A Metallo-Capped Polyrotaxane Containing Calix[4]arenes and Cyclodextrins and Its Highly Selective Binding for Ca^{2+}

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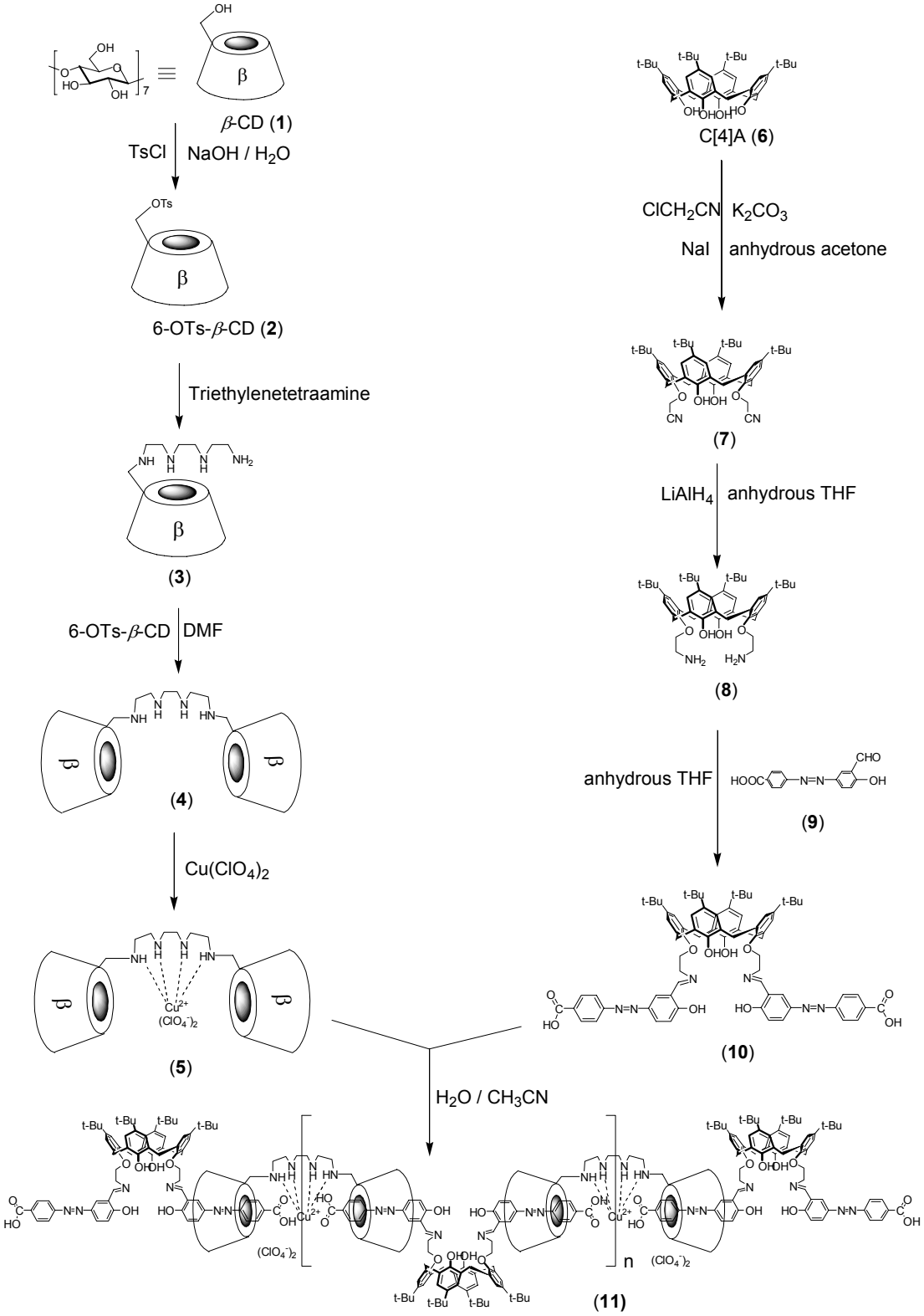
Supporting materials



Scheme 1

Experimental Section

General. *β*-CD was purchased from Wako, and all were used as received. NMR spectra were performed on a Varian INVOA 300 spectrometer in $CDCl_3$ using tetramethylsilane as an internal reference. UV-Vis spectra were recorded in a conventional quartz cell (10 x 10 x 45 mm) at 25 °C on a Shimadzu UV2401 spectrometer. The FTIR spectra were recorded on the Shimadzu Bio-Rad FTS 135 instruments in the range from 4000 to 500 cm^{-1} with a resolution of 2 cm^{-1}. GPC analysis was carried out with a HPLC workstation and waters 410 differential refractometer equipped with the PL Gel permeation columns. THF was used as an eluent at a flow rate of 2.7 $\mu L \cdot min^{-1}$ at 40 °C. Polystyrene standards are used to obtain a calibration curve. In the TEM experiments, a 50 μL portion of sample solution was dropped on a carbon-coated copper grid. The grid was then air-dried, which was then shaded with palladium-iridium alloy to thicken and make the images clearer.

The polyrotaxane **11** was prepared according to the procedures shown in Scheme 1. 6,6'-Triethylenetetraamine-bridged bis(*β*-cyclodextrin) (**4**) and its copper(II) complex (**5**) were synthesized from **1**. In this synthetic route, 6-OTs-*β*-CD (**2**), prepared by the reaction of **1** with *p*-toluenesulfonyl chloride in aqueous alkaline solution,[1] was converted to mono(6-triethylenetetraamino-6-deoxy)- *β* -cyclodextrin (**3**) in 68% yield on heating in excess triethylenetetramine at 70°C for 7 h.[2] Subsequent reaction of this intermediate with a slight excess of the 6-OTs-*β*-CD in N,N-dimethylformamide at 80°C for 3 days, followed by being poured into acetone to give the crude bis(*β*-cyclodextrin) (**4**) as a precipitate. The crude product was purified on a CM Sephadex C-25 ionic column with 1 mol dm^{-3} aqueous ammonia as an eluent and a Sephadex G-25 column with water as an eluent, respectively (yield 15%).[3] Treatment of copper(II) perchlorate and bis(*β*-cyclodextrin) **4** obtained the Cu(II)-complex **5** in 52% yield.[3] **7** was synthesized by the reaction of C[4]A (**6**) with chloroacetonitrile in the presence of potassium carbonate and sodium iodide in anhydrous acetone, according to the literature procedure.[4] Calix[4]arene derivative (**8**) was obtained by reducing **7** with $LiAlH_4$ in anhydrous THF.[5] The azosalicylaldehyde intermediate (**9**),

