

Simple Molecule-Based Fluorescent
Sensors for Vapor Detection of TNT

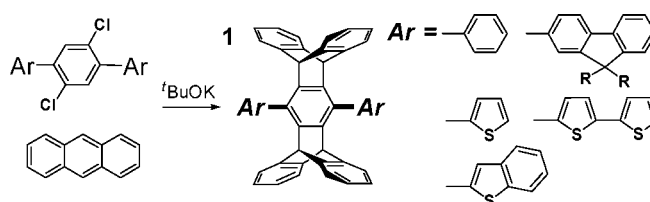
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ABSTRACT



1,4-Diarylpenttiptycenes (1a–e) were synthesized from 1,4-dichloro- or 1,4-difluoro-2,5-diarylbenzene derivatives by double base-promoted dehydrohalogenation to give corresponding arynes, which in the presence of anthracene undergo cycloaddition providing 1,4-diarylpenttiptycenes in moderate overall yields. The resulting 1,4-diarylpenttiptycenes show fluorescence modulated by the 1,4-aryl residues. The fluorescence is quenched in the presence of vapors of nitroaromatic compounds suggesting potential application in sensing of explosives.

Host materials that form inclusion complexes with small molecules are the subject of considerable interest owing to potential applications in the preparation of sensors and materials for selective sequestration of substrates of interest. Growing attention is currently devoted to studying supramolecular complexes of a wide variety of lipophilic hosts for electroneutral species that include calixarenes¹ and related macrocycles, cyclodextrins,² cycloveratrylenes,³ cryptophanes,⁴ cucurbiturils,⁵ and their derivatives.

The interest in penttiptycene receptors was sparked by the discovery that iptycenes bind nitroaromatic explosives⁶

used in landmines and improvised explosive devices.⁷ The materials successfully used for detection of nitroaromatics are fluorescent polymers with the ability to form complexes with nitroaromatics while changing their emission. Examples are polyphenyleneethynylenes with integrated penttiptycene receptors,^{8a} polyphenylenebutadiynylenes,^{8b} polyacetylenes,^{8c} and polymetalloles^{8d} such as polysiloles.^{8e}

As a part of our work on polythiophene conductivity-based sensors⁹ we decided to investigate electropolymerizable penttiptycene receptors carrying thiophene moieties to be deposited as electrochemical sensors for TNT.

Penttiptycene derivatives are most frequently synthesized by the Clar synthesis, which involves double Diels–Alder

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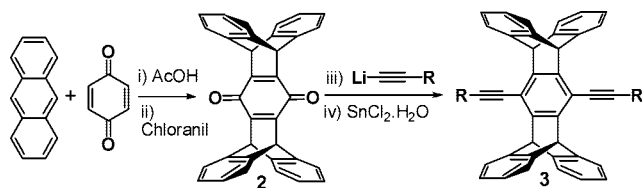
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cycloaddition of an acene to benzoquinone.¹⁰ The resulting pentiptycene quinone **2**¹¹ may then be reacted with organometallic reagents such as lithium acetylides to yield 1,4-substituted derivatives **3** according to Scheme 1, which was

Scheme 1. Synthesis of 1,4-Substituted Pentiptycenes



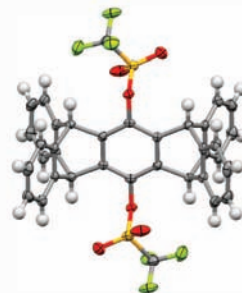
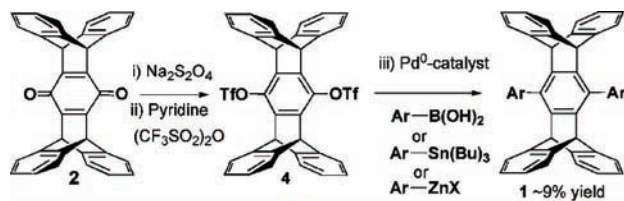
utilized by Swager to generate poly-(phenyleneethynylene)s comprising pentiptycene moieties.⁶ Unfortunately, there is no literature describing a similar approach using aryllithiums or arylmagnesium halides.

