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Inclusion Behavior of β-Cyclodextrin with Bipyridine Molecules: Factors Governing Host-Guest Inclusion Geometries

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Abstract: The 1:1 complexation of β-cyclodextrin (β-CD) with structurally similar bipyridine guests which lead to the formation of six inclusion complexes (**1**–**6**) of β-CD with 4,4′-vinylenedipyridine, 2,2′-vinylenedipyridine, 1-(2-pyridyl)-2-(4-pyridyl)ethylene, 4,4′-ethylene-dipyridine, 4,4′-dithiodipyridine, and 2,2′-dithiodipyridine has been investigated comprehensively by X-ray crystallography in the solid state and by ^{1}H NMR spectroscopy and microcalorimetric titration in aqueous solution. The complex formation constants (K_S) for the stoichiometric 1:1 host–guest inclusion complexation of β-CD with the bipyridine derivatives were determined in aqueous solution by microcalorimetry and the host–guest inclusion geometries of the complexes were deduced from ^{1}H ROESY NMR spectroscopy. It transpires that the guest bipyridine molecules are included in the β-CD cavity with a range of different inclusion geometries. In the solid state, the crystal superstructures for the β-CD complexes **1**, **4**, and **5** are characterized by the triclinic crystal system (space group $P1$) commensurate with AAAA type supramolecular aggregation. By contrast, the β-CD complexes **2**, **3**, and **6** display either monoclinic (space group $P2_1$) or orthorhombic (space group $C222_1$) crystal systems, characteristic of ABAB type supramolecular aggregation. The results demonstrate that the relative locations of the nitrogen atom positions and the bridge-bond links between the two pyridine rings in these bipyridine guests, not only lead to distinct crystal systems and space groups, but also to different binding geometries and thermodynamical parameters on complexation of the bipyridines with β-CD. The knowledge obtained from this research improves our understanding of the molecular recognition and self-assembly processes exhibited by β-CD, both in the solid state and in aqueous solution.

Keywords: crystal structures · cyclodextrins · host–guest systems · inclusion compounds · NMR spectroscopy

Introduction

As naturally abundant cyclic oligosaccharides, cyclodextrins (CDs) have been applied in the fields of molecular recognition and supramolecular assembly.[1–6] Indeed, CDs can form stable inclusion complexes in aqueous solution with various guest molecules through the simultaneous contributions of several noncovalent bonding interactions by which the guest molecules are included within their hydrophobic inner cavities. The commonly accepted model for CD complex formation suggests that a CD complex forms when a suitable hydrophobic molecule displaces "high energy" water from the CD cavity.[7] In the inclusion complexation process, besides several weak intermolecular noncovalent forces, such as dipole-dipole (ion), hydrophobic, electrostatic, van der Waals, and hydrogen bonding interactions, the solvent, environment, and geometries of hosts and guests also affect the stabilities of the inclusion complexes. The strong binding affinity of CDs to hydrophobic molecules in aqueous solution enables these hosts to be effective receptors for organic, inorganic, and biological substrates.[8–10] Therefore, the findings of the researchers who have investigated the geometrical properties associated with the binding of guest molecules by CDs during the past two decades have attracted a lot of attention. For example, several research groups have reported solution studies of CDs upon complexation with amino

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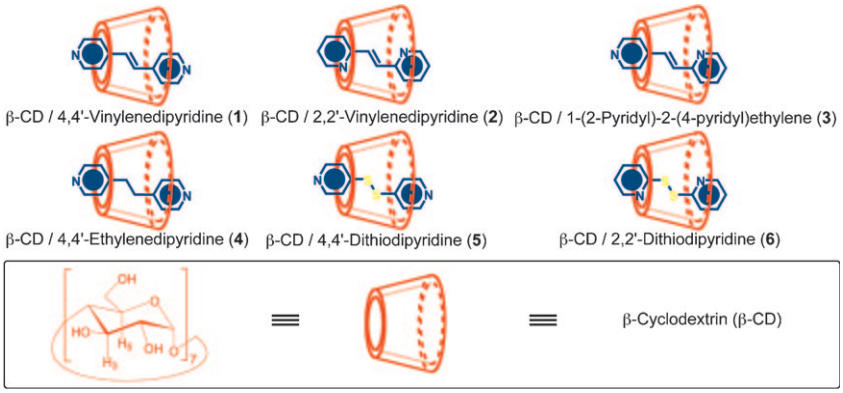
acids,[11,12] peptides,[13,14] drugs,[15,16] surfactants,[17,18] steroids,[19] and so forth, using different methods such as microcalorimetry in addition to NMR, UV/Vis, and fluorescence spectrometry. Through these studies, which were directed toward an understanding of the binding behavior and molecular/chiral recognition of CDs, these research groups have provided valuable information on the effects of changes in the functionality and chirality of guests that is not revealed in the crystal superstructures of the inclusion complexes. Nonetheless, it is much more valuable if the crystal superstructures of inclusion complexes can be obtained because they can provide direct insight into the binding mechanisms of substrates by CDs. Indeed, a number of crystallographic studies on inclusion complexes of CDs with guest molecules have been performed[20–32] during the past decade. Close examination of the crystal superstructures of a variety of inclusion complexes reveals that steric matching of the host and guest is certainly one of the most important factors determining the molecular geometry of a complex and its packing in the solid state.[20a] It is obvious that crystal superstructures can be affected by other factors, such as the type, length, functional group, and heteroatom content of the guests. This situation implies that the crystal superstructures of the CD complexes are designable through the precise control of interactions between the guests and CD hosts. Nevertheless, there are very few investigations focused on understanding how small differences in the structures of the guests affect the inclusion geometries and binding abilities of CDs, both in solution and the solid state. The nature of these variations could provide valuable insights into the complexity of the intermolecular interactions involving hydrophobic, hydrogen bonding, and π–π stacking interactions in the host–guest systems and serve to establish a correlation between the host–guest geometrical relationships and the molecular recognition abilities of CDs towards guests.

Herein, we report the preparation of six inclusion complexes (**1**–**6** in Scheme 1) of β-CD with 4,4′-vinylenedipyridine, 2,2′-vinylenedipyridine, 1-(2-pyridyl)-2-(4-pyridyl)ethylene, 4,4′-ethylenedipyridine, 4,4′-dithiodipyridine, and 2,2′-dithiodipyridine—and investigated systematically their binding abilities, their geometrical characteristics, and their assembly behavior towards β-CD, both in solution, by ^{1}H NMR spectroscopy and microcalorimetry, and in the solid state, by means of X-ray crystallography.



Scheme 1. Schematic representation of the inclusion complexes (**1**-**6**) of β-CD with 4,4′-vinylenedipyridine, 2,2′-vinylenedipyridine, 1-(2-pyridyl)-2-(4-pyridyl)ethylene, 4,4′-ethylenedipyridine, 4,4′-dithiodipyridine, and 2,2′-dithiodipyridine, respectively.

