

# A Pd<sub>8</sub> Tetrafacial Molecular Barrel as Carrier for Water Insoluble Fluorophore

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**S** Supporting Information

**ABSTRACT:** A new carbazole-based tetraimidazole ligand 1,3,6,8-tetra(1*H*-imidazol-1-yl)-9-methyl-9*H*-carbazole (**L**) has been synthesized. The unsymmetrical nature of **L** as well as the rotational freedom of imidazole donor moieties around C–N bond make it a special building unit, which upon treatment with *cis*-(*tmeda*)Pd(NO<sub>3</sub>)<sub>2</sub> produced an unprecedented single linkage-isomeric Pd<sub>8</sub> tetrafacial molecular nanobarrel (**PSMBR-1**) [*tmeda* = *N,N,N',N'*-tetramethylethane-1,2-diamine]. Unlike closed architectures, open barrel architecture of water-soluble **PSMBR-1** makes it an ideal host for some water insoluble polyaromatic hydrocarbons in aqueous medium; one such inclusion complex coronene**PSMBR-1** was characterized by X-ray diffraction study. Moreover, the potential application of **PSMBR-1** as carrier in aqueous medium for the transportation of water insoluble fluorophore (perylene) for live cell imaging is explored.

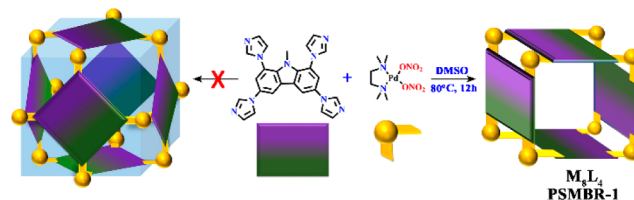
Metal–ligand coordination driven self-assembly has evolved as a powerful approach to achieve discrete nanometer-sized molecular architectures.<sup>1</sup> After the successful synthesis of the famous “molecular square” in 1990 via this approach, the next two decades have seen a tremendous growth in this field with the introduction of numerous fascinating two-dimensional (2D) and three-dimensional (3D) architectures of diverse shapes, sizes and functionality.<sup>2</sup> While, the “molecular library” suggested by Stang et al. has made it easy to design precursors for a desired architecture, the concept of “ship in a bottle” and “molecular flask” by Fujita et al. has illustrated their multifaceted applications in guest encapsulation, catalysis, peptide binding etc.<sup>3–7</sup> Symmetrical ligands have been extensively used due to the ease of convergence in discrete closed-shell architecture.<sup>8</sup> In this context, the use of a nonsymmetrical multitopic donor (number of donor sites >3) remains largely neglected due to the possibility of formation of multiple conformational isomers upon diverse orientation of the donors around the metal centers (Figure S1). However, in principle, such nonsymmetrical multidentate donors can yield unprecedented structural features which otherwise are not expected on the basis of the “molecular library” concept.

Most of the reported 3D discrete architectures of Pd(II)/Pt(II) have closed structures. Due to their closed-shell topology, they possess comparatively smaller windows with respect to their internal cavity size, which in turn restricts bigger guest molecules to go inside.<sup>9</sup> In this respect, cylindrical- or barrel-shaped

architectures are very promising as they possess windows similar to their cavity size. Moreover, release of guests is also expected to be easy through the open window. Even in biology, barrel-shaped protein structures, viz.  $\beta$ -barrels have immense importance in the diffusion process of small molecules and ions through cell membranes.<sup>10</sup> However, the synthesis of discrete barrel-shaped architectures by metal–ligand self-assembly remains very challenging and scarcely reported in the literature.<sup>11</sup>

Herein, we report the template free synthesis of an unprecedented water-soluble tetrafacial molecular barrel **PSMBR-1** via the self-assembly of a new asymmetric tetraimidazole donor **L** with 90° acceptor *cis*-Pd(*tmeda*)(NO<sub>3</sub>)<sub>2</sub> (**M**) [*tmeda* = *N,N,N',N'*-tetramethylethane-1,2-diamine] (Scheme 1). Such a self-assembly reaction may also

