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Versatile Transamination in Quinonediimine Chemistry: Towards a Novel Class of Water Soluble UV/violet Chromophores

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Abstract

Transamination reactions occurring on 2,5-diaminobenzoquinonediimine (**QDI**) in presence of ethylenediamine yields fluorescent 1,2,3,4-tetrahydropyrazino[2,3-g]quinoxaline (**1**). When the same reaction is carried out with *N,N'*-bis(aminoethyl)-1,3-propanediamine, a novel cationic quinoxalinium species (**2**) is isolated, which can be further condensed to a benzaldehyde derivative to afford a benzimidazolo-fused quinoxaline dye (**3**) that is a water-soluble fluorophore in the UV-visible range.

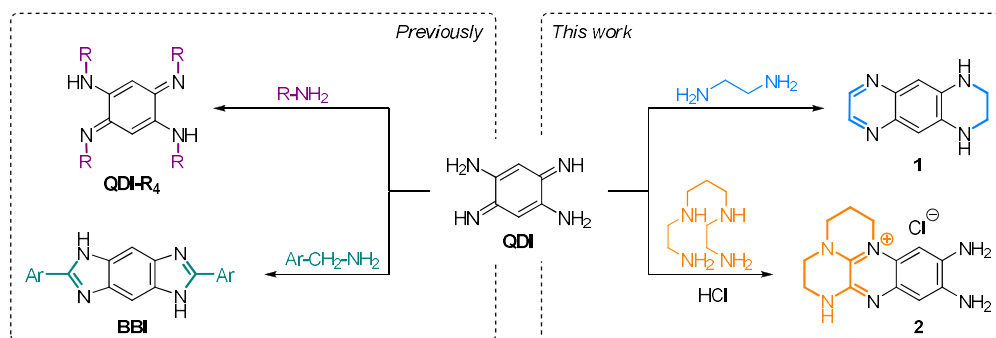
Introduction

2,5-Diaminobenzoquinone diimine (**QDI**) stands as a versatile class of ligands for the preparation of coordination complexes featuring catalytic, optical or magnetic properties [1], and as a building block to design specific chromophore families such as near-infrared aza-macrocycles [2-4], colorful π -zwitterions [5, 6] or benzobisimidazolium dyes [7-11]. Although molecule **QDI** was reported more than a century ago [12], its reactivity has been poorly investigated so far. Transamination reaction – well known reaction in biochemistry accomplished by transaminases [13, 14] – has been recently investigated on **QDI**. Using primary alkylamines, this approach appeared to be an efficient and green method to reach N-substituted **QDI** (**QDI-R₄**, Scheme 1) [15]. Interestingly, when the same reaction occurs with benzylamine derivatives (Ar-CH₂-NH₂), the corresponding aryl-substituted benzobisimidazole (BBI) is then obtained.

Herein, as an extension of this work, we investigated the reactions involving **QDI** and polyamines to enlarge the scope of this reaction in quinoid chemistry. This approach allows to reach two other classes of molecules from **QDI** depending on the number of amine functions of the precursor: 1) diamino quinoxaline derivatives **1** [16, 17], also known as 1,2,3,4-tetrahydro-1,4,5,8-tetraazaanthracene, could be obtained from an alkyl diamine, and 2) new diamino quinoxalinium **2** introducing a annelated alkylamino fragment reminiscent of azajulolidines [18, 19] was formed from a linear tetramine.

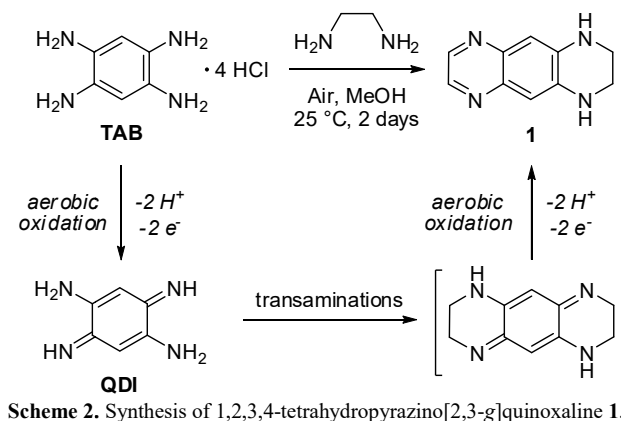
Results and discussion

When tetraaminobenzene tetrahydrochloride (TAB•4HCl) is mixed with an excess of ethylenediamine under aerobic conditions, the solution quickly turns brown, as a result of the oxidation of TAB to the corresponding **QDI** (Scheme 2). After two days of stirring at room temperature, the compound **1** is isolated in 40% yield as a yellow solid. This molecule was previously synthesized by high-temperature condensation of ethylenediamine on 2,5-dihydroxy-*p*-benzoquinone or catechol derivatives [17, 20, 21].



