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A new colorimetric sensor based on semithiocarbazone for some anions: 2-(1,3-dioxo-1,3-dihydro-*2H*-inden-2-ylidene)-N-phenylhydrazine-1-carbothioamide

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Keywords:
4-Phenylsemithiocarbazide,
Ninhydrin,
Anion receptor,
UV-Vis titration,
Naked eye

Abstract — Carbazones are molecules containing important functional groups in designing anion chemosensors due to proton donor and acceptor sites in their structures. In this paper, we synthesize a novel colorimetric receptor with 1,3-dioxo-indene and thiosemicarbazone moieties by the reaction of ninhydrin and 4-phenyl-thiosemicarbazide in quantitative yield. We then identify its structure by means of FT-IR, ^{1}H-NMR, ^{13}C-NMR, and MS spectroscopic techniques. Moreover, we observe the reaction of the title compound with biologically important F^-, OAc^-, CN^-, $H2PO4^-$, and OH^- anions in the presence of other anions, such as Cl^-, Br^-, I^-, SCN^-, and OCl^- in dimethylsulfoxide solution through a color change from yellow to orange-red that can easily be distinguished even by the naked eye under ambient light. Finally, we evaluate the anion-sensing ability of the title compound via UV-vis spectroscopic studies.

Subject Classification (2020):

1. Introduction

Anions are important in many medical, biological, and chemical processes [1,2]. One particular anion, fluoride, has been studied extensively for its role in preventing dental caries [3]. It is also being investigated as a treatment for osteoporosis, a kind of fluoride toxicity [4]. Acetate is essential in numerous metabolic processes [5]. Similarly, dihydrogen phosphate anion plays a key role in energy storage and signal transduction within the body [6]. However, cyanide is one of the most toxic anions and can harm the environment [7]. Besides, it is important in various industrial processes, such as gold mining, synthetic fibers, and resins [8].

Researchers have increasingly synthesized and applied new chemosensors in anion recognition system studies [9,10]. These studies focus on designing host molecules that selectively recognize and sense anion species [11]. Chemosensors use a chromophore to translate the receptor-anion association into an optical signal. Colorimetric chemosensors are attractive because they give a direct signal easily observed by the naked eye. It is widely used because it shows color changes that can indicate an event perceived with the naked eye, is low cost, and does not require much equipment. When designing an anion receptor, signaling subunit of synthetic anion receptors is generally important. Anion binding sites of receptors occur not only positively changed macrocyclic guanidinium [12], imidazolium [13]

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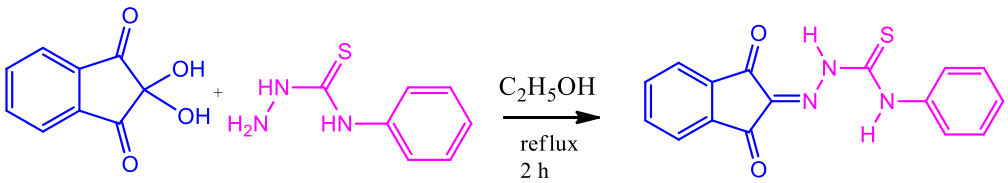
based on electrostatic interactions but also neutral H-bonding donor groups such as (thio)ureas [14–16] phenylhydrazone [17], indole [18], sulfonamide [19], functionalized calixarenes [20], Schiff bases [21], thiosemicarbazone [22], aromatics such as pyrrole [23], or BODIBY core [24], natural products [25] or particularly activated amides [26].

This study synthesized a novel receptor from ninhydrin and 4-phenyl-thiosemicarbazide (Scheme 1) and characterized using FT-IR, ^{1}H-NMR, ^{13}C-NMR, and MS spectroscopic techniques. The newly reported receptor was determined to contain both the –methylene-inden-1,3-dione and the thiosemicarbazone moiety. Since the title compound has active hydrogen atoms, their varying spectral responses in UV-vis absorption investigated the hydrogen binding with some anions. It was determined that the title compound showed sensitivity to F^- anion among halides and to OH^-, AcO^-, CN^-, and $H2PO4^-$ anions, anions of biological and environmental importance. The hydrogen binding of the title compound with anions was investigated by their spectral responses changed in UV-vis titration. In addition, a notable color change when adding these anions could also be observed by the naked eye.



