Review

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Molecular Selective Binding and Nanofabrication of Cucurbituril/Cyclodextrin Pairs

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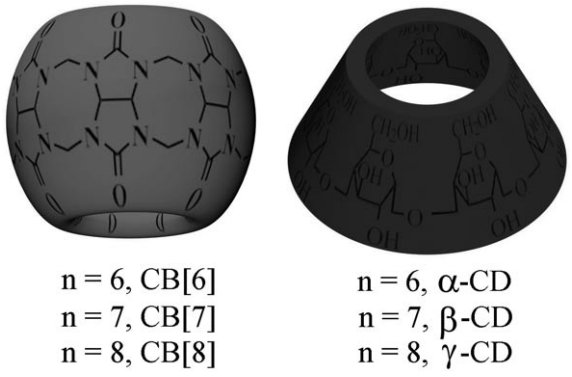
Abstract: Cucurbiturils (CBs) and cyclodextrins (CDs) are two important classes of macrocyclic molecules, both of which have the capability of forming stable complexes with various molecular or ionic substrates. These capabilities consequently make them attractive as both receptors for molecular recognition and building blocks for the construction of nano-scaled supramolecular systems. This review mainly deals with representative contributions in comparative studies of selective binding and molecular assembly behaviors of cucurbiturils and cyclodextrins possessing different types of hydrophobic cavities. It also gives a description of the construction of nanometer-scaled supramolecular architectures through the cooperative assembly employing cucurbiturils and cyclodextrins, as well as their functions. This review will be addressed to students and researchers interested in the supramolecular chemistry of cucurbiturils and cyclodextrins, especially that involving these two classes of macrocyclic receptors in a single system.

Keywords: cucurbiturils · cyclodextrins · nanofabrication · selective binding · supramolecular chemistry

1. Introduction

Cucurbiturils (CBs) and cyclodextrins (CDs) are two of the most important classes of macrocyclic compounds within the field of supramolecular chemistry, and have attracted more and more interest owing not only to their ability to successfully bind with various inorganic/organic/biological molecules and ions in both aqueous solution and the solid state, but also to their potential applications in the construction of supramolecular nanoarchitectures with unique material and biological properties.[1–15] It should be noted that the cavities of cucurbiturils and cyclodextrins, although both hydrophobic, are different to some extent (Scheme 1). For example, cucurbiturils are a class of cyclic compounds composed of mainly 6–8 glycoluril units linked by methylene bridges, and the shape of their cavity resembles that of a pumpkin. On the other hand, cyclodextrins are a class of cyclic oligosaccharides with 6–8 D-glucose units linked by α-1,4-glucose bonds, and the shape of CD cavities, in their most symmetrical forms, resembles that of a truncated cone. In terms of cavity size, cucurbit[6]uril (CB[6]), cucurbit[7]uril (CB[7]), and cucurbit[8]uril (CB[8]) resemble α-CD, β-CD, and γ-CD, respectively. However, CB cavities possess a highly symmetrical structure and two identical openings, while CD cavities have two different openings, that is, a wide opening composed of C2-OH and C3-OH groups and a narrow opening composed of C6-OH groups. These structural differences consequently lead to different behaviors in selective binding towards guest molecules and in the construction of supramolecular assemblies. Specifically, although cucurbiturils and cyclodextrins are both potential binding sites for hydrocarbon molecules, the cucurbituril cavity prefers cationic guests due to the existence of carbonyl-lined portals, while the cyclodextrin cavity tends to bind neutral or anionic guests. Meanwhile, we believe that appropriate combination of cucurbiturils



Scheme 1. Molecular structures of cucurbiturils (left) and cyclodextrins (right). n refers to the number of glycoluril or glucose units.

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and cyclodextrins may result in useful applications in many fields of chemistry and material science.

This review summarizes our recent endeavors and related works by other investigators on comparative studies of cucurbiturils and cyclodextrins, with a special emphasis on their selective binding and molecular assembly behaviors. It also gives a description of the construction of nanometer-scaled architectures through cooperative assembly employing cucurbiturils and cyclodextrins in a single supramolecular system, as well as their functions.

Yong Chen was born in Tianjin, China, in 1972, and obtained his Ph.D. degree in 2001 at Nankai University majoring physical organic chemistry based on cyclodextrins. He has been a faculty member at the Institute of Chemistry, Chinese Academy of Science, and a post-doctor at Ecole Normale Superieure (ENS, France). In 2003, he joined the Supramolecular Chemistry Laboratory of Nankai University as an Associate Professor and became a Full Professor at 2009. His research interests are mainly focused on supramolecular chemistry of cyclodextrins.

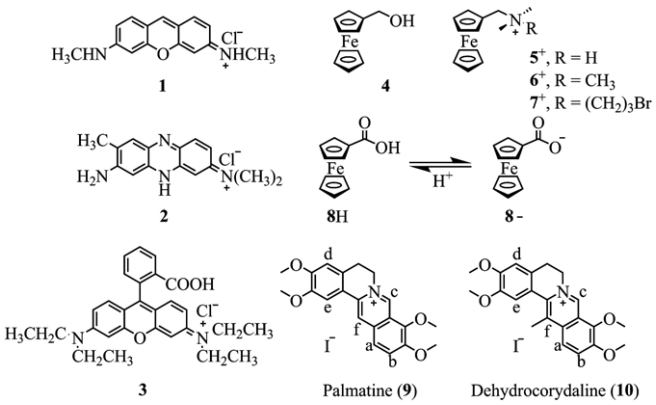
Ying-Ming Zhang graduated from Nankai University with a B.Sc. degree in 2005. During his doctoral studies from 2005 to 2010, his research focused on the molecular recognition and assembly of functional derivatives of cyclodextrin under the supervision of Professor Yu Liu. In 2010, Dr. Zhang joined the Supramolecular Chemistry Laboratory of Nankai University as a Lecturer.

