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Synthesis of A Novel Bridged Bis(β-cyclodextrin)s Possessing Phenanthroline Tether and Its Molecular Binding Ability with Dyes

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Abstract: A novel β-cyclodextrin dimer bearing 2, 9-diformyl-1, 10-phenanthroline tether **4** has been synthesized and its inclusion complexation behavior with two triangular model substrates (RhB and BG) has been investigated through fluorescence and ultraviolet spectrometry. The result obtained indicated that novel bridged bis(β-cyclodextrin)s could significantly enhance the original molecular binding ability of native β-cyclodextrin by cooperative binding of two hydrophobic cavities.

Keywords: Bis(β-cyclodextrin)s, inclusion complexation, dye, binding ability.

It is well known that the bridged bis(β-cyclodextrin)s tethered with a variety of linkers show higher binding constants by cooperative binding of one guest molecule in the closely located two hydrophobic cyclodextrin cavities as compared with the parent cyclodextrins[1]. Therefore, a lot of effect has been devoted to the design and synthesis of dimeric cyclodextrins with structural diversities in order to control the inclusion complexation behavior by cyclodextrins. Recently, we have demonstrated that several bridged bis(β-cyclodextrin)s with organoselenium and oligo(ethylenediamine) tethers not only gave much stronger binding ability for some fluorescent dyes than the parent cyclodextrin, but also showed the higher molecular selectivity[2]. In the present letter, we report our investigation on the synthesis and the inclusion complexation behavior of a novel bridged bis(β-cyclodextrin)s tethered with 2, 9-formyl-1, 10-phenanthroline linker in order to further explore the molecular recognition mechanism of bridged bis(β-cyclodextrin)s.

The bridged bis(β-cyclodextrin)s tethered with 2, 9-diformyl-1, 10-phenanthroline linker has been synthesized according to the **Scheme 1**. In this synthetic route, 0.5 mmol 2, 9-diformyl-1,10-phenanthroline[3] and 1.0 mmol mono (6-ethylene- diamino-6-deoxy)-β-cyclodextrin[4] were stirred for 6 h in the mixture solution of ethanol and water (5:1) at 80°C, then the mixture was cooled. The precipitate was collected and dissolved in water, the resultant solution was poured into acetone, and the precipitate formed was collected by filtration. This procedure repeated several times, and then the crude product was repeatedly purified by the column of Sephadex G-25 with the elution of

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water two times to give pure **4** in 12% yield. The pure sample is confirmed by elemental analysis and spectroscopic data[5].

Scheme 1

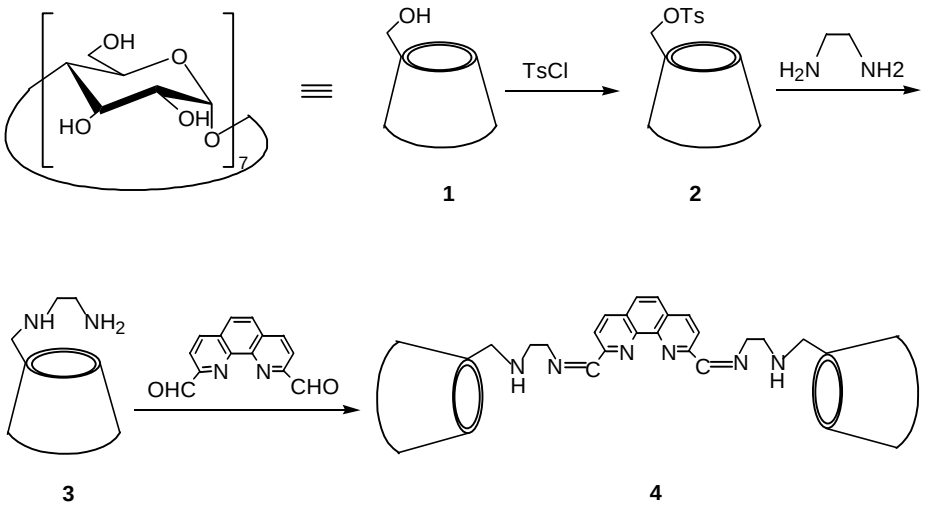
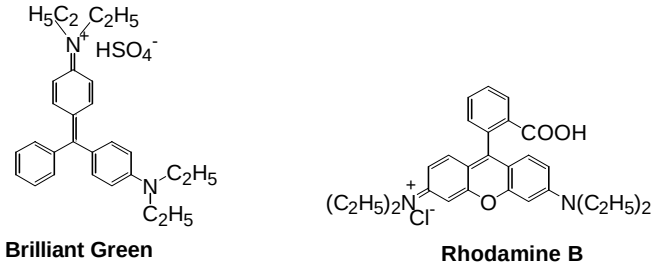