(1)

Scheme 1. Synthesis of the 2-(1,3-dioxo-1,3-dihydro-2H-inden-2-ylidene)-N-phenylhydrazine-1-carbothioamide (**1**)

2. Experimental Section

2.1. Material and Methods

All synthesized and application reagents were purchased commercially and did not require further purification. An anions solution was prepared from tetra-n-butylammonium (TBAX) salts purchased from Argos, Sigma-Aldrich Chemical, in the titration experiments. These salts were stored in a vacuum desiccator before use. The melting point of the compound was determined using the Electrothermal 9100® apparatus. Elemental analysis was performed on a LECO, CHNS-932 Elemental Analysis instrument. The Infrared spectrum was recorded using a Perkin Elmer Spectrum-100 FT-IR instrument with an ATR apparatus in the range 4000-650 cm^{-1}. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a JEOL ECX-400 FT-NMR spectrometer operating at 400 and 100 MHz, respectively. UV-visible measurements were carried out with a Perkin Elmer WinLab-25 series spectrophotometer in quartz cells of 1 cm path length. LC-MS analysis was performed with Shimadzu LC-MS/MS 8040 liquid chromatograph mass spectrometer equipped with an electrospray ionization source. The compound was named following IUPAC rules via ChemDraw 12.0 program.

2.2. Synthesis of the 2-(1,3-dioxo-1,3-dihydro-2H-inden-2-ylidene)-N-phenylhydrazine-1-carbothioamide (1)

4-Phenylsemithiocarbazide (0.836 g, 5 mmol) in ethanol (20 mL) was added dropwise to a solution of ninhydrin (0.980 g, 5 mmol) in ethanol (20 mL), and the mixture was refluxed by rapidly stirring. The progress of the reaction was monitored by thin-layer chromatography (TLC) analysis on 0.25-mm silica gel plates, visualized under UV light (254 nm) and by using ethyl acetate solvent.

After the completion of the reaction, for 2 h, the solvent was removed by evaporation. The crude product was purified by flash chromatography on silica gel (1:1 tetrahydrofuran/ethyl acetate as eluent) to give **1** as an orange-red solid, mp. 186 °C, 1.266 g (82%) yield. Analytically calculated for **$C_{16}H_{11}N_3O_2S$:** C 62.12%, H 3.58%, N 13.58%, O 10.34%, and S 10.37%; **Found:** C 62.50%, H 3.26%, N 13.03%, O 10.74%, and S 10.47%; **FT-IR (cm^{-1}):** 3342 (N-H), 3289 (N-H), 3208, 3059 ($C_{aromatic}$-H), 1720 (C=O), 1684 (C=O), 1594 (-C=N), 1523 (C=S), and 751 (C=S); **^{1}H-NMR (400.2 MHz; DMSO-*d*$_6$; δ ppm):** 13.41 (s, 1H, =N–NH-C=S), 9.88 (s, 1H, –NH-ph), 8.56 (d, 2H, Ar–H), 8.49 (d, 2H, Ar–H), 7.97 (d, 2H, ph–H), 7.79 (t, 2H, ph–H), and 7.55 (t, 1H, ph–H); **^{13}C-NMR (100 MHz, DMSO-*d*$_6$, δ ppm):** 161.30 (C=S), 158.35 (C=O), 112.00 (C=N-), 142.21, 125.09, 124.37, 119.27 (ph-C), 139.72, 136.17, 125.72, and 124.63 (Ar-C) ppm; **MS:** m/z, found $[M]^+$ 309.00, calculated for $C_{16}H_{11}N_3O_2S$ $[M]^+$ 309.06.

3. Results and Discussion

3.1. Spectral Studies

The title compound as a receptor was synthesized by reacting compounds in ethanol (Scheme 1) and characterized by FT-IR as well as ^{1}H and ^{13}C-NMR spectroscopic methods and MS technique. The FT-IR spectrum of the title compound is given in Figure 1. Figure 1 shows strong and broad bands in the 3342.00 and 3289.58 cm^{-1} range due to two N−H symmetrical and asymmetrical stretching vibrations. The two C=O stretching bands appear at 1720.12 and 1684.95 cm^{-1}. The strong bands at 1523.58 and 751.11 cm^{-1} are assigned to thioureido N-C=S and C=S stretching vibrations, respectively. Besides, vibration bands with the wave numbers, 3208.17 and 3059.47 cm^{-1} (υ: C-H, Ar-H) and 1594.96 cm^{-1} (υ: C=C, Ar), are observed for a compound.

