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Hydrogen-Bond-Assisted π-Stacking of Shape-Persistent Cyclophanes

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The π-stacking interaction between shape-persistent cyclophanes works cooperatively with multiple hydrogen bonding sites to form cyclophane dimers. These findings considerably broaden the applicability of π-stacking interactions as a driving force in self-assembly chemistry. A gel formation effect was also noticed in one of the cyclophanes.

Introduction

In the past two decades, π-stacking interactions between aromatic systems have been the focus of much research. Not only is the interaction of great theoretical interest,[1] it has also been proposed to be a pivotal assembly force in many important supramolecular systems including discotic liquid crystals,[2] nucleic acids,[3] molecular catalysts,[4] and various protein and enzyme−substrate complexes.[5] One important goal of this work is that scientists may one day employ the molecular stacking interaction to build controlled nanoscale structures.[6] However, before the goal can be accomplished, chemists need a much deeper understanding of the nature of the interactions and how they can be modulated.

The oligomerization of shape-persistent cyclophanes (SPCs, Figure 1) through π-stacking interactions in solution has attracted considerable interest since Moore first discovered the phenomenon in 1992.[7] Similar studies conducted by Tobe's and Yamaguchi's groups have revealed that the stacking interactions can be fine-tuned by altering the ring size,[8] the interior or exterior substitutions on the ring,[9] and stereochemistry of the ring.[10]

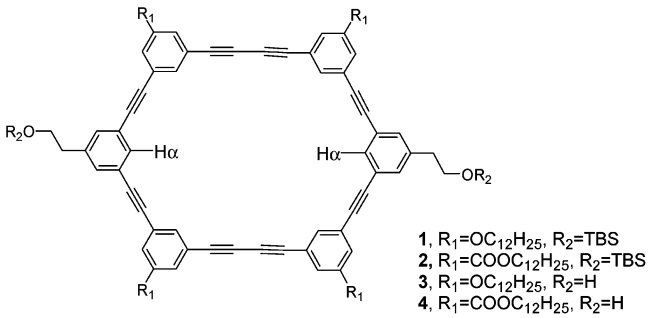

FIGURE 1. Examples of shape-persistent cyclophane.

More recently, higher order SPC aggregates such as liquid crystals[11] and hollow cylindrical brushes[12] have also been reported. Despite these prior works, the basic principle of using π-stacking interactions to build SPC-based nanostructures is still elusive.

We report here the first example of π-stacking between SPCs assisted by hydrogen bonding. When hydrogen-bonding hydroxyl groups were attached to the exterior of the SPCs, we detected enhanced dimerization in the ester-substituted SPCs. More remarkably, clear NMR evidence of the π-stacking was observed even for an alkoxyl-substituted SPC. These results open a new venue of SPC self-assembly that we believe can greatly extend the potential of intermolecular interactions in building nanostructures.

The general consensus from the literature is that the oligomerization (usually observed by NMR in $CDCl_3$) is

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much stronger in SPCs substituted with electron-withdrawing groups.[7] Alkyl- and alkoxyl-substituted SPCs showed no tendency to form aggregates under identical conditions. Conversely, our study on **1** and **3**, systems containing electron-donating groups, clearly indicated that π-stacking can be enhanced by hydrogen bonds. Likewise, the hydrogen-bonding-assisted stacking is also evident from the association behavior of electron-deficient cyclophanes **2** and **4**. This cooperative interaction allows us to observe for the first time the dimerization of an alkoxyl-substituted SPC in chloroform via π-stacking.

Synthesis and Measurement of the Dimerization Constant

The synthesis is outlined in Scheme 1. A retrosynthetic analysis revealed that cyclophanes **1**−**4** could be assembled from common components **5**−**7**. Compound **5** was made via alkylation and iodination of 3,5-dibromophenol.[13] The synthesis of **6** started with bromination (NBS/DMF) and deamination (isoamyl nitrite/ DMF) of 4-aminophenethyl alcohol to produce 3,5-dibromophenethyl alcohol.[14] The hydroxyl group was protected before the two alkyne units were introduced through Sonogashira coupling conditions to give **6.** To make **7**, 1,3,5-tribromobenzene was first converted into 3-bromo-5-trimethylsilylbenzoic acid through two consecutive lithiation reactions. Esterification followed by iodination furnished **7** in high yield**.**

The TMS-protected half-cyclophanes **8** and **9** were synthesized through a one-pot quadruple Sonogashira coupling in 70−80% yield. The dialkyne **6** and iodobromide **5** or **7** first underwent coupling to produce the intermediate dibromide (in situ). Excess trimethylsilyl acetylene (TMSA) and a fresh portion of Pd catalyst were then added to introduce the protected alkyne units.

The TBDMS-protected cyclophanes **1** and **2** were synthesized from half-cyclophanes **10** and **11**, respectively, using a modified Ellington coupling.[15] Removing the TBDMS protecting groups (TBAF/THF) furnished the corresponding diols **3** and **4**.

As expected, the chemical shift of the aromatic protons in **1**, an electron-rich cyclophane, was not concentration dependent (between 1 and 50 mg/mL in $CDCl_3$), indicating no self-association occurred in this reasonably wide range of concentrations. Also, consistent with the observations by Moore and Tobe, all the NMR signals in the aromatic region of **2**, an electron-deficient cyclophane, showed notable upfield shifts when the concentration increased from 2 to 100 mg/mL. Assuming the monomer−dimer equilibrium to be the dominating process in these moderately concentrated solutions, we found the dimerization constant in $CDCl_3$ at 25 °C to be 5.6 M^{-1} using the fitting method developed by Horman.[16] Variable temperature experiments were carried out between −20 and +25 °C. Employing a van't Hoff plot, we determined $\Delta H = -7.52$ kcal/mol, $\Delta S = -21.68$ cal/mol, and $\Delta G = -1.06$ kcal/mol for the dimerization of **2** (Table 1). The stacking force is rather weak compared to that for similar cyclophanes reported by Moore and Tobe **(**$\Delta G = -2.4$ and −3.4 kcal/mol at 20 °C, respectively) presumably because the two exterior alkyl groups in **2** interfere with the stacking.