## Scheme 1. Schematic Representation of the Expected Cube and the Synthesis of Molecular Barrel **PSMBR-1**



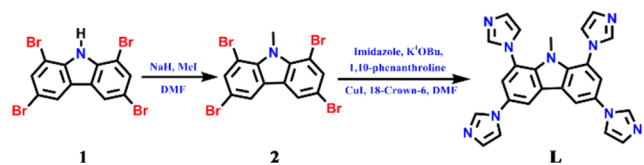
lead to the expected closed cubic architecture  $M_{12}L_6$  and numerous linkage isomeric structures due to the different connectivity of the two “pairs” of dissimilar imidazole units in the ligand **L**. Despite several possibilities, formation of a single linkage isomeric tetrafacial barrel in the present case is very surprising. The barrel has hydrophobic pocket surrounded by the four conjugated aromatic walls (**L**). The newly engineered molecular barrel with integrated hydrophobic pocket and water-soluble nature has shown to be suitable for the encapsulation of water-insoluble aromatic hydrocarbons in aqueous medium.<sup>12</sup> Moreover, the potential of this open barrel as carrier for the transportation of water insoluble perylene into HeLa cell in aqueous medium for live cell imaging without alteration of cell morphology has been explored.

**L** was synthesized in good yield from the *N*-methyl tetrabromo derivative of carbazole (2) by standard copper(I) catalyzed C–N coupling reaction as shown in Scheme 2. It was fully characterized by elemental analysis, multinuclear NMR spectroscopy, COSY, NOESY, and ESI-MS spectrometry, and its

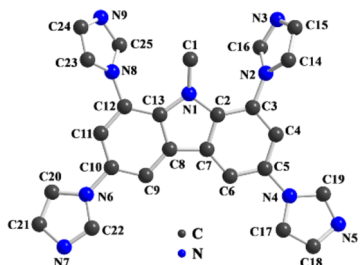
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## Scheme 2. Synthetic Strategy for the Donor L



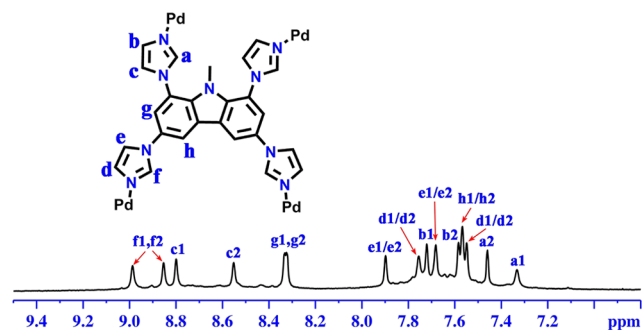
solid-state structure was elucidated by single crystal X-ray diffraction (XRD) analysis (Figure 1).



**Figure 1.** Ball and stick representation of the crystal structure of L. Hydrogen atoms are omitted for clarity.

The imidazoles at C3 and C12 are found to reside severely out of the carbazole plane compared to the rests due to steric repulsion with the *N*-methyl group, as is reflected from the torsional angles ( $\varphi_{C2-C3-N2-C16} = -62.8^\circ$ ;  $\varphi_{C13-C12-N8-C25} = 53.6^\circ$ ;  $\varphi_{C4-C5-N4-C19} = -16.9^\circ$ , and  $\varphi_{C9-C10-N6-C22} = 26.2^\circ$ ). Though the imidazoles at C3 and C12 as well as at C5 and C10 look different in terms of their orientations in the solid state, the differences remain untraced in the  $^1\text{H}$  NMR spectra due to their rapid rotation with respect to the NMR time scale (Figure S4).

