ORGANIC LETTERS

2007
Vol. 9, No. 17
3201−3204

Synthesis and Ion Sensing Properties of New Colorimetric and Fluorimetric Chemosensors Based on Bithienyl-Imidazo-Anthraquinone Chromophores

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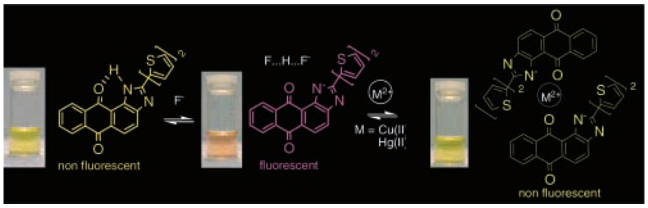
Received May 3, 2007

ABSTRACT



Novel colorimetric receptors for fluoride ion sensing containing anthraquinone as a chromogenic signaling unit and imidazo-2,2′-bithiophene binding sites are reported. Well-defined color change was observed upon addition of fluoride ions to acetonitrile solutions of receptors 2. Compounds 2a–c, deprotonated after fluoride ion addition, were studied as metal ion chemosensors in the presence of Zn(II), Hg(II), and Cu(II) in acetonitrile solutions, especially compound 2a which displayed a marked change from pink to yellow-gold colors upon complexation.

The design and synthesis of systems that are capable of sensing various biologically and chemically important anions are currently of major interest because anions play a fundamental role in chemical and biological processes.[1] Among various important anionic analytes, the fluoride ion is one of the most significant due to its role in dental care[2] and treatment of osteoporosis.[3]

Colorimetric sensors have attracted much attention for allowing so-called "naked-eye" detection in a straightforward and inexpensive manner, offering qualitative and quantitative information without using expensive equipment. A chemosensor usually consists of three parts, a recognition moiety, a spacer, and a signal reporter. Hydrogen-bonded donors such as pyrrole/calixpyrrole, (thio)urea, guanidinium, azophenol, dipyrrolylquinoxalines, indolocarbazoles, (di)amino, amide, and (benzo)imidazole usually act as anion binding sites. Anthraquinone derivatives are electron acceptor groups that,

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10.1021/ol071029b CCC: $37.00

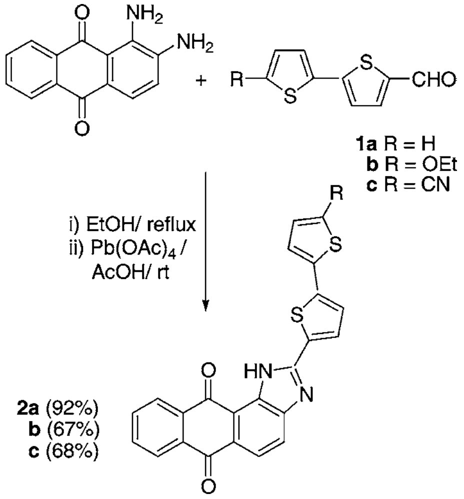
electronically connected with recognition sites, have proved suitable receptors for the colorimetric sensing of certain anions (e.g., fluoride).[1,4−7]

Donor−acceptor-substituted thiophene derivatives have been used recently due to their optical properties.[8] Bithienyl derivatives of anthra[1,2-*d*]imidazole-6,11-dione, which possess intramolecular hydrogen bonding between the NH of the imidazole ring with the neighboring quinone carbonyl group, are new candidates to investigate hydrogen-bond formation and proton transfer in the receptor−anion interactions. It should be noted for these kind of sensors that the acidity of the NH proton of the imidazole ring can be tuned by changing the electronic properties (donor or acceptor) of the thiophene substituents.[7,9] These compounds are very promising for applications in various areas, such as medical and environmental sciences, due to the combination of the two sensing effects, color and fluorescence.

Therefore, we propose the synthesis of new imidazo-anthraquinone sensors containing bithiophene moieties. The electronic nature of its substituents was used to tune the selectivity and the photophysical properties of the chemosensors. In this communication, we propose a simple synthetic route to the imidazo-bithienyl-anthraquinone derivatives **2** in which 1,2-diaminoanthraquinone and several formyl-bithiophenes are used as precursors for the synthesis of new fluorimetric and/or colorimetric sensors. To our knowledge, this is the first time that the synthesis and characterization of colorimetric/fluorimetric properties of anthraquinone derivatives containing imidazo-bithienyl moieties are reported and evaluated for halide and metal ion detection.