Abstract in Chinese:

为了系统地研究β-环糊精和结构相近的联吡啶客体的分子键合能力和聚集行为，我们制备得到了 6 个超分子包结配合物，即，β-环糊精/4,4′-乙烯撑联吡啶包结配合物(**1**)、β-环糊精/2,2′-乙烯撑联吡啶包结配合物(**2**)、β-环糊精/2,4′-乙烯撑联吡啶包结配合物(**3**)、β-环糊精/4,4′-乙烷基联吡啶包结配合物(**4**)、β-环糊精/4,4′-联硫基联吡啶包结配合物(**5**)和β-环糊精/2,2′-联硫基联吡啶包结配合物(**6**)，并且使用 X 射线晶体衍射分析、核磁和微量热滴定等方法对这些包结配合物进行了全面的研究。在溶液中，β-环糊精和联吡啶客体能够形成 1:1 的主-客体包结配合物，微量热滴定实验给出了这些包结配合物的配位形成常数(K_S)和热力学参数；二维核磁实验结果显示这些客体分子能够以不同的模式包结到环糊精空腔中。在固态，包结配合物 **1**、**4** 和 **5** 的晶体结构属于三斜晶系(*P*1 空间群)，能够形成 AAAA 型的超分子聚集体。包结配合物 **2**、**3** 和 **6** 则给出了单斜($P2_1$ 空间群)或者正交($C222_1$ 空间群)晶系，进而形成 ABAB 型的超分子聚集体。这些研究结果证明，联吡啶客体中的氮原子位置和连接两个吡啶环之间的桥键的差异能够导致截然不同的配合物晶系和空间群以及不同的主-客体包结模式和热力学参数，这为进一步揭示环糊精的分子识别和聚集机制提供了重要的实验依据。

Results and Discussion

Preparation of Inclusion Complexes and Their Crystal Structures

Bipyridine molecules have very interesting coordination properties and therefore are frequently used as building blocks to construct supramolecular architectures.[33–37] In the present work, we chose 4,4′-vinylenedipyridine, 2,2′-vinylenedipyridine, 1-(2-pyridyl)-2-(4-pyridyl)ethylene, 4,4′-ethylenedipyridine, 4,4′-dithiodipyridine, and 2,2′-dithiodipyridine as guests in order to prepare inclusion complexes with β-CD. These bipyridine guests vary in their constitutions, resulting in broad variations in their inclusion geometries and in the binding behavior of the complexes.

The inclusion complexes **1**–**6** of β-CD with all six bipyridine guests were prepared in aqueous ethanolic solution using a simple method, that is, an EtOH solution (10 mL) of

each guest (1 mmol) was added dropwise to an aqueous solution (40 mL) of β-CD (1 mmol). The turbid solutions were stirred and heated to 50 °C, in order to attain complete dissolution. After cooling down to room temperature, the precipitates which formed were isolated by filtration and washed with H_2O. The resulting solids were dried under vacuum to give powder-like samples. The inclusion complexes of β-CD were characterized by ^{1}H NMR spectroscopy and MALDI time-of-flight mass spectrometry. The inclusion geometries and binding behaviors of the complexes were investigated by ^{1}H ROESY (Rotating frame Overhauser Effect SpectroscopY) NMR spectroscopy and microcalorimetric titrations. Crystals of the complexes were then grown from saturated aqueous solutions. Single crystals of appropriate quality were chosen for X-ray crystallographic analyses.

Solution Investigation

In order to investigate the binding behavior of β-CD with bipyridine guests in aqueous solution, we have performed ^{1}H NMR spectroscopic experiments on the host–guest system at 25 °C in D_2O. First of all, the stoichiometries of the host–guest systems were determined by ^{1}H NMR spectroscopy employing experiments where the molar ratios of guest and β-CD were varied, while the overall molar concentrations of the two components were held constant. A typical Job plot for the β-CD/4,4′-ethylenedipyridine system at 25 °C in D_2O reveals (Figure 1) a minimum at 0.50, indicating the formation of a 1:1 host–guest inclusion complex between β-CD and 4,4′-ethylenedipyridine. Very similar results were obtained in the case of the inclusion complexes of β-CD containing the other guests.

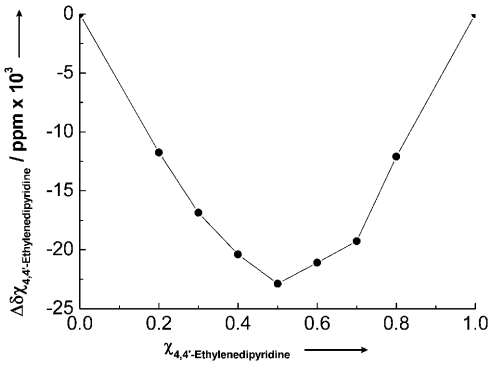


Figure 1. Job plot obtained for β-CD/4,4′-ethylenedipyridine ([β-CD]+[4,4′-ethylenedipyridine] = 5.0×10^{-3} mol dm^{-3}) in D_2O at 25 °C. The changes ($\Delta\delta$) in chemical shifts of the H_β protons on 4,4′-ethylenedipyridine. χ is the molar fraction of 4,4′-ethylenedipyridine.

Next, the changes of chemical shifts of proton probes in the guest molecules in the presence of β-CD were evaluated using the ^{1}H NMR titration method at 25 °C in D_2O. In general, the inclusion of a guest molecule into the CD cavity will result in changes in the chemical shifts of host and/or guest protons.[38–40] We can obtain some important information from these changes in chemical shifts. For instance, Figure 2 shows the protons present in 4,4′-ethylenedipyridine (1.03×10^{-3} mol dm^{-3}) to exhibit significant changes in chemical shifts in the presence of β-CD (0–2.37×10^{-3} mol dm^{-3}). The H_α and H_γ protons in 4,4′-ethylenedipyridine in the presence of β-CD display downfield shifts ($\Delta\delta$) of up to +0.02 and +0.07 ppm, respectively, while the H_β protons reveal upfield shifts ($\Delta\delta$) of up to −0.05 ppm under the same conditions. A possible explanation for these observations is that the interaction between the H_γ protons of 4,4′-ethylenedipyridine and the wall of β-CD is stronger than that between H_α or H_β and the wall. Furthermore, we have also performed the ^{1}H NMR titration experiments of β-CD in the presence of guests at 25 °C in D_2O. Typical ^{1}H NMR titration spectra of β-CD on addition of 4,4′-ethylenedipyridine are shown in Figure 3. The H3 and the H5 protons in β-CD experience upfield shifts ($\Delta\delta$) of about

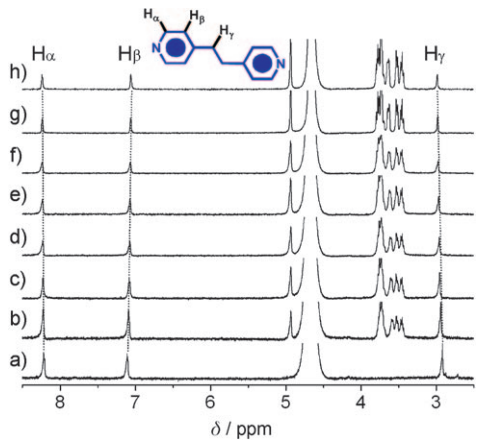


Figure 2. ^{1}H NMR spectra of 4,4′-ethylenedipyridine (1.03×10^{-3} mol dm^{-3}) recorded following the stepwise addition of β-CD (a–h: 0–2.37×10^{-3} mol dm^{-3}) in D_2O at 25 °C.

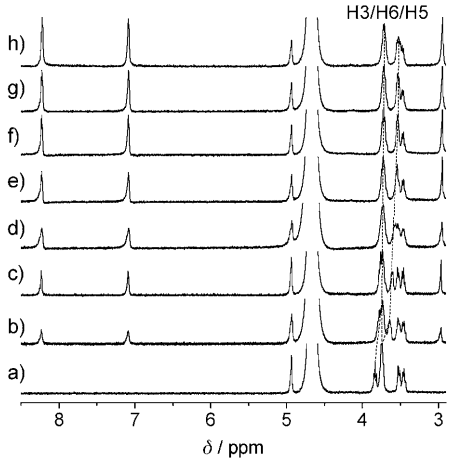


Figure 3. ^{1}H NMR spectra of β-CD (1.02×10^{-3} mol dm^{-3}) recorded following the stepwise addition of 4,4′-ethylenedipyridine (a–h: 0–2.06×10^{-3} mol dm^{-3}) in D_2O at 25 °C.