prepared according to the reported method,[6] further reacted with **8** in anhydrous THF to obtain azo-calixarene (**10**) as an orange powder in 42% yield. Metal capped polyrotaxane (**11**) was synthesized through the intermolecular inclusion complexation between Cu(II)-complex **5** and azo-calixarene (**10**) to give a product in 8% yield. The reagent grade chemicals LiCl, NaCl, KCl, RbCl, CsCl, $MgCl_2$, $CaCl_2$, $SrCl_2$, and $BaCl_2$ are dried in vacuum for three days before used.

Synthesis of azosalicylaldehyde intermediates 9:

p-Aminobenzoic acid (2.0 g), sodium nitrite (1.0 g), and concd. HCl (5.8 mL) were dissolved in water (10 mL). This mixture was stirred for 0.5 h in an ice bath. Then, carbamide (0.15 g) was added to remove the unreacted sodium nitrite. Sodium hydroxide (1.6 g) and salicylaldehyde (1.5 mL) in water (300 mL) were then slowly added to the above solution, which was stirred for another 2 h at 0 °C. The precipitate was collected and dried to give an orange powder, which was recrystallized with toluene to give pure products in a yield of 52 %.

Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,27-bis[2-[(2-hydroxy-5-(4-carboxyl –azo)benzylidene)amino]ethoxy]-26,28–dihydroxycalix[4]arene (10) The reaction mixture containing *p*-carboxylazosaliayl-aldehyde (0.74 g, 2.72 mmol) and 1,3-alternately substituted 25,27-bis(2-aminoethoxy)-26,28-calix[4]arene (**8)** (1.0 g, 1.36 mmol) in anhydrous THF (40 mL) was stirred for 4 hours at 70 °C under N_2. After cooling, the precipitate obtained was collected by filtration and recrystallized with anhydrous THF to give an orange powder of **4 (**0.7g, 42 %), m. p. > 300 °C. ^{1}H-NMR ($CDCl_3$), δ: 0.92 (s, 18H, $C(CH_3)_3$), 1.29(s, 18H, $C(CH_3)_3$), 3.27 (d, 4H, J = 12 Hz, $ArCH_2Ar$), 4.11 (t, 4H, J = 5.2 Hz, NCH_2), 4.19 (d, 4H, J = 12 Hz, $ArCH_2Ar$), 4.31 (t, 4H, J = 5.2 Hz, OCH_2), 6.69 (s, 2H, ArH), 6.72 (s, 4H, ArH), 6.98 (d, 2H, J = 9.0 Hz, ArH), 7.02 (s, 4H, ArH), 7.92~8.04 (m, 6H, ArH), 8.25~8.29 (m, 4H, ArH and NCH), 8.57(s, 2H, ArOH); ^{13}C NMR (75 Hz, $CDCl_3$) δ: 31.6, 33.8, 57.5, 74.6, 118.0, 119.0, 122.9, 124.7, 125.0, 125.7, 127.3, 127.6, 129.6, 132.0, 141.7, 144.6, 147.3, 148.1, 149.4, 150.2, 155.9, 167.1, 167.4. 175.9. Anal.: Calcd. for $C_{76}H_{82}N_6O_{10}$: C, 73.64; H, 6.67; N, 6.78; Found: C, 73.72, H 6.52, N 6.54. FT-IR ν (KBr)/cm^{-1} 3524, 2958, 2902, 2867, 1641, 1617, 1484, 1338, 1105, 855. UV/Vis (H_2O) λ_{max}/nm (ε / M^{-1}cm^{-1}) 390.5 (78241).

Synthesis of polyrotaxane 11:

Azo-calixarene **10** (0.08 mmol) in 10mL of acetonitrile was dropwisely added to the solution of the Cu(II)-complex **5** (0.05 mmol) in 30mL of water under vigorous stirring at room temperature. With the addition of azo-calixarene **10**, the color of the mixture turned from light blue to brown. After titration, the solution was stirred for another 24 h, and then continued the reaction at 70^{o}C for another 2 days. The mixture was filtered and the filtrate was concentrated under vacuum. The resultant solution was kept in 4^{o}C. The obtained precipitate was collected by filtration, washed successively with a small amount of water and chloroform, and then dried in vacuum to give polyrotaxane **11** in 8% yield. m.p. 270°C. (decomposed). Elemental Analysis Calcd. (%) for $[C_{90}H_{154}N_4{\cdot}C_{76}H_{80}N_6O_{10}{\cdot}Cu{\cdot}2ClO_4{\cdot}4H_2O]_n$: C, 69.61; H, 8.52; N, 4.89. Found: C, 69.34; H, 8.65; N, 4.82. UV/Vis (H_2O) λ_{max}/nm (ε / $M^{-1}cm^{-1}$) 390.0 (69075).

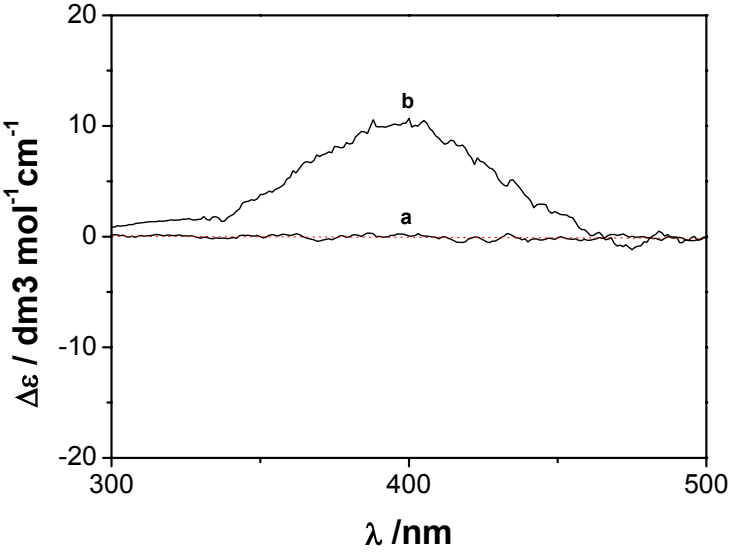


Figure 1S Circular dichroism (*a*) azo-calixarene **10** (10 μM) in CH_3CN and (*b*) polyrotaxane **11** (11 μM) in H_2O: CH_3CN (V:V / 95:5) at 25 °C.

