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Original article

Synthesis of a bistable [3]rotaxane and its pH-controlled intramolecular charge-transfer behavior

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ABSTRACT

A [3]rotaxane **1** involving two naphtho-21-crown-7 (N21C7) rings and a dumbbell-shaped component **4** was synthesized. The dumbbell-shape molecule **4** contains one viologen nucleus, two secondary alkyl ammonium sites and two phenyl stoppers. After threading the N21C7 ring with the thread-like ammonium guest **3**, the copper(I)-catalyzed Huisgen alkyne-azide 1,3-dipolar cycloaddition (CuAAC "click" reaction), was performed to connect the pseudorotaxanes with viologen unit **2** and generate **1**. Through treating the [3]rotaxane by the base and acid circularly, the two N21C7 rings can make shuttling motion along the axle. Meanwhile the distance between the electron-deficient viologen unit and the electron-rich naphthol group can be adjusted precisely along with a remarkable intramolecular charge-transfer (CT) behavior.

1. Introduction

The mechanically interlocked molecules have several components which are not covalently linked [1]. These molecules can exhibit various functions through integrating the features of the components and controlling them by changing the external stimulation such as light, electrochemical potential, pH and solvent. Rotaxanes, one of the most useful members in this family, have been developed and used widely in construction of various artificial molecular devices and machines such as molecular shuttles [2], nanovalves [3], molecular muscles [4]. Among various macrocycles, 24-crown-8 (24C8) has been widely applied in lots of bistable rotaxanes [5] because of its unique binding properties toward the positively charged guests in low polar solvents. Recently, 21-crown-7 (21C7) was found to have a much stronger binding affinity toward the secondary ammonium guests and its size was small enough to be stoppered by phenyl group [6]. Several rotaxanes based on this property have been reported [7]. However, the switchable behavior of 21C7-based rotaxane has not been investigated.

Herein, we designed and synthesized a switchable [3]rotaxane that containing two N21C7 rings and a dumbbell-shaped molecule. The dumbbell-shaped molecule has a viologen unit in its center. In the original state, the N21C7 rings located on the secondary ammonium sites which were far away from the viologen. After treated by base, the secondary ammonium sites were deprotonated and the positively charged viologen unit attracted the rings to move toward the center. The distance between the viologen unit and the naphthol group could be close enough to exhibit a strong CT interaction.

2. Experimental

All chemicals were commercially available unless noted otherwise. Compound **9** was prepared according to the literature procedure [6]. NMR data were recorded on Bruker AV400 spectrometer, and chemical shifts were recorded in parts per million (ppm). Mass spectra were recorded using Agilent 6520 Q-TOF LC/MS (ESI).

Preparation of **1** (*Scheme 1*): To a solution of **2** (174.1 mg, 0.3 mmol), **3** (238.3 mg, 0.63 mmol), N21C7 (426.8 mg, 1.05 mmol) in CH_2Cl_2 (1.0 mL) and CH_3CN (1.0 mL) was added $Cu(MeCN)_4PF_6$ (352.2 mg, 0.945 mmol) and 2,6-lutidine (11 μL, 0.095 mmol). The reaction mixture was stirred for 24 h at room temperature. Then the solvent was removed under reduced pressure, and purified by column chromatography over silica gel (eluent: CH_2Cl_2/MeOH, 50:1) to afford **1** as a yellow solid (528.9 mg, 82%). ^1H NMR (400 MHz, CD_3CN): δ 8.95 (d, 4 H, J = 6.3 Hz), 8.35 (d, 4 H, J = 6.2 Hz), 7.71 (m, 4 H), 7.61 (s, 4H), 7.52 (s, 2 H), 7.34 (m, 18 H), 4.67 (m, 4 H), 4.45 – 4.33 (m, 12 H), 4.10 (m, 4 H), 3.92 (m, 8 H), 3.59 (m, 28 H), 3.39 – 3.31 (m, 8 H), 2.72 (m, 4 H), 2.34 (m, 4 H), 1.67 (m, 4 H), 1.58 – 1.48 (m, 4 H), 1.28 (m, 4 H), 1.19 – 1.12 (m, 4 H). ^{13}C NMR (100 MHz, CD_3CN): δ 150.6, 148.1, 146.6 133.5, 130.8, 129.8, 129.7, 129.3, 127.8, 126.9, 125.2, 108.4, 71.8, 71.6, 71.1, 71.0, 70.2, 69.4, 51.3, 47.6, 29.9, 26.6, 26.3. HRMS (ESI): m/z calcd. for $C_{90}H_{123}N_{10}O_{14}^{3+}$: $[M-4PF_6-H]^{3+}$ 522.9745; found: 522.9757.