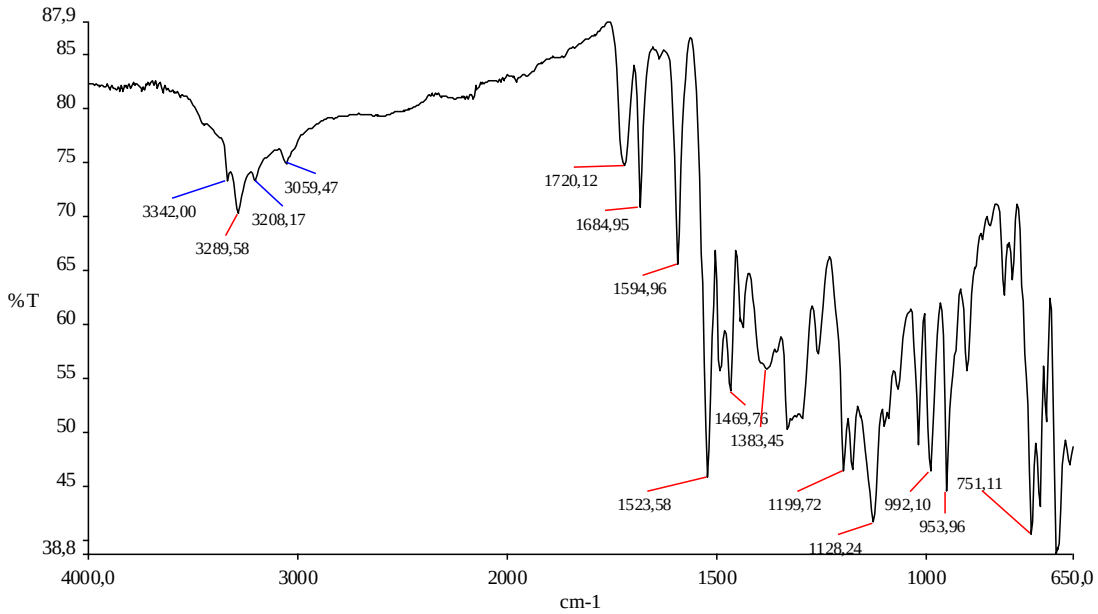


Figure 1. FT-IR spectrum of the compound (**1**)

In the ^{1}H-NMR spectrum, the broad signals at 13.41 and 9.88 ppm confirm the presence of two –NH protons. The peaks at 7.97, 7.79, 7.55 ppm and 8.56, 8.50 ppm show phenyl and inden-1,3-dione aromatic moieties protons, respectively (Figure 2, Scheme 2-a).

In the ^{13}C NMR spectrum, the peak at 161.30 ppm confirms the presence of the amide thiocarbonyl group. The peak at 158.35 ppm appears in the presence of keto carbonyl carbons. The peaks in the range of 119.27-142.21 ppm show aromatic carbons. The peak at δ: 112.00 ppm shows the presence of carbazide carbon (C=N-) (Figure 3, Scheme 2-b).

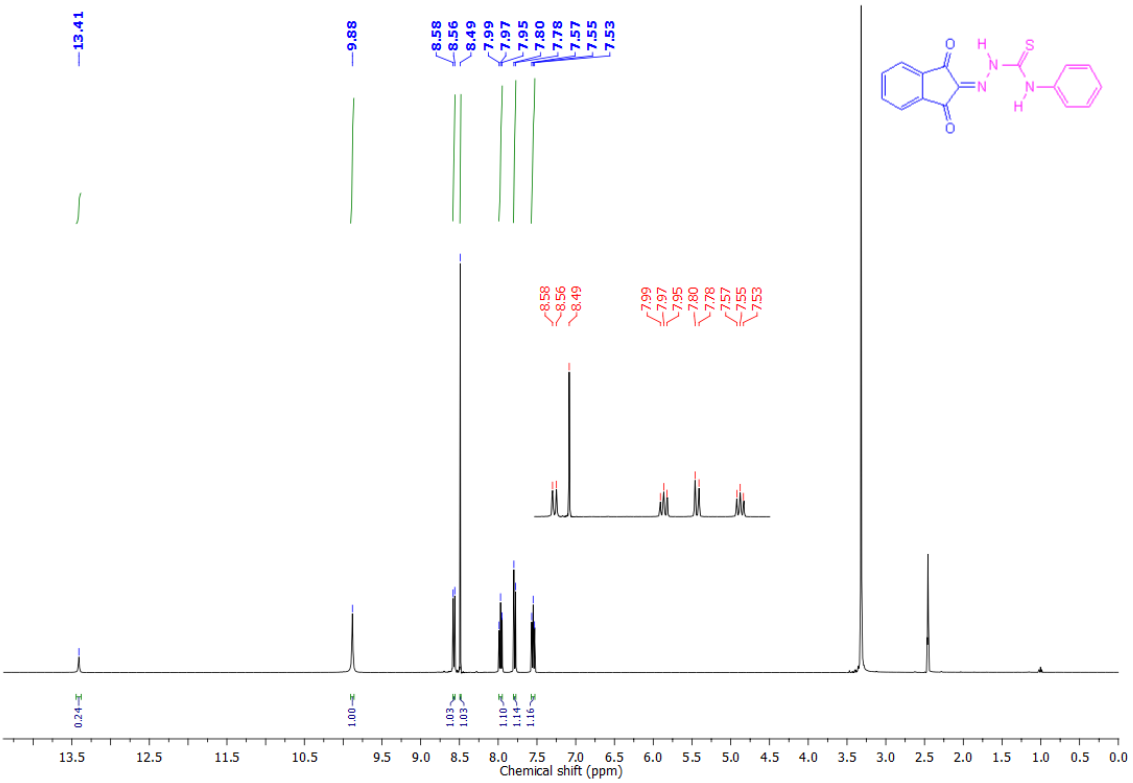


Figure 2. ^{1}H-NMR spectrum of the compound (**1**)

