JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

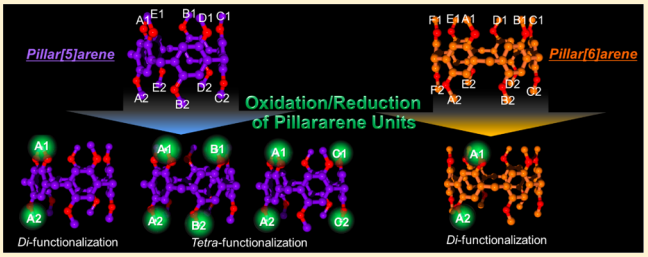
Clickable Di- and Tetrafunctionalized Pillar[*n*]arenes (*n* = 5, 6) by Oxidation−Reduction of Pillar[*n*]arene Units

Tomoki Ogoshi,* Daiki Yamafuji, Daisuke Kotera, Takamichi Aoki, Shuhei Fujinami, and Tada-aki Yamagishi

Department of Chemistry and Chemical Engineering, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa, 920-1192, Japan

Supporting Information

ABSTRACT: We report a new route for the selective synthesis of di- and tetrafunctionalized pillararenes via oxidation and reduction of the pillararene units. Hypervalent-iodine oxidation of perethylated pillar[5]arene afforded pillar[5]arene derivatives containing one benzoquinone unit and two benzoquinones at the A,B- and A,C-units. A pillar[6]arene derivative containing one benzoquinone unit was also synthesized. Reduction of the benzoquinone units yielded position-selective di- and tetrahydroxylated pillararene derivatives. This methodology avoids the generation of many constitutional isomers and overcomes the isolation problem of numerous constitutional isomers. From these hydroxylated pillararenes, Huisgen reaction-based clickable di- and tetraalkynylated pillar[5]arenes were prepared. Because of the highly selective and reactive nature of Huisgen alkyne−azide cycloaddition, these pillar[5]arenes can serve as key compounds for a large library of di- and tetrafunctionalized pillararenes. Based on these di- and tetrafunctionalized pillar[5]arenes as key compounds, fluorescent sensors were created by the modification of di- and tetrapyrene moieties via Huisgen-type click reactions.



INTRODUCTION

The functionalization of macrocyclic host molecules such as cyclodextrins,[1] calixarenes,[2] and cucurbiturils[3] has expanded the possibilities for their application. For the functionalization of these host molecules, there are mainly two protocols. One is introduction of a reactive group to the host molecule. Monotosylated cyclodextrins,[1a−c] monohydroxylated calixarenes,[2a−d] and cucurbiturils[3a] are useful key compounds to prepare monofunctionalized hosts. The second is cocyclization of a functional monomer. Incorporation of a functional group during the synthesis of calixarenes[2e] and cucurbiturils[3b,c] has been demonstrated. On the basis of these protocols, monofunctionalized macrocyclic hosts were synthesized. These derivatives have provided a useful platform for construction of various supramolecules, including self-inclusion complexes,[4] dimers,[5] supramolecular polymers,[6] and chemosensors.[7] However, the synthesis of multifunctionalized macrocyclic hosts has proved to be a challenging proposition because multifunctionalization by these two protocols generates various constitutional isomers. For example, modification of two functional groups of a cyclodextrin to OH groups affords numerous constitutional isomers, and isolation of particular constitutional isomers from a mixture is quite difficult.[8] Synthesis of multifunctionalized macrocyclic hosts by new approaches is therefore of high interest and has been extensively studied by organic and supramolecular chemists.[9]

We first reported the preparation of the macrocyclic host molecules "pillararenes" (Figure 1) in 2008.[10a] To date, two

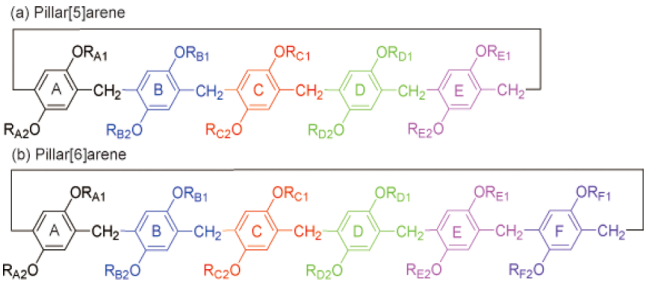


Figure 1. Assignments of positions of pillar[5]arene and pillar[6]-arene. Stereoisomers generated by rotation of units are not included.

kinds of pillararenes, pillar[5]arenes and pillar[6]arenes, containing five and six repeating units, respectively, have been synthesized.[10] The units in this macrocycle are connected by methylene bridges in the para-positions of the benzene rings, affording a highly symmetric pillar-shaped structure. Similar to cyclodextrins, pillar[5]arenes and pillar[6]arenes have 10 and 12 substituent groups, respectively. Figure 1 shows the assignment of position of pillar[5]arene and pillar[6]arene. There is only one constitutional isomer (A1) in the monofunctionalized pillar[5]arenes and pillar[6]arenes. Thus, synthesis of monofunctionalized pillararenes is relatively easy and has recently been accomplished by the following typical

