

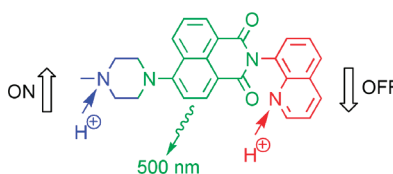
OFF-ON-OFF Fluorescence Switch with
T-Latch FunctionVânia F. Pais,[†] Patricia Remón,[†] Daniel Collado,[‡] Joakim Andréasson,[§]
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ABSTRACT



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 receptor₁-fluorophore-receptor₂ 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.^{1–5} This has been manifested by the availability of molecular mimics for all essential logic gates (AND, OR, NOR, NAND, INH, XOR, etc.)^{1,3} and for rather complex logic devices such as adders/subtractors, encoders/decoders, and multiplexers/demultiplexers.^{2,6–10} Such logic functions are of elevated interest for

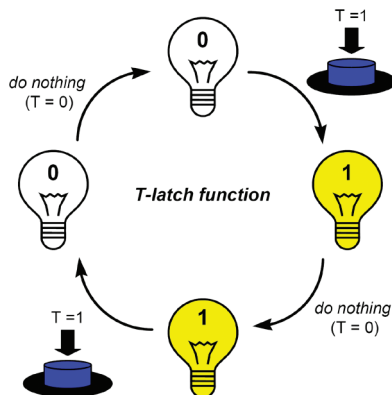
applications such as object coding,¹¹ intelligent materials,^{12–14} pro-drug activation,^{15–17} and diagnostics/actuation.^{18–20} While these systems work independently of the order of input application (combinational logic), the molecular memorization of information is a precondition for applications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

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function of molecular keypad locks^{10,23–28} and memory devices.^{29–35}

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.^{29,31–35} 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_{current}) and upon each T input application, the new state (Q_{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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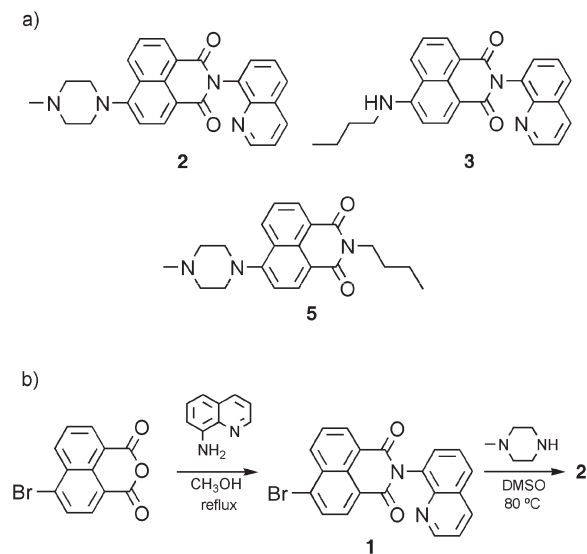
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Scheme 2. (a) Structures of Triad **2** and the Naphthalimide Models **3** and **5** with One Receptor Unit and (b) Synthesis of Triad **2** (for Compound **4**, an Intermediary Product, see Supporting Information)



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.^{3,4,36–38} The integrated receptor₁-fluorophore-receptor₂ architecture **2** (Scheme 2a) was identified as an excellent candidate to put the molecular T-latch function into practice.

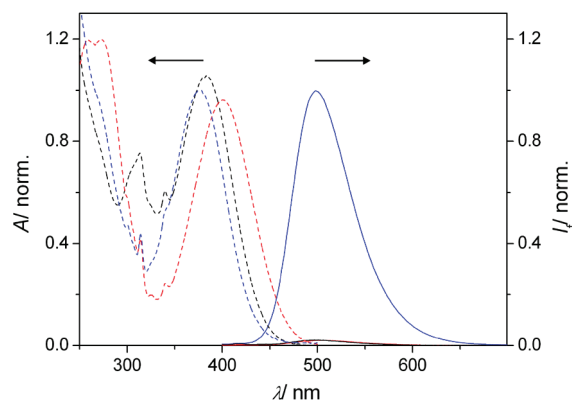


Figure 1. Relative absorption spectra (dashed lines) and normalized fluorescence spectra (solid lines) for **2** (red), 2H^+ (blue), and 2H_2^{2+} (black). Note that the low fluorescence emissions of **2** and 2H_2^{2+} are hardly distinguishable.