TABLE 1. Thermodynamic Parameters of 2A ↔ A_2 Equilibrium

	ΔG (kcal/mol at 25 °C)	ΔH (kcal/mol)	ΔS (cal/K·mol)
1	∼0		
2	−1.06	−7.52	−21.68
3	−0.87	−7.11	−20.94
4	−1.47	−5.52	−13.6

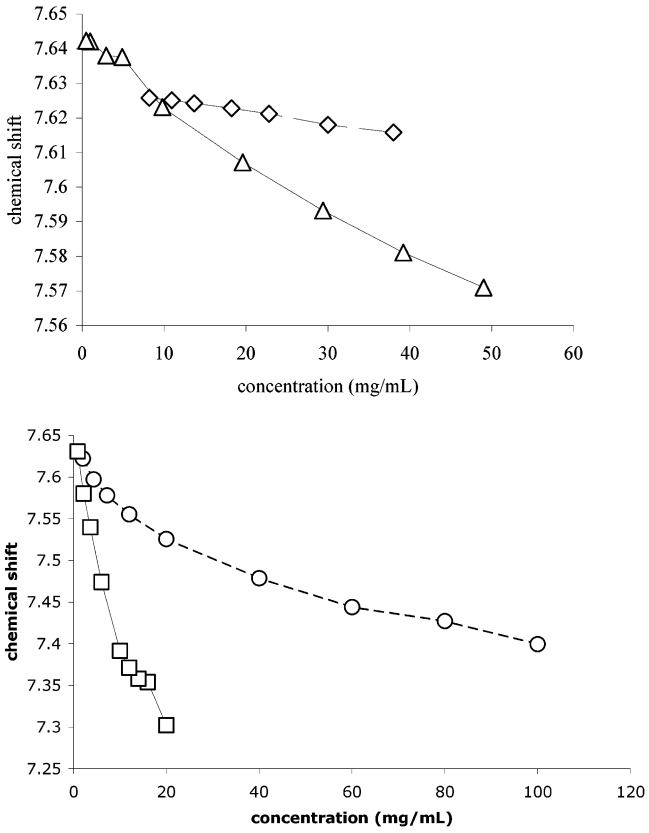

FIGURE 2. (a) Concentration vs chemical shift (H_α, see Figure 1) plot for cyclophanes **1** (diamonds) and **3** (triangles). (b) Concentration vs chemical shift (H_α, see Figure 1) plot for cyclophanes **2** (circles) and **4** (squares).

Similar NMR studies were also performed with very diluted to nearly saturated solutions of **3** and **4**. To our surprise, the NMR spectrum of **3** is unequivocally concentration dependent, and the association constant was found to be 3.7 M^{-1} at 25 °C (Figure 2a). Hydroxyl groups evidently have a strong influence on this behavior. The aggregation behavior of **4** also supported this hypothesis (Figure 2b). Under similar conditions, its association constant near room temperature was estimated to be 25 M^{-1},[17] nearly five times that of **2**. All the binding study results are listed in Table 1. Given the present results,

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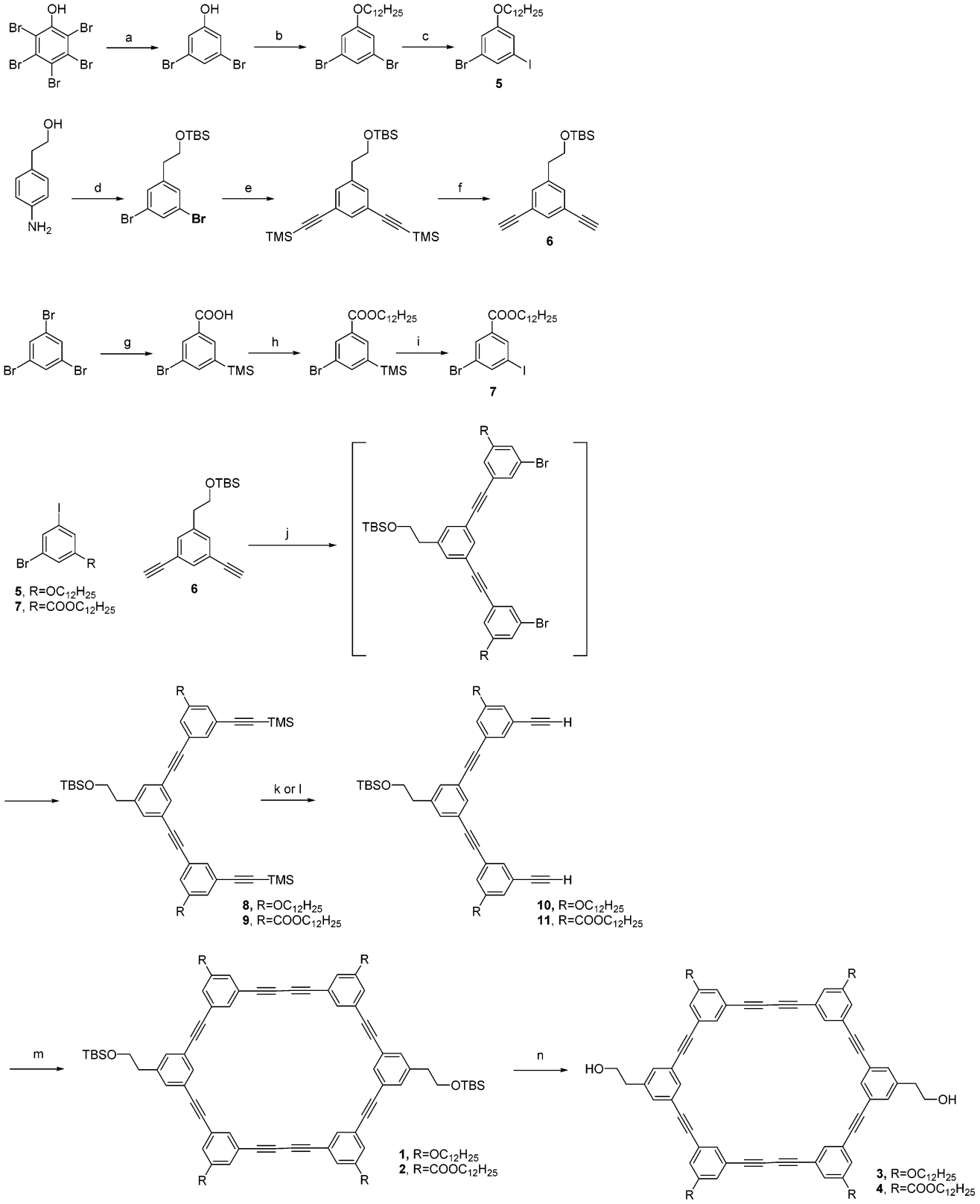
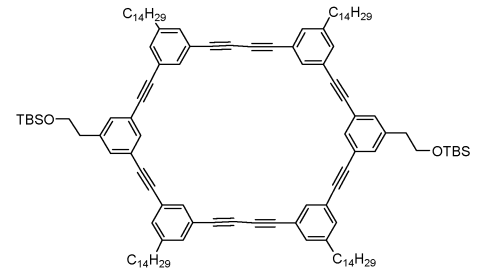
(17) The equilibrium constant at 25 °C was intrapolated from the van't Hoff plot.