Received: October 16, 2012
Published: December 3, 2012

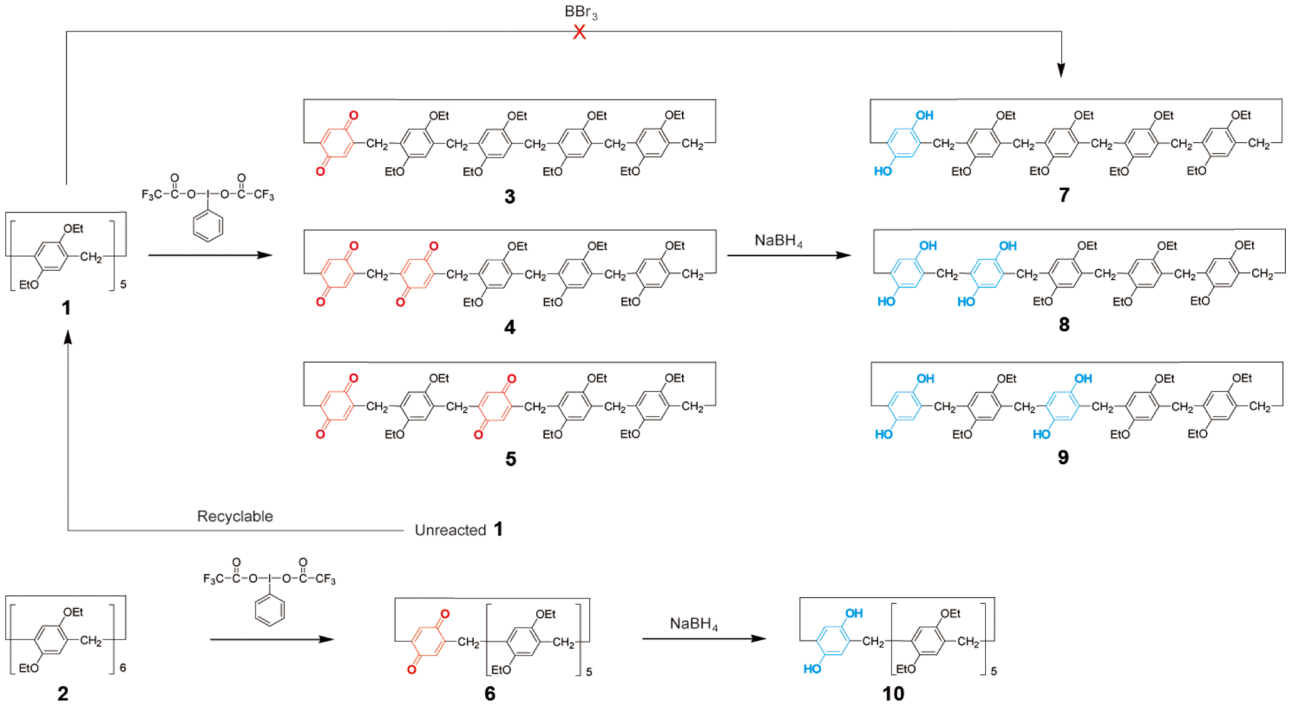


Figure 2. Synthesis of di- and tetrahydroxylated pillararenes by oxidation−reduction of 1,4-diethoxybenzene units.

protocols.[11] Stoddart and co-workers synthesized a monofunctionalized pillar[5]arene by incorporation of a functional group by cocyclization of a monofunctional monomer.[11a] Our group reported introduction of a reactive group to a pillar[5]arene by deprotection of a single alkoxy group.[11b] A monofunctionalized pillar[6]arene was also prepared by the same deprotection method.[11c] Difunctionalized pillar[5]arenes and pillar[6]arenes have possible five (A1/B2, A1/C1, A1/A2, A1/B1, and A1/C2) and seven isomers (A1/B1, A1/C1, A1/D1, A1/A2, A1/B2, A1/C2, and A1/D2), respectively. Among them, A1/A2 and A1/B2 pillar[5]arene isomers have been synthesized by cocyclization of different monomers by Huang and co-workers[12a] and in situ cyclization−deprotection approaches by our group,[12b] respectively. However, new synthetic strategies are needed to synthesize functionalized pillararenes containing more than three different substituents, because these functionalized pillararenes afford many constitutional isomers, which gives isolation problems similar to that in cyclodextrins. For example, there are 10 constitutional isomers (A1/B1/C1, A1/B1/D1, A1/B1/C2, A1/B1/D2, A1/A2/B1, A1/A2/B2, A1/A2/C1, A1/A2/C2, A1/B2/C1, and A1/B2/D1) in trifunctionalized pillar[5]arenes. To date, isolation of functionalized pillar[5]arene derivatives containing more than three substituents has not been accomplished owing to the difficult separation of these constitutional isomers. In this study, we report a new route for synthesis of difunctionalized pillararenes (A1/A2) and tetrafunctionalized pillar[5]arenes (A1/A2/B1/B2 and A1/A2/C1/C2) via oxidation−reduction of the pillararene units. The methodology avoids the generation of many constitutional isomers and overcomes isolation problems of constitutional isomers of these di- and tetrafunctionalized pillar[5]arenes. We also synthesized the first difunctional pillar[6]arene. Based on these di- and tetrafunctionalized pillar[5]arenes as key compounds, fluorescent sensors were created by the modification of di- and tetrapyrene moieties via Huisgen-type click reaction.[13]

RESULTS AND DISCUSSION

We investigated postfunctionalization of pillararenes by hypervalent-iodine oxidation of pillararene units. The hypervalent-iodine oxidation is an efficient method for oxidation of *p*-dialkoxybenzenes to benzoquinone.[16] Oxidation of perethylated pillar[5]arene **1** with 2 equiv of bis[trifluoroacetoxy)iodo]-benzene gave a red-colored solid containing unreacted **1** and pillar[5]arene derivatives containing one to five benzoquinone units (Figure 2). The solid was purified by column chromatography on silica gel with hexane/ethyl acetate = 20/1 as the eluent. The first fraction was the unreacted product **1** (white solid, yield: 20%), which can be reused for the oxidation reaction. The second red-colored fraction was a pillar[5]arene derivative containing one benzoquinone unit **3**. The third and fourth red-colored fractions were pillar[5]arene derivatives containing two benzoquinones at the A,B (**4**) and A,C units (**5**), respectively. Derivatives **3**−**5** were red-colored products owing to the intramolecular charge-transfer (CT) complex between dimethoxybenzene and benzoquinone units. It is therefore very easy to separate these red-colored fractions with the naked eye. The direct monitoring of the red-colored fractions overcomes the isolation problem of these constitutional isomers. The oxidation of perethylated pillar[6]arene (**2**) was also performed. A red-colored solid of a pillar[6]arene containing one benzoquinone unit (**6**) was isolated by silica gel column chromatography. These pillararenes containing benzoquinone units were soluble in a wide variety of solvents such as alcohols, chloroform, acetone, acetonitrile, DMF, and DMSO. Crystals suitable for X-ray analysis were grown by slow evaporation of a solution of **3** in methanol at room temperature. As with permethylated pillar[5]arene,[10a] the structure of **3** was an equilateral pentagon when viewed from the top (Figure 3). From the side view, **3** is seen to be composed of one benzoquinone and four diethoxybenzene units.

dx.doi.org/10.1021/jo302283n | J. Org. Chem. 2012, 77, 11146−11152

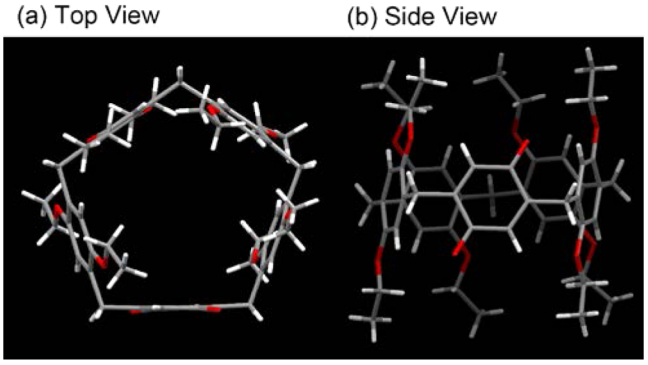


Figure 3. Crystal structure of **3** from (a) top and (b) side view. Solvent molecules are omitted for clarity.

