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Dual-mode tunable viscosity sensitivity of a rotor-based fluorescent dye

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ABSTRACT

The design and fabrication of new type viscosity sensor on molecular scale will enrich the detection means in both physical and life sciences. In this work, a rotor-containing fluorescent dye was prepared, which can reveal a typical viscosity-sensitive behavior due to the environment-induced non-radiative decay. The viscosity-sensitive behavior of this dye could be tunable (locked and activated) in aqueous environment, either with the reversible light-driven *trans*/*cis*-photoisomerization of the cyanostilbene moiety, or with the reversible assembly/disassembly process of β-cyclodextrin (β-CD) to the rotor part. Such dual-mode tunable viscosity sensitivity can be well distinguished by fluorescent spectra. A slope method, on double-logarithmic plots of the fluorescent signal to the corresponding environmental viscosity, makes a quantitative estimation to the tunable viscosity sensitivity, featuring the 'Activated' and the 'Locked' state in this molecular-scale viscometer.

1. Introduction

The design and development of viscosity chemosensors or probes[1] is of considerable current interest in modern viscosity test. In particular, changes in biofluid viscosity are usually linked to the perturbations and diseases in organisms. Because of its high sensitive and low detection limit in these fluid media, the molecular-scale viscometers may play a significant role in such areas where mechanical measurement apparatus are hard to reach. Generally, the microscopic viscosity test is realized by the sensing function of a molecular-scale viscometer, whose output signal (e.g., the fluorescence) varies indicatively in response to the change of the environmental viscosity. Hitherto, most of the viscosity tests at molecular level are continuous and forward.[1,2] Sometimes, temporary halt and reset of the viscosity tests are needed in a comprehensive determination program. Thus, a tunable way in practice, to make the viscosity-response ability of the sensory species controllably locked and activated using simple chemical switching elements, is of great concern. In this case, we have focused on the conception of molecular switch or molecular machinery behaviors,[3] and tried to combine such tunable functions with the viscosity sensitivity in a molecular platform, for control of the viscosity-sensitive behavior by multiple input operations.

p-(Dialkylamino)-benzylidenemalonitrile derivative is a typical molecular-rotor architecture.[4] Its non-radiative decay of the fluorescent excited state can be influenced by the viscosity of the medium, for test of the local viscosity by the change of fluorescence quantum yield. A β-cyclodextrin (β-CD) polypseudorotaxane system, comprising a light-tunable fluorescent rotor with combination of cyanostilbene (a light-active moiety) and tetramethyljulolidine (a rotator), was reported more recently.[5] It showed a clear photo-lockable viscosity-sensitive behavior with the *trans*/*cis*-photoisomerization process, and this light-driven tunable viscometer could be remotely operated as photon is clean and long-range control element. For the interest of fabricating multi-responsive functional dyes and multi-controllable sensors, however, other more efficient approaches to modulate the rotor's viscosity sensitivity are required. Considering the suitable space configuration and hydrophobic structure of the rotor part, we tried the supramolecular assembly (host–guest encapsulation) of cyclodextrins,[6] to influence and control the rotor's relative rotation in fluid together with its viscosity-sensitive behavior.

In this work, we synthesized a novel fluorescent dye (compound **1**; see Schemes 1 and 2)[7] by introduction the hydrophilic viologen group linked to the above-mentioned light-active rotor (also a fluorophore). Such viologen-containing dye could be easily encapsulated by β-CD in aqueous environment.[8] The long alkyl chain is used to avoid the intramolecular electron transfer from the rotor to the viologen group, keeping the individual but viscosity-dependent fluorescent emission of the rotor itself. A reversible dual-mode (light-driven *trans*/*cis*-photo-isomerization and β-CD assembly/disassembly process) switchable system based on compound **1** is presented. The new format of tunable viscosity-sensitive effect induced by β-CD supramolecular assembly could be also well distinguished by fluorescence signals. The two locked viscosity sensitivity states of this dye could be reactivated by corresponding

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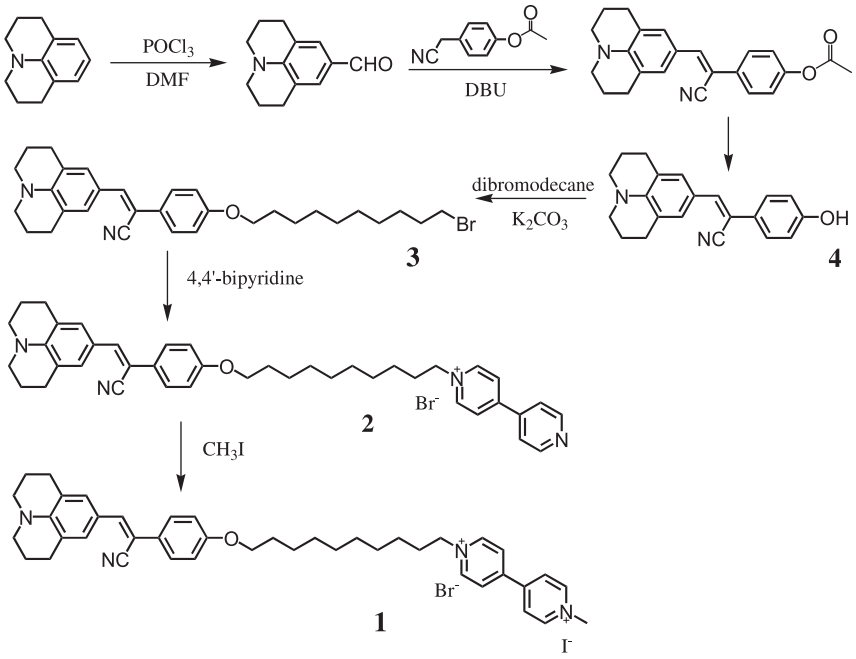
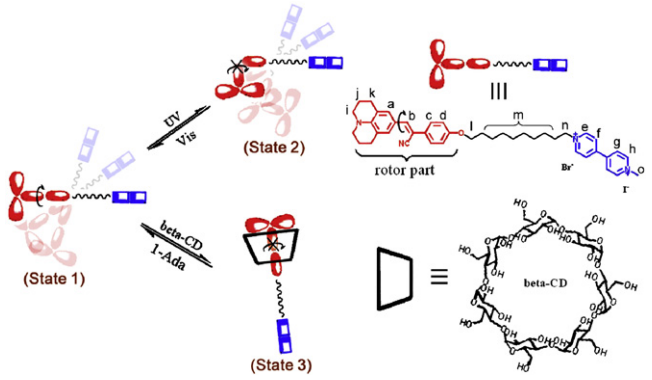


