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A Large Conformational Change of a Bridged β-Cyclodextrin Dimer in Aqueous Solution

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Abstract: A novel bridged β-CD dimer in which two β-cyclodextrins were linked by a naphthalene at positions 2 and 7 has been synthesized. ^{1}H and ^{13}CNMR measurements showed that a large change in the conformation of the dimer occurred in aqueous solution. The dimer interacted with methyl and ethyl orange to form stable inclusion complexes *via* "induced fit" mechanism.

Keywords: Cyclodextrin dimer, ethyl orange, enzyme mimic, induced fit.

As artificial enzymes, the binding constants of cyclodextrins (CDs) and their substrates are expected to be high[1]. For this purpose, many kinds of bridged cyclodextrin dimers[2] whose two cyclodextrins are linked by various spacers have been constructed. It was of interest to make the dimers, whose binding constants would exceed 10^{8}dm^{3}/mol[3]. Up to date, the bridged cyclodextrin dimers have been extensively studied as enzyme models and as molecular receptors[4-6].

Recently, we synthesized a bridged β-CD dimer **1** in which two β-cyclodextrin molecules were linked by a naphthalene at positions 2 and 7 (**Figure 1**). The interaction of dimer with methyl and ethyl orange to form stable inclusion complexes *via* "induced fit" mechanism are reported.

Experimental

1 was obtained by the reaction of mono-(6-O-*p*-tolylsulfonyl)-β-cyclodextrin with 2,7-disulfydryl naphthalene in CH_3OH in the presence of CH_3ONa. ^{1}H, ^{13}C NMR spectra and ^{1}H-^{1}H NOESY were measured with a Bruker AM-400 NMR spectrometer. Fluorescence emission spectra were measured with a Hitachi MP850 spectrometer in degassed solution at 25°C and pH 7.0.

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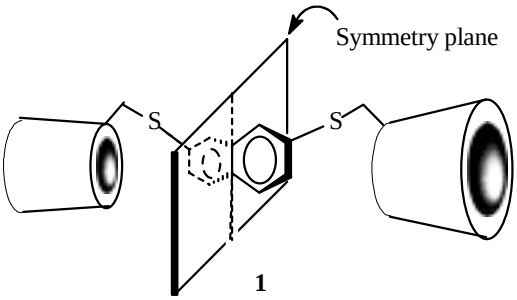
Figure 1 The structure of **1** with a plane symmetry

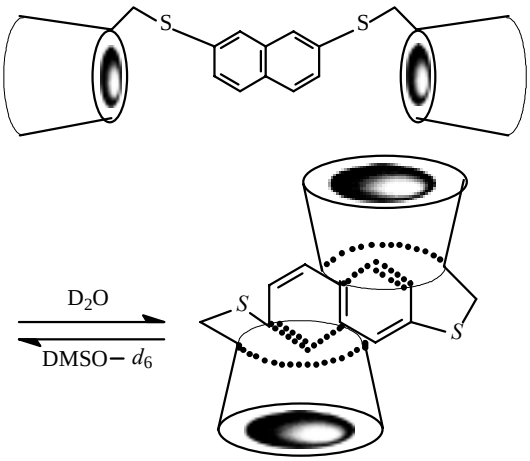


Results and Discussion

^{1}H NMR spectral data showed that the chemical shifts of aromatic protons of **1** are 7.76 (d, 2H, H-3 and H-6), 7.72 (s, 2H, H-1 and H-8) and 7.38 (d, 2H, H-4 and H-5) ppm. ^{13}C NMR showed the chemical shifts of six kinds of aromatic carbons are 124.3, 125.9, 128.4, 128.9, 133.8 and 135.6 ppm, respectively. According to the NMR data, the geometry of the dimer is symmetrical and the conformation in DMSO is shown in **Figure 1**.

Interestingly, the ^{1}H NMR spectrum of **1** in D_2O solution was different from that in DMSO. The chemical shifts of the aromatic protons are 7.39 (d, 1H, H-5), 7.79 (d, 1H, H-4), 7.81 (d, 1H, H-3), 7.90 (d, 1H, H-6), 7.93 (s, 1H, H-8), and 7.96 (s, 1H, H-1) ppm. Obviously, the chemical environment of each aromatic proton is different. This finding indicated that the self-inclusion of the dimer occurred in D_2O solution due to the hydrophobic properties of the aromatic moiety and the cyclodextrin cavity (**Figure 2**).

Figure 2 The large conformation change of **1** in DMSO and in D_2O



The self-inclusion of **1** in water was strongly supported by the experimental data of NOESY (**Figure 3**). From **Figure 3** it can be seen that there is interaction between the bridged aromatic protons H-4 (7.79 ppm), H-8 (7.93 ppm) and cyclodextrin protons at wider rim H-5 (3.70 ppm) and H-6 (4.02 ppm). This finding demonstrated that the bridge naphthalene was partially included by the cyclodextrins.

Although the self-inclusion conformation of **1** was formed in water, the binding with methyl orange and ethyl orange was observed. The binding constants for **1** with methyl orange and ethyl orange were determined by the fluorescence spectroscopy, the results are listed in **Table 1**.

