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Hexakis(*m*-phenylene ethynylene) Macrocycles with Multiple H-Bonding Side Chains and Modified Cavities: Altered Stacking Strength and Persistent Tubular Assembly

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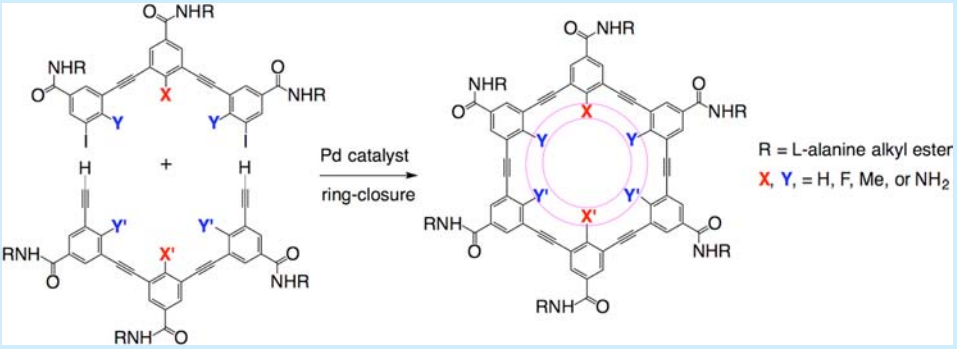
Supporting Information



ABSTRACT: Hexakis(*m*-phenylene ethynylene) macrocycles **1** bearing multiple hydrogen-bonding side chains and containing inner cavities modified with different functional groups are synthesized based on Pd-catalyzed (Sonogashira) coupling of monomeric building blocks to trimeric precursors that are recombined and coupled to give macrocycles with different substitution patterns of inward-pointing groups. Examining four representative macrocycles indicates that they all undergo the same helical tubular assembly previously observed for macrocycle **1a** but with different stacking strengths.

The development of molecular components that engage in the same or similar assembly allows structural and functional tuning on supramolecular assemblies by performing modification at the molecular level based on established synthetic methods. Persistent supramolecular motifs are invaluable in uncovering unusual properties and functions that are only expressed at the supramolecular level.[1] For example, the stacking of ringlike molecules leads to tubular assemblies with outer and inner surfaces, along with internal pores that are defined by the cyclic molecular constituents.[2,3] Among various ring-shaped molecules, those having rigid backbones and nondeformable cavities are of particular interest[4−6] since the stacking of such macrocycles results in tubular assemblies with precisely defined outer and inner diameters, along with the possibility of placing functional groups at specific sites. Of the nanopores with defined diameters, those having a subnanometer (<1 nm) range have been found to exhibit unique and, in many cases, unexpected properties.[1]

One class of rigid macrocycles are those having oligo(phenylene ethynylene) backbones and have been extensively studied.[4,5] A major objective in developing such rigid macrocycles is to realize their tubular assembly.[3d,e,4] However, the tubular stacking of these macrocycles is known to be case-dependent, which often fails with even minor structural modification on the macrocyclic building blocks.

We recently reported a strategy for enforcing the tubular stacking of rigid macrocycles.[7] Equipping a class of well-studied hexakis(*m*-phenylene ethynylene) (*m*-PE) macrocycles with side chains capable of engaging in intermolecular H-bonding led to several six-residue *m*-PE macrocycles as shown by general structure **A** (Figure 1a).

Our study indicates that macrocycles **A**, with their H-bonding side chains, undergo reliable tubular stacking, forming well-defined helical nanotubular assemblies that are encased in 6-fold H-bonded networks and further stabilized by $\pi-\pi$ stacking involving the backbones. With a noncollapsible, hydrophobic sub-nanometer inner pore, the self-assembling tubes of **A** exhibited extraordinary mass-transporting capabilities across lipid bilayers by serving as ion channels with superb ion selectivity and as efficient water channels.[7]

We have also probed the tubular stacking and mass transport of several generations of rigid macrocycles we developed in recent years.[8] Modifying the periphery of *meta*-linked aromatic oligoamide (*m*-OA) macrocycles **B** (Figure 1b) resulted in the

