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Photochemistry

Photoswitchable “Turn-on” Fluorescence Diarylethenes: Substituent Effects on Photochemical Properties and Electrochromism

Qi Ai, Shichong Pang, and Kwang-Hyun Ahn*[a]

Abstract: A series of “turn-on” fluorescence diarylethenes derived from 2,3-bis(2-methylbenzo[*b*]thiophen-3-yl)-5,6-dihydro-4*H*-thieno[2,3-*b*]thiopyran-4-one (**1**) with alkyl and acetyl substituents were synthesized. The photochemical and photophysical properties of these derivatives, including the photoreaction of crystalline **1**, were thoroughly investigated to reveal substituent effects on their properties. The results indicated that alkyl substituents did not significantly affect the absorption and emission spectra of the diarylethenes. However, large absorption and emission wavelength shifts were observed for the diarylethene with an acetyl substituent due to extension of π–π conjugation. Significantly, all of the fluorescent ring-closed forms of the compounds isomerized to their ring-open forms in the presence of Cu^{2+} in the dark. EPR results provide clear evidence for the formation of the compound **1** radical cation intermediate that might be generated in the reaction between c-**1** and Cu^{2+}. DFT calculations found that the ground-state activation energy for ring-opening of $\mathbf{1}^{\bullet+}$ was approximately 9.2 kcal mol^{-1} lower than that of **1** without Cu^{2+}, such that a Cu^{2+}-catalyzed oxidative cycloreversion reaction at room temperature might be possible.

Introduction

In recent years, fluorescence regulation of fluorescent molecules by external stimuli such as light has received a great deal of attention because light is non-invasive, and it is easily tuned and focused to provide a high degree of spatial and temporal control.[1] Among these fluorescent molecules, “turn-on” fluorescence diarylethenes, the initial non-fluorescent open isomers of which are converted to closed isomers that emit green or red fluorescence upon UV irradiation, have attracted much attention.[2] Such derivatives may be useful for PALM[3] (photoactivated localization microscopy), STORM[4] (stochastic optical reconstruction microscopy), and RESOLFT[5] (reversible saturable optical fluorescence transition) applications.

Photochemical properties of diarylethenes are strongly dependent upon the particular substituents.[6–8] Information related to substituent effects may contribute to a broad understanding of the specific photochromic characteristics of diarylethenes. In a recent study, a few effective “turn-on” fluorescence diarylethenes with various substituents were developed.[9]

Besides photochemical reactions, many diarylethenes are reported to undergo cyclization and cycloreversion reactions in electrochemical oxidation or reduction processes.[10] The ring-opening reaction can also take place in the presence of oxidizing reagents.[11] Such electrochromism[12] resembles photochromism[13] in that it provides a pathway to bypass the large ground-state thermodynamic barrier required for isomerization. For diarylethenes, electrochromism offers a valuable additional means of accessing the two switching states, and this unique dual chromism behavior has been exploited for molecular switches.[14]

Recently, we reported a novel “turn-on” fluorescent diarylethene—2,3-bis(2-methylbenzo[*b*]thiophen-3-yl)-5,6-dihydro-4*H*-thieno[2,3-*b*]thiopyran-4-one (**1**)—and its successful application to live cell imaging (Scheme 1).[15] The fluorescence of the compound was thought to be due to the bridge unit containing the six-membered ring with sulfur and carbonyl groups forming a “push–pull” system.[16] Thus, to improve the photochromic properties, and especially the fluorescence of diarylethene **1**, a series of derivatives, **2**–**7**, retaining the “push–pull system” was synthesized, and their photophysical properties were studied. Interestingly, during our study with **1**–**7**, we unexpectedly found that the diarylethenes had electrochromic properties. The ring-closed forms of the diarylethenes readily transformed to ring-open forms in the presence of an external oxidant. Detailed results of this study are described herein.

Results and discussion

Synthesis

To investigate substituent effects on the fluorescence of compound **1**, various diarylethenes (**2**–**7**) with alkyl and acetyl groups at the R_1, R_2, and R_3 positions were prepared according to methods described in Schemes 2 and 3.

