ORGANIC LETTERS

2012
Vol. 14, No. 24
6286–6289

Three-Stage Binary Switching of Azoaromatic Polybase

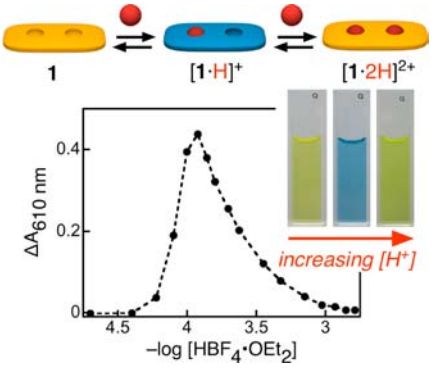
Ho Yong Lee, András Olasz, Chun-Hsing Chen, and Dongwhan Lee*

Department of Chemistry, Indiana University, 800 East Kirkwood Avenue, Bloomington, Indiana 47405, United States

dongwhan@indiana.edu

Received November 6, 2012

ABSTRACT



An OFF−ON−OFF-type three-stage binary switching was realized with an azoaniline-based polybase 1. The optical properties of 1 and $[1\cdot 2H]^{2+}$ are essentially indistinguishable to the naked eye but distinctively different from those of $[1\cdot H]^{+}$ to produce an unusual *bell-shaped response as a function of protonation state*; the underlying molecular mechanism was unraveled by a combination of experimental and DFT computational studies.

Carbon-based π-conjugation can be structurally engineered with functional groups that respond to external stimuli. With appropriate structure design, the geometric and/or electronic properties of such hybrid π-systems can be modulated in a predictable and controllable fashion.[1] Azoaromatics represent one important class of such a functional motif,[2] which have found applications as chemical sensors and switches that exploit either (i) light-driven *trans*−*cis* isomerization around the —N=N— bond for *mechanical signaling*[3] or (ii) binding-induced perturbation of the electronic structure of the extended π-conjugation for *optical signaling*.[4]

In this paper, we report *three-stage binary signaling* of an azopyrrole system **1** (Scheme 1) having multiple Brønsted basic sites embedded along the π-conjugated molecular backbone. Unlike simple **ON**−**OFF** or **OFF**−**ON** switching (Scheme 1b) of typical receptors/indicators as chemical models of logic operation,[5] the implementation of three-stage binary switching, such as the **OFF**−**ON**−**OFF** or **ON**−**OFF**−**ON** sequence shown in Scheme 1a requires a structural platform **I** that has *multiple binding sites* for *common substrates* functioning as an input signal. In addition, a stepwise and reversible binding event of **I** should generate discrete and experimentally identifiable adducts,

(1) (a) Balzani, V.; Venturi, M.; Credi, A. *Molecular Devices and Machines: A Journey into the Nanoworld*; Wiley−VCH: Weinheim, 2003. (b) Kay, E. R.; Leigh, D. A.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 72–191. (c) de Silva, A. P.; Vance, T. P.; West, M. E. S.; Wright, G. D. *Org. Biomol. Chem.* **2008**, *6*, 2468–2481. (d) Stoddart, J. F. *Chem. Soc. Rev.* **2009**, *38*, 1802–1820. (e) *Molecular Switches*, 2nd ed.; Feringa, B. L., Browne, W. R., Eds.; Wiley-VCH: Weinheim, 2011.

(2) (a) *The Chemistry of the hydrazo, azo and azoxy groups*; Patai, S., Ed.; John Wiley & Sons: London, 1975. (b) Tamai, N.; Miyasaka, H. *Chem. Rev.* **2000**, *100*, 1875–1890. (c) Hamon, F.; Djedaini-Pilard, F.; Barbot, F.; Len, C. *Tetrahedron* **2009**, *65*, 10105–10123. (d) Merino, E. *Chem. Soc. Rev.* **2011**, *40*, 3835–3853. (e) Beharry, A. A.; Woolley, G. A. *Chem. Soc. Rev.* **2011**, *40*, 4422–4437.