−0.13 and −0.21 ppm, respectively. In the cases of the other guests, the upfield shifts ($\Delta\delta$) for the H3 and the H5 protons of β-CD are in the order of −0.08 to −0.15 ppm and −0.13 to −0.24 ppm, respectively. These results indicate that the inclusion of an aromatic guest inside the CD cavity can cause major upfield shifts of the H3 and/or the H5 protons on account of the ring currents generated by the aromatic portions of the guests and/or hydrogen bonding interactions between the host and guests.[41]

It is also interesting to note that the complexation of guests with β-CD produces larger upfield shifts for H5 than those for H3. An investigation by Goldberg and co-workers[41] has suggested that the magnitude of the upfield shifts of the CD's H3 and H5 protons, $\Delta\delta$(H3) and $\Delta\delta$(H5), and their relative ratios, $\Delta\delta$(H5)/$\Delta\delta$(H3), can be used, respectively, as a measure of (1) the complex stability and (2) the inclusion depth of the guests within the β-CD cavity, that is, the larger is the value of $\Delta\delta$, the more stable the complex is and the larger the relative ratio of $\Delta\delta$(H5)/$\Delta\delta$(H3) is, the deeper the guest enters inside the cavity. In the experiments reported here, the order of average values of $\Delta\delta$(H3) and $\Delta\delta$(H5) in the presence of a guest under the same conditions is 4,4′-dithiodipyridine > 4,4′-ethylenedipyridine > 1-(2-pyridyl)-2-(4-pyridyl)ethylene > 4,4′-vinylenedipyridine > 2,2′-dithiodipyridine > 2,2′-vinylenedipyridine. This trend indicates that the complex formation constants of guests with β-CD should also follow the above sequence. In fact, the sequence is almost consistent with the results obtained from calorimetric titration experiments. On the other hand, the $\Delta\delta$(H5)/$\Delta\delta$(H3) values of guests with β-CD are around 1.6, a value which indicates that the inclusion depth of the guests inside the β-CD cavity does not display obvious differences. The results obtained from the crystal superstructures, however, show that the depths are variable.

^{1}H ROESY NMR spectroscopy has recently become an important analytical method for investigating the interactions and included geometries between CD hosts and guest molecules. When the guest molecule is included inside the β-CD cavity, the NOE correlations between the protons of the guest molecule and the inner protons (H3 and H5) inside the β-CD cavity can be measured.[38] In order to obtain further evidence about the inclusion geometries of the complexes **1**–**6** in solution, ^{1}H ROESY NMR experiments were performed on them at 25 °C in D_2O. The ROESY spectrum (see Figure S1 a of the Supporting Information) of **1** (3.0×10^{-3} mol dm^{-3}) displays clear NOE cross-peaks between the H3 protons of β-CD and the H_α (peak A), H_β (peak B), and H_γ (peak C) protons of 4,4′-vinylenedipyridine, as well as between H5 and H_α (peak D) and H_β (peak E). All these observations demonstrate that the 4,4′-vinylenedipyridine guest is deeply included into the hydrophobic cavity of β-CD as shown in Figure S1b of the Supporting Information. In the case of **2** (see Figure S2 a of the Supporting Information), the ROESY spectrum of **2** (3.1×10^{-3} mol dm^{-3}) recorded in D_2O reveals NOE cross-peaks between the H3 protons of β-CD and the H_δ (peak A) and H_ε (peak B) protons of 2,2′-vinylenedipyridine, and between the H5 protons of β-CD and the H_α (peak C), H_β (peak D), H_δ (peak E), H_ε (peak F), and H_γ (peak G) protons, indicating distinctly that the 2,2′-vinylenedipyridine guest is also included inside the β-CD cavity. The fact that the correlation (peak E) of H3 with the H_δ protons is slightly weaker than the others suggests that the H_δ protons in 2,2′-vinylenedipyridine should be removed from H3. A possible inclusion geometry for **2** is shown in Figure S2 b of the Supporting Information. For complex **3** (4.6×10^{-3} mol dm^{-3}), the NOE cross-peaks between the H3/H5 protons of β-CD and the H_α/H_η (peak A) and H_ε (peak C) protons of 1-(2-pyridyl)-2-(4-pyridyl)ethylene molecule, and between the H3 protons and the H_δ protons (peak B) are shown in the ROESY spectrum (Figure S3 a of the Supporting Information), indicating that the 1-(2-pyridyl)-2-(4-pyridyl)ethylene molecule is included in the cavity of β-CD. Notably, it shows the interaction between the H3 and the H_δ protons (peak B), implying the 2-pyridyl moiety of 1-(2-pyridyl)-2-(4-pyridyl)ethylene molecule is located on the secondary side of the β-CD cavity. This interesting result indicates that the β-CD can direct the orientation of the 1-(2-pyridyl)-2-(4-pyridyl)ethylene molecule inside the cavity. According to the results of the ROESY NMR experiment, a possible geometry of β-CD with 1-(2-pyridyl)-2-(4-pyridyl)ethylene is given in Figure S3 b of the Supporting Information.

The nonconjugated guests, 4,4′-ethylenedipyridine, 4,4′-dithiodipyridine, and 2,2′-dithiodipyridine have more flexible skeletons than those of the conjugated guests, that is, 4,4′-vinylenedipyridine, 2,2′-vinylenedipyridine, and 1-(2-pyridyl)-2-(4-pyridyl)ethylene. Thus, the nonconjugated guests can be included in the cavity of β-CD with better matching geometries. In the case of the complex **4** (4.7×10^{-3} mol dm^{-3}), its ROESY spectrum (Figure S4 a of the Supporting Information) reveals NOE cross-peaks between the H3/H5 protons of β-CD and the H_α (peak A), H_β (peak B), and H_γ (peak C) protons of 4,4′-ethylenedipyridine molecule. Similarly, the ROESY spectrum (Figure S5 a of the Supporting Information) of the complex **5** (3.4×10^{-3} mol dm^{-3}) shows NOE cross-peaks between the H3/H5 protons of β-CD and the H_α (peak A) and H_β (peak B) protons of 4,4′-dithiodipyridine molecule. For the complex **6** (2.5×10^{-3} mol dm^{-3}), the ROESY spectrum (Figure S6 a of the Supporting Information) reveals NOE cross-peaks between the H5 protons of β-CD and the H_α (peak A) and H_δ (peak B) protons of 2,2′-dithiodipyridine molecule, as well as between the H3 protons and the H_δ (peak C) protons. Based on the results of these ROESY NMR experiments, possible inclusion geometries of β-CD with the three nonconjugated guests are shown in Figures S4 b, S5 b, and S6 b of the Supporting Information, respectively. Although a series of complex geometries may be present in the β-CD inclusion complexes in aqueous solution,[42,43] the inclusion geometries in the systems under investigation should be an optimum one for the various host–guest geometries adopted between β-CD and the bipyridine guests. Therefore, the results of the ^{1}H ROESY NMR experiments serve to establish the correlation between the geometrical features of the inclusion

complexes and the molecular recognition mechanism of β-CD toward bipyridine guests. The different inclusion geometries and strict size/shape fitting relationships between the host and guest explain reasonably well the different binding affinities and guest selectivities of β-CD.

