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Oxidized Bis(indolyl)methane: A Simple and Efficient Chromogenic-Sensing Molecule Based on the Proton Transfer Signaling Mode

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ABSTRACT

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Oxidized bis(indolyl)methane, 1, a simple chromophore containing an acidic H-bond donor moiety and a basic H-bond acceptor moiety, can act as a selective colorimetric sensor either for F^- in aprotic solvent or for HSO_4^- and weak acidic species in water-containing medium. The deprotonation/protonation of oxidized bis(indolyl)methane 1 is responsible for the dramatic color change.

The search of colorimetric sensors for various chemically or biologically significant anions is emerging as an area of great interest.[1] Most of synthetic chemosensors generally involve the covalent linking of an optical-signaling chromophoric fragment to a neutral anion receptor containing urea,[2] thiourea,[3] amide,[4] phenol,[5] or pyrrole[6] subunits, which can provide one or more H-bond donor sites for selective binding and sensing of some anions, especially for F^-, AcO^-, $H_2PO_4^-$, etc. The selectivity can be related to the structure of the hydrogen bond complex and the basicity of the anions. Among anions, F^-, the most electronegative atom, usually forms the strongest H-bond interaction with an NH or OH

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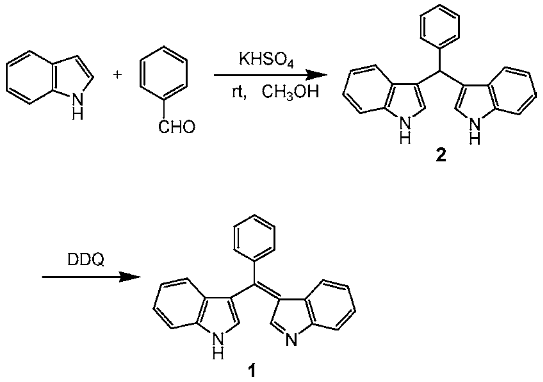
fragment of the artificial receptor, and further the interaction should likely arouse an advanced stage of the proton transfer reactions, which partially depend on the intrinsic acidity of the H-bond donor group of the artificial receptor. Such features have been observed in few amide-, phenol-, and urea-based receptors containing electron-withdrawing chromogenic substituents.[7] Indeed, the colorimetric sensor based on the deprotonation of the binding moiety by anions is very efficient and highly sensitive. Here we report an easy-to-make and simple indole-based chemosensor for selected anions based on the proton-transfer signaling mode.

Numerous bis(indolyl)methanes and their derivates, a new kind of aza-heterocycles, have been isolated from various terrestrial and marine natural sources. These natural products have novel structures and exhibit important biological activities.[8] Therefore, there is a great interest in the synthesis of the bisindole compounds,[9] occurring naturally or not. In our research, it was found that bis(indolyl)methanes containing an H atom in the *meso* position were unstable and easy to spontaneously oxidize to the corresponding conjugated products. It also led us to consider that the conjugated compound might display interesting anion binding and sensing characteristics. The choice of oxidized bis(indolyl)methane as the chromogenic-sensing molecule was mainly based on the fact that the conjugated bisindole skeleton could act not only as a color-reporting group but also as a binding affinity control group containing an acidic H-bond donor moiety and a basic H-bond acceptor moiety. The strong hydrogen bonding to, or deprotonation/protonation of, the indolyl moiety might modulate the internal charge transfer (ICT) state of oxidized bis(indolyl)methane and give rise to large color changes.

The synthesis of **1** is shown in Scheme 1. The *meso*-phenyl bis(indolyl)methane **2** was prepared in 92% yield by condensation of indole with benzaldehyde in CH_3OH.[9b] Compound **1** was formed by treating the precursor **2** with DDQ in CH_3CN in about 37% yield.

