Organic LETTERS

Letter

pubs.acs.org/OrgLett

Monomer Emission and Aggregate Emission of TPE Derivatives in the Presence of γ-Cyclodextrin

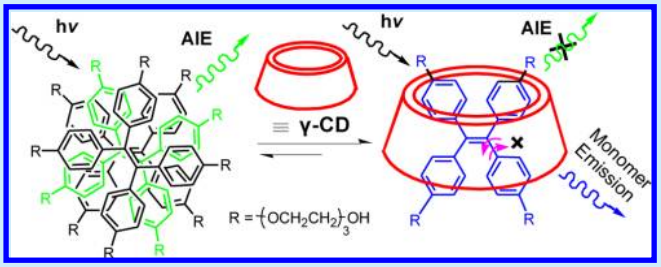
Song Song,[†] Hua-Fei Zheng,[‡] Dong-Mi Li,[†] Jin-Hua Wang,[†] Hai-Tao Feng,[†] Zhi-Hua Zhu,[†] Yi-Chang Chen,[†] and Yan-Song Zheng*[,†]

[†]Key Laboratory for Large-Format Battery materials and System, Ministry of Education, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan 430074, China

[‡]School of Chemistry and Materials Science, University of Science and Technology of China, Hefei 230026, China

Supporting Information

ABSTRACT: It was found for the first time that neutral amphiphilc tetraphenylethylene (TPE) derivatives showed an enhanced monomer emission and a decreased aggregate emission when they were included in the cavity of γ-cyclodextrin. This result provided a new insight into the aggregation-induced emission (AIE) effect.



Recently, a new class of organic compounds with an amazing property of aggregation-induced emission (AIE) effect is attracting increasing interest because of their tremendous potential in chemosensors, bioprobes, and solid-state emitters.[1,2] Since the AIE effect was discovered in 2001,[2] a huge number of AIE compounds have been garnered, and successful studies regarding application have been conducted.[1] However, the mechanism underlying this novel AIE phenomenon is still bewildering and in dispute[1,3,4] due to limited direct evidence.[5] The AIE compounds, especially the most studied tetraphenylethylene (TPE) derivatives, do not emit light but display a strong fluorescence in the aggregation state. At low temperature, in viscous solvent, and even under high pressure, the AIE compounds also have an AIE enhancement because of slowed motions.[1b] After absorption onto biopolymers such as DNA,[6] protein,[7] and peptides,[8] these compounds also exhibit strong aggregation fluorescence resulting from the restriction of their motions by the biopolymer backbone or groove. Moreover, upon loading into mesopores of silica nanoparticles, the AIE molecules have an increased AIE effect due to narrow space that limits their motions.[9] If an AIE molecule is put into a cavity of a host compound such as crown ethers, cyclodextrins (CDs),[10] calixarenes, curcubiturils, and so on, the cavity will confine the motions of the AIE molecules and result in an enhanced AIE effect. Here we report for the first time that a stable 1:1 inclusion complex of neutral amphiphilic tetraphenylethylene derivatives with γ-CD arouses a significantly attenuated aggregate emission and an increased monomer emission, which provided a new insight into the fluorescence of AIE compounds.

As shown in Figure 1, compounds **2a**, **2b**, and **2c** were synthesized by the reaction of tetra(*p*-hydroxyphenyl)ethylene **1**[11a] with oligo(ethylene glycol) monotosylate. Because of a

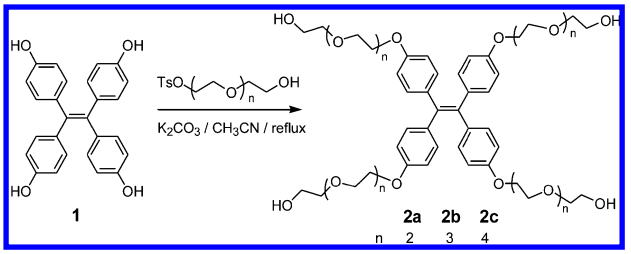


Figure 1. Synthesis of the AIE compounds **2a**−**2c**.

typical AIE property of the known **1**,[11] compounds **2a**−**2c**, as colorless sticky solids, emitted a brilliant green light under a 365 nm lamp. A solution of **2a**, **2b**, or **2c** in 1,2-dichloroethane had no fluorescence but started to emit fluorescence at 485 nm when turbidity appeared upon addition of nonsolvent hexane up to 70% volume fraction. Afterward, the fluorescence intensity increased rapidly with hexane (Supplementary Figure S13). Therefore, **2a**−**2c** were AIE compounds.