SCHEME 1. Synthetic Strategy for Cyclophanes 1−4[a]



[a] Key: (a) $AlCl_3$, benzene reflux (78%); (b) *n*-dodecyl iodide, K_2CO_3, DMF, 70 °C (83%); (c) (i) *n*-BuLi, THF, −78 °C, (ii) 1,2-diiodoethane (87%); (d) (i) NBS, DMF 0 °C → rt, (ii) isoamyl nitrite, DMF, 70 °C, (iii) TBSCl, imidazole, CH_2Cl_2 (41%); (e) $Pd(dba)_2$, PPh_3, CuI, TMSA, Et_3N, 65 °C (82%); (f) K_2CO_3, CH_2Cl_2/MeOH, (100%); (g) (i) *n*-BuLi, ether, −78 °C (ii) TMSCl, (iii) *n*-BuLi, ether, −78 °C, (vi) CO_2 (56%); (h) *n*-dodecyl iodide, K_2CO_3, DMF, 70 °C (95%); (i) ICl, CH_2Cl_2 (100%); (j) (i) $Pd(dba)_2$, PPh_3, CuI, Et_3N, 50 °C, (ii) $Pd(dba)_2$, PPh_3, CuI, TMSA, Et_3N, 70 °C (72% and 84% for **8** and **9**, respectively); (k) same as (f), (99% for **10**); (l) 10% TBAF, CH_2Cl_2, (90% for **11**); (m) $CuCl_2$/CuCl, pyridine, slow addition for 96 h at 65 °C, overnight at rt (50% and 35% for **1** and **2**, respectively); (n) excess TBAF, THF (72% and 94% for **3** and **4**, respectively).



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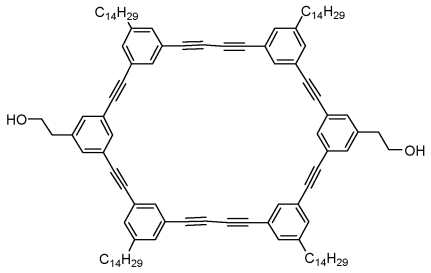

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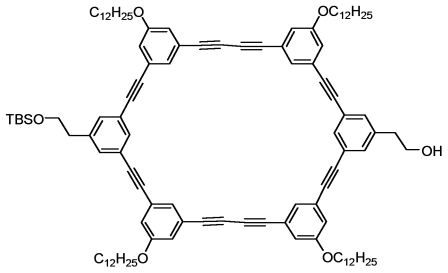

14

FIGURE 3. Structures for cyclophane **12**−**14**.

we postulate that the dimerization of **3** and **4** should most accurately be described as π-stacking assisted by the hydrogen bonding.

To the best of our knowledge, **3** is the first example of an alkoxyl-substituted SPC that forms dimers in $CDCl_3$.[18] Compared to previous results, the association constant is admittedly only moderate. However, it is already comparable to that for **2**, which is a more appropriate reference compound.[19]

The scope and limitation of the hydrogen-bonding assisted π-stacking was further investigated by studying **12,** an alkyl-substituted SPC, **13**, an alkyl-substituted bis-hydroxyl SPC, and **14**, a monohydroxyl SPC (Figure 3). While no evidence of self-association was detected for **12** in $CDCl_3$, **13** formed dimers under identical conditions (observed by both NMR and TLC). The stacking interaction is evidently weaker than in **2** or **3**. Unfortunately, we could not determine the association constant of **13** because of poor solubility at the available temperature range. This demonstrated the adaptability of this hydrogen-bonding-assisted π-stacking interaction that operates with electron-deficient (**4**), electron-neutral (**13**), and electron-rich (**3**) cyclophanes.

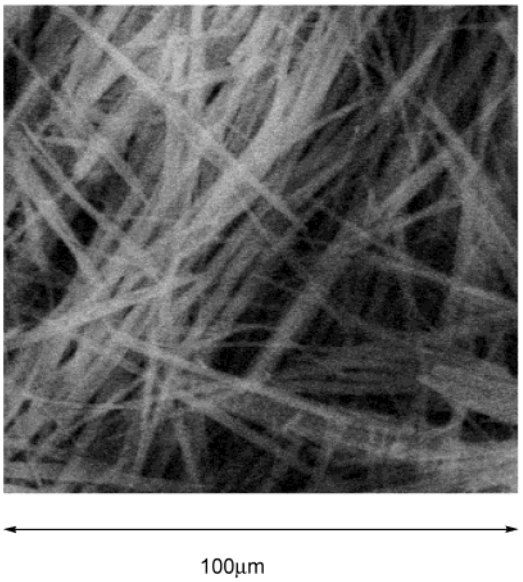

FIGURE 4. SEM image of xerogel from the CH_2Cl_2 solution of **3**.

Since the dimerization could involve up to three different forces (two hydrogen bonds, one π-stacking), it is important to know whether these forces work cooperatively. Preliminary results showed the association force of **14** is much weaker than in **3**, indicating that such interaction is indeed cooperative. Due to extremely small changes of chemical shifts, the dimerization constant of **14** cannot be unequivocally determined.

During the course of our NMR study, we also found that **3** can act as a gelling agent for chlorinated solvents ($CHCl_3$ and CH_2Cl_2) near room temperature. Compound **3** was soluble in CH_2Cl_2 at 40 °C. When the solution (3% w/w) was cooled back to room temperature, it slowly became a nonflowing mass. The gelation is thermally reversible. The microstructure of the xerogel of **3** was examined by SEM (Figure 4). We postulated that the network was directed by the cooperative interaction of hydrogen bonds and π-stacking. Similar phenomenon were recently observed by two other groups in their studies of organogels formed from oligo(phenylenevinylene)s and porphyrins.[20]

Discussion

The current interest in SPCs is at least partly due to their potential to self-assemble into channel-like superstructures. In principle, it is possible to control the size and transportation properties of the channels by altering the size and substitutions (both interior and exterior) of the cyclophanes.[8,9] However, early studies have already shown some limitations of this approach. According to

(18) An oligoethylene glycol-alkoxyl-substituted SPC did form a dimer in acetone solution (ref 9c). However, the nature of the driving force is proposed to be solvophobic.

(19) Interestingly, we discovered that thin-layer chromatography (TLC), in addition to NMR, can be used to detect the dimerization in this class of compounds. When developed on TLC plates, the monomeric cyclophane (**1**) showed a regular inverted-V-shaped tailing trail. In contrast, all the aggregating cyclophanes (**2**−**4**) exhibited very unusual V-shaped reverse-tailing trails. A similar phenomenon was also observed in alkyl-substituted cyclophanes (vide infra). Whether this phenomenon is the result of the π-stacking remains an open question.

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both theoretical and empirical data,[21] pure π-stacking interaction always directs two aromatic systems into a "staggered face-to-face" geometry in which the hollow space in every SPC is eclipsed (at least partly) by its neighboring SPCs. The staggered structure is expected to be dynamic. As a result, to attain static tubular structure would be very difficult.

Early studies also showed that the stacking interaction is very sensitive to substitutions on SPCs. Although it is generally accepted that electron-withdrawing substitutions are necessary for the aggregation to occur, too many electron-withdrawing groups seem to inhibit the dimerization. Our current knowledge of π-stacking force is insufficient to predict whether certain SPCs will oligomerize, let alone to predict the precise geometry of the aggregates.

