

Chemical approaches for mimicking logic functions within fluorescent MPT dyes

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The progress of the design, synthesis, fluorescence properties and application of a new family of fluorescent molecular switches towards information processing at the molecular level was reviewed. On the basis of the high fluorescence quantum yields and surroundings-sensitive fluorescent properties of the 5-methoxy-2-(2-pyridyl)-thiazole (2-MPT, 1) and a series of its derivatives as prepared, multiple binary logic and arithmetic functionalities were realized through encoding the controllable fluorescence switching properties with binary digit. Combined with the microfluidic platform, the fabrication of the molecular logic devices was attempted.

5-methoxy-2-(2-pyridyl)-thiazole (2-MPT), surroundings-sensitive fluorescence properties, logic and arithmetic functionalities

1 Introduction

The increasing exploration of the novel fluorescent molecular switches over the recent decades is shedding light on the application potentials in many multi-disciplinary fields, such as environmental hazard detection^[1–6], disease diagnostics^[7–9] and digital processing^[10–15]. In principle, if a fluorescent molecular switch exhibits the unique spectral response towards a particular molecule or ion in the presence of various interfering chemical species, it can be employed to detect or label special targets with high sensitivity and selectivity^[16]. Recently, those molecular switches with the surroundings-sensitive fluorescence behaviors have attracted more and more attention, due to their single-molecule resolution^[17], sub-nanomolar detection limit^[18] and ease for *in situ* detection^[19]. However, if a fluorescent molecular switch exhibits the diverse fluorescence responses towards different guest ions or molecules, and then the interplays between different competing chemical recognition processes with the fluorescent substrate can be expressed through the distinct fluorescent spectral profiles. Hereby, with encoding the low and high concentra-

tions of the input guest molecules and the output fluorescent intensities with binary 0 and 1 respectively, the Boolean logic system (Scheme 1) can be introduced to describe the mutually dependent interactions of different competitive chemical-recognition processes within a unique fluorescent switch^[20–24]. Therefore, a specific binary algebraic issue can be executed by the specific combination of multiple recognition processes within one or more molecular or supramolecular systems^[25].

With this strategy, de Silva and his colleagues firstly reported the realization of a 2-input molecular Boolean AND gate within an anthracene-derived fluorescent switch that bears two specific binding sites respectively towards proton and sodium cation^[26]. Since this enlightening prototype was reported, plenty of logic gates and circuits with all kinds of digital functionalities have been constructed at the molecular level, including the entire set of 2-input Boolean logic gates^[27–43], some 3-input

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| Input | | Output | | | |
|-------|--|--------|---|---|---|
| A | | | | | |
| 0 | | 0 | 1 | 1 | 0 |
| 1 | | 1 | 0 | 1 | 0 |

| Input | | Output | | | |
|-------|---|--------|---|---|---|
| A | B | | | | |
| 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 1 | 0 | 1 | 1 | 0 |
| 1 | 0 | 0 | 1 | 1 | 0 |
| 1 | 1 | 1 | 0 | 1 | 0 |

| Input | | Output | | | |
|-------|---|--------|---|---|---|
| A | B | | | | |
| 0 | 0 | 0 | 1 | 0 | 1 |
| 0 | 1 | 1 | 1 | 1 | 0 |
| 1 | 0 | 0 | 0 | 1 | 0 |
| 1 | 1 | 0 | 1 | 0 | 1 |

Scheme 1 Truth tables and electronic representation symbols of binary Boolean logic operations. From left to right, top: YES, NOT, PASS 1, PASS 0; middle: AND, NAND, OR, NOR; bottom: INHIBIT, IMPLICATION, XOR, XNOR.

Boolean logic gates^[44–52], binary calculators for addition and subtraction^[53–70], comparators^[66,68], multi-layer circuits^[71], multiplexer/demultiplexer^[72–75], encoders/decoders^[76], keypad locks^[77–79] and game devices^[80]. Besides the advancement of computing capability, concerns about device fabrication^[62,81], reset capacity^[61,67,82], security level^[77–80] and communication addressability^[21,44–46,59,83] of molecular devices have also attracted more and more research interest in recent years, in order to improve the performance of a molecule in digital processing.

Compared with the conventional silicon-based electronic devices, molecular computation devices are still limited in computing power and speed, but they exhibit some other intrinsic and significant potential advantages^[22]. First, molecules are small in size, far smaller than a conventional electronic logic gate due to the physical and fabrication limits, which qualifies the molecular platform to be a potential candidate for mimicking the functionalities of many digital processing operations in a small scale and enhancing the integrity of logic circuits^[84]. Second, molecular logic systems show the advantage of parallel processing, as chemical recognition processes often result in several nondegenerate changes at different output channels^[30,31,33,34,41,85], which endows a molecular device with various distinct logic processing functionalities and offers the parallel proc-

essing capacities, while multiple executions can only be accomplished with several processing units together in silicon-based devices. Third, the reconfiguration of functionalities is achieved more easily compared with the silicon-based devices by further introducing a particular chemical species as an extra input signal. For a molecular logic system, the input and output signals are usually heterogeneous, which avoids the interplay between the input of one gate and the output of another one^[23], whereas for conventional electronic devices, complicated logic functions are realized by physical connection among the three fundamental silicon-based logic units.

In order to synthesize multi-responsive molecular fluorescent switches for performing logic functionalities, several design strategies that emphasize the derivation of organic fluorophores with different binding sites^[21,33,50,51,54,58,86–89], have been proposed. Through the specific recognition with the input chemicals, the fluorescent substrate undergoes inter-conversion from one binding state to another one, such as transition between different protonation, redox, coordination or constitution states^[13,15,20–24]. With the perturbation of the frontier molecular orbitals by structural modification, the substrate molecule shows the controllable intra-/inter-molecular charge transfer phenomena at the ground or excited state and switchable fluorescence behaviors, which can be interpreted with the logic functionalities. Notably, the same set of chemical input signals may trigger distinct fluorescent switching behaviors for different fluorescent molecules or different states of the same molecule, which also contributes to the construction of different logic functionalities in parallel (Figure 1).

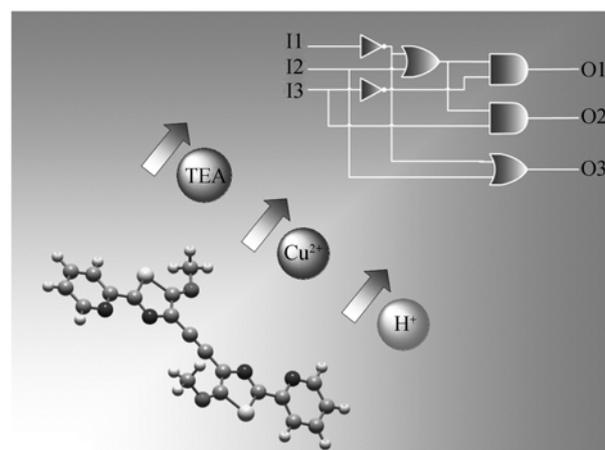


Figure 1 Schematic representation of the construction of Boolean logic functions with chemical inputs at the molecular level.