Yu Liu is a Professor at Nankai University. He graduated from the University of Science and Technology of China in 1977, and received his Ph.D. from Himeji Institute of Technology, Japan, in 1991. Then, he spent about two years (1991–1992) as a postdoctoral fellow at Lanzhou Institute of Chemical Physics. In 1993, he moved to Nankai University as a Full Professor. He is now the chairman of Asian and Oceanian Cyclodextrin League, a member of the International Cyclodextrin League, and the specially-appointed professor of the "Cheung Kong Scholars Programme of China". His research interests are mainly focused on molecular recognition and assembly of crown ethers, cyclodextrins, cucurbiturils, and calixarenes.

2. Discussions

2.1. Molecular Selective Binding of Cucurbiturils vs. Cyclodextrins

As described above, owing to the structural difference between cucurbituril and cyclodextrin cavities, the main non-covalent interactions governing their molecular binding are different to some extent. For cyclodextrins, hydrophobic interactions are the main dominating forces during the course of molecular binding,[16–18] while for cucurbiturils, both hydrophobic interactions and ion–dipole interactions are the dominant forces.[2,9,19,20] This section will describe comparative studies of molecular selective binding behaviors of cucurbiturils and cyclodextrins towards various guest molecules (Scheme 2).



Scheme 2. Molecular structures of guest molecules used in comparative studies of binding behaviors of cucurbiturils and cyclodextrins. (refs. [21–24])

Since they possess good structural diversity and spectral sensitivity, dyes are regarded as good spectral probes for comparative studies of binding behaviors of CBs and CDs. Table 1 lists the binding constants of some representative dyes with cucurbiturils and cyclodextrins in aqueous solution.[21–24] As seen in Table 1, CB[7] forms moderately stable complexes with positively charged guests in buffer solution, showing a K_S order of **2** > **1** > **3** in pH 6.0 buffer solution. A reasonable explanation for the highest binding ability of CB[7] towards **2** is that CB[7] can effectively bind the positive-charge portion of **1** or **3** mainly through ion–dipole interactions, while for **2**, the hydrogen bond interactions between the middle NH group in **2** and C=O group in CB[7] possibly also play a crucial role in the host–guest complexation besides the ion–dipole interactions. In sharp contrast to CB[7], the K_S sequence of β-CD with these dyes is in the order of **3** > **1** > **2**, where the inclusion complexation of β-CD with **2** can hardly be determined because not only two ends but also the middle part is highly polar and unfavorable to the hydrophobic interactions between the β-CD cavity and **2**. In addition

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Table 1. Binding constants (K_s) of cucurbiturils and cyclodextrins with some guest molecules

Guest	β-CD	CB[7]
1	1.38×10^3 [a]	6.89×10^3 [a]
2	– [a]	3.33×10^4 [a]
3	5.88×10^3 [a]	5.05×10^3 [a]
4–8	$10^3\sim10^4$ [b]	$10^9\sim10^{13}$ [c]
9	0.63×10^3 [d]	4.26×10^4 [d]
		2.42×10^6 [e]
10	0.59×10^3 [d]	7.86×10^3 [d]
		3.24×10^5 [e]

[a] Ref. [21], in pH 6.0 buffer. [b] Ref. [23], in pure water. [c] Ref. [23,24], in pure water or pD 4.74 buffer. [d] Ref. [22], in pH 7.2 buffer. [e] Ref. [22], in pure water.

to dyes, some drug molecules and ferrocene derivatives are also utilized as typical guest molecules for comparative studies of CBs and CDs. Also in Table 1, CB[7] presents the binding constants of $4.26\times10^4\,M^{-1}$ and $7.86\times10^3\,M^{-1}$ for the inclusion complexation of two positively charged alkaloids (palmatine **9** and dehydrocorydaline **10**, respectively) in pH 7.2 buffer solution, which are 14–68 times higher than the corresponding values for β-CD under the same conditions, due to the strong ion–dipole interactions between the cucurbituril cavity and the cationic guest molecule. Interestingly, a close comparison shows that the substitution of hydrogen for methyl in **10**, affording **9**, dramatically increases the K_S value by 5.4 times for CB[7]. This observation indicates that, besides the ion–dipole, hydrophobic interactions are also active in the binding of cucurbiturils with cationic alkaloid guests. The replacement of -H by a -CH_3 group makes palmatine more hydrophobic than dehydrocorydaline, which consequently leads to stronger hydrophobic interactions between palmatine and the cucurbituril.

More surprising enhancement of the binding ability of cucurbiturils as compared with that of cyclodextrins comes from the association with cationic ferrocene derivatives. Due to the major contribution in the cucurbituril complex of ion–dipole interactions, which are not significant in the cyclodextrin complex, as well as the match between guest shape and host cavity, K_S values determined for the binding of ferrocene derivatives **4–6** with cucurbiturils, particularly cationic $\mathbf{5}^+$ and $\mathbf{6}^+$, are extremely high for synthetic host–guest systems (up to $10^9 \sim 10^{13}\,M^{-1}$), even exceeding the stability of typical antibody–antigen complexes. However, because of the intense charge repulsion between the carboxylate group of guest $\mathbf{8}^-$ and the carbonyl oxygens on the CB[7] portals, the negatively charged guest $\mathbf{8}^-$ is not bound at all by CB[7], although all of these ferrocene-containing guests can form stable inclusion complexes with β-CD regardless of their charge.[22–24]

From the results described above, one can conclude that CB[7] is a better host for cationic guests than β-CD, especially in pure water. It should be noted that the addition of salt greatly affects the binding abilities of cucurbiturils in aqueous solution. That is, using buffer solution as solvent or adding salt always weakens the binding of cucurbiturils with cationic guests, mainly because of the competing ion–dipole interactions between salts and cationic guest molecules. Therefore, the binding strength of cationic guests with cucurbiturils can be effectively modulated by the adjustment of the salt concentration and the type of salt.[22,25]