Microcalorimetric titration (ITC) experiments have been performed in aqueous phosphate buffer solutions (pH 7.0) at 25 °C. The formation constants (K_S) and the thermodynamic parameters of the bipyridine guests upon complexation with β-CD are listed in Table 1. The formation constants (K_S) for the inclusion complexation of host with guest decrease in the following order—4,4′-dithiodipyridine > 1-(2-pyridyl)-2-(4-pyridyl)ethylene > 4,4′-ethylenedipyridine > 4,4′-vinylenedipyridine > 2,2′-dithiodipyridine > 2,2′-vinylenedipyridine. We note that the association of β-CD with 4,4′-dithiodipyridine affords the highest formation constant of $1102 \pm 58\,M^{-1}$, a value which is 7.7 times more than that for 2,2′-vinylenedipyridine ($144 \pm 29\,M^{-1}$). This relatively good molecular selectivity can be attributed to strict size/shape matching and hydrophobic interactions between the host and guest. The guests, 4,4′-ethylenedipyridine, 4,4′-dithiodipyridine, and 2,2′-dithiodipyridine, have more flexible skeletons than those of 4,4′-vinylenedipyridine and 2,2′-vinylenedipyridine. They can find a match with the β-CD cavity more easily by changing their geometries, leading to higher formation constants except in the case of 2,2′-dithiodipyridine. Furthermore, the guests with nitrogen atoms in the 2,2′-positions afford lower formation constants compared with guests which have nitrogen atoms in their 2,4′- and 4,4′-positions, most likely because of their lower hydrophobicities.

Table 1. Complex formation constant (K_S), standard enthalpy ($\Delta H°$), and entropy changes ($T\Delta S°$) for the inclusion complexation of β-CD with bipyridine guests in phosphate buffer solution (pH 7.0) at 25 °C.

Host[a]	Guest[b]	K_S [M^{-1}]	$-\Delta G°$ [kJ mol^{-1}]	$-\Delta H°$ [kJ mol^{-1}]	$T\Delta S°$ [kJ mol^{-1}]
β-CD	4,4′-Vinylenedipyridine	327 ± 63	14.3 ± 0.1	1.8 ± 0.2	12.6 ± 0.2
β-CD	2,2′-Vinylenedipyridine	144 ± 29	12.3 ± 0.4	3.6 ± 0.6	8.6 ± 1.0
β-CD	1-(2-Pyridyl)-2-(4-pyridyl)ethylene	572 ± 26	15.8 ± 0.1	2.2 ± 0.1	13.5 ± 0.1
β-CD	4,4′-Ethylenedipyridine	523 ± 14	15.5 ± 0.3	13.7 ± 0.2	1.9 ± 0.5
β-CD	4,4′-Dithiodipyridine	1102 ± 58	17.3 ± 1.0	10.8 ± 0.3	6.6 ± 1.3
β-CD	2,2′-Dithiodipyridine	255 ± 37	13.8 ± 2.5	29.8 ± 2.9	−16.0 ± 0.4

[a] [Host] = 11.789–13.163 mM. [b] [Guest] = 1.008–1.306 mM.

The thermodynamic parameters listed in Table 1 show that complex formation of bipyridine guests with β-CD in phosphate buffer solution is accompanied by favorable enthalpic changes and positive entropic contributions, except in the case of 2,2′-dithiodipyridine ($T\Delta S° = -16.0 \pm 0.4$ kJ mol^{-1}). It is well-known[8] that the negative enthalpy changes can be accounted for by the hydrogen bonding and van der Waals interactions arising from the size/shape matching between the host and guest. When the guests are embedded in the cavity of β-CD, the previously existing hydrogen bonding between the nitrogen atoms and water molecules will become weaker or even non existent as a result of the hydrophobicity inside the β-CD cavity. Furthermore, the larger K_S values for the guests with nitrogen atoms in their 2,4′- and 4,4′-positions as compared with the guests which have nitrogen atoms in their 2,2′-positions mean that there exists a more extensive desolvation effect for the guests with nitrogen atoms in their 2,4′- and 4,4′-positions upon complexation with β-CD. The difference in desolvation effect of the guests with nitrogen atoms in their 2- and 4-positions can be ascribed to their differing orientations within the β-CD cavity, cf., the ROESY experiments. In the case of 2,2′-dithiodipyridine with β-CD, the larger entropy loss ($T\Delta S° = -16.0 \pm 0.4$ kJ mol^{-1}) may be attribute to the smaller geometrical change and/or weaker desolvation effect between the host and guest as compared with other complexes. These results help us understand the thermodynamic origins at work in the process of the molecular inclusion.

Crystal Superstructures

Direct evidence for the formation of inclusion complexes **1**–**6** has been obtained in the solid state. Single crystals of the β-CD complexes **1**, **4**, and **5** were triclinic and had space group $P1$. The single crystal for the complex **2** was monoclinic and had space group $P2_1$. The single crystals for the complexes **3** and **6** were orthorhombic and had space group $C222_1$. The crystal data and experimental and refinement parameters for the superstructures **1**–**6** are listed in Table 2 and their unit cells are shown in Figure 4 and Figure S9 of the Supporting Information. In these crystal superstructures, the skeleton of β-CD with its approximate seven-fold axis and toroidal shape, as well as the coplanarity of the seven glycosidic oxygen atoms, are not significantly changed with the inclusion of the bipyridine molecules. There is a little conformational variability in the β-CD torus, that is, the two primary OH groups for complexes **1** and **2** and one primary OH group for complex **4** are disordered over two sites, one site a (+)-gauche conformer (the primary OH groups point toward the interior of β-CD), and the other a (−)-gauche conformer (the primary OH groups point toward the exterior of β-CD). Some H_2O molecules are distributed throughout the unit cells of crystals **1**–**6**, and these H_2O molecules are almost located on the exterior of the β-CD cavities, an observation which indicates the presence of strong hydrophobic interactions between the β-CD cavities and guests.

In the unit cell of **1** (Figure 4a and Figure S9a of the Supporting Information), two 4,4′-vinylenedipyridine molecules with the *trans* configuration are embedded into two β-CD cavities in different directions, forming a head-to-head dimer arrangement, which is somewhat different from the inclusion complexes produced by β-CD and guests in the solid state.[20a] In particular, there is an H-bonding interaction between an *ortho*-hydrogen atom (H_α) in pyridine ring A of 4,4′-vinylenedipyridine molecule and an O atom on the

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Table 2. Crystal data, experimental and refinement parameters for crystals **1**–**6**.

	Crystal **1**	Crystal **2**	Crystal **3**	Crystal **4**	Crystal **5**	Crystal **6**
Molecular Formula	$C_{97}H_{153}N_2O_{94}$	$C_{108.50}H_{162}N_4O_{92.50}$	$C_{54}H_{101.25}N_2O_{45.50}$	$C_{110}H_{170}N_4O_{96}$	$C_{104}H_{196}N_4O_{90}S_4$	$C_{52}H_{105}N_2O_{48.50}S_2$
M_r [g mol^{-1}]	2851.21	3002.42	1506.62	3084.50	3070.89	1598.50
Crystal System	Triclinic	Monoclinic	Orthorhombic	Triclinic	Triclinic	Orthorhombic
Space Group	*P*1	$P2_1$	$C222_1$	*P*1	*P*1	$C222_1$
Z	1	2	8	1	1	8
a [Å]	15.2244(12)	15.3151(9)	19.413(3)	15.216(2)	15.2813(12)	19.382(4)
b [Å]	15.4858(12)	31.5498(18)	23.698(4)	15.514(2)	15.4039(12)	23.852(5)
c [Å]	18.0318(15)	15.3818(9)	32.864(6)	17.791(2)	17.8904(14)	32.311(7)
α [°]	99.619(2)	90	90	99.249(2)	99.662(1)	90
β [°]	113.2770(10)	101.661(1)	90	112.618(2)	113.423(1)	90
γ [°]	102.8770(10)	90	90	103.041(2)	102.481(1)	90
V [Å^3]	3649.2(5)	7278.9(7)	15119(5)	3630.7(8)	3618.4(5)	14937(5)
ρ_{calcd} [g cm^{-3}]	1.297	1.370	1.324	1.411	1.409	1.422
F (000)	1501.0	3162.0	6426.0	1626.0	1632.0	6808.0
T [K]	100(2)	100(2)	100(2)	100(2)	100(2)	100(2)
μ (M_o K_α) [mm^{-1}]	0.118	0.122	0.117	0.126	0.178	0.179
Crystal Dimensions [mm]	0.60×0.40×0.40	0.40×0.20×0.20	0.40×0.40×0.40	0.60×0.40×0.40	0.60×0.40×0.40	0.60×0.40×0.40
No. of Reflections Collected	14554	15176	18455	20154	24893	13203
No. of Unique Reflections	9589	11337	11758	15385	18111	11534
R_1 (I > 2σ (I))	0.0761	0.0662	0.0852	0.0769	0.0962	0.1059
wR_2 (all data)	0.2173	0.1951	0.2407	0.2343	0.2853	0.2926