Scheme 1. Previously reported transamination on 2,5-diaminobenzoquinone diimine (**QDI**) to reach N-substituted benzoquinone diimines (**QDI-R₄**) (R = alkyl) or C-substituted benzobisimidazoles (**BBI**, Ar = aryl), and diamino quinoxalin(ium) derivatives **1** and **2**.

The presence of two ethylenediamine moieties on the final compound indicates that the four transaminations occur on the quinone derivative before its aromatization step. When TAB•4HCl is stirred overnight in presence of *N,N'*-bis(aminoethyl)-1,3-propanediamine, a precipitate is formed and isolated as the hygroscopic salt **2** with 54% yield (Scheme 3). Noteworthy, this molecule can be obtained with comparable yield by reaction between **QDI** and a stoichiometric amount of *N,N'*-bis(aminoethyl)-1,3-propanediamine in presence of a catalytic amount of acid.



Scheme 3. Synthesis of diamino quinoxalinium derivative **2**.

The structure of the isolated compound **2** was supported by high-resolution mass spectrometry (HRMS) and combined 1D and 2D NMR experiments (see Supplementary Data). The ^1H NMR spectrum (Figure 1) has been recorded in $\text{DMSO}-d_6$ and clearly shows, on one hand, the presence of two inequivalent protons at δ 6.63 and 6.75, corresponding to hydrogen born by the aromatic ring (positions 6 and 7). On the other hand, three broad singlets at δ 5.09, 5.32 and 7.65 are attributed to NH_2 and NH protons (positions 8, 9 and 10). Finally the five multiplets found between δ 2.25 and 4.16 correspond to the bridging propyl and ethyl moieties (positions 1-5), each signal integration corresponding to two protons. A tentative mechanism of formation of compound **2** is proposed in Supplementary Data (Scheme S1) based on the synthesis of bis-aminals from glyoxal and polyamines [22, 23].

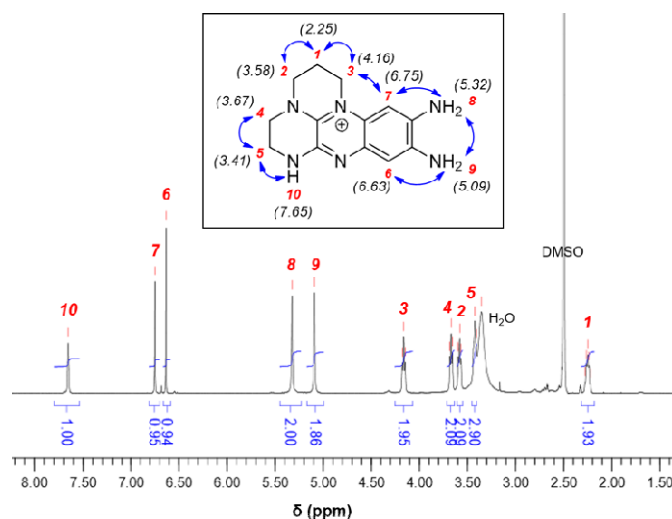
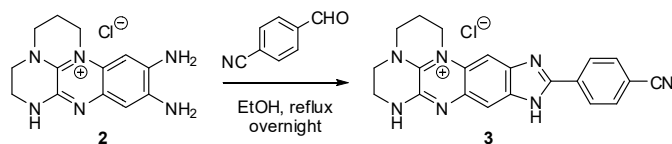


Figure 1. ^1H NMR (400 MHz, 298 K) spectrum of compound **2** recorded in $\text{DMSO}-d_6$. Values in parentheses are the measured chemical shifts (ppm) and blue arrows correspond to the correlations detected between protons by 2D experiments (see Supplementary Data).

Next, to assess the reactivity of the amine functions in compound **2**, it was further condensed to *p*-cyanobenzaldehyde to yield the hybrid benzimidazole-quinoxalinium derivative **3** with 90% yield (Scheme 4). Unfortunately, attempts to condense benzaldehyde reagents featuring electron-enriching substituents lead to the formation of intractable mixtures or isolation of remaining starting material.



Scheme 4. Synthesis of diamino quinoxalinium derivative **3**.

The UV-vis absorption spectra of chromophores **1-3** were recorded in spectrophotometric grade water and all display broad lower energy transitions located in the violet spectral range (see Figure 2 and Table 1). While quinoxaline **1** presents a broad and Gaussian-shaped absorption transition with a maximum at 410 nm, cationic dye **2** features two absorption bands centered at 415 and 345 nm with molar extinction coefficients of *ca.* 7000 and 12000 M⁻¹cm⁻¹, respectively.

Table 1. Optical properties of the chromophores **1-3** in water.

Dye	λ_{abs} (nm)	ϵ (M ⁻¹ cm ⁻¹)	λ_{em} (nm)	Φ^a
1	410	10900	509	0.14
2	415	7600	-	-
3	398	10600	469	0.35

^a Quantum yields relative to anthracene ($\Phi = 0.28$ in ethanol) [24].