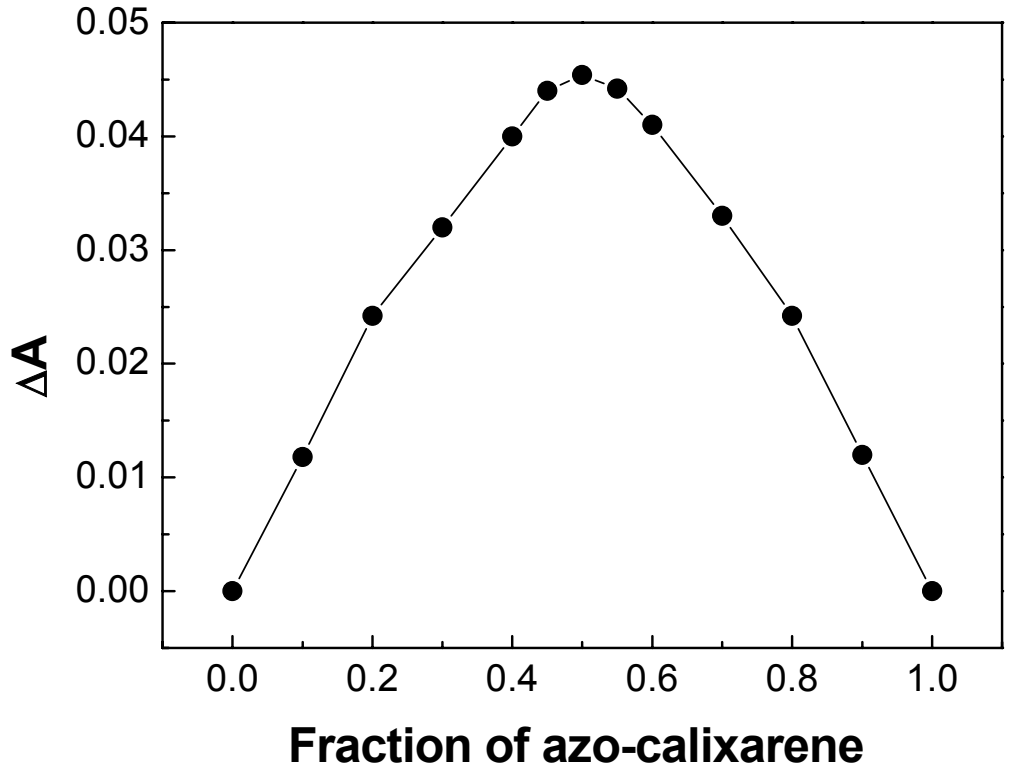
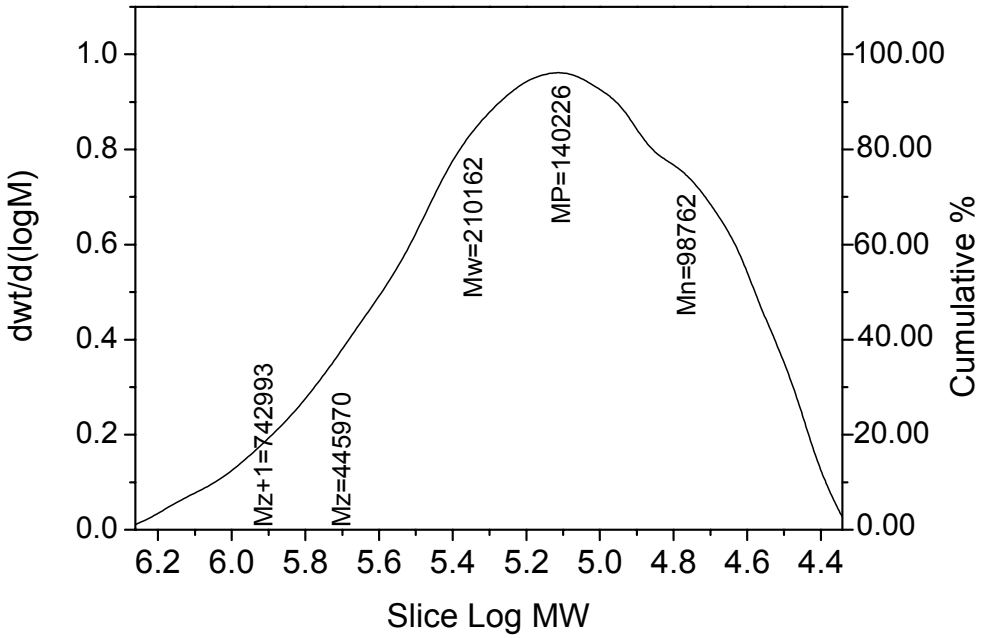


Figure 2S Job's plot for the complexation of metallobridged bis-cyclodextrins **5** with azo-calixarenes **10** in H_2O: CH_3CN (V:V / 95:5) at 25°C ([**5**] + [**10**] = 1.0×10^{-5} mol dm^{-3}).



GPC Results

Dist Name	Mn	Mw	MP	Mz	Mz+1	Polydispersity
1	98762	210162	140226	445970	742993	2.127971

Figure 3S GPC trace of polyrotaxane **11** in THF elution *vs.* polystyrene standards.