Scheme 1



The color changes were observed in a first step in acetonitrile and acetonitrile/water (4:1, v/v) by addition of 10 equiv of various anions (F^-, Cl^-, Br^-, I^-, AcO^-, $H_2PO_4^-$, and HSO_4^- added as their tetrabutylammonium salts) to dilute solutions of receptor **1**. Specifically, as shown in Figure 1, the receptor **1** in aprotic organic solvent changes color in the presence of F^- and AcO^- anions. The most pronounced effect is the F^--induced color change from yellow to red. However, in a water-containing system, a significant color-based response was observed only upon the addition of HSO_4^-. The dramatic combination of anion-specific response/nonresponse makes receptor **1** an especially effective colorimetric anion sensor under the solution-phase conditions.

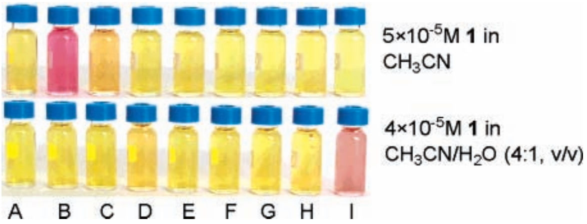


Figure 1. Color changes of **1** upon addition of 10 equiv of anions in different medium (from A to I: free, F^-, AcO^-, $H_2PO_4^-$, Cl^-, Br^-, I^-, ClO_4^-, HSO_4^-).

The anion binding and sensing properties of receptor **1** have been studied by using UV/vis spectroscopic techniques. The receptor **1** itself displays two strong absorption bands at 277 and 423 nm and one weak band at 347 nm in acetonitrile. In contrast to the absorption spectrum of bis(indolyl)methane **2** (λ_{max} = 224 and 283 nm), the strong absorption band at 423 nm, which has the effect of making the solution of **1** yellow, can be assigned to the ICT absorption band of the conjugated bisindole skeleton. Another less strong shoulder peak at 500 nm is related to its intermolecular hydrogen bond interaction, which disappeared when adding a polar protic solvent such as H_2O or CH_3OH to this system. Figure 2 shows the anion-induced spectral changes of the CH_3CN solution of **1** (5.0×10^{-5} M). In the

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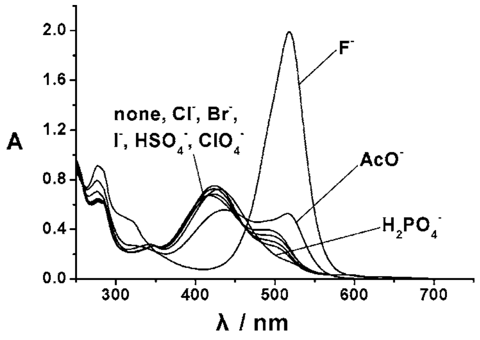
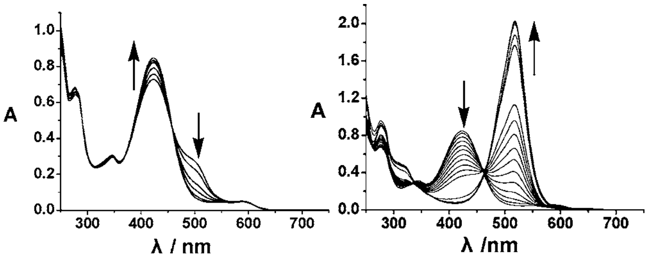


Figure 2. UV/vis spectra of **1** recorded in CH_3CN (5.0×10^{-5} M) after addition of 25 equiv of various anions (none, F^-, AcO^-, Cl^-, Br^-, I^-, HSO_4^-, ClO_4^-, $H_2PO_4^-$).

presence of 25 equiv of F^-, the absorption band at 423 nm vanished, while a new red-shifted absorption band appeared at 517 nm with the effect that the solution instantaneously changed color from yellow to red (near-complete color conversion). A similar, but less remarkable spectral change was observed upon addition of AcO^-, and complete color change from yellow to red was achieved upon addition of not less than 100 equiv of AcO^-. As for $H_2PO_4^-$, however, there was only a slight red shift of the band at 423 nm along with the disappearance of the shoulder peak at 500 nm. On the other hand, no noticeable changes in color and absorption spectra were observed in the cases of Cl^-, Br^-, I^-, ClO_4^-, or HSO_4^-, even at high concentration up to 1000 equiv each. Similar anion sensing properties were also observed in the more polar DMSO.