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[a] *Dr. Q. Ai, Dr. S. Pang, Prof. Dr. K.-H. Ahn*
Department of Applied Chemistry
Kyung Hee University, Yongin, 446-701 (Republic of Korea)
E-mail: khahn@khu.ac.kr

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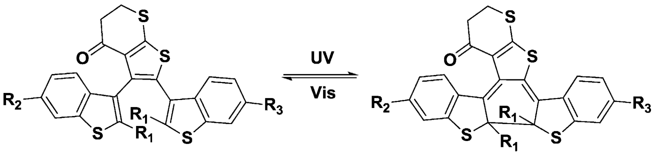


1; $R_1 = CH_3$, $R_2 = R_3 = H$,
2; $R_1 = CH_2CH_3$, $R_2 = R_3 = H$,
3; $R_1 = (CH_2)_6CH_3$, $R_2 = R_3 = H$,
4; $R_1 = CH_3$, $R_2 = R_3 = COCH_3$,
5; $R_1 = CH_3$, $R_2 = R_3 = CH_2CH_3$,
6; $R_1 = CH_3$, $R_2 = CH_2CH_3$, $R_3 = H$,
7; $R_1 = CH_3$, $R_2 = H$, $R_3 = CH_2CH_3$,

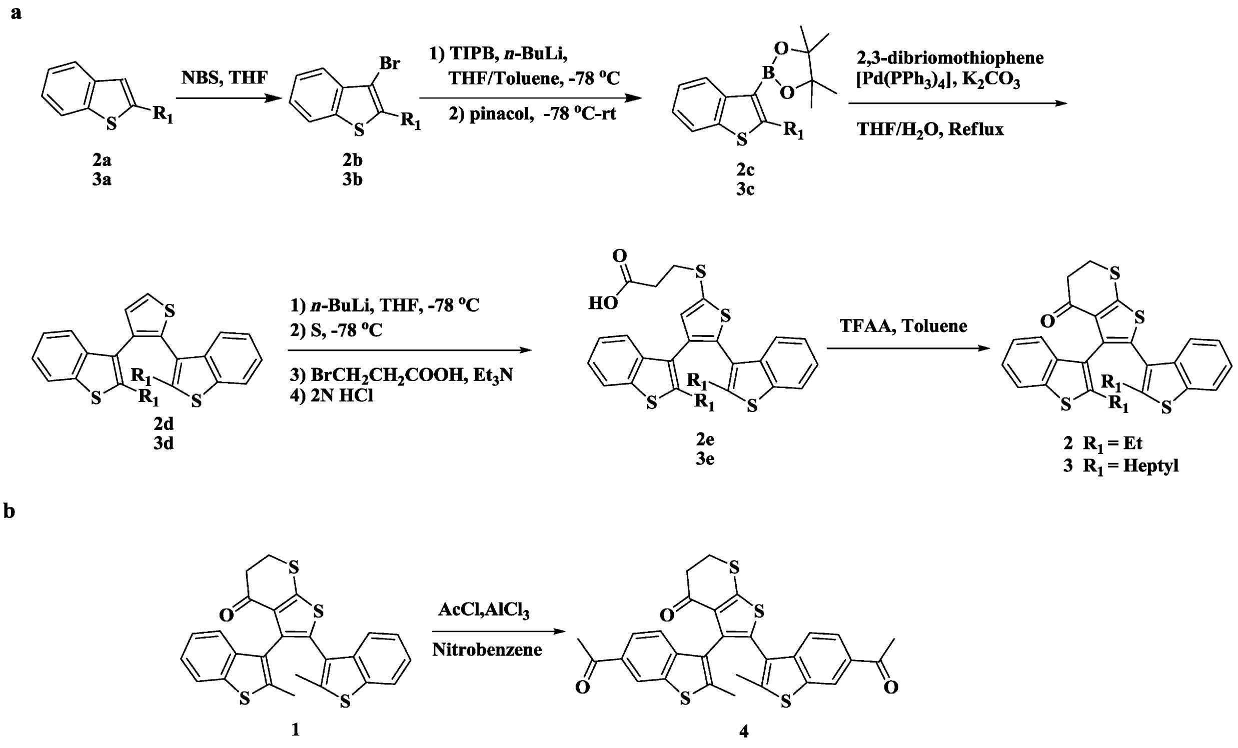
Scheme 1. Photochromic reactions of **1** and derivatives.

