DOI: 10.1002/ejoc.201100698

Preparation of Pillar[*n*]arenes by Cyclooligomerization of 2,5-Dialkoxybenzyl Alcohols or 2,5-Dialkoxybenzyl Bromides

Yingjie Ma,[a] Zibin Zhang,[a] Xiaofan Ji,[a] Chengyou Han,[a] Jiuming He,[b] Zeper Abliz,[b] Weixiang Chen,[a] and Feihe Huang*[a]

Keywords: Supramolecular chemistry / Host–guest systems / Cyclooligomerization / Calixarenes / Macrocycles / Arenes / Pillar[*n*]arenes

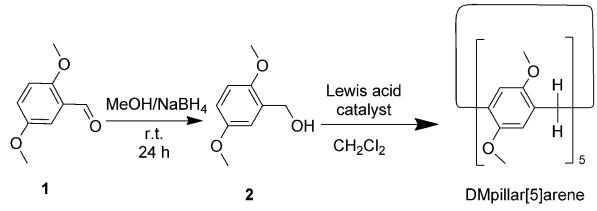
The facile and efficient preparation of pillar[*n*]arenes (n = 5 or 6) was achieved by cyclooligomerization of 2,5-dialkoxybenzyl alcohols or 2,5-dialkoxybenzyl bromides with an appropriate Lewis acid catalyst at room temperature. The mechanism for this cyclooligomerization is presumed to be a Friedel–Crafts alkylation.

Introduction

The preparation of new macrocyclic hosts plays an important role in supramolecular chemistry, as every generation makes their supramolecular chemistry more versatile.[1] A new kind of macrocyclic host, called pillar[*n*]arenes,[2] has attracted increasing attention over the past few years. Their structures are similar to those of calixarenes,[3,4] but they are more symmetrical and rigid, which provides them with some interesting physical, chemical, and host–guest properties. Until now, two kinds of pillararenes, pillar[5]arenes and pillar[6]arenes, containing five and six units, respectively, have been reported. Their syntheses,[2a,2c,2f,5a,5b,6a,6c] conformational mobility,[2e,2g,6] derivatization,[2b,11a] host–guest complexation with organic salts,[6a,6c,7,8,12] and self-assembly[2d,6b,11b] have been explored. However, methods to make pillararenes are still limited. To date, only three methods have been reported. In 2006, Kanai et al. reported the first method, by which a five-membered ring was synthesized successfully from 1,4-dimethoxy-2,5-xylylenedibromide in low yield using a Friedel–Crafts reaction.[13,14] In 2008, Ogoshi et al. reported the second method, by which 1,4-dimethoxypillar[5]arene (DMpillar[5]arene) was prepared rapidly and easily by condensation of 1,4-dimethoxybenzene and paraformaldehyde with $BF_3{\cdot}O(C_2H_5)_2$ as the catalyst.[2a] However, this method is limited to the preparation of pillar[5]arenes. More recently, Cao and Meier et al. reported the third method by the condensation of 1,4-dialkoxy-2,5-bis(alkoxymethyl)benzenes using *p*-toluenesulfonic acid as the catalyst at room temperature.[5a] With this method, both 1,4-dialkoxypillar[5]arenes and 1,4-dialkoxypillar[6]arenes can be synthesized. Nevertheless, the preparation of the starting reactants, 1,4-dialkoxy-2,5-bis(alkoxymethyl)benzenes, is not easy. For the further investigation of pillararenes in supramolecular chemistry, the search for facile and efficient preparation methods is a necessary and urgent mission.

Results and Discussion

Herein, we report a new method to synthesize DMpillar[5]arene by condensation of 2,5-dimethoxybenzyl alcohol (**2**) with an appropriate Lewis acid catalyst in CH_2Cl_2 at room temperature (Scheme 1). In this reaction, various Lewis acids, such as $FeCl_3$, $AlCl_3$, $SnCl_4$, and $BF_3{\cdot}O(C_2H_5)_2$, can be used as a catalyst.



Scheme 1. Synthesis of DMpillar[5]arene from the condensation of **2**.

First, we investigated the effect of different Lewis acids on the cyclization reaction using CH_2Cl_2 as the solvent. The results showed that a solution of **2** in CH_2Cl_2 turned green immediately when $SnCl_4$ or $BF_3{\cdot}O(C_2H_5)_2$ was added. The reactant **2** was consumed in about one minute. This showed that both $SnCl_4$ and $BF_3{\cdot}O(C_2H_5)_2$ can promote the cyclization reaction efficiently. In addition, $FeCl_3$ and $AlCl_3$ can also promote the reaction. With either $FeCl_3$ and $AlCl_3$ as

[a] Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China
Fax: +86-571-8795-3189
E-mail: fhuang@zju.edu.cn
[b] Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, P. R. China
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201100698.