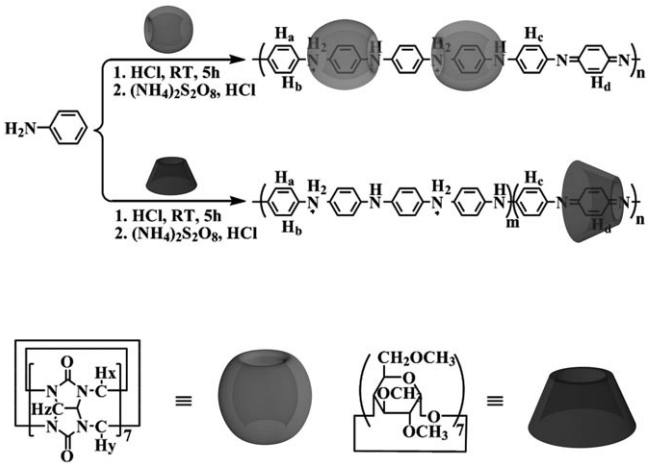
2.2. Binding Thermodynamics of Cucurbiturils vs. Cyclodextrins

To determine the thermodynamic parameters for the binding of cucurbiturils with guest molecules, the most used method is isothermal microcalorimetric titration (ITC). Since the binding constants and thermodynamic parameters are very large, ITC experiments are usually performed using the one- or two-step competition method.[14,23] Similar to most cases of cyclodextrins, the binding of cucurbiturils are mainly driven by favorable enthalpic gains, accompanied by either positive or negative entropic changes. As a result of strong ion–dipole interactions, the binding of cucurbiturils with cationic guests always give more negative enthalpic changes than the corresponding values for cyclodextrins.[23,26,27] For example, the binding of CB[7] with ferrocene derivative guests gives very large negative enthalpic changes (ΔH) up to ca. $-370\,kJ\,mol^{-1}$ accompanied by negative entropic changes up to -17 to $-34\,kJ\,mol^{-1}$.[23] However, the binding of similar ferrocene derivative guests by β-CD gives only moderate negative enthalpic changes ($T\Delta S$), up to -12 to $-33\,kJ\,mol^{-1}$, accompanied by entropic changes up to -15 to $6\,kJ\,mol^{-1}$.[28,29] More interestingly, in the cooperative binding of cucurbiturils and cyclodextrins towards a guest molecule possessing different types of binding sites, such as a positively charged site and a hydrophobic site, they will give different thermodynamic origins, which will be described in the later part of this paper.

2.3. Nanofabrication of Cucurbiturils vs. Cyclodextrins

The capability of forming stable complexes with cationic or neutral molecules makes cucurbiturils and cyclodextrins attractive as building blocks for the construction of supramolecular architectures. However, comparative studies of their nanofabrication are still rare, because templates suitable for the molecular assembly of not only cucurbiturils but also cyclodextrins are somewhat difficult to select. Recently, we choose polyaniline as a versatile template to compare the molecular assembly behaviors of forming polypseudorotaxanes by cucurbiturils and cyclodextrins.[30,31] A simple reason for choosing polyaniline as a template is that there are numerous doped (cationic) and undoped (neutral) units in a polyaniline chain, which are favorable to the association of cucurbiturils and cyclodextrins, respectively. In this work, the CB/polyaniline or

CD/polyaniline polypseudorotaxane is conveniently constructed by a polycondensation reaction of aniline in the presence of CB[7] or permethylated β-CD by using a method similar to that used for the preparation of polyaniline,[32] and the centrifugation experiment gives the approximate molecular weight of these polypseudorotaxanes up to ca. 10^5 g mol^{-1}. By comparing the integration area of ^{1}H NMR signals of doped phenyl unit protons (including H_a protons ($\delta = 7.30$ ppm) and H_b protons ($\delta = 7.16$ ppm)) in polyaniline, undoped phenyl unit protons (including H_c protons ($\delta = 6.58$ ppm) and H_d protons ($\delta = 5.39$ ppm)) in polyaniline, H_y protons of CB[7] (a CB[7] containing 14 H_y protons ($\delta = 4.12$ ppm)), and H1 protons of permethylated β-CD (a permethylated β-CD containing 7 H1 protons ($\delta = 5.12$ ppm)), one can conclude that two doped phenyl units of polyaniline chain thread through a CB[7] unit, while 5 phenyl units of polyaniline chain thread through a permethylated β-CD unit. Moreover, the use of sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) as the internal standard shows that the ^{1}H NMR signals assigned to the doped phenyl protons of polyaniline show a clear upfield shift, while those assigned to the undoped phenyl protons show a slight downfield shift after treatment with CB[7]. Whereas the ^{1}H NMR signals assigned to the doped phenyl protons of polyaniline show no obvious chemical shifts, those assigned to the undoped phenyl protons of polyaniline give a considerable downfield shift upon association with permethylated β-CD. These phenomena demonstrate that CB units mainly complex to the doped units, but CD units mainly complex the undoped aromatic rings of the polyaniline chain, when forming polypseudorotaxanes (Scheme 3).



Scheme 3. Construction of cucurbituril/polyaniline and cyclodextrin/polyaniline polypseudorotaxanes.