(a) (b)

Figure 3. The changes in UV/vis spectra of **1** recorded in CH_3CN (5.0×10^{-5} M) after addition of (a) 0, 0.1, 0.2, 0.3, 0.4, and 0.5 equiv of F^- or (b) 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 50, and 100 equiv of F^-.

The interaction of receptor **1** with F^- was investigated in detail through the UV/vis spectroscopic titration, and complicated spectral behaviors were observed (Figure 3). On addition of F^- from 0 to 2.0 equiv, the intensity of the band at 423 nm increases, while the shoulder peak at 500 nm decreases. In the presence of 0.5 equiv of F^-, the band at 423 nm almost reaches the maximum and the band at 500 nm completely disappears (Figure 3a). However, in this process, no noticeable changes in color were observed. The changes suggested that F^- first forms a H-bond complex with **1** and meantime disturbs the intermolecular hydrogen bond assembly of **1** itself (approximately 0.5 equiv of F^- are sufficient to effect near-complete disassembly). With further increasing F^- concentration, the solution color gradually turned from yellow to red, correspondingly, the band at 423 nm decreased gradually and a new and substantially red-shifted band at 517 nm evolved and reached its limiting value after the addition of about 25 equiv of F^- (Figure 3b). Two clearly isosbestic points at 332 and 461 nm were observed. The new band that develops at 517 nm pertains to the deprotonated receptor $[L]^-$, which was confirmed by the Brønsted acid−base reaction of adding strong base $[Me_4N]OH$. The spectral behavior revealed that deprotonation of the NH fragment by F^- and not hydrogen bonding to it is responsible for the drastic color change, as a result of altering the optical properties of the chromogenic bisindolyl skeleton. Such deprotonation was related to the acidity of the H-bond donor site and the particular stability of the $[HF_2]^-$ H-bond complex.[10] In contrast, the addition of $[Me_4N]OH$ and F^- (or other anions) to a colorless acetonitrile solution of the nonconjugated precursor **2** does not induce a color change and modification of the corresponding absorption spectrum. A control experiment indicated that the conjugated structure of **1** enhances the proton activities of the NH group (as H-bond donor), and then helps to stabilize the negative charge state of the deprotonated receptor. However, no color changes were observed upon addition of organic amines such as NEt_3.

The interaction of receptor **1** with F^- was corroborated by ^1H NMR titration experiments carried out in DMSO-d_6 (solubility problems prevented the studies in CD_3CN solution). Different patterns are observed in the titration ranges of 0−2.5 and 2.5−10.0 equiv. It was found that the aromatic proton signals underwent continuous upfield shifts with increasing F^- concentration from 0 to 2.5 to 5.0 equiv. The upfield shifts are stopped after a 5.0 equiv addition, and the proton signals of the bisindolyl skeleton were broadened. These observations further revealed that the first added F^- establishes H-bond interaction with the NH subunit of **1**, while the second F^- induces the deprotonation of the NH fragment, which brings electron density onto the π-conjugated framework with a through-bond propagation, thus causing a shielding effect and inducing upfield shift. In the full deprotonated form, the polarization effect is no longer present since the anion does not remain in proximity to the receptor.

It has been noted that the deprotonation of receptor **1** is also induced by basic anion AcO^-, and appearance of the band at 517 nm and development of the red color were observed after large excess addition. No deprotonation took place in the presence of less basic anion such as $H_2PO_4^-$, Cl^-, Br^-, I^-, ClO_4^-, or HSO_4^-. However, the added $H_2PO_4^-$ can establish weak H-bond interaction with receptor **1** and disturbs the intermolecular hydrogen bond assembly of **1**. The above results indicate that the receptor **1** exhibits

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[10] Gronert, S. *J. Am. Chem. Soc.* **1993**, *115*, 10258−10266.

excellent selective sensing for F^- ($F^- > AcO^- \gg$ other anions) in aprotic organic solvent.