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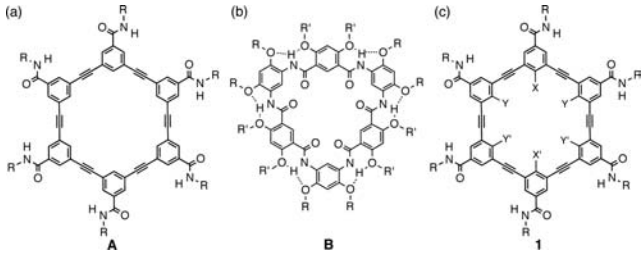


Figure 1. (a) *m*-PE macrocycles **A** equipped with H-bonding (secondary amide) side chains; (b) first-generation *meta*-linked aromatic oligoamide (*m*-OA) macrocycles **B**; (c) cavity-modified *m*-PE macrocycles **1** derived from **A**.

second-generation macrocycles that stack into discrete tetramers[9] and the third-generation macrocycles that undergo extremely strong stacking.[10]

Exceptional mass-transport capabilities of sub-nanometer pores was observed with the hydrophilic pores of the tubular assemblies of *m*-OA macrocycles **B** and their derivatives. The first-generation macrocycles **B** stack into transmembrane ion channels with very large conductance.[11] More recently, we developed the fourth-generation macrocycles by merging the backbones of the *m*-PE and *m*-OA macrocycles, which allows the placement of an inward-pointing functional group inside the cavity of the resultant macrocycle. The tubular stacks of these hybrid macrocycles, with different functional groups in the inner pores, exhibited drastically different transmembrane ion transport behavior such as the surprising rejection of proton or altered cation/anion selectivities.[12]

Our study shows that even a simple structural modification, e.g., introducing just one functional group in the inner cavity of a macrocycle, can have a major impact on the property of its supramolecular assembly. The dramatic effect of simple structural modification on the behavior of self-assembling pores prompted us to perform systematic modification on the inner cavities of rigid macrocyclic building blocks.[13]

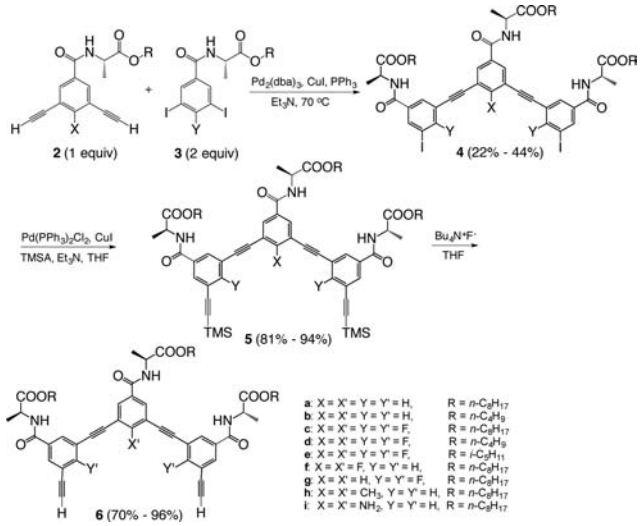
With numerous aromatic hydrogens that can be replaced with other groups, *m*-PE macrocycles are very attractive for systematic structural modification. Surprisingly, of the many known examples of *m*-PE and other analogous macrocycles, few with multiple H-bonding side chains were known until our recent report.[7] In addition, except for small alkyl or alkoxy groups, almost no other functional groups have been introduced into the cavities of *m*-PE and analogous macrocycles.

Herein, we report the design and synthesis of macrocycles **1** (Figure 1c). By keeping the same set of H-bonding side chains, macrocycles **1** are designed to build on the assembly of **A** to also undergo tubular stacking. The inward-pointing groups of **1** will not only alter the inner cavities but will also change the electronic features of the *m*-PE backbones, which will lead to different stacking propensities for the macrocycles. Achieving these systematic tunings relies on the development of a synthetic protocol that accommodates the needed modifications.

The preparation of **1** follows a convergent synthetic sequence that involves (1) synthesis of monomeric building blocks bearing different X groups that end up as the inward-pointing groups in the cavities of the target macrocycles, (2) the preparation of trimeric precursors by coupling different combinations of monomers, and (3) ring-closure reaction involving different pairs of the trimeric precursors.