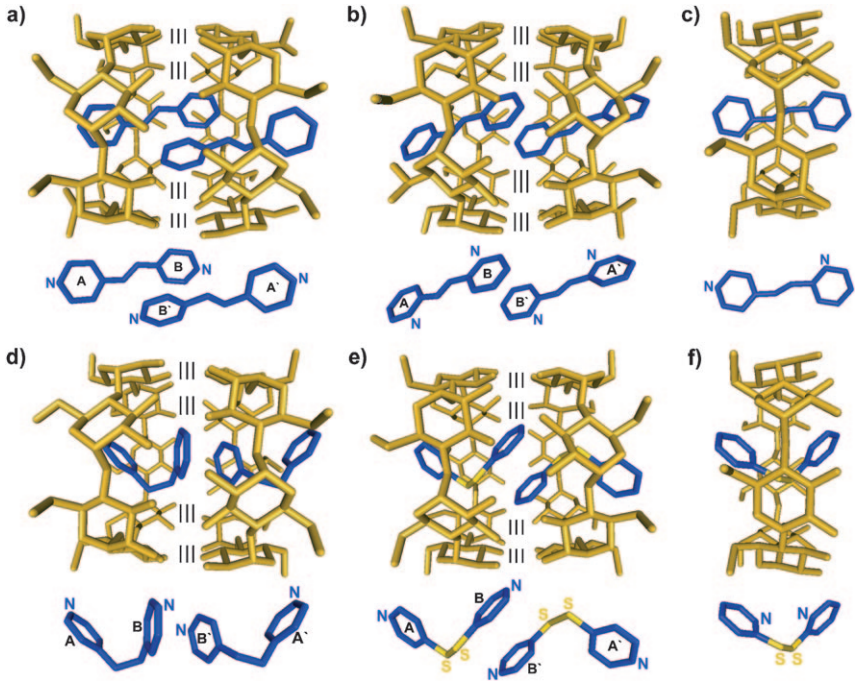

Figure 4. a–f) The cell superstructures of inclusion complexes **1**–**6**, respectively. The hydrogen atoms and H_2O molecules are omitted for the sake of clarity. β-CDs are colored orange and the bipyridine guests are colored blue except, for the sulfur atoms which are colored yellow.

primary side of the β-CD ($d_{C-H\cdots O}$ = 2.41 Å), which fixes the orientation of the guest molecule inside the β-CD cavity. This dimerization can be attributed to the cooperative interactions of ten H-bonding interactions between the secondary OH groups of two adjacent β-CD units, as well as the π–π stacking of two pyridine rings B and B′ (13° dihedral angle and 3.72 Å centroid–centroid separation) in the two guest molecules. Furthermore, the dihedral angles between the plane of these pyridine rings A (A′) or B (B′) in 4,4′-vinylenedipyridine and the heptagons composed of seven glycosidic oxygen atoms (O4-heptagon) in β-CD are 67° (101°) or 89° (84°), and the centroid–centroid separations between them are 1.43 (3.63) Å or 5.19 (3.73) Å, indicating that one 4,4′-vinylenedipyridine molecule with pyridine rings A and B is included shallowly in a β-CD cavity while the other one with pyridine rings A′ and B′ is deeply included in the cavity. The dihedral angle between the pyridine rings A (A′) and B (B′) in 4,4′-vinylenedipyridine is 40° (39°). However, the crystal superstructure[44] of 4,4′-vinylenedipyridine (Figure 5), obtained from H_2O, shows that the dihedral angle between the pyridine rings A and B is 20°. The 4,4′-vinylenedipyridine molecules are self-assembled through three H-bonding interactions linked by H_2O molecules

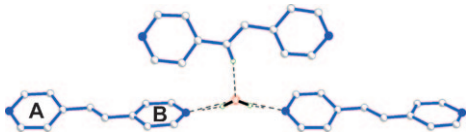

Figure 5. The crystal superstructure of 4,4′-vinylenedipyridine.

($d_{C-H\cdots O}=2.39$ Å, $d_{O-H\cdots N}=2.00$ Å, $d_{O-H\cdots N}=2.05$ Å). No π–π interactions can be found in the superstructure. These results indicate that the geometry and packing mode of the guest molecule can be altered by the complexation inside the cavity of β-CD.

In the case of complexes **4** and **5** with nonconjugated guests (Figures 4d and 4e and Figures S9d and S9e of the Supporting Information), although their crystal system and space group are the same as that for complex **1**, the inclusion geometry of host and guest in the superstructures **4** and **5** have several differences compared with that in **1**. Two 4,4′-ethylenedipyridine or two 4,4′-dithiodipyridine molecules with the *cis* configuration are included inside the cavities of β-CD in two different directions, forming dimeric superstructures. Some key dihedral angles and centroid–centroid separations in the dimers are listed in Tables 3 and 4, respectively, indicating that the two 4,4′-ethylenedipyridine molecules are included shallowly in the cavities, whereas one 4,4′-dithiodipyridine molecule with A and B pyridine rings is included shallowly, while the other one with A′ and B′ pyridine rings is located almost in the middle of the cavity. In the unit cell of **4**, the two β-CDs of the dimer are connected by ten H-bonding interactions between the OH groups on the secondary faces of the β-CD rings. In particular, there are three H-bonding interactions between the host and guest, that is, an H atom (H_i) in 4,4′-ethylenedipyridine and a glycosidic O atom in the β-CD ring ($d_{C-H\cdots O}=2.55$ Å), a N atom in 4,4′-ethylenedipyridine and a secondary OH group in the β-CD ring ($d_{O-H\cdots N}=2.61$ Å), and the N atom and an H atom in a glucopyranose ring of adjacent β-CD ($d_{C-H\cdots N}=2.45$ Å)—and a weak π–π interaction between two pyridine rings B and B' in a face-to-face arrangement (17° dihedral angle and 3.89 Å centroid–centroid separation). Hydrogen bonding interactions involving glycosidic O atom are not common in crystal superstructures of β-CD with guest molecules. In the unit cell of **5**, the two β-CD rings in the dimer are connected by five H-bonding interactions between the OH groups on the secondary sides of the β-CD rings. There are two H-bonding interactions between the host and guest, that is, a N atom in 4,4′-dithiodipyridine and a secondary OH group in an adjacent β-CD ring ($d_{O-H\cdots N}=2.53$ Å), as well as an S atom in 4,4′-dithiodipyridine and an H atom in a glucopyranose ring of β-CD ($d_{C-H\cdots S}=2.93$ Å) and the π–π interaction of two pyridine rings B and B' in a face-to-face arrangement (4° dihedral angle and 3.76 Å centroid–centroid separation). We attribute the different guest orientations to the stabilization afforded by the H-bonding interaction between the guest and host β-CD.