Chart 1

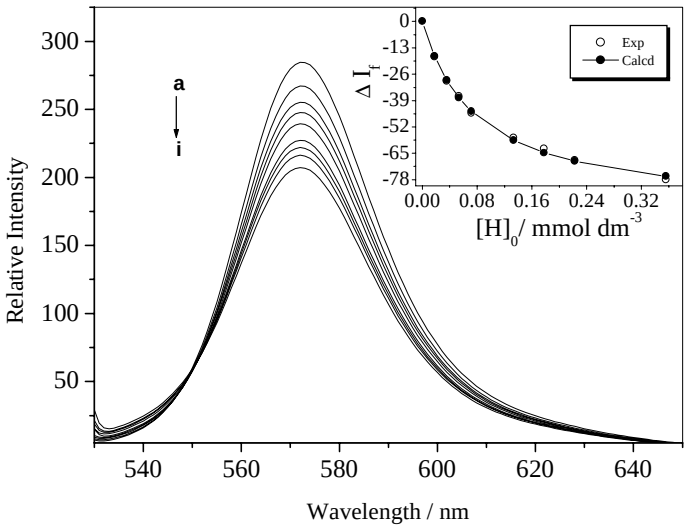


Brilliant Green **Rhodamine B**

The inclusion complexation behavior of cyclodextrin dimer **4** with Rhodamine B (RhB) and Brilliant Green (BG) **(Chart 1)** as representative guest molecules was studied by fluorescence and ultraviolet spectrometric titrations. It is well known that RhB and BG are sensitive to the change of environment, and then both of them could be used as a spectrum probe to investigate binding ability with cyclodextrin. As can be seen from **Figure 1**, the fluorescence intensity of RhB was gradually decreased upon addition of host compound **4**. One possible explanation for this phenomenon is that RhB has been embedded in the cavities of bridged bis(β-cyclodextrin)s as a lactonic form leading to the quenched fluorescence. It is noted from **Table 1** that the log K_S values for the inclusion complexation of native β-cyclodextrin with RhB and BG have been reported as 3.34 and 3.63, respectively. The hydrophobic lactonic neutral form of RhB matched the size of

native β-cyclodextrin and gave the relative high binding constant. Comparing with RhB, BG has only one benzene ring can be penetrated into the β-cyclodextrin cavity according to the topology. Hence, the binding ability of β-cyclodextrin with Brilliant Green is lower than that with RhB. Possessing two hydrophobic cavities, cyclodextrin dimer **4** form much more stable inclusion complex with RhB and BG through the cooperative binding of one guest molecule in the closely located two cavities, giving the higher binding constant. The stability sequence upon the inclusion complexation with cyclodextrin dimer **4** is RhB > BG. The binding ability of **4** has been enhanced by a factor of 3.0 for RhB, and of 3.4 for BG , respectively.

Figure 1 The changes of the Rh B upon addition of **4** in aqueous buffer solution.



*Using the nonlinear least-squares analysis (inset) of the differential intensity (Δ*I*) to calculate the complex stability constant (log K_S). $[M]_{Rh\ B}$ = 1.9 μ mol/L; $[M]_{host\ 4}$ = 0–355 μ mol/L (from a to i)

Table 1 The complex stability constant (K_S) and the gibbs free energy change (-Δ*G*°) for 1:1 inclusion complexation of RhB and BG with *β*-cyclodextrin **1**, and bis(*β*-cyclodextrin)s **4** in aqueous buffer solution (pH 7.20) at 25.0°C

Host	Guest	K_S	log K_S	$-\Delta G°(kJ\cdot mol^{-1})$	Methods	Ref
1	BG	2187	3.34	19.10	UV	a
	RhB	4240	3.63	20.70	FL	a
4	BG	7460	3.87	22.10	UV	b
	RhB	12900	4.11	23.46	FL	b

[a] Ref 6; [b] This work

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References and Notes

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5. ^{1}H-NMR(300 MHz, D_2O, δ, ppm) of compound **4**: 2.5 (s, 2H), 2.6-2.8 (m, 8H), 3.4–3.8 (m, 84H), 4.9 (m, 14H), 7.7–8.3 (m, 8H). Anal. Calcd. for $C_{102}H_{156}O_{68}N_6.7H_2O$ C, 45.71; H, 6.39; N, 3.14. Found: C, 45.88; H, 6.75; N 3.23. UV/vis(water) λ_{max}/ nm (ε/ $M^{-1}cm^{-1}$) 279 (21700).
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