The synthesis of trimers **4a–i** and **6a–i** is shown in Scheme 1 by coupling 2 equiv of **2a–g** with 1 equiv of **3a–g** (Scheme S1).

Scheme 1. Synthesis of Trimeric Precursors



This strategy allows the generation of **4** and **6** with a variety of substitution patterns by combining different pairs of **2** and **3**, as exemplified by, but not limited to, the nine trimers of **4** or **6** prepared. The combinations of **2** and **3** and the yields of **4–6** are shown in Table 1. The yields of **4** and **6** demonstrate that the various types of X (and Y) groups do not compromise the coupling reactions.

Table 1. Synthesis and Yields of Compounds 4,[a] 5,[b] and 6[c]

entry	3	2	4 (%)	5 (%)	6 (%)
1	**3a**	**2a**	**6a**, 24	**5a**, 88	**6a**, 96
2	**3b**	**2b**	**6b**, 40	**5b**, 94	**6b**, 93
3	**3c**	**2c**	**6c**, 38	**5c**, 90	**6c**, 92
4	**3d**	**2d**	**6d**, 44	**5d**, 92	**6d**, 92
5	**3e**	**2e**	**6e**, 22	**5e**, 81	**6e**, 70
6	**3a**	**2c**	**6f**, 34	**5f**, 90	**6f**, 93
7	**3c**	**2a**	**6g**, 38	**5g**, 91	**6g**, 94
8	**3a**	**2f**	**6h**, 28	**5h**, 94	**6h**, 94
9	**3a**	**2g**	**6i**, 23	**5i**, 90	**6i**, 93

[a]Formed from **2** and **3** by treatment with $Pd_2(dba)_3$, CuI, and PPh_3 (**2**/**3**/$Pd_2(dba)_3$/CuI/PPh_3 = 1:2:0.03:0.06:0.3) at 75 °C for 12 h. [b]Formed from **4** and TMSA (trimethylsilylacetylene) by treatment with $Pd(PPh)_3Cl_2$ and CuI (**4**/TMSA/$Pd(PPh)_3Cl_2$/CuI = 1:4:0.03:0.06) in THF/Et_3N (15/8, v/v) at room temperature for 12 h. [c]Formed from **5** by treatment with Bu_4NF (**5**/Bu_4NF = 1:3) in THF at room temperature for 0.5 h.

Pd-catalyzed bimolecular coupling/unimolecular cyclization[5] of **4** and **6** was performed under pseudohigh dilution conditions (Scheme 2). The availability of the two types of trimeric precursors allows a large number of macrocycles **1** to be constructed. The pairings of **4** and **6** that correspond to the 12 macrocycles (**1a–l**) and their yields are shown in Table 2.

Macrocycles **1** were obtained in yields ranging from ~8% to 20% after extensive purification. While **1b**, **1d**, and **1e** were successfully synthesized, these macrocycles, which bear short alkyl (*n*-butyl or isobutyl) side chains, were obtained in lower yields most likely due to their limited solubilities that complicated their purification. It was also found that maintaining the reaction temperature at near 85 °C was important for the formation of the macrocyclic products. At temperatures lower

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Scheme 2. Synthesis of Macrocycles 1

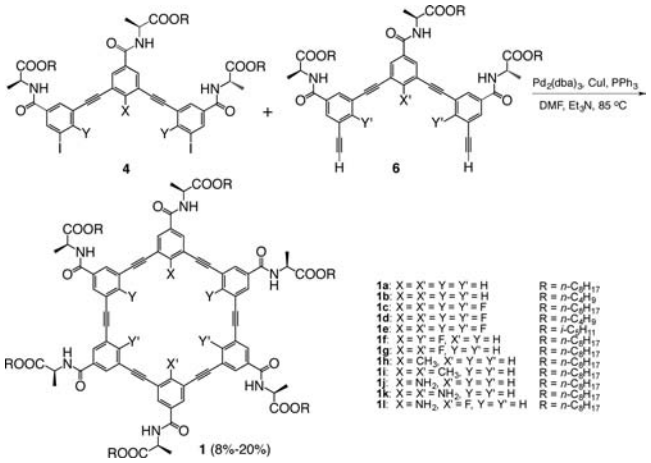

Table 2. Synthesis of Macrocycles 1[a]

entry	trimer 4[b]	trimer 6[b]	macrocycle 1 (%)
1	4a	6a	1a, 20
2	4b	6b	1b, 9
3	4c	6c	1c, 18
4	4d	6d	1d, 11
5	4e	6e	1e, 8
6	4f	6g	1f, 18
7	4f	6f	1g, 16
8	4a	6h	1h, 18
9	4h	6h	1i, 16
10	4a	6i	1j, 14
11	4i	6i	1k, 14
12	4i	6f	1l, 12