Compound **4** was synthesized from **1** in a reaction with acetyl chloride and $AlCl_3$ in 90% yield (Scheme 2b). Since **1** has an asymmetric structure, electronic effects due to substituents at either the R_2 or R_3 position were expected to be different. Thus, compounds with asymmetric substituents, such as **6** and **7**, were prepared. To prepare these two compounds (Scheme 3a), stepwise Suzuki coupling reactions were employed with 2,3-dibromothiophene to form the 2-heteroaryl-3-bromothiophene intermediates. To confirm the structures of the intermediates, debromination of **6b** was performed with *n*-butyl lithium to prepare **6′b** (Scheme 3b). The ^1H NMR spectrum of **6′a** prepared from 3-bromothiophene showed a distinct singlet peak for the thiophene ring. Meanwhile, the ^1H NMR of **6′b** had no such singlet peak, indicating that the initial Suzuki coupling with 2,3-dibromothiophene took place regioselectively at the 2-position. The chemical structures of **2**–**7** were confirmed by ^1H and ^{13}C NMR spectroscopy, and HRMS.

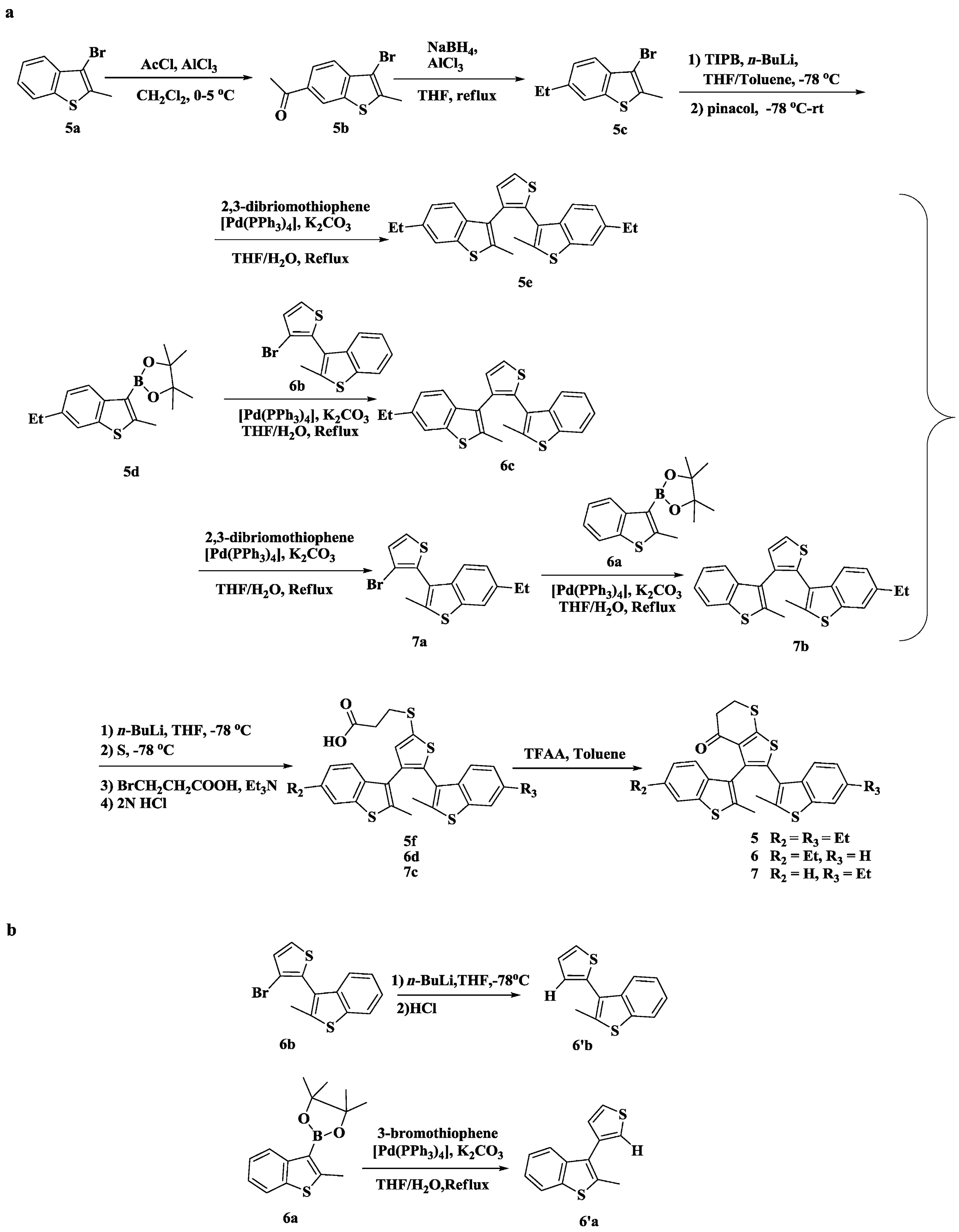
A single crystal of **1** in its open form was obtained from its solution in hexane and ethyl acetate.[17] Interestingly, the crystal showed "turn-on" fluorescence behavior in the solution with UV or visible light irradiation. The yellow non-fluorescent ring-open form was converted to the red fluorescent ring-closed form upon irradiation with 365 nm light. The red color of the crystal reverted to yellow after exposure to visible light (Figure 1b). The crystal structure was solved by X-ray crystallographic analysis. The ORTEP drawing of the crystal structure in Figure 1a exhibits the open isomer of **1** with approximately C_2 symmetry. It was packed in a photoactive anti-parallel conformation in the crystalline phase, suitable for the photocyclization reaction. It has been reported that photocyclization of a diarylethene molecule in the single crystalline phase was possible when the distance between the two reacting carbon atoms packed in the crystal was less than 4.0 Å.[18] The distance between C8 and C24 of the open isomer of **1** was determined to be 3.58 Å, which is close enough for the photocyclization reaction in the single-crystalline phase to occur.