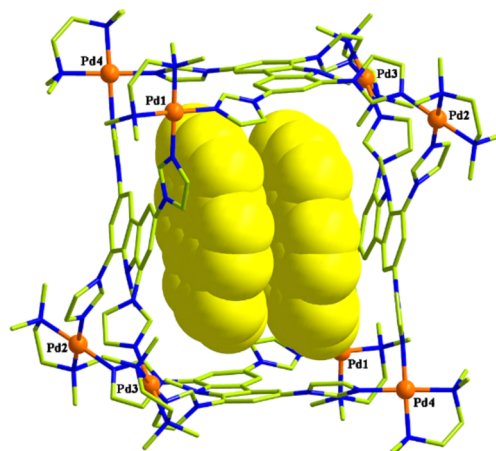
Overnight heating of a clear solution of L and *cis*-(*tmeda*)Pd( $\text{NO}_3$ )<sub>2</sub> (**M**) in DMSO at 80 °C in 1:2 molar ratio resulted a clear brown solution which upon treatment with excess ethyl acetate yielded **PSMBR-1** as off-white precipitate in quantitative yield. The product is completely soluble in water which is known as the “solvent of nature”.  $^1\text{H}$  NMR spectra in D<sub>2</sub>O showed the presence of 14 peaks between 9.0 and 7.3 ppm (Figure 2), which could be due to different orientation of the imidazole moieties around metal centers or the formation of mixture of products. Diffusion ordered NMR spectroscopy (DOSY, DMSO-*d*<sub>6</sub>), however, corroborated the formation of a single product with hydrodynamic radius of ~11.8 Å (Figure S11). Variable-temperature  $^1\text{H}$  NMR spectra in DMSO-*d*<sub>6</sub> showed no



**Figure 2.**  $^1\text{H}$  NMR spectra of **PSMBR-1**. Only aromatic region is shown for the sake of clarity. The peaks were assigned with the help of the  $^1\text{H}$ - $^1\text{H}$  COSY spectra (Figure S10) as well as the single crystal X-ray structure of the coronene**PSMBR-1** complex (Figure 3).

permanent change in the peak positions or any deformation upon heating up to 125 °C, strictly advocated the stability of **PSMBR-1** in a wide range of temperature in solution (Figure S12). The composition of the assembly was precisely determined by ESI-MS spectrometry of the  $\text{PF}_6^-$  analogue of **PSMBR-1**. The presence of several prominent peaks at  $m/z = 1815.51$ , 1325.38, and 1031.31 with isotopic distribution patterns corresponding to [**PSMBR-1-3PF<sub>6</sub><sup>-</sup>**]<sup>+3</sup>, [**PSMBR-1-4PF<sub>6</sub><sup>-</sup>**]<sup>+4</sup>, and [**PSMBR-1-5PF<sub>6</sub><sup>-</sup>**]<sup>+5</sup> charge fragments, respectively, confirmed the formation of a  $\text{M}_8\text{L}_4$  species (Figures S13–14). Though the formation of tetrafacial barrel was quite evident from the NMR and ESI-MS analyses, the  $^1\text{H}$  NMR spectra was inconclusive about the exact orientation of the imidazole moieties around metal centers in the assembly.

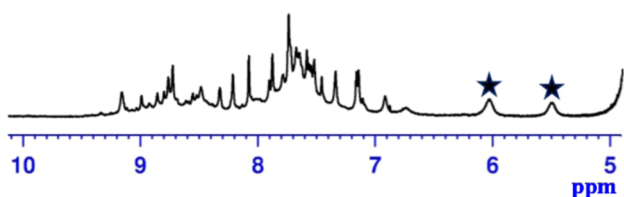
Unfortunately, several attempts to obtain diffraction quality single crystals of **PSMBR-1** remained unsuccessful. However, the coronene encapsulated **PSMBR-1** was successfully crystallized by diffusion of acetone vapor into aqueous solution of the encapsulated complex. Single crystal XRD analysis unambiguously established the open tetrafacial barrel architecture of the assembly (Figure 3). The inclusion complex (corone-



**Figure 3.** Crystal structure of coronene**PSMBR-1**. Guest molecules are represented in space filled model. Color codes: green = carbon, blue = nitrogen. Hydrogen atoms, counteranions, and solvent molecules are omitted for clarity.

