

Reversible Formation and Destruction of Micelles of Amphiphilic Compounds in Aqueous Media. Competition with Pseudorotaxane Formation

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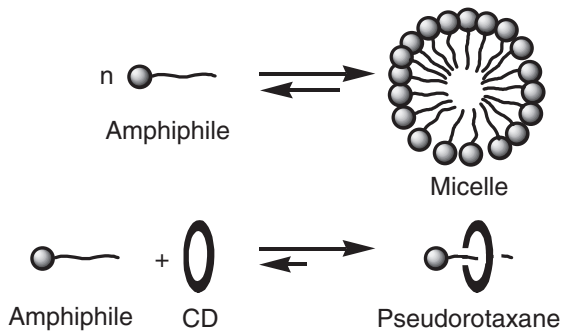
N-Alkyl-4,4′-bipyridiniums $[4,4'\text{-bpy-}N\text{-}(CH_2)_nOAr]^+(Cl^-)$ ($n = 6$ and 10, Ar = C_6H_3-3,5-*t*-Bu_2, C_6H_3-3,5-$(OMe)_2$, and C_6H_2-2,4,6-Me_3), having the cationic bipyridinium group and a long hydrophobic alkyl chain, were prepared from the reaction of 4,4′-bipyridine with the corresponding alkyl chlorides. The amphiphilic compounds in water form micelles which encapsulate added pyrene in the hydrophobic core. Addition of α-cyclodextrin to the micellar solution converts a part of the aggregated amphiphilic molecules to their pseudorotaxane with α-cyclodextrin. Formation of the pseudorotaxanes is favored at lower temperature, as is observed by temperature dependent change of the absorption spectra.

Amphiphilic compounds possessing both hydrophilic and hydrophobic parts in the molecule, such as CTAB (cetyltrimethylammonium bromide), SDS (sodium dodecyl sulfate), and Triton X-100 (octylphenoxypolyethoxyethanol), form micelles or other self-assembled aggregates, such as vesicles and bilayer sheets, in water.[1,2] The micelle particles composed of the amphiphiles often contain added pigment or dye molecules in their hydrophobic cavity. Such encapsulation of the micellar solution is widely used to estimate critical micelle concentration (CMC) of the amphiphiles in water.[3] Spectroscopic measurement of the micellar solution of various amphiphiles in the presence of pyrene provide a good means to determine their CMCs as well as to obtain information of the environment around the pyrene.[4] Addition of cyclodextrins (CDs), cyclic-oligoglucoses composed of six to eight 1,4-linked D-glucopyranose units,[5] to the micellar solution has been reported to change properties of the solution, such as surface activity,[6] surface intensity,[7] and conductivity[8] as well as the spectroscopic and physicochemical results.[9] They were attributed to the formation of their pseudorotaxanes in which cyclodextrins were threaded by the long alkyl chain of the amphiphile.[10–12] In these mixtures of cyclodextrin and amphiphile in water, formation of the micelle and of the pseudorotaxane competes with each other as shown in Scheme 1.[8b,8c,13–15]

Studies on the mixture of β-cyclodextrin and SDS revealed that formation of the pseudorotaxane with β-CD is much more favored than that of the micelle because of more significant interaction between β-CD and SDS than that among the amphiphilic molecules in the micellar system.[16] Recent kinetic study of the β-CD–SDS system by EPR spectroscopy also showed the complex formation of β-CD and SDS which occurs with a higher association constant than that of micellization of SDS in water.[17] In these systems, high stability of the pseudorotaxane prevents formation of micelles or the change of the ratio of the pseudorotaxanes to the micelles in aqueous media. On–off regulation of competing supramolecular assembly systems between pseudorotaxane formation and micellar aggregation may lead to switching of the solution properties, although reports on this subject are rare.[6]



Scheme 1. Competitive formation of micelles and pseudorotaxanes.

In this paper, we report the reversible formation of micelles and of pseudorotaxanes in an aqueous mixture of α-CD and amphiphilic molecule by temperature alternation. It was achieved by use of *N*-alkyl-4,4′-bipyridiniums. A part of this work has been reported in a preliminarily form.[18]

Results and Discussion

Chart 1 lists *N*-alkyl-4,4′-bipyridiniums used in this study. Reaction of 4,4′-bipyridine with $Cl(CH_2)_nOAr$ ($n = 6$ and 10; Ar = C_6H_3-3,5-*t*-Bu_2, C_6H_3-3,5-$(OMe)_2$, and C_6H_2-2,4,6-Me_3) in DMF produces, $[4,4'\text{-bpy-}N\text{-}(CH_2)_nOAr]^+(Cl^-)$ (**1a**: $n = 10$, Ar = C_6H_3-3,5-*t*-Bu_2; **1b**: $n = 10$, Ar = C_6H_3-3,5-$(OMe)_2$; **1c**: $n = 10$, Ar = C_6H_2-2,4,6-Me_3; and **1d**: $n = 6$, Ar = C_6H_3-3,5-$(OMe)_2$). Compounds **1a**–**1c** show amphiphilic nature; they are soluble both in water and in common organic solvents, such as dmso, acetone, CH_2Cl_2, and $CHCl_3$. Compound **1d**, however, is soluble in water, sparingly soluble in dmso, and insoluble in other organic solvents, due to the shorter polymethylene chain than that of the other compounds.

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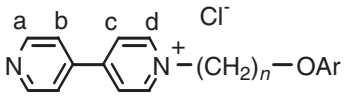


1a: $n = 10$, Ar = C_6H_3-3,5-*t*-Bu_2
1b: $n = 10$, Ar = C_6H_3-3,5-$(OMe)_2$
1c: $n = 10$, Ar = C_6H_2-2,4,6-Me_3
1d: $n = 6$, Ar = C_6H_3-3,5-$(OMe)_2$

Chart 1. Structure of *N*-alkyl-4,4′-bipyridinium compounds, **1a**–**1d**.

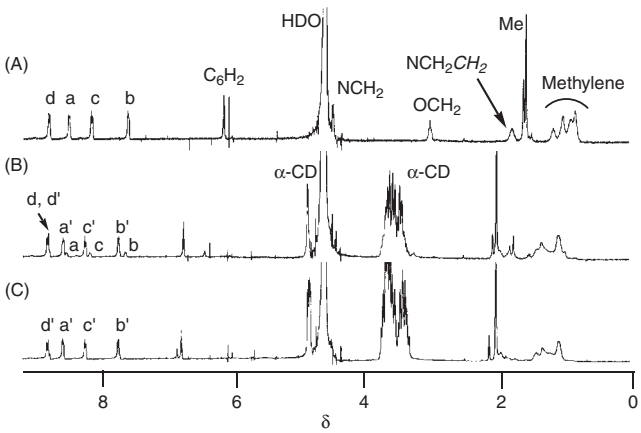
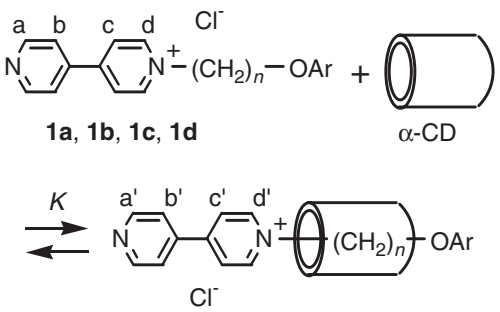


Figure 1. ^{1}H NMR spectra (D_2O, 300 MHz, 25 °C) of (A) **1c** ([**1c**] = 10 mM), (B) **1c** and α-CD ([**1c**] = 10 mM, [α-CD] = 10 mM), and (C) **1c** and α-CD ([**1c**] = 10 mM, [α-CD] = 30 mM).