(3) (a) Russew, M.-M.; Hecht, S. *Adv. Mater.* **2010**, *22*, 3348–3360. (b) Stoll, R. S.; Hecht, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 5054–5075. (c) Yu, H.; Ikeda, T. *Adv. Mater.* **2011**, *23*, 2149–2180. (d) Wegner, H. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 4787–4788.

(4) (a) Zollinger, H. *Color Chemistry: Syntheses, Properties, and Applications of Organic Dyes and Pigments*, 3rd ed.; VHCA: Zurich, 2003. (b) Chudgar, R. J.; Oakes, J. In *Kirk-Othmer Encyclopedia of Chemical Technology*, 5th ed.; John Wiley & Sons: Hoboken, 2007; Vol. 9, pp 349−430.

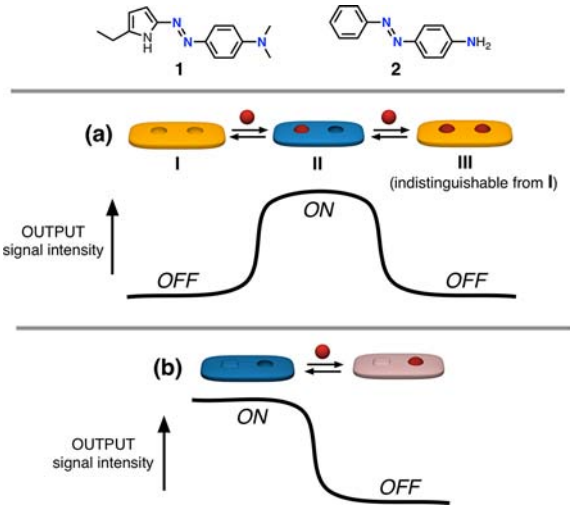
(5) (a) de Silva, A. P.; Uchiyama, S. *Nat. Nanotechnol.* **2007**, *2*, 399–410. (b) Szaciłowski, K. *Chem. Rev.* **2008**, *108*, 3481–3548. (c) Andréasson, J.; Pischel, U. *Chem. Soc. Rev.* **2010**, *39*, 174–188.

10.1021/ol303039s
Published on Web 12/03/2012

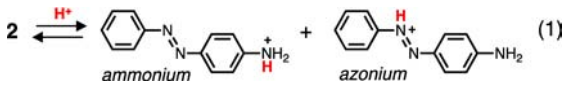
II and **III** (Scheme 1a). Most importantly, the signal output from the "fully-saturated" product **III** should be distinctively different from that of the "intermediate" **II**, but *operationally indistinguishable* from that of the initial state **I**, so that a bell-shaped response curve (Scheme 1a) is obtained with an increasing level of input signal.

When all these functional requirements are satisfied, the **ON** signal from such a system is observed only for a finite input signal window that maximizes the population of **II**. By design, the system automatically turns **OFF** when the input signal level is either lowered (toward **I**) or raised (toward **III**) away from this predefined zone of **II**. A fluorogenic polybase reported by de Silva is a seminal example of such a molecular switch,[6] which uses protons as an input signal to produce a bell-shaped response curve (Scheme 1a) resulting from pH-dependent PET mechanisms.[1c,7]

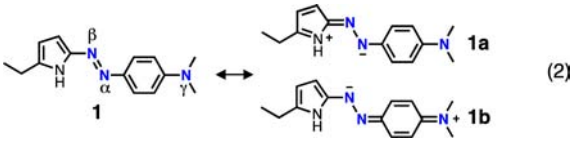
Scheme 1. Chemical Structures of **1** and **2** (top), and Schematic Representations of (a) Three-Stage vs (b) Two-Stage Binary Switching upon Substrate (Shown As a Red Sphere) Binding



Our entry into this chemistry was motivated by **2** (Scheme 1), a prototypical azoaniline that we came across during our studies of electron-rich azo derivatives for chemical sensing and actuation.[8] As a simpler structural analogue of pH indicator methyl yellow or methyl orange, **2** has a *p*-phenylene linker which supports three Brønsted basic nitrogen atoms constituting the extended π-conjugation. Previous studies have shown that its protonation product $[\mathbf{2}\cdot\mathrm{H}]^+$ exists as a tautomeric mixture of "ammonium" and "azonium" species (eq 1).[9]



Using **2** as a structural template, we designed **1**.[10] We anticipated that the Brønsted basicity of *both* of the azo nitrogen atoms, Nα and Nβ, in **1** should be enhanced through contributions from the quinoid-type and zwitterionic resonance structures **1a** and **1b** (eq 2).



