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Synthesis and Chemosensory Behavior of Anthracene Bisimide Derivatives

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Intermolecular interactions may be signaled by changes in photoinduced properties, such as absorption, emission intensity or wavelength, and luminescence lifetime.[1] Quenching of photoluminescence intensity is of particular interest as sensitivity is inherently enhanced due to a distinct contrast between signaling events (i.e., luminescent and nonluminescent states).[1] Researchers have utilized photoinduced electron transfer (PET), energy transfer, and others to produce “on/off” sensors based on aromatic and polycyclic aromatic hydrocarbons, aromatic heterocycles, and transition metal complexes.[1] Each approach targets specific sensing applications and maintains distinct advantages and disadvantages that warrant continued investigations.

Recently, chemical sensing of warfare agents has gained increasing attention.[2] Swager et al. reported an elegant example of functional group specific chemosensors that incorporated a transduction/cyclization process specific to highly reactive organophosphates and related compounds.[2c] Our design of chemical sensors is based on creating new luminescent species that may be functionalized to respond to generic or specific target molecules.

Anthracene-based sensors encompass all areas of molecular recognition; for example, anion sensors,[1d,1e] glucose sensors,[1d,3] and metal-organic switches.[4] Anthracene is exploited due to its relative abundance (i.e., low cost) and depth of synthetic manipulation. Anthracene also possesses favorable photophysical properties, such as strong absorption and high quantum yield. Limitations include photoinduced cycloaddition reactions and formation of peroxides in the presence of oxygen.[5] We report herein the synthesis and optical-based chemical sensing properties of two chromophores, **4** and **5** (vide infra), based on highly substituted anthracene bisimides.[6]

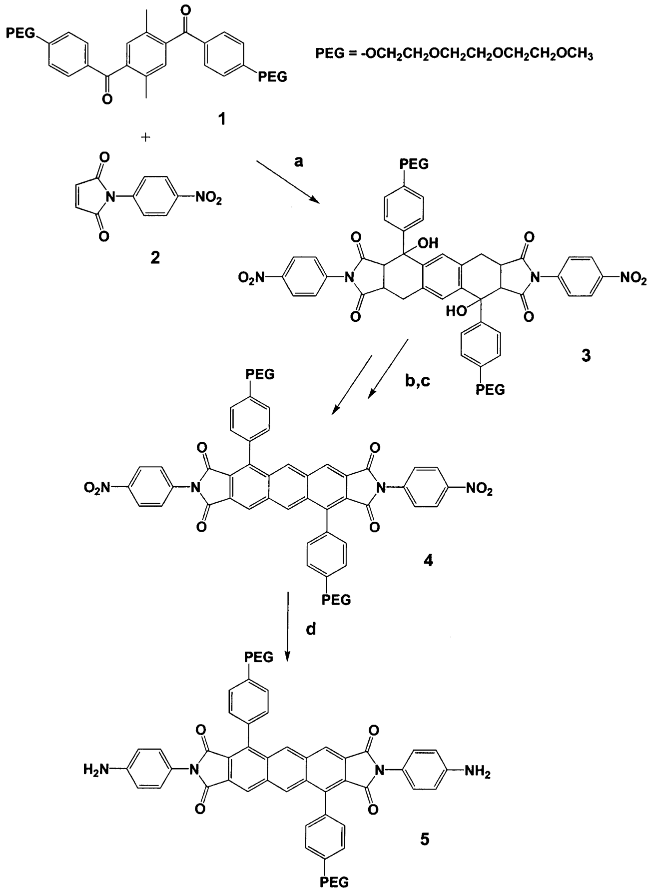

Figure 1. (a) $h\nu$, benzene; (b) *p*-toluene sulfonic acid monohydrate, toluene; (c) DDQ, chlorobenzene; (d) 5% Pd/C, formic acid, DMF.