Hence, exploring novel fluorescent molecular switches lays the foundation for the development of the highly functional integrated molecular computing platform.

Motivated by this goal, our group has been studying on processing digital information within a family of molecular switches bearing a blue emissive fluorophore 5-methoxy-2-pyridyl-thiazole (MPT) (Figure 2), which was reported in our previous work^[90]. From the view of molecular structure, MPT skeleton is composed of an electron donor methoxy group, an electron acceptor pyridine ring and a spacer thiazole ring to transfer electronic coupling between the electron donor and the electron acceptor, which is similar to that in the well-known fluorescent labeled Thiazole Orange (TO)^[91]. Furthermore, MPT is highly fluorescent in water and common organic solvents and the quantum yield increases in an order of **1a** < **1b** < **1**^[90]. In addition, as a structural analog of 2,2'-bipyridine, 2-MPT is able to bind with cupric ion and proton, which reveals its potential in multiple recognition processes.

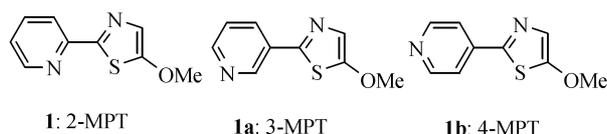


Figure 2 Molecular structures of the three MPTs.

With some functional groups conjugated to the MPT unit, such as a photo-active core (perfluorocyclopentene moiety)^[92], an electro-active group (tetrathiafulvalene (TTF))^[93,94], or a coordination-active site (another MPT moiety^[95] and an amino group^[96]), a series of multi-sensitive fluorescent switches are achieved, which exhibit optical responses to the interplay of coordination, protonation, redox and irradiation (Figure 3). Boolean logic gates, reconfigurable digital circuits, algebraic calculators and secured molecular platform providing user-specific algebra have been achieved within MPT-derived molecular switches.

In this paper, we will briefly discuss our recent research results on the MPT families with chemical approaches to process digital information. The results are presented from the preparation of MPT-derived dyes to the binary logic gates and devices implemented therein.

2 Synthesis and photophysical properties

The preparation route of the MPT fluorophore is devel-

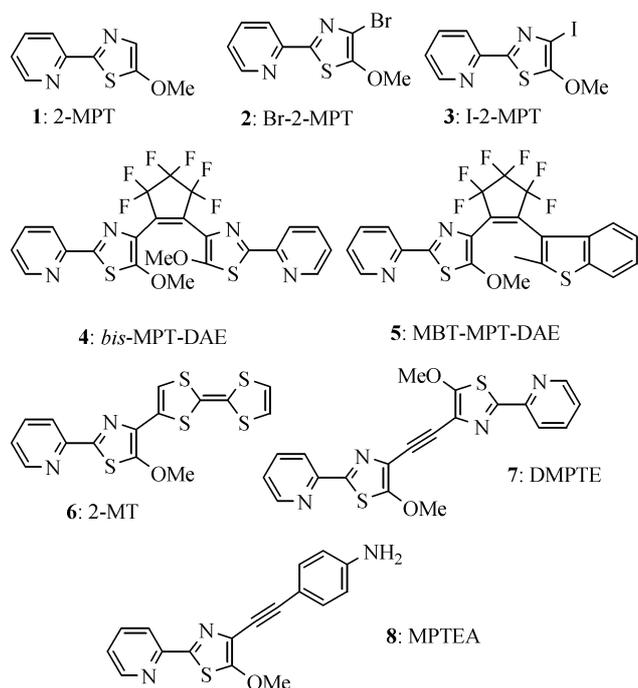


Figure 3 Chemical structures of MPT-containing molecules.

oped from the synthesis of 5-methoxy-2-phenylthiazole. Pyridyl carboxylic acid was treated with sulfurous dichloride in benzene and then with glycine methyl ester hydrochloride in presence of triethylamine in chloroform to produce the corresponding amide. Further treatment with Lawesson's reagent leads to the formation of MPT through a ring-closing process (Figure 4)^[90].

Derivation of MPT skeleton with a halogen atom, either bromine or iodine, at the 4-position of thiazole ring, renders the MPT active and able to conjugate other groups. The introduction of halogen atom on the thiazole ring is accomplished through the treatment with *N*-bromosuccinimide (NBS) or *N*-iodosuccinimide (NIS) (Figure 4), producing 4-bromo-5-methoxy-2-(2-pyridyl)-thiazole (Br-2-MPT, **2**) or 4-iodo-5-methoxy-2-(2-pyridyl)-thiazole (I-2-MPT, **3**).

Next, depriving the halogen atom on the thiazole ring with a strong base affords a nucleophilic MPT anion intermediate that can react with the perfluorocyclopentene moiety to form symmetric or asymmetric photo-active diarylethene (DAE) compounds (Figure 4)^[92]. The fluorescence behaviors are different in ring-open and ring-closed isomers because of the different energy and charge transfer phenomena in both ground and excited states resulted from the different extensions of π -nature frontier orbitals. The obtained symmetric DAE

