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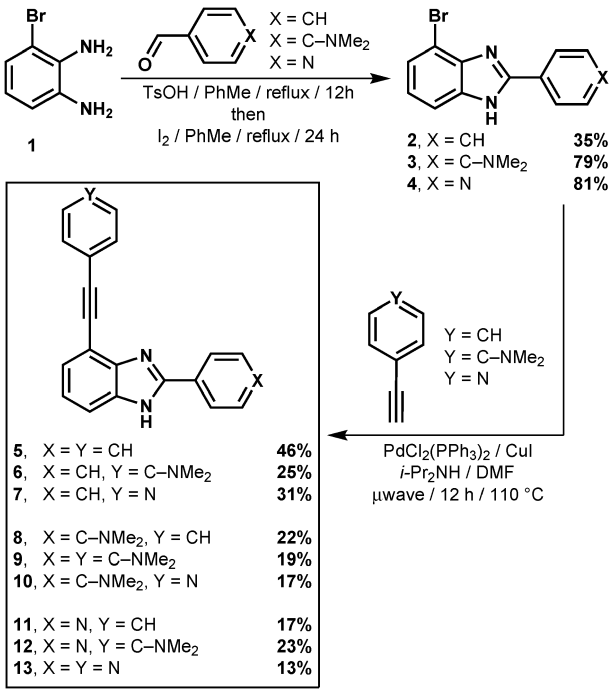
L-shaped benzimidazole fluorophores: synthesis, characterization and optical response to bases, acids and anions†‡

Rio Carlo Lirag,§ Ha T. M. Le§ and Ognjen Š. Miljanić*

Nine L-shaped benzimidazole fluorophores have been synthesized, computationally evaluated and spectroscopically characterized. These "half-cruciform" fluorophores respond to bases, acids and anions through changes in fluorescence that vary from moderate to dramatic.

Molecular cruciforms[1]—cross-conjugated molecules in which two conjugation circuits intersect at a central core—have been prominently used as fluorescent sensors for carboxylic[2] and boronic acids,[2b] amines,[3] metal ions,[1,4] small organic and inorganic anions[3a,5] and phenols.[2b] With appropriate substitution, cruciforms localize their HOMO and LUMO orbitals on different "arms" of the molecule; this spatial separation of frontier molecular orbitals (FMOs) is essential to the use of cruciforms as sensors, since analyte binding to the cruciform invariably affects its HOMO–LUMO gap and the associated optical properties. Our group was particularly focused on the synthesis and study of cruciforms based on the benzobisoxazole nucleus.[6] In this communication, we introduce a new class of L-shaped fluorophores based on the related *benzimidazole*[7] nucleus. Formally, these systems represent "cruciforms cut in half", and this structural simplification permits us to explore minimal systems which preserve spatially isolated FMOs. At the same time, the dual acidic–basic nature of the benzimidazole nucleus could potentially allow the use of this sensing motif in the direct identification and quantification of both acidic and basic analytes.

Benzimidazole fluorophores **5–13** were synthesized (Scheme 1) in two steps starting from 3-bromo-*o*-phenylenediamine (**1**).[8] Its oxidative condensation[9] with three commercially available aldehydes produced brominated imidazoles **2–4**, which were subjected to Sonogashira couplings with either phenylacetylene, 4-ethynylpyridine, or 4-ethynyl-*N*,*N*-dimethylaniline, to generate the final desired products in moderate yields. Fluorophores **5–13** were isolated as off-white, yellow or light green powders, following chromatography and/or recrystallization. In the case of donor–acceptor systems **10** (Fig. 1, right) and **12** (not shown), their



Scheme 1 Synthesis of fluorophores **5–13**.

University of Houston, Department of Chemistry, 136 Fleming Building, Houston, TX 77204-5003, USA. E-mail: miljanic@uh.edu; Fax: +1 (713)743-2709; Tel: +1 (832)842-8827

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‡ Electronic supplementary information (ESI) available: Synthesis and full characterization data for all new compounds, detailed orbital diagrams for all synthesized compounds, plots of UV/Vis absorption and fluorescence spectral changes during acid and base titrations. See DOI: 10.1039/c2cc37120k

§ These authors contributed equally to this work.

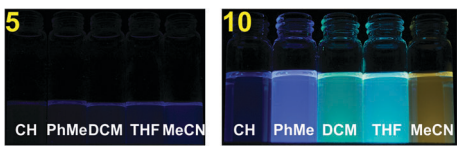

Fig. 1 Emission colours of benzimidazoles **5** (left) and **10** (right) in five different solvents (CH = cyclohexane, DCM = dichloromethane, THF = tetrahydrofuran). Excitation was achieved using a handheld UV lamp, λ_{exc} = 365 nm.