Reaction of α-CD with **1a**–**1d** leads to formation of their pseudorotaxanes as shown in eq 1.



(1)

1a(α-CD): $n = 10$, Ar = C_6H_3-3,5-*t*-Bu_2
1b(α-CD): $n = 10$, Ar = C_6H_3-3,5-$(OMe)_2$
1c(α-CD): $n = 10$, Ar = C_6H_2-2,4,6-Me_3
1d(α-CD): $n = 6$, Ar = C_6H_3-3,5-$(OMe)_2$

Inclusion complexes of α-CD with **1a** in D_2O/dmso-d_6 (=3/1) and [3]pseudorotaxane of two α-CDs and **1b** were reported in our previous reports.[19,20] The MALDI-TOF MS spectrum obtained from the mixtures of α-CD and **1c** (and **1d**) showed peaks assigned to 1:1 complexes, **1c**(α-CD) ($m/z = 1401.7$) and **1d**(α-CD) ($m/z = 1363.7$), respectively. Figure 1 compares the ^{1}H NMR spectra of **1c** and of mixtures of α-CD and **1c**. An equimolar mixture ([α-CD] = [**1c**] = 10 mM) shows a set of the signals at δ 7.75 (b′), 8.24 (c′), 8.59 (a′), 8.82 (d′) and

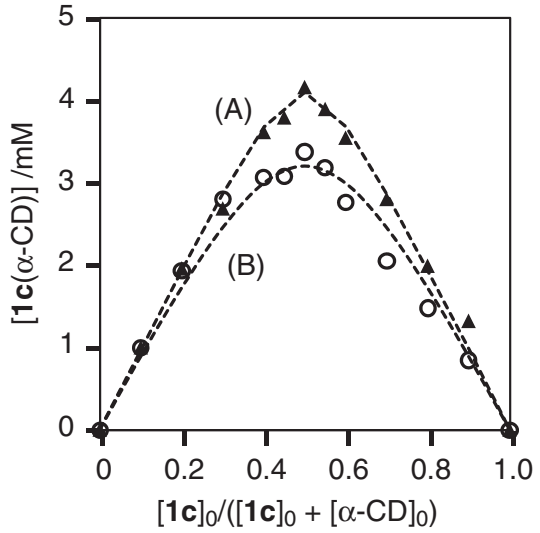


Figure 2. Job's plots for **1c** and α-CD (A) at 25 °C and (B) at 60 °C based on ^{1}H NMR peak area ratio of bipyridinium protons (b and b′). $[\mathbf{1c}]_0 + [\alpha\text{-CD}]_0 = 10$ mM. The curve calculated by assuming formation of a 1:1 pseudorotaxane with association constants of 5000 and of 1000 M^{-1} is shown in (A) and (B), respectively.

Table 1. Association Constants *K* for [2]Pseudorotaxane Formation Reaction of α-CD with **1a**–**1d** in D_2O[a]

[2]Pseudorotaxane	K/M^{-1} at 25 °C	K/M^{-1} at 60 °C
1a(α-CD)	102[b]	29[b]
1b(α-CD)	25000	12000
1c(α-CD)	5000	1000
1d(α-CD)	400	N.D.
CTAB(α-CD)	1110[c]	—

a) Unless noted association constants *K* were estimated from Job's plot obtained from ^{1}H NMR spectroscopy. b) Association constants *K* were estimated from single point ^{1}H NMR measurement. c) Ref. 21.

the signals of free **1c** (δ 7.62 (b), 8.17 (c), 8.51 (a), 8.81 (d)) in the aromatic hydrogen region (Figure 1B). The former signals (a′, b′, c′, d′) are assigned to the bipyridinium moiety of an inclusion complex, **1c**(α-CD). Further addition of α-CD to the mixture causes disappearance of the signals of free **1c** (Figure 1C). Signals of the C_6H_2 hydrogens in Figure 1C were observed as two peaks with different intensity (δ 6.82, 6.91), indicating the presence of two isomers of **1c**(α-CD) with different orientations of α-CD. The ratio of the isomers was determined to be 82:18 by comparison of the integrations of the ^{1}H NMR peak area. Job's plots obtained from the peak area ratio between b and b′ show maximum at a molar fraction of 0.5 both at 25 and 60 °C (Figure 2), which confirms exclusive formation of 1:1 complex, [2]pseudorotaxane. The corresponding association constants *K* were determined to be 5000 M^{-1} (25 °C) and 1000 M^{-1} (60 °C), respectively. Table 1 summarizes association constants of α-CD and **1a**–**1d**. Large dependence of [2]pseudorotaxane formation on the structures of the axle molecule (K = 102–25000 M^{-1} at 25 °C) was observed. The thermodynamic parameters of the [2]pseudorotaxane

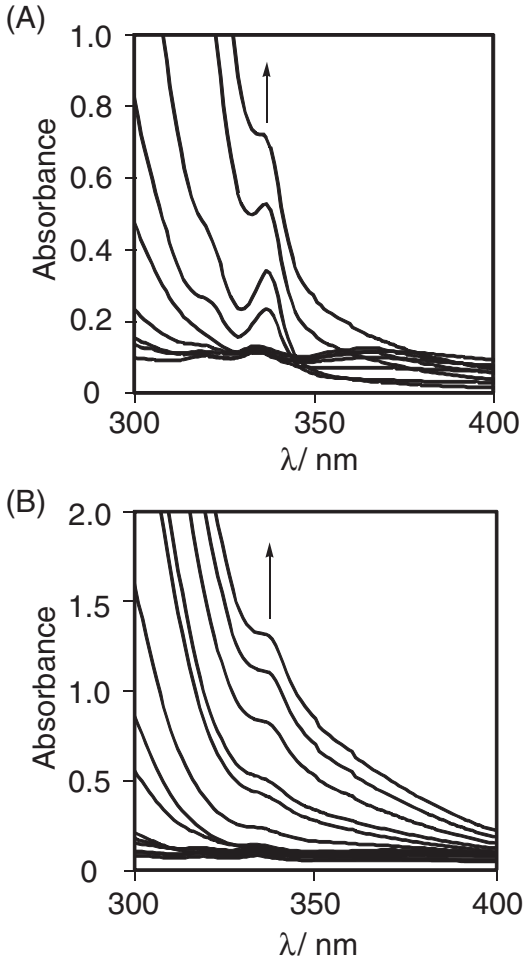


Figure 3. Absorption spectra of (A) pyrene (10 μM) and [**1a**] ([**1a**] = 5×10^{-6} to 2.5×10^{-3} g mL^{-1}) and (B) pyrene (10 μM) and [**1b**] ([**1b**] = 1.25×10^{-6} to 2.5×10^{-3} g mL^{-1}) in water at 25 °C.