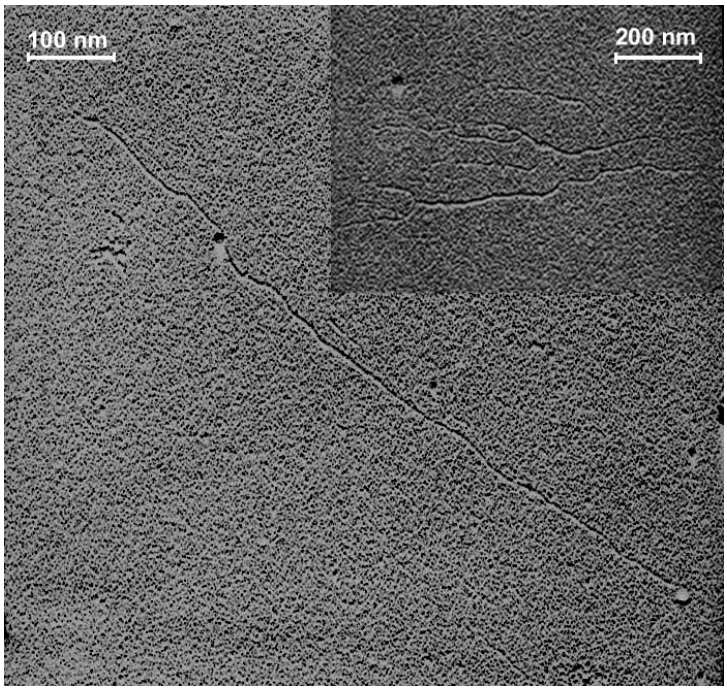


Figure 4S TEM images of polyrotaxane **11**

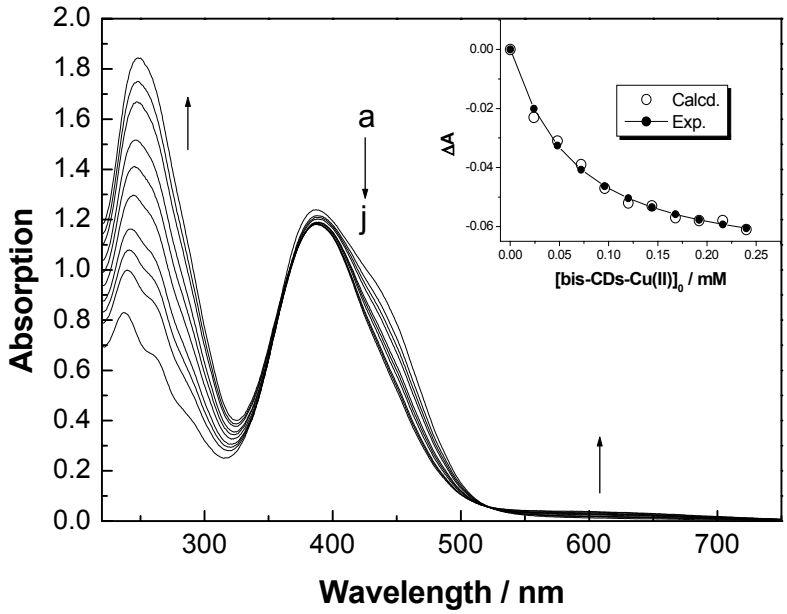


Figure 5S UV-Vis spectral changes of azo-calixarene **10** (17 μM) and the nonlinear least-squares analysis at 386 nm (inset) of differential intensity (ΔA) to calculate the stability constants upon the addition of metallobridged cyclodextrins **5** (0-240 μM from a to j) in H_2O: CH_3CN (V:V / 95:5).

Spectral titrations and curve-fitting analysis

In the UV-Vis spectral titrations experiment, the absorption intensity of the chromophoric group, embedding into the β-cyclodextrin cavity, gradually change upon the addition of a varying concentration of metal ions. Hence, curve-fitting analysis is available for us to determine the effective binding constants (K_{ES}) of the complexation process. However, confirmation of stoichiometry between polyrotaxanes and metal ions is a key step before we apply the appropriate fitting equation. It can be easily recognized that the polyrotaxanes involves numerous identical binding sites, which promote us to investigate only one repeated unit (one azo-calixarene and two cyclodextrins, seeing scheme 1). So, it is logical that formation 1:1 repeated unit-metal complex. The complexation of polyrotaxanes **11** (including n repeated units, and each repeated unit is defined as a host binding sites, H) with guest metal ions (G) are expressed by equation 1, and the effective binding constants (K_{ES}) are given by equation 2,

$$\mathrm{nH} + \mathrm{nG} \overset{K_{ES}}{\rightleftharpoons} \mathrm{n\,H \cdot G} \qquad (1)$$

$$K_{ES} = \frac{[\mathrm{H \cdot G}]}{[\mathrm{H}] \cdot [\mathrm{G}]} \qquad (2)$$

where [H], [G], and [H·G] represent the equilibrium concentration of the host, the guest, and the formed complex, respectively.

From eq 1, we can obtain the following equations. (In this case, the host is the chromophore.)

$$A_0 = \varepsilon[\mathrm{H}]_0 \qquad (3)$$

$$A = \varepsilon[\mathrm{H}] + \varepsilon'[\mathrm{H \cdot G}] = \varepsilon[\mathrm{H}]_0 + (\varepsilon' - \varepsilon)[\mathrm{H \cdot G}] \qquad (4)$$

where $[\mathrm{H}]_0$ signifies the initial concentration of the host chromophore, ε and ε' represent the molar fluorescence intensity of the free host and the complexed host, i.e. the formed complex (H·G).

Substracting eq 3 from eq 4, we obtain,

$$\Delta A = A - A_0 = (\varepsilon' - \varepsilon)[\mathrm{H}\cdot\mathrm{G}] = \Delta\varepsilon[\mathrm{H}\cdot\mathrm{G}] \qquad (5)$$

where ΔA and $\Delta\varepsilon$ denote the changes in the absorption intensity and molar absorption intensity of host unit upon complexation with metal ions

Further, from eqs 2 and 5, eq 6 can be derived,

$$\Delta A^2 - \Delta\varepsilon([\mathrm{G}]_0 + [\mathrm{H}]_0 + \frac{1}{K_{\mathrm{ES}}})\Delta A + \Delta\varepsilon^2[\mathrm{H}]_0[\mathrm{G}]_0 = 0 \qquad (6)$$

and solving eq 6 for ΔF , we obtain,

$$\Delta A = \frac{\Delta\varepsilon([\mathrm{G}]_0 + [\mathrm{H}]_0 + \frac{1}{K_{\mathrm{ES}}}) \pm \sqrt{\Delta\varepsilon^2([\mathrm{G}]_0 + [\mathrm{H}]_0 + \frac{1}{K_{\mathrm{ES}}})^2 - 4\Delta\varepsilon^2[\mathrm{H}]_0[\mathrm{G}]_0}}{2} \qquad (7)$$

where the initial concentrations were designated $[\mathrm{H}]_0$ and $[\mathrm{G}]_0$ for the host and the guest, respectively.