This pattern of limited reactivity of both iptycene-benzoquinone carbonyls was also observed by Yang et al.,^{12,13} who synthesized pentiptycenes with middle ring substituents (described here as 1,4-positions based on the *p*-benzoquinone).¹⁴ Yang et al. successfully attached a variety of substituents to 1,4-positions, however, carbon substituents proved difficult to introduce to both 1,4-positions. Notable exceptions are the acetylene derivatives introduced following the outline in Scheme 1.

Originally, we believed the lack of a direct coupling method to be due to the limited availability of the 1,4-dihalo derivatives.^{12,15,16} However, Yang et al.^{12,13} were able to successfully perform a Suzuki-Miyaura¹⁷ coupling on 1-alkoxy-4-iodopentiptycene in 72% yield. In an effort to circumvent the problem of limited availability of 1,4-dihalo derivatives, we synthesized the corresponding 1,4-triflate **4**, which we hoped would react in Pd⁰-catalyzed reactions such

as the Stille,¹⁸ Suzuki-Miyaura,¹⁶ and Negishi¹⁹ couplings (Scheme 2). The reduction of quinone **2** to the corresponding

Scheme 2. Alternative Synthesis of 1,4-Diaryl Pentiptycenes^a



^aX-ray ORTEP representation of **4** (displacement ellipsoids are scaled to the 50% probability level).

hydroquinone form²⁰ followed by reaction with triflic anhydride in pyridine at 0 °C gave the corresponding bis-triflate **4** in a quantitative yield (>99%). Triflate **4** is a stable crystalline compound that can be prepared at a multigram scale. The coupling procedures, however, failed to yield 1,4-diaryl pentiptycenes **1** in yields exceeding 9%. The starting material **4** was recovered regardless of the coupling method or reaction conditions.

Simultaneously with the above approach, we attempted to construct the 1,4-diaryl pentiptycene using the aryne-anthracene [4 + 2] cycloaddition approach.²¹ Toward this end we considered several strategies to generate a 1,4-diaryl bisaryne precursor **5** to be reacted with anthracene.

Numerous methods of generating benzyne are known from the literature,²² starting, for example, from haloaromates using sodium amide or other strong bases, 1,2-dihaloarenes,²³ from arenediazonium ions derived from anthranilic acid,²⁴ 2-(trimethylsilyl)phenyl triflates, aminotriazoles,^{25,26} and aryl[2-(trimethylsilyl)phenyl]iodonium triflates,²⁷ etc. Compared to the double dehydrohalogenation, these methods of generating aryne are often carried out using mild conditions and furnish moderate to high yields of corresponding arynes. However, the preparation of the hexasubstituted benzene precursors requires multiple-steps syntheses that with exception of tetrahalo-1,2-diarylbenzenes in our hands did not

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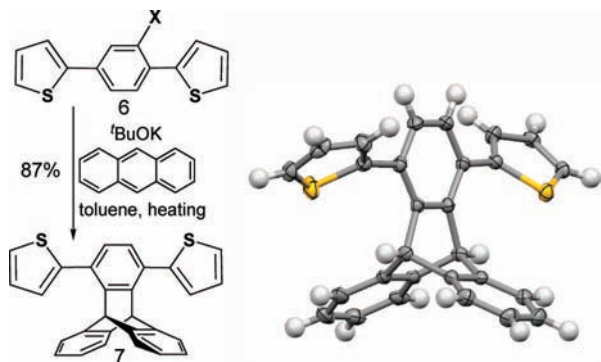
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result in overall yields exceeding 40% of the precursor for the preparation of diaryl bisaryne **5**. Because we are targeting low-cost precursors for the sensor polymers, we decided to focus on a more straightforward method that would utilize few synthetic steps and would be easy to scale up.