formation are determined to be $\Delta H^{o} = -8.8$ kcal mol^{-1}, $\Delta S^{o} = -14$ cal mol^{-1} K^{-1}, and $\Delta G^{o} = -4.7$ kcal mol^{-1} for **1c**(α-CD) and to be $\Delta H^{o} = -7.3$ kcal mol^{-1}, $\Delta S^{o} = -13$ cal mol^{-1} K^{-1}, and $\Delta G^{o} = -3.4$ kcal mol^{-1} for **1d**(α-CD), respectively, by temperature dependence of association constant obtained by ^{1}H NMR spectroscopy of the mixture of amphiphiles and α-CD in D_2O. The large negative values of ΔH^{o} and ΔG^{o} suggest that hydrophobic interaction between the cavity of α-CD and the polymethylene chain of **1c** contribute to enthalpy-controlled thermodynamic stability of the [2]pseudorotaxane.[5]

The critical micelle concentrations (CMCs) of **1a**–**1c** in water were obtained by dye solubilization, while dynamic light scattering (DLS) measurement was also conducted to determine particle size of the formed aggregates. Figure 3 shows absorption spectra of a mixture of pyrene ([pyrene] = 10 μM) and **1a** with different concentrations ([**1a**] = 5×10^{-6} to 2.5×10^{-3} g mL^{-1}). The absorbance at 338 nm significantly increases at concentrations of [**1a**] above 5×10^{-4} g mL^{-1} due to the formation of micelles which encapsulate pyrene in the hydrophobic core. CMC values of **1a** become larger at higher temperatures or by addition of α-CD. The CMC of **1a** was determined to be 0.26 mM at 25 °C (0.50 mM at 60 °C) based

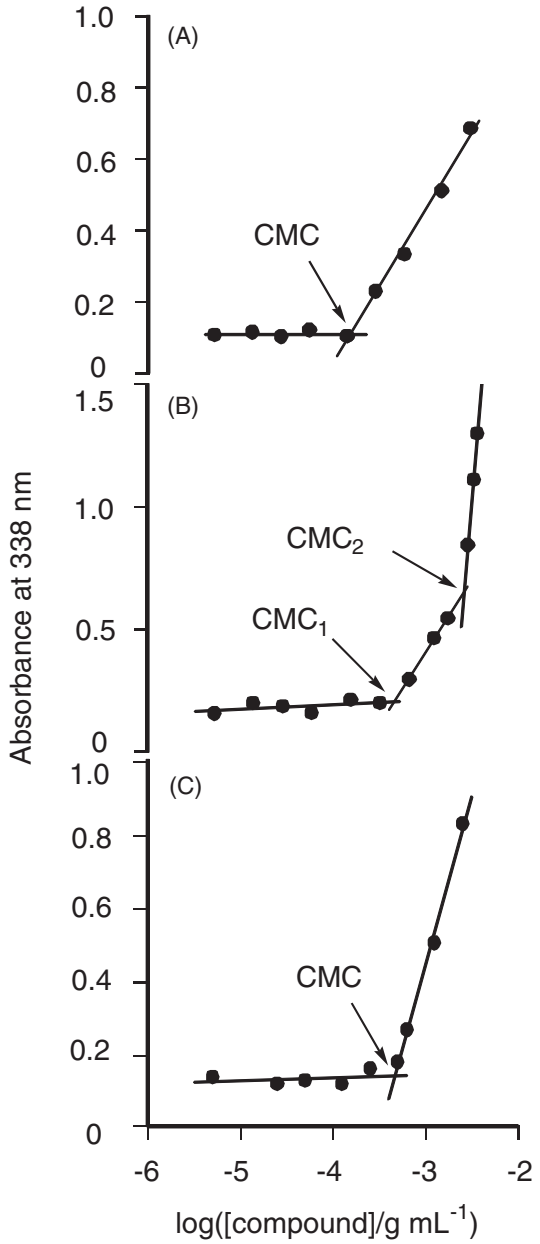


Figure 4. Plots of the absorbance at 338 nm of the aqueous mixture of pyrene ([pyrene] = 10 μM) and **1a**–**1c** at 25 °C on concentrations of (A) [**1a**], (B) [**1b**], and (C) [**1c**].

on plots of the absorbance vs. concentration of **1a** (Figure 4). DLS measurement shows the hydrodynamic radius of a micelle in an aqueous solution of **1a** ([**1a**] = 18.6 mM) as 61 nm at 25 °C. CMCs of **1b**–**1d** were determined similarly (Figure 4 and Table 2). The mixture of pyrene and **1b** shows change in slope at [**1b**] = 0.65 mM (CMC_1) and 2.1 mM (CMC_2), which is attributed to stepwise aggregation of **1b**. The CMC value of **1c** is similar to that of CTAB (0.92 mM) while those of **1a** and **1b** (CMC_2) are smaller. DLS measurement of solution of **1b** ([**1b**] = 5 mM at 25 °C) indicates a large particle with hydrodynamic radius of 2.6×10^{3} nm where formation of suspended solution due to further aggregation of **1b** was observed at high concentration. The hydrodynamic radius of micelle of **1b** does not depend significantly on temperature (hydrodynamic

Table 2. CMC and Averaged Particle Sizes of **1a**–**1d** in Water

Compound	Temperature /°C	CMC[a] /mM	Averaged particle size[b]/nm
1a	25	0.26	61
	25	0.19[c]	N.D.
	50	0.34[c]	N.D.
	60	0.50	N.D.
1a + α-CD[d]	25	0.30	N.D.
1a + α-CD[e]	25	0.56	N.D.
1b	25	0.65 (CMC_1)	2.6×10^3 [f]
		2.1 (CMC_2)	
1c	25	1.0	110[g]
CTAB	25	0.92[e]	2.6[h]

a) Determined by dye solubilization method using pyrene. b) Determined by DLS. c) DPH (1,6-diphenylhexatriene) was used as dye. d) [α-CD]/[**1a**] = 0.4. e) [α-CD]/[**1a**] = 10. f) Suspension. g) At 19 °C. h) Ref. 21.

radius = 1.5×10^3 to 2.6×10^3 nm at 25–75 °C). The hydrodynamic radius of micelle of **1c** ([**1c**] = 20 mM at 19 °C) was determined to be 110 nm. So, the amphiphiles in this study form micelles with much larger particle size than those of CTAB.