[a]Formed from **4** and **6** by treatment with $Pd_2(dba)_3$, CuI, and PPh_3 (**4**/**6**/$Pd_2(dba)_3$/CuI/PPh_3 = 1:1:0.5:1:5) in DMF/Et_3N at 85 °C for 60 h. [b]Reactants **4** and **6**, each dissolved in 10 mL of DMF, were added dropwise to Et_3N (20 mL) in DMF (40 mL) over 48 h at 85 °C, followed by stirring for an additional 12 h at the same temperature.

than 85 °C the coupling reaction failed to proceed, while at temperatures above 85 °C only byproducts were obtained.

Except for their side chains, macrocycles **1a**–**l** have cavities with different substitution patterns. Macrocycles **1a** and **1b**, which have only H atoms in their cavities, were previously reported by us.[7] Macrocycles **1h** and **1j** have a methyl and an amino group, respectively. Multiple groups were also introduced as shown by **1g** (two fluorines), **1i** (two methyls), **1k** (two amino groups), and **1f** (three fluorines), as well as **1c**, **1d**, and **1e** (six fluorines). The versatility of our strategy is further demonstrated by the preparation of **1l** that has two different groups, an amino group and a fluorine atom, in its cavity.

In addition to modifying cavities, the introduced groups also result in *m*-PE backbones with different electronic features, which should influence the stacking propensity of the resultant macrocycles. For example, electron-withdrawing groups decrease the electron density of the *m*-PE backbone and are known to enhance the $\pi-\pi$ stacking, while electron-donating groups increase electron density and weaken such stacking.[4c]

Our previous study established the tubular stacking of macrocycles **1a** and **1b** both in solution and in the solid state.[7] To probe the effect of backbones with altered electronic properties on the assembly of *m*-PE macrocycles, an initial study was performed by comparing macrocycles **1g**, **1i**, and **1k**, each of which has two functional groups in its cavity, and **1c**, which has six fluorine atoms in its cavity, with **1a**.

The ^{1}H NMR signals of these four macrocycles, like those of **1a**, are broadened in spectra recorded in $CDCl_3$ (Figure S37) but not in DMF-d_7 or DMSO-d_6 (Figures S1–24) in the micromolar range, indicating that these molecules undergo decreased motion due to aggregation in $CDCl_3$.

The stacking propensities of the macrocycles were assessed by comparing absorption spectra measured in CCl_4, $CHCl_3$, THF, and DMF (Figure S38). Macrocycle **1a** (5 μM) is known[7] to aggregate only in CCl_4 with a λ_{max} of 277 nm, while in the other three solvents the λ_{max} of **1a** shifts to 290 nm, corresponding to the molecularly dissolved form (Figure S38a). Similar to **1a**, macrocycles **1g**, **1i**, and **1k** (5 μM) give absorption bands around 277 nm in CCl_4, which t indicate aggregation, and bands around 290 nm in $CHCl_3$, THF, and DMF, which are due to a lack of aggregation (Figure S38c–e). In contrast, the absorption bands of **1c** in both CCl_4 and $CHCl_3$ (5 μM) are around 277 nm, which indicates aggregation, and in THF and DMF the bands shift to 290 nm, which suggests free molecules (Figure S38b). Thus, in $CHCl_3$, with its six fluorine atoms, macrocycle **1c** aggregates while **1a** and the other three macrocycles do not.

Absorption spectra measured in CCl_4 at different temperatures provide additional insights into the stacking strength of the macrocycles (Figure S39). The absorption bands of **1a**, **1i**, and **1k** were found to undergo red shifts between 45 and 50 °C, from around 276 nm toward about 290 nm, indicating the dissociation of stacked molecules with rising temperature. A similar red shift of bands was not observed for **1c** and **1g**, which have two and six fluorines, respectively, in their cavities, at up to 55 °C. These observations suggest that fluorine substituents, which reduce electron densities of the *m*-PE backbones, enhance the stacking of macrocycles **1c** and **1g**.