Figure 4a shows UV–vis spectra of **1**–**6** in chloroform. Compared with perethylated pillar[5]arene **1** and pillar[6]arene

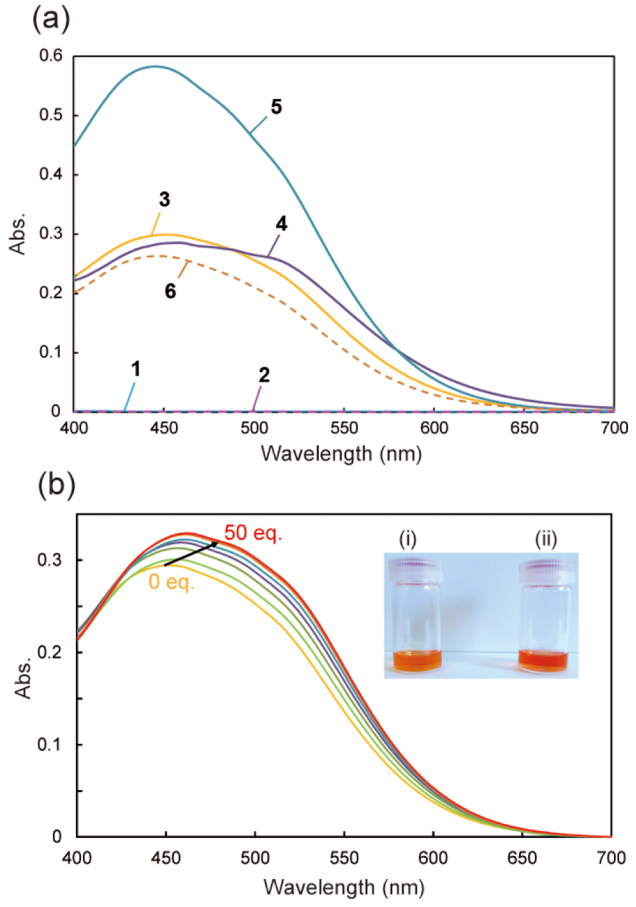


Figure 4. (a) UV–vis spectra of **1**–**6** (0.50 mM) in $CHCl_3$. (b) UV–vis spectra of **3** (0.50 mM) upon addition of 1,4-dicyanobutane (0–50 equiv) (insert: photos of **3** (ii) with and (i) without 1,4-dicyanobutane).

2, pillararene derivatives containing quinone units **3**–**6** showed a new absorption band at around 450 nm. This is due to the formation of the intramolecular CT complex between 1,4-diethoxybenzene and benzoquinone units. The absorption band of **5** was approximately two times larger than those of **3**, **4**, and **6**. Derivative **5** should preferentially form the intramolecular CT complex compared with the other pillar[5]arene derivatives containing benzoquinone units owing to the arrangement of the benzoquinone parts at the A,C units.

On the basis of the CT band, the complexation event of a guest molecule was monitored by the color change of the solution. Because 1,4-dicyanobutane forms stable host–guest complexes with pillar[5]arenes,[17] we employed 1,4-dicyanobutane as a guest. The absorption of the CT band for **3** increased and the peak showed a redshift upon addition of 1,4-dicyanobutane to **3** (Figure 4b). Addition of 1,4-dicyanobutane induced a color change of the solution from orange to red (Figure 4b, insert). Inclusion of 1,4-dicyanobutane into the cavity of **3** could be directly monitored by the color change with the naked eye. The inclusion of 1,4-dicyanobutane into **3** should change the intramolecular CT complex. Based on the intensities of the CT bands, the stoichiometry of the CT complex determined from a Job plot was 1:1 (Figure S13, Supporting Information), and the association constant (K) for the complex was $(3.0 \pm 0.5) \times 10^2$ M^{-1} at 25 °C (Figure S14, Supporting Information).

By reduction of the benzoquinone units with $NaBH_4$, dihydroxylated pillar[5]arene **7** and tetrahydroxylated pillar[5]-arenes at the A,B- and A,C-units (**8** and **9**) were obtained in high yields. These di- and tetrahydroxylated pillar[5]arenes could not be isolated by deprotection of **1** with BBr_3 because the obtained product is a mixture of multideprotected pillar[5]arene derivatives. The synthesis of these tetrafunctionalized pillar[5]arenes was quite difficult by the cocyclization approach owing to the difficult isolation of these constitutional isomers. The synthetic pathway of oxidation–reduction of pillar[5]arene units is therefore a useful strategy for the preparation of selectively di- and tetrahydroxylated pillar[5]-arenes. Reduction of **6** also afforded dihydroxylated pillar[6]-arene **10**. We attempted to obtain difunctionalized pillar[6]-arenes by the cocyclization approach but could not obtain them because the major products were pillar[5]arene derivatives. Thus, the oxidation–reduction approach is especially useful for the synthesis of difunctionalized pillar[6]arenes. These di- and tetrahydroxylated pillararenes are reactive, and thus introduction of any functional group is possible.

Dubbed the "click" reaction, the Huisgen 1,3-dipolar cycloaddition between terminal alkynes and azides is high-yielding, functional-group-tolerant, and compatible with a wide range of substrates.[11a,13,18] To attach functional groups via the Huisgen reaction, intermediates dialkynylated pillar[5]arene **11** and tetraalkynylated pillar[5]arene **12** were prepared from **7** and **9**, respectively (Figure 5). Because of the highly selective and reactive nature of the alkyne–azide cycloaddition, **11** and **12** can serve as key compounds for a large library of di- and tetrafunctionalized pillar[5]arenes.

Compounds bearing more than two pyrene moieties to form excimers have been widely employed for supramolecular design and for probing the structural properties of macromolecular systems.[7,19] We therefore chose to react the azide-substituted pyrene derivative **13** with **11** and **12** to give dipyrene moiety-functionalized pillar[5]arene **14** and tetrapyrene moiety-functionalized pillar[5]arene **15**. The concentration dependence of fluorescence spectra of **14** and **15** was measured (Figures S15 and S16, Supporting Information). At high concentrations, an emission quenching was observed, suggesting the formation of intermolecular associates. However, under dilute conditions, the emission quenching was not observed. The critical association concentration (cac) values of **14** and **15** determined from the concentration-variable emission spectra