Addition of α-CD to the solution of pyrene and **1a** ([α-CD] = 47.5 mM, [pyrene] = 10 μM, [**1a**] = 9.5 mM) at 25 °C causes significant decrease in the absorption at 338 nm (Figures 5A-(i) and 5A-(ii)) due to degradation of micelles of **1a** and formation of the [2]pseudorotaxane **1a**(α-CD). Heating the solution to 60 °C caused partial recovery of the absorbance, suggesting reformation of micelle particles of **1a**. Re-cooling the solution to 25 °C decreases the absorbance again (Figures 5A-(iii) and 5A-(iv)). Repetition of the temperature change between 25 and 60 °C results in swinging of the spectra between (ii) (or (iv)) and (iii), as shown in Figure 6. Addition of α-CD to the aqueous solution of pyrene and amphiphiles, **1b**–**1d** and CTAB, causes similar decrease of the absorbance at 338 nm, while change of the spectra by temperature alternation between 25 and 60 °C lacked reversibility in these solutions (Figures 5B and 5C).

The aqueous solution of the mixture of **1a** and pyrene ([**1a**] = 2 mM, [pyrene] = 5 μM) shows weak emission at λ = 375 (I_1), 386 (I_3) nm due to π–π^* transition of pyrene with the I_3/I_1 ratio of 1.01 (λ_{ex} = 335 nm) (Figure 7A). Addition of α-CD (10 mM) to the solution causes significant increase in the intensity of the emission (Figure 7B). The intensity of emission and I_3/I_1 ratio from the mixture of α-CD, **1a**, and pyrene (I_3/I_1 = 0.67) are similar to those from solution containing pyrene (5 μM) (I_3/I_1 = 0.66). This change of emission can be ascribed as follows. Pyrene is solubilized in water via encapsulation into the cavity of micelle of **1a** where the photoexcited pyrene is quenched by bipyridinium unit of **1a**. Addition of α-CD to the micellar solution of **1a** forms individual pseudorotaxane species, **1a**(α-CD), via degradation of the micelle structure. The small I_3/I_1 values (<0.70) in Figures 7B and 7C indicate that these emissions are from the pyrene molecule dissolved in water.[4] Similar aqueous solutions of the mixture of pyrene and **1b** (and **1c**) show emission with the I_3/I_1 ratio of 0.72 and 0.85, respectively, indicating their micelle also encapsulate pyrene in the cavity.

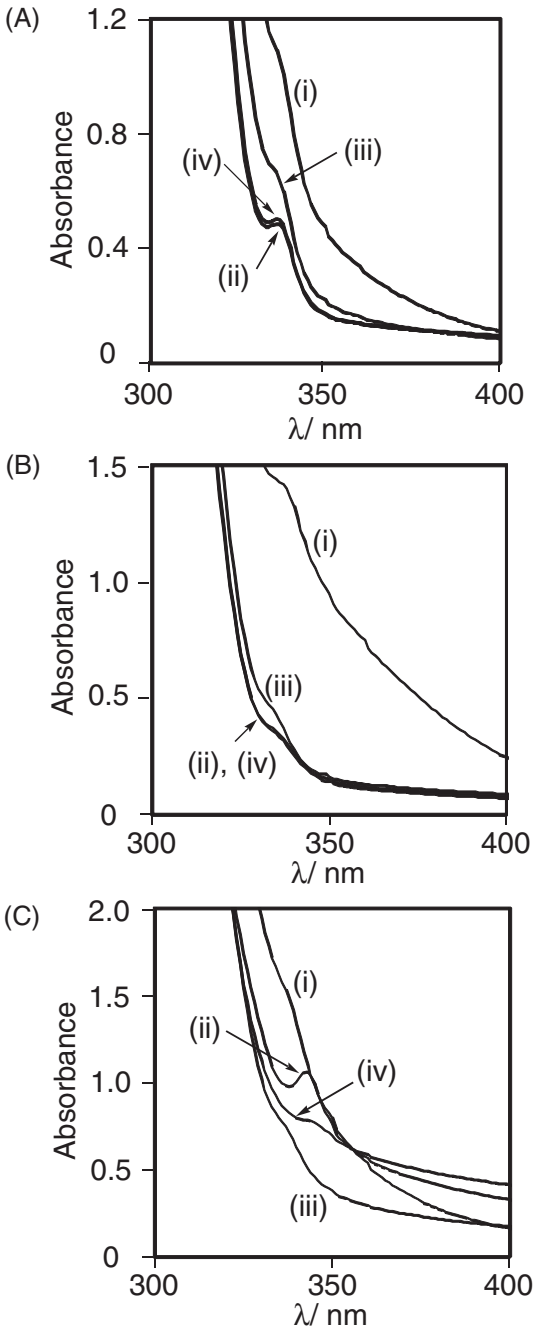


Figure 5. (A) Absorption spectra of α-CD, pyrene, and [**1a**] ([pyrene] = 10 μM, [**1a**] = 9.5 mM, [α-CD] = 47.5 mM), (B) absorption spectra of α-CD, pyrene, and [**1b**] ([pyrene] = 10 μM, [**1b**] = 5.0 mM, [α-CD] = 30 mM), (C) absorption spectra of α-CD, pyrene, and [**1c**] ([pyrene] = 10 mM, [**1c**] = 5.0 mM, [α-CD] = 30 mM). The spectra were recorded in the following order: (i) before addition of α-CD at 25 °C, (ii) after addition of α-CD at 25 °C, (iii) after heating to 60 °C, (iv) after cooling to 25 °C.

Scheme 2 summarizes a plausible mechanism for the spectroscopic changes of a solution containing pyrene, α-CD,

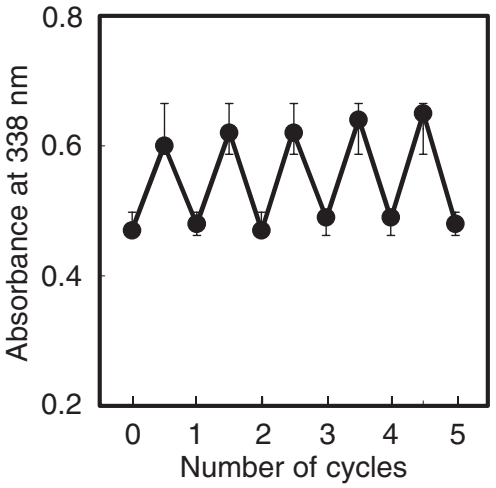


Figure 6. Switching cycles of absorbance of mixture of **1a**, α-CD, and pyrene at 338 nm between 25 and 60 °C ([pyrene] = 10 μM, [**1a**] = 9.5 mM, [α-CD] = 47.5 mM). The normal distribution within 2 standard deviations of the mean ($\mu + 2\sigma$) was included.