Table 3. Some dihedral angles in the pyridine rings A (A′) and B (B′), and O4-heptagon of crystal superstructures **1**–**6**.

Dihedral Angle [°]	**1**	**2**	**3**	**4**	**5**	**6**
A/B	40	1	23	51	80	99
B′/A′	39	15	–	47	77	–
A (A′)/O4-heptagon	67 (101)	64 (65)	85	18 (33)	59 (58)	125
B (B′)/O4-heptagon	89 (84)	65 (65)	90	42 (37)	50 (48)	52
B/B′	13	1	21	17	4	32

Table 4. Some centroid-centroid separations in the pyridine rings A (A′) and B (B′), and O4-heptagon of crystal superstructures **1**–**6**.

Centroid–Centroid Separation [Å]	**1**	**2**	**3**	**4**	**5**	**6**
A (A′)/O4-heptagon	1.43 (3.63)	3.92 (3.46)	3.71	0.94 (3.87)	2.72 (3.27)	2.96
B (B′)/O4-heptagon	5.19 (3.73)	2.67 (3.04)	4.01	3.84 (1.10)	3.46 (3.11)	3.16
B/B′	3.72	3.73	3.80	3.89	3.76	3.02

Superstructure **2** belongs to monoclinic crystal system (Figure 4b and Figure S9b of the Supporting Information). Two 2,2′-vinylenedipyridine molecules with *trans* configurations are included inside two β-CD cavities, forming a head-to-head dimer arrangement. The seven H-bonding interactions between secondary OH groups in two adjacent β-CD units and the π–π stacking between two pyridine rings B and B′ (1° dihedral angle and 3.73 Å centroid–centroid separation) in the 2,2′-vinylenedipyridine molecules can be found in the dimer. The dihedral angles between the plane of the pyridine rings A (A′) or B (B′) in the 2,2′-vinylenedipyridine molecule and the O4-heptagon in β-CD are 64° (65°) or 65° (65°), and the centroid–centroid separations between them are 2.92 (3.46) Å or 2.67 (3.04) Å, values which indicate that the two 2,2′-vinylenedipyridine molecules are located almost at the middle of the β-CD cavities. This result is different from that in superstructure **1**.

Compared with complexes **1**, **2**, **4**, and **5**, the unit cells for superstructures **3** and **6** (Figures 4c, 4f, and Figures S9c and S9f of the Supporting Information) show only one inclusion geometry between the host and the guests. Although they do not form dimers in the unit cells, their complexes self-assemble to form the dimeric superstructures as shown in Figure 6 and Figure S10 of the Supporting Information. In the case of complex **3**, the 1-(2-pyridyl)-2-(4-pyridyl)ethylene molecule with *trans* configuration is located on one side

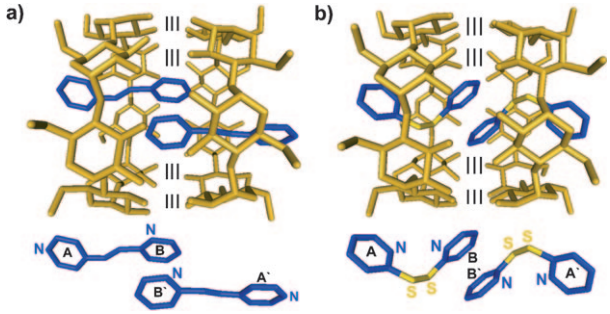

Figure 6. The dimeric superstructures of the inclusion complexes a) **3** and b) **6**. The H atoms and H_2O molecules are omitted for the sake of clarity. The β-CD rings are colored orange and the bipyridine guests are colored blue, except for the sulfur atoms which are highlighted in yellow.

of the β-CD cavity. The dihedral angles between the plane of the pyridine rings A or B in the 1-(2-pyridyl)-2-(4-pyridyl)ethylene molecule and the O4-heptagon in β-CD are 85° or 90°, respectively, and the centroid–centroid separations between them are 3.71 or 4.01 Å. There are 12 H-bonding interactions between secondary OH groups of two adjacent β-CD units and a weak π–π stacking between the two pyridine rings B and B′ (21° dihedral angle and 3.80 Å centroid–centroid separation) of 1-(2-pyridyl)-2-(4-pyridyl)ethylene in the dimeric superstructure. For the complex **6**, the 2,2′-dithiodipyridine molecule with *cis* configuration is located almost at the middle of the β-CD cavity. The dihedral angle between the plane of the pyridine rings A or B in the 2,2′-dithiodipyridine molecule and the O4-heptagon in β-CD is 125° or 52°, and the centroid–centroid separations between them are 2.96 or 3.16 Å. There are 16 H-bonding interactions between secondary OH groups of two adjacent β-CD units and no π–π stacking between the two pyridine rings B and B′ (32° dihedral angle and 3.02 Å centroid–centroid separation) of the 2,2′-dithiodipyridine molecules in the dimer. Interestingly, two H-bonding interactions ($d_{C-H\cdots S}=2.82$ Å and $d_{C-H\cdots S}=2.82$ Å) between the S atoms and H atoms (H_β) in the 2,2′-dithiodipyridine molecules are present in the dimeric superstructure.

The head-to-head dimers of the complexes **1**–**6** self-assemble to form polymeric supermolecules, by means of an H-bonding network (see Figure 7 and Figure S11 of the Supporting Information). For superstructures **1**, **4**, and **5**, each dimer connects tightly with the adjacent dimers through a relatively complicated inter dimer H-bonding system involving the β-CD's C6-OHs, the guest molecules, and H_2O molecules. Notably, there is a kind of H-bonding interaction ($d_{O-H\cdots N}=1.83$ Å) between a N atom in the pyridine ring A of 4,4′-vinylenedipyridine in the dimer and a primary OH group in adjacent dimers in the superstructure **1**. These interconnections enable the dimers to form a linear supramolecular aggregate (AAAA type) in the solid state of the complexes **1**, **4**, and **5**. In the case of complex **2**, the adjacent head-to-head dimers self-assemble, resulting in the formation of wave-like polymeric supermolecules (ABAB type) involving inter dimer H-bonding interactions. In particular, there is a kind of H-bonding interaction between an H atom (H_α) in the pyridine ring B of 2,2′-vinylenedipyridine molecule in the dimer and a primary O atom in the adjacent dimer ($d_{C-H\cdots O}=2.43$ Å). In the case of the superstructures **3** and **6**, the adjacent head-to-head dimers self-assemble to form large wave-like polymeric supermolecules (ABAB type) involving inter dimer H-bonding interactions. Moreover, the strong H-bonding network formed by the OH groups of β-CD, guest molecules, and intervening H_2O molecules stabilize the aggregations **1**–**6** and further extend the aggregations to a higher architecture level. That is to say, H-bonding interactions play a central role in the formation of the polymeric supermolecules.