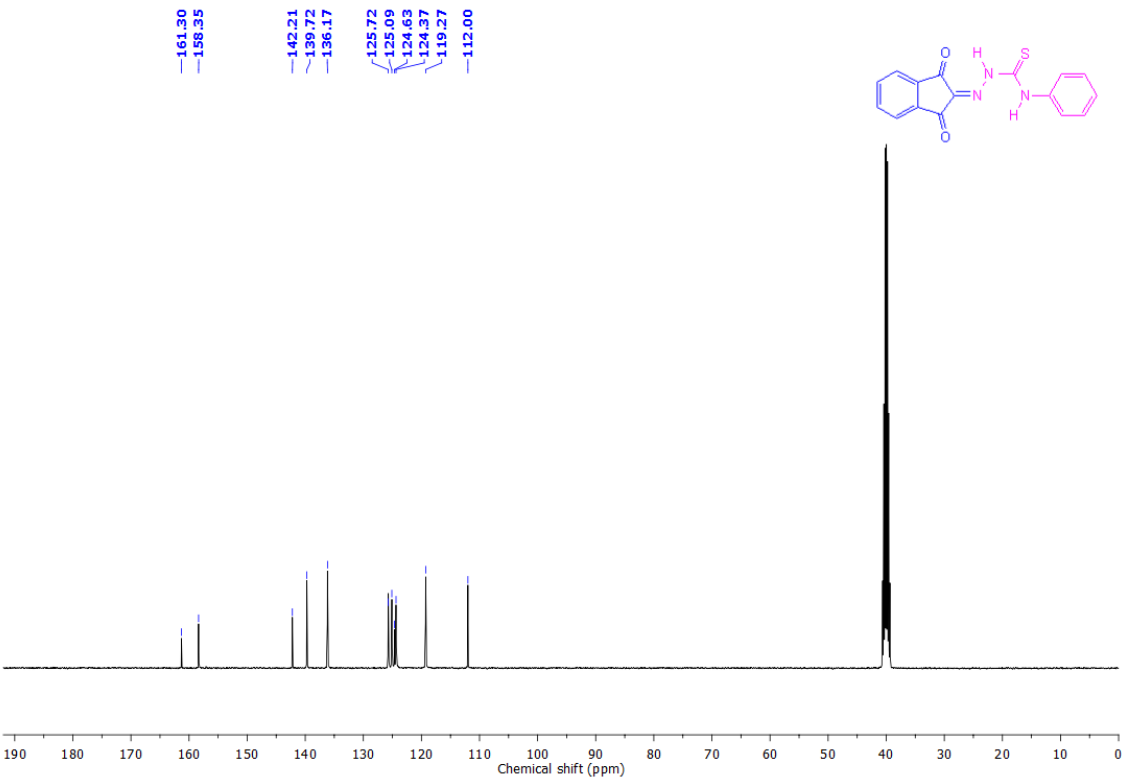
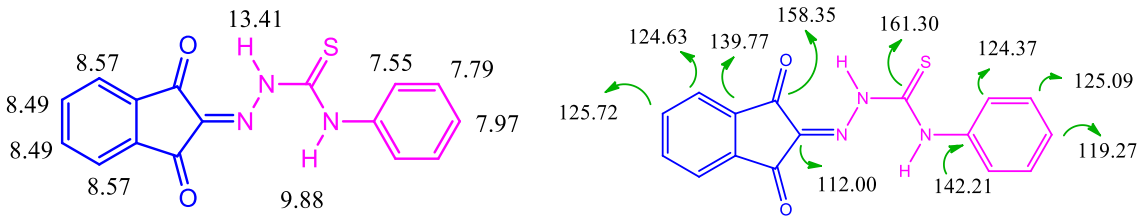


Figure 3. ^{13}C-NMR spectrum of the compound (**1**)



(**a**) (**b**)

Schema 2. ^{1}H-NMR and ^{13}C-NMR data for the compound (**1**)