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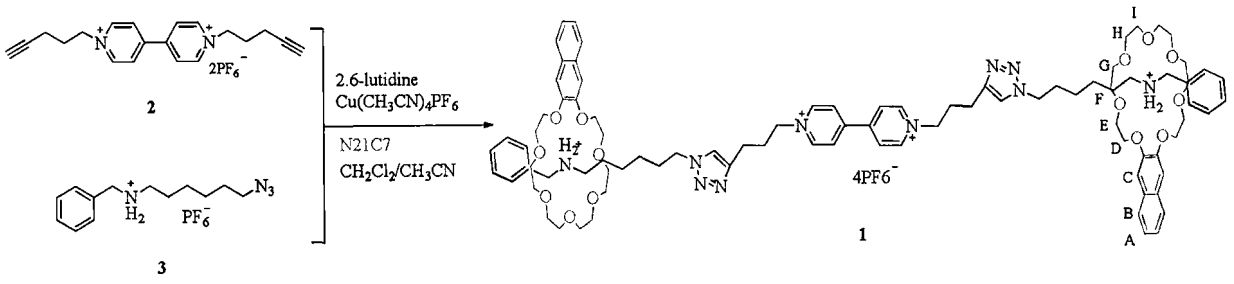
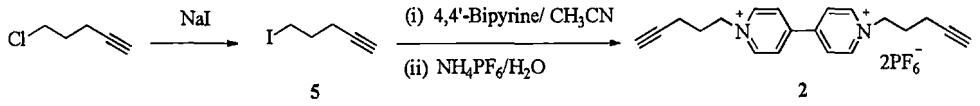


Scheme 1. Synthesis of [3]rotaxane **1**.



Scheme 2. Synthesis of viologen **2**.

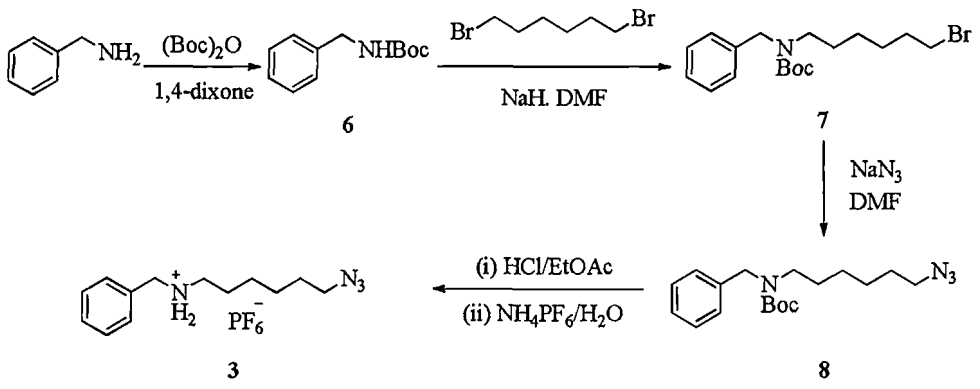
Preparation of **2** (*Scheme 2*): Compound **5** (2.91 g, 15 mmol) and 4,4′-bipyridine (780.9 mg, 5.0 mmol) were dissolved in DMF (30 mL), stirred at 80 °C under N_2 for 1d. After cooled, the precipitate was filtered off, washed with CH_3CN, then suspended in acetone (50 mL). A saturated aqueous solution of NH_4PF_6 was added until the suspension became clear. The solvent was removed in vacuo, and water (50 mL) was added to the residue. The resulting mixture was then filtered, washed with water, and dried to give **2** as a white solid (2.15 g, 74%). ^{1}H NMR (400 MHz, CD_3CN): δ 8.95 (d, 4 H, J = 5.9 Hz), 8.42 (d, 4 H, J = 5.4 Hz), 4.76 (t, 4 H, J = 7.0 Hz), 2.41 – 2.32 (m, 6 H), 2.28 (m, 4 H). ^{13}C NMR (100 MHz, CD_3CN): δ 150.8, 146.4, 127.9, 82.1, 71.5, 61.5, 29.8, 15.2. HRMS (ESI): m/z calcd. for $C_{20}H_{22}F_6N_2P^+$: $[M-PF_6]^+$ 435.1419; found: 435.1413.