Photophysical properties

The photophysical properties of diarylethenes **2**–**7** were investigated in ethyl acetate (1.0×10^{-5} M) at room temperature. Figure 2 shows absorption spectra of the open and closed diarylethenes in ethyl acetate. All of the closed isomers showed a broad band near 520–560 nm. The reddish color of the solutions, which represents ring-closed isomers, disappeared after irradiation with visible light due to the ring-opening reaction.



Scheme 2. a) Synthesis of compounds **2** and **3**. b) Synthesis of compound **4**.



Scheme 3. a) Synthesis of compounds **5**–**7**. b) Synthesis of compounds **6′b** and **6′a**.

The photochromic properties of these compounds are summarized in Table 1. The results showed that alkyl substituents at the R_1, R_2, and R_3 positions had a slight effect on the photochromic features of diarylethenes, including absorption maxima, molar absorption coefficients, and quantum yields of the photoreaction. However, a large absorption shift of 33 nm was observed in the absorption spectrum of **4** compared to **1** due to extension of the π–π conjunction of the benzothiophene with the carbonyl substituent, and the photoconversion ratio of **4** increased to 82 %. These results indicate that the carbonyl group had a significant effect on the photochromic properties of **1**.

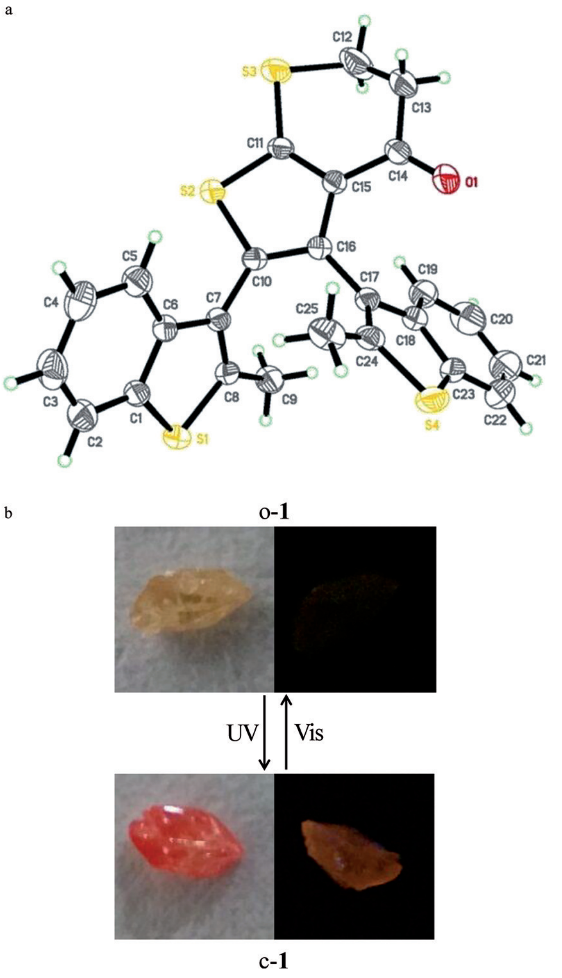


Figure 1. a) ORTEP drawing of the open-ring isomer of **1** with 30% probability ellipsoids. b) Photochromism of **1** in the crystalline phase.