Scheme 1. Synthetic route of compound **1**.



Scheme 2. Illustration of the dual-mode molecular switch of **1** accompanied with the interconversions network of its conformational species in water. (The initial state 'State 1' can be translated to the photostationary 'State 2' by irradiation upon 254 nm for ca. 2 h, while can be reversibly returned by irradiation of visible light; The initial state 'State 1' can be also interconversed to encapsulation equilibrium state 'State 3' via addition of 10 equiv of β-CD at room temperature, while can be disassembled via addition of excessive 1-adamantanol to form a competitive complex.).

visible-light irradiation or supramolecular disassembly of β-CD, and it exhibits a promising application in the area of multi-mode tunable viscosity detection.

2. Experimental part

2.1. Instruments

^{1}H NMR, ^{13}C NMR, and 2D-ROESY NMR spectra were measured on a Brüker AV-400, or AV-500 spectrometer with tetramethylsilane (TMS) as the internal standard. The high-resolution ESI mass spectrum was tested on a HP5989 mass spectrometer. Absorption spectra were done on a Varian Cary 500 UV/Vis spectrophotometer (1 cm quartz cell used). Fluorescent spectra were recorded on a Varian Cary Eclipse fluorescence spectrophotometer. All the fluorescent spectra recorded in this work were on an excitation at 370 nm. Fluorescence lifetime measurements were performed on an Edinburgh FL 900 Fluorescence Spectrometer equipped with a laser (λ=372 nm). The ICD spectra were recorded on a Jasco J-815 CD spectrophotometer in a 1 cm quartz cell. The photoirradiation was carried on a CHF-XM 500-W high-pressure mercury lamp with a filter for 254 nm in a sealed Ar-saturated 1 cm quartz cell. The distance between the lamp and the sample cell was 20 cm. Melting points were determined by using an X-6 micro-melting point apparatus. The scanning electron microscopy (SEM) was tested on JEOL (JSM-6360LV) electron microscope, while the transmission electric microscopy (TEM) was tested on a JEOL-JEM2100F electron microscope. Solvent viscosities were carried on a NDJ-79 rotatory viscometer. The surface tension was measured by Thermo Cahn DCA-315 surface tension analysis system.

2.2. Materials

β-Cyclodextrin (β-CD), phosphorus oxychloride, 1,10-dibromodecane, 18-Crown-6,4,4′-bipyridine and the inorganic reagents were commercially available and used without further purification. 1-Adamantanol (1-Ada), julolidine, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were purchased from Alfa Aesar and used as received. Dextran (70 kDa average MW) was purchased from Tokyo Chemical Industry Corp. Pyridine was dried over potassium hydroxide while DMF and dichloromethane were dried over calcium hydride, and then distilled under reduced pressure. Acetone and acetonitrile were dried by 4A molecular sieve and distilled before used.

2.2.1. Preparation of 9-formyl-julolidine. $POCl_3$ (5 ml) was slowly added to 11 ml anhydrous DMF under argon at 0 °C. The mixture was vigorously stirred for 2 h and then julolidine (5 g, 28.9 mmol) dissolved in 10 ml anhydrous DMF was added. After stirring for 12 h at room temperature under argon, the solution was added dropwise to ice and then NaOAc (aq) was added until pH of 7–8 was achieved. A great deal of yellow solid was gradually crystallized from the solution. The solid was filtered, washed with petroleum ether several times and then dried in vacuo. Yield was 67.6%. Mp 70–72 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ=9.60 (s, 1H), 7.30 (s, 2H), 3.30 (t, J=6.0 Hz, 4H), 2.77 (t, J=6.4 Hz, 4H), 1.97 (tt, $J1$=6.4 Hz, $J2$=6.0 Hz, 4H).

2.2.2. Preparation of Compound ***4****.* 4-(Cyanomethyl) phenyl acetate[5] (3.0 g, 17.1 mmol), 9-formyl-julolidine (3.6 g, 17.9 mmol), and

DBU (4.8 g, 28.2 mmol) were dissolved in pyridine (17 ml) and stirred for 48 h at 120 °C under argon, then cooled, and poured into de-ionized water (120 ml). Here the product had hydrolyzed to be a corresponding phenol. The solution was extracted three times with dichloromethane (150 ml) and the underlayer was washed with water (80 ml). After drying with anhydrous $MgSO_4$ and concentrated in vacuo, the residue was applied to silica gel chromatography (petroleum ether–ethyl acetate=5:1) to afford orange compound **4** (2.83 g, 52.4%). Mp 198–201 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ=7.48 (d, J=8.0 Hz, 2H), 7.39 (s, 2H), 7.17 (s, 1H), 6.86 (d, J=8.0 Hz, 2H), 3.26 (t, J=6.0 Hz, 4H), 2.77 (t, J=6.4 Hz, 4H), 1.97 (tt, $J1$=6.4 Hz, $J2$=6.0 Hz, 4H). ^{13}C NMR (500 MHz, $CDCl_3$): δ=156.117, 145.231, 141.850, 129.332, 127.520, 121.639, 120.475, 116.435, 103.477, 54.111, 50.667, 30.391, 28.376, 22.231. HRMS (EI): m/z: 316.1573.

