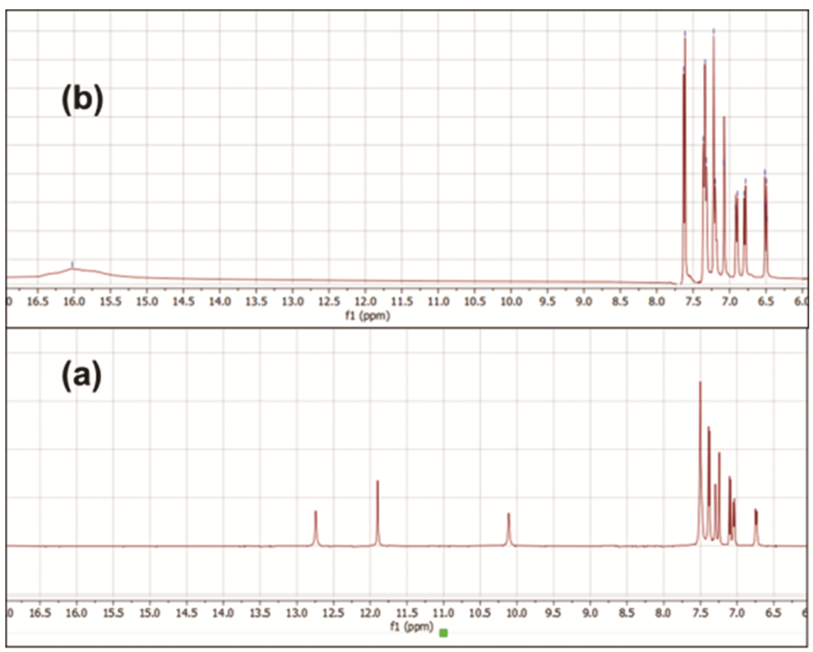


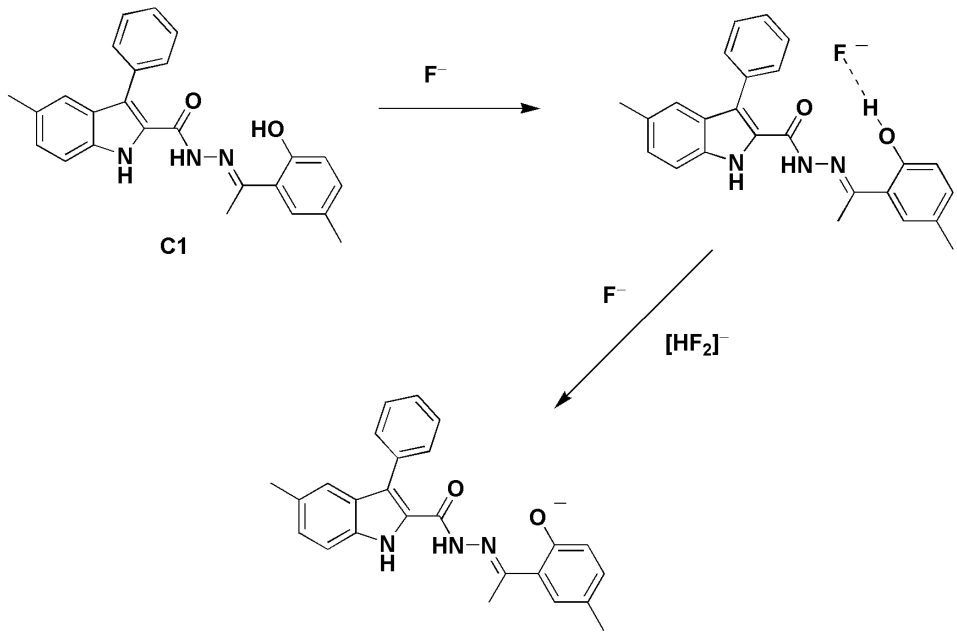
Fig. 5 — ^{1}H NMR spectra of chemosensor **C1** in DMF (a) Absence of TBAF and (b) in presence of excess (4 equivalent) of TBAF

formula LOD= 3σ/n; where σ represents the standard deviation for blank response and n denotes the slope of the calibration curve[19].

The sensitivity of chemosensor **C1** towards other anions (Br^-, Cl^-, I^-, NO_3^-, HSO_4^-, ClO_4^-, PF_6^-) under similar experimental condition is shown in Fig. 4. The UV-visible spectra does not show any considerable change upon addition of TBA salts of Br^-, Cl^-, I^-, NO_3^-, HSO_4^-, ClO_4^-, PF_6^-. Though the peak intensity gets slightly decreased (which may be attributed to dilution effect), the UV-visible pattern of chemosensor C1 remain same (except F^- ion) in presence of the aforementioned ions. Thus chemosensor **C1** shows strong selectivity for fluoride ions.

^{1}H NMR titration of chemosensor **C1** was carried out with fluoride ions to explain the binding mechanism (Fig. 5). Chemosensor **C1** exhibits the signals at δ 12.78, δ 11.94 and δ 10.15 corresponding to –OH and –NH protons (Fig. 5a)[20,21].

The signals due to –OH and –NH protons disappeared while a new signal at around δ 16.0 was observed upon



Scheme 2 — Proposed mechanism for F^- ion sensing with chemosensor **C1**

addition of excess of F^- ion, due to the formation of $[HF_2]^-$ ion (Fig. 5b)[6, 20]. This can be attributed to the deprotonation of the –OH proton (Scheme 2).

Conclusion

In summary, we have successfully designed and synthesized an indole based chemosensor **C1** which serves as highly selective robust colorimetric sensor for fluoride ions. The anion detection ability of the chemosensor **C1** has been validated by naked-eye detection, UV-visible titrations and ^{1}H NMR titrations. Chemosensor **C1** shows low limit of detection (LOD=1.02 μM) values in micromolar range with high selectivity towards fluoride ions. The current studies can be beneficial for designing indole based fluoride ion sensor.

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