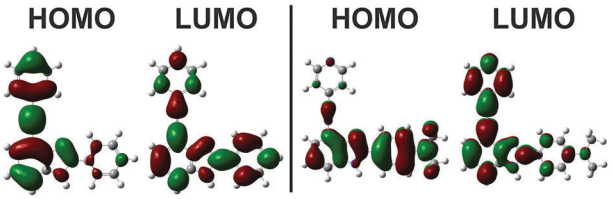

Fig. 2 Frontier molecular orbitals of L-shaped benzimidazole fluorophores **5** (left) and **10** (right). Only one of the two possible tautomers was considered (see ESI‡ for the FMOs of the other tautomers, as well as other L-shaped fluorophores).

fluorescence emission is highly solvent-dependent; on the other extreme, the very weak fluorescence of "neutral" diphenyl substituted compound **5** is independent of the solvent (Fig. 1, left). It should also be noted that the NMR spectra of **5–13** are often more complex than structures in Scheme 1 would suggest (see ESI‡ for details), because of the N–H tautomerization between the imidazole's two nitrogen atoms.

Computational insight into the FMOs of **5–13** was obtained using Gaussian 09W[10] software package and its accompanying graphical interface program GaussView 5.0, at the B3LYP/6-31G^{++} level of theory. Fig. 2 shows the HOMO and LUMO orbitals of two extreme cases: diphenyl substituted compound **5** and the donor–acceptor system **10** (see ESI‡ for FMOs of all other L-shaped fluorophores). In these two compounds, trends previously observed for benzobisoxazole[6a] (and other) cruciforms are again borne out. Both the HOMO and the LUMO of compound **5** are significantly delocalized across the molecule. In contrast, **10** shows considerably localized FMOs: most of the LUMO density is placed along the pyridine-bearing arm of the half-cruciform, while most of the HOMO density resides along the electron-rich dimethylaniline-group. In both compounds, HOMO is the more localized of the two FMOs.

Compounds **5** and **10** will be the chief subjects of discussion in this communication, as they allowed us to separate the effects of the benzimidazole nucleus alone (in **5**) from those introduced by the donor–acceptor substitution and the resultant FMO spatial isolation (in **10**). Analogous experiments for all other benzimidazole fluorophores are described in ESI.‡ In light of the spatially separated FMOs in **10**, its solvatochromicity can be rationalized by the apparent charge separation in the excited state.

Our next set of experiments focused on the titration of the solutions of the prepared benzimidazole fluorophores with a concentrated aqueous solution of tetrabutylammonium hydroxide (TBA^+OH^-). In both fluorophores, red shifts in absorption (Fig. 3, top; +45 nm for **5** and +18 nm for **10**) and emission (Fig. 3, bottom; +54 nm for **5** and +43 nm for **10**) were observed, with clear isosbestic points suggesting simple interconversion between just two species: compounds **5** and **10** and their conjugate bases deprotonated at the benzimidazole ($pK_a \approx 12.8$).[11] These red shifts indicate that deprotonation destabilizes HOMO more than the LUMO; the largely analogous responses of **5** and **10** are a consequence of the fact that both FMOs in both compounds have significant densities along the imidazole N–H bond being cleaved.

Perhaps surprisingly, response of the prepared half-cruciform sensors to acids was more difficult to rationalize. Both **5** and **10** are largely unresponsive to trifluoroacetic acid (TFA) until −log[TFA] of approx. 2.30 is reached. At this point, **5** shows a minimal blue shift in absorption (Fig. 4, top left; −7 nm) and a much larger red shift

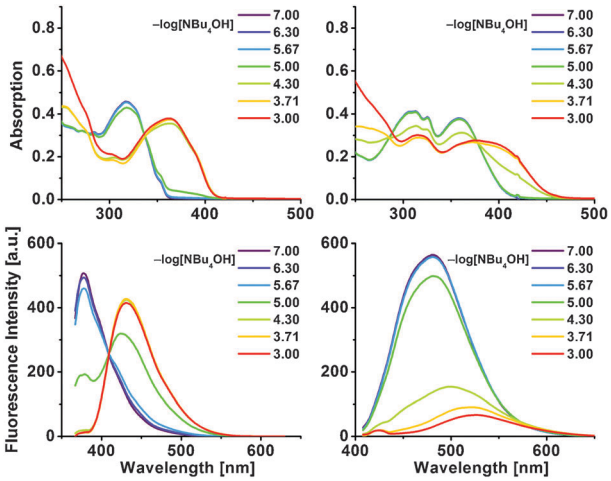

Fig. 3 UV/Vis absorption (top) and emission (bottom) spectra for the titrations of THF solutions of fluorophores **5** (left two spectra) and **10** (right two spectra) with a concentrated aqueous solution of TBA^+OH^-. Excitation wavelengths for fluorescence emission titrations of **5** and **10** were 337 and 378 nm, respectively.