Preparation of **7** [8] (*Scheme 3*): Compound **6** (1.15 g, 6 mmol) was dissolved in dry DMF (18 mL), then NaH (172.8 mg, 7.2 mmol) was added to the solution at 0 °C. After stirring for 30 min at room temperature, 1,6-dibromohexane (4.4 g, 18.06 mmol) was added in three portions to the solution at 0 °C. After stirring for another 18 h at room temperature, water was added to stop the reaction. After solvent was evaporated off under vacuum, the residue was dissolved with CH_2Cl_2 (100 mL) and washed with water (50 mL) twice. Then the residue was purified by column chromatography over silica gel [eluent: from petrol ether to petrol ether/EtOAc (10:1)] to afford **7** as a colorless oil (1.44 g, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (m, 5 H), 4.41 (s, 2 H), 3.38 (m, 2 H), 3.15 (m, 2 H), 1.82 (m, 2 H), 1.46 (m, 13 H), 1.26 (m, 2 H).

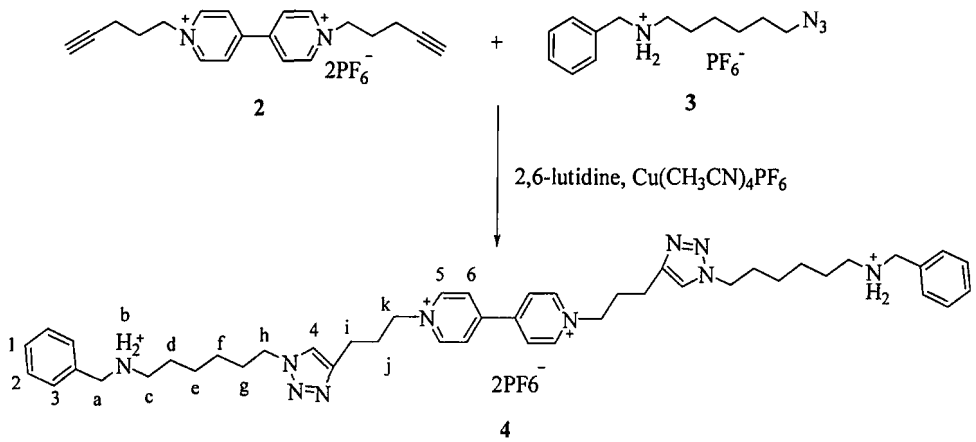
Preparation of **8** (*Scheme 3*): Compound **7** (2.03 g, 5.48 mmol) was dissolved in DMF (150 mL), NaN_3 (3.57 g, 55.0 mmol) was added to the solution. After stirring for 24 h at 80 °C, the solvent was evaporated off under vacuum, the residue was dissolved with CH_2Cl_2 (100 mL) and washed with water (50 mL) twice. The organic phase was dried and evaporated off to afford **8** as a colorless oil (1.69 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.29 (m, 2 H), 7.26–7.19 (m, 3 H), 4.42 (m, 2 H), 3.20 (m, 4 H), 1.57 (m, 2 H), 1.43 (m, 11 H), 1.38–1.32 (m, 2 H), 1.27 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 128.4, 127.6, 127.0, 79.4, 51.2, 50.5, 49.9, 46.4, 28.7, 28.4, 27.9, 27.7, 26.4, 26.3. HRMS (ESI): m/z calcd. for $C_{18}H_{29}N_4O_2^+$: $[M+H]^+$ 333.2285; found: 333.2282.