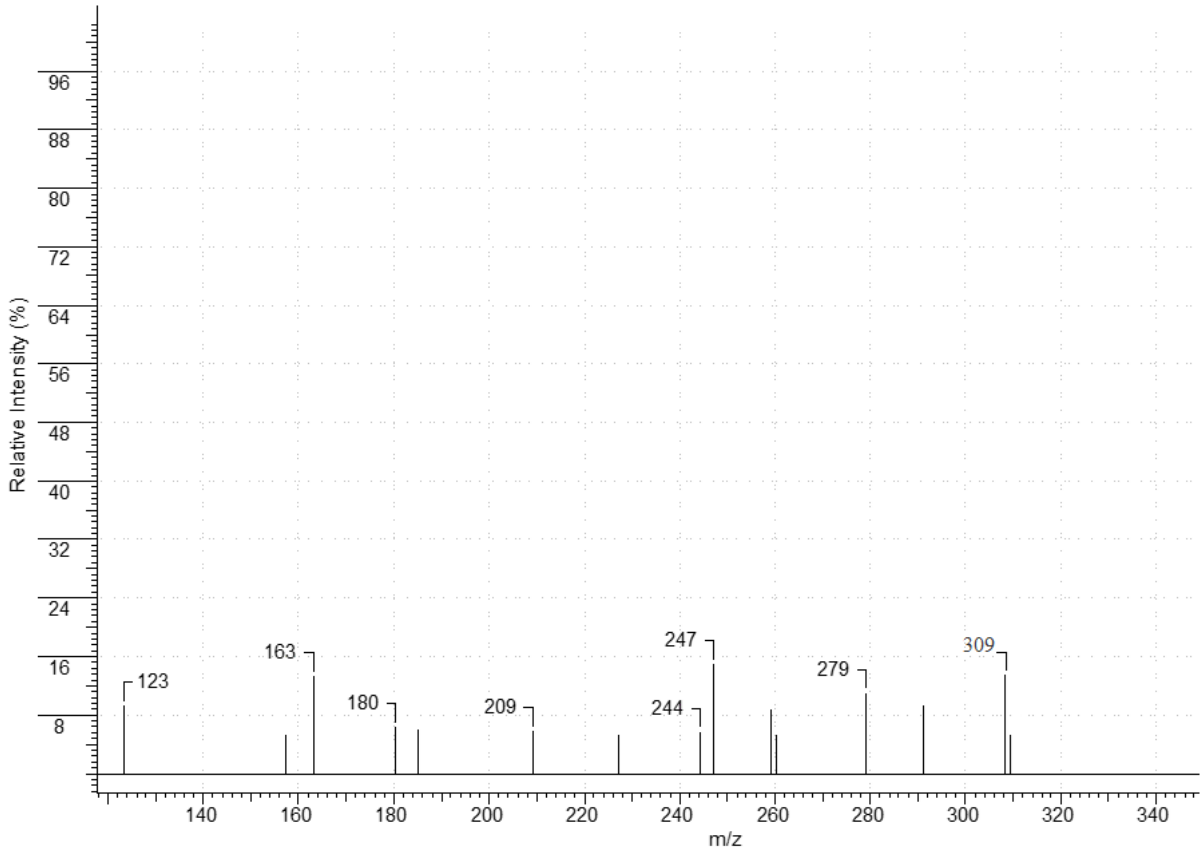
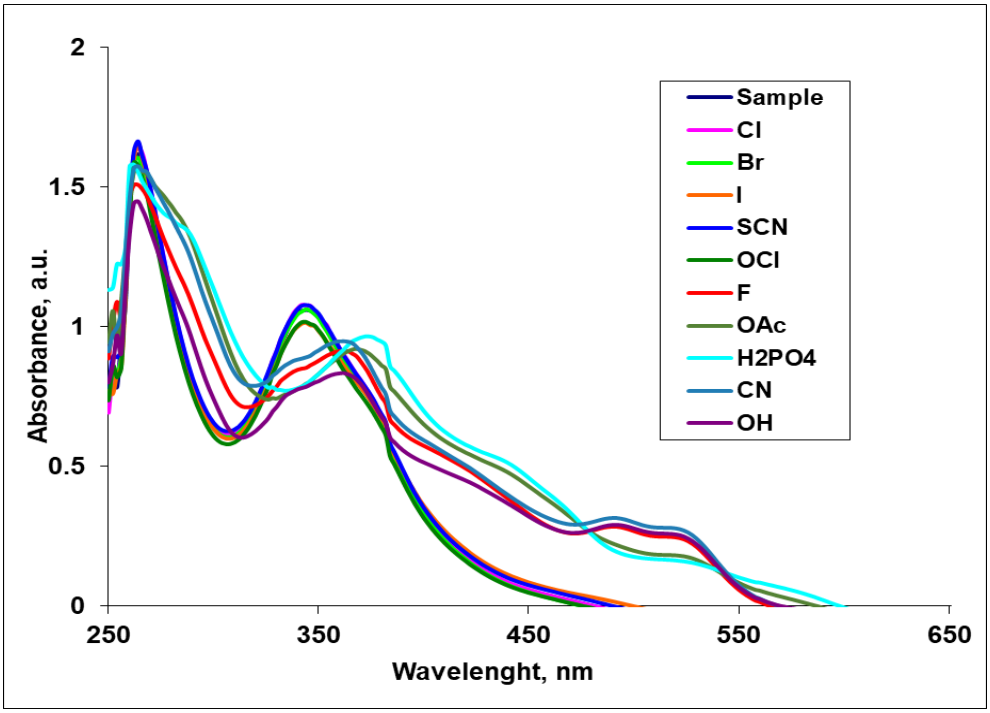