Figure 3 NOESY spectrum for dimer **1** in D_2O

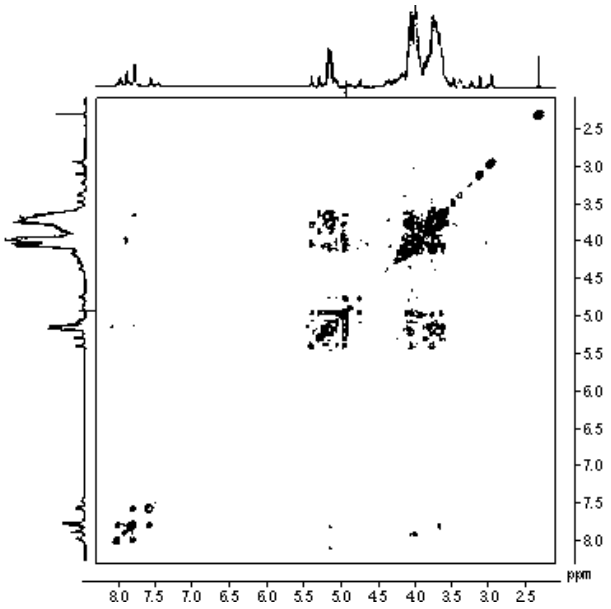


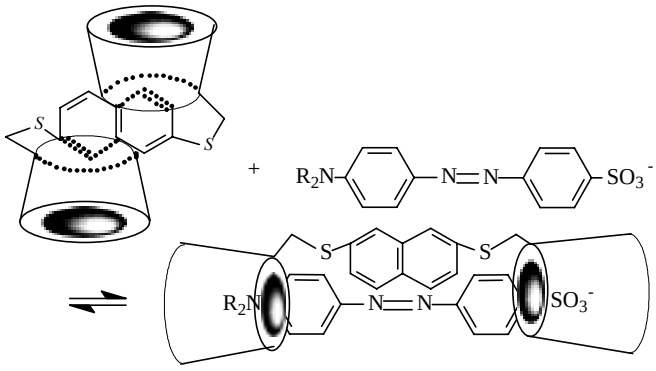
Table 1 Binding constants for the complexation of dimer **1** and *β*-CD with methyl and ethyl orange

	K_b (dm^3/mol)			
Host	Methyl Orange		Ethyl Orange	
1	3.2×10^6		2.4×10^5	
β-CD[7]	K_1	K_2	K_1	K_2
	9030	388	2970	606

From **Table 1** it can be seen that the binding constants of dimer with methyl orange and ethyl orange are greater than *β*-CD. It demonstrated that the inclusion complexes were formed through two sites recognition and binding of the *β*-CD dimer with the substrates.

Interestingly, this finding revealed the conformation of *β*-CD dimer must change for adapting the rigid linear shape of methyl and ethyl orange (**Figure 4**).

Figure 4 Inclusion complexation of **1** with methyl and ethyl orange in aqueous solution



R=Methyl, Ethyl

In other words, the *β*-CD dimer would be stretched out from the self-inclusion form to fit the request of the substrate. The similar phenomena called "induced fit"[8] were often occurred in the enzymatic process. The observation in this work is a good example of "induced fit" mode in artificial species.

In conclusion, we have synthesized a novel enzyme model compound bridged *β*-CD dimer. The NMR data showed that a self-inclusion of the dimer occurred in D_2O. The dimer could change its conformation to fit the shape of its substrate methyl and ethyl orange to form stable inclusion complexes *via* induced fit mechanism. This property could mimic the recognition and binding progress of enzyme to its substrates. Synthesis and molecular recognition of more *β*-CD dimers are undergoing.

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References

1. R. Breslow, N. Greenspoon, T. Guo, R. Zarzychi, *J. Am. Chem. Soc.,* **1989**, *111*, 8296.
2. F. Venema, C. M. Baselier, C. van Dienst, B. H. M. Ruel, M. C. Feiters, J. F. J. Engbersen, D. N. Reinhoudt, R. J. M. Nolte, *Tetrahedron Lett.*, **1994**, *35*, 1773.
3. B. Zhang, R. Breslow, *J. Am. Chem. Soc*., **1997**, *119*, 1676.
4. R. Breslow, B. Zhang, *J. Am. Chem. Soc*., **1994**, *116*, 7893.
5. R. R. French, P. Holzer, M. G. Leuenberger, W.-D. Woggon, *Angew. Chem.Int. Ed. Engl.*, **2000**, *39*, 1267.
6. T. J. Brett, J. M. Alexander, J. J. Stezowski, *J. Chem. Soc. Perkin Trans. 2*, **2000**, 1105.
7. T. Jiang, D. K. Sukumaran, S. D. Soni, D. S. Lawrence, *J. Org. Chem.*, **1994**, *59*, 5149.
8. D. E. Jr. Koshland, *Proc. Natl. Acad. Sci. USA*, **1958**, *44*, 98.

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