Several 5-formyl-2,2′-bithiophenes **1** with different substituents at the 5′-position (hydrogen, ethoxy, and cyano) were used in the synthesis of sensors **2**. 5-Formyl-2,2′-bithiophene **1a** was available commercially, while the synthesis of 5-ethoxy-5′-formyl-2,2′-bithiophene **1b** was recently reported.[8a] Aldehyde **1c** was synthesized by a Pd(PPh_3)$_4$-catalyzed cross-coupling reaction of 5-formyl-2-thiophene boronic acid with 2-bromo-5-cyanothiophene in 61% yield.

Scheme 1. Synthesis of Sensors **2**



The synthesis of sensors **2** is outlined in Scheme 1. In the first step, mixtures of 1,2-diaminoanthraquinone and the appropriate formyl-bithiophenes **1a**−**c** were refluxed for 12 h in ethanol, with formic acid as catalyst, to yield the corresponding imine intermediates which were used in the second step without isolation or further purification. The cyclization of the imines to the imidazo-anthraquinone derivatives **2** was achieved with lead tetraacetate in acetic acid at room temperature.[10]

Recrystallization of the crude products gave the pure heterocyclic sensors **2** in good to excellent yields (67−92%). Compounds **2** were completely characterized by ^1H and ^{13}C NMR, IR spectroscopy, and HRMS. In DMSO-d_6 at 25 °C, the ^1H NMR signals of NH proton of compounds **2a**−**c** were observed from 13.3 to 13.6 ppm. The signal of NH appearing downfield indicated high acidity and strong hydrogen-bonding ability.

Compounds **2a**−**c** were protonated in an acidic acetonitrile solution of HBF_4 or methanesulphonic acids, which resulted in a blue shift in the band centered at 444 (**2a**), 462 (**2b**), and 512 nm (**2c**) to 432 (**2a**), 450 (**2b**), and 417 nm (**2c**) (see Supporting Information, Figures S1−S3).

Interaction with basic anions (CN^-, $H_2PO_4^-$, CH_3COO^-) and halide ions (F^-, Cl^-, Br^-, and I^-) was investigated using spectrophotometric and spectrofluorimetric titrations, by adding a standard acetonitrile solution of the corresponding tetrabutylammonium salts to an acetonitrile solution of compounds **2a**−**c** at room temperature. In the case of the basic anions, no change occurred upon interaction with cyanide anions and a small red shift was observed only when a large amount of CH_3COO^- or $H_2PO_4^-$ was added. In both cases, the yellow color of the solution changed to pale orange

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and no emission was detected. After addition of 100 equiv of each anion, a plateau was observed (see Supporting Information, Figure S4).

In the case of chloride, bromide, and iodide ions, no change was observed upon addition of up to 20 molar equiv (see Figures S5−S7 in Supporting Information). However, addition of fluoride ions produced a marked red shift in the absorption for all systems and also an increase in the intensity of the emission spectra. Due to the deprotonation of the NH to N^- in the imidazole ring in an alkaline medium, the UV−visible absorption band was shifted to a longer wavelength. The deprotonation lowers the steric hindrance between the thiophene unit and the NH group and enables the formation of a more extended π-conjugated system. As can be observed for compound **2a**, the UV−vis band centered at 444 nm that can be assigned to the $\pi-\pi^*$ transition of the chromophore disappeared gradually and a new band centered at 503 nm appeared, which was assigned to the charge transfer (CT) band. The yellow color of the sensor solution turned to light pink at the same time. Two well-defined isosbestic points were observed at 389 and 470 nm for **2a**, which suggested that the stoichiometry of the **2a**−fluoride interaction was 1:1 (Figure 1). For systems **2b** and **2c**, similar results were observed. The initial color observed for compound **2b** was orange and for **2c** was red. The intensity of these colors resulted in a weaker naked-eye effect than that observed for compound **2a** (see Figure S13 in the Supporting Information).