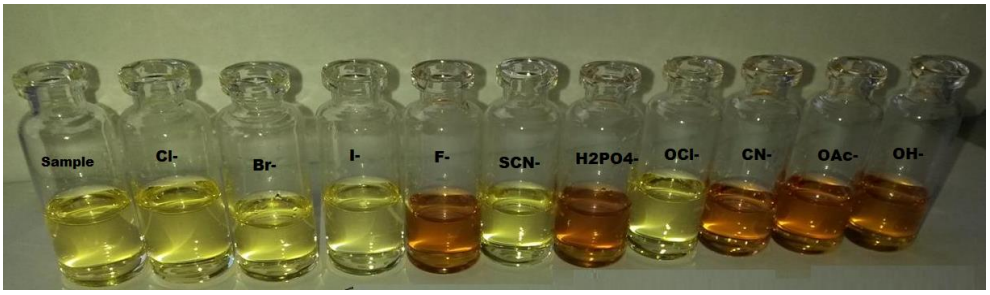
Figure 4. MS spectrum of the compound (**1**)

3.2. Colorimetric anion sensing

The sensing property of receptor (**1**) was first examined by mixing it with various anions as tetrabutylammonium salts in DMSO. Upon addition of various anions (F^-, Cl^-, Br^-, I^-, OAc^-, CN^-, $H_2PO_4^-$, SCN^-, OCl^-, and OH^-) to the DMSO solution of the title compound, it was also found that F^-, OAc^-, CN^-, $H_2PO_4^-$, and OH^- could induce significant changes in the UV-vis absorption spectra of a compound, as shown in Figure 5-a. However, the absorption spectra did not exhibit any change upon the Cl^-, Br^-, I^-, SCN^-, and OCl^-. The color change of receptor from yellow to orange-red upon the addition of F^-, OAc^-, CN^-, $H_2PO_4^-$, and OH^- was easily observed by the naked eye even at low concentration natural light and under a UV lamp (Figure 5-b, c).



(a)



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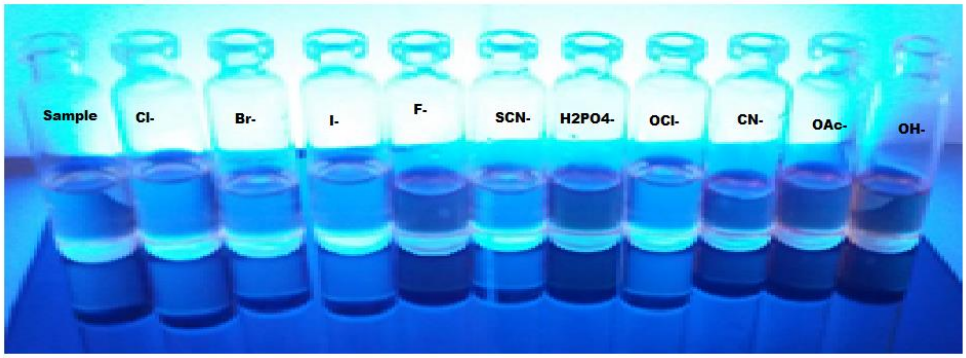

(c)

Figure 5. (a) UV-vis absorption spectrum of the compound (**1**), (b) naked-eye color change observed under natural light, (c) under a UV lamp, upon the addition of TBAX salts in DMSO solution left to right sample, Cl^-, Br^-, I^-, F^-, SCN^-, $H_2PO_4^-$, OCl^-, CN^-, OAc^-, CN^-, and OH^-.

At first, the band at 344 nm was progressively shifted to 494 nm upon titrations of F^- (0-1 equiv) and CN^-, OAc^-, $H_2PO_4^-$, and OH^- followed a very similar pattern to F^- in the titration (Fig 6a-e). Absorption values and exchange rates were investigated to evaluate the detection potential of anions with the title compound. The spectrum data plots the ratio of the absorption value at 494 nm to the absorption value at 344 nm (A494/A344) (Figure 6f). The title compound showed the largest ratiometric absorption value with the addition of $F^-$and CN^- and moderate value for OAc^-, $H_2PO_4^-$, and OH^-.

Thiosemicarbazone derivatives containing units such as isatin, anthracene and substituted benzene have also shown specific anion selective properties for similar anions [27-30].