Preparation of **3** (*Scheme 3*): Compound **8** (1.0 g, 3.0 mmol) was dissolved in a mixed solvent 10% conc. HCl/EtOAc (80 mL), and then stirred overnight. After evaporated off the solvent under vacuum, the residue was suspended in acetone (50 mL). A saturated aqueous solution of NH_4PF_6 was added until the suspension became clear. The solvent was removed in vacuo, and water (50 mL) was added to the residue. The resulting mixture was then filtered, washed with water, and dried to give **3** as a yellow solid (1.06 g, 93%). ^{1}H NMR (400 MHz, CD_3CN): δ 7.49 (m, 5 H), 4.16 (s, 2 H), 3.32 (t, 2 H, J = 6.6 Hz), 3.03 (t, 2 H, J = 7.7 Hz), 1.73–1.64 (m, 2 H), 1.63–1.55 (m, 2 H), 1.40 (m, 4 H). ^{13}C NMR (100 MHz, CD_3CN): δ 131.4, 130.6, 130.3, 129.7, 52.1, 51.5, 48.4, 28.7, 26.3, 26.1, 26.0. HRMS (ESI): m/z calcd. for $C_{13}H_{21}N_4^+$ 233.1761: $[M-PF_6]^+$; found: 233.1762.

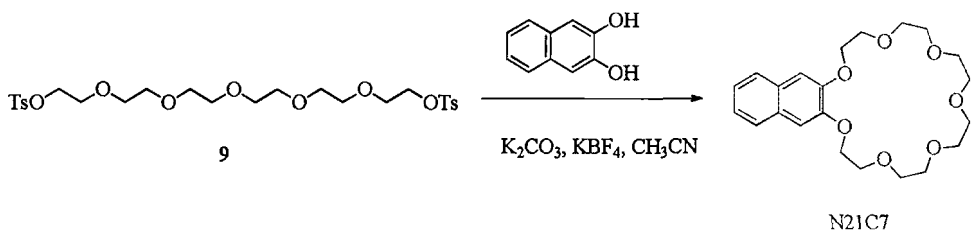
Preparation of **4** (*Scheme 4*): To a solution of **2** (174.1 mg, 0.3 mmol), **3** (238.3 mg, 0.63 mmol), in CH_3CN (3.0 mL) was added $Cu(MeCN)_4PF_6$ (352.2 mg, 0.945 mmol) and 2,6-lutidine (11 μL, 0.095 mmol). The reaction mixture was stirred for 24 h at room temperature. Then the solvent was removed under reduced



Scheme 3. Synthesis of secondary ammonium guest **3**.



Scheme 4. Synthesis of dumbbell-shaped molecule **4**.



Scheme 5. Synthesis of N21C7.

pressure, and purified by column chromatography over silica gel (eluent: CH_2Cl_2/MeOH, 30:1) to afford **4** as a yellow solid (528.9 mg, 82%). ^{1}H NMR (400 MHz, CD_3CN): δ 8.97 (d, 4 H, J = 6.9 Hz), 8.37 (d, 4 H, J = 6.8 Hz), 7.58 (s, 2 H), 7.47 (m, 10 H), 4.83 – 4.59 (m, 4 H), 4.41 – 4.22 (m, 4 H), 4.20 – 3.96 (s, 4 H), 3.13 – 2.86 (m, 4 H), 2.76 (m, 4 H), 2.42 – 2.26 (m, 4 H), 1.88 – 1.75 (m, 4 H), 1.71 – 1.54 (m, 4 H), 1.40 – 1.23 (m, 8 H). ^{13}C NMR (100 MHz, CD_3CN): δ 149.7, 145.5, 145.0, 130.3, 129.7, 129.4, 128.8, 126.8, 121.7, 68.3, 63.0, 60.9, 51.2, 49.3, 47.5, 30.1, 29.2, 25.0, 21.0. HRMS (ESI): m/z calcd. for $C_{46}H_{62}N_{10}^{2+}$: $[M-4PF_6-2H]^{2+}$ 377.2574; found: 377.2579.