We have recently developed a method for preparing substituted anthracenes based on the photoenolization of 2,5-dibenzoyl-*p*-xylene (DBX) derivatives.[7] The photoenol of DBX is trapped in situ by a reactive dieneophile to produce a bisadduct.[7] Dehydration of this compound and subsequent aromatization yields highly substituted anthracene derivatives.[7b−d] Following this methodology, 2,5-bis(*p*-(tetraethyleneglycoloxy)benzoyl)-*p*-xylene, **1**, was irradiated for 18 h in the presence of 2 equiv of *N*-(*p*-nitrophenyl) maleimide, **2**, to produce **3** in high yield (98%) as a mixture of stereoisomers (Figure 1). This is a synthetically mild step that has the potential to be used with a wide array of functional groups. Furthermore, addition of tetraethyleneglycoloxy (PEG) units enhanced solubility in common organic

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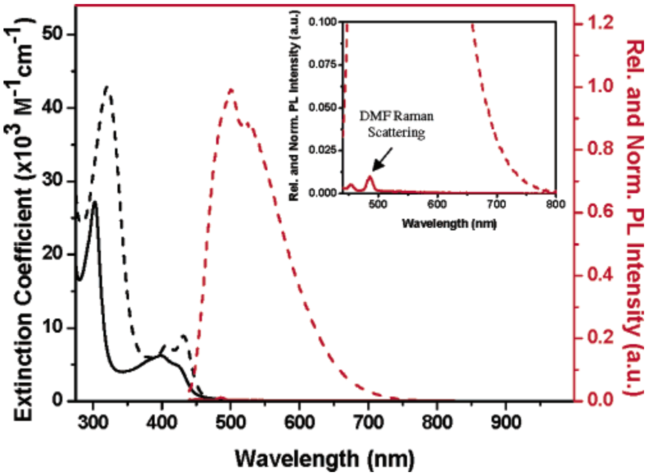

Figure 2. Absorption spectra (black lines) and relative, normalized emission spectra (red lines) for **5** (solid lines) and **4** (dashed lines). Spectra were recorded in anhydrous DMF with 425 nm excitation. Inset: Expanded view of the normalized emission spectra.

media. Subsequent dehydration and aromatization of **3** produced *N*,*N*′-bis(*p*-nitrophenyl)-1,5-bis(*p*-(tetraethyleneglycoloxy)phenyl)anthracene-2,3,6,7-tetracarboxyl bisimide (**4** or ABI–NO_2) in moderate overall yield (34%). This sequence represents more vigorous experimental conditions and care must be taken to design a system that will maintain its chemical integrity).

Photophysical evaluation of ABI–NO_2 (DMF, $\sim 1 \times 10^{-5}$ M) revealed properties unlike traditional anthracene derivatives;[8] Figure 2 exhibits these data. The absorption spectrum displayed two vibrational bands in the visible region ($\lambda_{max} = 408$ and 432 nm, $\epsilon = 7800$ and 8900 M^{-1} cm^{-1}, respectively). Steady-state fluorescence experiments revealed a broad, green emission ($\lambda_{max} = 499$ nm with a shoulder near 530 nm). Although the quantum yield of ABI–NO_2 in anhydrous DMF ($\Phi = 0.05$) was significantly less than that of anthracene in cyclohexane ($\Phi = 0.34$), the bisimide derivative demonstrated good photostability (<5% loss of signal intensity in 24 h) when continuously irradiated at 425 nm (150 W Xe lamp) in the presence of oxygen. The resistance of ABI–NO_2 to excited state reaction with oxygen is likely due to dramatic changes in electronic structure, which is supported by unique absorption and emission spectra. Further investigation of ABI–NO_2 showed no unexpected reactivity with traditional acids or acid halides.

Reduction of ABI–NO_2 with formic acid and Pd/C gave *N*,*N*′-bis(*p*-aminophenyl)-1,5-bis(*p*-(tetraethyleneglycoloxy)phenyl)anthracene-2,3,6,7-tetracarboxyl bisimide (**5** or ABI–NH_2) in high yield (88%).[9] Initial inquiry into the properties of ABI–NH_2 showed an absorption spectrum similar to that of ABI–NO_2 (Figure 2). Unlike the nitro-substituted compound, however, emission from ABI–NH_2 was nearly completely quenched. It is reasonable to suggest that this quenching is due to intramolecular PET from the amine substituents.[1,10] ABI–NH_2 also displayed similar stability toward reaction with oxygen that was noted with ABI–NO_2. Continuous irradiation with 425 nm light from a 150 W Xe lamp in the presence of oxygen resulted in minimal changes of absorption intensity and no fluorescence intensity changes.