*2.2.3. Preparation of Compound **3**.* Compound **4** (2.2 g, 6.9 mmol) was added with magnetic stirring to 1,10-dibromodecane (20.7 g, 69 mmol) acetone solution. The mixture was then added upon K_2CO_3 (1.9 g, 13.9 mmol) and trace of 18-Crown-6. The solution was stirred refluxing for 8 h under Ar protection. The solution was poured into 200 ml ethanol and the mixture was concentrated in vacuo to ca. 60 ml left. A great deal of solid was crystallized from the solution while cooled in an ultrasonator. The solid was filtered, washed with 300 ml petroleum ether overnight, and then with 100 ml water to obtain orange compound **3** (2.5 g, 67.1%). Mp 73–74 °C. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ=7.51 (d, J=8.6 Hz, 2H), 7.39 (s, 2H), 7.17 (s, 1H), 6.90 (d, J=8.6 Hz, 2H), 3.97 (t, J=6.6 Hz, 2H), 3.41 (t, J=6.8 Hz, 2H), 3.25 (t, J=6.0 Hz, 4H), 2.77 (t, J=6.4 Hz, 4H), 1.97 (tt, $J1$=6.4 Hz, $J2$=6.0 Hz, 4H), 1.75–1.88 (m, 4H), 1.20–1.51 (m, 12H). ^{13}C NMR (500 MHz, $CDCl_3$): δ=159.589, 145.287, 141.619, 129.290, 127.229, 121.580, 121.490, 120.505, 115.477, 103.520, 68.808, 54.106, 50.613, 34.731, 33.503, 30.111, 30.030, 30.001, 29.894, 29.421, 28.841, 28.394, 26.681, 22.261. HRMS (EI): m/z: 534.2247 (^{79}Br), 536.2239 (^{81}Br).

*2.2.4. Preparation of Compound **2**.* A solution of compound **3** (2.5 g, 4.7 mmol) and 4,4′-bipyridine (4.4 g, 28 mmol) in acetonitrile (100 ml) was stirred for two days at 80 °C. The solvent was removed in vacuo, and the residue was dissolved in some acetone to applied to silica gel chromatography (dichloromethane–methanol=50:3) to afford orange compound **2** (1.12 g, 34.8%). Mp 118–120 °C. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ=9.46 (d, J=6.4 Hz, 2H), 8.87 (d, J=6.4 Hz, 2H), 8.32 (d, J=6.4 Hz, 2H), 7.67 (d, J=6.4 Hz, 2H), 7.50 (d, J=8.6 Hz, 2H), 7.38 (s, 2H), 7.17 (s, 1H), 6.89 (d, J=8.6 Hz, 2H), 4.96 (t, J=7.4 Hz, 2H), 3.97 (t, J=6.6 Hz, 2H), 3.24 (t, J=6.0 Hz, 4H), 2.77 (t, J=6.4 Hz, 4H), 1.98–2.08 (m, 2H), 1.97 (tt, $J1$=6.4 Hz, $J2$=6.0 Hz, 4H), 1.72–1.84 (m, 2H), 1.22–1.49 (m, 12H). ^{13}C NMR (500 MHz, DMSO-d_6): 152.223, 150.939, 146.943, 145.243, 140.807, 137.587, 134.814, 128.302, 127.615, 126.099, 125.348, 122.386, 121.853, 120.205, 115.192, 114.904, 108.251, 67.532, 60.347, 52.395, 49.131, 30.641, 28.768, 28.635, 28.548, 28.305, 27.156, 27.000, 25.3087, 20.0666. HRMS (ESI): m/z: 611.3757 [**2**−Br]$^+$

*2.2.5. Preparation of Compound **1**.* Compound **2** (1.12 g, 1.62 mmol) was dissolved in 40 ml acetonitrile. The solution was then added upon iodomethane (1.6 g, 11.3 mmol) and stirred for one day at 60 °C. A great deal of orange solid was gradually crystallized from the solution. The solid was filtered, washed with acetonitrile several times and then dried in vacuo to afford Compound **1** (1.02 g, 75.6%). Mp 219–220 °C. ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): δ=9.39 (d, J=6.4 Hz, 2H), 9.28 (d, J=6.4 Hz, 2H), 8.79 (d, J=6.4 Hz, 2H), 8.76 (d, J=6.4 Hz, 2H), 7.54 (d, J=8.6 Hz, 2H), 7.50 (s, 1H), 7.39 (s, 2H), 6.98 (d, J=8.6 Hz, 2H), 4.67 (t, J=7.4 Hz, 2H), 4.43 (s, 3H), 3.99 (t, J=6.6 Hz, 2H), 3.25 (t, J=6.0 Hz, 4H), 2.64 (t, J=6.4 Hz, 4H), 1.92–2.02 (m, 2H), 1.88 (tt, $J1$=6.4 Hz, $J2$=6.0 Hz, 4H), 1.67–1.76 (m, 2H), 1.22–1.44 (m, 12H). HRMS (ESI): m/z: 313.2000 [**1**−Br−I]$^{2+}$.