Preparation of N21C7 (*Scheme 5*): While stirring vigorously under argon atmosphere, a suspension of K_2CO_3 (1.38 g, 10 mmol) and KBF_4 (629.5 mg, 5 mmol) in dry CH_3CN (100 mL) was heated to reflux. To the suspension was added dropwise a solution of compound **9** (1.97 g, 3.33 mmol) and 2,3-dihydroxynaphthalene (533.3 mg, 3.33 mmol) in dry CH_3CN (100 mL) during 12 h. The reaction mixture was stirred under reflux for another 3 d. After cooled, the mixture was filtered and washed with CH_2Cl_2 (100 mL). The filtrate was evaporated off under vacuum. The residue was partitioned between CH_2Cl_2 (100 mL) and water (100 mL), and the aqueous phase was extracted twice by CH_2Cl_2 (50 mL). Then the organic phase was dried over anhydrous Na_2SO_4, then concentrated. The crude product was purified by column chromatography over silica gel (eluent: EtOAc/petrol ether from 1:5 to 2:1) to afford N21C7 as a yellowish solid (879.8 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (dd, 2 H, J = 6.0, 3.3 Hz), 7.32 (dd, 2 H, J = 6.1, 3.2 Hz), 7.12 (s, 2 H), 4.30–4.23 (m, 4 H), 4.03–3.97 (m, 4 H), 3.85 (m, 4 H), 3.76 (m, 4 H), 3.68 (m, 8 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 129.3, 126.3, 124.2, 108.1, 71.4, 71.2, 71.1, 70.5, 69.6, 69.0. HRMS (ESI): m/z calcd. for $C_{22}H_{30}NaO_7^+$: $[M+Na]^+$ 429.1884; found: 429.1891.

3. Results and discussion

The rotaxanes based on crown ether were commonly synthesized following the "threading-followed-by-stoppering" protocol [9]. Attaching two semirotaxanes (that is, *pseudo*rotaxane with one stopper) onto a bifunctional stopper can be an effective way to generate a [3]rotaxane [10]. We synthesized an azide-containing secondary ammonium guest **3** to bind with N21C7 ring. A viologen **2** with two alkyne groups was chosen to connect with the semirotaxanes. The CuAAC "click" reaction has been widely used in rotaxane synthesis because of the mild condition and high efficiency [11]. Using the $Cu(CH_3CN)_4PF_6$ as the catalyst, we can obtain the [3]rotaxane **1** in high yield. The ^{1}HNMR, ^{13}C NMR and HRMS have been used to characterize the compounds. We assigned all the resonances by analyzing their 1D NMR and 2D NMR spectra (see the Supporting information for ^{1}H–^{1}H COSY spectra).

The structure of **1** was confirmed through the comparison of the ^{1}H NMR spectra of **1**, uncomplexed dumbbell-shaped component **4** and N21C7 (Fig. 1). The downfield shifts of H_a and H_c adjacent to the ammonium site and the split and the shifts of the ethylidene protons on the crown ether ring confirmed the threading of the

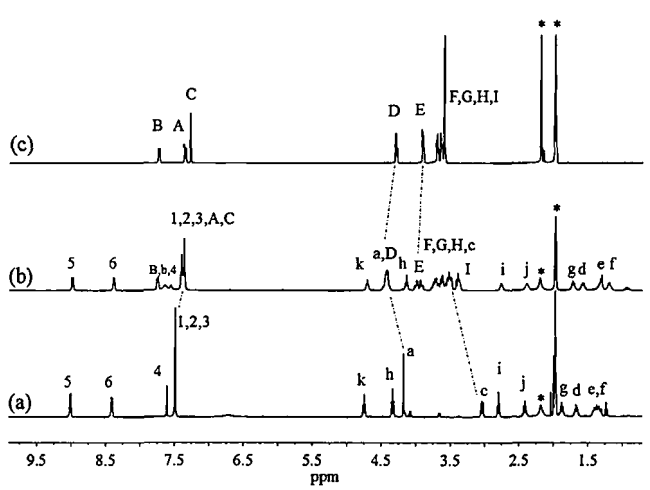


Fig. 1. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 5 mmol/L, 298 K) of (a) the uncomplexed dumbbell-shaped thread **4**, (b) **1**, and (c) the uncomplexed host N21C7. * = solvent signal.

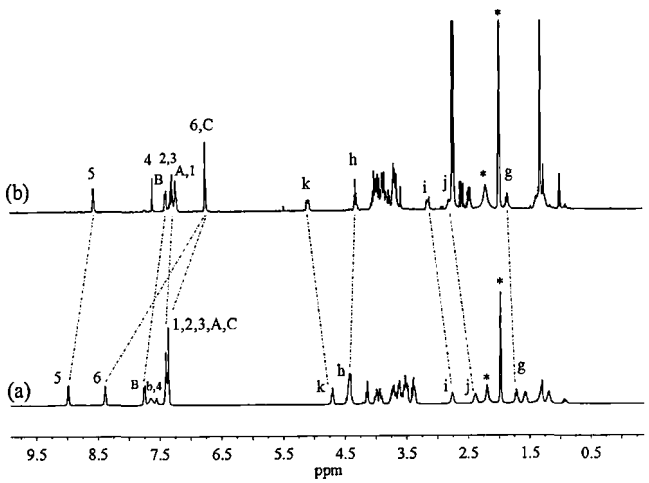


Fig. 2. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 5 mmol/L, 298 K) of **1** (a) the original spectrum, (b) after addition of 2.0 equivalents P_1–*t*-Bu. * = solvent signal.

