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Synthesis and properties of bis(pyrazino[2′,3′:4,5]imidazole)-fused 1,2,5,6-tetrahydro-1,4,5,8,9,10-hexaazaanthracenes: a new fluorescent nitrogen-rich heterocycle

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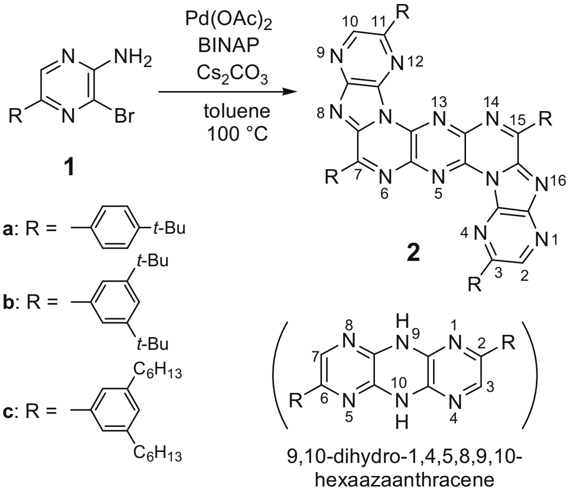
ABSTRACT

Nitrogen-rich heterocycles, bis(pyrazino[2′,3′:4,5]imidazole)-fused 1,2,5,6-tetrahydro-1,4,5,8,9,10-hexaazaanthracenes (BPI-HAAs) were prepared by conventional Pd(OAc)$_2$/BINAP-catalyzed C–N coupling reactions of 5-aryl-3-bromoaminopyrazines. The BPI-HAA core is a planar structure with aromaticity, and this heterocycle exhibits red fluorescence and moderate electron-accepting characteristics.

Fluorescent compounds are widely used in applications such as fluorescent sensors for live-cell imaging and light-emitting components for organic light-emitting devices.[1] Many fields depend on advances in new fluorescent compounds.[2] Fluorescent compounds based on bioluminescence[3] are promising because of their high-performance for light generation. Aminopyrazine is the core structure of the bioluminescence-related compound ethioluciferamine, derived from the ostracod *Cypridina*,[4] and AF-350, derived from the jellyfish *Aequorea*.[5] Aminopyrazines are also useful precursors for preparing bioluminescent substrates and light-emitter compounds.[4b,6] In this study we then have attempted to prepare a new fluorescent compound by modification of an aminopyrazine derivative. As one of our target compounds, we tried to prepare 9,10-dihydro-1,4,5,8,9,10-hexaazaanthracene by C–N cross-coupling reactions[7–9] with 3-bromoaminopyrazine (**1**) and serendipitously generated a fluorescent nitrogen-rich heterocycle, bis(pyrazino[2′,3′:4,5]imidazole)-fused 1,2,5,6-tetrahydro-1,4,5,8,9,10-hexaazaanthracene (BPI-HAA, **2**) (Scheme 1).[10] We report herein the synthesis and fundamental properties of the new heterocycle **2**.

We applied a typical Pd(OAc)$_2$/BINAP-catalyzed C–N cross-coupling condition [Pd(OAc)$_2$ (3 mol %), BINAP (4 mol %), Cs$_2$CO$_3$, toluene, 100 °C] reported by Buchwald and co-workers[9] to 5-(4-*t*-butylphenyl)-3-bromoaminopyrazine (**1a**), which produced a complex mixture containing various colored products. Careful separation of the products using silica gel chromatography resulted in the isolation of red compound **2a** in 13% yield as the major product together with several purple, green, and red compounds in low yields (<5%). Because **2a** has low solubility in typical organic solvents, including ethyl acetate, chloroform, and methanol, we also examined C–N coupling reactions with **1b** and **1c**, which have a 3,5-dialkylphenyl group. The reactions mainly produced red compounds **2b** and **2c** in 7% and 6% yields, respectively. Molecular weights of **2** indicate that four molecules of **1** make up **2**, and the ^{1}H NMR spectra of **2** indicate their symmetric structures. X-ray crystal structure analysis of **2b** confirmed its BPI-HAA structure (Fig. 1A) (cf. Supplementary data). Crystals of **2b** contain two chloroform molecules per unit cell. The solid-state structure of **2b** has a planar core seven-fused ring system, and 3,5-di-*t*-butylphenyl groups are twisted with dihedral angles of 27° (C3 and C11) and 43° (C7 and C15). The core seven-fused ring system shows a bond length alternation (Fig. 1B).