The helical columnar stacking of **1a** leads to similar CD spectra in CCl_4 (Figure S40f) and in the solid state, with maxima between 295 and 350 nm and minima around 275 nm.[7] Macrocycles **1c**, **1g**, **1i**, and **1k** also show the same general features, with maxima between 295 and 350 nm and minima around 275 nm in spectra measured in CCl_4 (Figure 2). The CD spectra of **1i** (Figure 2c) are nearly the same as those of **1a**. Plotting the minima at 277 nm against temperature reveals a

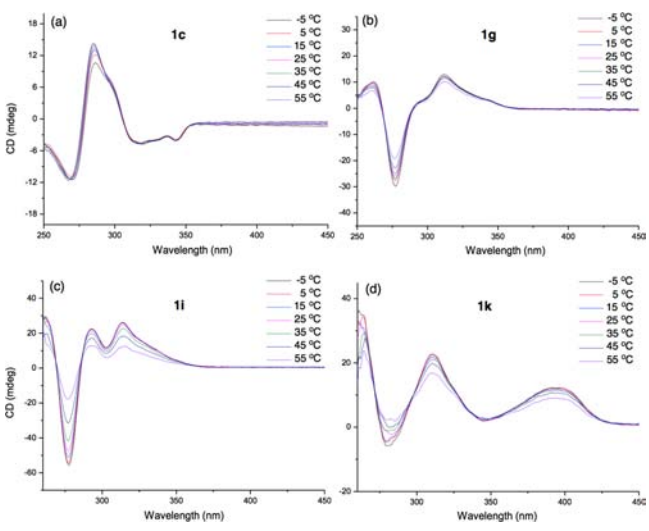

Figure 2. Variable-temperature CD spectra of (a) **1c**, (b) **1g**, (c) **1i**, and (d) **1k** measured in CCl_4 (10 μM).

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partial sigmoidal curve, indicating a cooperative assembly desassembly transition (Figure S40e). These results suggest that, like **1a**, macrocycles **1c**, **1g**, **1i**, and **1k** also stack into helical assemblies. The additional band around 390 nm in the spectra of **1k** is due to the red-shifted B-band caused by $\pi-\pi^*$ transition associated with the two benzene rings bearing amino groups.

In $CHCl_3$, macrocycles **1c**, **1g**, and **1i** give CD signals with the same features observed in CCl_4, while **1k** gives weak, poorly defined signals (see Figure S40a–d). The different CD spectra of **1k** measured in CCl_4 and $CHCl_3$ thus indicate that the strength of its stacking interaction is reduced due to the presence of the two amino groups.

In summary, Pd-catalyzed coupling of monomeric building blocks leads to the generation of a variety of trimeric building blocks. Pairwise combinations of the trimeric building precursors make it possible to synthesize a large number of different macrocycles **1** that bear different types of side chains and, more importantly, have cavities featured by different substitution patterns of introduced groups, which demonstrates the feasibility and efficiency of this strategy. In CCl_4, four representative macrocycles with distinctly different inward-pointing functional groups adopt the same helical tubular assembly previously observed for macrocycles **1a** but show different stacking strength. The aggregation of the macrocycles is interrupted in solvents of high polarity. The availability of cavity-modified *m*-PE macrocycles that stack into the same nanotubular motif offers new opportunities for constructing self-assembling nanotubes containing functionally diverse and tunable subnanometer pores.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00718.

Synthetic and experimental details; NMR, mass, UV, and CD spectra (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Bayley, H.; Cremer, P. S. *Nature* **2001**, *413*, 226. (b) Sakai, N.; Mareda, J.; Matile, S. *Acc. Chem. Res.* **2008**, *41*, 1354. (c) Rebek, J. *Acc. Chem. Res.* **2009**, *42*, 1660. (d) Childers, W. S.; Ni, R.; Mehta, A. K.; Lynn, D. G. *Curr. Opin. Chem. Biol.* **2009**, *13*, 652. (e) Gong, B.; Shao, Z. F. *Acc. Chem. Res.* **2013**, *46*, 2856.