the catalyst, the reaction was finished in about three minutes, a little longer than when $SnCl_4$ or $BF_3{\cdot}O(C_2H_5)_2$ was used. When $ZnCl_2$ was used as the catalyst, the cyclization occurred very slowly, and a reaction time of 10 h was required. Furthermore, the color of the reaction mixture after completion of the reaction was white, whereas the color was deep green when the other Lewis acids were used. Using different Lewis acids as the catalyst gave different yields (Table 1). Similar yields of DMpillar[5]arene were achieved with $FeCl_3$, $AlCl_3$, and $BF_3{\cdot}O(C_2H_5)_2$ and a lower yield was obtained with $SnCl_4$. However, when $ZnCl_2$ was used as the catalyst, the amount of the product obtained was so little that it could be detected only by MS. Therefore, $FeCl_3$, $AlCl_3$, or $BF_3{\cdot}O(C_2H_5)_2$ are the best choice of catalyst in the preparation of DMpillar[5]arene from the condensation of **2** in CH_2Cl_2.

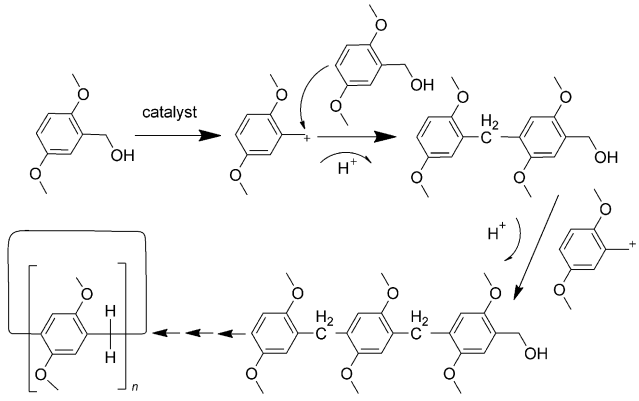
Table 1. Cyclization reactions using different Lewis acids as the catalyst for the room temperature condensation of **2** in CH_2Cl_2.

Catalyst (1 equiv.)	Reaction time (min)	Yield (%)
$FeCl_3$	3	39
$BF_3{\cdot}O(C_2H_5)_2$	3	38
$AlCl_3$	3	35
$SnCl_4$	3	25
$ZnCl_2$	3	trace

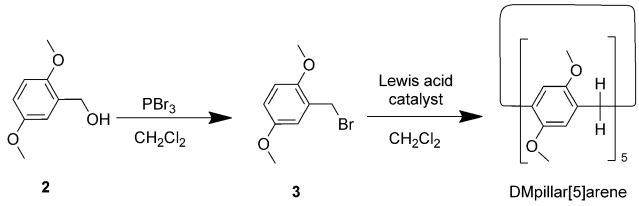
The mechanism of this cyclization reaction is presumably based on a Friedel–Crafts alkylation (Scheme 2).[9,10] With the catalyst, **2** is converted to its carbocation, which undergoes reaction with the benzene ring of another molecule of **2**. Because of the orientation effect of the benzyl alcohol group, the benzyl carbocation group is attached at the 4-position of **2** to give a dimer. In the same way, other oligomers can form. At last, these oligomers form rings through cyclocondensation to give the corresponding macrocyclic compounds. We wondered why the five-membered ring, DMpillar[5]arene, was the main product. Its crystal structure shows that it is a regular pentagon,[2a] so the angle between the two bridging carbon–carbon bonds is 108°, which is very close to the normal bond angle of the sp^3 carbon atom, 109°28′. Therefore, the DMpillar[5]arene structure should have a lowest energy and be the most stable macrocycle compared to other cyclic compounds containing different numbers of repeat units.

If the mechanism is correct, 2,5-dimethoxybenzyl bromide (**3**) could also be used to synthesize DMpillar[5]arene, similar to a reported method for calixarenes,[4] as it could also be converted to the carbocation under the influence of a Lewis acid and undergo Friedel–Crafts alkylation.[10] Therefore, we replaced **2** with **3** and repeated the cyclization reaction (Scheme 3 and Table 2). DMpillar[5]arene was obtained as expected, consistent with the proposed mechanism.

The Lewis acids, $FeCl_3$, $AlCl_3$, $BF_3{\cdot}O(C_2H_5)_2$, $ZnCl_2$, and $SnCl_4$ were also investigated for this reaction and all were found to promote the cyclization reaction. When $FeCl_3$, $AlCl_3$, $ZnCl_2$, or $SnCl_4$ was added, the solution of **3** in CH_2Cl_2 turned green immediately. However, 24 h



Scheme 2. Possible mechanism of the cyclization reaction of **2** to form DMpillar[*n*]arene.



Scheme 3. Synthesis of DMpillar[5]arene from the condensation of **3**.

Table 2. Cyclization reactions using different Lewis acids as the catalyst for the room temperature condensation of **3** in CH_2Cl_2.