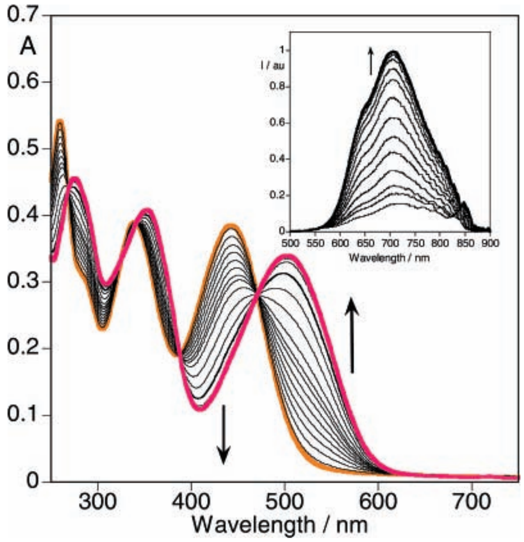

Figure 1. Changes in UV−vis and fluorescence (inset) spectra for compound **2a** (1.75×10^{-5} M) in CH_3CN with addition of CH_3CN solution of $[(Bu)_4N]F$. Absorptions read at 444 and 503 nm.

The selectivity toward the fluoride ion in compounds **2a**−**c** was achieved through the introduction of substituents at the 5′-position of the bithienyl moiety with different electronic properties (**2b**, electron-donating ethoxy group, and **2c**, electron-withdrawing cyano group), as the number of fluoride ion equivalents needed to fully deprotonate the system varied from 4 equiv for **2b**, 3 equiv for **2a** to 2 equiv for **2c**. As expected, system **2c** showed the strongest interaction with fluoride ions. Stability constants for the interaction of ligands **2a**−**c** in the presence of the fluoride ion were calculated using SPECFIT/32 software[11] and are summarized in Table 1.

Table 1. Stability Constants for Ligands **2a**−**c** in the Presence of Fluoride Ion and Some Metal Cations in Acetonitrile

ligand	interaction	log K
2a	F^-	4.80 ± 5.39E−02
	(**2a**)$_2$Cu	8.84 ± 1.59E−02
	(**2a**)$_2$Hg	12.43 ± 4.79E−02
2b	F^-	4.68 ± 1.12E−02
	(**2b**)$_2$Zn	6.73 ± 6.75E−02
	(**2b**)$_2$Hg	8.99 ± 9.57E−02
2c	F^-	5.02 ± 1.15E−02
	(**2c**)$_2$Cu	9.81 ± 2.09E−02

Recently, Han and co-workers[7] reported the synthesis and characterization of phenylimidazo-anthraquinone derivatives as selective F^- sensors. The highest sensitivity was achieved for the sensor possessing a *p*-nitro group at the phenyl ring (40 equiv of fluoride ion), which is 20 times higher than the amount needed in the case of our best system **2c**, probably due to the presence of the more efficient electron transfer bithienyl unit.

A great advantage presented by our deprotonated **2a**−**c** systems is that they are emissive and at the same time provide a chelating site with recognition effects formed by the deprotonated N from the imidazole ring and the O from the quinone group. Metal ion complexes can be formed with ligands provided with the 9,10-anthraquinone donor unit with free electron pairs to coordinate to the metal ions.[12] Therefore, we investigated the behavior of compounds **2a**−**c** in the presence of Zn(II), Cu(II), and Hg(II) cations, after fluoride ion addition. In all cases, a blue shift in the absorption band centered at ca. 503−505 nm was observed, and the original band, related to the free ligand, centered at 444 nm was restored, suggesting the formation of metal complexes in solution. With increasing addition of metal ions, a plateau was achieved for a 1:2 metal to ligand molar ratio, except for the complex formed by **2a** with Zn(II), where the molar ratio observed was 1:1 (see Figures S15−S19 in Supporting Information). In Table 1, some stability constants of ligands **2a**−**c** with Cu(II), Hg(II), and Zn(II) are presented. The strongest interaction was observed for ligand **2a** in the presence of Hg(II). The mononuclear complex formed by **2a** with Zn(II) could be attributed to the great ability of this

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(11) SPECFIT/32 Global Analysis System, v. 3.0; Spectrum Software Associates, Malborough, MA, U.S.A.