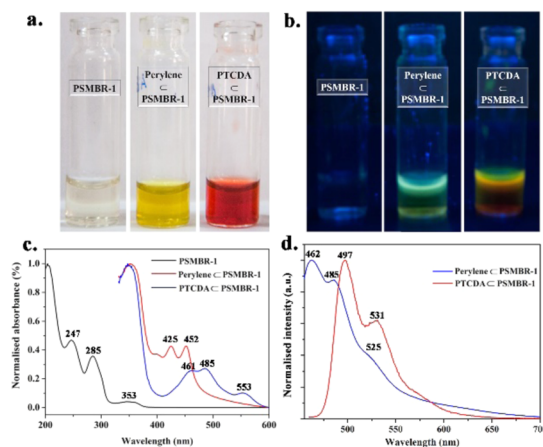
ne**PSMBR-1**) was crystallized in triclinic space group *P*-1, where the asymmetric unit contains only one molecule. The four panel-like ligands are connected together in head-to-head fashion by eight Pd(II) acceptors which furnishes the square barrel topology. The dimension of the cavity is found to be  $11.7 \times 11.4 \times 10.5 \text{ \AA}^3$ , and the farthest methyl groups associated with the diagonal metal centers are ~25 Å apart from each other (Figure 3), which is quite close to the hydrodynamic radius of **PSMBR-1** as obtained from the DOSY experiment. All the four *N*-methyl groups of the ligands are found to be tilted inward the cavity. The crystal structure also showed that the opposite ligand panels of the centrosymmetric molecular barrel are identical, however, different from the adjacent ones which clearly explains the origin of 14 peaks in the  $^1\text{H}$  NMR spectra of **PSMBR-1**. Interestingly, though the distances between the opposite walls of the cavity are differ by ~2.7 Å (Figure S26), the two coronene molecules are found to be comfortably aligning within the smaller gap. The coronene–coronene shortest distance is 3.90 Å, while they are 3.72 Å apart from the walls.

Polyaromatic hydrocarbons (PAHs) and their derivatives are generally  $\pi$ -electron-rich and possess attractive luminescence properties and hence have found immense importance in optoelectronics and dye industries.<sup>13</sup> But, their poor solubility in water limits their use in aqueous medium. To judge the efficiency of the newly engineered molecular barrel as a host for PAHs and their derivatives in aqueous medium, naphthalene, anthracene, pyrene, perylene, and perylene tetracarboxylic acid dianhydride (PTCDA) along with the coronene were selected as analytes, which are mostly insoluble in water.<sup>14</sup> To our great delight, all the guests molecules were found to be efficiently encapsulated by PSMBR-1 upon overnight stirring at room temperature in water, and the inclusion of guests was confirmed by <sup>1</sup>H NMR, UV-vis, and fluorescence studies. Encapsulations caused significant changes in peak positions in the aromatic region as observed in the <sup>1</sup>H NMR spectra for all the encapsulated complexes except PTCDA (Figures 4 and S15–



**Figure 4.** Aromatic region of the <sup>1</sup>H NMR spectra of peryleneCPSMBR-1 inclusion complex. Star marked peaks correspond to the encapsulated perylene molecules.

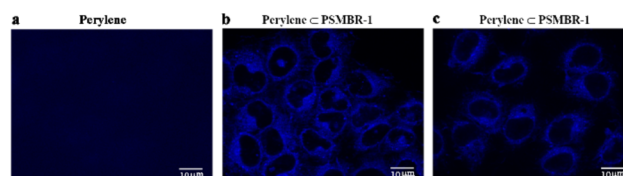
S20), attributed due to the strong  $\pi$ - $\pi$  interaction of the guest molecules with the walls of the cavity. Moreover, the encapsulated guests molecules showed new set of peaks in the range of 7–5 ppm, which were significantly shielded due to the ring current effect inside cavity. Remarkable visual color changes of the aqueous solutions were observed from pale yellow to intense yellow and red in case of perylene and PTCDA, respectively (Figure 5), upon encapsulation, which was also reflected in their UV-vis spectra with the presence of additional bands assigned to the guest molecules. In addition, the inclusion complexes of anthracene, perylene, and PTCDA showed characteristic luminescence of the guest molecules respectively (Figure 5) in aqueous medium. The stoichiometry of the host–



**Figure 5.** Aqueous solutions of PSMBR-1, peryleneCPSMBR-1, and PTCDA CSMBR-1 complexes under (a) normal and (b) UV lights and their corresponding (c) absorption and (d) emission spectra.

guest complexes could not be determined by conventional spectroscopic titrations due to the poor aqueous solubility of the analytes. NMR study was also not much helpful for this purpose because of broadened <sup>1</sup>H NMR peaks as a result of tumbling motion of the guests inside the cavity. Albeit, the successful single crystal XRD analysis of the coroneneCPSMBR-1 inclusion complex unambiguously confirmed the host–guest stoichiometry to be 1:2.