3. Results and discussion

3.1. Conformational switches of compound 1 with photo-isomerization and β-CD inclusion

Compound **1** has an excellent solubility and exists as a free monomeric form in some high-polar solvents such as DMSO. In this case, ^{1}H NMR signals of **1** can be well assigned (Fig. 1A). As expected, the *trans*-cyanostilbene unit of compound **1** was photo-isomerized upon 254 nm irradiation to its *cis*-form. It resulted in a cluster of new peaks of rotor part arising in ^{1}H NMR spectrum with a photo-isomerization efficiency of nearly 70% (Fig. 1B). When **1** was dispersed in water, it self-organized to an aggregated form immediately if only above its critical aggregate concentration (CAC: 1.70×10^{-5} M, see Supplementary data, Fig. S5). In this case, compound **1** shows some surfactant properties, which results in a relative low solubility at room temperature with the surface tension falling down to 55.23 mN/m. As shown in Figure 1C, the H_a–H_d and H_i–H_n signals, which belong to the rotor and the alkyl chain part, respectively, are obviously turned to be broad. But the signals of H_e–H_h and H_o, which are associated with the viologen part, still keep split. Hence, it is inferred that the hydrophobic part of **1** is stacked up to each other, whereas hydrophilic viologen unit is exposed to the aqueous environment.[8] This aggregated vesicles can be clearly observed from SEM image (Fig. 2A). *Trans*-to-*cis* photoisomerization process of **1** could also take place in water. The aggregation would be slightly weakened, which should be caused by the

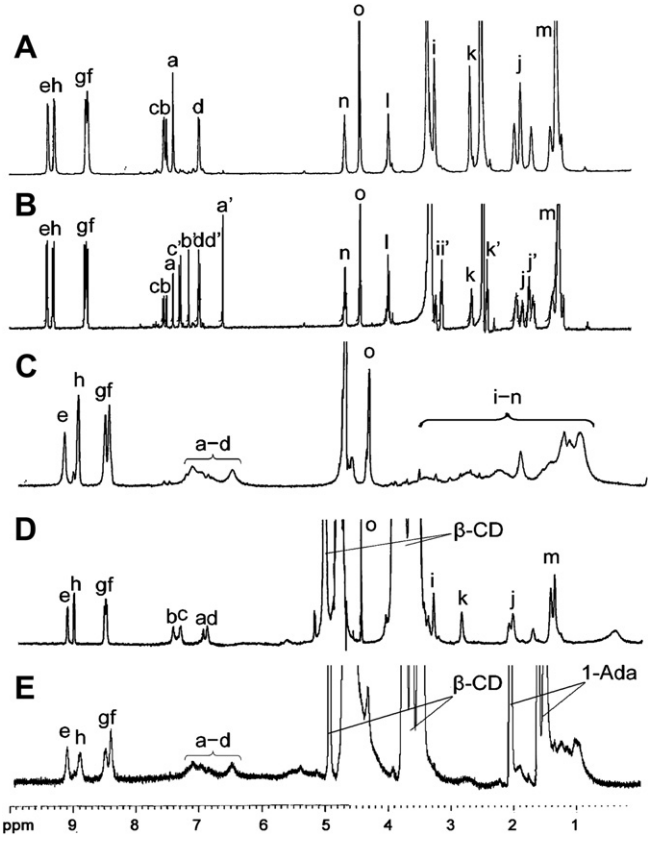


Figure 1. ^{1}H NMR spectra (500 MHz, 293 K) of **1**, (A) in DMSO-d_6, (B) in DMSO-d_6 upon sufficient irradiation at 254 nm, (C) in D_2O, (D) in the presence of excessive β-CD in D_2O, and (*E*) after addition of excessive 1-adamantanol in D_2O. The concentration of **1** was maintained at 1.5×10^{-3} M.

unfavorable π–π stack of the *cis*-fluorophore confirmed by the reduced vesicle-size shown in Figure 2B. For the encapsulation behavior of the β-CD cavity to a configuration matched guest, the hydrophobic part of compound **1** could be complexed with β-CD in water. Introduction of 10 equiv of β-CD to the aggregated system of **1** in water would lead to a new monomeric form. It was indicated by the reproduction of the peaks of H_a–H_d and H_i–H_n in ^{1}H NMR spectrum (Fig. 1D), as well as a disappearance of aggregated vesicles observed from SEM image (Fig. 2C).