Scheme 1. Synthesis of BPI-HAA **2**.

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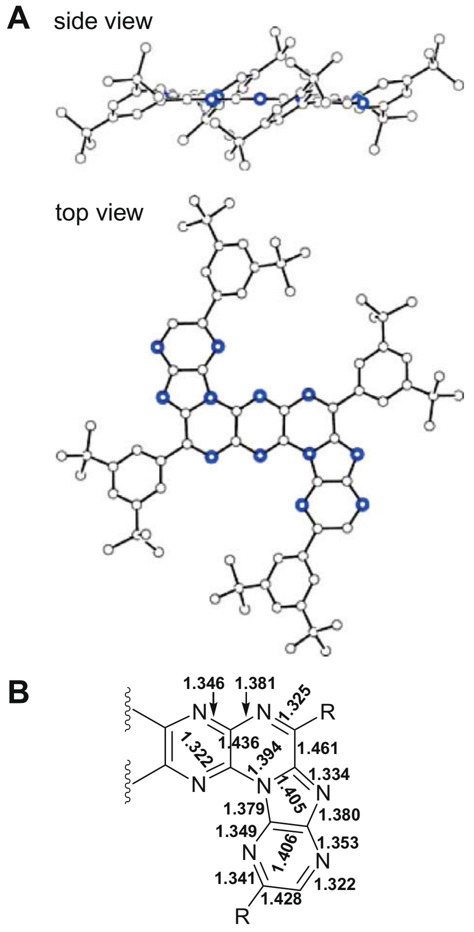
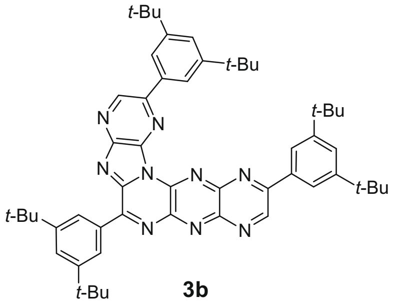


Figure 1. Molecular structure of **2b** (A) whose hydrogen atoms were omitted for clarity and selected bond distances in a partial structure of **2b** (B).

Generation of **2** suggests that the C–N coupling reactions of **1** produce 9,10-dihydro-1,4,5,8,9,10-hexaazaanthracenes as intermediates, and further condensation reactions of dihydrohexaazaanthracenes with **1** produce **2**. The reaction processes that generate **2** include four Pd-catalyzed C–N couplings, two nucleophilic C–N couplings, and three dehydrogenations. In an attempt to regulate the preparation of **2b**, we increased the amount of $Pd(OAc)_2$ (55 mol %) and BINAP (50 mol %), resulting in the generation of orange compound **3b** (22% yield) instead of **2b**. Compound **3b** consists of three molecules of **1b**.[11]



3b

Figure 2 shows UV–vis absorption and fluorescence spectra of **2** in $CHCl_3$, and the spectral data are summarized in Table 1. The lowest energy absorption bands of **2** were observed at around 550 nm, and fluorescence emission maxima of **2** were observed at around 570 nm with quantum yields (Φ_f) over 0.7. The lowest energy absorption and fluorescence emission bands exhibited vibrational structures. The absorption maxima (λ_{ab}) and fluorescence emission maxima (λ_f) of **2b** showed a slight blue shift compared to those of **2a** and **2c**, indicating that the bulky 3,5-di-*t*-butylphenyl groups of **2b** are twisted against the planar BPI-HAA skeleton more than the 4-*t*-butylphenyl and 3,5-dihexylphenyl groups of **2a** and **2c**, respectively. The λ_{ab} and λ_f values of **2b** in various solvents indicate a slight dependency on solvent polarity (cf. Supplementary data).

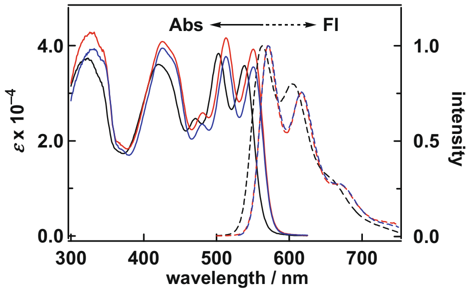


Figure 2. UV–vis absorption (Abs) and fluorescence (Fl) spectra of **2a** (blue), **2b** (black), and **2c** (red) in $CHCl_3$ at 25 °C.