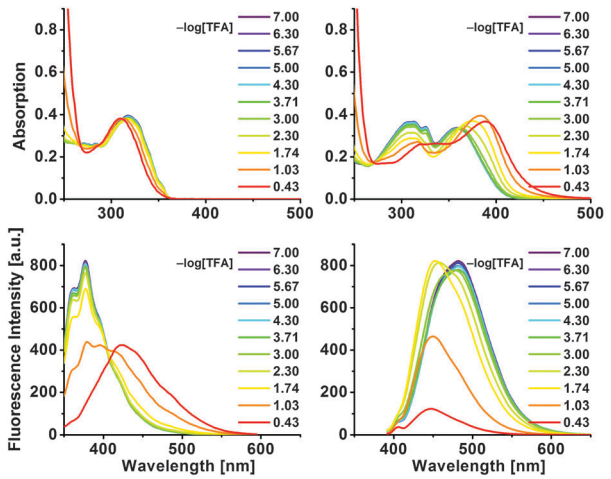

Fig. 4 UV/Vis absorption (top) and emission (bottom) spectra for the titrations of THF solutions of fluorophores **5** (left two spectra) and **10** (right two spectra) with a concentrated solution of TFA in THF. Excitation wavelengths for fluorescence emission titrations of **5** and **10** were 313 and 362 nm, respectively.

and slight attenuation of its emission (Fig. 4, bottom left; +47 nm). Since this compound can be protonated only at benzimidazole, it would follow that this protonation preferentially stabilizes the LUMO. Compound **10**, on the other hand, responds by a red shift in absorption (Fig. 4, top right; +29 nm) and a blue shift and significant attenuation of its emission (Fig. 4, bottom right; −35 nm). In **10**, there are three possible protonation sites: dimethylaniline, pyridine and imidazole, with quite similar pK_a values for their conjugated acids of 5.15, 5.25 and 5.53, successively.[11,12] The observed blue shift in the emission is consistent with the stabilization of HOMO, which would suggest that pyridine protonation is probably not operational, since HOMO has essentially no density on the pyridine nucleus. It is still unclear, however, which of the other two sites is protonated first, and why absorption and emission maxima shift in the opposite directions. In order to obtain more predictable optical response to protonation—similar to those of our

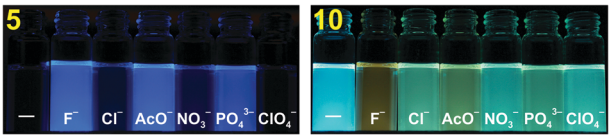

Fig. 5 Changes in the emission colour of benzimidazole sensors **5** (left) and **10** (right) upon exposure to anions. Anions were added in excess as their TBA^+ salts. Emission colours were recorded in THF, using a handheld UV lamp (λ_{exc} = 365 nm) as the excitation source.

previously reported benzobisoxazole cruciforms,[6a] it appears that a more basic pyridine nucleus (substituted *e.g.* with electron-donating methyl groups) would be a better choice.

Finally, we attempted to qualitatively assess whether half-cruciforms **5** and **10** can be used as fluorescent sensors for small inorganic and organic anions.[13] Dilute solutions of **5** and **10** in THF were exposed to excess of TBA^+ salts of several representative anions. Fig. 5 summarizes the emission colour changes resulting from these additions. Both sensors minimally changed their fluorescence when exposed to the weakly basic Cl^-, NO_3^- and ClO_4^- anions. However, more basic F^-, AcO^- and PO_4^{3-} anions turned ON the fluorescence of **5** and also significantly modulated the emission colour of **10**—particularly in the case of fluoride.

In conclusion, benzimidazole fluorophores described here can be easily synthesized in two steps. Their optical response to acids is moderate and somewhat difficult to rationalize, presumably on the account of (a) similar basicities of several possible protonation sites, and (b) incomplete spatial separation of FMOs within the molecules. On the other hand, their response to bases is much more dramatic, as all but two members of this class consistently shift their emission maxima toward the red region. The fact that these fluorophores preserve their fluorescence upon deprotonation is intriguing, as it suggests that benzimidazolate anions of **5–13** could potentially be used as building blocks for the porous zeolitic imidazolate frameworks (ZIFs),[14] thus opening up routes to crystallographically ordered solid-state sensors. We are exploring this and other applications of the L-shaped benzimidazole fluorophores and will report our findings in due course.

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