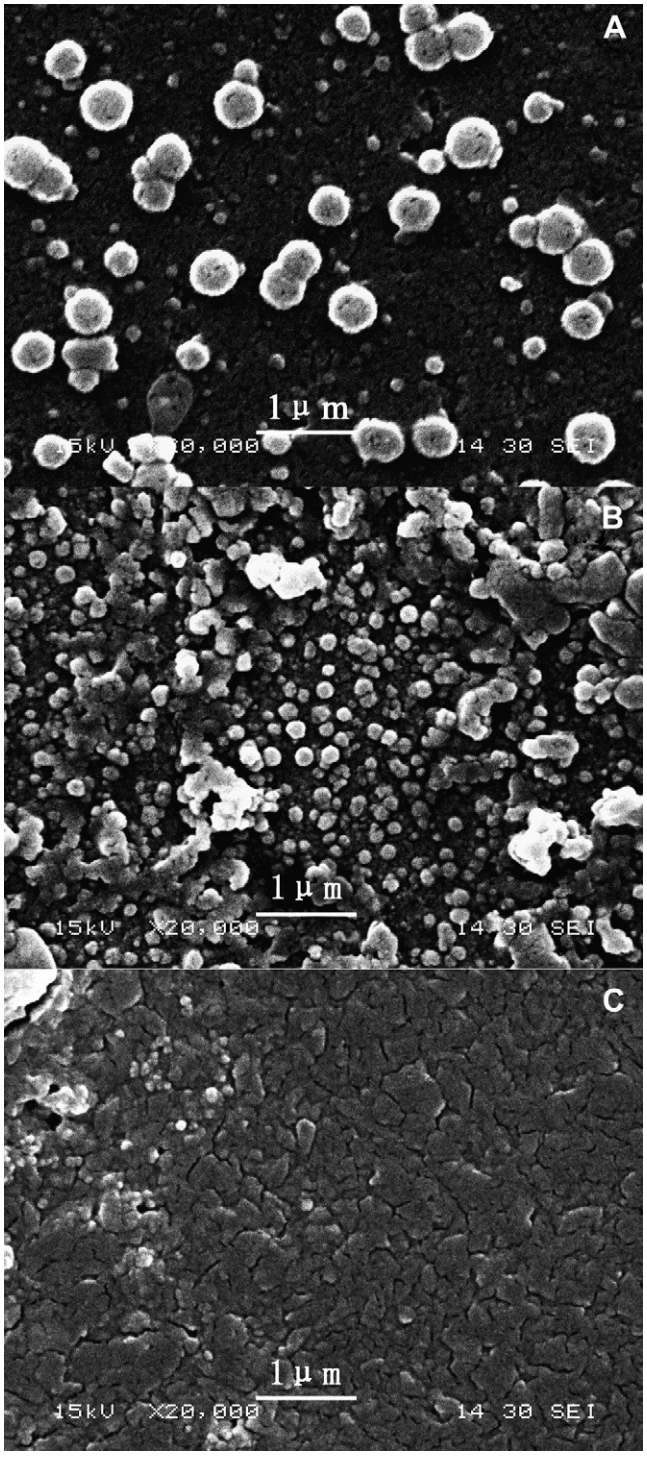


Figure 2. SEM images of (A) **1**, (B) after sufficient irradiation at 254 nm and (C) **1** mixed with excessive β-CD. The concentration of **1** is 1.01×10^{-4} M, which is larger than its critical aggregate concentration (CAC) (1.70×10^{-5} M).

The maximum absorption band for compound **1** in water appears at wavelength of around 420 nm, which decreases remarkably upon irradiation with UV light at 254 nm. When the complex of compound **1** with β-CD was formed, the maximum absorption was red-shifted about 20 nm (see Fig. 3). A sufficient transformation of **1** to the encapsulation complex at 1.01×10^{-4} M concentration needs ten-fold β-CD, attribute to a relative small association constant K (4.82×10^2 M^{-1}, see Supplementary data, Fig. S6) between **1** and β-CD. The 2D ROESY spectrum (see Supplementary data, Fig. S3) of **1** mixed with excessive β-CD and the generation of positive induced circular dichroism (ICD) signal at around 425 nm (attributed to $\pi\rightarrow\pi^*$ transition of the rotor part, see the inset of Fig. 3), indicate that the cyanostilbene unit is located in the cavity of β-CD in this system, because a positive ICD signal arises when the electric transition dipole moment of the guest inside the host cavity is aligned parallel to the axis of the chiral host.[9] This location is also confirmed by the finding of a similar ICD signal and locked viscosity-sensitive behavior of the encapsulation complex of compound **4** and β-CD (see Supplementary data, Fig. S7). Compound **1** will be extruded from the β-CD cavity to reform an aggregated form while excessive 1-adamantanol (1-Ada) is added, due to a very high association constant between the β-CD host and the 1-Ada guest. This process is also confirmed by ^{1}H NMR spectroscopy (shown in Fig. 1E and 1C).

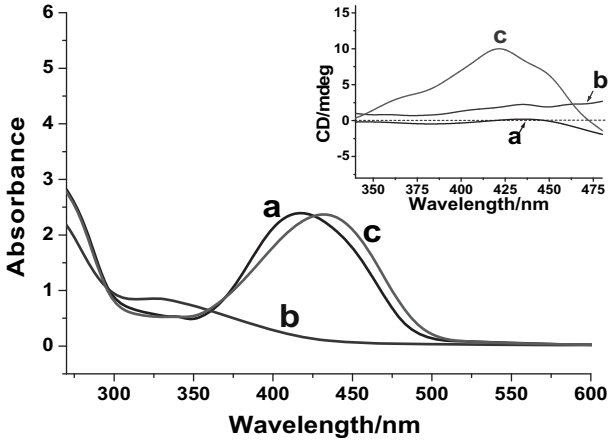


Figure 3. Absorption spectra of **1** (curve a), after irradiation at 254 nm to photostationary state (curve b) and **1** mixed with excessive β-CD (curve c). The inset shows their corresponding ICD signals. These optical spectra of **1** were measured in water with the concentration of 1.01×10^{-4} M at 293 K.

3.2. Viscosity response of compound 1 detected by fluorescent spectroscopy

The rotor part of **1** belongs to a class of fluorophore, which can form twisted intramolecular charge transfer (TICT) states upon photo-excitation. The competition of fluorescence emission and non-radiative decay is environmental viscosity or fluid flow dependent. The intramolecular rotation of the phenyl group (here is the julolidine group) is relatively free when the fluid outside is not sheared, whereas it is readily inhibited by high viscosity of the microenvironment. Hence the balance of relaxation will shift with the variation of environmental viscosity and the fluorescence intensity increases with increased viscosity of the solvent.[2,4]

The viscosity sensitivity of compound **1** described by fluorescent intensity [10] could be clearly observed in mixtures of ethylene glycol and glycerol with different ratio. Increased glycerol content is known to increase viscosity with only minimal changes of solvent polarity. Glycerol contents of 0, 20, 40, 60, 80% resulted in viscosities of 19, 32, 72, 155 and 368 mPa s, respectively. Fluorescence measurements of **1** made in glycol/glycerol mixtures of different

viscosities (Fig. 4A), show that the fluorescence intensity increases dramatically with increasing solvent viscosity. Interestingly, the logarithm of its fluorescence has a good linear relationship with the logarithm of viscosity according to the Főrster–Hoffmann equation (Eq. 1).[11] This result also suggest this fluorescent dye has a representative viscosity response.

