Benzothiadiazoles And Dipyrrrolyl Quinoxalines With Extended Conjugated Chromophores-fluorophores And Anion Sensors

Dmitry Aldakov
Manuel A. Palacios
Pavel Anzenbacher Jr.

Follow this and additional works at: https://scholarworks.bgsu.edu/chem_pub

Repository Citation
Aldakov, Dmitry; Palacios, Manuel A.; and Anzenbacher, Pavel Jr., "Benzothiadiazoles And Dipyrrrolyl Quinoxalines With Extended Conjugated Chromophores-fluorophores And Anion Sensors" (2005). Chemistry Faculty Publications. 178.
https://scholarworks.bgsu.edu/chem_pub/178

This Article is brought to you for free and open access by the Chemistry at ScholarWorks@BGSU. It has been accepted for inclusion in Chemistry Faculty Publications by an authorized administrator of ScholarWorks@BGSU.
Benzothiadiazoles and Dipyrryl Quinoxalines with Extended Conjugated Chromophores—Fluorophores and Anion Sensors

Dmitry Aldakov, Manuel A. Palacios, and Pavel Anzenbacher, Jr.*

Department of Chemistry and Center for Photochemical Sciences, Bowling Green State University, Bowling Green, Ohio 43403

Received May 11, 2005 Revised Manuscript Received August 22, 2005

Stable fluorescent chromophores find use in a growing number of practical applications, including their utility as laser dyes,1 emitters in light-emitting diodes,2 photodectors,3 optical data storage,4 and optical switches.5 Stable fluorophores with high quantum yields are widely used in anions, the hydrogen bonding nature of the DPQ binds anions via hydrogen bonding between pyrrole NH and the sensor complex was demonstrated by H NMR.10a In this paper, we provide a full account of our efforts including synthesis and photophysical properties of DPQ-based fluorescent anion sensors with extended conjugated chromophores S1–S6 (Figure 1), including their benzothiadiazole precursors F1–F6, which appears to be an interesting set of highly stable fluorescent chromophores.

Sensors S1–S6 with the extended aryl substituents of varying electronic nature were designed to provide a tool for systematic modulation of electronic density in the quinoxaline chromophore. This, in turn, was expected to lead to tuning the output emission wavelength as well as the anion binding affinity in the sensors S1–S6. Our previous studies suggest that even small changes in electronic density in the quinoxaline moiety affect the pyrrole hydrogen-bonding donors and the stability of the anion—sensor complex.9a

The synthesis of complexes S1–S6 (Scheme 1) departs from 1,2,3-benzothiadiazole 1, which was converted to the corresponding bromo derivative 2.11 In pathway A (Scheme 1), intermediate 2 was coupled via Stille reaction12 with a suitable arylobutylstannyl derivative to yield benzothiadiazole precursors F1–F6, which appears to be an interesting set of highly stable fluorescent chromophores.

**Scheme 1. Synthesis of 5,8-Diaryl-2,3-dipyrrylquinoxaline Sensors**

*Conditions: (a) HBr, H2O2, reflux; (b) PdCl2(TPP), THF, 100–120 °C; (c) LiAlH4, THF, reflux; (d) AcOH, reflux; (e) NaBH4-EtOH; (f) Pd(TPP), toluene-aq. K2CO3.

Figure 1. Structures of DPQ sensors with extended conjugated chromophores S1–S6 and their benzothiadiazole precursors F1–F6.
diazo fluorophores F1–F6, which were then reduced by LiAlH4 to the corresponding phenylene-diamines of general formula 3. We note that the reduction of benzothiadiazole derivatives did not proceed smoothly and required LiAlH4 in THF at reflux for 2 h, and the resulting diamines showed signs of photochemical degradation. Diamine intermediates 3 were then condensed with 1,2-di(1H-pyrrol-2-yl)ethane-1,2-dione 4 in refluxing acetic acid to give 5,8-diaryl-2,3-di(1H-pyrrol-2-yl)quinoxalines S1–S6.

The difficult reduction of diaryl benzothiadiazoles F1–F6 and photochemical instability of intermediates 3 prompted us to develop an alternative route. Pathway B was designed to use the advantage of easily accessible 1,2-diamino-3,6-dibromobenzene 5,13 which was condensed with 4 to give 5,8-dibromo-2,3-di(1H-pyrrol-2-yl)quinoxaline 7. Intermediate 7 was then coupled with suitable aryltributylstannyl derivatives (Stille reaction)13 or aryl-boronic acids (Suzuki reaction)14 to yield sensors S1–S6.

The synthesized benzothiadiazole precursors F1–F6 display emission color tuning mediated by the aryl substituents, which is easily observed by a naked eye examination of their fluorescence in solution (Figure 2). While the strong emission (Table 1) was not entirely unexpected given the frequent use of benzothiadiazole in fluorescent materials and conjugated polymers,15 we found that F1–F6 are also very stable fluorophores that did not show appreciable photobleaching in oxygenated solutions even after several weeks. More importantly, F1–F6 displayed absorption/emission tuning that to a large extent follows the electronic properties of the extended aryl substituents (Table 1).