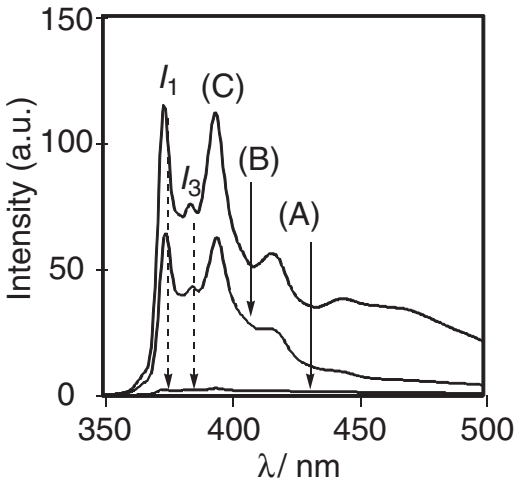
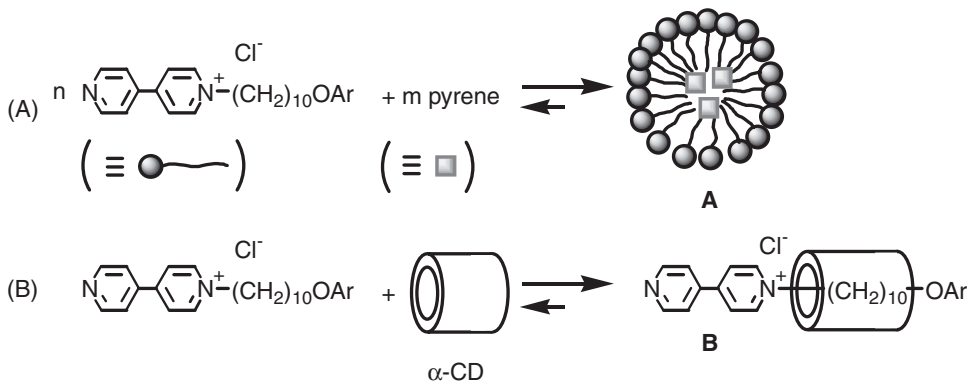


Figure 7. Emission spectra of (A) **1a** and pyrene ([pyrene] = 5 μM, [**1a**] = 2 mM), (B) **1a**, α-CD, and pyrene ([pyrene] = 5 μM, [**1a**] = 2 mM, [α-CD] = 10 mM), and (C) pyrene ([pyrene] = 5 μM) in water.



Scheme 2. Plausible mechanism for competing supramolecular assembly of amphiphiles.

and **1a** at different temperatures. The amphiphilic molecules aggregate via encapsulation of pyrene to form micelle **A** in water (Scheme 2A). Although almost all of the molecule in aqueous media are involved in the micelle, addition of α-CD causes degradation of micellar aggregate and forms pseudorotaxane with α-CD, **B**, leading to separation of pyrene from the solution as a solid and consequent decrease of the absorbance (Scheme 2B). Pseudorotaxane of **1a**, upon heating, tends to cause dethreading to separate α-CD from free amphiphile which forms micelle **A** again, leading to encapsulation of pyrene even in the presence of α-CD. Assemblies of **1a** to form micelles and to form pseudorotaxane with α-CD compete with each other in the presence of α-CD due to comparable stabilities of the two kinds of supramolecular aggregation. The association constants for formation of the pseudorotaxane **1a**(α-CD) ($K = 102\,M^{-1}$ at 25 °C, $29\,M^{-1}$ at 60 °C) are much smaller than those for the pseudorotaxane of **1b**–**1d**. The mixture of **1a** and α-CD in Figure 5A ([**1a**] = 9.5 mM, [α-CD] = 47.5 mM) is estimated to contain **1a**(α-CD) in 80% at 25 °C and 55% at 60 °C, respectively. Micelle formation of **1a** is also affected by temperature alternation (CMC of **1a** = 0.26 mM at 25 °C, 0.50 mM at 60 °C). As a result, the ratio of concentration of **1a** in the micelles and **1a**(α-CD) varies significantly by temperature alternation. Reaction of α-CD with **1b** (or **1c**, CTAB) forms their pseudorotaxanes dominantly in solution at both 25 and 60 °C under the conditions shown in Figures 5B and 5C. Yields of the pseudorotaxanes, **1b**(α-CD) and **1c**(α-CD), in these solutions are estimated to be higher than 96% even at 60 °C from their large association constants ($K = 5000$, $25000\,M^{-1}$ at 25 °C, $K = 1000$, $12000\,M^{-1}$ at 60 °C). Negligible changes in the absorption spectra of these mixtures by temperature alternation are ascribed to high stability of the pseudorotaxanes.

Conclusion

The competitive supramolecular assembly in water was investigated to reveal the micelle formation of amphiphilic *N*-alkyl-4,4′-bipyridiniums and pseudorotaxane formation of it with α-CD. The association constants of [2]pseudorotaxane formation of α-CD and $[4,4'\text{-bpy-}N\text{-}(CH_2)_nOAr]^+(Cl^-)$ ($n = 6$ and 10; Ar = C_6H_3-3,5-*t*-Bu_2, C_6H_3-3,5-$(OMe)_2$, and C_6H_2-2,4,6-Me_3) vary in the range, $K = 102$–$25000\,M^{-1}$, at 25 °C depending on the amphiphiles. Molecules having proper length of methylene chain, $n = 10$, show amphiphilic properties and

form stable micelles in water. Aqueous mixtures of α-CD and the amphiphiles produce solutions which exhibit competitive formation of micelle and pseudorotaxane. The amphiphilic molecule, [4,4′-bpy-*N*-$(CH_2)_{10}O(C_6H_3$-3,5-*t*-$Bu_2)]^+(Cl^-)$ (**1a**), forms pseudorotaxane **1a**(α-CD) with a relatively small association constant, in which significant change of the ratio of pseudorotaxane and micelles is induced reversibly by temperature alternation. This supramolecular transformation system may provide new means for artificial molecular materials that respond to an external stimulus.

Experimental

General. [4,4′-bpy-*N*-$(CH_2)_n$OAr]$^+(Cl^-)$ (**1a**; $n = 10$, Ar = C_6H_3-3,5-*t*-Bu_2 and **1b**; $n = 10$, C_6H_3-3,5-$(OMe)_2$) were prepared according to a literature method.[18,19] The other chemicals were commercially available and used without further purification. ^{1}H and $^{13}C\{^1H\}$ NMR spectra were recorded on Varian MERCURY300 and JEOL EX-400 spectrometers. 3-(Trimethylsilyl)-1-propanesulfonic acid sodium salt (DSS) was used as an external standard in the $^{13}C\{^1H\}$ NMR measurements in D_2O. Matrix-assisted laser desorption ionization time of flight mass spectra (MALDI-TOF MS) were obtained from a Shimadzu AXIMA-CFR Plus spectrometer (matrix, 2-hydroxy-5-methoxybenzoic acid (super DHB)). The absorption spectra were recorded using a JASCO V-530 UV–vis spectrometer. A 10 μL aliquot of a 2.0 M solution of pyrene in dmso was transferred to 2.0 mL of each sample. Before measuring, the samples were stored at adequate temperature using a JASCO EHC-477 peltiere-type thermostated cell holder. The emission spectra were recorded using a JASCO FP-6300 Spectrofluorometer. Elemental analysis was carried out with a LECO CHNS-932 CHNS or Yanaco MT-5 CHN autorecorder at the Center for Advanced Materials Analysis, Technical Department, Tokyo Institute of Technology. The hydrodynamic size of the micelles in aqueous solution was measured using an Otsuka Electronics Co., Ltd. DLS-7000 spectrophotometer equipped with a 10 mW He-Ne laser operating at 632.8 nm. Measurement was performed at an angle of 90°, and the data obtained were fitted using the CONTIN algorithm.