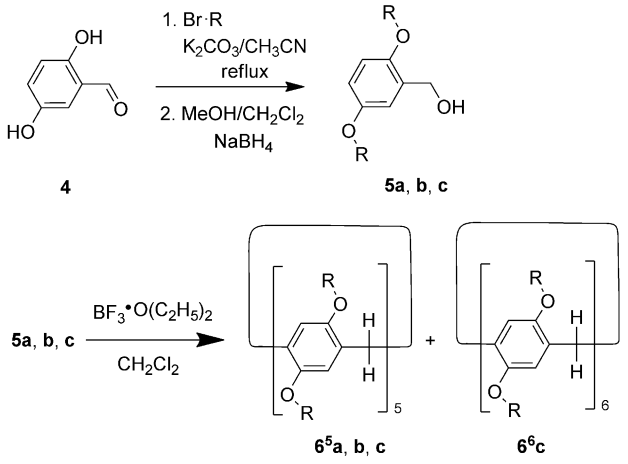
Catalyst (1 equiv.)	Reaction time [min]	Yield [%]
$ZnCl_2$	3	40
$AlCl_3$	3	37
$SnCl_4$	3	35
$FeCl_3$	3	34
$BF_3{\cdot}O(C_2H_5)_2$	3	trace

was required for the condensation to finish when $BF_3{\cdot}O(C_2H_5)_2$ was used as the catalyst. The yields of the reactions using different catalysts in CH_2Cl_2 for three minutes are shown in Table 2, and $ZnCl_2$ produced the highest yield. With $BF_3{\cdot}O(C_2H_5)_2$ as the catalyst, trace product was obtained. When $FeCl_3$, $AlCl_3$ or $SnCl_4$ was used, the yields were about the same. These results are different to those using **2** as the reactant. However, the highest yield of DMpillar[5]arene using **3** is very close to that obtained with **2**.

A detailed study of the reactions of starting compounds **5a**–**c** [R = pentyl (**5a**), hexyl (**5b**), and octyl (**5c**)] revealed that the corresponding pillararenes were obtained (Table 3). Using **5a** or **5b** as the starting compound, the cyclic pentamers were obtained with similar yields, which were higher than those reported (Table 3).[2c] However, **5c** yielded not only the cyclic pentamer 1,4-dioctyloxypillar[5]arene (**6^5c**), but also the higher cyclooligomer 1,4-dioctyloxypillar[6]arene (**6^6c**) in yields of 14 and 13%, respectively. Furthermore, the yield of **6^6c** was higher than those (8,[5a] 11,[5a] and 4.6%[8]) of all the other pillar[6]arenes reported to date. Both **6^5c** and **6^6c** are white solids and their melting points

are 97.9–99.4 and 76.0–78.9 °C, respectively. These values are lower than that of DMpillar[5]arene (248.8 °C),[2a] probably due to the incorporation of longer, flexible alkyl chains.

Table 3. Preparation of $\mathbf{6^5a–c}$ and $\mathbf{6^6c}$ with different alkoxy substituents R.



Starting compound	R	Product	Yield [%]	Product	Yield [%]
5a	pentyl	$\mathbf{6^5a}$	41[a]	–	–
5b	hexyl	$\mathbf{6^5b}$	43[b]	–	–
5c	octyl	$\mathbf{6^5c}$	14	$\mathbf{6^6c}$	13

[a] The reported yield was 13.7%.[2c] [b] The reported yield was 18.2%.[2c]

^{1}H NMR spectra of $\mathbf{6^5c}$ and $\mathbf{6^6c}$ show that the signal arising from the phenylene protons H^1 shifted upfield from 6.85 for $\mathbf{6^5c}$ to 6.70 ppm for $\mathbf{6^6c}$, and the methylene protons H^3 shifted from 3.84 for $\mathbf{6^5c}$ to 3.70 ppm for $\mathbf{6^6c}$ (Figure 1). A possible reason is that $\mathbf{6^6c}$ contains more benzene rings than $\mathbf{6^5c}$ so the shielding is stronger. Furthermore, it was found that the signals of methylene protons H^2 and H^3 of $\mathbf{6^6c}$ overlap, and those of $\mathbf{6^5c}$ do not.

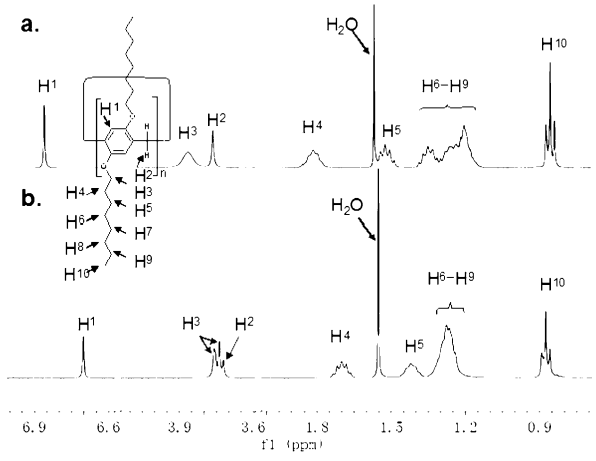


Figure 1. ^{1}H NMR spectra (400 MHz, $CDCl_3$, 20 °C) of (a) $\mathbf{6^5c}$ and (b) $\mathbf{6^6c}$.