dx.doi.org/10.1021/jo302283n | J. Org. Chem. 2012, 77, 11146–11152

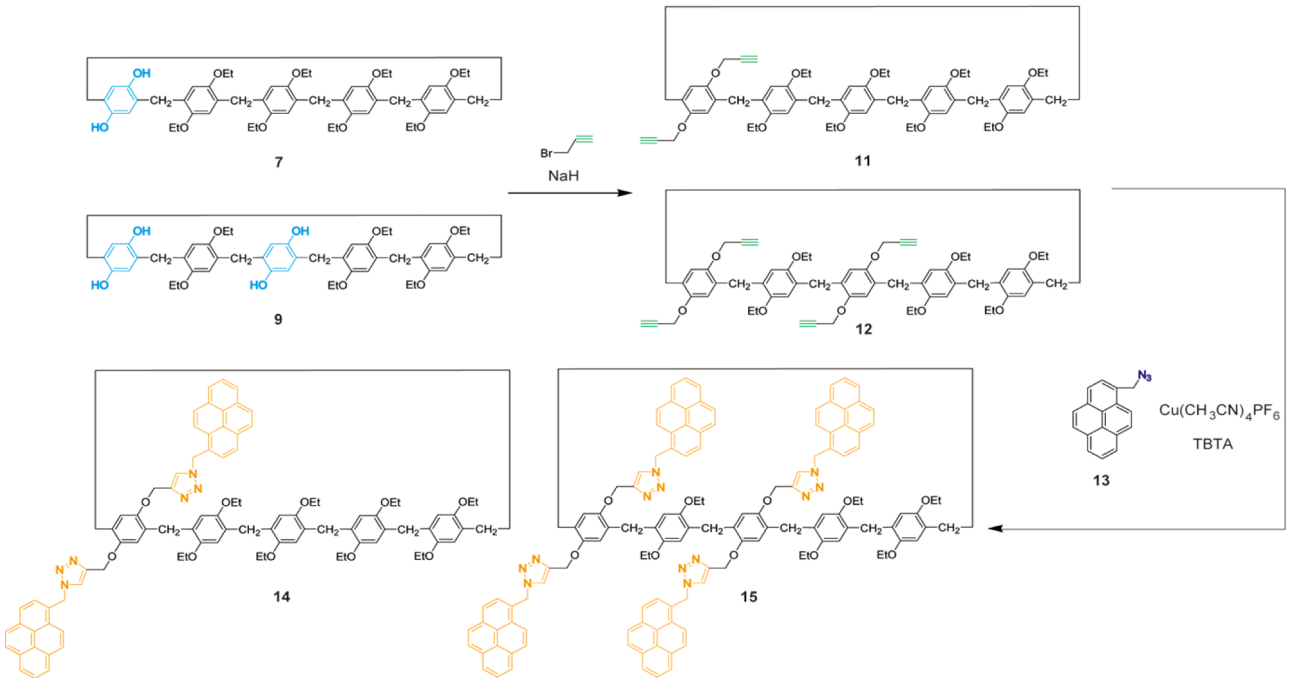


Figure 5. Synthesis of di- and tetrapyrene group-modified pillararenes via the Huisgen reaction.

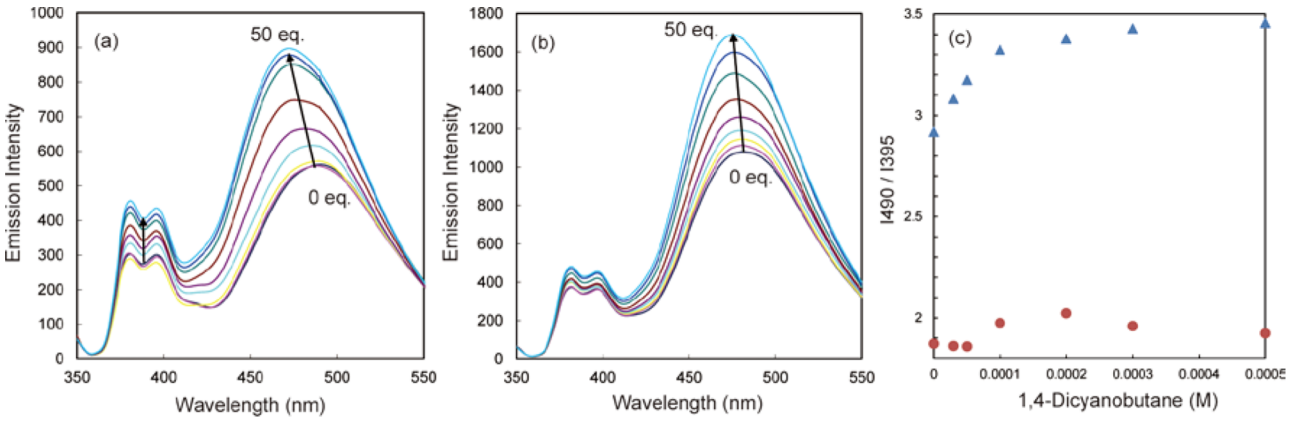


Figure 6. Emission spectra (excited at 340 nm) of (a) **14** and (b) **15** in chloroform (1.0×10^{-5} M) upon addition of 1,4-dicyanobutane. (c) The emission intensity ratios [I_{490} (excimer emission)/I_{395} (monomer emission)] of **14** (brown circles) and **15** (blue triangles) upon addition of 1,4-dicyanobutane (0−50 equiv).

were 2.0×10^{-5} M. To remove the effects of the intermolecular associates, the fluorescence measurements were carried out at concentrations below the cac. Figure 6a and 6b (black line) show emission spectra of **14** and **15**. Compounds **14** and **15** exhibited emission peaks near 370−400 nm and an emission peak at 470 nm, which were assigned as monomer and excimer emissions from the pyrene moiety, respectively. The emission intensity ratios [I_{490} (excimer emission)/I_{395} (monomer emission)] of **14** and **15** were found to be 1.9 and 2.9, respectively. In **15**, four pyrene moieties appended on both rims were sterically fixed to be in close proximity to allow the formation of the excimer compared with **14**.

Upon addition of the guest molecule 1,4-dicyanobutane to **14**, the monomer and excimer emissions increased. On the basis of the change in the fluorescence, the stoichiometry of the complex determined from a Job plot was 1:1 (Figure S17, Supporting Information) and the association constant for the complex was found to be $(8.5 \pm 1.7) \times 10^3$ M^{-1} (Figure S18, Supporting Information). The emission intensity ratios I_{490}/I_{395} hardly change in the range of 1.9−2.0 upon addition of 1,4-dicyanobutane. Because inclusion of 1,4-dicyanobutane decreased mobility of the units, both the monomer and excimer emissions increased. On the other hand, when **15** was mixed with 1,4-dicyanobutane, the excimer emission increased but the monomer emission did not. On the basis of the change in the fluorescence, the stoichiometry of the complex determined from a Job plot was 1:1 (Figure S19, Supporting Information) and the association constant for the complex was $(6.1 \pm 0.8) \times 10^3$ M^{-1} (Figure S20, Supporting Information). The emission intensity ratios I_{490}/I_{395} increased from 2.9 to 3.5 upon addition of 1,4-dicyanobutane. Decreasing the mobility of the units by the complexation allows the formation of the excimer on both rims because the pyrene moieties are in close proximity on both rims in **15**. The number and position of the pyrene moieties had a large effect on the fluorescence change induced by complexation of 1,4-dicyanobutane.

dx.doi.org/10.1021/jo302283n | J. Org. Chem. 2012, 77, 11146−11152

CONCLUSION

We have devised a synthetic strategy of oxidation and reduction of the pillararene units to prepare selective di- and tetrafunctionalized pillararenes. This simple method gives access to selectively modified pillararenes suitable for advanced applications. A pillar[5]arene containing one benzoquinone unit showed a guest-induced color change. This is a first example of a color-changeable chemosensor using the pillararene platform. We have also shown the first syntheses of tetrafunctionalized pillar[5]arenes and difunctionalized pillar[6]arene. We developed Huisgen reaction-based clickable di- and tetrafunctionalized pillar[5]arenes from di- and tetraalkynylated functionalized pillar[5]arenes. By installation of pyrene moieties by the Huisgen reaction, new fluorescent chemical sensors using changes in the monomer and excimer emission were constructed. Because of the highly selective and reactive nature of the alkyne−azide cycloaddition, these di- and tetraalkyne-modified pillar[5]arenes could act as starting points for the creation of new sophisticated supramolecular systems.