Using the nonlinear curve-fitting approach, the effective binding constant (K_{ES}) and the change in molar absorption intensity ($\Delta\varepsilon$) were calculated according to eq 7 using the data of ΔA observed at each initial guest concentration $[\mathrm{G}]_0$. Good curve-fitting plots further verify the 1:1 complex stoichiometry for each host–guest system. Typical spectral change and curve-fitting plots are shown in Figures 5S and 7S, respectively. The results are summarized in Table 1S.

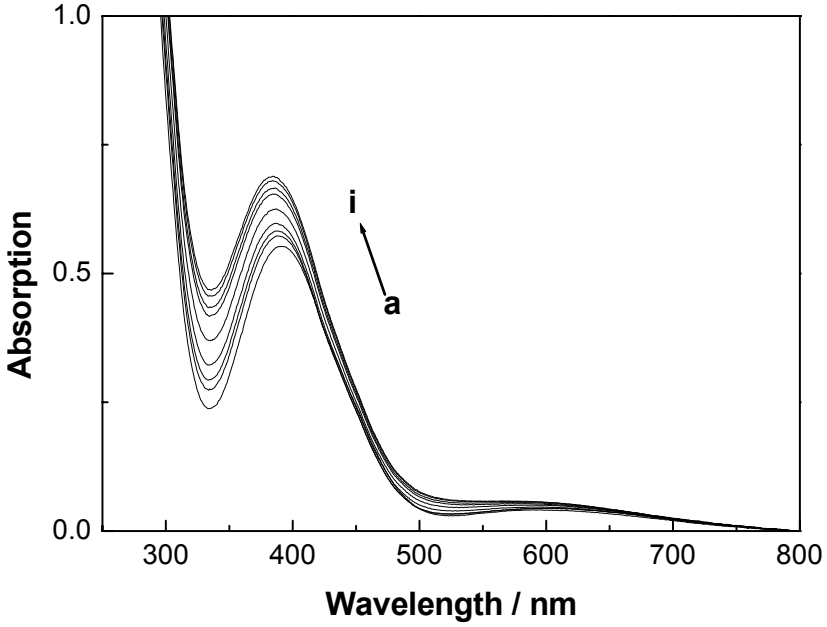


Figure 6S UV-Vis spectral changes of polyrotaxane **11** (8 μM, calculated based on repeat unit) upon the addition of Ca^{2+} (0-510 μM from a to i) in H_2O: CH_3CN (V:V / 95:5).

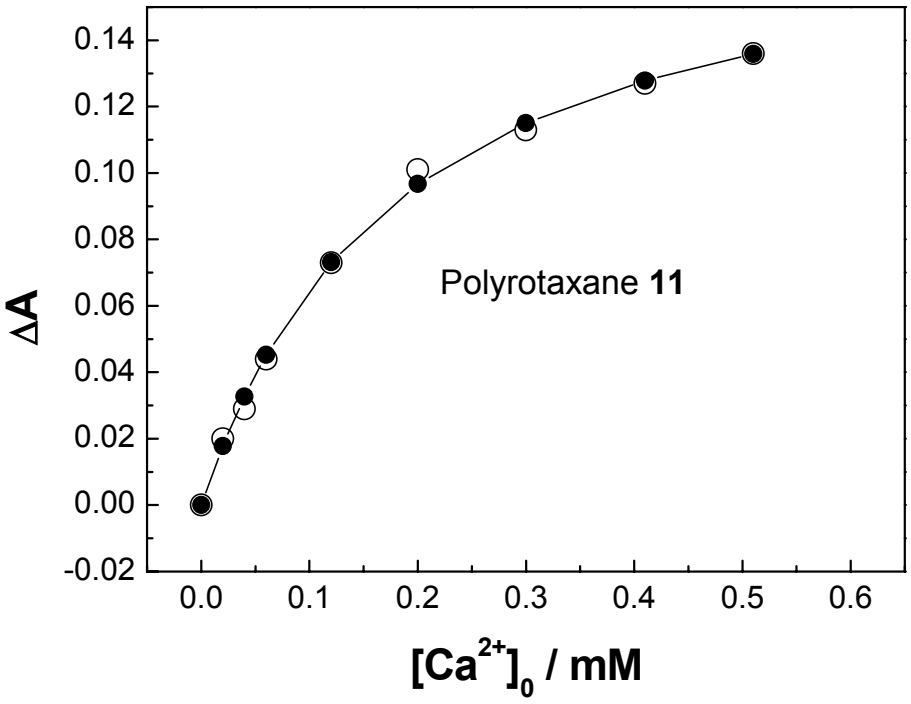


Figure 7S Curve-fitting analysis for the binding ability of polyrotaxane **11** with Ca^{2+} at 391 nm, upon the addition of Ca^{2+} in H_2O: CH_3CN (V:V / 95:5).

Table 1S. Effective binding constants (logK_{ES}) and Gibbs free energy changes ($-\Delta G^o$) (in kJ·mol^{-1}) for complexation of polyrotaxane **11** with alkali and alkaline metal ions in H_2O: CH_3CN (V:V / 95:5) 25^{o}C

Hosts	Ions	logK_{ES}	$-\Delta G^o$ / kJ mol^{-1}
Polyrotaxane **11**	Li^+	1.48	8.43
	Na^+	1.93	11.01
	K^+	1.65	9.44
	Rb^+	1.34	7.66
	Cs^+	<1.00	<5.71
	Mg^{2+}	3.10	17.70
	Ca^{2+}	4.00	22.78
	Sr^{2+}	2.71	15.45
	Ba^{2+}	2.63	15.03

When repeated measurements were performed, the K_{ES} value was reproducible within an error of 5%, which corresponding to an estimated error of 0.13 kJ mol^{-1} in the Gibbs free energy changes (ΔG^o).