Conclusions

We have demonstrated that pillararenes can be obtained by the condensation of 2,5-dialkoxybenzyl alcohol (**2**) and 2,5-dialkoxybenzyl bromide (**3**) with an appropriate Lewis acid catalyst at room temperature in a short time. The mechanism of this cyclization reaction is presumed to be a Friedel–Crafts alkylation. The effect of different Lewis acids on the cyclization reaction was investigated. The results showed that the effects of different Lewis acids on the cyclization reactions of **2** and **3** were different. When **2** was used as the reactant, the appropriate catalyst was $FeCl_3$, $AlCl_3$, $SnCl_4$, or $BF_3{\cdot}O(C_2H_5)_2$, whereas when **3** was used, the appropriate catalyst was $FeCl_3$, $AlCl_3$, $ZnCl_2$ or $SnCl_4$. Using this method, pillar[*n*]arenes (n = 5, 6) with different alkoxy substituents were prepared successfully. Our method makes it possible to prepare pillar[5]arenes and pillar[6]arenes easily and efficiently from the cyclization of relatively available 2,5-dialkoxybenzyl alcohols and 2,5-dialkoxybenzyl bromides. This should be helpful for investigations on the applications of pillararenes, especially pillar[6]arenes, in host–guest chemistry.

Experimental Section

General: 2,5-Dimethoxybenzaldehyde, 2,5-dihydroxybenzaldehyde, bromooctane, bromopentane, bromohexane, boron trifluoride ethyl ether complex, $FeCl_3$, $ZnCl_2$, $SnCl_4$, $AlCl_3$, and CH_2Cl_2 were reagent grade and used as received. Solvents were either employed as purchased or dried according to procedures described in the literature. ^{1}H NMR spectra were collected with a Varian Unity INOVA-400 spectrometer with TMS. ^{13}C NMR spectra were recorded with a Varian Unity INOVA-400 spectrometry at 100 MHz. Mass spectra were performed with a Bruker Esquire 3000 plus mass spectrometer (Bruker–Franzen Analytik GmbH Bremen, Germany) equipped with ESI interface and ion trap analyzer. High resolution mass spectra were obtained with a Bruker 7-Tesla FT-ICRMS equipped with an electrospray source (Billerica, MA, USA). The melting points were measured with an automatic melting point apparatus (SHPSIC WRS-2).

Synthesis of 2: To a solution of 2,5-dimethoxybenzaldehyde (3.32 g, 20.0 mmol) in MeOH, $NaBH_4$ (1.13 g, 30.0 mmol) was added at 0 °C. The mixture was stirred overnight at room temperature. The solvent was removed by evaporation. To the residue, H_2O/CH_2Cl_2 (v/v = 1:1, 100 mL) was added. The organic layer was dried with anhydrous Na_2SO_4. After filtration, solvents were evaporated to give a colorless oil (3.32 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.90 (s, 1 H), 6.78 (s, 2 H), 4.64 (s, 2 H), 3.79 (s, 3 H), 3.75 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, room temperature): δ = 153.7, 151.4, 130.3, 114.6, 112.9, 111.2, 61.60, 51.80 ppm. ESI-MS: m/z = 191.1 $[M + Na]^+$ (100). HRMS: m/z calcd. for $[M]^+$ $C_9H_{12}O_3$, 168.0786; found 168.0788, error 0.2 ppm.

Synthesis of DMpillar[5]arene from 2: To a solution of **2** (0.673 g, 4.00 mmol) in CH_2Cl_2, catalyst [4.00 mmol: $BF_3{\cdot}O(C_2H_5)_2$, $FeCl_3$, $ZnCl_2$, $SnCl_4$ or $AlCl_3$] was added. After the mixture was stirred at room temperature for 3 min, the mixture was washed twice with deionized water (30 mL). The organic layer was dried with anhydrous Na_2SO_4 and evaporated to afford the crude product, which was isolated by flash column chromatography using petroleum

ether/ethyl acetate (*v*/*v* = 6:1) as the eluent to give the product as a white solid [BF_3·$O(C_2H_5)_2$: 0.225 g, 38%; $FeCl_3$: 0.235 g, 39%; $ZnCl_2$: trace; $SnCl_4$: 0.15 g, 25%; $AlCl_3$: 0.210 g, 35%]; m.p. 248.1–249.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.88 (s, 10 H), 3.78 (s, 10 H), 3.74 (s, 30 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, room temperature): δ = 151.02, 128.43, 114.29, 55.99, 29.88 ppm. ESI-MS: *m*/*z* = 773.4 $[M + Na]^+$ (100%), 751.4 $[M + H]^+$, 768.5 $[M + NH_4]^+$. HRMS: *m*/*z* calcd. for $[M]^+$ $C_{52}H_{46}O_5$, 750.3345; found 750.3352, error 0.2 ppm.