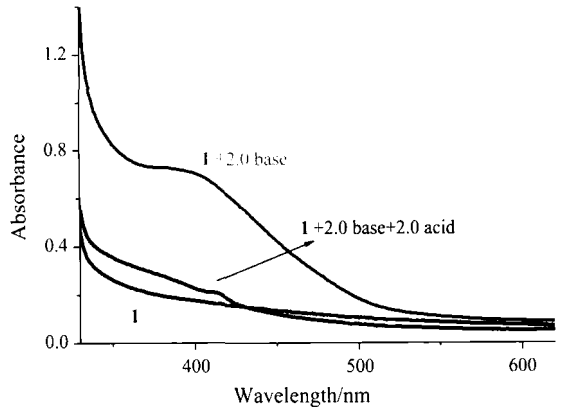


Fig. 3. Absorption spectra of **1** (a) the original spectrum, (b) after addition of 2.0 equivalents P_1–*t*-Bu; and (c) further addition of 2.0 equivalents TFA.

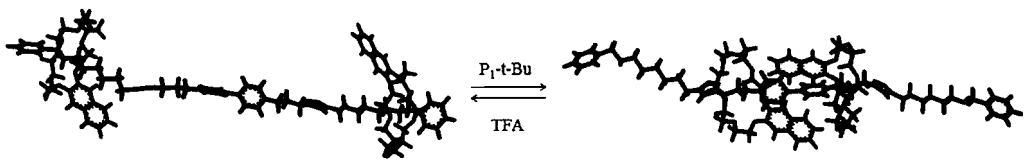


Fig. 4. Molecular energy minimization of **1** before (left) and after (right) the addition of base. The geometries were optimized by the molecular mechanics method with dreiding force field.

secondary ammonium group into the 21C7 ring. The protons H_5 and H_6 of the viologen and H_A, H_B and H_C of the naphthol group were almost unchanged, which indicated that the viologen and naphthol groups were far away from each other.

We used the ^{1}H NMR to investigate the base-acid controlled movement of **1** (Fig. 2). Through addition of phosphazene base *N*-*t*-butyl-*N*′,*N*′,*N*″,*N*″,*N*″,*N*‴-hexamethyl-phosphorimidic triamide (P_1–*t*-Bu) to the solution of **1**, it can be found that viologen protons H_5 and H_6 and H_A, H_B and H_C of the naphthol group were all shifted upfield. This observation suggested that the electron-deficient viologen unit and the electron-rich naphthol group were close to each other to form a strong CT interaction. Protons H_j, H_k and H_i near the viologen were shifted downfield, which should be attributed to the existence of the C–H···O interaction between the axle and crown ether and the deshielding effect of the naphthol group. These observations indicated that the crown ether rings located around the N terminals of viologen unit after addition of base.

The base–acid controlled behavior was also investigated by UV/vis spectroscopy (Fig. 3). In the original state, the CT interaction was weak. After addition of P_1–*t*-Bu, a characteristic CT band centered around 390 nm can be found in the UV/vis spectrum, which indicated the strong CT interaction between the naphthol and viologen groups. Then addition of trifluoroacetic acid (TFA) can restore the original spectrum which suggested that the process was reversible. The energy-minimized structures of **1** (before and after the addition of base) obtained by molecular modeling were also consistent with the proposed structures (Fig. 4).

4. Conclusion

In conclusion, a bistable [3]rotaxane **1** has been prepared by CuAAC "click" reaction. The shuttling motion of N21C7 ring along the axle molecule can be realized upon the addition of base and acid circularly. The intensity of CT interaction between the naphthol and viologen groups can be adjusted through the motion of rotaxane. Through adjusting the spacial distance between donor and acceptor under external stimulation, the result presented here offers a new prototype of performing photophysical function in mechanically interlocked molecules.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.cclet.2013.04.007.

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Comment

It offers a new prototype of performing photophysical function through adjusting the special distance under external stimulation.