EXPERIMENTAL SECTION

Materials. All solvents and reagents were used as supplied. Perethylated pillar[5]arene (**1**) and pillar[6]arene (**2**), and the pyrene derivative containing the azide moiety (**13**), were prepared according to previous papers.[14]

Measurements. The ^{1}H NMR spectra were recorded at 500 MHz, and ^{13}C NMR spectra were recorded at 125 MHz. UV−vis absorption spectra and fluorescence spectra were recorded at room temperature. For UV−vis and fluorescence measurements, 1 cm quartz cuvets were used. High-resolution mass spectra (HRMS) were obtained on a high resolution sector type double-focusing mass spectrometer (ionization mode: FAB) and a time-of-flight (TOF) analyzer (ionization mode: ESI).

Determination of Association Constants. The association constant (K) of 1,4-dicyanobutane-**3** complex was determined by the change in the CT band of **3** upon addition of 1,4-dicyanobutane by UV−vis spectroscopy and employing the titration method. Addition of 1,4-dicyanobutane (guest) to a solution with the same concentration of **3** (host) resulted in an increase of the CT band intensity of the complex. By nonlinear curve-fitting methods,[15] K for the complex in $CHCl_3$ at 25 °C was determined to be $(3.0 \times 0.5) \pm 10^2$ M^{-1} for 1:1 stoichiometry.

The K of the complexes 1,4-dicyanobuane with **14** and **15** complex were determined by the change in the fluorescence of **14** and **15** upon addition of 1,4-dicyanobutane by fluorescence spectroscopy and employing the titration method. Addition of 1,4-dicyanobutane (guest) to a solution with the same concentration of **14** and **15** (host) resulted in an increase of the fluorescence intensity. By nonlinear curve-fitting methods,[15] K for the complexes of 1,4-dicyanobutane with **14** and **15** in $CHCl_3$ at 25 °C were determined to be $(8.5 \times 1.7) \pm 10^3$ M^{-1} and $(6.1 \times 0.8) \pm 10^3$ M^{-1}, respectively, for 1:1 stoichiometry.

Oxidation of Perethylated Pillar[5]arene. To a solution of perethylated pillar[5]arene (**1**, 9.50 g, 10.7 mmol) in THF (300 mL) and H_2O (50 mL) was added [bis(trifluoroacetoxy)iodo]benzene (9.12 g, 21.3 mmol). The mixture was stirred at 25 °C for 48 h. The resulting solution was concentrated under vacuum. The obtained product was dissolved in dichloromethane and washed with saturated sodium bicarbonate. The organic layer was dried over anhydrous Na_2SO_4. After filtration, the filtrate was evaporated to give a red solid. The solid was purified by column chromatography on silica gel with hexane/ethyl acetate = 20/1 as the eluent. The first fraction was the unreacted perethylated pillar[5]arene (**1**, 1.92 g, 2.18 mmol, yield: 20%). The second fraction was the pillar[5]arene derivative containing one benzoquinone unit (**3**, 2.30 g, 2.76 mmol, yield: 26%). The third fraction was the pillar[5]arene derivative containing two benzoquinones at the A,C units (**5**, 182 mg, 0.240 mmol, yield: 2.2%). The fourth fraction was a pillar[5]arene derivative containing two benzoquinones at the A,B units (**4**, 52 mg, 0.0672 mmol, yield: 0.3%). **3.** ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 6.80, 6.79, 6.74, 6.65, 6.63 (s, 10H), 3.57−3.95 (m, 26H), 1.20−1.42 (m, 24H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 188.6, 146.6, 133.4, 150.2, 149.9, 149.8, 129.7, 128.7, 128.0, 123.4, 115.2, 115.1, 114.9, 114.5, 64.1, 63.8, 63.7, 63.4, 29.5, 29.3, 28.3, 15.2, 14.9. HRFABMS: m/z calcd for $C_{51}H_{60}O_{10}$ $[M]^+$: 832.4186, found 832.4199. Melting point (T_m): 104−108 °C. **4.** ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 6.87, 6.86, 6.75, 6.67, 6.61 (s, 10H), 3.86−3.96 (m, 12H), 3.80 3.58 (s, 8H), 3.45 (s, 2H), 1.33−1.45 (m, 18H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 187.8, 187.7, 146.9, 143.1, 136.0, 134.0, 150.4, 150.0, 149.8, 129.8, 128.3, 123.0 115.1, 114.9, 114.5, 64.1, 63.8, 63.6, 29.3, 28.4, 25.9, 15.4, 15.3, 15.2. HRFABMS: m/z calcd for $C_{47}H_{50}O_{10}$ $[M]^+$: 774.3404, found 774.3422. Melting point (T_m): 96−97 °C. **5.** ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 6.85, 6.71, 6.68, 6.67 (s, 10H), 3.86−4.00 (m, 12H), 3.80 (s, 2H), 3.60 (s, 8H), 1.31−1.50 (m, 18H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 188.7, 188.5, 146.8, 146.2, 133.6, 133.3, 150.7, 150.3, 149.8, 129.5, 124.7, 123.8, 115.5, 115.0, 114.4, 64.4, 64.0, 63.6, 29.4, 28.1, 27.8, 15.3, 15.1. HRFABMS: m/z calcd for $C_{47}H_{50}O_{10}$ $[M]^+$: 774.3404, found 774.3417. Melting point (T_m): 180−182 °C.

Oxidation of Perethylated Pillar[6]arene. To a solution of perethylated pillar[6]arene (**2**, 800 mg, 0.749 mmol) in THF (100 mL) and H_2O (17 mL) was added [bis(trifluoroacetoxy)iodo]benzene (633 mg, 1.50 mmol). The mixture was stirred at 25 °C for 48 h. The resulting solution was concentrated under vacuum. The obtained product was dissolved in dichloromethane and saturated sodium bicarbonate. The organic layer was dried over anhydrous Na_2SO_4. After filtration, the filtrate was evaporated to give a red solid. The solid was purified by column chromatography on silica gel with hexane/ethyl acetate = 15/1 as the eluent. The first fraction was the unreacted perethylated pillar[6]arene (**2**, 352 mg, 0.330 mmol, yield: 44%). The second fraction was a pillar[6]arene derivative containing one benzoquinone unit (**6**, 100 mg, 0.099 mmol, yield: 13%). **6.** ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 6.75, 6.69, 6.88, 6.67, 6.61, 6.43 (s, 12H), 3.75−3.91 (m, 28H), 3.56 (s, 4H), 1.19−1.39 (m, 30H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 188.4, 146.7, 133.7, 150.7, 150.6, 150.5, 129.4, 128.3, 128.0, 127.4, 122.8, 115.6, 115.4, 115.3, 115.2, 114.6, 64.3, 64.2, 64.1, 64.0, 63.7, 31.1, 30.7, 30.4, 15.3, 15.2, 15.0. HRFABMS: m/z calcd for $C_{62}H_{74}O_{12}$ $[M]^+$: 1010.5180, found 1010.5209. Melting point (T_m): 108−110 °C.