Synthesis of 3: To a solution of **2** (7.52 g, 44.7 mmol) in CH_2Cl_2, PBr_3 (7.97 mL, 83.9 mmol) was added. After the mixture was stirred at room temperature overnight, deionized water (30 mL) was added. The organic layer was washed twice with deionized water (100 mL). The organic layer was dried with anhydrous Na_2SO_4 and evaporated to afford the product as a white solid (9.58 g, 93%); m.p. 67.0–68.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.91 (d, *J* = 2.2 Hz, 1 H), 6.82 (m, 2 H), 4.54 (s, 2 H), 3.85 (s, 3 H), 3.77 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, room temperature): δ = 153.54, 151.79, 127.04, 116.52, 115.16, 112.31, 55.32, 55.89, 29.11 ppm. HRMS: *m*/*z* calcd. for $[M]^+$ $C_9H_{11}O_2Br$, 229.9942; found 229.9947, error 0.2 ppm.

Synthesis of DMpillar[5]arene from 3: To a solution of **3** (0.924 g, 4.00 mmol) in CH_2Cl_2, catalyst [4 mmol: BF_3·$O(C_2H_5)_2$, $FeCl_3$, ZnCl2, $SnCl_4$ or $AlCl_3$] was added. After the mixture was stirred at room temperature for 3 min, the mixture was washed twice with deionized water (30 mL). The organic layer was dried with anhydrous Na_2SO_4 and evaporated to afford the crude product, which was isolated by flash column chromatography using petroleum ether/ethyl acetate (*v*/*v* = 6:1) as the eluent to give the product as a white solid [BF_3·$O(C_2H_5)_2$: trace; $FeCl_3$: 0.205 g, 34%; $ZnCl_2$: 0.241 g, 40%; $SnCl_4$: 0.214 g, 35%; $AlCl_3$: 0.220 g, 37%]; m.p. 248.1–249.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.88 (s, 10 H), 3.78 (s, 10 H), 3.74 (s, 30 H) ppm.

Synthesis of 5a: A mixture of 2,5-dihydroxybenzaldehyde (5.52 g, 40 mmol), K_2CO_3 (16.56 g, 120 mmol), and 1-bromopentane (19.7 mL, 160 mmol) in CH_3CN (250 mL) was heated to reflux overnight. After cooling, the mixture was filtered to obtain a black solution. The solution was concentrated and purified by silica gel flash column chromatography (petroleum ether/ethyl acetate, *v*/*v* = 10:1) to obtain the product as a brown oil (9.2 g). The brown oil (2.92 g, 10 mmol) was dissolved in CH_2Cl_2/MeOH (*v*/*v* = 1:1) and $NaBH_4$ (0.760 g, 20 mmol) was added at 0 °C. The resulting mixture was stirred overnight at room temperature and the solvent was removed by evaporation. To the residue, H_2O/CH_2Cl_2 (*v*/*v* = 1:1, 100 mL) was added. The organic layer was dried with anhydrous Na_2SO_4. After filtration, solvents were evaporated to give the product as a brown liquid (2.80 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.86 (d, *J* = 1.9 Hz, 1 H), 6.74 (d, *J* = 3.4 Hz, 2 H), 4.63 (s, 2 H), 3.92 (t, *J* = 6.5 Hz, 2 H), 3.88 (t, *J* = 6.6 Hz, 2 H), 1.78–1.73 (m, 4 H), 1.43–1.35 (m, 8 H), 0.94–0.91 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, room temperature): δ = 153.21, 150.97, 130.44, 115.49, 113.83, 112.23, 68.72, 62.10, 29.24, 28.42, 22.62, 14.17 ppm. HRMS: *m*/*z* calcd. for $[M]^+$ $C_{17}H_{28}O_3$, 280.2039; found 280.2038, error 0.4 ppm.