Fluorescence of diarylethenes

The fluorescence properties of diarylethenes **2–7** close form were measured in ethyl acetate (1.0×10^{-5} M) at room temperature. Because of the bridge unit forming a "push–pull" balance with the sulfur atom and carbonyl group, the ring-closed form for all of the diarylethenes showed good fluorescence in solution upon UV irradiation. The fluorescence spectra of diarylethenes at their photostationary states are shown in Figure 3 and Table 2.

As presented in Table 2, emission peaks of **2** and **3** upon photoexcitation at the absorption maxima were observed at 594 and 597 nm, respectively, which are approximately 14 and 17 nm bathochromic shifts compared with **1**. At the same time, the fluorescence quantum yields decreased to 0.050 and 0.044, respectively. These results indicate that an increase in the alkyl chain length at R_1 is accompanied by a red-shift of emission maxima and a decrease in emission intensities. For **4**, the emission maximum was red-shifted by 31 nm. Although, a carbonyl substituent lowered the fluorescence quantum yield, it may offer a new method for the synthesis of "turn-on" fluorescence NIR photoswitching materials for biological probe applications.

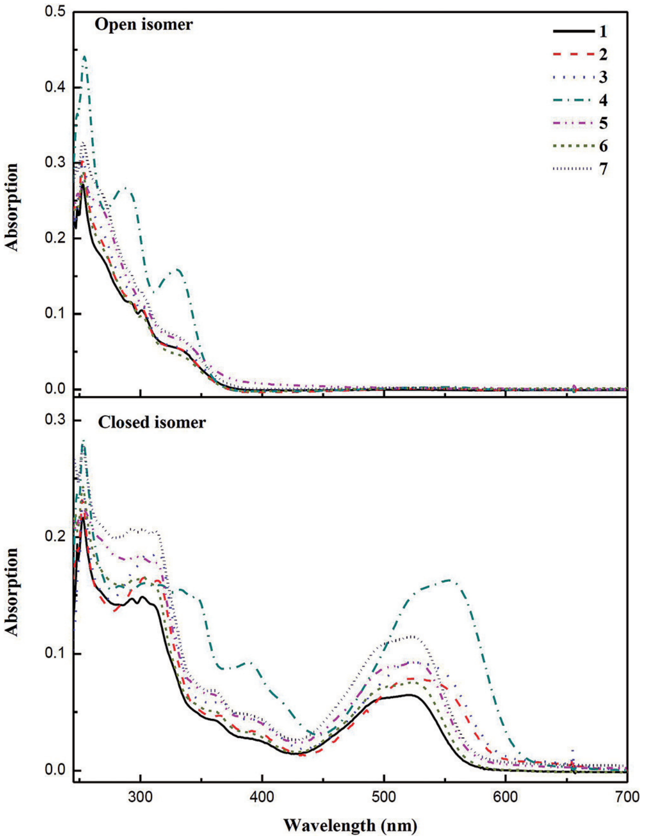


Figure 2. Absorption spectra for **1**–**7** in ethyl acetate (1.0×10^{-5} M) at room temperature. Cycling between the open and closed isomers was performed by alternating illumination with 312 nm and visible light.

Table 1. Photophysical properties of diarylethene derivatives.

	AP:P[a]	$\Phi_{o\rightarrow c}$[b,c]	$\Phi_{c\rightarrow o}$[b,d]	conversion	λ_{max} [nm]/ε [10^3 M^{-1} cm^{-1}] open ring	closed ring
1	65:35	0.25	0.17	50	252/27.2	520/3.2
2	73:27	0.35	0.17	35	252/30.3	524/4.0
3	–[e]	0.20	0.07	40	252/30.8	526/3.7
4	60:40	0.16	0.016	82	254/44.1 286/26.7	553/13.4
5	70:30	0.21	0.14	35	253/27.6	527/3.3
6	65:36	0.24	0.17	48	252/28.9	523/3.6
7	66:34	0.14	0.084	57	253/32.8	523/6.6

[a] Antiparallel (AP) to parallel (P) ratio as observed in ^{1}H NMR spectra in $CDCl_3$ (5.0×10^{-3} M). [b] BTF6 was used as a reference. [c] Cyclization quantum yield, measured at 312 nm in ethyl acetate. [d] Ring-opening quantum yield in ethyl acetate measured at the λ_{max} of the closed-ring isomer. [e] Not determined due to complex peaks.