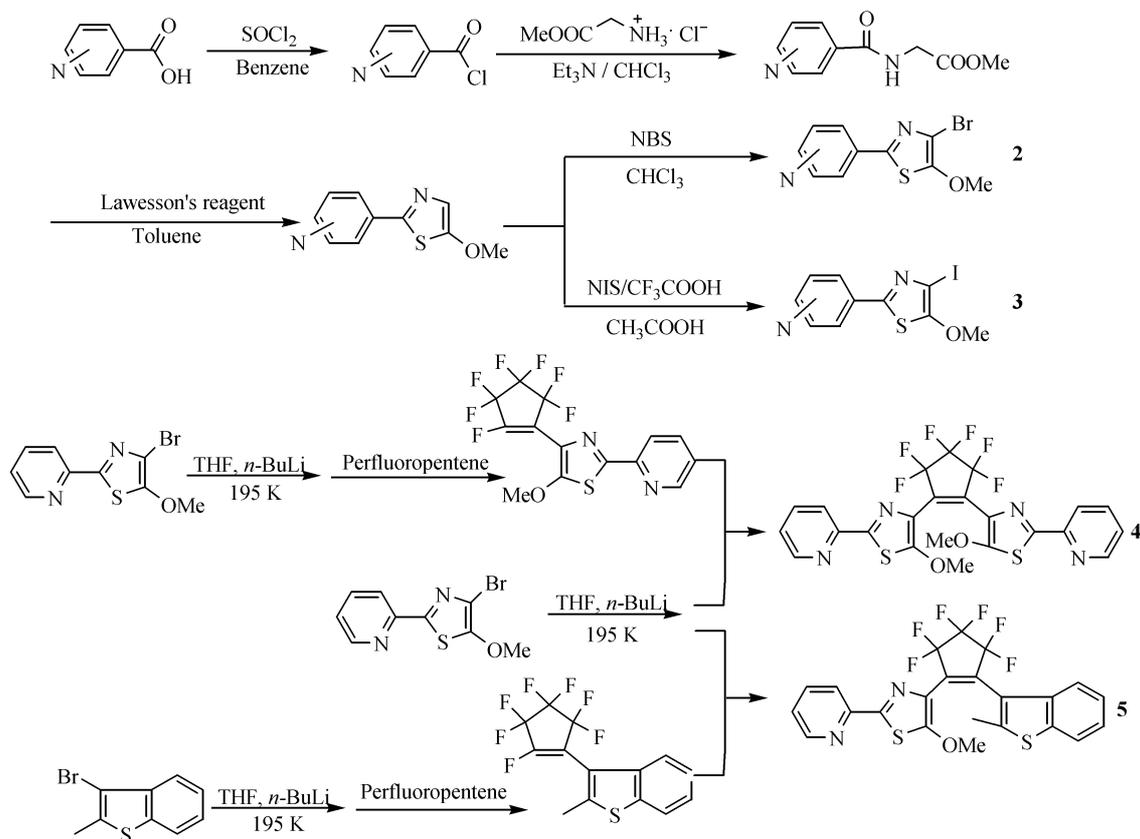


Figure 4 Synthetic route of MPT and I/Br-MPT (top) and synthetic route of molecules **4** and **5** through a nucleophilic substitution reaction (bottom).

(1,2-bis-[5-methoxy-2-(2-pyridyl)thiazolyl]perfluoropentene (*bis*-MPT-DAE, **4**) is fluorescent in ring-open form but nonfluorescent in ring-closed form, while for the asymmetric 1-{4-(5-methoxy-2-(2-pyridyl)thiazolyl)}-2-{3-(2-methylbenzo[*b*]thiophenyl)}hexafluorocyclopentene (MBT-MPT-DAE, **5**), both the ring-open form and the ring-closed form are fluorescent, which is ascribed to the presence of an electron-donating 2-methylbenzothio-phenene (MBT) and energy transfer process^[92].

Besides, the MPT skeleton can conjugate with another aromatic ring or an ethynyl group via the cross-coupling with the catalysis of palladium (Figure 5)^[93–96]. This synthetic procedure is applicable to conjugate the MPT moiety with either an electron-donating or electron-withdrawing group with relative high yield. Notably, the introduction of halogen atom at the 4-position of the thiazole ring ensures that the MPT skeleton structure is retained after further derivation, and then its intrinsic fluorescence emission is remained, except that in the TTF-conjugated MPT compound 2-[4-(2,2'-bi-1,3-dithiol-4-yl)-5-methoxy-1,3-thiazol-2-yl]-pyridine (2-MT, **6**), the fluorescence of the MPT skeleton structure is

totally quenched in the neutral state due to an efficient photo-induced electron transfer (PET) at the excited state^[93,94]. Especially, if a new binding site is attached to the aromatic ring, such as another MPT moiety inside 1,2-di[5-methoxy-2-(2-pyridyl)thiazolyl]ethyne (DMPTE, **7**) or an amino group inside 2-(4-aminophenylethyl)-5-methoxy-2-(2-pyridyl)thiazole (MPTEA, **8**), the coupling reaction affords a product with multiple binding sites^[93–96]. In the meanwhile, the π -nature frontier orbitals have been extended through the coupling, which results in the new electronic transitions in the absorption spectra, red shift of spectral maxima and lowering of quantum yield in fluorescence. The maximum absorption/emission wavelengths and the fluorescence emission quantum yields of the above compounds are summarized in Table 1.

3 Elementary logic gates within MPT

MPT in neutral aqueous solution exhibits an absorption peak around 320 nm and an emission peak at about 400 nm with excitation at 320 nm^[90]. Its fluorescence emis-

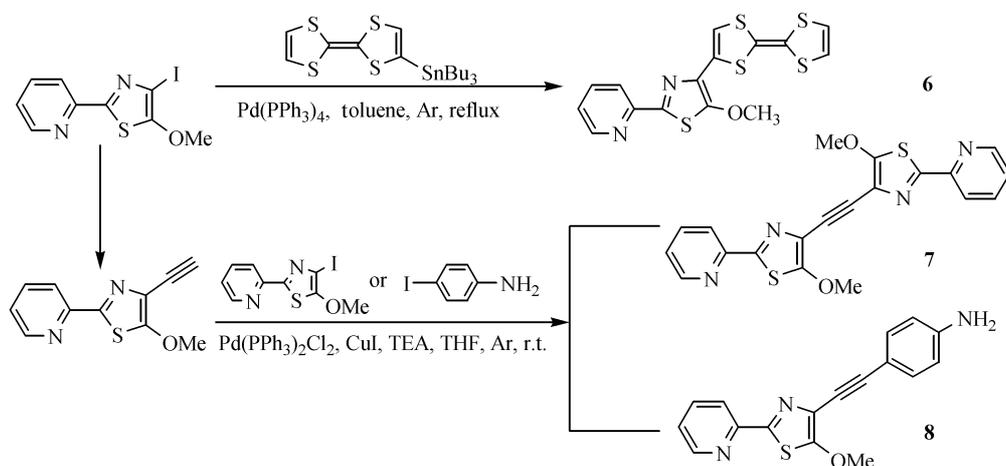


Figure 5 Synthetic route of molecules **6**, **7** and **8** through a palladium-catalyzed coupling reaction.

Table 1 Photophysical data of all the MPT family in acetonitrile

| Compound | $\lambda_{\max}^{\text{abs}}$ (nm) | $\lambda_{\max}^{\text{em}}$ (nm) | ϕ |
|-----------------------------|------------------------------------|-----------------------------------|--------|
| 2-MPT | 320 | 397 | 0.88 |
| 3-MPT | 311 | 388 | 0.20 |
| 4-MPT | 318 | 391 | 0.59 |
| bis-MPT-DAE-O | 337 | 460 | 0.10 |
| bis-MPT-DAE-C | 566 | – | – |
| MBT-MPT-DAE-O | 323 | 394 | 0.004 |
| MBT-MPT-DAE-C ^{a)} | 322, 408, 540 | 394 | 0.009 |
| 2-MT | 385 | – | – |
| 2-MT ⁺ | 417, 466, 522, 730 | – | – |
| 2-MT ²⁺ | 400, 565 | 450 | 0.11 |
| DMPTE | 322, 344 | 154 | 0.10 |
| MPTEA | 307, 355 | 525 | 0.025 |
| Ad | 307, 355 | 435 | 0.028 |
| H ₂ M | 300, 400 | 500 | 0.19 |

a) The photostationary state.

sion originated from the intramolecular charge transfer (ICT) is from the highest occupied molecular orbital (HOMO) localized at the methoxy group to the lowest unoccupied molecular orbital (LUMO) localized at the pyridine ring. In an acidic environment, protonation occurs at the nitrogen atom of the pyridine ring, which lowers the energy gap between the frontier molecular orbitals and induces red shifts both in absorption and fluorescence emission spectra (emission at 450 nm with excitation at 350 nm).

