

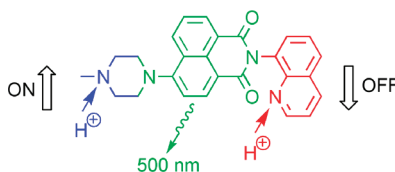
OFF-ON-OFF Fluorescence Switch with  
T-Latch FunctionVânia F. Pais,<sup>†</sup> Patricia Remón,<sup>†</sup> Daniel Collado,<sup>‡</sup> Joakim Andréasson,<sup>§</sup>  
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## ABSTRACT



A novel molecular system with characteristics of an OFF-ON-OFF fluorescence switch was designed to integrate the function of a T-latch. In detail, a receptor<sub>1</sub>-fluorophore-receptor<sub>2</sub> architecture was adopted to achieve fluorescence switching upon addition of protons.

The idea to use molecular systems for information processing has attracted a great deal of interest during the recent years.<sup>1–5</sup> This has been manifested by the availability of molecular mimics for all essential logic gates (AND, OR, NOR, NAND, INH, XOR, etc.)<sup>1,3</sup> and for rather complex logic devices such as adders/subtractors, encoders/decoders, and multiplexers/demultiplexers.<sup>2,6–10</sup> Such logic functions are of elevated interest for

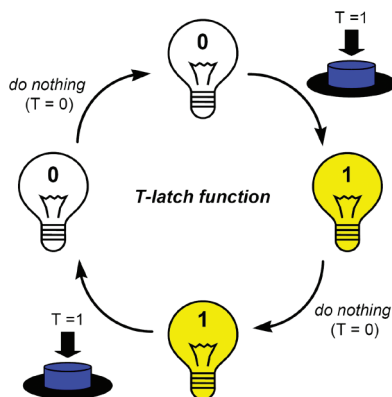
applications such as object coding,<sup>11</sup> intelligent materials,<sup>12–14</sup> pro-drug activation,<sup>15–17</sup> and diagnostics/actuation.<sup>18–20</sup> While these systems work independently of the order of input application (combinational logic), the molecular memorization of information is a precondition for applications which profit from a sequential application of input signals.<sup>21,22</sup> This behavior is reflected in the

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function of molecular keypad locks<sup>10,23–28</sup> and memory devices.<sup>29–35</sup>

The set-reset (S-R) latch was one of the first memory devices that was implemented at the molecular level by using electrochemical, chemical, and photonic signaling.<sup>29,31–35</sup> The device is characterized by a high state (binary 1) whenever the set input is applied ( $S = 1$ ) and which upon reset ( $R = 1$ ) has a binary 0 (low) state. The herein described toggle-latch (T-latch) is a different logic switch with memory capacity. Its working principle is well illustrated with the function of a conventional light switch or of the push button of a ballpoint pen: every time the toggle input is activated, the state  $Q$  of the system changes (see Scheme 1). The device “remembers” if a 0 or a 1 state was memorized ( $Q_{\text{current}}$ ) and upon each T input application, the new state ( $Q_{\text{next}}$ ) has the opposite value ( $0 \rightarrow 1$  and  $1 \rightarrow 0$ ). The “do nothing” situation leaves the system state unchanged.

**Scheme 1.** Presentation of the T-Latch Function



We anticipated that a molecular OFF-ON-OFF fluorescent switch could integrate this function. In detail, we needed a switch which upon single application of an input changes to the ON state and is set back to the OFF state by

