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A Novel Heterocyclic Thiosemicarbazone: Synthesis, Characterization and Preliminary Sensing Studies for Ions †

M. Lene F. Jardim, M. Manuela M. Raposo and Susana P. G. Costa *

Centre of Chemistry, Campus de Gualtar, University of Minho, 4710-057 Braga, Portugal; jardimmlf@gmail.com (M.L.F.J.); mfox@quimica.uminho.pt (M.M.M.R.)
* Correspondence: spc@quimica.uminho.pt

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Abstract: Over the past decades, the interest in the fast and sensitive recognition and detection of molecules and ions with biological and/or environmental relevance has increased. Therefore, the search of new molecules capable of coordinating these analytes is an important topic of investigation, especially those with an optical response (via color or fluorescence changes). Thiosemicarbazones are versatile organic compounds due to their wide range of biological activities and interesting optical, electronic and redox properties. Also, they possess various binding sites, whose complexing ability can be tuned by the introduction of substituents of different electronic character. Having this in mind, we report the synthesis of a new thiosemicarbazone derivative functionalized with a nitrogen heterocyclic moiety. The new compound was characterized by ^{1}H and ^{13}C NMR, UV-Vis absorption and fluorescence spectroscopies. Moreover, a preliminary chemosensory study was undertaken in acetonitrile solutions in the presence of relevant ions with biological, medicinal and environmental relevance showing that this receptor has potential application as a fluorimetric chemosensor.

Keywords: thiosemicarbazone; quinoline; synthesis; optical chemosensor

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1. Introduction

The molecular recognition of ionic and neutral species is one of the most studied areas of supramolecular chemistry [1]. In recent years, new colorimetric and fluorimetric molecular chemosensors for anions and cations with biological, industrial and environmental importance have been investigated due to their potential applications [2].

A chemical sensor should have a receptor (recognition) unit that interacts with the substrate or analyte, and a transduction unit that signals recognition, causing changes at an electronic level in the host molecule (receptor) and giving a measurable response to the presence of the coordinated analyte, making its quantification possible [3,4]. Receptors or host molecules are designed in such a way that, upon coordination with an analyte, a measurable signal is observed, such as changes in color or fluorescence [4,5].

In this context, the thiosemicarbazone functional group has been widely studied and used in supramolecular chemistry, especially due to its potential application in the detection of anions and cations. (Thio)urea-containing compounds can be used for the formation of complexes with anions because the hydrogen-bonding ability of these functional groups commonly results in the formation of stable complexes. The hydrogen bonding ability of the (thio)urea moiety depends on the acidity of the ureido NH protons and the number of binding sites [6]. However, as multiple binding sites can be present in the molecule, they can also act as cation sensors [5].

Thiosemicarbazones are usually obtained through the equimolar condensation of aldehydes or ketones with thiosemicarbazides. The versatility of these compounds can be attributed to their easy synthetic methodology, their ability to be modulated and, most importantly, their structural properties, which allow their integration in different applications [7]. Thiosemicarbazones also have biological activities such as antitumor, antiviral, antifungal, antibacterial, antimalarial agents, among others [8]. This work reports the synthesis, spectroscopic characterization and evaluation of the sensing capacity of a novel thiosemicarbazone derivative in ACN.

2. Methods and Materials

Commercial reagents were supplied by Sigma-Aldrich, Acros, Fluka, Panreac and were used as received. The ion salts used (in the form of tetrabutylammonium salts for anions and perchlorate for cations, except for Cu(I), Pd(II) and Li(I), in the form of tetrafluoroborate and Sn(II) in the form of chloride) and the solvents are from Sigma-Aldrich, Acros and Fluka and were used as received.

Thin layer chromatography (TLC) was performed on silica gel 60 plates with fluorescence indicator F254 (Macherey-Nagel). The ^{1}H and ^{13}C nuclear magnetic resonance spectra were recorded using a Bruker Avance III device at 400 MHz and 100.6 MHz, respectively, using the solvent peak as an internal reference. The assignment of the ^{1}H and ^{13}C signals was performed using two-dimensional heteronuclear correlation techniques, using as solvent DMSO-d_6 with a 99.9% deuteration degree, containing 0.1% *v*/*v* tetramethylsilane from Sigma-Aldrich. The UV-visible absorption and fluorescence spectra were obtained using a Shimadzu UV/2501PC spectrophotometer and a Horiba Jobin-Yvon FluoroMax-4 spectrofluorometer, respectively, in UV-grade solvents and quartz cells.