On the basis of the pH-sensitive fluorescence properties of MPT, YES and NOT logic gates are directly constructed by correlating the presence or absence of protons with the emission intensity at two different wavelengths (403 nm and 455 nm with excitation at 350 nm), for its dual-emissive fluorescence can be modulated by protons. By modulating the pH values of the solution of MPT by addition of trifluoroacetic acid (TFA), detection

at 455 nm shows a high fluorescence intensity (denoted as logic 1) at pH 1.0 and a low intensity (denoted as logic 0) at pH 5.5, which corresponds to the YES logic. Meanwhile, detection at 403 nm shows a strong fluorescence at pH 5.5 (denoted as logic 1) and a weak emission (denoted as logic 0) at pH 1.0, which corresponds to the NOT logic. Thus, working at a single excitation wavelength (355 nm) allows us to integrate the YES and NOT logic in parallel.

Furthermore, as MPT is a structural analog of 2,2'-bipyridine (bpy), it may chelate with the transition metal ions. Upon the introduction of paramagnetic cupric ion to the MPT solution, the fluorescence emission is quenched thoroughly due to the formation of a stable non-fluorescent Cu²⁺-2-MPT complex.

On the basis of the nondegenerate responses of the fluorescent emissions at two wavelengths with the introduction of proton (I1) and cupric ion (I2), parallel logic gates can be constructed (Figure 6). If the fluorescence at 403 nm is regarded as the output signal (O1), either one or both of inputs lead to the fluorescence quenching, that is, O1 is turned off as 0. The truth table illustrates a NOR logic operation. Meanwhile, if the

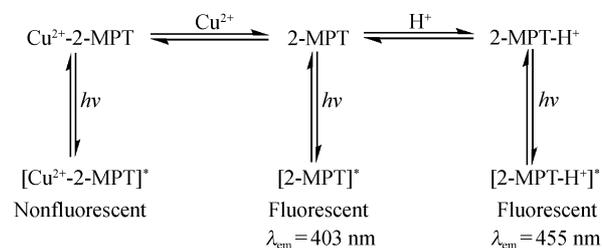


Figure 6 Schematic representation of the protonation and coordination equilibria of 2-MPT at the ground and excited state.

emission at 456 nm was recorded as output O2, an INHIBIT operation is set up. Therefore, parallel logic gates have been simulated on the basis of the pH-sensitive dual emissions of the fluorescent MPT. Moreover, all-fluorescence output is the most appreciated feature of this unimolecular system.

However, the number of reception sites in these molecules is still limited, which greatly restricts their binding capability and recognition selectivity to metal ions and other guest species. Moreover, MPT displays a rather small Stokes shift in fluorescence emission, which brings a relatively high background signal and a decreased ON-OFF contrast during the signal detection at the specific output channel. In order to improve the chemical and photophysical properties of MPT, further derivation of the molecular structures is necessary, for instance, extension of the molecular skeleton, introduction of certain switching units or recognition groups.

4 Combinational logic circuits within several MPT derivatives

If one molecule exhibits different responses to the multiple input signals, the cooperative effect among inputs may produce a multilayer digital circuit within one molecule, thus enlarging the variety of logic functions and enhancing the computing power. Under this strategy, a photo-switch and an electro-switch were introduced to conjugate with the MPT skeleton, and their fluorescence behaviors were investigated.

4.1 Cascade logic circuits within MBT-MPT-DAE

In modern electronics, gates can be physically wired together to form cascade digital circuits. Thus the computing power is enhanced with the increase of cascade layers, which affords the desired functions. However, the molecular systems cannot employ the same strategy as that in electronics due to the incompatibility of input and output signals. For a molecular substrate, the binding of a specific chemical input not only gives out a logic operation, but also usually produces or activates another recognition site, which can interact with the next input signal, and then the communication of the information is accomplished. Hence, by modulating the fluorescence properties of a multiswitchable molecule through the cooperative effect among inputs, cascade logic circuits can be realized within a molecule. Based on the same principle, the information transmission from

sequential logic units to combinatorial logic units can also be completed, which will be discussed later in this paper.

Photochromic molecules have been applied in molecular logic due to the different responsive properties of both isomers which can be switched with particular irradiation^[97]. Many examples have been reported that their photochromic behaviors are utilized to realize many logic functions^[15,20,35,39,43–48,60]. By covalently conjugating chemical binding sites with photo-switching skeleton in one fluorescent molecule, the chemical-sensitive fluorescence properties can be further modulated by particular irradiation signals, providing an extra pathway toward constructing a set of logic gates in cascade. Therefore, we were devoted to the realization of cascade digital circuits in a novel asymmetric diarylethene derivative **5** (Figure 7)^[92].

In this asymmetric diarylethene molecule, one MPT unit and a MBT unit occupy both aryl arms in adjacent to the perfluorocyclopentene core, where MBT can modulate the fluorescence behaviors as an electron donor. Addition of TFA into **5O** or **5C** solution results in a bathochromic shift in the emission spectra (Figure 7), which is attributed to the decrease of the energy gap between HOMO and LUMO after the formation of **5OH** or **5CH**, respectively. Similar to the parent compound MPT, addition of cupric ion quenches the fluorescence because of the formation of nonfluorescent complexes (**5OC** or **5CC**), which are little influenced by protons. Triethylamine (TEA) alone does not affect the fluorescence properties of **5O** or **5C**, but it can remove the proton within **5OH** or **5CH** due to the neutralization reaction, or serve as a competing ligand that can prohibit the coordination of cupric ion with MPT moiety, so as to recover the initial emission spectra. Thus, with different combinations of the several chemical or optical inputs (I1, irradiation at 350 nm; I2, TFA; I3, cupric ion; I4, TEA; I5, irradiation at 560 nm) introduced, **5** can be interconverted among six different states and exhibit different fluorescence behaviors (Figure 7). Therefore, multiple logic gates are yielded at each output channel. The value of every output signal is determined by the cooperation effect of the four input signals with a cascade digital circuit^[92].