Interestingly, CB/polyaniline and CD/polyaniline polypseudorotaxanes also differ from each other in their morphology. As seen in Figure 1 a–c, the atomic force microscopic (AFM) images show that, at a low concentration, cucurbituril/polyaniline polypseudorotaxane mainly exists as discrete curving lines with an average length of 1.5 nm (similar to the outer diameter of CB[7][33]), while cyclodextrin/polyaniline polypseudorotaxane presents a morphology of curving strand-like structures with an average length of 1.7 nm (similar to the outer diameter of permethylated β-CD[34]) and a much larger width than that of cucurbituril/polyaniline polypseudorotaxane. In the control experiment, the AFM image of free polyaniline shows many small particles, which is distinctly different

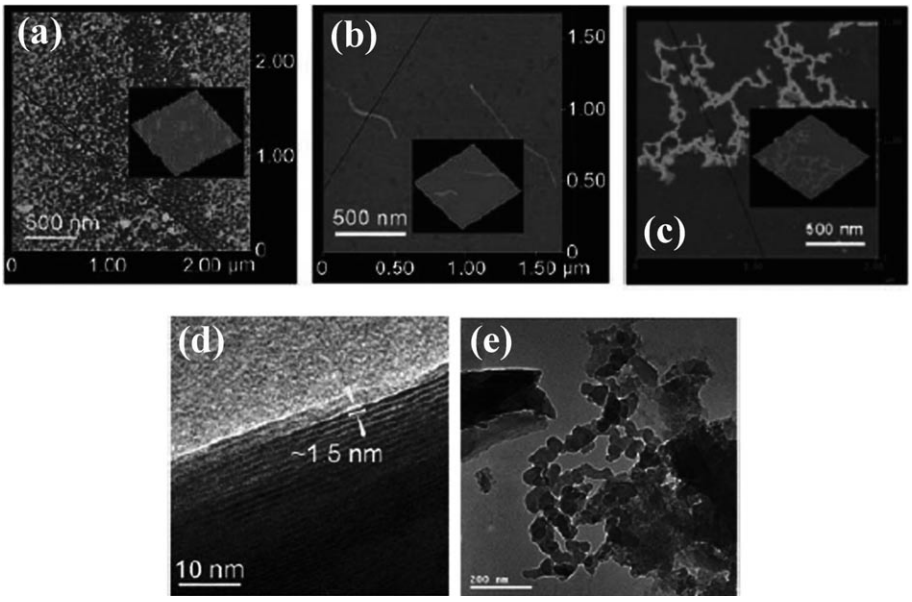


Figure 1. AFM (a–c) and TEM (d, e) images of (a) polyaniline, (b and d) cucurbituril/polyaniline polypseudorotaxane and, (c and e) cyclodextrin/polyaniline polypseudorotaxane.

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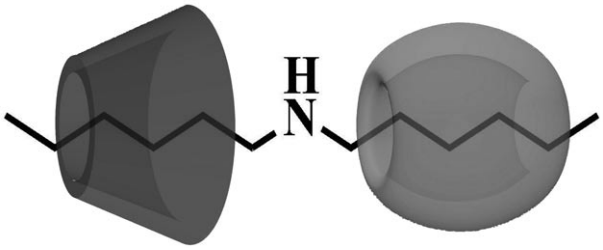
from the structural features of cucurbituril/polyaniline and cyclodextrin/polyaniline polypseudorotaxanes. In addition, the transmission electron microscopic (TEM) images show that, at a relative high concentration, the curving lines of cucurbituril/polyaniline polypseudorotaxanes shown in the AFM images become linear structures that are located side by side to form a straight fiber (Figure 1d). However, the cyclodextrin/polyaniline polypseudorotaxanes appear as curving strand-like structures consisting of many small aggregates (Figure 1e).

Due to the high solubility of CBs and CDs, the resultant cucurbituril/polyaniline and cyclodextrin/polyaniline polypseudorotaxanes are not only more soluble in water than free polyaniline, but also can remain soluble for more than 10 h. The water solubility of cucurbituril/polyaniline and cyclodextrin/polyaniline polypseudorotaxanes can reach approximately 1.4 $mg\,mL^{-1}$ and 1.7 $mg\,mL^{-1}$, respectively, compared to 0.3 $mg\,mL^{-1}$ for free polyaniline. More interestingly, although cucurbiturils and cyclodextrins associate with different moieties of polyaniline, the complexation of cucurbiturils and cyclodextrins both show the enhanced radical cation stabilization effect towards polyaniline. Compared with that of free polyaniline, the EPR spectra of cucurbituril/polyaniline and cyclodextrin/polyaniline polypseudorotaxanes both show the clear broadening of signal peaks. Moreover, the EPR signals of CB/polyaniline polypseudorotaxane exhibit a slower attenuation rate and a smaller attenuation ratio of the signal intensity than polyaniline, and the stabilization effect of CD/polyaniline polypseudorotaxane is even better than that of CB/polyaniline polypseudorotaxane. In addition, cyclic voltammetry experiments also show that both CB/polyaniline polypseudorotaxane and CD/polyaniline polypseudorotaxane present more negative first anodic peaks than polyaniline, indicating that the formation of radical cations in both combinations is easier than in free polyaniline. This phenomenon is consistent with the electrochemistry of the CB[7]/oligoaniline system reported by Anderson and coworkers.[35] Although both CBs and CDs give a satisfactory radical cation stabilization effect towards polyaniline, their detailed mechanisms are actually different. For the cucurbituril/polyaniline polypseudorotaxane, the radical cation stabilization effect is attributed to the strong complexation of cucurbituril macrocycles with the cationic units of polyaniline protecting the doped form, that is, the conductive form, of polyaniline. But for the cyclodextrin/polyaniline polypseudorotaxane, the mechanism is similar to that reported for the radical cation stabilization by the complexation of β-CD or polysaccharide, where the restricted mobility of the supramolecular system may play an important role. It should also be noted that the cyclodextrin/polyaniline polypseudorotaxane can be further wrapped on the surface of carbon nanotubes, like the reported cyclodextrin-based polypseudorotaxane/carbon nanotube system,[36] but the association of the cucurbituril-based polypseudorotaxane with carbon nanotubes has not been reported so far, to the best of our knowledge.