Dihydroxylated Pillar[5]arene at A1/A2 Positions, 7. To a solution of **3** (1.25 g, 1.50 mmol) in THF (20 mL) and methanol (4 mL) was added $NaBH_4$ (285 mg, 7.50 mmol). The mixture was stirred at 25 °C for 30 min. The reaction was quenched by pouring into 1 M HCl aqueous solution. Then dichloromethane and water were added to the mixture. The organic layer was dried over anhydrous Na_2SO_4. After filtration, solvents were evaporated to give a white solid (**7**, 1.24 g, 1.49 mmol, yield: 99%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.21, 6.92, 6.98, 6.77, 6.59, 6.57 (s, 12H), 3.58−4.08 (m, 26H), 1.29−1.46 (m, 24H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 151.4, 149.9, 149.8, 147.5, 147.4, 129.4, 128.6, 127.7, 127.3, 126.9, 118.1, 116.1, 115.1, 114.8, 113.9, 65.3, 63.9, 63.7, 31.0, 30.2, 29.3, 15.3, 15.2, 14.7. HRFABMS: m/z calcd for $C_{51}H_{62}O_{10}$ $[M]^+$: 834.4343, found 834.4358.

Tetrahydroxylated Pillar[5]arene at A1/A2/C1/C2 Positions, 8. To a solution of **4** (40 mg, 0.0517 mmol) in THF (4 mL) and methanol (1 mL) was added $NaBH_4$ (19 mg, 0.517 mmol). The mixture was stirred at 25 °C for 30 min. The reaction was quenched by pouring into 1 M HCl aqueous solution. Then dichloromethane and water were added to the mixture. The organic layer was dried over anhydrous Na_2SO_4. After filtration, solvents were evaporated to give a white solid (**8**, 39 mg, 0.0503 mmol, yield: 97%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 6.98, 6.85, 6.68, 6.62, 6.59, 6.63, 5.00 (s, 14H), 3.68−4.02 (m, 22H), 1.18−1.40 (m, 18H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 151.3, 149.9, 147.9, 145.8, 129.5, 128.0, 127.4, 127.1, 126.9, 118.3, 117.6, 116.3, 115.1, 113.8, 65.3, 64.0, 63.9, 34.3, 30.7, 30.1, 29.8, 15.1, 15.0, 14.8. HRFABMS: m/z calcd for $C_{47}H_{54}O_{10}$ $[M]^+$: 778.3717, found 778.3721.

dx.doi.org/10.1021/jo302283n | J. Org. Chem. 2012, 77, 11146−11152

Tetrahydroxylated Pillar[5]arene at A1/A2/B1/B2 Positions, 9. To a solution of **5** (200 mg, 0.258 mmol) in THF (20 mL) and methanol (4 mL) was added $NaBH_4$ (96 mg, 2.58 mmol). The mixture was stirred at 25 °C for 30 min. The reaction was quenched by pouring into 1 M HCl aqueous solution. Then dichloromethane and water were added to the mixture. The organic layer was dried over anhydrous Na_2SO_4. After filtration, solvents were evaporated to give a white solid (**9**, 198 mg, 0.0256 mmol, yield: 99%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.22, 7.10, 6.94, 6.70, 6.60, 6.59, 6.54 (s, 14H), 3.39−4.27 (m, 22H), 1.43−1.51 (m, 18H). ^{13}C NMR (DMSO-d_6, 125 MHz, ppm): δ149.5, 149.3, 147.1, 146.7, 128.9, 128.7, 128.0, 127.0, 126.8, 118.6, 118.0, 115.2, 114.5, 64.2, 63.9, 63.7, 31.0, 29.8, 29.5, 29.2, 15.6, 15.5, 15.4. HRFABMS: m/z calcd for $C_{47}H_{54}O_{10}$ $[M]^+$: 778.3717, found 778.3711.

Dihydroxylated Pillar[6]arene at A1/A2 Positions, 10. To a solution of **6** (50 mg, 0.0495 mmol) in THF (4 mL) and methanol (1 mL) was added $NaBH_4$ (9 mg, 0.278 mmol). The mixture was stirred at 25 °C for 30 min. The reaction was quenched by pouring into 1 M HCl aqueous solution. Then dichloromethane and water were added to the mixture. The organic layer was dried over anhydrous Na_2SO_4. After filtration, solvents were evaporated to give a white solid (**10**, 50 mg, 0.0494 mmol, yield: 99%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.20, 6.85, 6.75, 6.68, 6.67, 6.61, 6.60 (s, 14H), 3.69−4.06 (m, 32H), 1.22−1.47 (m, 30H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 151.8, 150.6, 150.5, 150.4, 147.8, 147.5, 129.0, 128.4, 128.0, 127.2, 126.7, 126.4, 117.8, 115.8, 115.2, 114.9, 114.1, 65.1, 64.5, 64.3, 64.2, 63.9, 31.3, 31.2, 30.9, 15.3, 15.2, 14.8. HRFABMS: m/z calcd for $C_{62}H_{76}O_{12}$ $[M]^+$: 1012.5337, found 1012.5320.

Dialkynylated Pillar[5]arene at A1/A2 Positions, 11. Under a nitrogen atmosphere, **7** (623 mg, 0.747 mmol) was dissolved in DMF (20 mL). Sodium hydride (108 mg, 4.5 mmol) was added, and the reaction mixture was stirred. Then propargyl bromide (0.25 mL, 3.00 mmol) was added, and the reaction mixture was heated at 80 °C for 24 h. After removal of the solvent, the resulting solid was dissolved in dichloromethane and water. The organic layer was dried over anhydrous Na_2SO_4. After filtration, solvents were evaporated to give a solid. Column chromatography (silica gel; hexane/ethyl acetate = 10/1) afforded a white solid (**11**, 408 mg, 0.448 mmol, yield: 60%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 6.81, 6.75, 6.74, 6.73, 6.64 (s, 10H), 4.45 (d, 4H), 3.77−3.88 (m, 26H), 2.04 (t, 2H), 1.19−1.34 (m, 24H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 150.0, 149.9, 149.4, 129.4, 128.8, 128.7, 128.5, 128.2, 116.2, 115.3, 115.2, 115.0, 78.9, 74.9, 64.0, 63.9, 63.8, 56.6, 30.0, 29.9, 29.8, 15.3, 15.2, 15.1. HRFABMS: m/z calcd for $C_{57}H_{66}O_{10}$ $[M]^+$: 910.4656, found 910.4648. Melting point (T_m): 96−98 °C.