Considering the four output channels together, with either **5O** or **5C** as the initial state, a cascade structure of 12 or 13 fundamental NOT, OR and AND gates inte-

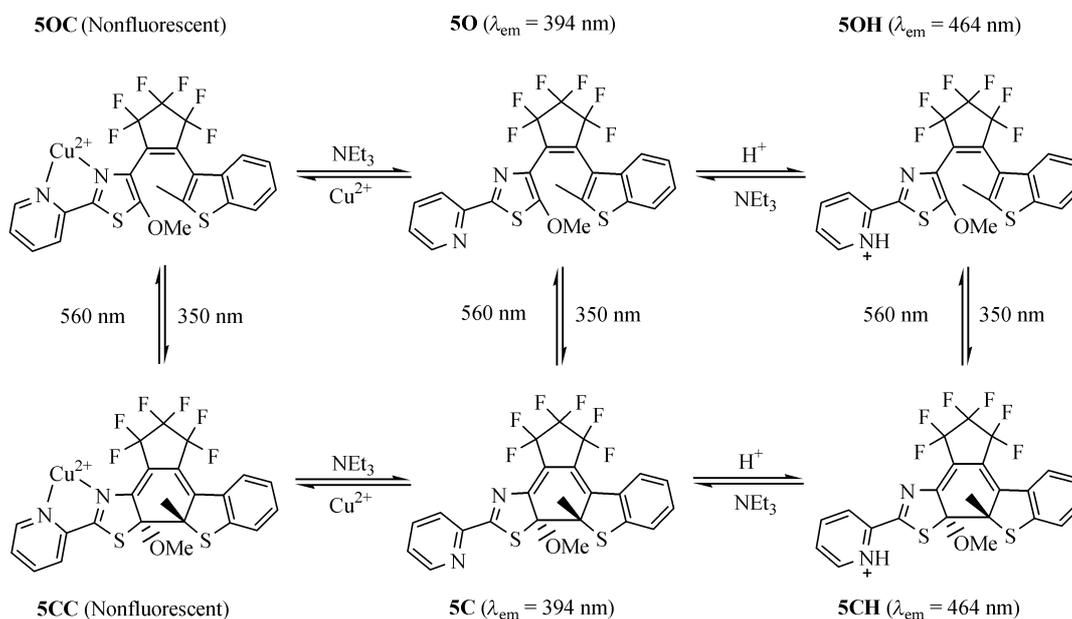


Figure 7 Schematic representation of the interconversion of **5** among different chemical states that exhibit distinct fluorescent behaviors.

grated in three layers is achieved through the cooperation of chemical and optical inputs in fluorescence mode^[92]. From this viewpoint, it can be envisaged that the introduction of more nondegenerate switches in a molecular system will result in a more complicated molecular cascade digital circuit.

4.2 Parallel logic gates within TTF-MPT

As described, the input signals and output signals of molecular logic systems are heterogeneous. Therefore, it is difficult to integrate the chemical-driven independent fundamental logic gates into a unimolecular system. One efficient approach is to assemble other switching units into a molecular fluorescent molecule, such as an electro-active group.

TTF is a widely employed electron donor in many molecular or supramolecular systems, and it can modulate the electron transfer process and the fluorescence properties of an organic fluorophore greatly with its sequential and reversible oxidation^[98]. The redox-controlled fluorescence behaviors of an TTF-anthracene dyad have been utilized to perform logic functions^[37]. Hence, we attempted to realize multiple switching spectral properties and investigate the multifunctional logic behaviors of a TTF-MPT dyad **6** by conjugating an electro-active TTF moiety with the MPT fluorophore^[93]. In **6**, the MPT fluorophore can be bound with proton or metal ions, while the TTF moiety is sensitive to the chemical oxidant. Therefore, its fluorescence exhibits

various changes with different combinations of inputs, and thus various reconfigurable logic gates are constructed in parallel.

Oxidation of the TTF moiety can be completed by introduction of several chemical oxidants. Excessive NOBF_4 can oxidize TTF to the dicationic state and Ce(IV) ion also exhibits such a property in presence of proton, both of which can promote a strong fluorescence emission. While cupric can only oxidize TTF to the cationic radical form, maintaining the negligible fluorescence emission (Figure 8). Addition of reductant to the solution of dicationic $\mathbf{6}^{2+}$ restores the system to the neutral state, quenching the fluorescence emission (Figure 8). Introduction of metal ions also affects the fluorescence properties of dicationic $\mathbf{6}^{2+}$, and the results depend on the nature of metal ions. Cu(II) , Fe(III) and Eu(III) quench the fluorescence emission, while Fe(II) barely influences the emission. In the meanwhile, the coordination of such metal ions with **6** is prohibited in the presence of competing ligands. Especially, $\text{Na}_2\text{S}_2\text{O}_3$ not only acts as a reductant, but also serves as a competing ligand that can bind with cupric ion strongly when sufficient proton is present to conjugate with the pyridine ring (Figure 8). In addition, the fluorescence quenching induced by Fe(III) can be realized by simultaneous addition of Fe(II) and NOBF_4 (Figure 8)^[93].

When protonation, coordination and redox reactions are executed within this system simultaneously. The

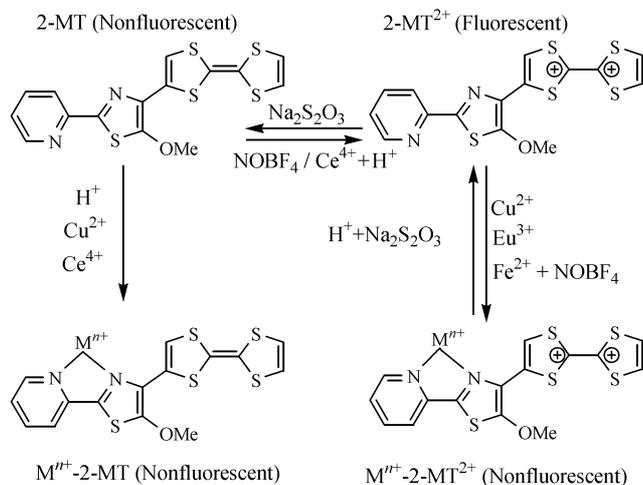


Figure 8 Schematic representation of the protonation, coordination and redox equilibria of molecule **6**.

fluorescence properties displayed more various switching behaviors, which could be described in the discipline of many Boolean logic functions. Starting from the non-fluorescent neutral **6** or the highly luminescent dicationic $\mathbf{6}^{2+}$, introduction of different combinations of the above chemical inputs would lead to the different fluorescence switching phenomena. Furthermore, through investigating the fluorescence spectral properties of 2-MT at the different oxidation and binding states, various Boolean logic gates, such as AND, OR, NOT, NOR, INHIBIT, XNOR and NAND, are realized by rational selection of the initial states and combinations of chemical inputs, which affords an efficient approach to the molecular logic reconfiguration^[93].

5 Basic numeracy performances within MPT derivatives

As described, it is common that the input and output signals of the molecular logic systems are heterogeneous. So it is difficult to integrate several chemical-driven arithmetic functionalities into a unique functional molecule. To break through this bottleneck, multiple spectral states can be employed as the output channels, such as different spectroscopic techniques, different signals at different wavelengths or the sum, difference or ratio of the signals at different wavelengths^[30,31,33,34,41,85].