2.1. Synthesis and Spectroscopic Characterization of Thiosemicarbazone Derivative 1

4-Phenyl-3-thiosemicarbazide (0.4 mmol) and 8-hydroxy-quinoline-2-carbaldehyde (0.4 mmol) were dissolved in methanol (30 mL). The reaction mixture was left at room temperature and protected from light for 70 h. The reaction was monitored by TLC, using DCM/MeOH (50:1) as eluent. Compound **1** (Figure 1), was obtained after evaporation of the solvent under reduced pressure. Thiosemicarbazone **1** was characterized by ^{1}H and ^{13}C NMR spectroscopy, with the characteristic signs of the NH groups, at 10.35 and 12.19 ppm, and of the imine CH at 8.35 ppm.

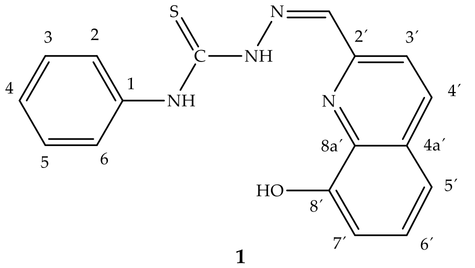

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Figure 1. Structure of thiosemicarbazone **1**.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.09 (dd, J = 1.6 and 7.6 Hz, 1H, H7′), 7.23 (dt, J = 0.8 and 7.6 Hz, 1H, H4), 7.41-7.36 (m, 3H, H3 + H5 + H5′), 7.43 (t, J = 8.0 Hz, 1H, H6′), 7.53 (dd, J = 1.2 and 7.6 Hz, 2H, H2 + H6), 8.28 (d, J = 8.8 Hz, 1H, H4′), 8.35 (s, 1H, N=CH), 8.54 (d, J = 8.4 Hz, 1H, H3′), 9.91 (s, 1H, OH), 10.35 (s, 1H, NH-C=S), 12.19 (s, 1H, NH-N) ppm.

^{13}C NMR (DMSO-d_6, 100.6 MHz): δ = 112.32 (C7′), 118.02 (C5′), 118.92 (C3′), 125.91 (C4), 126.49 (C2 + C6), 128.37 (C3 + C5), 128.42 (C6′), 129.05 (C4a′), 136.35 (C4′), 138.37 (C8a′), 139.10 (C1), 143.23 (N=CH), 151.82 (C2′), 153.54 (C8), 176.75 (C=S) ppm.

2.2. Photophysical Characterization of Thiosemicarbazone 1

This characterization was carried out to evaluate the absorption and emission properties, in order to collect the necessary information for the subsequent evaluation of its ability as colorimetric and/or fluorimetric ion sensor.

Solutions of compound **1** in acetonitrile in concentrations of 1 × 10^{-5} and 1 × 10^{-6} M were analyzed by UV-vis absorption and fluorescence spectroscopies, respectively. The relative quantum fluorescence yield of the compound was calculated using the fluorescence standard 9,10-diphenylanthracene (DPA), in ethanol, whose absolute fluorescence quantum yield is 0.95 [9].

2.3. Preliminary Chemosensing Studies of Thiosemicarbazone 1, in ACN

The solution of the synthesized compound and ions were prepared with concentrations of 1 × 10^{-5} and 1 × 10^{-2} M, respectively, in ACN. Then, 50 equivalents of each ion were added to 1 mL of solution of thiosemicarbazone **1**. The evaluation of the color/fluorescence changes was evaluated by "naked eye" and in a UV-Vis chamber, under ultraviolet light of wavelength 365 nm.

3. Results and Discussion

3.1. Synthesis and Spectroscopic Characterization of Thiosemicarbazone Derivative 1

The synthesis of thiosemicarbazone derivative **1** was performed from commercially available 8-hydroxy-quinoline-2-carbaldehyde (I) and 4-phenyl-3-thiosemicarbazide (II) that were dissolved in methanol (Figure 2), and stirred at room temperature. After evaporation of the solvent under reduced pressure, the pure derivative **1** was obtained in the form of a yellow solid in 83% yield and melting point in the range 203–205 °C.

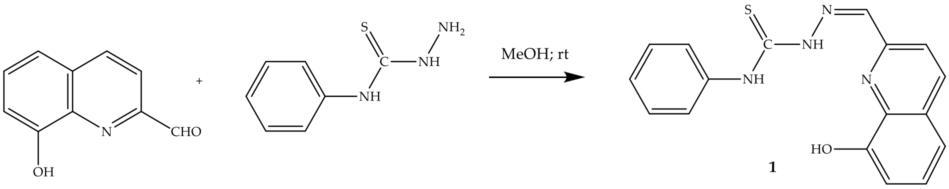

Figure 2. Synthesis of thiosemicarbazone derivative **1**.

3.2. Photophysical Characterization of Thiosemicarbazone 1

The photophysical properties of thiosemicarbazone derivative **1** were caried out in ACN solutions. The compound showed an intense absorption band (log ε = 4.4) at 346 nm and an emission band at 603 nm. The relative fluorescence quantum yield, determined by using DPA as standard, was found to be 0.05.