2.4. Nanofabrication by Cooperative Assembly of Cucurbituril and Cyclodextrin

In the preceding sections, we gained a deep insight into the different structural features and binding behaviors of cucurbiturils and cyclodextrins. The judicious application of these properties can allow the rational construction of highly ordered supramolecular architectures through the cooperative assembly of cucurbiturils and cyclodextrins. The first example of this cooperativity comes from the construction of a ternary assembly consisting of dihexylammonium, CB[6], and cyclodextrin (Scheme 4),[26]

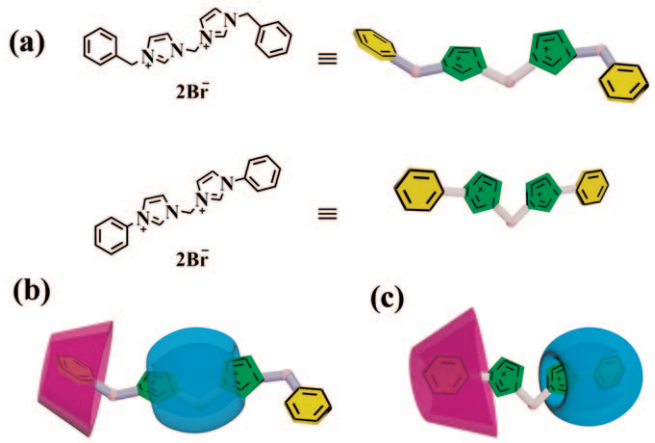


Scheme 4. Ternary assembly constructed of cyclodextrin, dihexylammonium, and cucurbituril.

where dihexylammonium, a positively charged compound with two separate aliphatic chains, is selected as the template. As the first step in supramolecular assembly, CB[6] strongly interacts with dihexylammonium to give a very stable 1:1 complex ($K_s \sim 10^5\ M^{-1}$). Microcalorimetric titration experiments show that this binding is driven both enthalpically ($\Delta H^\circ < 0$) and entropically ($T\Delta S^\circ > 0$), indicating that the CB[6]/dihexylammonium association is greatly assisted not only by van der Waals interactions of dihexylammonium with CB[6]'s inside walls but also by the ion–dipole interactions of the cationic ammonium with the carbonyl array of CB[6] portal. Moreover, microcalorimetric titration and NMR experiments demonstrate that the other aliphatic chain of dihexylammonium stays outside the cavity rather than forming an inclusion complex with CB[6], perhaps because the small CB[6] cavity cannot accommodate two aliphatic chains simultaneously. Subsequently, the second aliphatic chain of dihexylammonium gives a weak association with γ-CD ($K_s = 240\ M^{-1}$), a moderately strong association with α-CD ($K_s = 800\ M^{-1}$), and the strongest association with β-CD ($K_s = 2150\ M^{-1}$), accompanied by the less enthalpic and entropic contributions ($\Delta H^\circ = -11.1 \sim 20.5\ kJ\,mol^{-1}$, $T\Delta S^\circ = -3.9 \sim 3.5\ kJ\,mol^{-1}$) than those ($\Delta H^\circ = -24.9\ kJ\,mol^{-1}$, $T\Delta S^\circ = 7.7\ kJ\,mol^{-1}$) for the binding of the first aliphatic chain of dihexylammonium with CB[6]. These thermodynamic data from microcalorimetric titration experiments and the

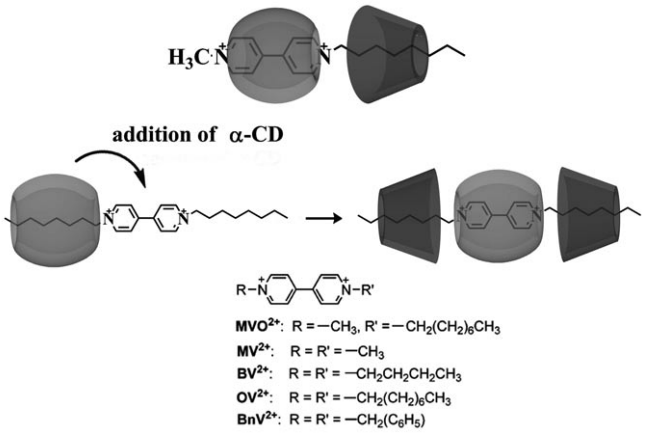
2D NMR results, which present clear NOE cross-peaks between hexyl protons of dihexylammonium and the cyclodextrin's interior protons (H3, H5, and H6 protons), jointly confirm the formation of the ternary assembly. It should be noted that the stability of the ternary assembly is determined not only by guest–cyclodextrin interactions but also by cucurbituril–cyclodextrin interactions, leading to the strongest association with β-CD.

Developing from the above ternary assembly, another successful example of the 1:1:1 assembly including cucurbiturils and cyclodextrins is designed and constructed (Scheme 5) by mixing *N*,*N*′-disubstituted methylenediimidazolium bromide salt, cucurbiturils, and cyclodextrins in stoichiometric proportion (Scheme 5).[37] High resolution mass spectrometric measurements using electrospray ionization demonstrate the formation of 1:1:1 ternary assembly at 4 mM concentration of each component. Interestingly, by altering the substituents of *N*,*N*′-disubstituted methylenediimidazolium templates from phenyl to benzyl groups, the binding position of cucurbituril can be effectively controlled. Based on their structural features, disubstituted methylenediimidazolium templates possess two different binding sites, that is, the external aromatic residues and the central diimidazolium dication. In the case of the 1:1 binding of cucurbituril or cyclodextrin with disubstituted methylenediimidazolium, the macrocycle (cucurbituril or cyclodextrin) prefers the external aromatic residues. But for the construction of 1:1:1 ternary assembly, the assembly mode is different. For the cooperative assembly of cucurbituril, cyclodextrin, and benzyl-disubstituted methylenediimidazolium, the cyclodextrin binds the external benzyl group by shallowly including the aromatic ring within its cavity, and the cucurbituril is positioned symmetrically around the diimidazolium site (Scheme 5b). When altering the benzyl groups of the disubstituted methylenediimidazolium template to the phenyl groups, the cyclodextrin cavity tends to include the phenyl ring more deeply, while the cucurbituril is positioned asymmetrically positioning around the diimidazolium site and located near to another external phenyl group (Scheme 5c). Here, the different structural geometry of disubstituted methylenediimidazolium templates, that is, the linear geometry of phenyl imidazolium vs. the bent geometry of benzyl imidazolium, may be the main factor controlling the binding sites of cucurbituril and cyclodextrin on the same template. Besides in solution, these different assembly modes also occur at the air–water interface, leading to the different surface activities of the resultant ternary assembly. That is, the CB/CD/benzyl-disubstituted methylenediimidazolium assembly adopts a perpendicular geometry at the air–water surface, with one benzyl terminal exposed to the air and the other, cyclodextrin-encased benzyl terminal pointed to the body of solution, presenting moderate surface tension (σ) measurements and lowering the interfacial free energy. However, the CB/CD/phenyl-disubstituted methylenediimidazolium assembly, where two phenyl terminals are respectively encompassed by the cucurbituril and cyclodextrin, are found to be completely surface inactive.