Synthesis of 5b: A mixture of 2,5-dihydroxybenzaldehyde (5.52 g, 40 mmol), K_2CO_3 (16.56 g, 120 mmol) and bromohexane (22.5 mL, 160 mmol) in CH_3CN (250 mL) was heated to reflux overnight. After cooling, the mixture was filtered to obtain a black solution. The solution was concentrated and purified by silica gel flash column chromatography (petroleum ether/ethyl acetate, *v*/*v* = 10:1) to obtain the product as a brown oil (15 g). The brown oil (10.33 g, 33.7 mmol) was dissolved in CH_2Cl_2/MeOH (*v*/*v* = 1:1, 200 mL) and $NaBH_4$ (2.55 g, 67.4 mmol) was added at 0 °C. Then the mixture was stirred overnight at room temperature and the solvent was removed by evaporation. To the residue, H_2O/CH_2Cl_2 (*v*/*v* = 1:1, 200 mL) was added. The organic layer was dried with anhydrous Na_2SO_4. After filtration, solvents were evaporated to give the product as a brown liquid (9.4 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.87 (d, *J* = 1.9 Hz, 1 H), 6.75 (d, *J* = 2.6 Hz, 2 H), 4.64 (s, 2 H), 3.91 (m, 4 H), 2.49 (s, 1 H), 1.44 (m, 4 H), 1.38–1.28 (m, 8 H), 0.92–0.89 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, room temperature): δ = 153.27, 150.96, 130.55, 115.44, 113.87, 112.31, 68.77, 62.10, 31.37, 29.51, 25.92, 22.74, 14.14 ppm. HRMS: *m*/*z* calcd. for $[M]^+$ $C_{19}H_{32}O_3$, 308.2356; found 308.2351, error 1.6 ppm.

Synthesis of 5c: A mixture of 2,5-dihydroxybenzaldehyde (5.52 g, 40 mmol), K_2CO_3 (16.56 g, 120 mmol) and bromooctane (27.9 mL, 160 mmol) in CH_3CN (250 mL) was heated to reflux overnight. After cooling, the mixture was filtered to obtain a black solution. The solution was concentrated and purified by silica gel flash column chromatography (petroleum ether/ethyl acetate, *v*/*v* = 200:1) to obtain the product as a brown oil (13.9 g). The brown oil (13.9 g, 38.3 mmol) was dissolved in CH_2Cl_2/MeOH (*v*/*v* = 1:1) and $NaBH_4$ (2.90 g, 76.7 mmol) was added at 0 °C. The mixture was stirred overnight at room temperature and the solvent was removed by evaporation. To the residue, H_2O/CH_2Cl_2 (*v*/*v* = 1:1, 100 mL) was added. The organic layer was dried with anhydrous Na_2SO_4. After filtration, solvents were evaporated to give the product as a white solid (13.7 g, 98%); m.p. 38.4–39.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.88 (d, *J* = 2.2 Hz, 1 H), 6.78 (m, 2 H), 4.67 (d, *J* = 5.3 Hz, 2 H), 3.97 (t, *J* = 6.5 Hz, 2 H), 3.92 (t, *J* = 6.6 Hz, 2 H), 2.45 (s, 1 H), 1.83–1.72 (m, 4 H), 1.56–1.41 (m, 4 H), 1.38–1.28 (m, 16 H), 0.90 (t, *J* = 6.6 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, room temperature): δ = 153.25, 151.07, 130.45, 115.49, 113.93, 112.29, 68.81, 62.44, 32.02, 29.46, 26.26, 22.66, 14.29 ppm. HRMS: *m*/*z* calcd. for $[M]^+$ $C_{23}H_{40}O_3$, 364.2977; found 364.2973, error 0.2 ppm.

Synthesis of 6^5a: To a solution of **5a** (1.16 g, 4.14 mmol) in CH_2Cl_2, BF_3·$O(C_2H_5)_2$ (1.04 mL, 4.14 mmol) was added. After the mixture was stirred at room temperature for 3 min, the mixture was washed twice with deionized water (100 mL). The organic layer was dried with anhydrous Na_2SO_4 and evaporated to afford the crude product, which was isolated by flash column chromatography using petroleum ether/ethyl acetate (*v*/*v* = 40:1) as the eluent to give the product as a white solid (0.44 g, 41%). ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.70 (s, 10 H), 3.90 (s, 10 H), 3.83 (t, *J* = 6.1 Hz, 20 H), 1.73 (m, 20 H), 1.42–1.29 (m, 40 H), 0.91 (t, *J* = 6.9 Hz, 30 H) ppm.

Synthesis of 6^5b: To a solution of **5b** (0.617 g, 2.00 mmol) in CH_2Cl_2, BF_3·$O(C_2H_5)_2$ (0.501 mL, 2.00 mmol) was added. After the mixture was stirred at room temperature for 3 min, the mixture was washed twice with deionized water (100 mL). The organic layer was dried with anhydrous Na_2SO_4 and evaporated to afford the crude product, which was isolated by flash column chromatography using petroleum ether/ethyl acetate (*v*/*v* = 80:1) as the eluent to give the product as a white solid (0.25 g, 43%). ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.66 (s, 10 H), 3.86 (s, 10 H), 3.79 (t, *J* = 6.2 Hz, 20 H), 1.71–1.58 (m, 20 H), 1.39 (m, 20 H), 1.29–1.27 (m, 40 H), 0.87 (t, *J* = 6.9 Hz, 30 H) ppm.