Due to these difficulties, we believe π-stacking alone might be inadequate as a driving force in constructing some supramolecular structures. However, these problems can be amended when the π-stacking interaction is supplemented by hydrogen bonds. As our results suggested, by installing two hydroxyl groups, existing stacking interactions can be amplified. More importantly, the π-stacking induced aggregation can be extended to systems where examples of such phenomenon were hitherto scarce. Our findings attest that the hydrogen-bond-assisted π-stacking force is stronger than π-stacking alone. This concept should be applicable to wide range of systems.

Furthermore, since the interaction is cooperative, both hydrogen bonds have to be intact for the dimer to maintain its structure. As a result, the sliding motions of the SPCs within the dimers of **3** and **4** should be much more restricted than that in **2**. Dimers of **3** and **4** should be more static and therefore have a better-defined inner diameter.

Summary

In conclusion, we have discovered that the well-known π−stacking forces between SPCs can be enhanced through hydrogen-bonding interactions. Due to the enhanced stacking interaction, we observed SPC dimerization in solution and gel formation at moderate concentration. This new mode of π-stacking is quite versatile and cooperative. Using such interactions to construct nano-sized channels is an obvious application.

Experimental Section

General Procedures. The starting compounds and reagents were purchased from Aldrich or Acros. The TMSA was obtained FAR Laboratories. The reactions were all carried out under 1 atm of N_2 with magnetic stirring. Some reaction solvents were distilled before use (THF and ether from Na/benzophenone; CH_2Cl_2 and triethylamine from CaH_2). The TLC plates (40 F_{254}) and silica gel (230−400 mesh ASTM) used for flash chromatography were from EM Science.

3,5-Dibromophenol.[13] Pentabromophenol (30.00 g, 0.04 mol) and $AlCl_3$ (80.00 g, 0.60 mol) were placed in a 500 mL round-bottom flask. Benzene (300 mL) was added, and the mixture was heated to reflux under N_2 for 18 h. The reaction was cooled back to room temperature and slowly poured unto crushed ice. The solid residue in the flask was quenched with cold water (caution, HCl evolved) before being combined with the icy slurry. The mixture was extracted with EtOAc (3×). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The dark residue was purified by flash chromatography (hexane then CH_2Cl_2) to give 3,5-dibromophenol (12 g, 78%) as a white solid. The ^{1}H NMR spectrum (400 MHz, $CDCl_3$) was identical with the literature value.[13]

3,5-Dibromododecyloxylbenzene. 3,5-Dibromophenol (8.01 g, 0.032 mol) was dissolved in DMF (50 mL). *n*-Dodecyl iodide (10.00 g, 0.033 mol) and K_2CO_3 (7.00 g, 0.051 mol) were added to the mixture. The suspension was then stirred under N_2 for 18 h at 70 °C. The reaction was poured into petroleum ether and the mixture was washed with water (5×). The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified on flash chromatography (petroleum ether) to furnish the product (11.4 g, 83%) as a light yellow oil that solidified after several days at room temperature: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (t, J = 2 Hz, 1 H), 7.02 (d, J = 2 Hz, 2 H), 3.95 (t, J = 7 Hz, 2 H), 1.79 (q, J = 7 Hz, 2 H), 1.30 (m, 18 H) 0.92 (t, J = 7 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.79, 126.57, 123.50, 117.43, 69.04, 32.40, 30.13, 30.11, 30.06, 30.02, 29.19, 29.83, 29.78, 29.48, 26.39, 23.16, 14.57; IR (KBr) 2922, 2852, 1584, 1557, 1465, 1254, 1027, 829, 743 cm^{-1}; HRMS found m/z = 420.0484, $C_{18}H_{28}Br_2O$ required 420.0488.

3-Iodo-5-bromododecyloxylbenzene (5). 3,5-Dibromododecyloxylbenzene (10.00 g, 0.024 mol) was dissolved in THF (200 mL). The solution was cooled to −78 °C in a dry ice−acetone bath under N_2. *n*-BuLi (11.5 mL, 2.46 M in hexane, 0.0264 mol) was added during 10 min via a syringe, and the exchange reaction was allowed to proceed for another 45 min. A solution of 1,2-diiodoethane (8.20 g in 10 mL THF, 0.0288 mol) was slowly added to the lithium reagent. The reaction then was warmed back to room temperature and stirred for 2.5 h. The solvent was removed in vacuo, and the residue was redissolved in ether. The solution was washed with Na_2SO_3 solution, saturated $NaHCO_3$ solution, and water (1× each) before being dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether) to give the product (9.75 g, 87%) as a colorless liquid that solidified to form a large crystal after standing at room temperature for several days: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (t, J = 2 Hz, 1 H), 7.19 (t, J = 2 Hz, 1 H), 7.03 (t, J = 2 Hz, 1 H), 3.92 (t, J = 7 Hz, 2 H), 1.77 (q, J = 7 Hz, 2 H), 1.29 (m, 18 H), 0.91 (t, J = 7 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.58, 132.19, 123.50, 123.23, 118.64, 94.56, 66.99, 32.34, 30.06, 30.05, 29.99, 29.95, 29.76, 29.71, 29.43, 26.33, 23.10, 14.53; IR (KBr) 2920, 2846, 1571, 1550, 1432, 1253, 1026, 826, 723 cm^{-1}; HRMS found m/z = 468.0350, $C_{18}H_{28}BrIO$ required 468.0350.

***O-tert*-Butyldimethylsilyl-2-(3,5-dibromophenyl)ethyl Alcohol.** 4-Aminophenethyl alcohol (10.00 g, 0.073 mol) was dissolved in DMF (40 mL), and the solution was cooled to 0 °C in an ice bath. To this solution was added an NBS solution (28.02 g in 50 mL of DMF, 0.156 mol) in 30 min. The dark mixture was stirred at room temperature for 4 h to give 4-amino-3,5-dibromophenethyl alcohol. An isoamyl nitrite solution (13.00 g in 50 mL of DMF, 0.11 mol) was heated to 70 °C. The dibromoaniline solution was added to the hot nitrite solution over 20 min with a pipet (N_2 gas evolved). The reaction was kept at 70 °C for another 30 min after the addition was completed. The solvent was removed in vacuo, and the black residue was dissolved in ether and washed with water (5×). The organic phase was dried (Na_2SO_4) and concentrated in vacuo to give the crude 2-(3,5-dibromophenyl)ethyl alcohol as a brown liquid. The crude alcohol was dissolved in CH_2Cl_2 (100 mL), and to this solution were added TBDMSCl (13.00 g, 0.087 mol) and imidazole (7.00 g, 0.1 mol). The solution was stirred under N_2 at room temperature for 2.5 h. The reaction was washed with water (3×) before being dried over Na_2SO_4 and

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concentrated in vacuo. The crude product was purified by flash chromatography (10−20% CH_2Cl_2 in hexane) to give the protected alcohol (11.70 g, 41%) as a transparent liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (t, J = 2 Hz, 1 H), 7.34 (d, J = 2 Hz, 2 H), 3.80 (t, J = 7 Hz, 2 H), 2.76 (t, J = 7 Hz, 2 H), 0.89 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.95, 132.12, 131.52, 122.91, 63.87, 39.09, 26.25, 18.65, −5.10; IR (KBr) 2295, 2929, 2856, 1585, 1553, 1422, 1254, 1100, 836, 777 cm^{-1}; HRMS found m/z 336.9072, $C_{10}H_{13}Br_2OSi$ required 336.9083.