Live cell imaging has become an indispensable method for diagnostics as well as biological studies in order to track dynamics and functions of various cellular processes. The foremost important factors associated with a cell imaging fluorophore are membrane permeability, cell viability, solubility, and stability.<sup>15</sup> Various probes have been developed for this purpose from simple organic dyes to metal–ligand complexes.<sup>16</sup> However, special attention is still required to overcome the common problems such as solubility, aggregation-induced quenching, pH sensitivity, etc. Our target in that context is can we use simple organic fluorophores such as PAHs as cell imaging agents by delivering them inside cell via water-soluble host like PSMBR-1? To answer this question, HeLa cells were incubated with an increasing concentration of PSMBR-1 or peryleneCPSMBR-1 complex for a period of 30 min. PeryleneCPSMBR-1 complex readily internalizes inside the cells without causing toxicity (Figures S31–32). Microscopy images of the treated cells show brilliant blue emission from the cytoplasm without alteration of cell morphology (Figure 6). In a



**Figure 6.** Microscopy images show blue emission from the cytoplasm of HeLa cells after the incubation with aqueous solution of peryleneCPSMBR-1 complex (b, c). Perylene alone is not able to go inside the cell, and hence no fluorescence was observed (a).

control experiment, no fluorescence was detected upon treatment of the cells with perylene itself due to the lack of solubility. The successful membrane penetration of the inclusion complex could be attributed to the presence of 32 lipophilic methyl groups associated with the palladium acceptors.

In conclusion, we report the selective formation of a single linkage isomeric unprecedented tetrafacial nanobarrel employing a new nonsymmetric tetraimidazole ligand with 90° Pd(II) ditopic acceptor. Despite of the possibility of expected closed cubic structure as well as several linkage isomeric barrels due to different connectivity of the nonsymmetric tetra-topic donor, the formation of a single isomeric tetrafacial barrel in the present case is remarkable. The water-soluble nature in combination with the presence of hydrophobic pocket make it a novel host for the encapsulation of water insoluble PAHs, as evident from spectroscopic studies including X-ray analysis of coroneneCPSMBR-1 complex. Moreover, the preliminary investigation has demonstrated the Pd<sup>II</sup><sub>8</sub> molecular barrel (PSMBR-1) to be a potential carrier to transport water insoluble perylene molecules inside the live cell in aqueous medium in order to use as a cell imaging probe. The “proof of concept” of transportation of water insoluble analyte to live cells using a water-soluble carrier has huge impact to explore the scope of using a wide range of water

insoluble dye molecules for live cell imaging as well as in drug delivery.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b08008.

Experimental procedures and characterization data (NMR, ESI MS, UV–vis spectra) for **L**, **PSMBR-1**, and encapsulated complexes along with cell imaging protocol (PDF) (CIF) (CIF)