Scheme 5. Molecular structures of (a) disubstituted methylene diimidazolium templates, (b) cucurbituril/cyclodextrin/benzyl-disubstituted methylenediimidazolium assembly, and (c) cucurbituril/cyclodextrin/phenyl-disubstituted methylenediimidazolium assembly.

Cooperative assembly with cyclodextrins can even drive the movement of cucurbiturils (Scheme 6).[27] In such a system, asymmetric viologen compounds, that is, *N*-methyl-*N*′-octyl-4,4′-bipyridinium (MVO^{2+}), and symmetrical viologen compounds, that is, *N*,*N*′-dimethyl-4,4′-bipyridinium (MV^{2+}), *N*,*N*′-dibutyl-4,4′-bipyridinium (BV^{2+}), *N*,*N*′-dioctyl-4,4′-bipyridinium (OV^{2+}), and *N*,*N*′-dibenzyl-4,4′-bipyridinium (BnV^{2+}), are respectively selected as templates to investigate the cooperativity of cucurbituril and cyclodextrin. For the asymmetric template MVO^{2+}, the associated CB[7] is equilibrating between the bipyridinium and the octyl moieties in $[MVO{\cdot}CB[7]]^{2+}$, but mainly locates at the octyl moiety.

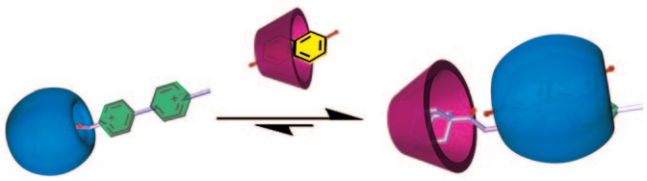


Scheme 6. Cooperative assembly mode of cucurbituril and cyclodextrin with asymmetric or symmetric viologen template.

Upon the addition of a excess amount of α-CD to the $[MVO{\cdot}CB[7]]^{2+}$ solution, CB[7] moves to the bipyridinium moiety of MVO^{2+} instead of shuttling between the octyl and the bipyridinium moieties, forming the 1:1:1 MVO·CB[7]·α-CD cooperative assembly similar to those described above. Thermodynamically, the association of MVO^{2+} with CB[7] presents a large favorable free energy change ($\Delta G^{\circ} = -31.56\ kJ\,mol^{-1}$), resulting from the contributions of both the enthalpy term originating from ion–dipole interactions between N^+ groups of MVO^{2+} and carbonyl groups of CB[7] and the entropy term from the desolvation effect of N^+ groups. Then, the further association of $[MVO{\cdot}CB[7]]^{2+}$ with α-CD is driven by both favored enthalpy change and entropy change. Herein, the favored enthalpy change may come from not only the complexation of the octyl moiety with α-CD but also the hydrogen-bonding interactions between CB[7] and α-CD.

For the symmetric templates OV^{2+}, CB[7] is docked at an octyl moiety of OV^{2+} to form the $[OV{\cdot}CB[7]]^{2+}$ complex with the other octyl moiety exposed in solution. Then, the added α-CD first binds at the free octyl moiety of $[OV{\cdot}CB[7]]^{2+}$, and then the binding of the second α-CD with another octyl chain of OV^{2+} forces CB[7] to move from the octyl moiety to the bipyridinium moiety. Thermodynamically, the free energy changes for the association of CB[7] or α-CD with OV^{2+} approximate those with MVO^{2+}, but their enthalpy changes and entropy changes are different. In comparison to the latter, the complexation of CB[7] with OV^{2+} gives a favorable entropy change and a less unfavorable enthalpy change. In contrast, the association of α-CD and OV^{2+} is enthalpically favorable and entropically unfavorable. Furthermore, the free energy changes for the formation of the 1:1 complex of α-CD and $[OV{\cdot}CB[7]]^{2+}$ is larger than that of α-CD and OV^{2+}, attributing to the OV^{2+} charge density decreasing with the binding of CB[7] and resulting in α-CD easily binding at the octyl moiety. For the case of other symmetric templates, BV^{2+} and BnV^{2+} can form the external inclusion complexes with CB[7] as OV^{2+}, but the addition of abundant α-CD cannot push CB[7] to the viologen nucleus. One possible reason is that both the external butyl and benzyl groups are too short to be included by α-CD. In addition, CB[7] binds MV^{2+} at the viologen nucleus directly, and the addition of α-CD cannot change the binding mode of $[MV{\cdot}CB[7]]^{2+}$.