Table 1
UV–vis absorption, fluorescence emission, and reduction potentials of **2**

Compounds	λ_{ab}[a] (nm) [$\varepsilon/10^4$]	λ_f[a] (nm) [Φ_f]	E^{red} (V)[b]
2a	551 [3.9], 513 [4.2], 425 [4.1], 329 [4.2]	616, 571 [0.75]	−1.00 −1.35
2b	538 [3.6], 503 [3.8], 420 [3.6], 323 [3.7]	603, 563 [0.71]	−0.97 −1.50
2c	550 [3.6], 513 [3.8], 426 [4.0], 334 [3.9]	616, 570 [0.75]	−1.00 −1.51

[a] In $CHCl_3$.

[b] 0.10 M *n*-Bu_4NClO_4 in CH_2Cl_2, Pt electrode, scanning rate 100 mV s^{-1}, *V* versus Fc/Fc^+.

Because the core ring system of **2** is a nitrogen-rich heterocycle, **2** is expected to have electron-accepting characteristics.[12] Square wave voltammograms (SWVs) of **2** showed two reduction peaks at −1.0 and −1.5 V versus Fc/Fc^+ in CH_2Cl_2. Cyclic voltammograms of **2** indicated that the first reduction at −1.0 V showed reversible waves, whereas the waves of the second reduction at −1.5 V were semi-reversible (cf. Supplementary data). The values of the first reduction potentials indicate that **2** has an electron-accepting ability similar to that of *p*-benzoquinone.[13]

To better understand the observed properties of **2**, DFT calculations on the core BPI-HAA [**2**(H), R = H] and tetraphenyl-substituted BPI-HAA [**2**(Ph), R = Ph] were conducted at the B3LYP/6-31G(d) level.[14–17] Optimized structures of **2**(H) and **2**(Ph) have a planar core seven-fused ring, and bond length alternation of their core ring systems is similar to that observed by X-ray structure of **2b**. Calculated dihedral angles of the phenyl groups against the core ring system in **2**(Ph) are 16° (C3 and C11) and 3° (C7 and C15). These values are smaller than the corresponding values observed for **2b** in crystals, indicating that steric hindrance between bulky 3,5-di-*t*-butylphenyl groups at the C3 and C7 (C11 and C15) positions causes a twist of the 3,5-di-*t*-butylphenyl groups. HOMO and LUMO levels were calculated to be −6.77 and −3.57 eV for **2**(H), respectively, and −5.97 and −3.35 eV for **2**(Ph), respectively. The LUMO levels are similar to that (−3.53 eV) of *p*-benzoquinone calculated by the same method, and this result supports the electron-accepting property of the BPI-HAA core structure. Transition

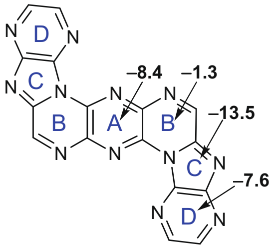


Figure 3. NICS values of **2**(H).

energy from S_0 to S_1 for **2**(Ph) was calculated by TD-DFT [B3LYP/6-31G(d)] to be 2.30 eV (540 nm, oscillator strength = 0.60), which is well similar to those of the observed lowest energy absorption bands of **2**. Nucleus induced chemical shift (NICS) values[18] at the centers of the A–D rings in **2**(H) were calculated to range from -1.3 to -13.5 at the GIAO-B3LYP/6-31+G(d)//B3LYP/6-31G(d) level (Fig. 3). The values for the A and D rings are similar to that of pyrazine, and the value for the C ring is similar to that of imidazole.[18] These negative NICS values for the A, C, and D rings predict that the BPI-HAA ring system has aromatic characteristics, while the B rings show a small negative value.

In conclusion, we successfully prepared a heterocyclic seven-fused ring system, BPI-HAA **2** by conventional Pd(OAc)$_2$/BINAP-catalyzed C–N coupling reactions of **1**. The BPI-HAA core is a planar structure with aromatic characteristics. Because **2** has both fluorescent and electron-accepting characteristics, it will be useful as a new fluorophore and as a new electron-carrier for biological and materials science. The nitrogen-rich structure of **2** will also be useful as a ligand for making metal ion-complexes, and an investigation of metal ion-complex formation with **2** is now in progress.

Acknowledgments

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Supplementary data

Supplementary data (experimental details, ^{1}H NMR spectra of **1**, **2**, and **3b**, single crystal X-ray analysis, UV–vis absorption and fluorescence spectra, and DFT calculation data) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.01.015.

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