Tetraalkynylated Pillar[5]arene at A1/A2/C1/C2 Positions, 12. Under a nitrogen atmosphere, **9** (150 mg, 0.193 mmol) was dissolved in DMF (20 mL). Sodium hydride (68 mg, 2.84 mmol) was added, and the reaction mixture was stirred. Then propargyl bromide (0.16 mL, 1.90 mmol) was added, and the reaction mixture was heated at 80 °C for 24 h. After removal of the solvent, the resulting solid was dissolved in dichloromethane and water. The organic layer was dried over anhydrous Na_2SO_4. After filtration, solvents were evaporated to give a solid. Column chromatography (silica gel; hexane/ethyl acetate = 5/1) afforded a white solid (**12**, 40 mg, 0. 0430 mmol, yield: 22%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 6.83, 6.79, 6.76, 6.69, 6.65 (s, 10H), 4.48, 4.45 (d, 8H), 3.76−3.88 (m, 22H), 2.15, 2.10 (t, 4H), 1.17−1.34 (m, 18H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 150.0, 149.9, 149.5, 129.5, 129.3, 128.8, 128.3, 128.1, 116.1, 115.8, 125.2, 115.1, 115.0, 79.2, 79.1, 74.9, 74.8, 64.0, 63.9, 56.7, 56.6, 30.0, 29.9, 29.8, 15.3, 15.2, 15.1. HRFABMS: m/z calcd for $C_{59}H_{62}O_{10}$ $[M]^+$: 930.4343, found 930.4342. Melting point (T_m): 98−100 °C.

Dipyrene Moiety-Functionalized Pillar[5]arene at A1/A2 Positions, 14. To a solution of **11** (200 mg, 0.220 mmol) and **13** (130 mg, 0.506 mmol) in dichloromethane (2 mL) were added tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA, 268 mg, 0.506 mmol) and $Cu(CH_3CN)_4PF_6$ (188 mg, 0.506 mmol). The mixture was stirred at 25 °C for 24 h. The resulting solution was concentrated under vacuum. Column chromatography (silica gel; ethyl acetate/dichloromethane = 1/10) afforded a pale yellow solid (**14**, 304 mg, 0.213 mmol, yield: 97%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.89−8.24 (m, 18H), 7.39, 6.71, 6.65, 6.55, 6.54, 6.43 (s, 12H), 6.22 (dd, 4H), 4.86 (s, 4H), 3.47−3.75 (m, 26H), 0.97−1.20 (m, 24H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 185.1, 150.0, 149.9, 149.8, 149.6, 132.2, 131.2, 130.6, 129.3, 129.2, 129.1, 128.6, 128.5, 128.4, 128.3, 128.1, 127.5, 127.3, 127.0, 126.5, 126.0, 125.9, 125.1, 125.0, 124.5, 122.5, 121.9, 115.7, 115.3, 115.1, 114.7, 63.9, 63.8, 63.7, 63.1, 52.5, 30.1, 29.9, 29.7, 15.1, 15.0, 14.9. HRESIMS: m/z calcd for $C_{91}H_{88}N_6O_{10}Na_1$ $[M+Na]^+$: 1447.64596, found 1447.64597. Melting point (T_m): Melting point (T_m): 104−105 °C.

Tetrapyrene Moiety-Functionalized Pillar[5]arene at A1/A2/C1/C2 Positions, 15. To a solution of **12** (30 mg, 0.0344 mmol) and **13** (41 mg, 0.172 mmol) in dichloromethane (1 mL) were added TBTA (85 mg, 0.172 mmol) and $Cu(CH_3CN)_4PF_6$ (60 mg, 0.0.172 mmol). The mixture was stirred at 25 °C for 24 h. The resulting solution was concentrated under vacuum. Column chromatography (silica gel; ethyl acetate/dichloromethane = 1/10) afforded a brown solid (**15**, 30 mg, 0.0152 mmol, yield: 44%). ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 7.83−8.22 (m, 36H), 7.31, 7.30, 6.66, 6.61, 6.38, 6.33 (s, 14H), 6.18, 6.14 (dd, 8H), 4.78, 4.74 (dd, 8H), 3.35−3.57 (m, 22H), 0.80−0.96 (m, 18H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 149.9, 149.6, 149.5, 145.2, 132.1, 131.1, 130.6, 129.3, 129.1, 128.3, 128.1, 127.5, 127.3, 127.0, 126.4, 126.0, 125.9, 125.1, 125.0, 124.5, 122.5, 121.9, 115.8, 115.3, 114.9, 114.7, 63.8, 63.7, 63.6, 52.4, 29.8, 29.6, 14.9, 14.8. HRESIMS: m/z calcd for $C_{127}H_{106}N_{12}O_{10}Na$ $[M + Na]^+$: 1981.80525, found 1981.80502. Melting point (T_m): 128−129 °C.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of all new compounds, Job plot, UV and fluorescence titrations of the host−guest complexes, and variable-concentration emission spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Tel: +81-76-234-4775; fax: +81-76-234-4800; e-mail: ogoshi@t.kanazawa-u.ac.jp.

Notes

The authors declare no competing financial interest.

■ REFERENCES

(1) (a) Takahashi, K.; Hattori, K.; Toda, F. *Tetrahedron Lett.* **1984**, *25*, 3331−3334. (b) Ikeda, H.; Nagano, Y.; Du, Y Q.; Ikeda, T.; Toda, F. *Tetrahdron Lett* **1990**, *31*, 5045−5048. (c) Melton, L. D.; Slessor, K. N. *Carbohyd. Res.* **1971**, *18*, 29−37.

(2) (a) Gutsche, C. D.; Dhawan, B.; Levine, J. A.; No, K. H.; Bauer, L. J. *Tetrahedron* **1983**, *39*, 409−426. (b) Beer, P. D.; Shade, M. *Chem. Commun.* **1997**, 2377−2378. (c) Ho, Z. C.; Ku, M. C.; Lin, L. G. *Tetrahedron* **1996**, *41*, 13189−13200. (d) Shirakawa, S.; Kimura, T.; Murata, S.; Shimizu, S. *J. Org. Chem.* **2009**, *74*, 1288−1296. (e) Colasson, B.; Reinaud, O. *J. Am. Chem. Soc.* **2008**, *130*, 15226−15227.

(3) (a) Zhao, N.; Lloyd, G. O.; Scherman, O. A. *Chem. Commun.* **2012**, *48*, 3070−3072. (b) Ahmed, M. M.; Koga, K.; Fukudome, M.; Sasaki, H.; Yuan, D. Q. *Tetrahedron Lett.* **2011**, *52*, 4646−4649. (c) Lucas, D.; Minami, T.; Iannuzzi, G.; Cao, L.; Wittenberg, J. B.; Anzenbacher, P.; Isaacs, L. *J. Am. Chem. Soc.* **2011**, *133*, 17966−17976.