Synthesis of 6^5c and 6^6c: To a solution of **5c** (7.29 g, 20 mmol) in CH_2Cl_2, BF_3·$O(C_2H_5)_2$ (5.04 mL, 20.0 mmol) was added. After the mixture was stirred at room temperature for 3 min, the mixture was washed twice with deionized water (100 mL). The organic layer was dried with anhydrous Na_2SO_4 and evaporated to afford the crude

product, which was isolated by flash column chromatography using petroleum ether/ethyl acetate (*v*/*v* = 200:1) as the eluent to give the products, **6⁵c** and **6⁶c**, both of which were white solids (**6⁵c**: 1.00 g, 14%; m.p. 97.9–99.5 °C. **6⁶c**: 0.92 g, 13%; m.p. 76.0–79.1 °C). Compound **6⁵c** was separated first and then **6⁶c** was eluted. **6⁵c**: ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.85 (s, 10 H), 3.84 (s, 20 H), 3.73 (s, 10 H), 1.81 (s, 20 H), 1.53–1.47 (m, 20 H), 1.35–1.23 (m, 80 H), 0.85 (t, *J* = 6.8 Hz, 30 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, room temperature): δ = 149.86, 128.30, 114.23, 68.28, 32.18, 30.38, 30.01, 29.63, 29.42, 26.67, 22.95, 14.34 ppm. ESI-MS: *m*/*z* 1749.9 $[M + NH_4]^+$ (100%). HRMS: *m*/*z* calcd. for $[M + NH_4]^+$ $C_{115}H_{194}N_1O_{10}$, 1749.47027; found 1749.47080, error 0.3 ppm. **6⁶c**: ^{1}H NMR (400 MHz, $CDCl_3$, room temperature): δ = 6.70 (s, 12 H), 3.76–3.72 (m, 36 H), 1.72–1.68 (m, 24 H), 1.42 (s, 24 H), 1.32–1.23 (m, 96 H), 0.87 (t, *J* = 6.7 Hz, 36 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, room temperature): δ = 150.70, 127.94, 115.20, 68.75, 32.22, 31.18, 30.18, 29.91, 29.66, 26.64, 22.97, 14.35 ppm. ESI-MS: *m*/*z* 1749.9 $[M + NH_4]^+$(100%). LRESIMS: *m*/*z* 2078.3 $[M + H]^+$ (100%). HRMS: *m*/*z* calcd. for $[M + NH_4]^+$ $C_{138}H_{232}N_1O_{12}$, 2095.75745; found 2095.75517, error –1.09 ppm.

Supporting Information (see footnote on the first page of this article): Product characterizations.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (NSFC) (grant numbers 20834004 and 91027006), the Fundamental Research Funds for the Central Universities (2010QNA3008), the Zhejiang Provincial Natural Science Foundation of China (R4100009), the MOE Key Laboratory of Macromolecular Synthesis and Functionalization of Zhejiang University (2010MSF02), and the Open Project of State Key Laboratory of Supramolecular Structure and Materials.

[1] a) W. Ong, M. Gómez-Kaifer, A. E. Kaifer, *Org. Lett.* **2002**, *4*, 1791–1794; b) F. Huang, K. A. Switek, L. N. Zakharov, F. R. Fronczek, C. Slebodnick, M. Lam, J. A. Golen, W. S. Bryant, P. E. Mason, A. L. Rheingold, M. Ashraf-Khorassani, H. W. Gibson, *J. Org. Chem.* **2005**, *70*, 3231–3241; c) S. J. Vella, J. Tiburcio, J. W. Gauld, S. J. Loeb, *Org. Lett.* **2006**, *8*, 3421–3424; d) C. Zhang, S. Li, J. Zhang, K. Zhu, N. Li, F. Huang, *Org. Lett.* **2007**, *9*, 5553–5556; e) D. J. Hoffart, J. Tiburcio, A. de la Torre, L. K. Knight, S. J. Loeb, *Angew. Chem. Int. Ed.* **2008**, *47*, 97–101; f) L. M. Klivansky, G. Koshkakaryan, D. Cap, Y. Liu, *Angew. Chem. Int. Ed.* **2009**, *48*, 4185–4189; g) S. Li, M. Liu, B. Zheng, F. Wang, N. Li, X. Zhao, F. Huang, *Org. Lett.* **2009**, *11*, 3350–3353; h) S. Rieth, B. Wang, X. Bao, J. D. Badjić, *Org. Lett.* **2009**, *11*, 2495–2498; i) Y. Hua, A. H. Flood, *Chem. Soc. Rev.* **2010**, *39*, 1262–1271; j) S. Rieth, X. Bao, B. Y. Wang, C. M. Hadad, J. D. Badjić, *J. Am. Chem. Soc.* **2010**, *132*, 773–776; k) B. Qin, C. Ren, R. Ye, C. Sun, K. Chiad, X. Chen, Z. Li, F. Xue, H. Su, G. A. Chass, H. Zeng, *J. Am. Chem. Soc.* **2010**, *132*, 9564–9566; l) M. Zhang, K. Zhu, F. Huang, *Chem. Commun.* **2010**, *46*, 8131–8141; m) M. Liu, S. Li, M. Hu, F. Wang, F. Huang, *Org. Lett.* **2010**, *12*, 760–763; n) G. Koshkakaryan, D. Cao, L. M. Klivansky, S. J. Teat, J. L. Tran, Y. Liu, *Org. Lett.* **2010**, *12*, 1528–153; o) M. Liu, X. Yan, M. Hu, X. Chen, M. Zhang, B. Zheng, X. Hu, S. Shao, F. Huang, *Org. Lett.* **2010**, *12*, 2558–2561.