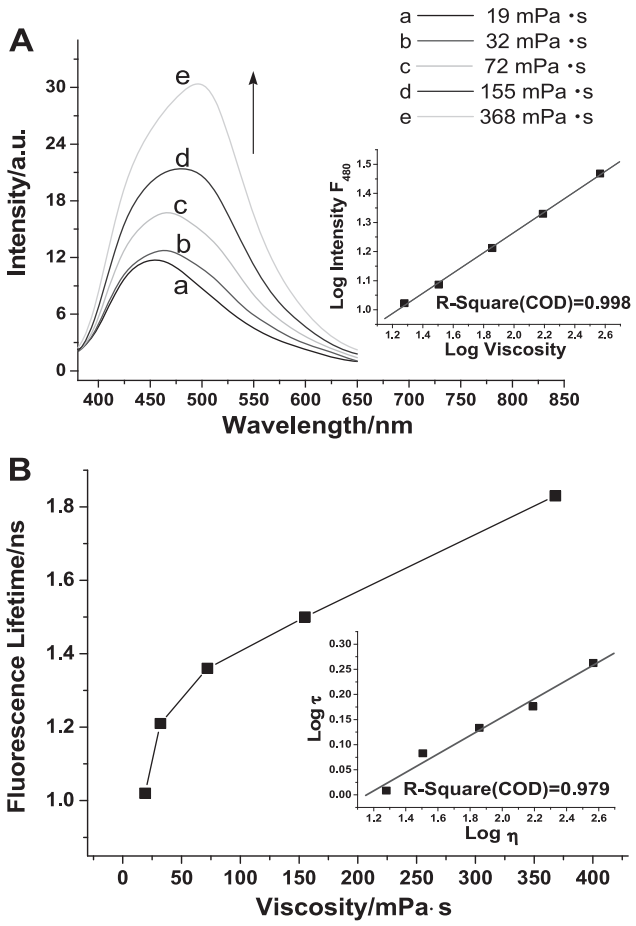


Figure 4. (A) Emission spectra of **1** (1.01×10^{-5} M, 293 K) in mixtures of ethylene glycol and glycerol with different viscosity (*ex*=370 nm). The insets show double-logarithmic plot between fluorescent intensity at 480 nm of **1** and the corresponding viscosity. (B) The changes of fluorescence lifetime for **1** as another indication of viscosity (*ex*=372 nm). The insets show double-logarithmic plot between fluorescence lifetime of **1** and the corresponding viscosity.

$$\log I = x\log \eta + C \tag{1}$$

I=fluorescent emission intensity; η=solvent viscosity; x=dye-dependent constant; C=conc. and temp. constant.

Currently, a new approach to image local viscosity using the fluorescence lifetime has been demonstrated,[12] as this measurement is also a reflection of environmental parameters and independent of fluorophore concentration. Fluorescence lifetime measurement has also been carried out on compound **1**. The calibration plot of fluorescence lifetime versus solvent viscosity for **1** is shown in Figure 4B, which is well described by Eq. 2.[11] The plot of $\log\tau$ versus $\log\eta$ (Fig. 4B, inset) is fitted by a straight line in agreement with the regularity that emission intensity changed with viscosity.

$$\tau = \zeta k_0 \eta^{\alpha} \tag{2}$$

τ=fluorescence lifetime; η=solvent viscosity; k_0=radiative rate constant; ζ, α=constant.

3.3. Viscosity sensitivity of compound 1 in aqueous environment

With the growing importance of viscosity measurements in aqueous solutions or biofluids, the viscosity sensitivity of compound **1** is required to be tested in water. The dextran was added to make the following weight/volume aqueous solutions, 2.5, 5.0, 7.5, and 10.0%, leading to viscosities of 1.6, 2.6, 4.2, and 6.5 mPa s, respectively. The monomeric form of **1** at the concentration of 1.01×10^{-5} M (below CAC) shows a good solvent-dependent viscosity-sensitive behavior. As shown in Figure 5A, the emission intensity of the fluorescent dye boosts obviously with the increase of the solvent's viscosity, i.e., from 4.5 to 8.3 a.u. in the viscosity test range.