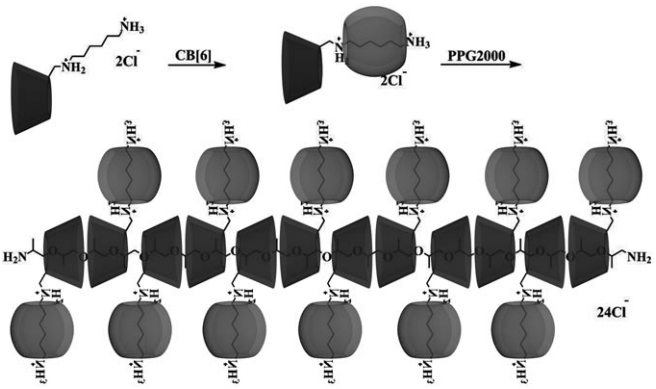
In addition to CB[6] and CB[7], the bigger CB[8] can also form cooperative assembly with cyclodextrins. For example, since it can facilitate the formation of a stable charge-transfer complex between viologen derivatives and hydroxynaphthalenes, CB[8] is used as one of the building blocks to construct the hetero-wheel [3]pseudorotaxane along with β-CD. In this route (Scheme 7), CB[8] and β-CD respectively form the 1:1 complexes with adamantanyl viologen and hydroxynaphthalene, which can be conveniently monitored by ^1H NMR spectroscopy and ESI-MS (Electrospray Ionization Mass Spectrometry). In



Scheme 7. Cooperative assembly of cucurbituril and cyclodextrin with adamantanyl viologen with hydroxynaphthalene.

the CB[8]/adamantanyl viologen complex, the adamantanyl moiety of the guest molecule is included in the cavity of CB[8], and the viologen moiety is near one of its portals. For the β-CD/hydroxynaphthalene complex, the naphthalene moiety penetrates into the β-CD cavity. Subsequently, the addition of β-CD/hydroxynaphthalene complex to the solution CB[8]/adamantanyl viologen complex leads to the formation of a cooperative cucurbituril/cyclodextrin/viologen/naphthalene quaternary assembly. During this process, CB[8] is moved to the viologen moiety facilitating the formation of a stable charge-transfer complex between viologen and hydroxynaphthalene, and β-CD correspondingly perches on the adamantanyl moiety. It should be noted that β-CD plays an important role in the construction of quaternary assembly. Without β-CD, CB[8]s mostly bind the adamantanyl moiety of the guest molecule, which makes the cavity of CB[8] not work for the formation of a stable charge-transfer complex of adamantanyl viologen with hydroxynaphthalene. However, the added β-CD will bind competitively the adamantanyl moiety of guest molecule, making partial CB[8] molecules move onto the viologen nucleus. This not only leads to the formation of a stable charge-transfer complex between adamantanyl viologen and hydroxynaphthalene, but also impels more CB[8] to move onto the viologen nucleus.[38]

The application of cooperative assembly of cucurbituril and cyclodextrin can also extend to the construction of more complicated supramolecular architecture, such as the two-dimensional pseudopolyrotaxanes. As shown in Scheme 8, the reaction of CB[6] with 6-[(6-aminohexyl) amino]-6-deoxy-β-CD dication produces the CB[6]/β-CD pseudorotaxane in more than 80% yield owing to the strong association of cucurbiturils with positively charged compounds, as described above. Then, the target two-dimensional pseudopolyrotaxane can be constructed by adding amino-terminated PPG2000 to a saturated aqueous solution of CB[6]/β-CD pseudorotaxane. By comparing the integral of ^1H NMR signals at 0.51 ppm ($H_{c/c'}$ of β-CD) or 4.34 ppm (H_y of CB[6]) with those at 1.15 ppm (CH_3 of PPG), the number of β-CD units can be calculated as 11.8 ± 0.7. This result means that a PPG2000 chain threads about 12 CB[6]/β-CD pseudorotaxanes to form the two-dimensional pseudopolyrotaxane, and no CB[6]s dethread off during this procedure.



Scheme 8. Construction of two-dimensional pseudopolyrotaxane through cooperative assembly of cucurbituril and cyclodextrin.

TEM images give the information about the size and shape of the two-dimensional pseudopolyrotaxane. As illustrated in Figure 2, the two-dimensional pseudopolyrotaxanes exist as sticklike nanowires on the TEM substrate (marked by circles). A further analysis of the length and width of these nanowires show that they vary in length in the range of 14–25 nm, which is consistent with those of PPG2000, and their width (about 3 nm) is basically equal to the sum of the outer diameter of the β-CD cavity (about 1.5 nm) and the height of the CB[6] cavity (about 0.9 nm). However, when the sample for TEM experiments is prepared in the presence of NaOH, the nanowires become thinner, attributed to the dethreading of CB[6]s from the side chain of pseudopolyrotaxane to form a familiar main-chain pseudopolyrotaxane. Interestingly, by adjusting the pH value to acidity, all CB[6]s will rethreaded on the cationic hexyldiamino side chain of β-CD to re-form two-dimensional pseudopolyrotaxane, and this process can be repeated at least four times upon the addition of base or acid. Furthermore, α-CDs can be threaded onto the hexyldiamino side chains of the main-chain pseudopolyrotaxane under basic condition, forming another PPG/β-CD/α-CD two-dimensional pseudopolyrotaxane; the alternation of this two-dimensional pseudopolyrotaxane with the PPG/β-CD/CB[6] two-dimensional pseudopolyrotaxane is made possible by the acid–base stimuli.[39]

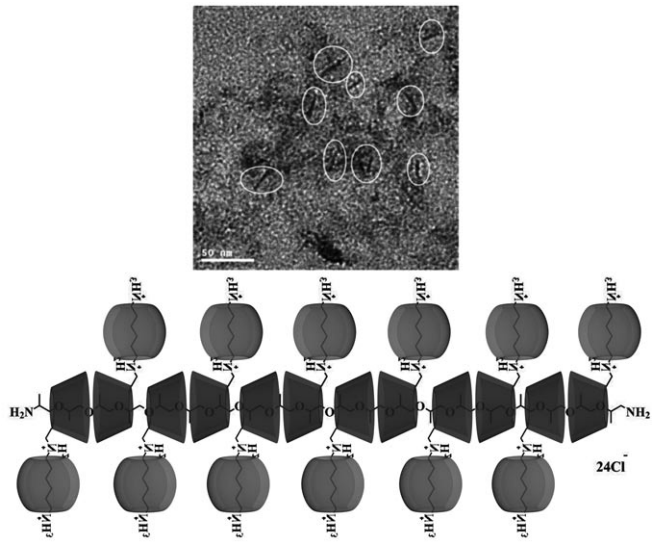


Figure 2. TEM image and schematic representation of two-dimensional pseudopolyrotaxane.