The crystallographic investigations of the inclusion complexes **1**–**6** of β-CD with bipyridine molecules have demonstrated that the guest molecules are enclosed inside the cavity of β-CD by hydrophobic and H-bonding interactions. In the present examples, the H-bonding interactions (especially for the C–H···O ones) between the host and guest act as a major driving force for the formation of the supramolecular species. It has already been demonstrated that C–H···O interactions are an important consideration in many biological situations and in supramolecular systems.[45,46] High-level theoretical investigations have provided computational support for interactions of 2–3 kcal mol^{-1} between α-CH bonds and peptide carbonyl O atoms in neutral systems such as amides, dimerizations, and protein folding.[46b] As the complexation of superstructures **1**–**6** occur in aqueous media, the driving force coming from numerous C–H···O hydrogen bonding interactions plays a substantial role. Accordingly, we can also deduce that the different arrangements of the guest molecules in the β-CD cavities can be ascribed to the differences of N atom position and bridge-bond links between the two pyridine rings in the bipyridine guests. In the com-

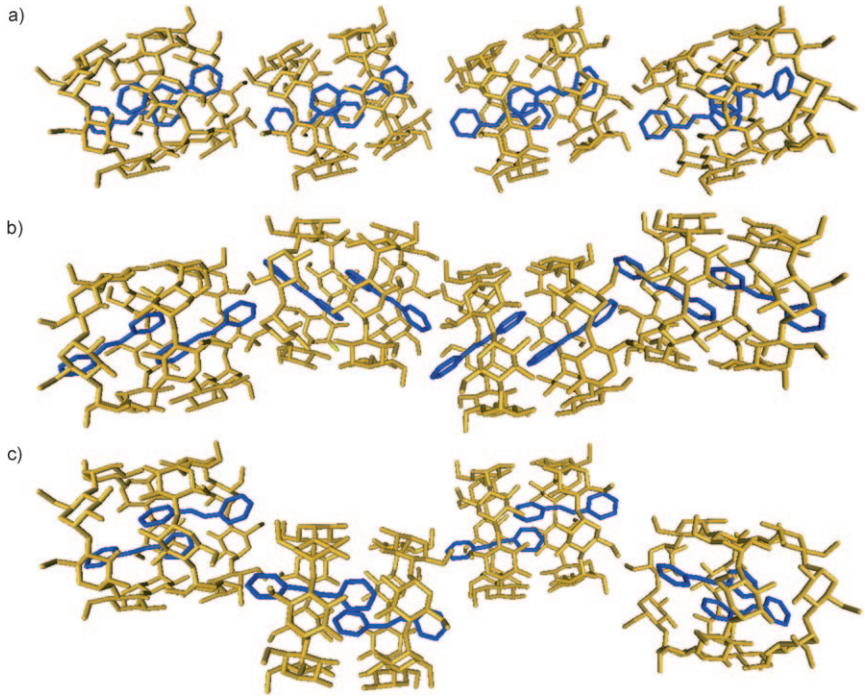

Figure 7. The packing arrangements of the complexes a) **1**, b) **2**, and c) **3**. The H atoms and H_2O molecules are omitted for the sake of clarity. The β-CD rings are colored orange and the bipyridine guests are colored blue.

plexes **1**, **4**, and **5**, the guest molecules possessing N atoms at their 4,4′-positions are included inside the β-CD cavities in two different orientations, thus leading to an "ordered" spatial arrangement of the resultant aggregates (AAAA type). However, in the superstructures **2**, **3**, and **6**, the bipyridine guests, possessing N atoms in their 2,2′- or 2,4′-positions, are included inside the β-CD cavity, which then form a "less-ordered" spatial arrangement of the aggregates (ABAB type). Thus, the present crystal superstructures of the complexes **1**–**6** not only shed significant light on solution work, but they also imply that structural features discussed in this section may be the essence of the molecular recognition of β-CD with the bipyridine molecules. These results provide valuable insight for the understanding of the spatial topology of biotic acceptors with different model substrates in the solid state, as well as on the inclusion complexation mechanism of β-CD with structurally similar guests.

Conclusions

The binding behavior and geometrical properties of β-CD complexes with structurally similar bipyridine molecules have been investigated in both solution and the solid state. It was of particular interest to us to investigate how and to what extent the difference of heteroatom position and bridge-bond links on the bipyridine framework of the guests affects the geometrical properties, binding ability, and self-assembly behavior of CD. Therefore, we sought to elucidate the correlations between the binding mode and the thermodynamic parameters of the host–guest complexation. The NMR and microcalorimetry investigations indicate that β-CD and bipyridine molecules can form 1:1 host–guest inclusion complexes with moderate complex formation constants. Unexpectedly, however, the guest molecules display different inclusion geometries in the β-CD cavity in aqueous solution, resulting in variable molecular recognition abilities by β-CD. The crystal structures for the complexes **1**, **4**, and **5** present "ordered" supramolecular aggregates (AAAA type), in which the guest molecules with two orientations are located in the β-CD cavities. By contrast, the complexes **2**, **3**, and **6** give "less-ordered" supramolecular aggregates (ABAB type). The complexation of β-CD with the guests is driven by H-bonding interactions. The H-bonding interactions between the host and guest result in the remarkable differences of both the guest shape and the location in the cavity, supporting significantly the induced-fit concept. These new observations, along with the easy synthesis of β-CD/bipyridine complexes, indicate that, with judicious design, highly ordered supramolecular arrays can be achieved conveniently in a controllable way, a situation which is useful for understanding of supramolecular recognition and aggregation phenomena on a more global scale.

Experimental Section

Materials and Instruments

β-Cyclodextrin (β-CD), 4,4′-vinylenedipyridine ($pK_{a1}=4.8$ and $pK_{a3}=5.9$),[47] 2,2′-vinylenedipyridine, 1-(2-pyridyl)-2-(4-pyridyl)ethylene, 4,4′-ethylenedipyridine, 4,4′-dithiodipyridine ($pK_{a1}=4.0$ and $pK_{a2}=5.1$),[48] and 2,2′-dithiodipyridine ($pK_{a1}<1.0$ and $pK_{a2}=2.5$)[48] were purchased from Aldrich and used as received. Based on the structural similarities of these bipyridine guests, the pH values used for the ^{1}H NMR and microcalorimetric titration experiments were well removed from the pK values at which protonation of the guests occurs. Thus, the complication of having more than one species of guest presented in the solutions was avoided.[41] ^{1}H NMR spectra were recorded on a Brüker Avance 500 spectrometer at 25 °C using D_2O as the solvent. The pD values of the solutions in the NMR experiments were determined to be about 6.7. Under the current conditions, the nitrogen atoms in the bipyridine guests will not be protonated. Chemical shifts are reported as parts per million (ppm) downfield from the signal of Me_4Si as internal standard for ^{1}H NMR spectroscopy. High-resolution matrix-assisted laser desorption/ionization spectra (HR-MALDI) were measured on an AppliedBiosystems DE-STR MALDI time-of-flight mass spectrometer. The reported molecular mass (m/z) values were the most abundant monoisotopic mass. An isothermal calorimeter (MicroCal Inc., Model No.: VP-ITC) was used for all microcalorimetric experiments (pH 7.0). All solutions were degassed and thermostatted using a ThermoVac accessory prior to the titration experiments. The X-ray intensity data were collected on a Bruker Smart 1000 CCD-based diffractometer at $T=100$ (2) K. The structures were solved by using the direct method and refined, employing full-matrix least squares on F^2 (Siemens, SHELXTL).

Syntheses

Inclusion Complex 1 of β-CD with 4,4′-Vinylenedipyridine: An ethanolic solution (10 mL) of 4,4′-vinylenedipyridine (0.18 g, 1 mmol) was added dropwise to an aqueous solution (40 mL) of β-CD (1.13 g, 1 mmol) and the mixture was stirred at 50 °C for 5 h. The solution was cooled to room temperature, and the precipitate which formed was filtrated and washed with H_2O. The product was dried in vacuo to give a colorless powder complex **1** (1.02 g, 78 %). ^{1}H NMR (500 MHz, D_2O, TMS): $\delta=3.46$–3.50 (m, 7H), 3.53–3.56 (m, 7H), 3.65–3.68 (m, 7H), 3.75–3.82 (m, 21H), 4.96–4.97 (d, 7H), 7.26 (s, 2H), 7.47–7.48 (d, 4H), 8.42–8.43 ppm (d, 4H); MS (HR-MALDI): calcd for $C_{54}H_{80}O_{35}N_2$ $m/z=1317.2054$, found $m/z=1316.2837$ [M^+].