For this reason, we decided to investigate the simple dehydrohalogenation/Diels–Alder cycloaddition of an *in situ* generated aryne to anthracene. There are literature precedents, albeit not for diarylpentiptycenes, suggesting that this reaction would proceed. For example, Hart²⁸ described a Bu-Li promoted reaction of 3,6-substituted 1,2,4,5-tetrabromobenzene derivatives in the presence of anthracene to yield pentiptycene, 1,4-dimethylpentiptycene, and 1,4-dimethoxy-pentiptycene in 26, 14, and 21% yield, respectively. An earlier report by Cadogan²⁹ describes the reaction of sterically crowded 1,4-dibromo-2,5-di-*t*-butylbenzene and *t*BuOK as a base in the presence of anthracene, which yielded *t*-butyl aryl ethers as well as a pentiptycene side-product, albeit in ~2% yield.

First, we explored the reaction conditions described by Cadogan²⁸ using 3-halo-1,4-bis(thien-2-yl)benzene and potassium *t*-butoxide in the presence of anthracene (Scheme 3). Reaction condition tuning allowed to generate the

Scheme 3. Base-Promoted Reaction of 3-Halo-1,4-bis(thien-2-yl)benzene (X = Br, Cl)^a



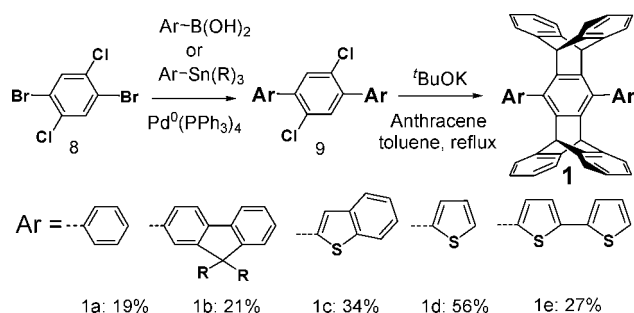
^aX-ray ORTEP representation of **7** (displacement ellipsoids are scaled to the 50% probability level).

corresponding di(thien-2-yl)trityptene **7** in up to 87% yield. The identity of **7** was confirmed by spectroscopic methods as well as X-ray crystallography.

Similar conditions were then used to synthesize 1,4-diaryl pentiptycenes **1a–e**. While the previous reaction was carried out using 3-bromo- or 3-iodo-1,4-bis(thien-2-yl)benzene, for the synthesis of **1a–e** we decided to use the 3,6-dichloro congener. While the chloride is certainly not as good a leaving group as

bromide or iodide, the preparation of the starting 1,4-diaryl-2,5-dichlorobenzenes **9a–e** in photonic purity³⁰ using appropriate arylboronic acid¹⁶ or aryl-tin derivative¹⁷ to give the corresponding dichloro-derivatives **9a–e** was easier. In the case of 1,4-diaryl-2,5-dibromobenzenes prepared from 1,4-dibromo-2,5-diiodobenzene using Pd⁰ coupling procedures, the presence of 1–5% of difficult to separate side-products was observed.³¹ Following the arylation of 1,4-dibromo-2,5-dichlorobenzene **8** the 1,4-diaryl-2,5-dichlorobenzenes **9a–e** were subjected to double *t*-BuOK-promoted dehydrohalogenation/cycloaddition to anthracene present in excess (~5 equiv) in the reaction mixture. Pentiptycenes **1a–e** were purified by column chromatography and the pure products were obtained in respectable yields of 20–56%. Similarly, sodium amide also furnished expected pentiptycenes, albeit in a lower amount. The synthesis of 1,4-diaryl pentiptycenes **1a–e** is shown in Scheme 4.