(2) (a) Bong, D. T.; Clark, T. D.; Granja, J. R.; Ghadiri, M. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 988. (b) Gin, D. L.; Gu, W. Q.; Pindzola, B. A.; Zhou, W. J. *Acc. Chem. Res.* **2001**, *34*, 973. (c) Keizer, H. M.; Sijbesma, R. P. *Chem. Soc. Rev.* **2005**, *34*, 226. (d) Block, M. A. B.; Kaiser, C.; Khan, A.; Hecht, S. *Top. Curr. Chem.* **2005**, *245*, 89. (e) Pasini, D.; Ricci, M. *Curr. Org. Synth.* **2007**, *4*, 59.

(3) (a) Ghadiri, M. R.; Granja, J. R.; Milligan, R. A.; McRee, D. E.; Khazanovich, N. *Nature* **1993**, *366*, 324. (b) Seebach, D.; Matthews, J. L.; Meden, A.; Wessels, T.; Baerlocher, C.; McCusker, L. B. *Helv. Chim. Acta* **1997**, *80*, 173. (c) Gattuso, G.; Menzer, S.; Nepogodiev, S. A.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1451. (d) Mindyuk, O. Y.; Stetzer, M. R.; Heiney, P. A.; Nelson, J. C.; Moore, J. S. *Adv. Mater.* **1998**, *10*, 1363. (e) Fritzsche, M.; Bohle, A.; Dudenko, D.; Baumeister, U.; Sebastiani, D.; Richardt, G.; Spiess, H. W.; Hansen, M. R.; Höger, S. *Angew. Chem., Int. Ed.* **2011**, *50*, 3030. (f) Frischmann, P. D.; Sahli, B. J.; Guieu, S.; Patrick, B. O.; MacLachlan, M. J. *Chem. - Eur. J.* **2012**, *18*, 13712. (g) Hjelmgaard, T.; Roy, O.; Nauton, L.; El-Ghozzi, M.; Avignant, D.; Didierjean, C.; Taillefumier, C.; Faure, S. *Chem. Commun.* **2014**, *50*, 3564. (h) Zhao, H. Q.; Sheng, S.; Hong, Y. H.; Zeng, H. Q. *J. Am. Chem. Soc.* **2014**, *136*, 14270.

(4) (a) Bunz, U. H. F.; Rubin, Y.; Tobe, Y. *Chem. Soc. Rev.* **1999**, *28*, 107. (b) Grave, C.; Schlüter, A. D. *Eur. J. Org. Chem.* **2002**, 3075. (c) Zhao, D. H.; Moore, J. S. *Chem. Commun.* **2003**, 807. (d) Yamaguchi, Y.; Yoshida, Z.-I. *Chem. - Eur. J.* **2003**, *9*, 5430. (e) Höger, S. *Chem. - Eur. J.* **2004**, *10*, 1320.

(5) (a) Moore, J. S.; Zhang, J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 922. (b) Höger, S.; Enkelmann, V. *Angew. Chem., Int. Ed. Engl.* **1996**, *34*, 2713. (c) Hensel, V.; Schlüter, A. D. *Chem. - Eur. J.* **1999**, *5*, 421. (d) Seo, S. H.; Jones, T. V.; Seyler, H.; Peters, J. O.; Kim, T. H.; Chang, J. Y.; Tew, G. N. *J. Am. Chem. Soc.* **2006**, *128*, 9264. (e) Yang, L. Q.; Zhong, L. J.; Yamato, K.; Zhang, X. H.; Feng, W.; Deng, P. C.; Yuan, L. H.; Zeng, X. C.; Gong, B. *New J. Chem.* **2009**, *33*, 729. (f) Sisco, S. W.; Moore, J. S. *J. Am. Chem. Soc.* **2012**, *134*, 9114. (g) Aggarwal, A. V.; Thiessen, A.; Idelson, A.; Kalle, D.; Würsch, D.; Stangl, T.; Steiner, F.; Jester, S.-S.; Vogelsang, J.; Höger, S.; Lupton, J. M. *Nat. Chem.* **2013**, *5*, 964. (h) Tahara, K.; Yamamoto, Y.; Gross, D. E.; Kozuma, H.; Arikuma, Y.; Ohta, K.; Koizumi, Y.; Gao, Y.; Shimizu, Y.; Seki, S.; Kamada, K.; Moore, J. S.; Tobe, Y. *Chem. - Eur. J.* **2013**, *19*, 11251.