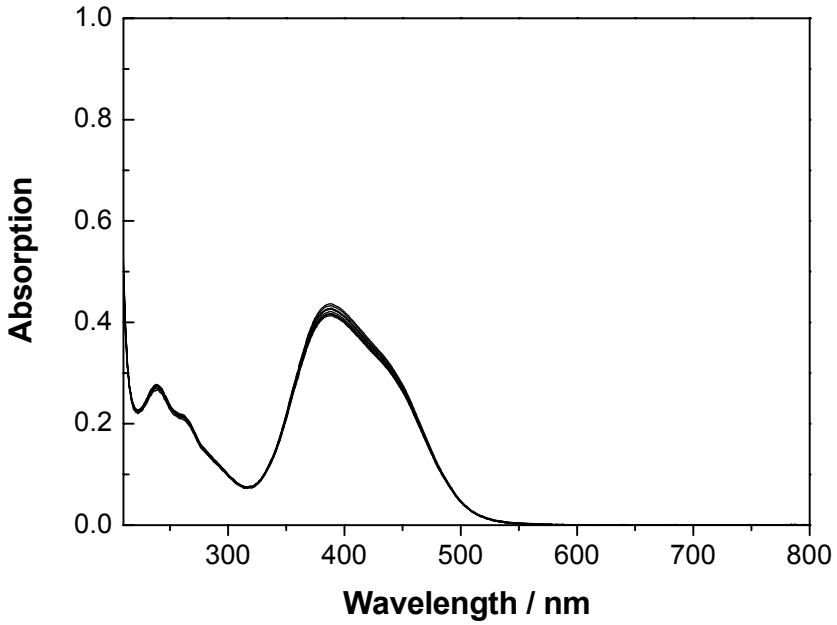


Figure 8S The UV spectral changes of azo-calixarene **10** (7 μM) with the addition of Ca^{2+} **(**0 to 1200 μM**)** in H_2O: CH_3CN (V:V / 95:5) at 25°C.

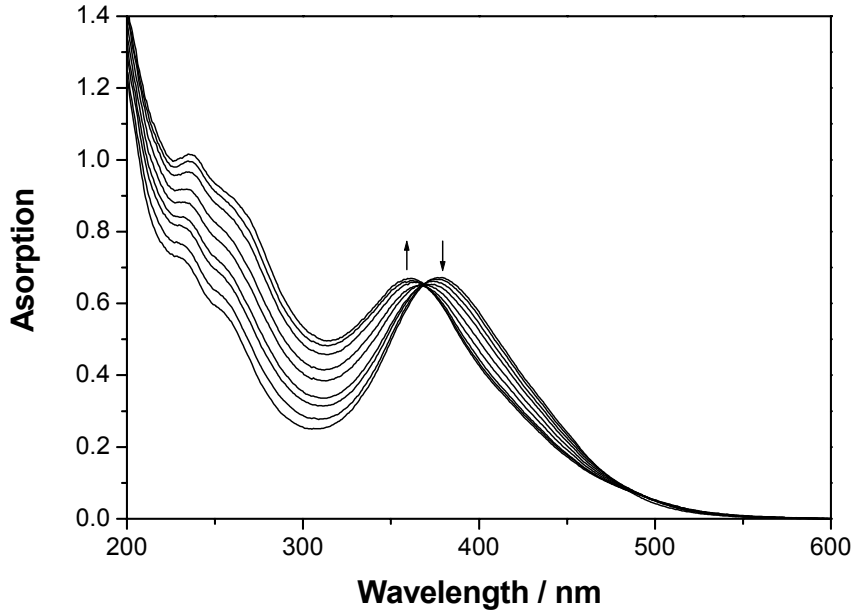


Figure 9S The UV spectral changes of azo-intermediate **9** (18 μM) with the addition of Cu^{2+} **(**0 to 150 μM**)** in H_2O: CH_3CN (V:V / 95:5) at 25°C.

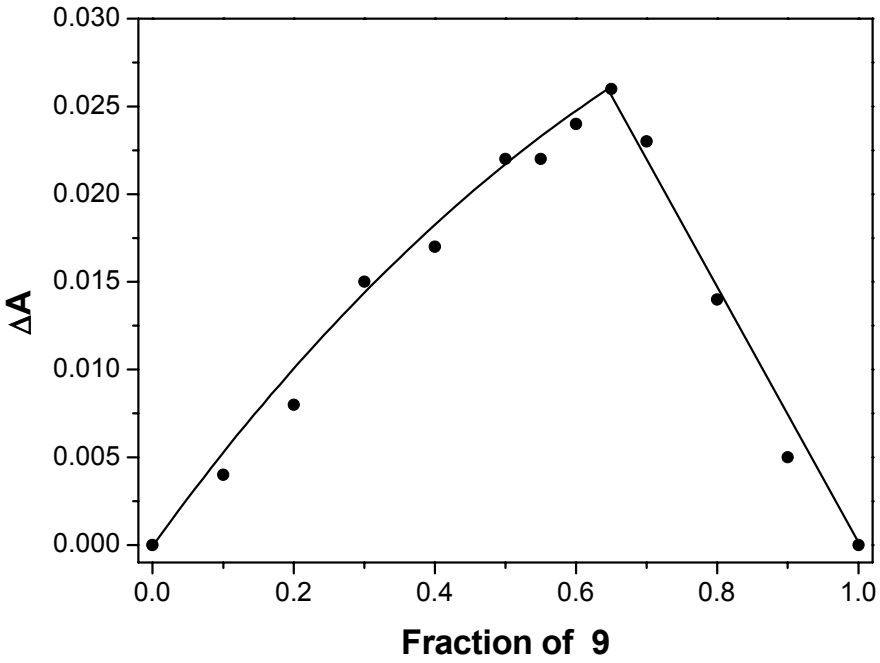


Figure 10S Job's plot for the complexation of azo-intermediate **9** with copper (II) ion in H_2O: CH_3CN (V:V / 95:5) at 25°C ([azo-intermediate **9**] + $[Cu^{2+}]$ = 1.8×10^{-5} mol dm^{-3}).