Scheme 4. Synthesis of 1,4-Diaryl Pentiptycenes



Thus far, we have prepared 1,4-diaryl pentiptycenes **1a–e**, and it seems that the reaction is fairly general: both arenes and heteroarenes may be used.

Additionally, we explored the flexibility of this synthetic protocol. The regioselectivity in the coupling step is determined by the preferential oxidative addition (C–I > Br > Cl) of the haloarene to the Pd⁰-catalyst. The combination of I and Br substituents gave the expected 1,4-diaryl-2,5-dibromobenzene, which underwent dehydrohalogenation-cycloaddition smoothly to give **1** in slightly higher (~5–10%) yields compared to the dichloro-compound **8**. Following the recently described double dehydrofluorination of 1,4-difluoro-2,5-dimethoxybenzene, which was also utilized in the Diels–Alder reaction³² we also tested the difluoro-analogs of **9**. Here too, the 1,4-diaryl-2,5-difluorobenzenes underwent dehydrohalogenation-cycloaddition, with only slightly diminished yields compared to the chloro-congeners. A step-wise dehydrohalogenation using BuLi at –78 °C as described in the literature³¹ resulted in only small (<5%) improvement. It seems that the sterical demands of the 1,4-aryl substituents

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(30) Photonic materials were purified to obtain satisfactory results using MS/NMR/elemental analyses, but also single-exponential luminescence lifetime decays. Even small amounts (<1%) of brightly fluorescent terphenyl-type impurities would invalidate the later spectroscopic measurements.

(31) These side-products were observed even when the reaction was carried out at low temperature (30–45 °C). According to MS spectra these minor products originated from deiodination and coupling to *m*-position (i.e., result of C–Br oxidative addition).

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rather than their electronic properties, the nature of the leaving group or the method generating the aryne determine the reaction yield.

The ability of 1,4-diarylpentipytcenes to act as TNT sensors was studied in solution and in the solid state following Swager's procedures^{33,34} utilizing fluorescence as a measure of the pentipytcene receptor-nitroaromate interaction. The fluorescence quantum yields were estimated as follows: **1a** (10%, 4.03 ns), **1b** (19%, ND), **1c** (15%, 0.3 ns), **1d** (~25%, 0.8 ns), **1e** (20%, 0.82 ns) using anthracene as a standard. Fluorimetric titration of **1a-e** by various nitroaromates such as nitrobenzene (NB), 2,4-dinitrotoluene (2,4-DNT), trinitrotoluene (TNT), 1-nitronaphthalene (NN), and 2,3-dimethyl-2,3-dinitrobutane taggant (DMDNB) in dichloromethane showed an expected decrease in fluorescence intensity (Figure 1). Fits of the first linear part of the

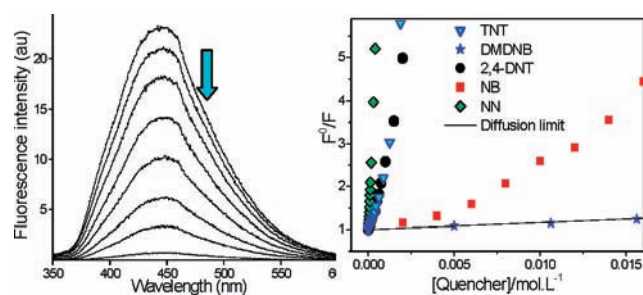


Figure 1. (Left) Emission quenching observed with **1e** (5.0 μM in CH_2Cl_2) upon DNT addition. (Right) Stern–Volmer plots for **1e** and various nitroaromates. Excited at 325 nm (abs. maximum).

Stern–Volmer plots allowed estimating apparent quenching constants to be in the range of 1000–3300 M^{-1} in the case of TNT. These values of quenching constants are comparable to the ones found for amplifying polymers.^{8a}

To estimate the ability of **1a-e** to sense nitroaromate vapors, we used a glass slide with round wells (1.3 mm diameter; 0.8 mm deep; 4 \times 3 wells, 3 compounds in 4 replicas), and the sensors **1d** and **1e** were cast in the wells as a polyurethane solution in THF. Tetraphenylporphyrin (TPP) was used as an internal standard.