As for **6** and **7** bearing an ethyl substituent at different positions, compound **7** had a better fluorescence quantum yield compared with **6**. However, compound **5**, which contains ethyl groups at both R_2 and R_3, exhibited the highest fluorescence quantum yield. This result demonstrates that the fluorescence quantum yield is quite sensitive to the position of alkyl group attachment.

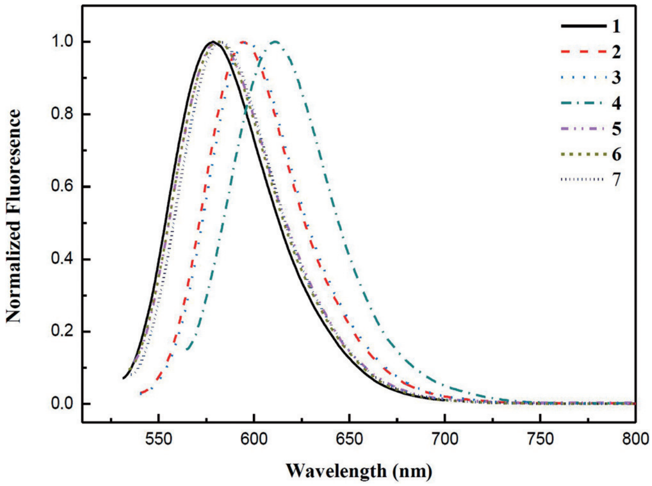


Figure 3. Normalized fluorescence spectra upon photo-excitation at the absorption maxima for the photostationary state of **1**–**7** close form in ethyl acetate (1.0×10^{-5} м) at room temperature.

Table 2. Fluorescence properties of diarylethene derivatives **1**–**7**.

	λ_{max} [nm][a]	Φ_F[b]		λ_{max} [nm][a]	Φ_F[b]
1	580	0.110	**5**	582	0.115
2	594	0.050	**6**	581	0.056
3	597	0.044	**7**	582	0.079
4	611	0.024			

[a] λ_{max} of the emission band following photo-excitation at absorption maxima. [b] Determined using rhodamine B (0.70:510 nm photoexcitation in EtOH) as the reference.

Electrochromism

It was recently reported that Cu^{2+} ions can oxidize the ring-closed form of certain diarylethenes to promote their ring-opening.[11] In our study of **1**, it was thought that fluorescence quenching by Cu^{2+} resulting from ring-opening of fluorescent ring-closed **1** (c-**1**) would be very interesting for the design of a logic gate.[18,19]

Since **1** is electron rich, one-electron oxidation of c-**1** by Cu^{2+} was presumed to be possible. As expected, the addition of Cu^{2+} (0.5 equiv) to a solution of c-**1** (1.0×10^{-5} м, CH_3CN) at its photostationary state in the dark promoted an immediate color change of the solution from red to colorless, accompanied by disappearance of the absorption band at 520 nm indicating that the ring-opening reaction of c-**1** had occurred. Furthermore, photoexcitation of the solution of ring-opened **1** (o-**1**) and Cu^{2+} with 365 nm light did not drive the open form into the ring-closed form, as evidenced by no clear change in the absorption spectra, that is, the photoisomerization of **1** from the open to closed form was completely inhibited by Cu^{2+}, representing a specific "lock" gate role of Cu^{2+} for the open form. Interestingly, the gate behavior was reversible. Quantitative titration of Cu^{2+} with EDTA recovered the photoswitching behavior of **1** (Figure 4), and the photochemical open/close cycle with Cu^{2+} and EDTA was repeated five times without a significant decrease in the absorption at 520 nm, which represents the concentration of c-**1** during the cycle.[20] Apparently, EDTA could be considered a "key" to the "lock". Further investigation with diarylethenes, **2**–**7** showed similar results.