On the other hand, this type of two-dimensional pseudopolyrotaxane can also be constructed by threading 6-[(6-aminohexyl) amino]-6-deoxy-β-CDs on the PPG backbone and then threading CB[6]s on the hexyldiamino arms of β-CDs. In addition, because of the strong binding ability between dicationic hexyldiamino arm and CB[6] in aqueous solution, the association is essentially quantitative, and the degree of substitution of CB[6]s in the two-dimensional pseudopolyrotaxanes that are obtained is controllable through this method. Interestingly, by adding various amount of CB[6]s during the construction, the obtained two-dimensional pseudopolyrotaxanes bearing different number of CB[6]s show different condensation abilities towards DNA, which is confirmed by both the agarose gel electrophoresis assay and AFM experiments. Surprisingly, the retardation of DNA by two-dimensional pseudopolyrotaxanes neither increases nor decreases linearly with the percentage of CB[6]s, and two-dimensional pseudopolyrotaxane bearing 70% CB[6] exhibits the highest efficiency to retard DNA in the gel well. Moreover, AFM images give similar results to those in the gel electrophoresis experiments. As shown in Figure 3a, the free plasmid DNAs deposit in their plectonemic form with several supercoils which cause the double helix to cross itself a number of times. After the addition of the main-chain pseudopolyrotaxane (without CB [6]), DNA is induced to form small nanoparticles with an approximate diameter of 120 nm (Figure 3b). When two-dimensional pseudopolyrotaxane bearing 70% CB[6] is added, larger nanoparticles with an approximate diameter of 600 nm are observed (Figure 3c). In the case of two-dimensional pseudopolyrotaxane bearing 100% CB[6], the diameter of the nanoparticles decreased. A possible explanation may be that, when the hexyldiamino moieties of two-dimensional pseudopolyrotaxane are included in the cavities of CB[6]s, the charged cations are shielded by the CB[6]s. As a result, the effective charges of the two-dimensional pseudopolyrotaxane interacting with the DNA decrease with the increasing of CB[6]s. However, the rigidity of two-dimensional pseudopolyrotaxane increases with the addition of CB[6]s, which is also an important factor for the interaction of two-dimensional pseudopolyrotaxane with DNA. The joint result of these two factors leads to an unusual binding interaction taking place in the system of DNA with two-dimensional pseudopolyrotaxane containing 70% CB[6]s, and the migra-

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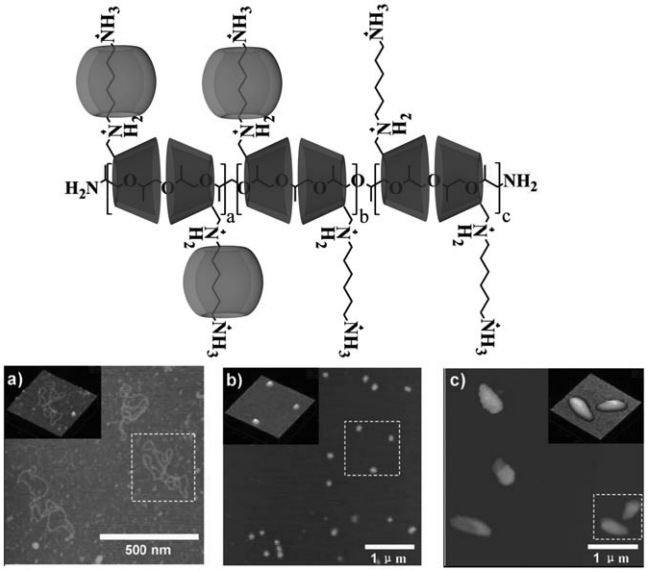

Figure 3. Molecular structure of PPG/β-CD/CB[6] two-dimensional pseudopolyrotaxane and AFM height images of a plasmid DNA (a) and its condensates induced by two-dimensional pseudopolyrotaxanes containing 0% (b) and 70% (c) CB[6]s.

tion of DNA/pseudopolyrotaxane conjugates in agarose gel electrophoresis is mainly dominated by particle size.[40]

3. Summary and Outlook

This review summarizes some recent works not only about the comparative studies on the selective binding and molecular assembly behaviors of cucurbiturils and cyclodextrins, but also, most importantly, the cooperativity of cucurbiturils and cyclodextrins in the nanofabrication of highly ordered supramolecular architectures. It is apparent from this review that, due to their different structural features, cucurbiturils and cyclodextrins exhibit the different binding sites, binding abilities, and thermodynamic origin upon association with the same guest molecules or assembly templates. Furthermore, the proper choice of templates containing both the charged and hydrophobic binding sites and the smart design of the construction route can achieve efficient cooperativity of cucurbiturils and cyclodextrins, which thus affords the opportunity to generate new and complicated nanometer-scaled structure with cucurbiturils and cyclodextrins as scaffolds. The next target of these studies may be, in the light of accumulated research accomplishments summarized here, to establish well-organized nanoarchitectures through the judicious alignments of cucurbituril and cyclodextrin building blocks as well as templates in a more ordered and more controllable manner. Past research has demonstrated the cucurbituril/cyclodextrin pair as a powerful platform of selective binding and nanofabrication. However, we believe that the development of new nanoarchitecture based on cucurbituril/cyclodextrin pairs and their expanded use will continue to energize the exciting findings.

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