$Cl(CH_2)_{10}O(C_6H_2$-2,4,6-$Me_3)$. A solution of 2,4,6-trimethylphenol (4.0 g, 29 mmol) and NaOH (1.6 g, 40 mmol) in DMF (20 mL) was stirred for 2 h at room temperature, followed by addition of 1,10-dichlorodecane (12.4 mL, 59 mmol). The mixture was stirred for another 26 h at 100 °C, before being quenched with 1 M HCl(aq) (50 mL). The water layer was extracted with Et_2O (30 mL, 4 times) and the combined organic extract was washed with water (20 mL, 2 times), dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield a crude product, which was purified by SiO_2 column chromatography (hexane/CH_2Cl_2 = 5/1, $R_f = 0.34$) to yield $Cl(CH_2)_{10}O(C_6H_2$-2,4,6-$Me_3)$ as a white powder (3.52 g, 11 mmol, 38%). ^{1}H NMR (300 MHz, $CDCl_3$, r.t.): δ 1.36–1.60 (CH_2, 12H), 1.75–1.88 ($ClCH_2CH_2$, NCH_2CH_2, 4H), 2.28 (s, Me, 9H), 3.56 (t, $ClCH_2$, 2H, $J = 7$ Hz), 3.76 (t, OCH_2, 2H, $J = 7$ Hz), 6.85 (s, C_6H_2, 2H); $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$, r.t.): δ 16.1 (C_6H_2-4-CH_3), 20.6 (C_6H_2-2,6-$(CH_3)_2$), 26.1 (CH_2), 26.8 (CH_2), 28.8 (CH_2), 29.4 (CH_2), 29.5 (CH_2, 2C), 30.4 (CH_2), 32.6 (CH_2), 45.1 ($ClCH_2$), 72.3 (OCH_2), 129.3 (C_6H_2), 130.5 (C_6H_2), 132.7 (C_6H_2), 153.7 (C_6H_2); Found: C, 73.37; H, 9.75; Cl, 11.42%. Calcd for $C_{19}H_{31}ClO$: C, 73.40; H, 10.05; Cl, 11.40%.

$Cl(CH_2)_6O\{C_6H_3$-3,5-$(OMe)_2\}$. A solution of 3,5-dimethoxyphenol (4.0 g, 26 mmol) and NaOH (1.6 g, 40 mmol) in DMF (10 mL) was stirred for 1 h at room temperature, followed by addition of 1,6-dichlorohexane (7.6 mL, 52 mmol). The mixture was stirred for another 23 h at 110 °C, before being quenched with 1 M HCl(aq) (100 mL). The water layer was extracted with CH_2Cl_2 (100 mL) and the organic extract was washed with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield a crude product, which was purified by SiO_2 column chromatography (2 times, hexane/CH_2Cl_2 = 3/1 ($R_f = 0.23$), hexane/AcOEt = 20/1 ($R_f = 0.34$)) and washing with hexane (15 mL) to yield $Cl(CH_2)_6O\{C_6H_3$-3,5-$(OMe)_2\}$ as a white powder (1.1 g, 4.0 mmol, 15%). ^{1}H NMR (300 MHz, $CDCl_3$, r.t.): δ 1.43–1.56 (CH_2, 4H), 1.73–1.86 (CH_2, 4H), 3.55 (t, $ClCH_2$, 2H, $J = 7$ Hz), 3.77 (s, CH_3, 6H), 3.92 (t, OCH_2, 2H, $J = 7$ Hz), 6.08 (s, C_6H_3, 3H); $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$, r.t.): δ 25.4 (CH_2), 26.6 (CH_2), 29.0 (CH_2), 32.4 (CH_2), 45.0 ($ClCH_2$), 55.3 (CH_3), 67.7 (OCH_2), 92.7 (C_6H_3), 93.2 (C_6H_3), 160.9 (C_6H_3), 161.4 (C_6H_3); Found: C, 61.47; H, 7.55; Cl, 13.09%. Calcd for $C_{14}H_{21}ClO_3$: C, 61.65; H, 7.76; Cl, 13.00%.

[4,4′-bpy-*N*-$(CH_2)_{10}O(C_6H_2$-2,4,6-$Me_3)]^+(Cl^-)$ (1c). A solution of $Cl(CH_2)_{10}O(C_6H_2$-2,4,6-$Me_3)$ (1.43 g, 4.6 mmol) and 4,4′-bipyridine (1.44 g, 9.2 mmol) in DMF (10 mL) was stirred at 100 °C for 28 h. The evaporation of the solvent yielded a brown solid, which was purified by washing with Et_2O, recrystallization from CH_2Cl_2/Et_2O (20 mL/200 mL) at room temperature, and washing with Et_2O to yield [4,4′-bpy-*N*-$(CH_2)_{10}O(C_6H_2$-2,4,6-$Me_3)]^+(Cl^-)$ (**1c**) as a white solid (945 mg, 2.0 mmol, 44%). ^{1}H NMR (300 MHz, $CDCl_3$, r.t.): δ 1.17–1.49 (CH_2, 12H), 1.70 (m, OCH_2CH_2, 2H), 1.75 (br, NCH_2CH_2, 2H), 2.17 (s, Me, 9H), 3.66 (t, OCH_2, 2H, $J = 7$ Hz), 4.94 (t, NCH_2, 2H, $J = 7$ Hz), 6.76 (s, C_6H_2, 2H), 7.75 (d, $C_{10}H_8N_2$, 2H, $J = 5$ Hz), 8.43 (d, $C_{10}H_8N_2$, 2H, $J = 6$ Hz), 8.77 (d, $C_{10}H_8N_2$, 2H, $J = 5$ Hz), 9.55 (d, $C_{10}H_8N_2$, 2H, $J = 6$ Hz); $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$, r.t.): δ 16.1 (C_6H_2-4-CH_3), 20.5 (C_6H_2-2,6-(CH_3)), 26.0 (CH_2, 2C), 28.9 (CH_2), 29.2 (CH_2), 29.3 (CH_2, 2C), 30.3 (CH_2), 31.8 (CH_2), 61.3 (NCH_2), 72.2 (OCH_2), 121.6 ($C_{10}H_8N_2$), 125.8 ($C_{10}H_8N_2$), 129.2 (C_6H_2), 130.4 (C_6H_2), 132.7 (C_6H_2), 141.0 ($C_{10}H_8N_2$), 145.7 ($C_{10}H_8N_2$), 151.1 ($C_{10}H_8N_2$), 153.2 ($C_{10}H_8N_2$), 153.6 (C_6H_2); Found: C, 69.48; H, 8.48; N, 5.61%. Calcd for $C_{29}H_{39}ClN_2O\cdot 2H_2O$: C, 69.23; H, 8.61; N, 5.57%.