Strong fluorescence as well as high chemical and photochemical stability of F1–F6, together with the ease of tuning the photophysical properties based on utilization of EWG/EDG attached to the 5,8-aryls, make these derivatives potentially useful as laser dyes. Interestingly, the fluorescence quantum yield and lifetimes within the F1–F6 series do not show a clear trend. Such effects are observed in aromatic chromophores16 and may be ascribed to varying oscillator strength of the chromophore.17 The effective electronic communication between the 5,8-substituted aryls and 1,2,3-benzothiadiazole is shown in the X-ray structure of F6. This structure shows how despite the steric hindrance of the phenyl ortho-hydrogens and the unshared electron pair on the benzothiadiazole nitrogen are almost coplanar with each other to maximize the conjugation (Figure 3).

Compared to the starting benzothiadiazole precursors F1–F6, sensors S1–S6 do not display the well-spaced emission signatures. As expected, the presence of 5,8-aryl substituents in sensors S1–S6 results in both a dramatic increase of emission intensity and shifted emission maximum as compared to the parent DPQ (λ<sub>e</sub> = 490 nm, Φ<sub>e</sub> = 0.15) (Figure 4, Table 2). This feature suggests that these sensors may be

\[ \text{compd} \quad \lambda_{\text{max}} \quad \lambda_{\text{e}} \quad \Phi_{\text{e}} \quad \tau_{\text{e}} \]

\[ \begin{array}{cccc}
F1 & 379 (9.1 \times 10^3) & 492 & 0.45 & 11.3 \\
F2 & 411 (1.10 \times 10^4) & 542 & 0.55 & 12.3 \\
F3 & 485 (6.60 \times 10^3) & 610 & 0.36 & 19.6 \\
F4 & 470 (16.9 \times 10^3) & 662 & 0.08 & 5.0 \\
F5 & 391 (15.5 \times 10^3) & 515 & 0.84 & 7.2 \\
F6 & 416 (12.2 \times 10^4) & 551 & 0.37 & 8.5 \\
\end{array} \]

\[ ^{a} \text{units of L mol}^{-1} \text{cm}^{-1}, \quad ^{b} \text{Determined using quinine sulfate} \]

\[ \text{compd} \quad \lambda_{\text{max}} \quad \lambda_{\text{e}} \quad \Phi_{\text{e}} \quad \tau_{\text{e}} \]

\[ \begin{array}{cccc}
\text{DPQ} & 410 (1.10 \times 10^4) & 490 & 0.15 & 1.8 \\
S1 & 422 (1.27 \times 10^4) & 500 & 0.25 & 2.1 \\
S2 & 346 (5.0 \times 10^3) & 506 & 0.38 & 2.6 \\
S3 & 419 (1.81 \times 10^4) & 514 & 0.24 & 2.5 \\
S4 & 416 (1.66 \times 10^4) & 520 & 0.13 & 2.7 \\
S5 & 450 (1.79 \times 10^3) & 595 & 0.22 & 10.1 \\
S6 & 425 (2.19 \times 10^4) & 610 & 0.26 & 3.1 \\
\end{array} \]

\[ ^{a} \text{units of L mol}^{-1} \text{cm}^{-1}, \quad ^{b} \text{Determined using quinine sulfate} \]
used in lower concentration thus allowing for achieving higher sensitivity.

Visual inspection of solutions of the sensors S1–S6 (10 μM in CH₂Cl₂) before and after addition of anions in the form of their hydrated tetra-n-butylammonium salts showed a dramatic change in fluorescence as well as in color after addition of both fluoride and pyrophosphate, which suggests strong binding. Conversely, addition of cyanide, dihydrogenphosphate, or chloride resulted in weak or no change in color, respectively (Figure 5). As expected, other anions such as bromide, sulfate, cyanate, thiocyanate, and nitrate did not show appreciable change in absorption/emission spectra and were not investigated further. Previous studies suggest that the affinity order F⁻ ≈ H₂PP₂⁻ ≫ H₂P⁻ ≥ Cl⁻ is a result of high surface charge concentration in a small fluoride anion and pyrophosphate dianion (H₂P₂⁻). This also explains why structurally similar but monoanionic dihydrogenphosphate (H₂P⁻) is not bound by our sensors.

Quantitative measurements of anion affinity were performed by monitoring the changes in the absorbance spectra of sensors S1–S6 upon addition of an anion. The titration experiments were performed using fluorescence for signal transduction. This is because the fluorescence is significantly more sensitive and allows for unambiguous sensing at low concentrations (0.5–100 μM). Examples of UV–Vis and fluorescence titration experiments are shown in Figure 6; see also Table 3.