In CH_3CN at $T = 298$ K, **1** displayed an intense yellow color, but immediately turned blue upon protonation (Figure 1a, inset). Such behavior was not unusual for an azo dye that functions as a simple acid–base indicator. To our surprise, however, subsequent addition of an increasing amount of acid *restored* the initial yellow color, which was visually similar to the neutral **1** (Figure 1a, inset).[11] This serendipitous finding of a rather peculiar protonation-dependent color switching did not make any intuitive sense and invited a detailed investigation.

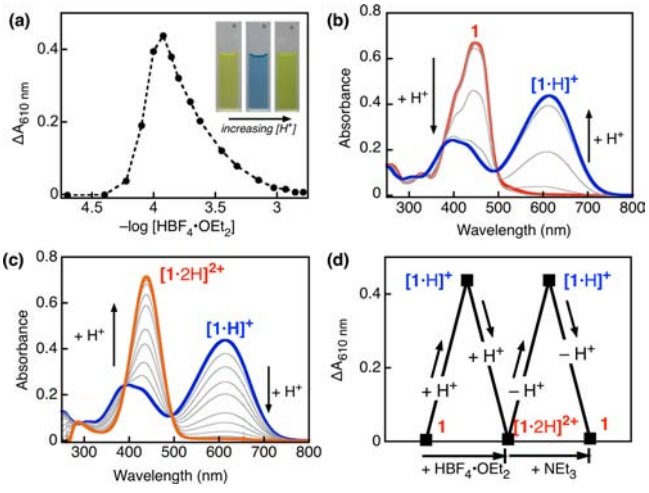


Figure 1. (a) A plot of $\Delta A_{610\ \mathrm{nm}}$ vs $-\log[HBF_4\cdot OEt_2]$, and yellow–blue–yellow color switching of **1** (inset: photographic images). (b) UV–vis spectra of **1** in the presence of $[HBF_4\cdot OEt_2]$ = 0 (orange), 0.02, 0.04, 0.06, 0.08, 0.10, and 0.12 (blue) mM. (c) UV–vis spectra of **1** in the presence of $[HBF_4\cdot OEt_2]$ = 0.12 (blue), 0.16, 0.20, 0.24, 0.35, 0.47, 0.70, 0.94, 1.20, 1.40, and 1.60 (orange) mM. (d) A reversible color switching monitored by $\Delta A_{610\ \mathrm{nm}}$ after addition of $HBF_4\cdot OEt_2$ and back-titration with Et_3N. For all measurements, [**1**] = 20 μM in MeCN; $T = 298$ K.

(6) de Silva, A. P.; Gunaratne, H. Q. N.; McCoy, C. P. *Chem. Commun.* **1996**, 2399–2400.

(7) For conceptually related luminescence-based **OFF–ON–OFF** signaling systems responding to protons, see: (a) Fabbrizzi, L.; Gatti, F.; Pallavicini, P.; Parodi, L. *New J. Chem.* **1998**, *22*, 1403–1407. (b) Gunnlaugsson, T.; Leonard, J. P.; Sénéchal, K.; Harte, A. J. *J. Am. Chem. Soc.* **2003**, *125*, 12062–12063. (c) Han, M.-J.; Gao, L.-H.; Lü, Y.-Y.; Wang, K.-Z. *J. Phys. Chem. B* **2006**, *110*, 2364–2371. (d) Evangelio, E.; Hernando, J.; Imaz, I.; Bardají, G. G.; Alibés, R.; Busqué, F.; Ruiz-Molina, D. *Chem.—Eur. J.* **2008**, *14*, 9754–9763. (e) Pais, V. F.; Remón, P.; Collado, D.; Andréasson, J.; Pérez-Inestrosa, E.; Pischel, U. *Org. Lett.* **2011**, *13*, 5572–5575. (f) Chen, Y.; Wang, H.; Wan, L.; Bian, Y.; Jiang, J. *J. Org. Chem.* **2011**, *76*, 3774–3781. (g) Sadhu, K. K.; Mizukami, S.; Yoshimura, A.; Kikuchi, K. *Org. Biomol. Chem.* **2013**, in press (DOI: 10.1039/C2OB26630J).