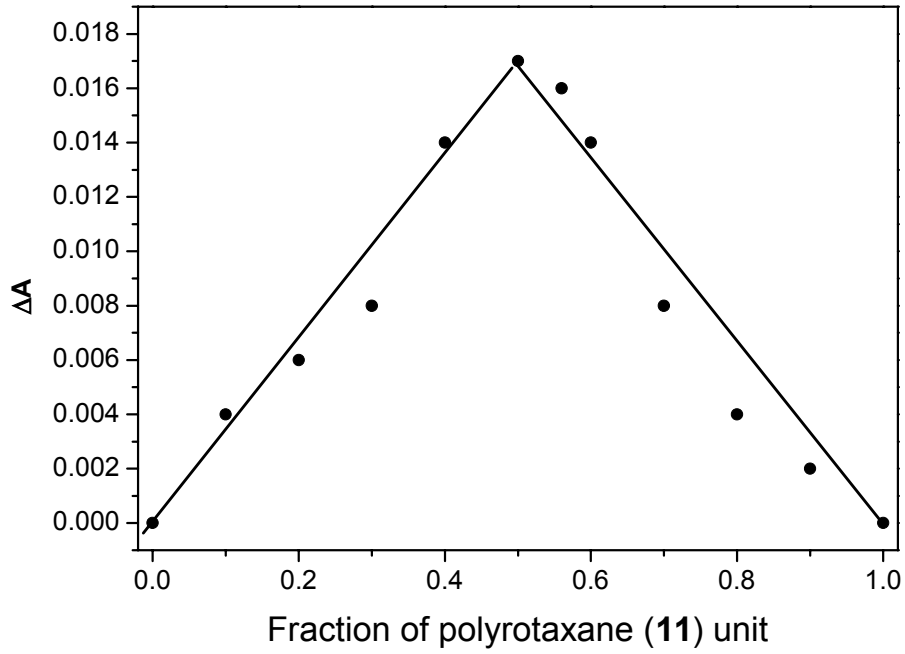


Figure 11S Job's plot for the complexation of polyrotaxane **11** unit with calcium ion in H_2O: CH_3CN (V:V / 95:5) at 25°C ([polyrotaxane unit] + $[Ca^{2+}]$ = 2.0×10^{-5} mol dm^{-3}).

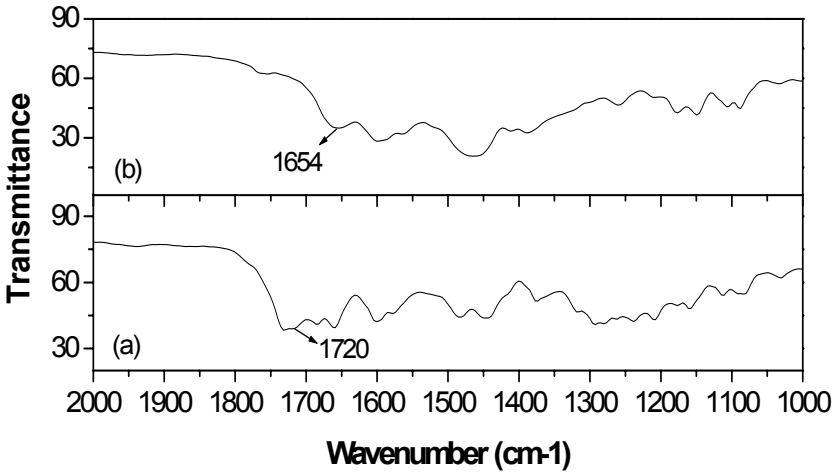


Figure 12S The IR spectra of (a) azo-intermediate **9**, and (b) **9**-Cu(II) complex.

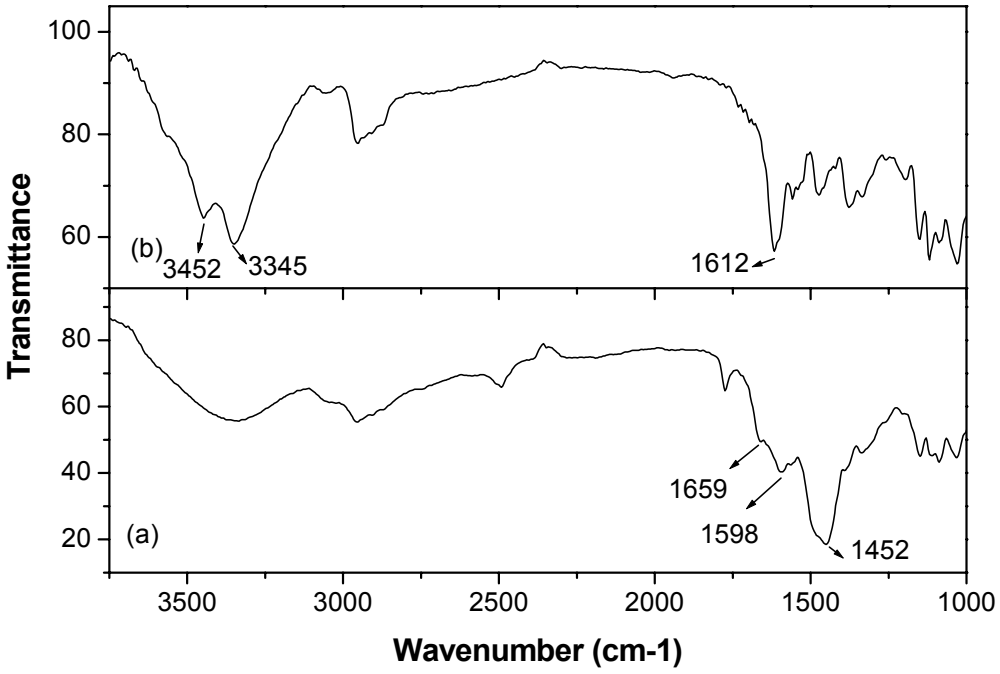


Figure 13S The IR spectra of (a) polyrotaxane **11** and (b) its corresponding complex with Ca^{2+}.