The fluoride- and acetate-induced deprotonation process is fully reversible—the addition of polar protic solvents (H_2O and CH_3OH) results in a reverse color change from red to yellow. This is presumably because protic solvent competes for F^- or AcO^- with the NH moiety, moreover, the presence of a relatively high amount of protic solvent disfavors the formation of the deprotonated receptor $[L]^-$. However, in water-containing medium, the excess addition of strong base $[Me_4N]OH$ could still deprotonate receptor **1** and induce a color change.

Interestingly, we also noted that the addition of H_2O to a CH_3CN solution of the mixture of receptor **1** and HSO_4^- results in a visual color change from yellow to red (see Figure 1), and the process is also fully reversible.[11] The sensing properties of receptor **1** in water-containing medium (CH_3CN/H_2O, 4:1, v/v) were then studied. As a result of the solvent effect of water, the band at 423 nm of receptor **1** shifts to 435 nm along with the disappearance of the shoulder peak at 500 nm. Upon addition of various representative anions, only HSO_4^- induced a great bathochromic shift from 435 to 500 nm (Figure 4). Since the HSO_4^- anion is a relatively strong acid ($pK_a = 1.99$ in aqueous solution), the HSO_4^--induced change, a different process from the deprotonation by basic anions, is mainly the consequence of a simple protonation of receptor **1**. The band that develops at 500 nm pertains to the protonated receptor $[H_2L]^+$, which was confirmed by the protonation of receptor **1** by using perchloric acid in CH_3CN/H_2O or in CH_3CN. In addition, the reversible protonation of receptor **1** can also take place in the presence of other weak acidic species, such as acetic acid, acidic amino acids, and nucleotides, etc., along with the same color change. We are currently investigating these features in greater detail.

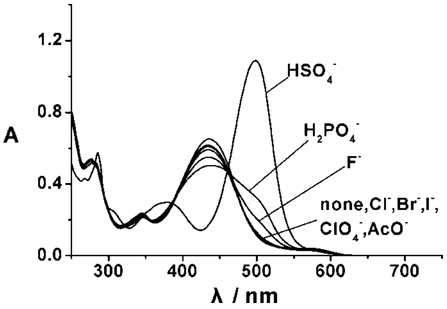

Figure 4. UV/vis spectra of **1** (4.0×10^{-5} M) after addition of 25 equiv of anions (none, F^-, Cl^-, Br^-, I^-, HSO_4^-, ClO_4^-, $H_2PO_4^-$, AcO^-) in CH_3CN/H_2O (4:1, v/v).

To sum up, oxidized bis(indolyl)methane compound, containing a conjugated bisindolyl skeleton, provides an easy-to-make, simple, and efficient chromogenic-sensing molecule model. The presence of strong base and acid can easily induce the deprotonation of the acidic H-bond donor moiety and the protonation of the basic H-bond acceptor moiety, respectively, which modulate the internal charge transfer state of oxidized bis(indolyl)methane and give rise to dramatic color changes. As a colorimetric anion sensor, the conjugated bisindole-based receptor has displayed highly selective coloration either for F^- in aprotic solvent or for HSO_4^- in water-containing medium based on the different proton-transfer signaling modes.

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Supporting Information Available: Synthesis, characteristics, and spectral data of compound **1** and **2** and ^1H NMR titration of **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] To the red mixed solution (CH_3CN/H_2O, 1: 1, v/v) of **1** and HSO_4^- (containing 4.0×10^{-5} M **1** and 2.0×10^{-3} M HSO_4^-) was added ether, with careful shaking. The upper organic phase turned yellow, while the aqueous phase became colorless. After evaporating the ether, the mixed solution gradually turned from yellow to pale-red.