The presence of an imidazole moiety featuring an electron-withdrawing *p*-cyanobenzene group causes a slight blueshift of the absorption to *ca.* 400 nm. Interestingly, while the molecule **2** shows no fluorescence, compounds **1** and **3** display strong emission in the blue-green region upon UV excitation (Figure 2), with maxima centered at 509 and 469 nm, characterized by quantum yield estimated to *ca.* 0.14 and 0.35, respectively.

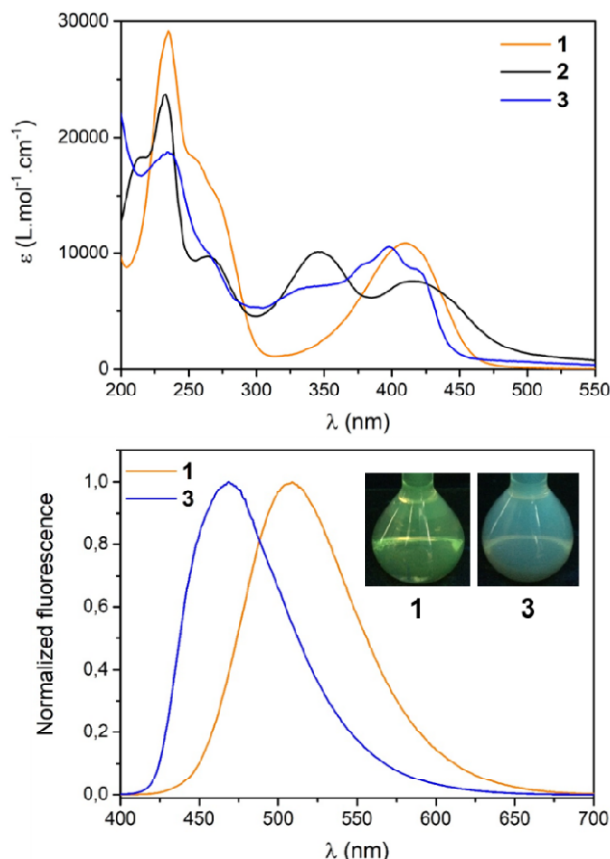


Figure 2. Top: UV-vis absorption spectra of the dyes **1-3** in water solution (*ca.* 2.10⁻⁵ M). Bottom: normalized fluorescence spectra of compounds **1** and **3** in water (excitation at 350 nm) and pictures of the solutions under 365 nm irradiation.

The pH-dependent optical behaviors of **1-3** were assessed in aqueous solution in presence of 0.1 M triethylamine or trifluoroacetic acid (see Figures 3 and S19). While a basic medium has minor influence on the optical properties of the series, the presence of TFA leads to noticeable hypsochromic and hyperchromic shifts of absorption maxima for compounds **2** and **3**, presumably due to the generation of dicationic species implying restrained electronic delocalization within the chromophores. In contrast, dye **1** shows noticeable redshifts of the absorption and emission maxima to 476 and 560 nm, respectively, probably due to the establishment of an intramolecular charge transfer in the mono-protonated species [25].

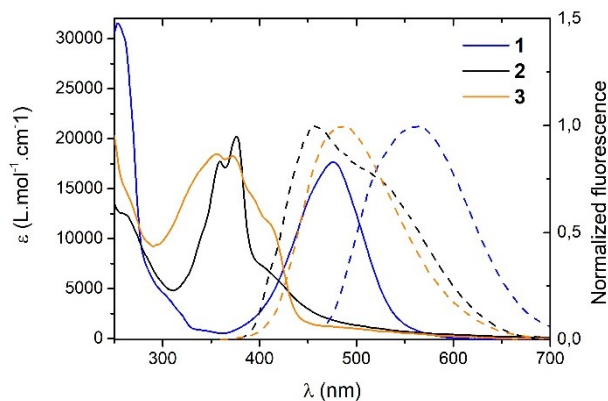


Figure 3. UV-vis absorption (plain lines) and normalized fluorescence (dotted lines) spectra of the dyes **1-3** in acidic water solution (TFA 0.1 M).

Conclusion

In summary, we further investigated the transamination reaction on **QDI** by using different polyamine precursors. If N-substituted **QDI (QDI-R₄)** and BBI derivatives could be obtained by using primary monoamines, we showed here that the use of diamine (ethylene diamine) or tetraamine (*N,N'*-bis(aminoethyl)-1,3-propanediamine) afforded quinoxaline and new quinoxalinium dyes. These latter are of particular interest as water soluble UV absorbers and blue-green emitters [26], but also because of the presence of two NH₂ functions which opens a wide range of chemical reactions towards benzimidazole derivatives of potent pharmaceutical or biological interest [27].

Acknowledgments

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