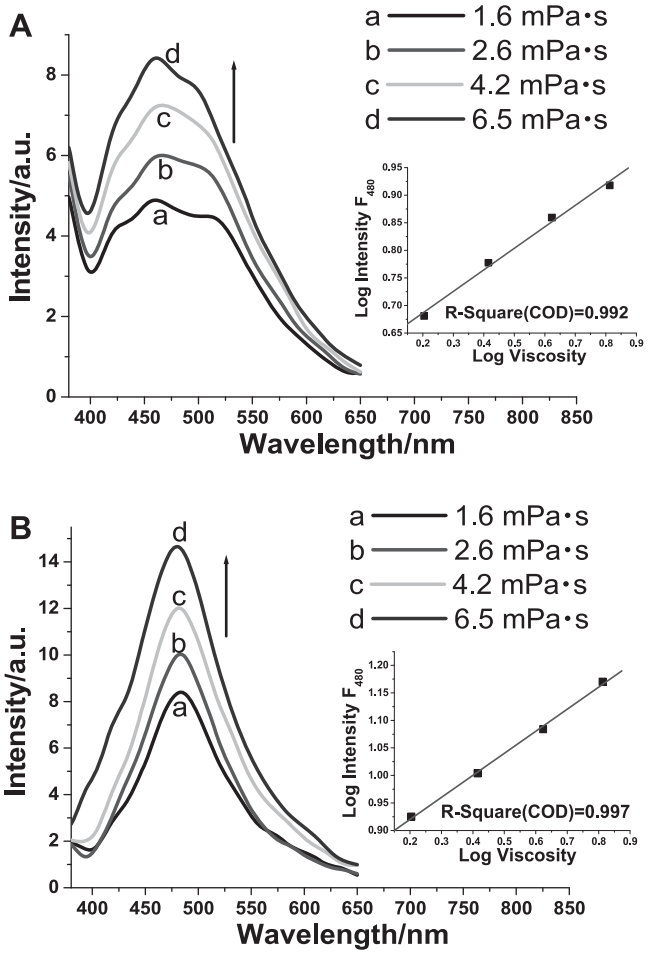


Figure 5. Emission spectra of **1** (A) 1.01×10^{-5} M and (B) 1.01×10^{-4} M in aqueous solutions at 293 K of dextran at different concentrations (*ex*=370 nm). The insets show double-logarithmic plot between fluorescent intensity at 480 nm of **1** and the corresponding viscosity.

On the other hand, although compound **1** comes to be aggregated form at the concentration above CAC, this rotor moiety can still feel the environmental viscosity change and show a similar linear relationship of the fluorescent intensity to the solvent viscosity (see Fig. 5B). In this case, the linear relationship here shows the non-radiative decay is also mainly affected by the viscosity change rather than the self-organized effect. It is suggested that the viscosity response of this dye is very sensitive in water.

3.4. Dual-mode tunable viscosity sensitivity in aqueous environment

The cyanostilbene moiety of **1** undergoes *trans-to-cis* photoisomerization by irradiation at 254 nm in water. The maximum

absorption of **1** is weakened by the photoisomerization, along with a stronger blue-shifted emission peak. After irradiation at 254 nm to the photostationary state, the new emission spectra of **1** (*cis*-form) almost does not change with the increase of the solvent's viscosity (Fig. 6A). A similar phenomenon was found when excessive β-CD was introduced to the initial system of **1**. Although the fluorescent intensity of the rotor was overall enhanced because of the β-CD inclusion, it remains a same level despite the environmental viscosity change (Fig. 6B).

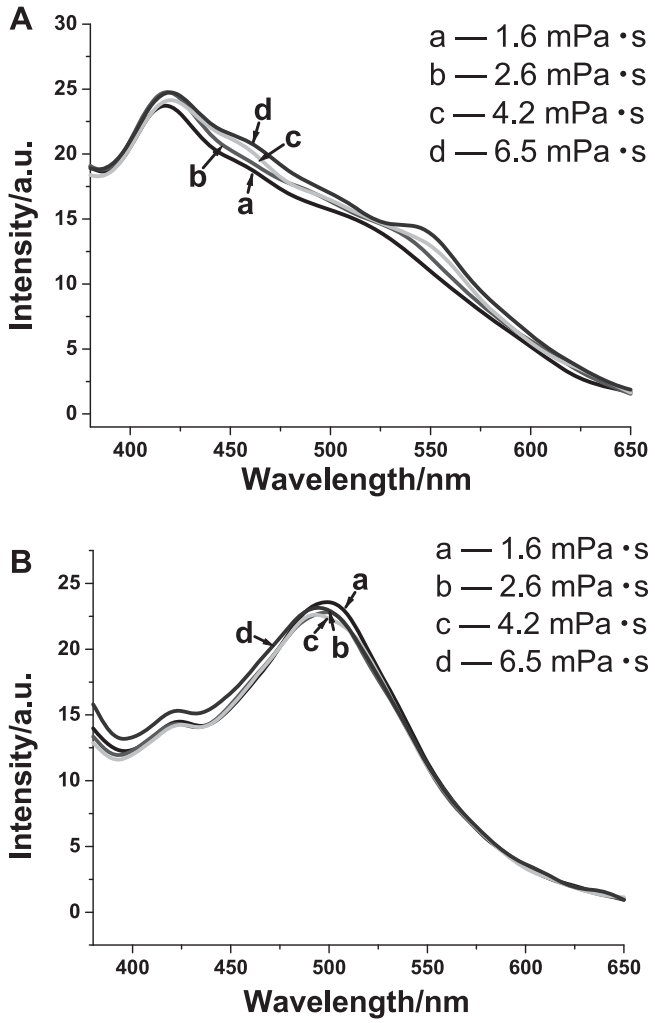


Figure 6. Emission spectra of (A) **1** after irradiation at 254 nm to photostationary state and (B) **1** mixed with excessive β-CD in aqueous solutions of dextran at different concentrations (*ex*=370 nm). The concentration of **1** is kept as 1.01×10^{-4} M at 293 K, and the solvent's viscosity was basically adjusted by addition of dextran at that test concentration of compound **1**.

Both the locked viscosity-sensitive phenomena are generally originated from the conformational restriction of the rotor part. According to our previous research,[5] the photo-lockable viscosity-sensitive behavior is induced by the UV stimuli. In that case, the cyanostilbene moiety is photoisomerized and the rotatory motion of julolidine moiety (the rotator) is hindered by the steric factor of the aromatic rings in the *cis*-isomer. That could be considered as a light-driven tunable viscosity sensitivity. Otherwise, the locked viscosity-sensitive behavior in this system can be also caused by the β-CD encapsulation. This phenomenon should be the result of the rigidity of the β-CD ring while locating on the fluorophore. Many structural experiments or theoretic calculations in the relative reports[6] interpret that guests are often prone to a unique optimized geometry in the cavity of cyclodextrins. Thus the intramolecular rotation of the rotator in compound **1** should be prevented, together with its environmental-viscosity sensitivity shielded. In this way, this process could be regarded as a supramolecular assembly induced tunable viscosity-sensitive behavior. High-temperature is unfavorable for this locked viscosity sensitivity (see Supplementary data, Fig. S10).