Although CH₂Cl₂ is not a solvent of choice for inorganic anions, we have been limited by the fact that our sensors are poorly soluble in polar solvents and may undergo aggregation. Naturally, we were also interested in exploring the anion sensing in polar/water compatible solvents such as MeCN or DMSO. Particularly water, albeit a natural medium for most anions, poses a challenge for anion binding and sensing as it is an effective competitor for hydrogen bonding. Nevertheless, we have carried out a series of titration experiments in MeCN as well as in DMSO using aqueous solutions of anions. While these experiments revealed similar behavior of sensors, the actual binding isotherms showed sigmoidal progression. We ascribe this to multiple equilibria, presumably involving solvation/hydration of ionic species. Although such isotherms did not allow for calculation of the actual affinity constants, these experiments (Figure 7) suggest that sensors S1–S6 may actually be used to sense anions administered in water.

Encouraged by the fact that even simple sensors utilizing hydrogen bonding may successfully be used to sense anions administered in the form of their aqueous solutions, we explored this idea further. Because sensors S1–S6 are not soluble in polar solvents, we decided to embed them in a compatible polymer matrixes and membranes. Particularly poly(vinyl chloride) (PVC) and polyurethane (PU) embedded sensors were reported in the literature. We reasoned that the hydrophilic PU matrix may provide low polarity environment that would accommodate the sensors while allowing the interaction with the anions administered as aqueous samples. We have devised a simple assay, in which complicates the binding equilibria and may render the fitting unreliable.

Table 3. Affinity Constants Recorded for Sensors S1–S6 (2.0 μM in CH₂Cl₂), Titrated by Anions at Room Temperature

<table>
<thead>
<tr>
<th>anion</th>
<th>fluoride</th>
<th>chloride</th>
<th>pyrophosphate</th>
<th>phosphate</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPQ</td>
<td>18 200</td>
<td>&lt;50</td>
<td>14 300</td>
<td>&gt;100</td>
</tr>
<tr>
<td>S1</td>
<td>51 300</td>
<td>&lt;100</td>
<td>93 700</td>
<td>&lt;200</td>
</tr>
<tr>
<td>S2</td>
<td>~12 200</td>
<td>&lt;100</td>
<td>~30 000</td>
<td>&lt;100</td>
</tr>
<tr>
<td>S3</td>
<td>24 700</td>
<td>&lt;100</td>
<td>58 900</td>
<td>&lt;100</td>
</tr>
<tr>
<td>S4</td>
<td>10 200</td>
<td>&lt;100</td>
<td>24 300</td>
<td>&lt;100</td>
</tr>
<tr>
<td>S5</td>
<td>25 600</td>
<td>&lt;100</td>
<td>57 300</td>
<td>&lt;100</td>
</tr>
<tr>
<td>S6</td>
<td>27 500</td>
<td>&lt;50</td>
<td>39 000</td>
<td>&lt;50</td>
</tr>
</tbody>
</table>

* All compounds were excited in their respective lowest lying isosbestic points.

References:

the individual wells in a multi-well dish were coated with a thin film of PU-embedded sensors (0.6% sensor in PU, w/w). Aqueous solutions of anions (25 or 50 μL, 10 mM, pH 7.4) were then applied into the individual wells, and the dish was incubated at 40 °C for 1 h. Interestingly, the same effect is also obtained when the assay is developed in a microwave oven for 1–2 min. The wells containing solutions of fluoride and pyrophosphate showed a characteristic change in color corresponding to binding. The wells containing only water or nonbinding anions such as chloride, bromide, cyanide, or dihydrogenphosphate did not show appreciable change in color (Figure 8).

In conclusion, a new class of fluorescent heterocycles potentially useful as chromophores and sensors were prepared by a simple methodology utilizing Suzuki and Stille cross-coupling. The resulting materials show bright fluorescence and remarkable emission tuning. Compounds S1–S6 were shown to display anion-induced fluorescence quenching thus acting as potential sensors for inorganic anions. The anion titration experiments using sensors S1–S6 revealed affinity for small or multiply charged anions such as fluoride and dihydrogenpyrophosphate. Preliminary experiments in water-miscible solvents showed that the anion binding/sensing process is not disrupted when anions are added in the form of aqueous solutions. Finally, multi-well assays utilizing polyurethane-embedded sensors allow for colorimetric screening of aqueous anion solutions indicating that the described compounds and approach may yield inexpensive yet effective fluorescence-based anion-sensor assays in the future. Further efforts toward this end are underway.

Acknowledgment. This work was supported by the NSF (DMR-0306117 and NER-0304320 grants to P.A.), BGSU (TIE and FRC grants to P.A.), Kraft Foods, Inc. grant to P.A., and by the Petroleum Research Fund (ACS-PRF 38110-G to P.A.). The Sloan Research Fellowship to P.A. and McMaster Junior Research Fellowship to D.A. are gratefully acknowledged.

Supporting Information Available: Synthetic procedures, UV–Vis and fluorescence titration experiments, binding isotherms, and crystallographic data for F4 in CIF format. This information is available free of charge at http://pubs.acs.org.