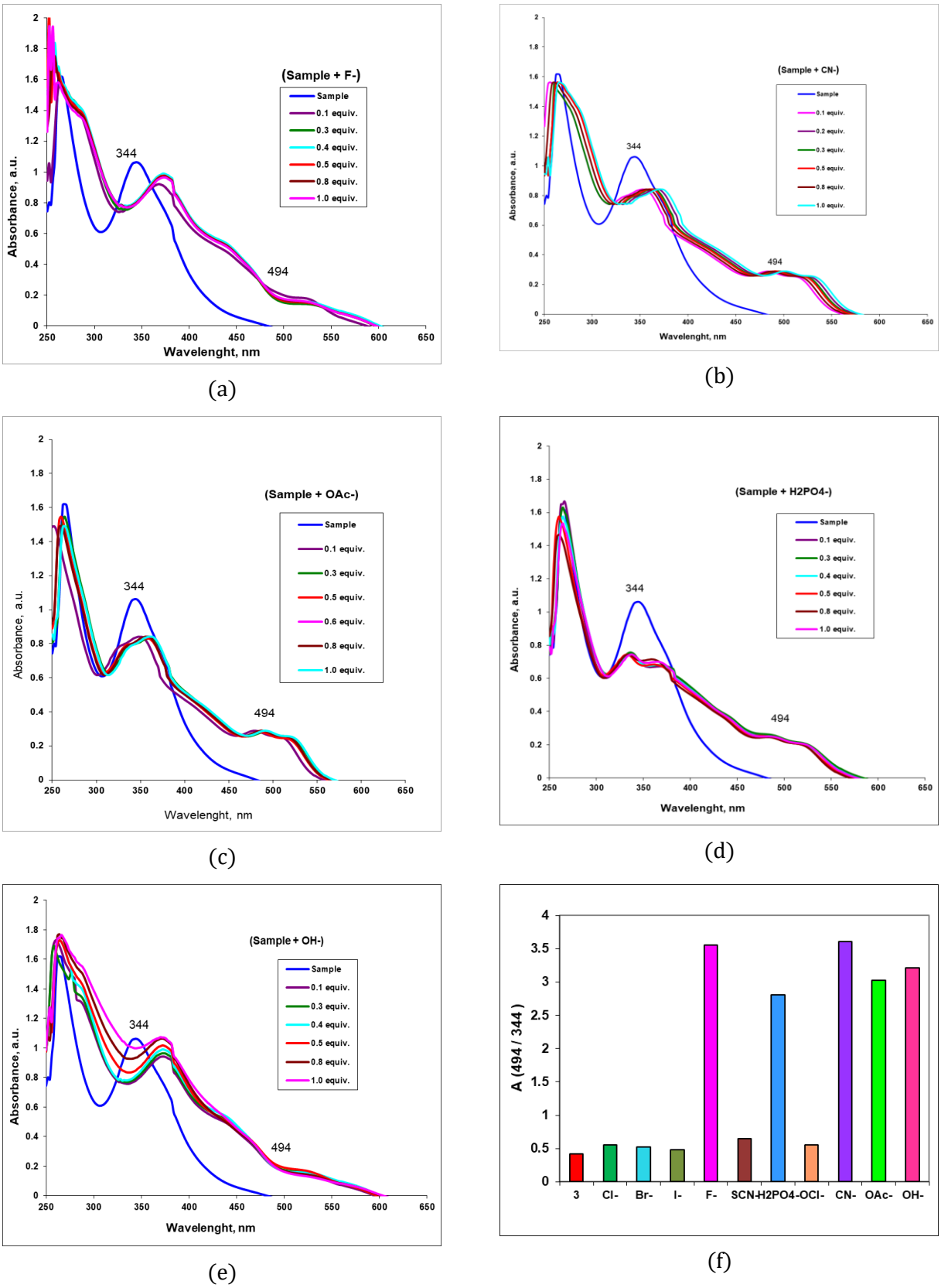

Figure 6. UV-vis spectra of the compound (**1**) (50 μM) upon the addition of increasing concentration of selective anions. (a) F^-, (b) CN^-, (c) AcO^-, (d) $H_2PO_4^-$ (e) OH^-, in DMSO solution, (f) ratiometric absorbance values (A_{494}/A_{344}) upon the addition of 1.0 equiv of various anions in DMSO solution.

3.3. Practical application to real sample analysis

In order to investigate the real application of probe towards the quantitative detection of fluoride anion in toothpaste and cyanide anion in natural sources like apple seeds, the applications were made. The apple seed contains a trace amount of cyanogenic glycosides. The apple seed sample was prepared from the reported procedure [31]. A sample of toothpaste containing fluoride was purchased from grocery stores. When the solution of the title compound was dropped on the prepared sample solution, color changes supporting the presence of these anions were observed, as well as the change in absorption in the UV-vis spectrum (Figure 7).