***O-tert*-Butyldimethylsilyl-2-(3,5-bis(trimethylsilylethynyl)phenyl)ethyl Alcohol.** In a screw-cap tube were dissolved *O-tert*-butyldimethylsilyl-2-(3,5-dibromophenyl)ethyl alcohol (11.00 g, 0.028 mol) and TMS-acetylene (11 mL, 7.8 g, 0.08 mol) in triethylamine (55 mL). PPh_3 (2.5 g, 9.5 mmol), $Pd(dba)_2$ (1.2 g, 2.1 mmol), and CuI (0.2 g, 1 mmol) were added in that order. The mixture was stirred under N_2 at room temperature for 45 min. The tube was then sealed, and the reaction was heated to 65 °C for 48 h in an oil bath. The reaction was diluted with ether and washed with water (3×). The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue orange oil was purified by flash chromatography (10% CH_2Cl_2 in hexane) to give pure product as a lightly yellow oil (9.8 g, 82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (t, J = 2 Hz, 1 H), 7.29 (d, J = 2 Hz, 2 H), 3.78 (t, J = 7 Hz, 2 H), 2.76 (t, J = 7 Hz, 2 H), 0.89 (s, 9 H), 0.26 (s, 18 H), 0.00 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.95, 133.54, 133.18, 123.52, 104.70, 94.84, 64.17, 39.27, 26.29, 18.66, 0.26, −5.07; IR (KBr) 2956, 2897, 2857, 2158, 1587, 1438, 1251, 1102, 842 cm^{-1}; HRMS found m/z = 371.1683, $C_{20}H_{31}OSi_3$ [M − t-C_4H_9]$^+$ required 371.1683.

***O-tert*-Butyldimethylsilyl-2-(3,5-bis(ethynyl)phenyl)-ethyl Alcohol (6).** *O-tert*-Butyldimethylsilyl-2-(3,5-bis(trimethylsilylethynyl)phenyl)ethyl alcohol (9.00 g, 0.21 mol) was dissolved in a mixed solvent of CH_2Cl_2 (100 mL) and MeOH (100 mL). K_2CO_3 was added (7.00 g, 0.051 mol), and the suspension was stirred under N_2 at room temperature for 2 h. The reaction was diluted with hexane and washed with water (4×). The organic phase was dried over Na_2SO_4 and concentrated in vacuo to give the pure product as a colorless viscous liquid (5.95 g, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (t, J = 2 Hz, 1 H), 7.35 (d, J = 2 Hz, 2 H), 3.81 (t, J = 7 Hz, 2 H), 3.08 (s, 2 H), 2.79 (t, J = 7 Hz, 2 H), 0.89 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.36, 133.08, 133.73, 122.65, 83.16, 77.87, 64.12, 39.26, 26.26, 18.66, −5.09; IR (KBr) 3297, 2856, 2110, 1587, 1471, 1255, 1093, 938, 840 cm^{-1}; HRMS found m/z 284.1599, $C_{18}H_{24}OSi$ [M − t-C_4H_9]$^+$ required 184.1596.

3-Bromo-5-trimethylsilylbenzoic Acid. 1,3,5-Tribromobenzene (12.00 g, 0.038 mol) was dissolved in diethyl ether (250 mL). The solution was cooled to −78 °C (in a dry ice−acetone bath), and it became a slurry. *n*-BuLi (17.5 mL, 2.4 M in hexane, 0.042 mol) was added over 20 min via a syringe, and the exchange reaction was allow to proceed for 3 h at −78 °C. TMSCl (6.0 mL, 5.14 g, 0.047 mol) was added to the mixture, and the reaction was warmed back to room temperature. The solvent and other volatile were evaporated. Hexane was added to the residue, and LiCl solid was removed by filtration. The filtrate was concentrated in vacuo to give the crude 3,5-dibromotrimethylsilylbenzene (11.02 g, crude yield 94%). The compound was used in the next step without further purification. Crude 3,5-dibromotrimethylsilylbenzene (11.00 g) was dissolved in diethyl ether (150 mL), and the solution was cooled to −78 °C in a dry ice−acetone bath. *n*-BuLi (17 mL, 2.4 M in hexane, 0.041 mol) was added slowly via a syringe (15 min), and the reaction was kept at −78 °C for 2.5 h. CO_2 was then bubbled into the solution for 40 min while the reaction was warmed back to room temperature. The reaction was stirred at room temperature for another 1 h before the reaction was quenched with saturated NH_4Cl. The organic phase was washed with water (3×), dried over Na_2SO_4, and concentrated in vacuo. Pure acid (5.82 g, 56% over two steps) was obtained after flash chromatography (30% diethyl ether in CH_2Cl_2) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (m, 1H), 8.20 (m, 1 H), 7.88, (m, 1 H), 0.36 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.68, 144.82, 141.67, 133.74, 133.70, 130.91, 123.26, −0.94; IR (KBr) 3500−2500 (broad), 2957, 2894, 2651, 1548, 1689, 1286, 1248, 877, 837 cm^{-1}; HRMS found m/z 273.9849, $C_{10}H_{13}BrO_2Si$ required 273.9839.

Dodecyl 3-Bromo-5-trimethylsilylbenzoate. 3-Bromo-5-trimethylsilylbenzoic acid (5.80 g, 0.021 mol) and 1-iodododecane (7.50 g, 0.026 mol) were dissolved in DMF (60 mL). K_2CO_3 (5.00 g, 0.037 mol) was added, and the suspension was heated to 70 °C for 14 h. The reaction was diluted with petroleum ether and then washed with water (4×). The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was purified by flash chromatography (20% CH_2Cl_2 in hexane) to give the desired ester as a colorless oil (8.8 g, 95%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (m, 1 H), 8.12 (m, 1 H), 7.81 (m, 1 H), 4.35 (t, J = 7 Hz, 2 H), 1.59 (m, 2 H), 1.3 (m, 18 H), 0.91 (t, J = 7 Hz, 3 H), 0.34 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.06, 144.47, 140.56, 133.12, 133.03, 132.23, 123.09, 65.92, 32.30, 30.04, 30.01, 29.96, 29.91, 29.73, 29.65, 29.07, 26.39, 23.07, 14.48. −0.94;. IR (KBr) 2925, 2851, 1728, 1556, 1462, 1265, 1122, 837, 754 cm^{-1}; HRMS found m/z 440.1745, $C_{22}H_{37}BrO_2Si$ required 440.1746.