(8) (a) Lee, H. Y.; Song, X.; Park, H.; Baik, M.-H.; Lee, D. *J. Am. Chem. Soc.* **2010**, *132*, 12133–12144. (b) Lee, H. Y.; Jo, J.; Park, H.; Lee, D. *Chem. Commun.* **2011**, *47*, 5515–5517. (c) Jo, J.; Lee, H. Y.; Liu, W.; Olasz, A.; Chen, C.-H.; Lee, D. *J. Am. Chem. Soc.* **2012**, *134*, 16000–16007.

As shown in Figure 1b, the absorption band of **1** at λ_{max} = 445 nm initially lost its intensity with increasing [H^+], with concomitant buildup of a broad longer-wavelength transition at λ_{max} = 615 nm along with a blue-shifted feature at λ_{max} = 400 nm. This yellow-to-blue color change, however, was essentially *reversed* upon further addition of acid (Figure 1c), which elicited the evolution of a new absorption band at λ_{max} = 440 nm and complete disappearance of the features at λ_{max} = 615 and 400 nm. Such protonation-driven spectral changes can be tracked best by a plot of ΔA_{610} (= changes in the absorption at λ = 610 nm) vs −log[H^+] (Figure 1a), which produces an **OFF−ON−OFF** response function (Scheme 1) with genuine reversibility in the forward (= protonation) and backward (= deprotonation) scans (Figure 1d).

In order to investigate the structural basis of this unusual color switching, we carried out ^{1}H NMR titration studies. As shown in Figure 2, protonation of **1** with $HBF_4 \cdot OEt_2$ in CD_3CN resulted in systematic downfield shifts of the signals from the phenyl protons that are *ortho* to the amine Nγ position. This spectral change is also accompanied by downfield shifts in the two pyrrolic C−H resonances.

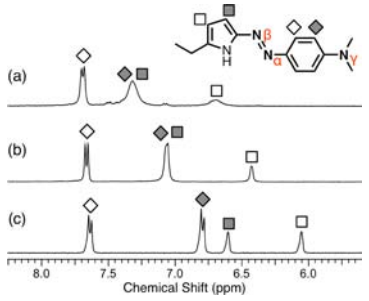
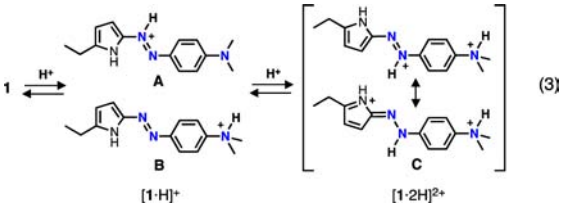


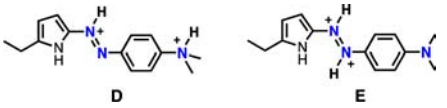
Figure 2. Partial ^{1}H NMR spectra of **1** (16 mM) in CD_3CN in the presence of (a) 2, (b) 1, and (c) 0 equiv of $HBF_4 \cdot OEt_2$ (T = 298 K).

In contrast, the phenyl C−H protons that are *ortho* to the azo Nα site remain essentially invariant under this condition. This observation suggests the solution equilibrium described by eq 3; protonation of **1** occurs at its Nβ or Nγ position to furnish a mixture of **A** and **B**. This interpretation is consistent with findings made for the benchmark system **2** (eq 1).[9]



Our subsequent DFT computational studies have confirmed that **A** and **B** share an essentially identical conformation, in which the pyrrolic N−H group makes a hydrogen bond with the azo Nα atom ($d_{N\cdots N}$ = 2.824 Å for **A**; 2.707 Å for **B**) to attenuate its basicity. On the other hand, contribution of the resonance structure **1b** (eq 2) enhances the basicity of the Nβ position to furnish **A**.