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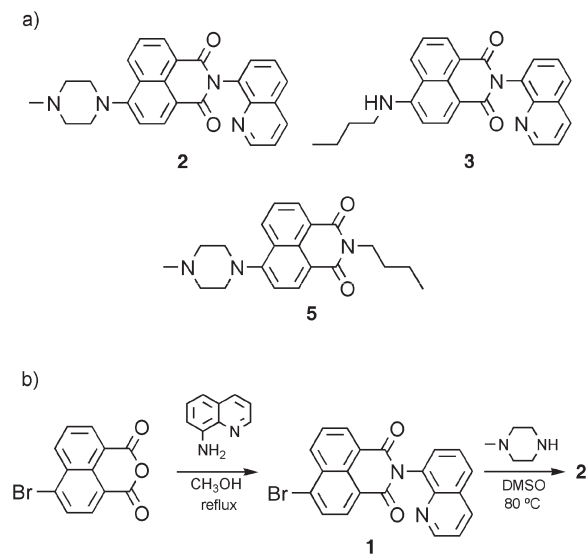
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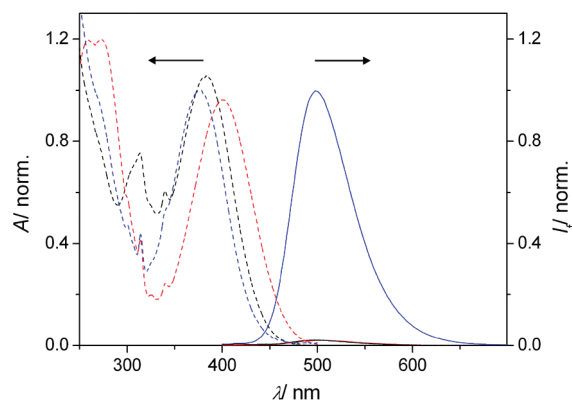
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**Scheme 2.** (a) Structures of Triad **2** and the Naphthalimide Models **3** and **5** with One Receptor Unit and (b) Synthesis of Triad **2** (for Compound **4**, an Intermediary Product, see Supporting Information)



a second equal input. Fluorescent systems, which change their emission properties upon application of chemical input information, have been often explored in the design of logic switches and chemical sensors.<sup>3,4,36–38</sup> The integrated receptor<sub>1</sub>-fluorophore-receptor<sub>2</sub> architecture **2** (Scheme 2a) was identified as an excellent candidate to put the molecular T-latch function into practice.



**Figure 1.** Relative absorption spectra (dashed lines) and normalized fluorescence spectra (solid lines) for **2** (red), **2H<sup>+</sup>** (blue), and **2H<sub>2</sub><sup>2+</sup>** (black). Note that the low fluorescence emissions of **2** and **2H<sub>2</sub><sup>2+</sup>** are hardly distinguishable.

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The synthesis of the new triad **2** is briefly sketched in Scheme 2b. The sequence started with the commercial 4-bromo-1,8-naphthalic anhydride, which was condensed with 8-aminoquinoline (74% yield). Further aromatic nucleophilic substitution of the intermediary 4-bromo-1,8-naphthalimide derivative with *N*-methylpiperazine resulted in the final product **2** with a yield of 52%. The synthesis of the naphthalimide derivatives **3** and **5** (Scheme 2a), which served herein as model structures, is described in the Supporting Information.

**Table 1.** Photophysical Properties of Compounds **2**, **3**, and **5** and Their Protonated Forms in Aerated Acetonitrile Solution

	$\lambda_{\text{abs,max}}/\text{nm}$	$\epsilon/\text{M}^{-1}\text{cm}^{-1}$	$\lambda_{\text{fluo,max}}/\text{nm}$	$\Phi_{\text{f}}$	$\tau_{\text{f}}/\text{ns}$
<b>2</b>	401	10100	504	0.017	<sup>a</sup>
<b>2H<sup>+</sup></b>	377	10500	499	0.67	8.90
<b>2H<sub>2</sub><sup>2+</sup></b>	383	11100	499	0.017	<sup>a</sup>
<b>3</b>	433	13000	520	0.56	10.00
<b>3H<sup>+</sup></b>	441	13400	519	0.006	<sup>a</sup>
<b>5</b>	398	9700	502	0.018	<sup>a</sup>
<b>5H<sup>+</sup></b>	374	10100	498	0.62	9.06

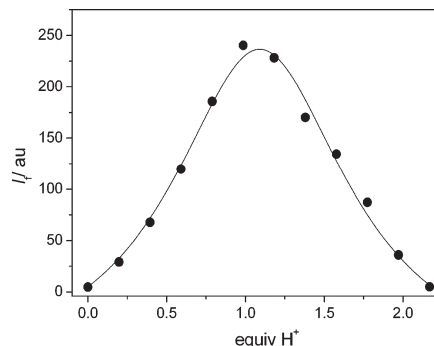
<sup>a</sup>Not determined due to low signal intensity.