[4,4′-bpy-*N*-$(CH_2)_6O\{C_6H_3$-3,5-$(OMe)_2\}]^+(Cl^-)$ (1d). A solution of $Cl(CH_2)_6O\{C_6H_3$-3,5-$(OMe)_2\}$ (800 mg, 2.9 mmol) and 4,4′-bipyridine (906 mg, 5.8 mmol) in DMF (8 mL) was stirred at 110 °C for 25 h. The evaporation of the solvent yielded a brown solid, which was purified by washing with Et_2O, reprecipitation from EtOH/Et_2O (50 mL/500 mL) at room temperature to yield [4,4′-bpy-*N*-$(CH_2)_6O\{C_6H_3$-3,5-$(OMe)_2\}]^+(Cl^-)$ (**1d**) as a gray solid (635 mg, 1.5 mmol, 52%). ^{1}H NMR (300 MHz, dmso-d_6, r.t.): δ 1.28–1.52 (CH_2, 4H), 1.68 (br, OCH_2CH_2, 2H), 1.98 (br, NCH_2CH_2, 2H), 3.67 (s, Me, 6H), 3.89 (t, OCH_2, 2H, $J = 6$ Hz), 4.67 (t, NCH_2, 2H, $J = 7$ Hz), 6.04 (s, C_6H_3, 3H), 8.05 (d, $C_{10}H_8N_2$, 2H, $J = 5$ Hz), 8.65 (d, $C_{10}H_8N_2$, 2H, $J = 6$ Hz), 8.86 (d, $C_{10}H_8N_2$, 2H, $J = 5$ Hz), 9.31 (d, $C_{10}H_8N_2$, 2H, $J = 6$ Hz); $^{13}C\{^1H\}$ NMR (100 MHz, dmso-d_6, r.t.): δ 25.0 (CH_2), 25.2 (CH_2), 28.4 (CH_2), 30.7 (CH_2), 55.1 (CH_3), 60.2 (NCH_2), 67.2 (OCH_2), 92.6 (C_6H_3), 93.1 (C_6H_3), 121.9 ($C_{10}H_8N_2$), 125.3 ($C_{10}H_8N_2$), 140.8 ($C_{10}H_8N_2$), 145.2 ($C_{10}H_8N_2$), 150.8 ($C_{10}H_8N_2$), 152.0 ($C_{10}H_8N_2$), 160.3 (C_6H_3), 161.0 (C_6H_3); Found: C, 65.51; H, 6.82; N, 6.27%. Calcd for $C_{24}H_{29}ClN_2O_3\cdot 0.5H_2O$: C, 65.82; H, 6.90; N, 6.40%.

[(α-CD){4,4′-bpy-*N*-$(CH_2)_{10}O(C_6H_2$-2,4,6-$Me_3)}]^+(Cl^-)$ (1c-(α-CD)). ^{1}H NMR data were obtained from a mixture of **1c** ([**1c**] = 10 mM) and α-CD ([α-CD] = 30 mM) in D_2O. ^{1}H NMR (300 MHz, D_2O, r.t.): δ 1.05–2.04 (CH_2, 16H), 2.06 (s, Me), 2.18

(s, Me), 3.35–3.79 (CH-α-CD, OCH_2, 38H), 4.50–4.54 (NCH_2, 2H), 4.82–4.88 (CH-α-CD, 6H), 6.82 (s, C_6H_2), 6.91 (s, C_6H_2), 7.75 (d, $C_{10}H_8N_2$, 2H, $J = 6$ Hz), 8.24 (d, $C_{10}H_8N_2$, 2H, $J = 5$ Hz), 8.59 (d, $C_{10}H_8N_2$, 2H, $J = 5$ Hz), 8.82 (d, $C_{10}H_8N_2$, 2H, $J = 7$ Hz); MS (MALDI-TOF) found m/z 1401.7 $[M - Cl]^+$, calcd for $C_{65}H_{99}N_2O_{31}$ m/z 1403.6.

[(α-CD){4,4′-bpy-*N*-$(CH_2)_6O(C_6H_3$-3,5-$(OMe)_2)$}]$^+(Cl^-)$ (1d-(α-CD)). ^{1}H NMR data were obtained from a mixture of **1d** ([**1d**] = 10 mM) and α-CD ([α-CD] = 50 mM) in D_2O. ^{1}H NMR (300 MHz, D_2O, r.t.): δ 1.19–1.69 (CH_2, 4H), 1.87 (m, OCH_2CH_2, 2H), 2.06 (m, NCH_2CH_2, 2H), 3.39–3.84 (CH-α-CD, OCH_2, 38H), 4.53–4.65 (NCH_2, 2H), 4.88–4.92 (CH-α-CD, 6H), 5.65 (s, C_6H_3), 6.16 (s, C_6H_3), 7.83 (d, $C_{10}H_8N_2$, 2H, $J = 6$ Hz), 8.30 (d, $C_{10}H_8N_2$, 2H, $J = 7$ Hz), 8.67 (d, $C_{10}H_8N_2$, 2H, $J = 6$ Hz), 8.89 (d, $C_{10}H_8N_2$, 2H, $J = 7$ Hz); MS (MALDI-TOF) found m/z 1363.7 $[M - Cl]^+$, calcd for $C_{60}H_{89}N_2O_{33}$ m/z 1363.6.

Determination of Equilibrium Constants for Formation of 1c(α-CD). A D_2O solution of **1c** ([**1c**] = 6 mM) and α-CD ([α-CD] = 4 mM) was charged to an NMR tube. Fixing temperature of the solution and comparison of the peaks at δ 7.62 (b) and 7.75 (b′) showed the equilibrium constant. $K = 2511$ (25 °C), 1734 (35 °C), 1173 (45 °C), 779 (55 °C), 566 (65 °C), 326 (75 °C), and 206 M^{-1} (85 °C).

Determination of Equilibrium Constants for Formation of 1d(α-CD). A D_2O solution of **1d** ([**1d**] = 10 mM) and α-CD ([α-CD] = 10 mM) was charged to an NMR tube. Fixing temperature of the solution and comparison of the peaks at δ 7.81 (b) and 7.93 (b′) showed the equilibrium constant. $K = 615$ (5 °C), 429 (15 °C), 289 (25 °C), 188 (35 °C), 125 (45 °C), and 83 M^{-1} (55 °C).