Upon illumination with black light (~ 360 nm), TPP as well as **1d** and **1e** showed emission in the solid state. The order of fluorescence intensity from the slides in Figure 2, that is, before being exposed to equilibrium vapors of DNT (0.18 ppm) or TNT (7.70 ppb), was **1e** > TPP > **1d**. The glass slide and sensor films were imaged before and after exposition to DNT or TNT vapors. Within 30 min the sensors fluorescence was quenched (Figure 2). Comparison of all slides shows the red TPP fluorescence did not change, presumably because the electron excited to the TPP LUMO level does not possess the energy to reduce the nitroaromates.^{8a} **1d** and **1e**, on the other hand, displayed DNT and TNT-mediated fluorescence quenching suggesting an interaction between **1d** and **1e** and DNT or TNT.

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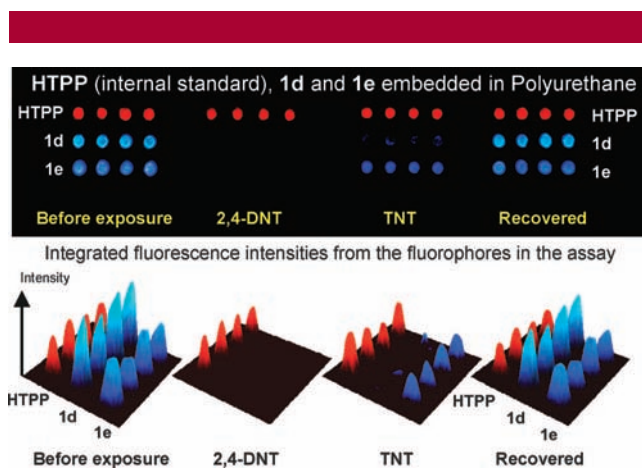


Figure 2. (Top) Photograph of the sensor slide before and after exposure to DNT and TNT in their equilibrium vapors at 22 $^{\circ}\text{C}$, and finally upon recovery in the stream of clean air. (Bottom) Integrated light output from the sensors represented as a quasi-3D graph (X-Y-Intensity) allows for signal quantitation.

Given the difference in the LUMO-levels of the two sensors as well as the quenchers it is not entirely surprising that the sensor films show a different degree of quenching for each vapor analyte. The fluorescence of the sensor films was largely restored when the films were washed by a stream of clean air. This suggests that these easy-to-make sensor films may be used in differential (array-based) sensors for nitroaromates.³⁵

In summary, we have developed a simple method for synthesis of 1,4-diarylpentipytcenes in two steps from 1,4-dibromo-2,5-dichlorobenzene that involves double dehydrohalogenation followed by aryne cycloaddition to anthracene. The yield of the respective 1,4-diarylpentipytcenes is moderate considering that four consecutive steps are involved (20–56% overall for four steps, i.e., 60–85% per step). Moreover, the synthesis is easy to perform from inexpensive starting materials. Preliminary fluorescence quenching experiments aimed at evaluation of 2,4-DNT and TNT interaction with 1,4-diarylpentipytcenes **1d** and **1e** showed a high degree of fluorescence quenching characterized by apparent quenching constant in the range of 1000–3300 M^{-1} for TNT. Solution-cast polyurethane films doped with **1d** and **1e** showed similar quenching patterns in the solid state. Taken together these observations suggest that 1,4-diarylpentipytcenes could be of potential interest for the fabrication of sensors for explosives. The preparation of such materials and devices is underway.

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Supporting Information Available: Experimental procedures and spectroscopic data for **8a-e**, **1a-e**, X-ray data for **3** and **6**. This material is available free of charge via the Internet at <http://pubs.acs.org>.