Upon addition of a second equivalent of proton, a single adduct **C** emerges as the lowest-energy tautomer of $[\mathbf{1}\cdot 2H]^{2+}$ (eq 3). Our DFT calculations suggested that alternative isomers **D** and **E** (shown below) would be significantly higher in energy, by ca. 11 and 22 kcal mol^{-1}, respectively, relative to **C**. Apparently, **C** benefits from charge delocalization through resonance (eq 3), which is not allowed for **D**. Adjacent positive charges make **E** the most unlikely tautomer.



From the electronic structure point of view, the singly protonated **A** has its (i) HOMO residing at the electron-rich amino group and the pyrrole π-system and (ii) LUMO dominated by the azo π^* orbital in the middle (Figure 3b).

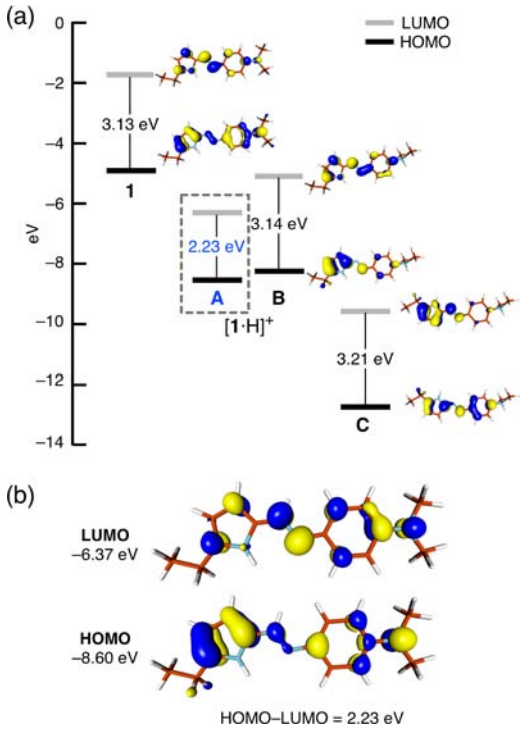


Figure 3. (a) Energy level diagram and FMO isosurface plots. (b) FMO isosurface plots of **A**.

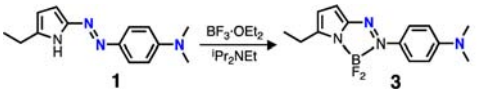
As a consequence, protonation at the Nβ position results in a smaller HOMO−LUMO gap (2.23 eV) of **A** and promotes longer-wavelength electronic transitions with significant charge-transfer character (Figure 1b). On the other hand, the HOMO−LUMO gap of **B** (3.14 eV) is essentially identical to that (3.13 eV) of

(9) (a) Kuroda, Y.; Lee, H.; Kuwae, A. *J. Phys. Chem.* **1980**, *84*, 3417–3423. (b) Liwo, A.; Tempczyk, A.; Widernik, T.; Klentak, T.; Czerminski, J. *J. Chem. Soc., Perkin Trans. 2* **1994**, 71–75. (c) Yatsenko, A. V.; Chernyshev, V. V.; Kurbakov, A. I.; Schenk, H. *Acta Crystallogr.* **2000**, *C56*, 892–894. (d) Matazo, D.; Ando, R.; Borin, A.; Santos, P. *J. Phys. Chem. A* **2008**, *112*, 4437–4443.

1 (Figures 3a and S1). The intense blue color of $[\mathbf{1}\cdot H]^+$ thus arises from **A**.

In the doubly protonated **C**, the amine Nγ site is effectively decoupled from the π-conjugation (Figure 3a and S1). The increased HOMO−LUMO gap of **C** (3.21 eV) happens to be close to that (3.13 eV) of **1**, which fully explains their indistinguishable yellow color despite markedly different protonation states (Figure 1a, inset).