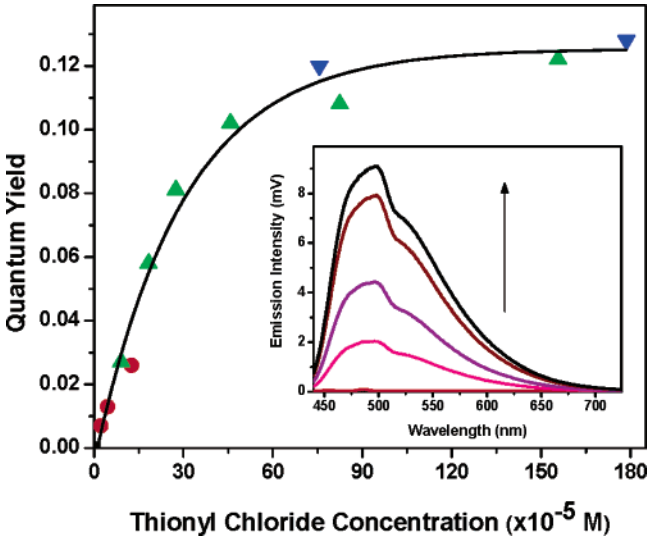

Figure 3. Luminescence titration curve in anhydrous DMF for **5** with additions of thionyl chloride. The complete curve represents three independent experiments with varying initial concentrations of thionyl chloride (● (red) = 2×10^{-5} M, ▲ (green) = 9×10^{-5} M, ▼ (blue) = 75×10^{-5} M). Inset: Selected emission spectra recorded with 425 nm excitation.

Reaction of ABI–NH_2 with organic acid halides, such as acetyl chloride, or with thionyl chloride ($SOCl_2$) gave rise to dramatic fluorescence enhancement. These acid halides mimic the behavior of organophosphonate-based nerve gases and offer a safer alternative to evaluating the effectiveness of luminescent nerve gas sensors.[2c] Figure 3 shows the luminescence titration curve for the reaction of ABI–NH_2 with $SOCl_2$. The response was converted to quantum yield for all data points due to the absence of a clear isospestic point. Conversion of the amines in ABI–NH_2 to the corresponding amides suppresses the PET quenching pathway and the resulting products display luminescence properties similar to ABI–NO_2.[10] Additionally, ABI–NH_2 dispersed on a silica support showed similar sensing behavior toward gas-phase $SOCl_2$, demonstrating its potential use as a solid-state sensor (Figure 4).

It is important to note that acids also increase the luminescence of ABI–NH_2 by reversible protonation of the pendant amines. Since hydrolysis of acid chloride analytes will produce HCl, it is reasonable to question whether the fluorescence activation of ABI–NH_2 in the presence of acid chlorides is due to amine protonation by the HCl byproduct rather than amide formation.

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(8) The present anthracene bisimide derivatives display photophysical properties similar to naphthalimides. For related structures see: (a) Middleton, R. W.; Parrick, J.; Clarke, E. D.; Wardman, P. J. *Heterocycl. Chem.* **1986**, *23*, 849. (b) Alexiou, M. S.; Tychopoulos, V.; Ghorbanian, S.; Tyman, J. H. P.; Brown, R. G.; Brittian, P. I. *J. Chem. Soc., Perkin Trans. 2* **1990**, 837.

(9) Analytically pure sample of ABI–NH_2 were obtained by reversed-phase HPLC and used for all quenching experiments.

(10) Related anthracene example: Herman, P.; Murtaza, Z.; Lakowicz, J. R. *Anal. Biochem.* **1999**, *272*, 87. Related perylene examples: (a) Zang, L.; Liu, R.; Holman, M. W.; Nguyen, K. T.; Adams, D. M. *J. Am. Chem. Soc.* **2002**, *124*, 10640. (b) Mohr, G. J.; Spichiger, U. E.; Jona, W.; Langhals, H. *Anal. Chem.* **2000**, *72*, 1084.

(11) From left to right, the luminescence was enhanced by exposure of ABI–NH_2 to vapor-phase $SOCl_2$. The experiment was performed by suspending liquid $SOCl_2$, held in a glass pipet, near the silica surface ($\sim$1–2 cm). The pictures were recorded in dim light using a 400-nm long pass filter to minimize scattered light.