[2] a) T. Ogoshi, S. Kanai, S. Fujinami, T. A. Yamagishi, Y. Nakamoto, *J. Am. Chem. Soc.* **2008**, *130*, 5022–5023; b) T. Ogoshi, K. Umeda, T. Yamagishi, Y. Nakamoto, *Chem. Commun.* **2009**, *45*, 4874–4876; c) T. Ogoshi, K. Kitajima, T. Aoki, S. Fujinami, T. A. Yamagishi, Y. Nakamoto, *J. Org. Chem.* **2010**, *75*, 3268–3273; d) T. Ogoshi, Y. Nishida, T. A. Yamagishi, Y. Nakamoto, *Macromolecules* **2010**, *43*, 7068–7072; e) T. Ogoshi, K. Kitajima, T. A. Yamagishi, Y. Nakamoto, *Org. Lett.* **2010**, *12*, 636–638; f) T. Ogoshi, T. Aoki, K. Kitajima, S. Fujinami, T. Yamagishi, Y. Nakamoto, *J. Org. Chem.* **2011**, *76*, 328–331; g) T. Ogoshi, R. Shiga, T. Yamagishi, *J. Org. Chem.* **2011**, *76*, 618–622.

[3] C. D. Gutsche, R. Muthukrishnan, *J. Org. Chem.* **1978**, *43*, 4903–4905.

[4] C. D. Gutsche, *Calixarenes: An Introduction*, 2nd ed., The Royal Society of Chemistry, Cambridge, **2008**; p. 77–78.

[5] a) D. R. Cao, Y. H. Kou, J. Q. Liang, Z. Z. Chen, L. Y. Wang, H. Meier, *Angew. Chem. Int. Ed.* **2009**, *48*, 9721–9723; b) Y. Kou, H. Tao, D. Cao, Z. Fu, D. Schollmeyer, H. Meier, *Eur. J. Org. Chem.* **2010**, 6464–6470.

[6] a) Z. Zhang, B. Xia, C. Han, Y. Yu, F. Huang, *Org. Lett.* **2010**, *12*, 3285–3287; b) Z. Zhang, Y. Luo, J. Chen, S. Dong, Y. Yu, Z. Ma, F. Huang, *Angew. Chem. Int. Ed.* **2011**, *50*, 1397–1401; c) Z. Zhang, Y. Luo, B. Xia, C. Han, Y. Yu, X. Chen, F. Huang, *Chem. Commun.* **2011**, *47*, 2417–2419.

[7] a) C. Li, Q. Xu, J. Li, F. Yao, X. Jia, *Org. Biomol. Chem.* **2010**, *8*, 1568–1576; b) C. Li, L. Zhao, J. Li, X. Ding, S. Chen, Y. Yu, X. Jia, *Chem. Commun.* **2010**, *46*, 9016–9018.

[8] C. Han, F. Ma, Z. Zhang, B. Xia, Y. Yu, F. Huang, *Org. Lett.* **2010**, *12*, 4360–4363.

[9] R. Nakane, O. Kurihara, A. Takenatsu, *J. Org. Chem.* **1971**, *36*, 2753–2756.

[10] P. S. Stapp, *J. Org. Chem.* **1974**, *39*, 2466–2467.

[11] a) X. Hu, L. Chen, W. Si, Y. Yu, J. Hou, *Chem. Commun.* **2011**, *47*, 4694–4696; b) W. Si, X. Hu, X. Liu, R. Fan, Z. Chen, L. Weng, J. Hou, *Tetrahedron Lett.* **2011**, *52*, 2484–2487.

[12] N. Strutt, R. Forgan, J. Spruell, Y. Botros, J. Stoddart, *J. Am. Chem. Soc.* **2011**, *133*,5668–5671.

[13] S. Kanai, Y. Nojiri, G. Konishi, Y. Nakamoto, *Polym. Prep. Jpn. J.* **2006**, *55*, 303; G. Konishi, *J. Synth. Org. Chem. Jpn.* **2008**, *66*, 705–713.

[14] H. Takemura, *Curr. Org. Chem.* **2009**, *13*.1633–1653.

Received: May 19, 2011
Published Online: August 2, 2011