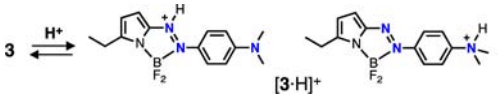
The Brønsted acid−base chemistry of **1** is significantly simplified in its derivative **3** (eq 4), in which protonation at the Nα site is effectively blocked through borylation.[10,12]



(4)

The X-ray structure of **3** (Figure 4a) revealed a significant contribution of the quinoid-type resonance structure, as reflected on the C−C bond length alternation in the phenyl ring (C−C = 1.405(1), 1.382(1), 1.417(1), 1.419(1), 1.376(1), and 1.401(1) Å) and the relatively long N−N distance (1.310(1) Å). This geometric property is reminiscent of **A** (= $[\mathbf{1}\cdot H]^+$) having similar resonance structures (Figure 4a). Indeed, **3** in MeCN displays an intense blue color with a broad absorption centered at λ_{max} = 600 nm (Figure 4b), which "mimics" the optical properties of **A** (Figure 1b).

In a manner similar to the conversion of $[\mathbf{1}\cdot H]^+$ to $[\mathbf{1}\cdot 2H]^{2+}$ (Figure 1c), protonation of **3** resulted in the disappearance of the longer-wavelength absorption with concomitant development of a new absorption at λ_{max} = 500 nm (Figure 4b). This spectral shift is accompanied by the change in color from blue to pink (Figure 4b, inset). Unlike the situation in **1**, coordination of the Lewis acidic $\{BF_2\}^+$ fragment disqualifies the Nα position from functioning as a Brønsted base. Consequently, protonation can occur only at the Nγ or Nβ position (Figure S2) to drive a conventional two-stage switching (eq 5; Scheme 1b).



(5)

In summary, two different dye molecules **1** and **3** were prepared which share a common azopyrrole platform. The stepwise protonation of **1** elicits differential shifts in the HOMO−LUMO gap of the conjugate acid to produce a bell-shaped response of **OFF−ON−OFF** type switching. A dynamic response to the stimuli in *both* directions from the predefined proton concentration window is a defining feature of the three-stage switch **1**, which distinguishes it from the conventional **ON−OFF** system such as **3**. The operation of the three-stage binary switching of **1** capitalizes on the presence of multiple Brønsted basic sites that communicate through the π-conjugation to modulate the energy levels of the frontier MOs as a function of protonation level. Efforts are currently underway in our laboratory to generalize this concept and structurally elaborate this proof-of-concept system for applications in chemical sensing.

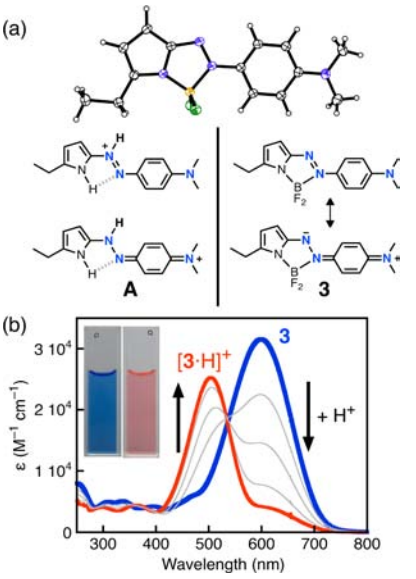


Figure 4. (a) X-ray structure of **3** with thermal ellipsoids at 50% probability (top), and benzoid vs quinoid resonance structures of **A** and **3** (bottom). (b) UV−vis spectra of **3** (20 μM in CH_3CN) in the presence of $[HBF_4\cdot OEt_2]$ = 0 (blue), 0.20, 0.22, 0.24, and 0.27 (red) mM (inset: photographic images). T = 298 K.

Acknowledgment. We thanks DTRA/Army Research Office (W911NF-07-1-0533) for financial support of this work.

Supporting Information Available. Experimental procedures, and spectroscopic, X-ray crystallographic, and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

(10) A structurally analogous azopyrrole was investigated previously as a synthetic precursor to NIR-absorbing molecules: Li, Y.; Patrick, B. O.; Dolphin, D. *J. Org. Chem.* **2009**, *74*, 5237–5243.

(11) In strongly acidic solvent (95% H_2SO_4), **2** shows similar color switching behavior.[9a]

(12) Coordination of $\{BF_2\}^+$ can also lower the energy of the azo $\pi-\pi^*$ transition. With appropriate structure design, the *trans*-to-*cis* photoisomerization can be driven by visible light. See: Yang, Y.; Hughes, R. P.; Aprahamian, I. *J. Am. Chem. Soc.* **2012**, *134*, 15221–15224.