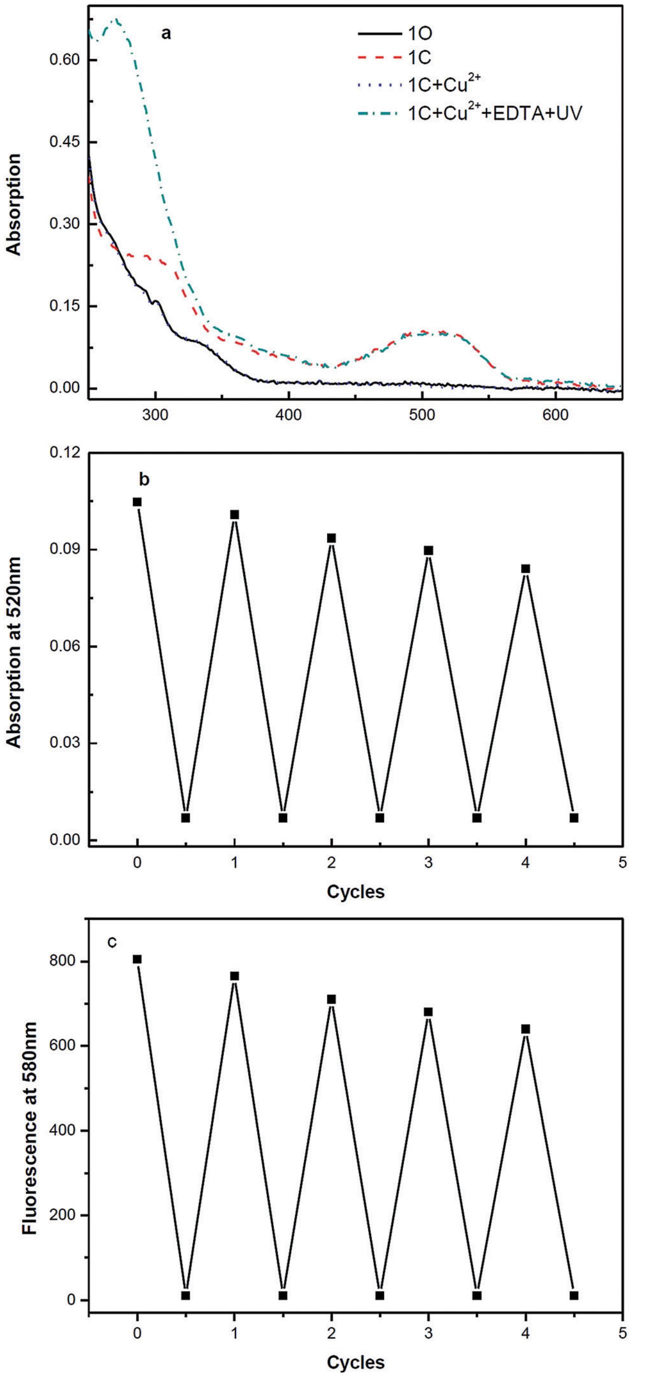


Figure 4. a) Absorption changes for the open form of **1** in CH_3CN (black line), close form (red line), upon addition of $Cu(ClO_4)_2$ (10^{-3} м) (blue line), and finally upon irradiation with 365 nm light (cyan line) after adding EDTA (10^{-3} м). b) Absorption switching of **1** monitored at 520 nm upon alternating additions of Cu^{2+} and EDTA in CH_3CN. c) Fluorescence switching of **1** monitored at 580 nm with excitation at 520 nm, upon alternating additions of Cu^{2+} and EDTA in CH_3CN.

The electrochromic ring-opening of c-**1** by Cu^{2+} is assumed to occur through the radical cation intermediate of **1**. Interestingly, the red c-**1** turned green upon the addition of Cu^{2+} at near $-40\,^{\circ}$C and the color was disappeared at room temperature, indicating the completion of ring-opening process (Figure S1 in the Supporting Information). The green intermediate was assumed to be $\mathbf{1}^{\bullet+}$. However, to get the EPR spectrum of the intermediate that might provide the clear evidence for the radical character, another one-electron oxidant was needed, because the strong EPR signal of copper itself might interrupt the observation of organic radical. We were lucky to find that ceric ammonium nitrate (CAN), which is a good one-electron oxidant frequently used in various organic reactions, including EPR studies for observation of organic radical cation intermediates,[21] promoted the ring-opening of c-**1** through the green intermediate in a similar fashion to Cu^{2+}. The EPR spectrum of the green solution obtained with c-**1** and CAN at 110 K exhibited a single isotropic line at $g=2.0041$ (Figure 5) indicating the radical character of the intermediate.