Dodecyl 3-Iodo-5-bromobenzoate (7). Dodecyl 3-bromo-5-trimethylsilylbenzoate (8.70 g, 0.0197 mol) was dissolved in CH_2Cl_2 (100 mL). An ICl solution (3.50 g in 10 mL CH_2Cl_2, 0.022 mol) was slowly added at 0 °C. The reaction was warmed back to room temperature and allowed to stir for 2 h. The reaction was washed with Na_2SO_3 solution, $NaHCO_3$ solution, and water (1× each) before being dried (over Na_2SO_4) and concentrated in vacuo. The residue was purified by flash chromatography (15% CH_2Cl_2 in hexane) to give the desired product as a white solid (9.70 g, 99%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (t, J = 2 Hz, 1 H), 8.14 (t, J = 2 Hz, 1 H), 8.05 (t, J = 2 Hz, 1 H), 4.34 (t, J = 7 Hz, 2 H), 1.78 (m, 2 H), 1.32 (m, 18 H), 0.90 (t, J = 7 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.27, 144.04, 137.52, 134.13, 132.32, 123.38, 94.38, 66.41, 32.31, 30.03, 29.97, 29.88, 29.74, 29.64, 29.01, 26.35, 23.08, 14.50; IR (KBr) 3066, 2923, 2848, 1712, 1549, 1269, 1128, 727 cm^{-1}; HRMS found m/z 494.0136, $C_{19}H_{28}BrIO_2$ required 494.0137.

8 (R = $OC_{12}H_{25}$). Compounds **6** (1.20 g, 4.2 mmol) and **5** (5.00 g, 10.7 mmol) were dissolved in triethylamine (40 mL), and the solution was transferred into a screw-cap tube. PPh_3 (0.6 g, 2.3 mmol), $Pd(dba)_2$ (0.3 g, 0.54 mmol), and CuI (80 mg, 0.42 mmol) were added in that order, and the mixture was stirred at room temperature for 40 min before being heated to 50 °C. The first step reaction was completed after 2 h as indicated by TLC. The yellow suspension was then cooled back to room temperature. Another portion of Pd/Cu catalyst [PPh_3 (0.6 g, 2.3 mmol), $Pd(dba)_2$ (0.3 g, 0.54 mmol), and CuI (80 mg, 0.42 mmol)] and TMSA (2 mL, 1.42 g, 14.5 mmol) were added to the reaction vessel. The tube was sealed, and the reaction was stirred at room temperature for 40 min before being heated to 70 °C for 16 h. The reaction was diluted with petroleum ether and washed with water (3×). The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash chromatography (15% CH_2Cl_2 in hexane). Compound **8** was obtained in ca. 90% purity as a yellow viscous liquid (3.03 g, 72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (t, J = 2 Hz, 1 H), 7.36 (d, J = 2 Hz, 2 H), 7.26 (t, J = 2 Hz, 2 H), 7.02 (m, 2 H), 6.99 (m, 2 H), 3.98 (t, J = 7 Hz, 4 H), 3.84 (t, J = 7 Hz, 2 H), 2.83 (t, J = 7 Hz, 2 H), 1.80 (m, 4 H), 1.32 (m, 36 H), 0.90 (s, 9 H), 0.89 (t, J = 7 Hz, 6 H), 0.28 (s, 18 H), 0.02 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.17, 140.33, 140.52, 133.19, 132.87, 128.06, 124.76, 124.59, 123.61, 118.51, 104.63, 94.99, 89.33, 89.28, 68.69, 64.26, 39.41, 32.34, 30.08, 30.05, 30.00, 29.99, 29.76, 29.57, 26.40, 26.32, 23.10, 18.70, 14.52, 0.32, −5.02; IR (KBr) 2854, 2157, 1577, 1470, 1249, 1206, 1158, 1099, 848 cm^{-1}; MS (MALDI) found m/z 997.84 ([M + H]$^+$, 1), required 997.67.

9 (R = $CO_2C_{12}H_{25}$). In a screw-cap tube, **6** (1.00 g, 3.52 mmol) and **7** (4.50 g, 9.1 mmol) were dissolved in triethylamine (50 mL). PPh_3 (600 mg, 2.3 mmol), $Pd(dba)_2$ 300 mg, 0.54 mmol) and CuI (80 mg, 0.42 mmol) were added in that order. The yellow suspension was stirred at room temperature for 40 min before being heated at 50 °C for 2 h. The reaction was cooled back to room temperature after being checked by TLC. Another portion of Pd/Cu catalyst (PPh_3 (600 mg, 2.3 mmol), $Pd(dba)_2$ (300 mg, 0.54 mmol), and CuI (80 mg, 0.42 mmol)) and TMSA (3 mL. 2.2 g, 2.3 mmol) were added to the reaction vessel. The reaction was then stirred at room temperature for 40 min before being heated to 70 °C for 16 h. After being cooled back to room temperature, the reaction was diluted with petroleum ether and washed with water (3×). The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography (30−50% CH_2Cl_2 in petroleum ether) to give the desired product as yellow viscous oil (3.15 g, 84%) that solidified to become a wax solid after several days at room temperature: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (t, J = 2 Hz, 2 H), 8.10 (t, J = 2 Hz, 2 H), 7.81 (t, J = 2 Hz, 2 H), 7.57 (t, J = 2 Hz, 1 H), 7.41 (d, J = 2 Hz, 2 H), 4.36 (t, J = 7 Hz, 4 H), 3.86 (t, J = 7 Hz, 2 H), 2.85 (t, J = 7 Hz, 2 H), 1.79 (m, 4 H), 1.29 (m, 36 H), 0.90 (s, 9 H), 0.89 (t, J = 7 Hz, 6 H), 0.29 (s 18 H), 0.02 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.67, 140.56, 139.03, 133.20, 132.92, 132.89, 132.70, 131.56, 124.42, 124.18, 123.30, 103.47, 96.61, 90.36, 88.39, 66.06, 64.17, 39.36, 32.30, 30.03, 30.01, 29.97, 29.89, 29.73, 29.67, 29.09, 26.37, 26.03, 23,07, 18.70, 14.47, 0.23, −5.3; IR (KBr) 2924, 2853, 2160, 1728, 1592, 1466, 1281, 1110, 895 cm^{-1}; MS (MALDI) found m/z 1076.42 ([M + Na]$^+$, 1), required 1076.72.