Inclusion Complex 2 of β-CD with 2,2′-Vinylenedipyridine: The colorless inclusion complex **2** (0.97 g, 74 %) was prepared from β-CD (1.13 g, 1 mmol) and 2,2′-vinylenedipyridine (0.18 g, 1 mmol), employing procedures similar to those described above. ^{1}H NMR (500 MHz, D_2O, TMS): $\delta=3.44$–3.48 (m, 7H), 3.51–3.54 (m, 7H), 3.71–3.77 (m, 21H), 3.81–3.85 (m, 7H), 4.94–4.95 (d, 7H), 7.27–7.29 (m, 2H), 7.43 (s, 2H), 7.58–7.59 (d, 2H), 7.77–7.80 (m, 2H), 8.42–8.43 ppm (d, 2H); MS (HR-MALDI): calcd for $C_{54}H_{80}O_{35}N_2$ $m/z=1317.2054$, found $m/z=1316.3521$ [M^+].

Inclusion Complex 3 of β-CD with 1-(2-Pyridyl)-2-(4-pyridyl)ethylene: The grayish inclusion complex **3** (0.89 g, 68 %) was prepared from β-CD (1.13 g, 1 mmol) and 1-(2-pyridyl)-2-(4-pyridyl)ethylene (0.18 g, 1 mmol), employing procedures similar to those described above. ^{1}H NMR (500 MHz, D_2O, TMS): $\delta=3.41$–3.51 (m, 14H), 3.64–3.79 (m, 28H), 4.91–4.92 (d, 7H), 7.22–7.24 (m, 1H), 7.30–7.31 (d, 2H), 7.46–7.47 (d, 2H), 7.50–7.51 (d, 1H), 7.72–7.75 (m, 1H), 8.37–8.39 ppm (m, 3H); MS (HR-MALDI): calcd for $C_{54}H_{80}O_{35}N_2$ $m/z=1317.2054$, found $m/z=1316.2469$ [M^+].

Inclusion Complex 4 of β-CD with 4,4′-Ethylenedipyridine: The colorless inclusion complex **4** (1.06 g, 81 %) was prepared from β-CD (1.13 g, 1 mmol) and 4,4′-ethylenedipyridine (0.18 g, 1 mmol), employing procedures similar to those described above. ^{1}H NMR (500 MHz, D_2O, TMS): $\delta=2.98$ (s, 4H), 3.43–3.53 (m, 21H), 3.66–3.73 (m, 42H), 4.92–4.93 (d, 7H), 7.04–7.05 (d, 4H), 8.23–8.24 ppm (d, 4H); MS (HR-MALDI): calcd for $C_{54}H_{82}O_{35}N_2$ $m/z=1319.2213$, found $m/z=1318.4428$ [M^+].

Inclusion Complex 5 of β-CD with 4,4′-Dithiodipyridine: The colorless inclusion complex **5** (1.00 g, 74%) was prepared from β-CD (1.13 g, 1 mmol) and 4,4′-dithiodipyridine (0.22 g, 1 mmol), employing procedures similar to those described above. ^{1}H NMR (500 MHz, D_2O, TMS): $\delta =$ 3.42–3.53 (m, 21H), 3.66–3.73 (m, 21H), 4.91–4.92 (d, 7H), 7.38–7.39 (d, 4H), 8.32–8.33 ppm (d, 4H); MS (HR-MALDI): calcd for $C_{52}H_{78}O_{35}N_2S_2$ $m/z = 1355.2981$, found $m/z = 1354.3167$ [M^+].

Inclusion Complex 6 of β-CD with 2,2′-Dithiodipyridine: The colorless inclusion complex **6** (0.97 g, 72%) was prepared from β-CD (1.13 g, 1 mmol) and 2,2′-dithiodipyridine (0.22 g, 1 mmol), employing procedures similar to those described above. ^{1}H NMR (500 MHz, D_2O, TMS): $\delta =$ 3.42–3.46 (m, 7H), 3.49–3.51 (m, 7H), 3.64–3.69 (m, 21H), 3.77–3.81 (m, 7H), 4.91–4.95 (m, 7H), 7.20–7.21 (d, 2H), 7.50–7.52 (d, 2H), 7.63–7.66 (m, 2H), 8.29–8.30 ppm (d, 2H); MS (HR-MALDI): calcd for $C_{52}H_{78}O_{35}N_2S_2$ $m/z = 1355.2981$, found $m/z = 1354.3353$ [M^+].

Preparation and Data Collection of Crystals 1–6: A powdered sample of the complex was dissolved in hot H_2O to make a saturated solution, which was then cooled to room temperature. After removing any precipitates by filtration, a small amount of H_2O was added to the filtrate. The resultant solution was kept at room temperature for several days. Crystals were collected for X-ray crystallographic analyses. The crystal data, experimental and refinement parameters for the complexes **1–6** are shown in Table 2. Because of the occurrence of many disordered H_2O molecules in the crystals, some of the oxygen atoms in these disordered H_2O molecules did not give reasonable O–H bond lengths. For the β-CD and guests, all non-hydrogen atoms were refined anisotropically and hydrogen atoms were placed at idealized positions in a riding model.

CCDC 610479 for **1**, CCDC 629367 for **2**, CCDC 629365 for **3**, CCDC 610480 for **4**, CCDC 629363 for **5**, CCDC 629364 for **6**, and CCDC 629366 for 4,4′-vinylenedipyridine contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk/data_request/cif.

General Methods

Job Plots: Typically, the total concentrations of guest and β-CD were maintained at 1.0 ~5.0×10^{-3} mol dm^{-3} in D_2O, while the molar ratios of guest and β-CD were varied from 1:0 to 0:1 in steps of 0.1. The ^{1}H NMR spectra of the samples were recorded at 25 °C. The Job plots were drawn based on the induced chemical shifts of the observed protons in the guest and β-CD, respectively.

^{1}H NMR Titration Experiments: Typically, a sample of guest (host) was dissolved in D_2O (generally concentrations of about 0.5–1.0×10^{-3} mol dm^{-3} were used). A portion of this solution was used as guest (host) NMR sample, and the remainder was used to dissolve a sample of the host (guest), so that the guest (host) concentration remained constant throughout the titration. Successive aliquots of the host (guest) solution (about 0–2.0×10^{-3} mol dm^{-3}) were added to the guest (host) NMR sample, and ^{1}H NMR spectra were recorded after each addition at 25 °C.

Microcalorimetric Titration: The microcalorimetric titrations were performed using an isothermal titration microcalorimeter at atmospheric pressure and 25 °C in aqueous phosphate buffer solution (pH 7.0). In each run, a buffer solution of the β-CD host in a 0.250 mL syringe was sequentially injected with stirring at 300 rpm into a buffer solution of the guest in the sample cell (1.4 mL volume). Each titration experiment was comprised of 30 successive injections. A control experiment was performed to determine the heat of dilution by injecting a host buffer solution into a pure buffer solution, containing no guest. The dilution enthalpy was subtracted from the apparent enthalpy obtained in each titration run, and the net reaction enthalpy was analyzed by using the "one-set-of-binding-sites" model. The Origin software (Microcal) was used to determine simultaneously the complex formation constant (K_S) and reaction enthalpy (ΔH^0) with the standard derivation on the basis of the scatter of data points from a single titration experiment. Two independent titration experiments were performed to afford self-consistent parameters and give the averaged values.

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