5.1 The reconfigurable half-adder and half-subtractor with multiple spectral channels

For the molecular systems, a three-state switch is required to construct a half-adder or a half-subtractor. A

reconfigurable arithmetic calculator must possess at least four spectral states in response to different input signals. As the TTF moiety within **6** can be sequentially and reversibly oxidized to the cationic radical and dicationic states, the occupancy of the frontier orbital is distinctly altered, not only endowing **6** various fluorescence switching abilities due to the different efficiencies of photoinduced electron transfer (PET) as described above, but also promoting the characteristic ICT phenomena of the oxidized TTF derivatives at the ground state, which can be observed in UV-vis absorption profiles. Introduction of other external chemical inputs also afford different alterations in both absorption and emission spectra at each oxidation state of **6**, due to the cooperative or competitive effects of redox, protonation and coordination reactions^[94]. Therefore, the asynchronous changing behaviors of the absorption and fluorescence spectra in response to different input signals thus provide parallel output channels with constructing reconfigurable molecule-based binary algebra functionalities (Figure 9).

Proton can bind with the nitrogen atom of the pyridine ring, enhancing the electron-withdrawing ability and lowering the transition energy from TTF-centered HOMO to MPT-centered LUMO, which leads to a red-shift of charge transfer band from 390 nm in the UV region to 530 nm in the visible region. The protonation also promotes the ICT process from the methoxy group to the pyridine ring to some extent, which slightly recovers the fluorescence at 450 nm (Figure 9).

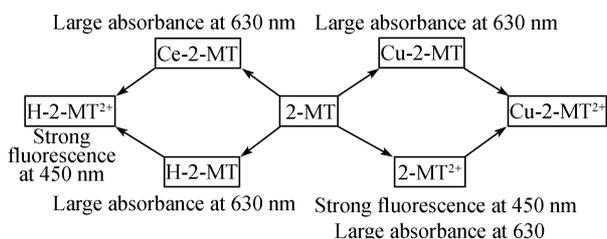


Figure 9 Chemical conversion processes with molecule **6** for the reconfigurable half-adder and half-subtractor.

Metal ions can interact with **6** in pure coordination mode or together with oxidation process. Cu(II) only oxidizes **6** to the monocationic radical state, inducing the characteristic ICT transition centered at 715 nm. While Ce(IV) can oxidize **6** to the dicationic state directly with the characteristic ICT band around 600 nm, and proton also promotes a large absorption around 600 nm. But addition of Cu(II) ion to the solution of dicationic $\mathbf{6}^{2+}$ leads the ICT absorption band centered at 600 nm dis-

appeared. Besides, simultaneous addition of proton and Ce(IV) to the neutral **6** solution does not promote such an ICT band. As for fluorescence properties, introduction of either Cu(II) or Ce(IV) is conducive for the non-radioactive relaxation of excited MPT at any oxidation state, thus quenching the fluorescence. The presence of proton blocks the coordination between Ce(IV) and MPT, restoring the fluorescence emission (Figure 9).

Above all, the same chemical introduction, either a single chemical input or a combination of several chemical inputs, may trigger different effects between ICT at the ground state and PET at the excited state. Taking the neutral **4** solution as the initial state and observing the output signal from ICT output channel of the absorbance at 630 nm (O1), the input set of either NOBF₄ (I1) and Cu(II) (I2) or TFA (I3) and Ce(IV) (I4) gives an XOR gate. If PET process is regarded as the output channel (emission at 450 nm, O2), the former input set as above enables the system to execute an INHIBIT function, while the latter generates an AND gate. Therefore, through recording the output signals at O1 and O2 simultaneously, a half-subtractor and a half-adder are assembled in the current system on the basis of the cooperative or competitive effects of the oxidation and coordination reactions in the parallel ICT and PET pathways^[94].

5.2 Reconfigurable molecular arithmetic with the full-fluorescence mode

The reconfiguration capacity of the arithmetic functions provides a feasible and facile pathway for promoting the functional integration and computing power at the molecular level. Herein, our interest is focused on performing reconfigurable half-adder and half-subtractor arithmetic functions solely in the fluorescence output mode. DMPTE is composed of two MPT moieties conjugated through a triple bond^[95]. Compared with the parent compound MPT, DMPTE bears more reception sites. Hence, it displays more coordination modes with proton and metal ions, and then various fluorescence behaviors can be observed upon different chemical inputs.

Neutral **5** exhibits an emission band centered at about 450 nm upon excitation at 350 nm. Upon sequential protonation of DMPTE to (H-DMPTE)⁺ and (H₂-DMPTE)²⁺, the fluorescence emission peak shows a bathochromic shift to 470 nm and then 550 nm (Figure 10). Addition of TEA to the acidic solution neutralizes the present TFA and restores the emission band at 450 nm,

while addition of TEA to neutral DMPTE brings neglectable change to the fluorescence behaviors. Upon addition of cupric ion to DMPTE solution, the emission is quenched, owing to the formation of a 2:1 nonfluorescent complex Cu₂-DMPTE^[95]. Cu₂-DMPTE solution exhibits different fluorescence responses toward proton from **5**, which is attributed to the competing binding between cupric ion and proton from **5** and the stepwise protonation of the two pyridine rings. A small portion of proton can only induce an emission band at 470 nm, and excessive amount of proton is required to promote the emission peak at 550 nm. Besides, formation of Cu₂-DMPTE is blocked by competing ligands that can precipitate cupric ion from solution, such as sulfide or hydroxyl anion, and the fluorescence emission at 450 nm is recovered. Notably, TFA may also affect the removal of cupric ion, because cupric hydroxide can be dissolved in acidic solution, quenching the fluorescence emission again, while cupric sulfide is stable against proton, remaining the restored fluorescence emission (Figure 10).

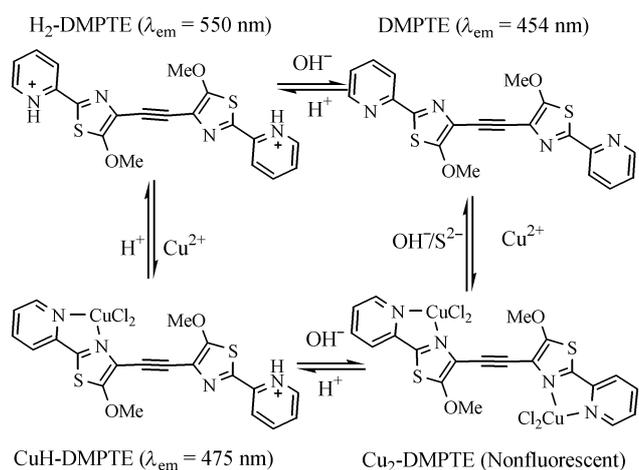


Figure 10 Schematic representation of the interconversion of molecule **7** among different fluorescent states.

Employing the solution of nonfluorescent Cu₂-DMPTE complex as the initial state, an OR gate at the output channel of emission intensity at 475 nm (O1), an AND gate at the output channel of emission intensity at 575 nm (O2), and an XOR gate at the output channel of the difference of the above two emission intensities (O3) are realized by the introduction of sodium sulfide and TFA, generating a half-adder. While a half-subtractor is constructed with sodium hydroxide and TFA (an XOR gate at O1 and an INHIBIT gate at O2). Thus, a half-adder

and a half-subtractor are assembled within DMPTE solely with the fluorescence output mode, and the functional reconfiguration is realized on the basis of the different stabilities of the two above cupric precipitations against protonation^[95].