Dialkyne 10 (R = $OC_{12}H_{25}$). Compound **8** (1.00 g, 1 mmol) was dissolved in a CH_2Cl_2/MeOH mix solvent (20 mL/20 mL). K_2CO_3 (1.00 g, 0.07 mol) was added to the solution, and the reaction was stirred at room temperature for 1.5 h. The reaction was poured into a water/petroleum ether mixture. The organic phase was washed with water (2×), dried (Na_2SO_4), and concentrated in vacuo. Pure product was obtained after flash chromatography (CH_2Cl_2/hexane = 1/2) as a thick yellow liquid (0.85 g, 99%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (t, J = 2 Hz, 1 H), 7.38 (d, J = 2 Hz, 2 H), 7.27 (t, J = 2 Hz, 2 H), 7.06 (m, 2 H), 7.02 (m, 2 H), 3.98 (t, J = 7 Hz, 4H), 3.85 (t, J = 7 Hz, 2 H), 3.09 (s, 2H), 2.84 (t, J = 7 Hz, 2 H), 1.81 (m, 4 H), 1.37−1.28 (m, 36 H), 0.93 (s, 9 H), 0.91 (t, J = 7 Hz, 6 H), 0.03 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.18, 140.36, 132.97, 132.88, 128.02, 124.70, 123.72, 123.50, 118.94, 118.65, 89.37, 89.18, 83.22, 77.85, 68.71, 64.26, 39.39, 32.34, 30.09, 30.06, 30.02, 29.99, 29.77, 29.54, 26.40, 26.32, 23.11, 18.72, 14.54, −5.04; IR (KBr) 3305, 2925, 2853, 1580, 1465, 1419, 1149, 839 cm^{-1}; MS (CI) found m/z 853.60 [(M + H)$^+$, 20], required 853.59.

Dialkyne 11 (R = $CO_2C_{12}H_{25}$). Compound **9** (1.00 g, 0.95 mmol) was dissolved in CH_2Cl_2 (30 mL), and the solution was cooled to 0 °C. Tetrabutylammonium fluoride (0.25 mL, 1 M solution in THF 0.25 mmol) was added. The reaction was stirred at 0 °C for 15 min. The reaction mixture was passed through a short silica gel column (eluted with CH_2Cl_2). The solvent was then removed in vacuo to give the terminal dialkyne as colorless sticky oil (0.78 g, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (t, J = 2 Hz, 2 H), 8.12 (t, J = 2 Hz, 2 H), 7.82 (t, J = 2 Hz, 2 H), 7.59 (t, J = 2 Hz, 1 H), 7.42 (d, J = 2 Hz, 2 H), 4.36 (t, J = 7 Hz, 4 H), 3.84 (t, J = 7 Hz, 2 H), 3.18 (s, 2 H), 2.85 (t, J = 7 Hz, 2 H), 1.80 (m, 4 H), 1.33 (m, 36 H), 0.92 (s, 9 H), 0.89 (t, J = 7 Hz, 6 H), 0.03 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.56, 140.59, 139.11, 133.31, 133.16, 133.14, 132.93, 131.66, 124.32, 123.39, 123.21, 90.52, 88.24, 82.24, 79.17, 66.14, 64.18, 39.35, 32.32, 30.58, 30.04, 30.00, 29.93, 29.76, 29.69, 29.07, 26.40, 26.30, 22.10, 18.71, 14.53, −5.03; IR (KBr) 3306, 2924, 2853, 1725, 1592, 1463, 1237, 1105 cm^{-1}; HRMS (CI) found m/z = 909.6 [(M + H)$^+$, 16], required 909.58.

General Procedure for the Synthesis of Cyclophane 1 and 2 (1, R = $OC_{12}H_{25}$, 2, R = $COOC_{12}H_{25}$). CuCl (8.00 g, 80 mmol) and $CuCl_2$ (1.60 g, 12 mol) (both grounded powder) were added to pyridine (250 mL). The dark green suspension was gently heated and sonicated to break up the lumps of Cu salt before it was heated to 65 °C in an oil bath. The terminal dialkyne **7** (0.84 g, 0.98 mmol) was dissolved in pyridine (50 mL) and was slowly added to the CuCl/$CuCl_2$ suspension in 96 h with a syringe pump. The reaction was cooled to room temperature and stirred overnight after the addition was completed. The reaction was diluted with CH_2Cl_2 (1000 mL), and the dark solution was washed with 4 M NH_4OH (4×), 1 M HCl (2×), saturated $NaHCO_3$ (1×), and water (1×). The remaining organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residual dark solid was purified by flash chromatography (20% CH_2Cl_2 in hexane). Cyclophane **1** was obtained as a white solid (0.42 g, 50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (t, J = 2 Hz, 2 H), 7.37 (m, 8 H), 7.07 (m, 4 H), 7.02 (m, 4 H), 3.99 (t, J = 7 Hz, 8 H), 3.85 (t, J = 7 Hz, 4 H), 2.84 (t, J = 7 Hz, 4 H), 1.82 (m, 8 H), 1.30−1.35 (m, 72 H), 0.92 (s, 18 H), 0.91 (t, J = 7 Hz, 12 H), 0.03 (s, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.23, 140.31, 132.68, 129.02, 124.93, 123.48, 123.31, 118.98, 118.58, 89.71, 89.16, 81.24, 74.45, 68.78, 64.29, 39.43, 32.34, 30.09, 30.06, 30.03, 30.00, 29.78, 29.53, 26.40, 26.33, 26.30, 23.11, 18.73, 14.55, −5.01; IR (KBr) 2924, 2853, 2219, 1578, 1467, 1416, 1370, 1198, 1097, 1056, 868, 838 cm^{-1}; MS (MALDI) found, m/z = 1724, ([M + Na]$^+$, <1), 1702 ([M + H]$^+$, <1), required 1724.13 and 1701.14.

Cyclophane**2** was synthesized from dialkyne **11** by a procedure similar to that for **1** from **10**. The only difference was the solvent polarity for the flash chromatography (70% CH_2Cl_2 in hexane). Cyclophane **2** was obtained as a yellow waxy solid (35% yield): ^{1}H NMR (400 MHz, $CDCl_3$, diluted solution) δ 8.30 (t, J = 2 Hz, 4 H), 7.94 (t, J = 2 Hz, 4 H), 7.86 (t, J = 2 Hz, 4 H), 7.50 (t, J = 2 Hz, 2 H), 7.30 (d, J = 2 Hz, 4 H), 4.35 (t, J = 7 Hz, 8 H), 3.83 (t, J = 7 Hz, 4 H), 2.78 (t, J = 7 Hz, 4 H), 1.81 (m, 8 H), 1.46−1.49 (m, 72 H), 0.94 (s, 18 H), 0.91 (t, J = 7 Hz, 12 H), 0.05 (s, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$, concentrated solution) δ 165.29, 140.57, 139.69, 133.49, 133.25, 133.06, 131.78, 124.61, 123.17, 122.83, 90.67, 88.23, 80.67, 75.41, 66.19, 64.13, 39.34, 32.32, 30.06, 30.04, 30.03, 29.94, 29.75, 29.72, 29.09, 26.41, 26.31, 23.08, 18.69, 14.49, −5.02; IR (KBr) 2924, 2853, 2217, 1752, 1593, 1456, 1254, 1110, 837, 770 cm^{-1}; MS (MALDI) found m/z 1922.65 ([M + Ag]$^+$, 1), required 1922.03.