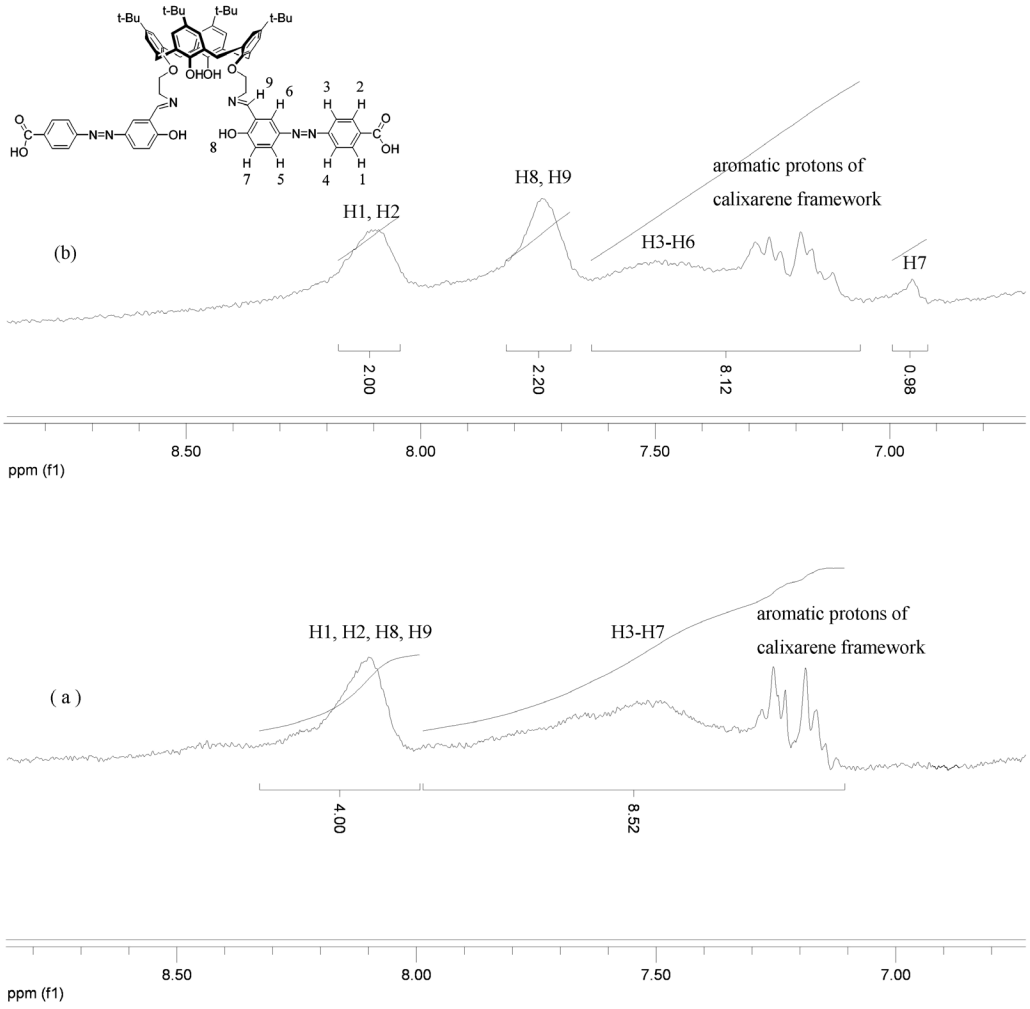


Figure 14S ^{1}H NMR spectra of (a) polyrotaxane **11** and (b) its corresponding complex with Ca^{2+} in D_6-DMSO.

Kinetics experiments

The determination of the kinetic data of the azo-calixarene-bis-CD-Cu (II) system in H_2O: CH_3CN (V:V / 95:5) mixture solution was performed by the time-dependent UV spectral changes. For 1:1 reaction the relaxation time τ is given by:

$$1 / \tau = k_R (C_{azo\text{-}CA}+C_{bis\text{-}CD}) + k_D$$

in which k_R is the recombination rate constant, k_D is the dissociation rate constant, $C_{azo\text{-}CA}$ is the concentration of the free azo-calixarene **10**, and $C_{bis\text{-}CD}$ is the concentration of the free bis-CD-Cu (II) **5**. If one of the components is in excess (bis-CD-Cu (II) **5** in this case), one can determine the rate constants by plotting $1 / \tau$ against $C_{bis\text{-}CD}$.

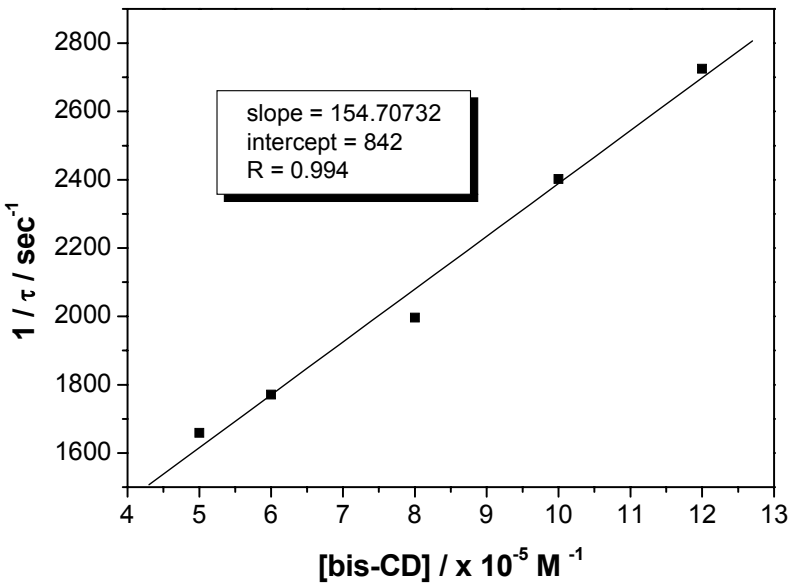


Figure 15S Reciprocal relaxation time for the azo-calixarene **10** and bis-CD **5** plotted against the concentration of bis-CD **5**.

Figure 15S showed the results of the measurements in H_2O: CH_3CN (V:V / 95:5) at 25°C. The slope gave the recombination rate constant k_R = 1.5 x 10^7 M^{-1} sec^{-1}; the intercept gave the dissociation rate constant k_D = 8.4 x 10^2 sec^{-1}. The quotient of the rate constants provided the effective binding constant log K_{es} = log (k_R/k_D) = 4.25 which was in good consistent with the thermodynamically measured constant 4.30. This confirmed that **10** formed a 1 : 1 assembly with the **5**. The obtained kinetic results were basically agreement with the reported values determined between the native cyclodextrins with azo guest molecules.[7]

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