(4) (a) Inoue, Y.; Miyauchi, M.; Nakajima, H.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* **2006**, *128*, 8994−8995. (b) Inoue, Y.; Kuad, P.; Okumura, Y.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* **2007**, *129*, 6396−6397. (c) Han, Y.; Cheng, K.; Simon, K. A.; Lan, Y.; Sejwal, P.; Luk, Y. Y. *J. Am. Chem. Soc.* **2006**, *128*, 13913−13920.

(5) (a) Kuad, P.; Miyawaki, A.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* **2007**, *129*, 12630−12631. (b) Ogoshi, T.;

Hashizume, M.; Yamagishi, T.; Nakamoto, Y. *Langmuir* **2010**, *26*, 3169−3173. (c) Takahashi, H.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Org. Chem.* **2006**, *71*, 4878−4883.
(6) (a) De Greef, T. F. A.; Smulders, M. J.; Wolffs, M.; Schenning, A. P. H. J.; Sijbesma, R. P.; Meijer, E. W. *Chem. Rev.* **2009**, *109*, 5687−5754. (b) Brunsveld, L.; Folmer, B. J. B.; Meijer, E. W.; Sijbesma, R. P. *Chem. Rev.* **2001**, *101*, 4071−4098.
(7) (a) Kim, J. S.; Quang, D. T. *Chem. Rev.* **2007**, *107*, 3780−3799. (b) Ogoshi, T.; Harada, A. *Sensors* **2008**, *8*, 4961−4982. (c) Kim, H. J.; Lee, M. H.; Mutihac, L.; Vicens, J.; Kim, J. S. *Chem. Soc. Rev.* **2012**, *41*, 1173−1190.
(8) (a) Yuan, D. Q.; Yamada, T.; Fujita, K. *Chem. Commun.* **2001**, 2706−2707. (b) M. Narita, M.; Hamada, F. *J. Chem. Soc., Perkin Trans. 2* **2000**, 823−832. Koga, K.; Yuan, D. Q.; Fujita, K. *Tetrahedron Lett.* **2000**, *41*, 6855−6857.
(9) (a) Pearce, A. J.; Sinaÿ, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 3610−3612. (b) Petrillo, M.; Marinescu, L.; Rousseaua, C.; Bols, M. *Org. Lett.* **2009**, *11*, 1983−1985. (c) Guieu, S.; Sollogoub, M. *J. Org. Chem.* **2008**, *73*, 2819−2828.
(10) (a) Ogoshi, T.; Kanai, S.; Fujinami, S.; Yamagishi, T.; Nakamoto, Y. *J. Am. Chem. Soc.* **2008**, *130*, 5022−5023. (b) Cragg, P. J.; Sharma, K. *Chem. Soc. Rev.* **2012**, *41*, 597−607. (c) Ogoshi, T. *J. Incl. Phenom. Macrocycl. Chem.* **2012**, *72*, 247−262. (d) Xue, M.; Yang, Y.; Chi, X.; Zhang, Z.; Huang, F. *Acc. Chem. Res.* **2012**, *45*, 1294−1308.
(11) (a) Strutt, N. L.; Forgan, R. S.; Spruell, J. M.; Botros, Y. Y.; Stoddart, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 5668−5671. (b) Ogoshi, T.; Demachi, K.; Kitajima, K.; Yamagishi, T. *Chem. Commum.* **2011**, *47*, 7164−7166. (c) Ogoshi, T.; Kayama, H.; Yamafuji, D.; Aoki, T.; Yamagishi, T. *Chem. Sci.* **2012**, *3*, 3221−3226.
(12) (a) Han, C.; Ma, F.; Zhang, Z.; Xia, B.; Yu, Y.; Huang, F. *Org. Lett.* **2010**, *12*, 4360−4363. (b) Ogoshi, T.; Kitajima, K.; Fujinami, S.; Yamagishi, T. *Chem. Commun.* **2011**, *47*, 10106−10108.
(13) (a) Ogoshi, T.; Shiga, R.; Hashizume, M.; Yamagishi, T. *Chem. Commun.* **2011**, 6927−6929. (b) Yu, G.; Zhang, Z.; Han, C.; Xue, M.; Zhou, Q.; Huang, F. *Chem. Commun.* **2012**, *48*, 2958−2960. (c) Ogoshi, T.; Yamafuji, D.; Aoki, T.; Kitajima, K.; Yamagishi, T.; Hayashi, Y.; Kawauchi, S. *Chem.—Eur. J.* **2012**, *18*, 7493−7500. (d) Nierengarten, I.; Guerra, S.; Holler, M.; Nierengarten, J. F.; Deschenaux, R. *Chem. Commun.* **2012**, *48*, 8072−8074. (e) Ogoshi, T.; Yamafuji, D.; Aoki, T.; Yamagishi, T. *Chem. Commun.* **2012**, *48*, 6842−6844.
(14) (a) Ogoshi, T.; Kitajima, K.; Aoki, T.; Fujinami, S.; Yamagishi, T.; Nakamoto, Y. *J. Org. Chem.* **2010**, *75*, 3268−3273. (b) Tao, H. Q.; Cao, D. R.; Liu, L. Z.; Kou, Y. H.; Wang, L. Y.; Meier, H. *Sci. China Chem.* **2012**, *55*, 223−228. (c) Xu, Z.; N. Singh, N. J.; Lim, J.; Pan, J.; Kim, H. N.; Park, S.; Kim, K. S.; Yoon, J. *J. Am. Chem. Soc.* **2009**, *131*, 15528−15533.
(15) Ashton, P. R.; Ballardini, R.; Balzani, V.; Bělohradský, M.; Gandolfi, M. T.; Philp, D.; Prodi, L.; Raymo, F. M.; Reddington, M. V.; Spencer, N.; Stoddart, J. F.; Venturi, M.; Williams, D. J. *J. Am. Chem. Soc.* **1996**, *118*, 4931−4951.
(16) (a) Yakura, T.; Yamauchi, Y.; Tian, Y.; Omoto, M. *Chem. Pharm. Bull.* **2008**, *56*, 1632−1634. (b) Yakura, T.; Omoto, M.; Yamauchi, Y.; Tian, Y.; Ozono, A. *Tetrahedron* **2010**, *66*, 5833−5840.
(17) Shu, X.; Chen, S.; Li, J.; Chen, Z.; Weng, L.; Jia, X.; Li, C. *Chem. Commun.* **2012**, *48*, 2967−2969.
(18) (a) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004−2021. (b) Ryu, E. H.; Zhao, Y. *Org. Lett.* **2005**, *7*, 1035−1037. (b) Bew, S. P.; Brimage, R. A.; L'Hermite, N.; Sharma, S. V. *Org. Lett.* **2007**, *9*, 3713−3716. (c) David, O.; Maisonneuve, S.; Xie, J. *Tetrahedron Lett.* **2007**, *48*, 6527−6530. (d) Mourer, M.; Hapiot, F.; Monflier, E.; Menuel, S. *Tetrahedron* **2008**, *68*, 7159−7163.
(19) Figueira-Duarte, T. M.; Müllen, K. *Chem. Rev.* **2011**, *111*, 7260−7314.