(6) Several examples of other rigid macrocycles: (a) Yuan, L. H.; Feng, W.; Yamato, K.; Sanford, A. R.; Xu, D. G.; Guo, H.; Gong, B. *J. Am. Chem. Soc.* **2004**, *126*, 11120. (b) Jiang, H.; Léger, J.-M.; Guionneau, P.; Huc, I. *Org. Lett.* **2004**, *6*, 2985. (c) Sessler, J. L.; Tomat, E.; Lynch, V. M. *Chem. Commun.* **2006**, 4486. (d) Nakao, K.; Nishimura, M.; Tamachi, T.; Kuwatani, Y.; Miyasaka, H.; Nishinaga, T.; Iyoda, M. *J. Am. Chem. Soc.* **2006**, *128*, 16740. (e) Holub, J. M.; Jang, H. J.; Kirshenbaum, K. *Org. Lett.* **2007**, *9*, 3275. (f) Campbell, F.; Plante, J.; Carruthers, C.; Hardie, M. J.; Prior, T. J.; Wilson, A. J. *Chem. Commun.* **2007**, 2240. (g) Qin, B.; Ren, C.; Ye, R.; Sun, C.; Chiad, K.; Chen, X.; Li, Z.; Xue, F.; Su, H.; Chass, G. A.; Zeng, H. Q. *J. Am. Chem. Soc.* **2010**, *132*, 9564. (h) Lee, S.; Chen, C.-H.; Flood, A. H. *Nat. Chem.* **2013**, *5*, 704.

(7) Zhou, X. B.; Liu, G. D.; Yamato, K.; Shen, Y.; Cheng, R. X.; Wei, X. X.; Bai, W. L.; Gao, Y.; Li, H.; Liu, Y.; Liu, F. T.; Czajkowsky, D. M.; Wang, J. F.; Dabney, M. J.; Cai, Z. H.; Hu, J.; Bright, F. V.; He, L.; Zeng, X. C.; Shao, Z. F.; Gong, B. *Nat. Commun.* **2012**, *3*, 949.

(8) Yamato, K.; Kline, M.; Gong, B. *Chem. Commun.* **2012**, *48*, 12142.

(9) Wu, X. X.; Liu, R.; Sathyamoorthy, B.; Yamato, K.; Liang, G. X.; Shen, L.; Ma, S. F.; Sukumaran, D. K.; Szyperski, T.; Fang, W. H.; He, L.; Chen, X. B.; Gong, B. *J. Am. Chem. Soc.* **2015**, *137*, 5879.

(10) Kline, M. A.; Wei, X. X.; Horner, I. J.; Liu, R.; Chen, S.; Chen, S.; Yung, K. Y.; Yamato, K.; Cai, Z. H.; Bright, F. V.; Zeng, X. C.; Gong, B. *Chem. Sci.* **2015**, *6*, 152–157.

(11) Helsel, A. J.; Brown, A. L.; Yamato, K.; Feng, W.; Yuan, L. H.; Clements, A.; Harding, S. V.; Szabo, G.; Shao, Z. F.; Gong, B. *J. Am. Chem. Soc.* **2008**, *130*, 15784.

(12) Wei, X. X.; Zhang, G. Q.; Shen, Y.; Zhong, Y. L.; Liu, R.; Yang, N.; Al-mkhaizim, F. Y.; Kline, M.; He, L.; Li, M. F.; Lu, Z. L.; Shao, Z. F.; Gong, B. *J. Am. Chem. Soc.* **2016**, *138*, 2749.

(13) (a) Endres, A.; Maas, G. *Tetrahedron* **2002**, *58*, 3999. (b) Kraszkiewicz, L.; Sosnowski, M.; Skulski, L. *Tetrahedron* **2004**, *60*, 9113. (c) Chang, K. J.; Kang, B. N.; Lee, M. H.; Jeong, K. S. *J. Am. Chem. Soc.* **2005**, *127*, 12214.

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