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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

	$\lambda_{\text{abs,max}}/\text{nm}$	$\epsilon/\text{M}^{-1}\text{cm}^{-1}$	$\lambda_{\text{fluo,max}}/\text{nm}$	Φ_{f}	$\tau_{\text{f}}/\text{ns}$
2	401	10100	504	0.017	^a
2H⁺	377	10500	499	0.67	8.90
2H₂²⁺	383	11100	499	0.017	^a
3	433	13000	520	0.56	10.00
3H⁺	441	13400	519	0.006	^a
5	398	9700	502	0.018	^a
5H⁺	374	10100	498	0.62	9.06

^aNot 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)³⁹ 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⁺** and **2**, respectively) of the 4-amino-1,8-naphthalimide chromophore ($\lambda_{\text{fluo,max}} = 504$ nm for **2** and 499 nm for **2H⁺**). 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.

(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.⁴⁰

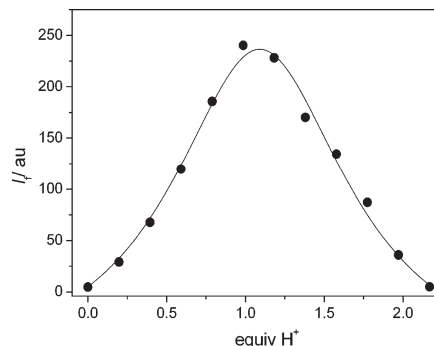


Figure 2. Fluorescence titration curve ($\lambda_{\text{exc}} = 388$ nm, $\lambda_{\text{obs}} = 499$ nm) of **2** (12.5 μM in acetonitrile) upon $\text{CF}_3\text{SO}_3\text{H}$ addition.

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

<i>T</i> input (1 equiv H ⁺)	Q_{current} (fluo)	Q_{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.^{41–43} The second equivalent of protons serves to transform the quinolinyl residue into a quinolinium cation. The hydrogen-bonding interaction of 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.⁴¹ However, PET from the singlet-excited fluorophore to the electron-accepting quinolinium cation may also be involved in the observed fluorescence OFF switching.^{44,45} Noteworthy, the control of 4-aminonaphthalimide fluorescence by a receptor linked to the “imide side” of the fluorophore has been rarely observed.^{41,42,46–48}

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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 2H^+ 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 2H^+ yields 2H_2^{2+} and concomitant fluorescence quenching, corresponding to a switching from $Q_{\text{current}} = 1$ to $Q_{\text{next}} = 0$.

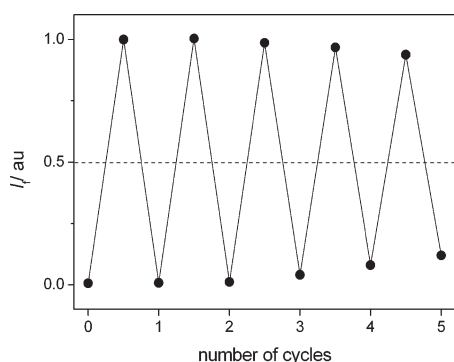


Figure 3. Recycling of fluorescence switching ($\lambda_{\text{obs}} = 499 \text{ nm}$) of **2** ($8.7 \mu\text{M}$ in acetonitrile) upon consecutive addition of 1 equiv of $\text{CF}_3\text{SO}_3\text{H}$ followed by 1 equiv of $\text{P}_2\text{-Et}$ phosphazene base. The dashed line marks the threshold. 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 2H_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.^{10,28,49,50} This control signal is provided herein by the absorption of the quinolinium cation at ca. 313 nm (fourth column in Table 2).⁵¹ 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**, ^1H and ^{13}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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