3.5. Reversible and repetitive operation of the tunable viscosity sensitivity of compound 1

The locked viscosity-sensitivity state of **1**, resulted from the dual-mode switch effect, generated much stronger fluorescent emissions than the ones in the corresponding initial state. In this way, the reversibility of these two switch processes could be simply described by the change of the fluorescent spectra. The photo-isomerized *cis*-form of **1** would turn back to *trans*-form upon the irradiation of visible-light, with the decrease of the emission nearly to the original level. On the other hand, compound **1** complexed with β-CD would be recovered to the initial conformation by adding 1-Ada. Moreover, the 1-Ada encapsulated in the β-CD cavity can be extracted out by introducing dichloromethane into this system; thereby the β-CD will be reassembled to compound **1**. These processes are obviously featured by the alternant fluorescent change (see Supplementary data, Fig. S11), indicating the dual-mode tunable viscometer could be repeatedly operated.

3.6. Quantitative estimation of the tunable viscosity-sensitive state by double-logarithmic scaled slopes

To a quantitative data processing of this dual-mode switch, we establish a method—comparing the slope of logarithm of the normalized fluorescent intensity to the logarithm of viscosity—to judge the tunable viscosity-sensitive effect in a logic way. To this rotor system, the logarithm of its fluorescence has a good linear relationship with the logarithm of viscosity according to the Förster–Hoffmann equation, but the activated and the locked viscosity-sensitive states exhibit significant difference on the slopes. Herein we recorded their normalized fluorescent intensity at 480 nm[13] and plotted in a double-logarithmic scale with respect to the environmental viscosity. Three straight lines, corresponding to an initial state and two converted states of **1**, are shown in Figure 7 with significant differences on the slopes. A threshold can be set between these slopes, displaying the '*Activated*' state of **1** in initial

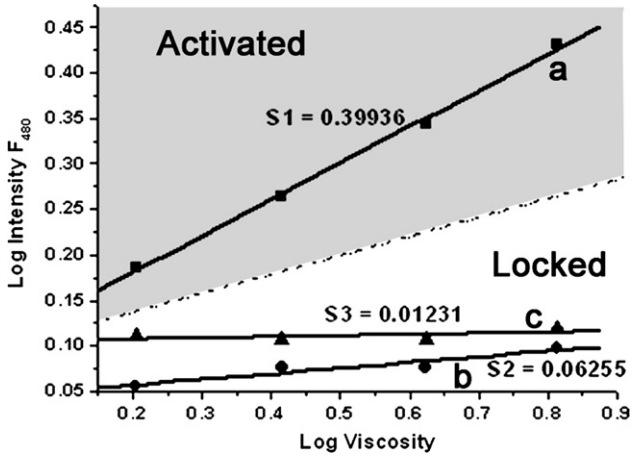


Figure 7. Double-logarithmic plot between normalized fluorescent intensity and viscosity corresponding to compound **1** (line a), after full irradiation at 254 nm (line b) and compound 1 mixed with excessive β-CD (line c). The dash line represents the threshold slope (0.18).

aqueous environment as the slope is big ($S1>0.18$), compared with the '*Locked*' state when this system reaches photostationary state or encapsulation equilibrium state as the slopes are small ($S2$, $S3<0.18$). The '*Activated*' and '*Locked*' states in this system are just corresponding to the turnon and turnoff of the fluorescent viscosity sensor function. By the way, $S3=0.01231$ is smaller than $S2=0.06255$, which features the fact that the conversion rate of supramolecular assembly is higher than that of photoisomerization in this system, for the fluorescence of some residual unconverted species will slightly ascend with increase of viscosity.

4. Conclusions

In summary, a new rotor-containing fluorescent dye has been synthesized and shows a good viscosity-sensitive behavior due to the environment-dependent non-radiative decay. With the reversible dual-mode switch driven by photoirradiation or assembly/disassembly process of β-cyclodextrin, the viscosity sensitivity of this molecular rotor could be locked and activated. These tunable viscosity-sensitive states can be distinguished by fluorescent signals. With establishment of a slope method, the viscosity-sensitive 'Activated' and the 'Locked' states of this dye could be quantitatively estimated.

This system provides a paradigm for the design and construction of multi-tunable molecular-scale viscosity sensor with characterized and read by fluorescent outputs. Indeed, the β-cyclodextrin encapsulation in this system performs efficiently and precisely on the tunable viscosity-sensitive behavior. There is a drawback of the relative inconvenient operation of the assembly/disassembly process yet. Our next goal is to translate this kind of molecular viscometers to a rotaxane-like architecture, which may bring in a high-speed tunable way with molecular-scale movement.

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Supplementary data

^{13}C NMR, and HRMS (ESI) spectra of compound **1**; 2D ROESY NMR spectrum of **1** mixed with β-CD; TEM images for a further magnified observation of Self-organized Conformational Switches of **1** in water; the measurement of CAC; the association constant between **1** and β-CD; the inclusion of **4** and β-CD; Data for the fluorescence life-time of compound **1** in mixtures of ethylene glycol and glycerol with different viscosity; Lockable viscosity sensitivity of **1** expressed by fluorescent emissions below CAC; Repetitive cycles of light-and ring-induced lockable viscosity sensitivity of **1** described in fluorescence signal. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.12.014.

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13. Here the normalized fluorescent intensity is defined as F/F_0, while F is the emission signals under each the viscosity condition, whereas F_0 is the one in the solvent without any addition of dextran.