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metal ion to form different complexes with coordination number from 2 to 6.

A CHEQ (chelation enhancement of the quenching) effect in the fluorescence emission for all metals studied, Zn(II), Hg(II), and Cu(II), was observed (Figure 2). This result suggested the involvement of the metal ion with both donor atoms, the O from the quinone ring and the N from the imidazole ring through two units of **2a**−**c** ligands, in the case of Cu(II) and Hg(II). The quenching effect could can be attributed to an energy transfer quenching of the π^* emissive state through low-lying metal-centered unfilled d-orbitals for Cu(II) and to an intersystem crossing mechanism due to the heavy atom effect for Hg(II).[13]

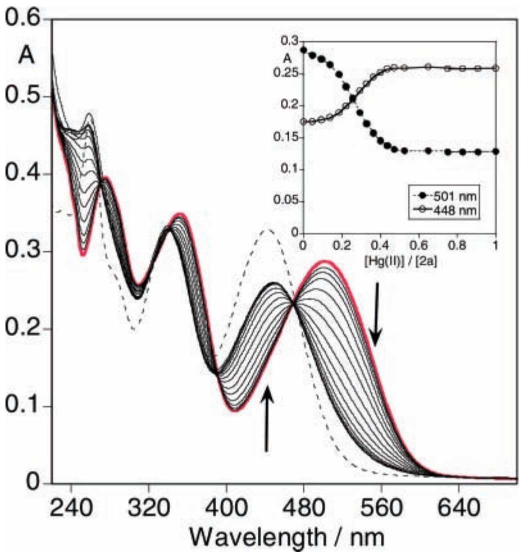

Figure 2. UV−vis titration of **2a** in CH_3CN with increasing amount of $Hg(CF_3SO_3)_2$, after addition of $[(Bu)_4N]F$ ($\lambda_{exc} = 470$ nm). Dotted line spectra: free ligand.

In the case of Zn(II) that normally produces a CHEF effect (chelation enhancement of fluorescence),[14] a quenching effect was also seen. Similar effects have been reported for systems bearing a coordinative aromatic nitrogen atom.[15] Previously, two different sensing mechanisms have been described for the anthraquinone chromophore. An inversion of excited luminescence states, n−π^* to π−π^*, proposed by Kadararaisamy[12d] involving the O atom from the quinone ring and a PET (photoinduced electron transfer) process proposed by Yoshida and co-workers[12a] involving a N from the imidazole and azacrown rings. In our case, involvement of both N and O donor atoms appears to suggest a PET process.

Taking into account the counterion used for all metal complexes, the triflate ion ($CF_3SO_3^-$), and its noncoordinative properties, the hypothesis of 1:2 M/L molar ratio observed is in agreement with the coordinative involvement of these metals (Cu(II) and Hg(II)) with at least four donor atoms (see Figure S20 for a schematic representation in Supporting Information).

In all cases, the pink color of the solution observed upon fluoride addition changed to yellow or gold upon metal complexation giving an on-off-on, yellow-pink-yellow, reversible colorimetric reaction (see Figure S14 in Supporting Information).

In summary, bithienyl-imidazo-anthraquinones **2a**−**c** were synthesized in good to excellent yields and were evaluated as colorimetric and/or fluorimetric sensors. Selectivity and sensitivity for the fluoride ion was observed for all systems. Moreover, the systems after deprotonation of the imidazole NH upon addition of the fluoride ion proved to be efficient sensors for metal ions such as Zn(II), Hg(II), and Cu(II), suggesting the formation of 1:2 complexes, except for the complex formed by **2a** with Zn(II), with a 1:1 molar ratio.

Acknowledgment. We are grateful to the Portuguese Foundation for Science and Technology for financial support through Center of Chemistry (UM) and FCT/UNL REQUIMTE through project POCI/QUI/55519/2004.

Supporting Information Available: Experimental procedures, characterization data including ^1H and ^{13}C spectral data of compounds and proton, basic anions, halide and metal ion sensing spectral studies and figures. This material is available free of charge via the Internet at http://pubs.acs.org.

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