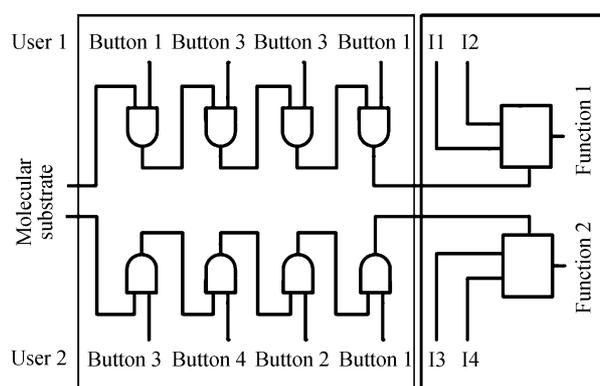
6 Construction of a secured molecular information platform

Due to the wide public concerns over the information security, the security feature of a molecular computing device also needs to be considered as the potential applications are expected. As for the information protection, several stages in security policy are involved as follows^[96]. First, users' authorities should be verified via passwords or tokens. Second, digital functionalities or databases specially tailored to users' identities should only be accessed after the prior authorization. Third, information transmission should be encrypted to prevent illegal wiretap if necessary.

To accomplish the first stage of the security policy, the logic molecule should perform as a keypad lock. So the unauthorized accesses cannot be admitted. As for a fluorescent molecular switch, the final fluorescent state of the substrate may be determined not only by the nature of the input signals but also by the addition sequence of the input signals, on condition that the kinetic or thermodynamic properties of the involved recognition reactions are affected by the input sequence. If the previous recognition process produces an inert intermediate product, the next recognition process cannot proceed smoothly within the limited timescale. By taking advantage of the kinetic hindrance, the identification of the input sequences has been reported by Shanzer and his coworkers^[77]. Besides the kinetic hindrance strategy, the input sequence can also be authenticated independently if there is only one possibility among the combination of the input sequence strings to produce the target compound. An example has been reported within 2-MT^[94]. Starting from the non-fluorescent neutral state, only two-step introduction of the equivalent oxidant can produce the fluorescent dicationic state, and the fluorescent signal can only be acquired after the excitation at 350 nm. For all the combinations of 3-digit input strings, any distorted input either fails to produce the dicationic state or lacks the excitation beam in the final step.

However, an information platform with the first-stage protection alone is still vulnerable against modification

chip or illegal duplication. Therefore, the security feature needs to be further strengthened by the second and third stage policies. However, this requires users' identity information to be transmitted from the authentication unit to the processing unit, which is difficult for a molecular device due to the heterogeneity of the chemical input and optical output signals. Notably, data processing functionalities, such as binary algebra, are based on the recognition processes between the fluorescent switch and the specific chemical input signals. If the binding site is activated only after an input-sequence-sensitive conversion, the differences in binding features between the initial and the activated form can ensure the digital functionalities to be achieved only after activation, which corresponds to the user identification process, and then the fluorescent switch is thus capable of performing user-specific digital functionalities (Scheme 2). If there is more than one activation pathway for the recognition sites, the molecular device will be capable of distinguishing multiple users^[96].



Scheme 2 Illustration for the operation procedure of user-specific binary algebra.

Following this strategy, the security policy for providing user-specific binary algebra has been implemented inside MPTEA molecule. Due to the distinct reaction activities of the amino group and the pyridine ring, MPTEA may be converted to either amide form Ad or diprotonated form H₂M with fluorescence maximum at 430 nm or 500 nm, respectively. In addition, the conversion from MPTEA to either Ad or H₂M is sensitive to the input sequence (Figure 11). Acylation reaction at the amino group produces a high-energy kinetic barrier to prevent the reverse reaction. For each conversion pathway, there is only one unique sequence among ten thousands of possible input sequences to achieve the desired

fluorescence information when the initial state is fixed (Figure 11). As for the conversion to Ad, the input sequence of 3421 is the only password entry that can complete the identification. While for the conversion to H₂M, the input sequence of 1331 is the only one that introduces two portions of proton and excitation at the right time. It should be noticed that the achievement of password authentication is based on the fact that distorted input cannot trigger the correct reaction in limited steps.

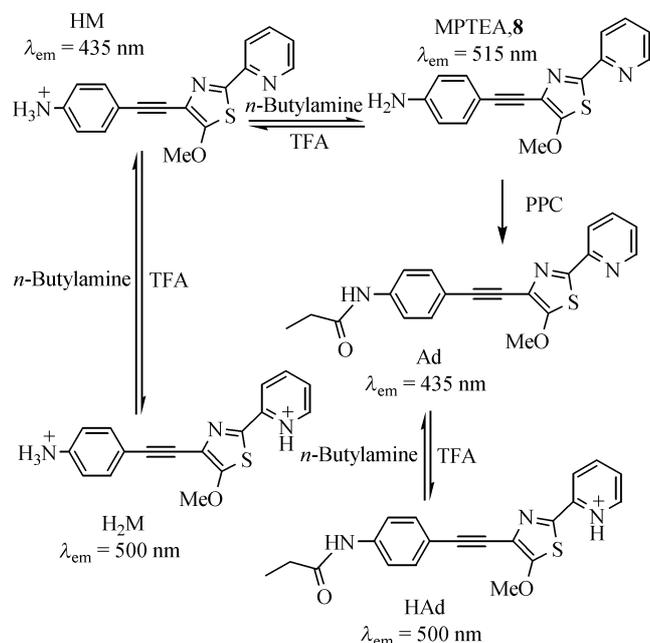


Figure 11 Fluorescence of different binding states of MPTEA. For the user authentication processes, MPTEA in acetonitrile solution ($0.02 \text{ mmol} \cdot \text{L}^{-1}$) containing *n*-butylamine ($0.1 \text{ mol} \cdot \text{L}^{-1}$) is set as the stand-by state of the secured platform. Buttons 1, 2, 3 and 4 in the keypad are represented with irradiation at 350 nm for 2 min, *n*-butylamine ($0.1 \text{ mol} \cdot \text{L}^{-1}$), trifluoroacetic acid (TFA, $0.1 \text{ mol} \cdot \text{L}^{-1}$), and propionyl chloride (PPC, $1 \text{ mmol} \cdot \text{L}^{-1}$)/CuCl₂ ($0.06 \text{ mmol} \cdot \text{L}^{-1}$), respectively. The other buttons are represented with a large amount introduction of quenchers.