Triad **2** contains two proton receptors: a piperazinyl and a quinolinyl moiety. The receptors have sufficiently different  $\text{p}K_{\text{a}}$  values (7.78 for *N*-benzoylpiperazine versus 4.60 for 8-methylquinoline as models)<sup>39</sup> so that they can be stepwise protonated. In accordance with this assumption and as shown in Figures 1 and 2, the addition of 1 equiv of protons (triflic acid;  $\text{CF}_3\text{SO}_3\text{H}$ ) yielded a pronounced fluorescence enhancement (fluorescence quantum yield  $\Phi_{\text{f}} = 0.67$  versus 0.017 for **2H<sup>+</sup>** and **2**, respectively) of the 4-amino-1,8-naphthalimide chromophore ( $\lambda_{\text{fluo,max}} = 504$  nm for **2** and 499 nm for **2H<sup>+</sup>**). However, the subsequent addition of a second equivalent of  $\text{CF}_3\text{SO}_3\text{H}$  caused practically quantitative fluorescence quenching (98% quenching). The photophysical properties of all investigated compounds and their protonated forms are summarized in Table 1. The independent actuation of both receptors in **2** was supported by the observation of the same differential photophysical effects upon protonation of the model compounds **3** and **5**, which contain each only one of the two receptors (Scheme 2a). In accordance with the fluorescence response of **2** upon stepwise protonation, **3** showed quenching and **5** enhancement of the emission for the addition of 1 equiv of protons (Supporting Information). The superposition of the photophysical

(39) The  $\text{p}K_{\text{a}}$  data were taken from [http://research.chem.psu.edu/brpgrp/pKa\\_compilation.pdf](http://research.chem.psu.edu/brpgrp/pKa_compilation.pdf).

(40) The protonation of the piperazinyl residue leads to a blue shift (by 24 nm) of the long wavelength aminonaphthalimide absorption band (for **2** and **5**), which is indicative of the destabilization of the charge transfer state through the repulsive interaction between the protonated distant methyl-substituted N and the positive pole of the charge transfer state at the aromatic N (cf. ref 47). The protonation of the quinolinyl moiety has stabilizing effects on the charge transfer state, which is expressed by a red shift (by 6–8 nm) of the long wavelength absorption band (for **2** and **3**).

trends of the model compounds in the triad was also noted for the absorption spectra.<sup>40</sup>



**Figure 2.** Fluorescence titration curve ( $\lambda_{\text{exc}} = 388$  nm,  $\lambda_{\text{obs}} = 499$  nm) of **2** (12.5  $\mu\text{M}$  in acetonitrile) upon  $\text{CF}_3\text{SO}_3\text{H}$  addition.

**Table 2.** Truth Table for the Implemented Molecular T-Latch

<i>T</i> input (1 equiv H <sup>+</sup> )	$Q_{\text{current}}$ (fluo)	$Q_{\text{next}}$ (fluo)	control channel (abs, 313 nm)
0	0	0	0
1	0	1	0
0	1	1	0
1	1	0	1

The fluorescence switching of triad **2** can be mechanistically rationalized as follows. The electron-donating methyl-substituted piperazinyl nitrogen atom is protonated upon the addition of the first equivalent of protons, which leads to blocking of photoinduced electron transfer (PET) and consequently fluorescence ON switching.<sup>41–43</sup> The second equivalent of protons serves to transform the quinolinyl residue into a quinolinium cation. The hydrogen-bonding interaction of  $\text{NH}^+$  with the imide carbonyl  $\text{C}=\text{O}$  is assumed to be at the origin of the fluorescence quenching of the 4-amino-1,8-naphthalimide derivative.<sup>41</sup> However, PET from the singlet-excited fluorophore to the electron-accepting quinolinium cation may also be involved in the observed fluorescence OFF switching.<sup>44,45</sup> Noteworthy, the control of 4-aminonaphthalimide fluorescence by a receptor linked to the “imide side” of the fluorophore has been rarely observed.<sup>41,42,46–48</sup>