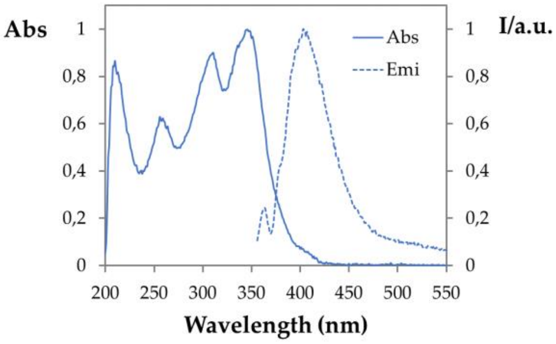

Figure 3. Normalized UV-Vis absorption and fluorescence spectra for thiosemicarbazone **1**, in ACN, with concentration 1 × 10^{-5} and 1 × 10^{-6} M, respectively.

3.3. Preliminary Studies of the Sensing Capacity of the Thiosemicarbazone Derivative 1

The solution of thiosemicarbazone **1** in ACN was analyzed for variations in color and fluorescence after the addition of 50 equivalents of the studied ions, at room temperature in “naked eye” visualization and in a UV-Vis chamber, under ultraviolet light of wavelength 365 nm, respectively.

3.3.1. Chemosensing of Anions in ACN

Regarding the interaction of compound **1** with anions, under natural light, color changes (from colorless to light yellow) after addition of BzO^- and CN^- anions were visible (Figure 4A). As for the fluorimetric behavior, compound **1** showed fluorescence quenching in the presence of BzO^- and CN^- ions and changes in λ_{flu} for the AcO^- ion (Figure 4B).

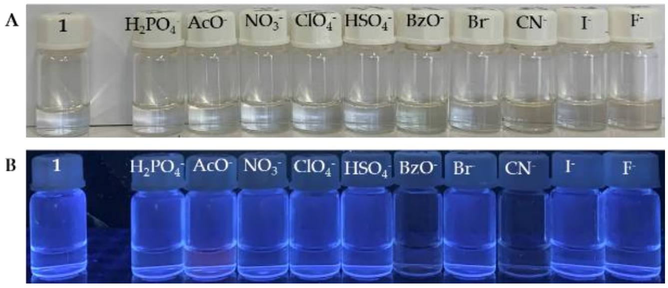

Figure 4. Solutions of compound **1**, in ACN, after addition of 50 equivalents of the various anions, visualized under natural light (**A**) and UV radiation at $\lambda = 365$ nm (**B**).

3.3.2. Chemosensing of Cations in ACN

Solutions of compound **1** in ACN experienced color changes (from colorless to light yellow) for Cu^+; TBT^+, Co^{2+}, Pb^{2+}, Zn^{2+}, Cd^{2+}, Pd^{2+} and Sn^{2+} ions, under natural light (Figure 5A). Under ultraviolet radiation, there was a quenching of fluorescence in the presence of Ag^+, K^+, Li^+, Pb^{2+}, Mn^{2+}, Fe^{2+}, Zn^{2+}, Cu^{2+}, Pd^{2+}, Sn^{2+} e Al^{3+} ions (Figure 5B).

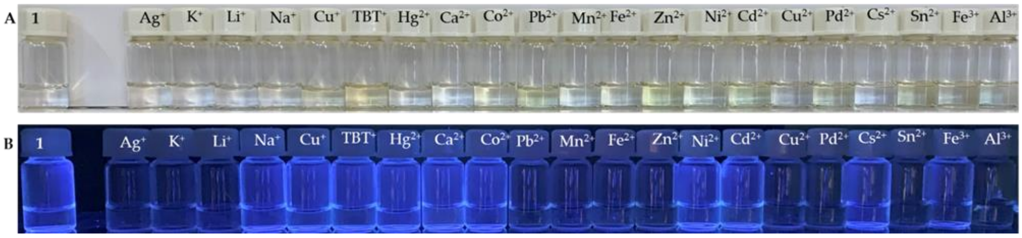

Figure 5. Solutions of compound **1**, in ACN, after addition of 50 equivalents of the various cations, visualized under natural light (**A**) and UV radiation at $\lambda = 365$ nm (**B**).

4. Conclusions

A novel thiosemicarbazone derivative functionalized with a quinoline moiety was synthesized in excellent yield, through a simple and straightforward method. The new compound was characterized by ^1H and ^{13}C NMR, UV-Vis absorption and fluorescence spectroscopies.

Considering the structure of thiosemicarbazone **1** with various potential binding groups, a preliminary chemosensory study was undertaken in acetonitrile solutions in the presence of relevant ions with biological, medicinal and environmental relevance showing that this receptor has potential application as a colorimetric/fluorimetric chemosensor. A more detailed study of the interaction of thiosemicarbazone **1** with the ions that gave the most interesting results will be undertaken through spectrophotometric and spectrofluorimetric titrations.

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