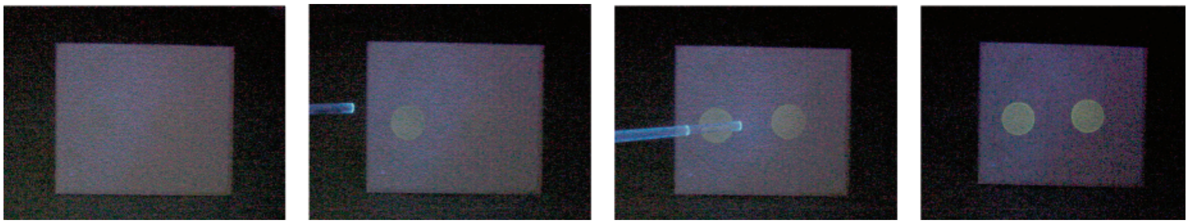

Figure 4. Luminescence sensing of gas-phase $SOCl_2$ by **5** dispersed on silica.[11]

Addition of acid chloride to a DMF solution of ABI−NH_2 containing triethylamine as an acid scavenger resulted in fluorescence enhancement (see Supporting Information). In addition, the fluorescence spectrum of isolated and purified bisamide formed from reaction of ABI−NH_2 with hexanoyl chloride was similar to that shown in Figure 3 for the titration of ABI−NH_2 with thionyl chloride. While it may be possible that some of the acid chloride induced ABI−NH_2 fluorescence enhancement is due to amine protonation, these experiments clearly demonstrate that amide formation also plays an important role in this process. In either case, ABI−NH_2 is an effective sensor for these analytes since it has the capacity to sense their presence both indirectly (from hydrolysis byproducts) and directly (by amide formation).

It should be noted that prolonged exposure of ABI−NH_2 to acidic conditions, either directly from mixing with acid or indirectly from acid halide reaction products, resulted in loss of emission intensity presumably due to acid-catalyzed hydrolysis of the imide ring. We are currently investigating this phenomenon.

To better mimic the behavior of organophosphate-based nerve gases, such as Sarin, four model phosphate derivatives were selected and subsequently added to ABI−NH_2 solutions. Figure 5 shows the reaction of ABI−NH_2 with dichlorothiophosphate (dCTP), methylphosphonic dichloride (MPdC), and dimethylphosphinic chloride (dMPC), all of which resulted in fluorescence enhancement. Thionyl chloride is included as reference. Dimethyl methylphosphonate (dMMP), a less reactive Sarin surrogate, showed no reaction under these conditions. The emission intensities were normalized to readily identify the reagents and do not reflect the relative reactivites of the analytes. Additional experiments are underway to determine reaction kinetics.

In summary, we have utilized the photoenolization reaction of a dibenzoyl-*p*-xylene derivative to synthesize two new, highly substituted anthracene-based molecules. ABI−NO_2 and ABI−NH_2 maintained photostability with longer wavelength absorption and emission spectra as compared to unsubstituted anthracene. Conversion of the terminal nitro groups to amines created an internal photoinduced electron-transfer scenario that quenched the luminescence of ABI−NH_2. Reversible or irreversible reaction of the attached amines resulted in fluorescence recovery. Sensitivity, of ABI−NH_2 and other potential derivatives, to toxic chemicals may prove useful for early detection systems.

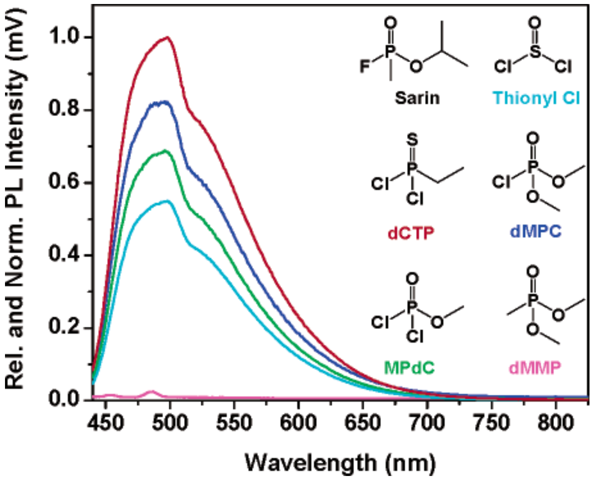

Figure 5. Relative, normalized emission spectra for **5** in the presence of excess dCTP (red line), MPdC (blue line), dMPC (green line), thionyl chloride (cyan line), and dMMP (magenta line). Spectra were recorded in anhydrous DMF with 425 nm excitation.

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Supporting Information Available: Data and synthetic preparations (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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