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

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## ■ REFERENCES

- (1) (a) Lehn, J. M. *Proc. Natl. Acad. Sci. U. S. A.* **2002**, *99*, 4763. (b) Fujita, M.; Tominaga, M.; Hori, A.; Therrien, B. *Acc. Chem. Res.* **2005**, *38*, 369. (c) Ronson, T. K.; Zarra, S.; Black, S. P.; Nitschke, J. R. *Chem. Commun.* **2013**, *49*, 2476. (d) Mukherjee, S.; Mukherjee, P. S. *Chem. Commun.* **2014**, *50*, 2239. (e) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853.
- (2) (a) Fujita, M.; Yazaki, J.; Ogura, K. *J. Am. Chem. Soc.* **1990**, *112*, 5645. (b) Pirondini, L.; Bertolini, F.; Cantadori, B.; Ugozzoli, F.; Massera, C.; Dalcanale, E. *Proc. Natl. Acad. Sci. U. S. A.* **2002**, *99*, 4911. (c) Beissel, T.; Powers, R. E.; Raymond, K. N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1084. (d) Bolliger, J. L.; Belenguer, A. M.; Nitschke, J. R. *Angew. Chem., Int. Ed.* **2013**, *52*, 7958. (e) Seidel, S. R.; Stang, P. J. *Acc. Chem. Res.* **2002**, *35*, 972. (f) Bhat, I. A.; Samanta, D.; Mukherjee, P. S. *J. Am. Chem. Soc.* **2015**, *137*, 9497. (g) Xu, L.; Wang, Y.-X.; Chen, L.-J.; Yang, H.-B. *Chem. Soc. Rev.* **2015**, *44*, 2148. (h) Saha, M. L.; Mittal, N.; Bats, J. W.; Schmittel, M. *Chem. Commun.* **2014**, *50*, 12189. (i) Soria, J. F.; Fernandez, A.; Pineda, E. M.; Varey, S. A.; Adams, R. W.; Tuna, F.; Timco, G. A.; Muryn, C. A.; Winpenny, R. E. P. *J. Am. Chem. Soc.* **2015**, *137*, 7644.
- (3) (a) Chakrabarty, R.; Mukherjee, P. S.; Stang, P. J. *Chem. Rev.* **2011**, *111*, 6810. (b) Kusukawa, T.; Fujita, M. *J. Am. Chem. Soc.* **1999**, *121*, 1397. (c) Ibukuro, F.; Kusukawa, T.; Fujita, M. *J. Am. Chem. Soc.* **1998**, *120*, 8561. (d) Aoyagi, M.; Biradha, K.; Fujita, M. *J. Am. Chem. Soc.* **1999**, *121*, 7457. (e) Yoshizawa, M.; Kusukawa, T.; Fujita, M.; Yamaguchi, K. *J. Am. Chem. Soc.* **2000**, *122*, 6311. (f) Ramsay, W. J.; Szczypliński, F. T.; Weissman, H.; Ronson, T. K.; Smulders, M. M. J.; Rybtchinski, B.; Nitschke, J. R. *Angew. Chem., Int. Ed.* **2015**, *54*, 5636. (g) Furrer, M. A.; Schmitt, F.; Wiederkehr, M.; Juillerat-Jeanneret, L.; Therrien, B. *Dalton Trans.* **2012**, *41*, 7201.
- (4) (a) Mahata, K.; Frischmann, P. D.; Wurthner, F. *J. Am. Chem. Soc.* **2013**, *135*, 15656. (b) Mal, P.; Breiner, B.; Rissanen, K.; Nitschke, J. R. *Science* **2009**, *324*, 1697.
- (5) (a) Simón, C. G.; Doria, R. G.; Raoufnoghaddam, S.; Parella, T.; Costas, M.; Ribas, X.; Reek, J. N. H. *J. Am. Chem. Soc.* **2015**, *137*, 2680. (b) Yoshizawa, M.; Tamura, M.; Fujita, M. *Science* **2006**, *312*, 251.