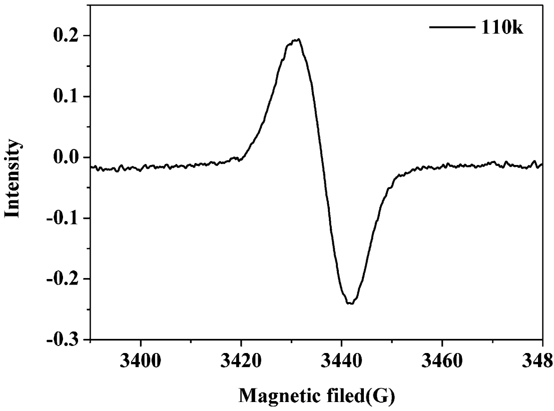
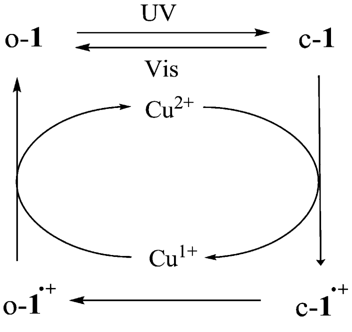


Figure 5. EPR spectrum of the green intermediate prepared from the reaction between c-**1** and CAN (1:1) in CH_3CN.

The proposed mechanism for the electrochromic cycloreversion of diarylethene **1** is illustrated in Scheme 4, which is similar to the mechanism suggested by You et al. based on systematic kinetic studies with dithienylcyclopentene (DTE).[11] The main idea of the mechanism is the ring-opening step of c-**1** radical cation (c-$\mathbf{1}^{\bullet+}$) is the rate-limiting step of the electrochromic cycloreversion process, because of the fast oxidation and reduction steps.



Scheme 4. Mechanism of electrocatalytic ring-opening of **1**.

The activation energy for the ring-opening of c-$\mathbf{1}^{\bullet+}$ calculated theoretically (DFT, uB3LYP/6-31+G(d)) was 16.6 kcal mol^{-1}. This activation energy is much lower than that of the ground-state ring-opening of c-**1**, which is 25.8 kcal mol^{-1}. The large difference in activation energies between the two steps supports the mechanism that reasonably rationalizes the fast room-temperature ring-opening of c-**1** in the presence of Cu^{2+} through an electrochromic cycloreversion process without irradiation from visible light.

Conclusion

We have synthesized a series of "turn-on" fluorescence diarylethene derivatives (**2**–**7**) with alkyl and acetyl groups at the reactive carbon and benzothiophene positions. The photochemical and photophysical properties of these derivatives were thoroughly investigated to reveal substituent effects on their properties. The results showed that alkyl substituents did not have a significant effect on the absorption and emission spectra of the diarylethenes. Meanwhile, a large absorption shift of 33 nm was observed in the absorption spectrum of the acetyl-substituted diarylethene (**4**) compared to the absorption of **1** due to the extension of π–π conjugation of the benzothiophene with the carbonyl substituent.

Interestingly, all of the ring-closed forms of diarylethenes **1**–**7** underwent cycloreversion upon addition of Cu^{2+} in the dark. EPR results provide clear evidence for the formation of the compound c-**1** radical cation intermediate that might be generated in the reaction between **1** and Cu^{2+}. DFT indicated that the ground-state activation energy for ring-opening of $\mathbf{1}^{\bullet+}$ was approximately 9.2 kcal mol^{-1} lower than that of **1** without Cu^{2+}, such that a Cu^{2+}-catalyzed oxidative cycloreversion reaction at room temperature might be possible.

Acknowledgements

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Keywords: diarylethenes · electrochromism · fluorescence · photochromism · substituent effects

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[17] Crystal data for **1**: $C_{25}H_{18}OS_4$; $M = 462.63$; $T = 296(2)$ K.; monoclinic; space group $P2_1/c$; $a = 11.4693(5)$ Å, $b = 12.2105(5)$ Å, $c = 15.7400(6)$ Å; $\beta = 90.067(2)^{\circ}$; $V = 2204.32(16)$ Å^3; $Z = 4$; $\rho_{\text{calcd}} = 1.394\,\text{mg}\,\text{m}^{-3}$; $\mu(\text{Mo}_{K\alpha}) = 0.446\,\text{mm}^{-1}$; 36391 reflections measured; 5448 independent reflections ($R_{\text{int}} = 0.0452$); R_1 $[I > 2\sigma(I)] = 0.0546$, wR_2 (all data) $= 0.1362$. CCDC 1414849 (**1**) contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

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