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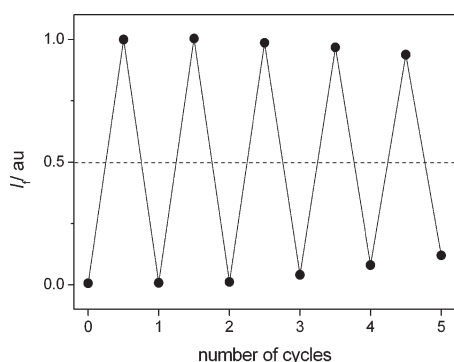
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The first three columns of the truth table (Table 2) describe the implementation of the T-latch function, which is mimicked by the above-discussed fluorescence switching. Starting with the triad in its unprotonated state (**2**), only low fluorescence is observed for  $T = 0$  (no addition of acid). This situation corresponds to  $Q_{\text{current}} = Q_{\text{next}} = 0$ . However, protonation of **2** with 1 equiv of acid ( $T = 1$ ) leads to  $2\text{H}^+$  and consequently a high fluorescence output (toggling from  $Q_{\text{current}} = 0$  to  $Q_{\text{next}} = 1$ ). Again, the “do nothing situation” ( $T = 0$ ) preserves the  $Q$  state (i.e.,  $Q_{\text{current}} = Q_{\text{next}} = 1$  in this case). The second addition of 1 equiv of acid ( $T = 1$ ) to  $2\text{H}^+$  yields  $2\text{H}_2^{2+}$  and concomitant fluorescence quenching, corresponding to a switching from  $Q_{\text{current}} = 1$  to  $Q_{\text{next}} = 0$ .



**Figure 3.** Recycling of fluorescence switching ( $\lambda_{\text{obs}} = 499 \text{ nm}$ ) of **2** ( $8.7 \mu\text{M}$  in acetonitrile) upon consecutive addition of 1 equiv of  $\text{CF}_3\text{SO}_3\text{H}$  followed by 1 equiv of  $\text{P}_2\text{-Et}$  phosphazene base. The dashed line marks the threshold. A conservative estimation yields that up to 10 cycles are possible, maintaining a dynamic switching range of  $I(\text{ON})/I(\text{OFF}) \geq 2$ .

The protonation state of the triad can be easily reset by application of a strong base ( $\text{P}_2\text{-Et}$  phosphazene), leading to the inverse titration curve (see Supporting Information). The consecutive protonation/deprotonation of **2** with

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acid/base can be repeated for at least five cycles without significant loss of the dynamic fluorescence switching range (Figure 3). The correct functioning of the T-latch requires that the initial device state is represented by the unprotonated triad **2**. However, by solely reading the fluorescence output  $Q$ , it cannot be decided whether at a random point of operation  $Q_{\text{current}} = 0$  corresponds to **2** or  $2\text{H}_2^{2+}$ . The unambiguous assignment of an output to a concrete input situation can be resolved by reading a control channel, as has been shown previously for the implementation of reversible logic functionality.<sup>10,28,49,50</sup> This control signal is provided herein by the absorption of the quinolinium cation at ca. 313 nm (fourth column in Table 2).<sup>51</sup> This spectral signature only evolves when the quinoline unit becomes protonated (Supporting Information). Hence, when the fluorescence is low and the absorbance at 313 nm is high, 2 equiv of base is needed to reset the system to its initial state (unprotonated **2**). If the fluorescence output and the absorbance at 313 nm are both low, then the system is already in its initial state. Hence, the two  $Q = 0$  situations are now clearly distinguishable.

In summary, we have shown that an OFF-ON-OFF fluorescence switch with two degenerate proton inputs can integrate the function of a molecular T-latch. The photo-physical design of the switch is based on the control of electron transfer and hydrogen-bond interaction. Work on an all-optical version, exploring photoinduced proton transfer as relay mechanism, is underway.

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**Supporting Information Available.** Details on the synthesis of **1–5**,  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra, additional spectroscopic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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