Diol 3 (R = $OC_{12}H_{25}$). Compound **1** (0.40 g, 0.245 mmol) was dissolved in THF (5 mL). Tetrabutylammonium fluoride (1.0 mL, 1 M solution in THF, 1 mmol) was added, and the reaction was stirred at room temperature for 2 h. The solution was passed through a short silica gel column (eluent 1:1 ether/chloroform), and the solvent was removed in vacuo. The crude product was purified by flash chromatography (5% diethyl ether in chloroform) to give the desired cyclophane diols as a white solid (0.25 g, 72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (t, J = 2 Hz, 2 H), 7.32 (d, J = 2 Hz, 4 H), 7.31 (t, J = 2 Hz, 4 H), 6.99 (m, 4 H), 6.93 (m, 4 H), 3.87−3.94 (m, 12 H), 2.84 (t, J = 7 Hz, 4 H), 1.76 (m, 8 H), 1.27 (m, 72 H), 0.89 (t, J = 7 Hz, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.14, 139.60, 133.93, 132.29, 129.02, 124.78, 123.92, 123.33, 118.88, 118.63, 89.53, 89.49, 81.24, 74.52, 68.76, 63.59, 39.10, 32.35, 30.11, 30.08, 30.05, 30.03, 29.83, 29.79, 29.57, 26.42, 23.12, 14.55; IR (KBr) 3354, 2921, 2851, 1579, 1416, 1368, 1198, 1050, 864, 844 cm^{-1}; MS (MALDI) found m/z 1474 ([M + H]$^+$, <1), required 1473.97.

Diol 4 (R = $CO_2C_{12}H_{25}$). Cyclophane **2** (0.15 g, 0.083 mmol) was dissolved in THF (5 mL). Tetrabutylammonium fluoride (0.4 mL, 1 M solution in THF, 0.4 mmol) was added, and the reaction was stirred at room temperature for 2 h. The solution was passed through a short silica gel column (50% ether in chloroform), and the solvent was removed in vacuo. The crude product was purified by flash chromatography (10−20% diethyl ether in chloroform) to give the desired cyclophane diol as an off-white solid (125 mg, 94%): ^{1}H NMR (400 MHz,

$CDCl_3$, concentrated solution) δ 8.02 (bs, 4 H), 7.90 (bs, 4 H), 7.78 (bs, 4 h), 7.47 (bs, 2 H), 7.31 (bs. 4 H), 4.35 (t, J = 7 Hz, 8 H), 3.92 (t, J = 7 Hz, 4 H), 2.84 (t, J = 7 Hz, 4 H), 1.82 (m, 8 H), 1.29 (m, 72 H), 0.89 (t, J = 7 Hz, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.23, 139.95, 139.53, 133.66, 133.09, 132.66, 131.55, 128.87, 124.41, 123.49, 122.77, 90.77, 88.49, 80.64, 75.47, 66.20, 63.35, 39.02, 32.32, 30.09, 30.06, 29.98, 29.91, 29.75, 29.09, 26.42, 23.08, 14.49; IR (KBr) 3431, 2921, 2851, 1724, 1592, 1461, 1239, 1114, 1044 cm^{-1}; MS (MALDI) found m/z 1694.33 ([M + Ag]$^+$, 1), required 1694.86.

12, 13 (12, R = TBDMS, 13, R = H). The two tetraalkyl-substituted cyclophanes were synthesized with the same strategy as **1**−**4**.

12: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (t, J = 2 Hz, 2 H), 7.62 (t, J = 2 Hz, 4 H), 7.39−7.39 (m, 8 H), 7.31 (t, J = 2 Hz, 4 H), 3.86 (t, J = 7 Hz, 4 H), 2.85 (t, J = 7 Hz, 4 H), 2.62 (t, J = 7 Hz, 8 Hz), 1.66 (m, 8 H), 1.29 (m, 88 H), 0.94 (s, 18 H), 0.91 (t, J = 7 Hz, 12 H), 0.04 (s, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.95, 140.27, 133.90, 132.63, 132.54, 132.41, 123.86, 123.61, 122.37, 89.64, 89.36, 81.39, 74.48, 64.34, 39.46, 35.91, 32.35, 31.47, 30.13, 30.11, 30.09, 30.08, 29.97, 29.89, 29.79, 29.59, 26.34, 23.12, 18.74, 14.54, −5.00; IR (KBr) 2912, 2852, 2219, 1590, 1463, 1252, 1095, 870, 834, 775 cm^{-1}; MS (MALDI) found m/z 1772 ([M + Na]$^+$, <1), required 1772.29.

13: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (t, J = 2 Hz, 2 H), 7.60 (t, J = 2 Hz, 4 H), 7.38 (d, J = 2 Hz, 4 H), 7.35 (t, J = 2 Hz, 4 H), 7.31 (t, J = 2 Hz 4 H), 3.92 (m, 4 H), 2.89 (t, J = 7 Hz, 4 H), 2.60 (t, J = 7 Hz, 8 H), 1.63 (m, 8 H), 1.30 (m, 88 H), 0.88 (t, J = 7 Hz, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.00, 139.68, 133.92, 133.97, 132.62, 132.49, 132.21, 124.06, 123.75, 122.42, 89.68, 89.43, 81.37, 74.49, 63.65, 39.16, 35.89, 32.32, 31.43, 30.09, 30.08, 30.05, 29.93, 29.85, 29.75, 29.56, 23.08, 14.49; IR (KBr) 3338, 2922, 2852, 1589, 1462, 1376, 1043, 874, 721, 688 cm^{-1}; MS (MALDI) found m/z 1544 ([M + Na]$^+$, <1), 1522 ([M + H]$^+$, <1), required 1544.11 and 1523.12.

NMR Determination of Self-Association Constant. NMR spectra were taken at various concentrations in $CDCl_3$ (from Cambridge Lab, contains 0.05% tetramethylsilane as internal standard). **1**, **2**, and **4** are all very soluble in chloroform. Diol **3**, on the other hand, was barely soluble. Fortunately, an oversaturated solution of **3** can stay clear for at least 60 min near room temperature without becoming turbid. The chemical shifts were therefore measured for these oversaturated solutions. However, care must be taken to ensure that the solution stays clear throughout the whole course of the spectrum acquisition. The most convenient concentration range for this analysis is 50−0.5 mg/mL. At these concentrations, the spectra exhibited reasonably discernible chemical shift changes and fairly sharp peaks, both of which are very important for precise measurement of the association constants.

The spectra were taken on a 500 MHz Buckner NMR spectrometer equipped with a 5 mm inverse probe. Prior to acquisition, every sample was gradiently shimmed to ensure maximum resolution. The spectrum digital resolution was set at 0.16 Hz. For each compound, a spectrum reference value was determined from the most diluted sample by set the TMS peak at exact 0 Hz. This reference number was then used for all other, more concentrated samples. This operation gave the most reliable chemical shifts values by minimizing the chemical shift uncertainty of the TMS chemical shift at different concentrations.

We employed Horman's procedure[16] to extrapolate the association constants from chemical shifts changes. Two proton signals (one exterior, one interior) were fitted for each compound. The curve fitting was performed on a Macintosh personal computer using the Kaleidagraph program.

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Supporting Information Available: Chemical shifts (in Hz) of selected protons of cyclophane **2** at various concentrations and temperatures. This material is available free of charge via the Internet at http://pubs.acs.org.

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