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References

1 C. Tanford, *The Hydrophobic Effect*, Wiley, Inc., New York, **1973**.

2 M. N. Jones, D. Chapman, *Micelles, Monolayers, and Biomembranes*, Wiley-Liss, Inc., New York, **1995**.

3 H. Schott, *J. Phys. Chem.* **1966**, *70*, 2966.

4 a) K. Kalyanasundaram, J. K. Thomas, *J. Am. Chem. Soc.* **1977**, *99*, 2039. b) N. J. Turro, A. Yekta, *J. Am. Chem. Soc.* **1978**, *100*, 5951.

5 a) T. Szejtli, *Topics in Inclusion Science: Cyclodextrin Technology*, Kluwer Academic, Boston, **1988**. b) J. F. Stoddart, *Carbohydr. Res.* **1989**, *192*, xii. c) G. Wenz, *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 803. d) A. Harada, *Coord. Chem. Rev.* **1996**, *148*, 115. e) A. Harada, *Carbohydr. Polym.* **1997**, *34*, 183. f) A. Harada, *Acc. Chem. Res.* **2001**, *34*, 456.

6 a) C. Park, I. H. Lee, S. Lee, Y. Song, M. Rhue, C. Kim, *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 1199. b) Y. Wang, N. Ma, Z. Wang, X. Zhang, *Angew. Chem., Int. Ed.* **2007**, *46*, 2823. c) J. Zou, F. Tao, M. Jiang, *Langmuir* **2007**, *23*, 12791.

7 T. Okubo, H. Kitano, N. Ise, *J. Phys. Chem.* **1976**, *80*, 2661.

8 a) T. Okubo, Y. Maeda, H. Kitano, *J. Phys. Chem.* **1989**, *93*, 3721. b) A. Diaz, P. A. Quintela, J. M. Schuette, A. E. Kaifer, *J. Phys. Chem.* **1988**, *92*, 3537. c) P. Sehgal, M. Sharma, R. Wimmer, K. L. Larsen, D. E. Otzen, *Colloid Polym. Sci.* **2006**, *284*, 916.

9 a) E. Junquera, E. Aicart, G. Tardajos, *J. Phys. Chem.* **1992**, *96*, 4533. b) G. González-Gaitano, A. Compostizo, L. Sánchez-Martín, G. Tardajos, *Langmuir* **1997**, *13*, 2235. c) G. González-Gaitano, A. Crespo, A. Compostizo, G. Tardajos, *J. Phys. Chem. B* **1997**, *101*, 4413. d) R. De Lisi, S. Milioto, A. Pellerito, A. Inglese, *Langmuir* **1998**, *14*, 6045. e) R. De Lisi, G. Lazzara, S. Milioto, N. Muratore, I. V. Terekhova, *Langmuir* **2003**, *19*, 7188. f) A. Guerrero-Martínez, T. Montoro, M. H. Viñas, G. González-Gaitano, G. Tardajos, *J. Phys. Chem. B* **2007**, *111*, 1368. g) A. Guerrero-Martínez, D. Domínguez-Gutiérrez, M. A. Palafox, G. Tardajos, *Chem. Phys. Lett.* **2007**, *446*, 92. h) G. Tardajos, T. Montoro, M. H. Viñas, M. A. Palafox, A. Guerrero-Martínez, *J. Phys. Chem. B* **2008**, *112*, 15691.

10 a) S. A. Nepogodiev, J. F. Stoddart, *Chem. Rev.* **1998**, *98*, 1959. b) G. Wenz, B.-H. Han, A. Müller, *Chem. Rev.* **2006**, *106*, 782. c) A. Harada, A. Hashidzume, H. Yamaguchi, Y. Takashima, *Chem. Rev.* **2009**, *109*, 5974.

11 a) G. Schill, *Catenanes, Rotaxanes, and Knots*, Academic Press, New York, **1971**. b) *Molecular Catenanes, Rotaxanes and Knots*, ed. by J.-P. Sauvage, C. Dietrich-Buchecker, Wiley-VCH, Weinheim, **1999**.

12 Y. Suzaki, T. Taira, K. Osakada, M. Horie, *Dalton Trans.* **2008**, 4823.

13 a) R. Palepu, V. C. Reinsborough, *Can. J. Chem.* **1988**, *66*, 325. b) M. Tunçay, S. D. Christian, *J. Colloid Interface Sci.* **1994**, *167*, 181. c) H. Mwakibete, R. Cristantino, D. M. Bloor, E. Wyn-Jones, J. F. Holzwarth, *Langmuir* **1995**, *11*, 57. d) R. Guo, X. J. Zhu, X. Guo, *Colloid Polym. Sci.* **2003**, *281*, 876. e) N. Funasaki, S. Ishikawa, S. Neya, *J. Phys. Chem. B* **2004**, *108*, 9593. f) A. A. Rafati, A. Bagheri, *Bull. Chem. Soc. Jpn.* **2004**, *77*, 485. g) P. Choppinet, L. Jullien, B. Valeur, *J. Chem. Soc., Perkin Trans. 2* **1999**, 249. h) G. M. Nicolle, A. E. Merbach, *Chem. Commun.* **2004**, 854.

14 Y. Wang, H. Xu, X. Zhang, *Adv. Mater.* **2009**, *21*, 2849.

15 T. Taira, Y. Suzaki, K. Osakada, *Chem. Commun.* **2009**, 7027.

16 a) L. García-Río, M. Méndez, M. R. Paleo, F. J. Sardina, *J. Phys. Chem. B* **2007**, *111*, 12756. b) A. J. M. Valente, M. Nilsson, O. Söderman, *J. Colloid Interface Sci.* **2005**, *281*, 218. c) C. Cabaleiro-Lago, M. Nilsson, O. Söderman, *Langmuir* **2005**, *21*, 11637.

17 E. Mileo, P. Franchi, R. Gotti, C. Bendazzoli, E. Mezzina, M. Lucarini, *Chem. Commun.* **2008**, 1311.

18 Y. Suzaki, T. Taira, D. Takeuchi, K. Osakada, *Org. Lett.* **2007**, *9*, 887.

19 a) Y. Suzaki, T. Taira, K. Osakada, *Dalton Trans.* **2006**, 5345. b) Y. Suzaki, T. Taira, K. Osakada, *Transition Met. Chem.* **2007**, *32*, 753.

20 a) T. Taira, Y. Suzaki, K. Osakada, *Chem. Lett.* **2008**, *37*, 182. b) T. Taira, Y. Suzaki, K. Osakada, *Chem. Asian J.* **2008**, *3*, 895.

21 N. C. Maiti, M. M. G. Krishna, P. J. Britto, N. Periasamy, *J. Phys. Chem. B* **1997**, *101*, 11051.