- (6) (a) Samanta, D.; Mukherjee, P. S. *Chem. Commun.* **2014**, *50*, 1595. (b) Samanta, D.; Mukherjee, P. S. *Chem. - Eur. J.* **2014**, *20*, 5649.
- (7) (a) Sato, S.; Yoshimasa, Y.; Fujita, D.; Utsumi, M. Y.; Yamaguchi, T.; Kato, K.; Fujita, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 8435. (b) Kikuchi, T.; Sato, S.; Fujita, D.; Fujita, M. *Chem. Sci.* **2014**, *5*, 3257.
- (8) (a) Stang, P. J.; Olenyuk, B. *Acc. Chem. Res.* **1997**, *30*, 502. (b) Cook, T. R.; Vajpayee, V.; Lee, M. H.; Stang, P. J.; Chi, K.-W. *Acc. Chem. Res.* **2013**, *46*, 2464. (c) Cook, T. R.; Stang, P. J. *Chem. Rev.* **2015**, *115*, 7001.
- (9) (a) MacGillivray, L. R.; Atwood, J. L. *Angew. Chem., Int. Ed.* **1999**, *38*, 1018. (b) Bruns, C. J.; Fujita, D.; Hoshino, M.; Sato, S.; Stoddart, J. F.; Fujita, M. *J. Am. Chem. Soc.* **2014**, *136*, 12027. (c) Samanta, D.; Mukherjee, P. S. *Chem. - Eur. J.* **2014**, *20*, 12483. (d) Sun, B.; Wang, M.; Lou, Z.; Huang, M.; Xu, C.; Li, X.; Chen, L.-J.; Yu, Y.; Davis, G. L.; Xu, B.; Yang, H.-B.; Li, X. *J. Am. Chem. Soc.* **2015**, *137*, 1556.
- (10) (a) Bishop, R. E. *Biochim. Biophys. Acta, Biomembr.* **2008**, *1778*, 1881. (b) Yamashita, D.; Sugawara, T.; Takeshita, M.; Kaneko, J.; Kamio, Y.; Tanaka, I.; Tanaka, Y.; Yao, M. *Nat. Commun.* **2014**, *5*, 4897.
- (11) (a) Yamanoi, Y.; Sakamoto, Y.; Kusukawa, T.; Fujita, M.; Sakamoto, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **2001**, *123*, 980. (b) Goeb, S.; Bivaud, S.; Croué, V.; Vajpayee, V.; Allain, M.; Sallé, M. *Materials* **2014**, *7*, 611. (c) Nakamura, T.; Ube, H.; Miyake, R.; Shionoya, M. *J. Am. Chem. Soc.* **2013**, *135*, 18790. (d) Bar, A. K.; Chakrabarty, R.; Mostafa, G.; Mukherjee, P. S. *Angew. Chem., Int. Ed.* **2008**, *27*, 316. (e) Riddell, I. A.; Hristova, Y. R.; Clegg, J. K.; Wood, C. S.; Breiner, B.; Nitschke, J. R. *J. Am. Chem. Soc.* **2013**, *135*, 2723.
- (12) (a) Hof, F.; Craig, S. L.; Nuckolls, C.; Rebek, J., Jr. *Angew. Chem., Int. Ed.* **2002**, *41*, 1488. (b) Dsouza, R. N.; Pischel, U.; Nau, W. M. *Chem. Rev.* **2011**, *111*, 7941. (c) Schmuck, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 5830.
- (13) (a) Weil, T.; Vosch, T.; Hofkens, J.; Peneva, K.; Müllen, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 9068. (b) Faulkner, E. B.; Schwartz, R. J.; Greene, M. *Perylene Pigments*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2009. (c) Yang, J.; Yan, D.; Jones, T. S. *Chem. Rev.* **2015**, *115*, 5570. (d) Zang, L.; Che, Y.; Moore, J. S. *Acc. Chem. Res.* **2008**, *41*, 1596.
- (14) (a) Li, K.; Zhang, L.-Y.; Yan, C.; Wei, S.-C.; Pan, M.; Zhang, L.; Su, C.-Y. *J. Am. Chem. Soc.* **2014**, *136*, 4456. (b) Bivaud, S.; Goeb, S.; Croué, V.; Dron, P. I.; Sallé, A. M. *J. Am. Chem. Soc.* **2013**, *135*, 10018.
- (15) (a) Herschman, H. R. *Science* **2003**, *302*, 605. (b) He, Y.; Su, Y.; Yang, X.; Kang, Z.; Xu, T.; Zhang, R.; Fan, C.; Lee, S.-T. *J. Am. Chem. Soc.* **2009**, *131*, 4434. (c) Tan, T. T. T.; Khaw, C.; Ng, M. M. L. *Microscopy: Science, Technology, Applications and Education*; A. Méndez-Vilas, J. Díaz, Eds.; Formatex Research Center: Badajoz, Spain, 2010; p 1495.
- (16) (a) Yuan, L.; Lin, W.; Zheng, K.; He, L.; Huang, W. *Chem. Soc. Rev.* **2013**, *42*, 622. (b) Wolfbeis, O. S. *Chem. Soc. Rev.* **2015**, *44*, 4743. (c) Mishra, A.; Ravikumar, S.; Song, Y. H.; Prabhu, N. S.; Kim, H.; Hong, S. H.; Cheon, S.; Nohe, J.; Chi, K.-W. *Dalton Trans.* **2014**, *43*, 6032. (d) Schmitt, F.; Freudenreich, J.; Barry, N. P. E.; Juillerat-Jeanneret, L.; Süß-Fink, G.; Therrien, B. *J. Am. Chem. Soc.* **2012**, *134*, 754.