When user 1 logs into the molecular platform through his password entry 1331, the molecular platform is converted from the stand-by state MPTEA to the operation state H₂M. In this case, $0.1 \text{ mol} \cdot \text{L}^{-1}$ *n*-butylamine plus the irradiation at 350 nm for 2 min (I1) and the irradiation at 410 nm for 2 min (I2) can perform an XOR gate and an INHIBIT gate when recording the emission intensity at 525 nm (O1) and calculating the ratio of emission intensities at 500 nm to that at 525 nm (O2) respectively. Thus, user 1 is then endowed with half-subtractor functionality. However, for the unauthorized users, the current input set only produces two PASS 0 gates, and

for user 2, a PASS 0 gate (O1) and an INHIBIT gate (O2) are accomplished. As for user 2, the operation state is Ad with *n*-butylamine-coordinated cupric ion. With the emission intensities detected at 485 nm (O3) and 520 nm (O4), respectively, an XOR gate and an AND gate are constructed by using two portions of TFA (I1, I2) as the inputs. In this way, a half-adder is realized specially for user 2^[96].

For each arithmetic step of the half-adder as described, original fluorescence spectra produced by the corresponding input signals can be further switched on and off by chemical-encoded keytexts ($0.8 \text{ mol} \cdot \text{L}^{-1}$ TFA and $0.8 \text{ mol} \cdot \text{L}^{-1}$ *n*-butylamine), due to the modulation of the protonation equilibrium between Ad and HAd. To decrypt the protected spectral information, both the encrypted fluorescent output signals and keytext inputs are required, which is only feasible for a trusted user holding the keytext entry. Besides, due to the distinct energy transfer efficiencies between the fluorescent substrate and the TTF unit at the different oxidation states, the fluorescent intensity at 435 nm of Ad can be utilized to label the oxidation state of TTF, which generates redox-controlled fluorescent-based information storage functionality to the molecular platform^[96].

7 Reset issue at the molecular level

One difference in running an electronic device and a molecular one lies in the reset capacity after each logic operation. An electronic device recovers its initial state immediately once electricity current is cut off. However, a molecular device retains its binding state even when the input signals are cut off, and thus prevents further operation, as the molecular system has been remaining in thermodynamic equilibrium with the input introduced. Therefore, the effect of the input signals must be removed or neutralized to restore the initial state of the molecular device, enabling the system to execute new logic operations^[99].

Usually, the resetting reagents are often introduced to recover the initial state of the molecular devices, the operation principle of which is based on the fact that the recognition reactions driving molecular logic devices, such as protonation, coordination, or redox reactions, are usually chemically reversible, which reveals that the direction of recognition reaction can be reversed if some reagents are introduced to consume the previous input signals. According to this strategy, protonated product

can be reset to the initial state when an equivalent amount of base is introduced^[61]. Oxidized product can be reset to the neutral state when reductant is present^[67]. For coordination reaction, either precipitation/dissolution equilibrium or coordination/dissociation equilibrium can be utilized to react with the input metal ions or ligands. Especially, if precipitation reaction is employed to remove the metals ion, after each resetting process, the residual metal concentration is negligible, which would not hamper further executions. By utilization of the proper resetting reagents, each signal of the fluorescent outputs triggered by the chemical inputs within DMPTE-(CuCl₂)₂ can be compensated (cupric ion resetting sulfide anion, TFA and NaOH resetting each other), restoring the initial state (Figure 12). Thus, the arithmetic functions can be performed in a single quartz-cell with a successive introduction of chemical inputs and resetting reagents with a high signal-to-noise ratio after 10 cycles of set/reset process^[95].

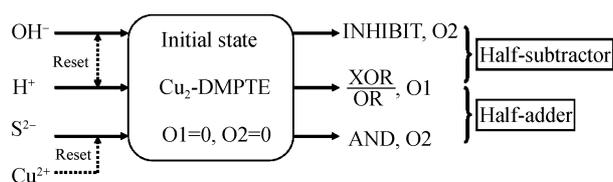


Figure 12 Schematic representation of the reset processes for the arithmetic functions within 7.

However, the utilization of the resetting reagents still faces other challenges. Because the recognition processes are executed in solution, repetitive introduction of the resetting reagents results in an increased solution volume and a decreased fluorescent substrate concentration. After several cycles, the chemical waste accumulated may also interfere with the operation of molecular logic functionalities. And the case would be even worse if the authentication processes are resettable in a secured molecular platform, where the latter user can know what the previous one has done by investigating the chemical waste composition related with the logic executions. Recently, the development of the molecular logic inside a microfluidic chip shows another solution for resetting the logic functions^[100]. After each logic execution, the nanoliter solution of the fluorescent substrate is refreshed, which obviates the concentration changes, accumulation of chemical waste and information risk. Primitive work has been attempted by us and some results have been obtained.

8 Conclusions and outlook

In summary, a series of MPT derivatives as synthesized show chemical-sensitive fluorescence behaviors. Such spectral tuning processes in response to external stimuli mimic the functions of molecular switches and logic gates, which are interesting for information processing at the molecular level. With other recognition groups conjugated to the MPT moiety, multiple reconfigurable fluorescence-based logic gates are constructed in a cascade mode or in parallel. Notably, the half-adder and half-subtractor can be loaded in a single fluorescent molecular system with different chemical input sets and different output channels running in parallel. The reconfiguration capacity of the arithmetic functions provides an additional approach for promoting the functional integration and computing power at the molecular level and circumventing the need for an additional processor. Concerning the issue of information security, the input-sequence-dependent spectral changes are employed to mimic the function of a keypad lock. In addition, a prototypical molecular secured computing platform, capable of performing user-specific functionalities under protection and data encryption and storage, is constructed. The authentication-prior-to-execution strategy is proposed to defend against information invasion at the molecular level. As for the reset issue in the molecular logic system, with a new efficient strategy employing the precipitation reactions, the binary arithmetic functionalities can be executed successively within a unique molecule in a single quartz-cell. In addition, microfluidic chips can perform as a promising alternative platform to execute digital functions resettably and refreshably, which avoids the concentration changes, accumulation of chemical waste or information risk.

Of course, as some inevitable defects exist in the current molecular system, such as a large amount of chemical waste produced in the reset process, the destructive readout and the incompatible input and output representations, the strategy for constructing multiple digital functions and carrying out reconfigurable arithmetic functions in a molecular or supramolecular system as discussed here only provides a prototype for molecular electronic devices, and we have only made some rudimentary contributions in this area. However, looking to the future, there are many opportunities for chemists in this ascendant field. Due to the small size and easy

modification of the structures and properties of organic functional molecules, constructing digital functionalities at the molecular level provides a promising direction to enhance the computing power and functional integration toward the future molecular computer, which is encouraging us to continue our efforts. Furthermore, the organic molecules display better biocompatibility, which may underline their significance in future molecular electronic devices. In the near future, some fundamental studies will still play important roles in many aspects,

such as the design strategies of functional molecules with targeted properties. In addition, with decreased information risk, the prototype of a secured molecular platform may inspire a diverse potential application of small molecules and biomolecules in this fast developing information era, such as the local drug delivery and release. At present, another great challenge is to localize these functional molecules in designed solid environment in order to be applied in reality, where they can still perform the excellent properties as that in solution.

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