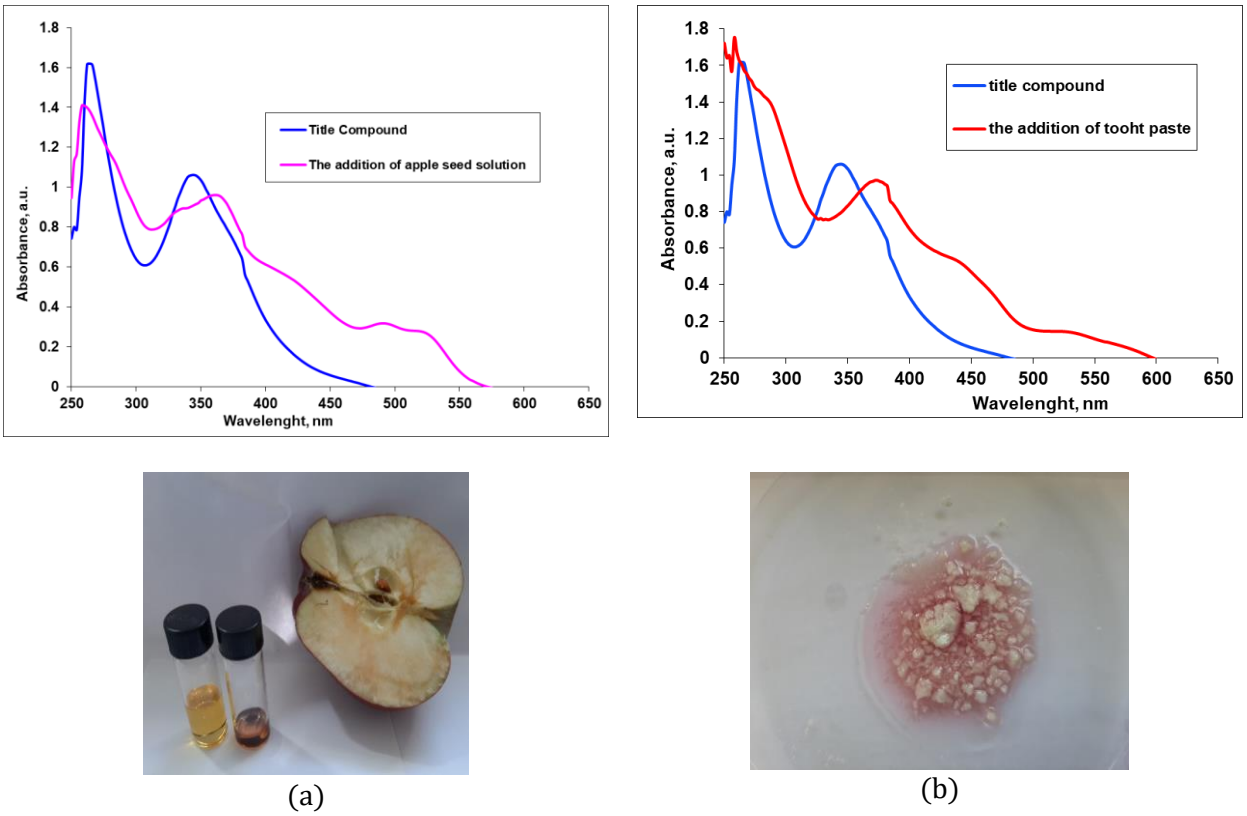

Figure 7. (a) UV-vis spectral change of the compound (**1**) in DMSO solution upon addition of apple seed sample, (b) toothpaste solution; photographs of source apple seed source cyanogenic glycoside and fluoride in toothpaste.

4. Conclusion

A new ninhydrin-thiosemicarbazone-based receptor (**1**) has been synthesized by simple steps with good yield. The receptor's interaction and colorimetric sensing properties with different anions were investigated by naked-eye, ultraviolet-visible (UV-Vis) spectroscopy in a DMSO solution. Its response in dimethyl sulfoxide (DMSO) solution in the presence of selected anions was studied by ultraviolet-visible (UV-Vis) spectroscopy. The results showed that the receptor had a higher affinity to fluoride, acetate, cyanide, dihydrogen phosphate, and hydroxide anions, but no evident binding with chloride, bromide, iodide, isothiocyanate, and hypochlorite anions. Upon addition of these anions to the receptor in DMSO at room temperature, the solution exhibited an obvious color change from yellow to orange-red that the naked eye could observe. It has been observed that the fluoride anion, due to its higher affinity, is determined more easily than other halide anions, such as chloride, bromide, and iodine. This compound's simple design may contribute to developing more elaborate colorimetric anion chemosensors.

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