Compounds **2a**−**2c** were soluble and light-emitting in water. The fluorescence intensity became larger with increasing concentration. Moreover, there appeared a minor emission with two fine vibration bands at 405 and 388 nm in addition to the main emission at 485 nm (Supplementary Figure S14). It is well-known that the neutral amphiphilic compounds bearing hydrophilic oligo(ethylene glycol) chains at both ends of one hydrophobic core easily self-assembly into one-dimensional aggregates.[12] For compounds **2a**−**2c**, they were prone to aggregate into a linear micelle by overlapping of molecules in order to avoid the hydrophobicity of the TPE core (Supplementary Figure S15A). The formation of the micelles

Received: February 28, 2014
Published: April 4, 2014

dx.doi.org/10.1021/ol500638c | *Org. Lett.* 2014, 16, 2170−2173

will lead to the main fluorescence emission at 485 nm, and the emission maximum wavelength was the same as that of the aggregates in the mixed solvent of 1,2-dichloroethane and hexane. Although the aqueous solutions of **2a**−**2c** were very clear and transparent, dynamic light scattering (DLS) disclosed that there were nanoparticles with a diameter of 5−12 nm (Supplementary Figure S16), indicating the formation of micelles or nanoaggregates.

Because of the two fine vibration bands at 405 and 388 nm, the weak emission at this area could probably be ascribed to the monomers of **2a**−**2c**. However, this weak emission was not observed in organic solvent, and therefore **2a**−**2c** in water should exist in a special state when they dismantle as monomers from a micelle. Due to the hydrophobicity of the TPE unit, the four hydrophilic and flexible chains will have a fold around the TPE core instead of pointing away from it in order to reduce its hydrophobic force (Supplementary Figure S15B). The four hydrophilic chains that wound around the TPE unit not only made the compound more compatible with water but also restricted the rotation of the phenyl rings, which would result in a monomer fluorescence of **2a**−**2c**.[13] The 2D NMR NOESY spectrum of **2c** in D_2O confirmed that the hydrophibic chains were truly bent toward the TPE unit instead of pointing off it (Supplementary Figure S15).

Interestingly, **2a**−**2c** exhibited a selective interaction with CD compounds. As shown in Figure 2 and Supplementary

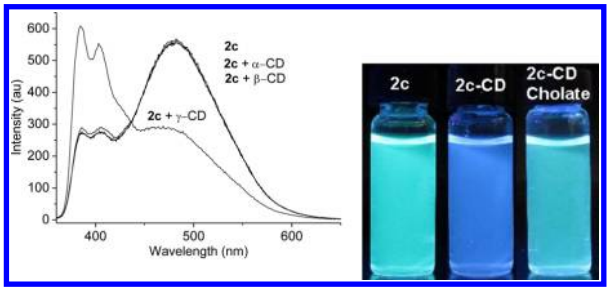


Figure 2. Fluorescence spectra of **2c** without and with α-CD, β-CD, and γ-CD in water. (Right) Photos of a solution of **2c**, **2c**-γ-CD, and **2c**-γ-CD-potassium ursodeoxycholate in water under a 365 nm lamp. [**2c**] = [α-CD] = [β-CD] = [γ-CD] = 1/3[cholate] = 5.0×10^{-5} M, λ_{ex} = 330 nm, ex/em slits = 5/5 nm.

Figure S17, α-CD or β-CD had almost no effect on the fluorescence of compounds **2a**−**2c**, but γ-CD significantly weakened the emission at 485 nm. Meanwhile, two weak emission peaks at 405 and 388 nm became strong and even much larger than that at 485 nm, and therefore a color change from green to blue could be observed under a 365 lamp (Figure 2). It is known that the inside diameter of the cavity of α-CD, β-CD, and γ-CD is 0.47−0.53, 0.60−0.65, and 0.75−0.85 nm, respectively.[14] The distance between two phenyl rings at different carbons and at the same carbon of the TPE double bond is about 0.74 and 0.90 nm, respectively;[15] therefore, only γ-CD could encapsulate just one molecule of **2a**−**2c** and affect their fluorescence, displaying a high selectivity for the size of CD compounds

The fluorescence titration of **2c** with γ-CD showed that the fluorescence intensity rapidly decreased at 485 nm while the emission significantly increased at 405 and 385 nm with addition of γ-CD. After the 1:1 molar ratio of γ-CD vs **2c**, all of the emissions displayed a slowed change (Figure 3). At 437 nm, a clear isoemissive point was observed, indicating formation of a

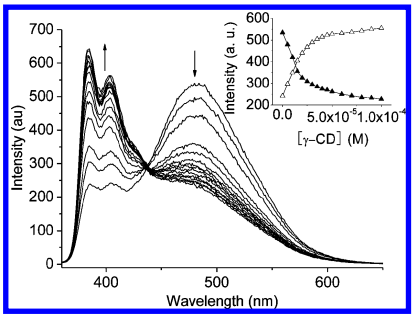


Figure 3. Change of fluorescence spectra of **2c** with γ-CD in water. λ_{ex} = 330 nm, ex/em slits = 5/5 nm. [**2c**] = 5.0×10^{-5} M. Inset, curves of fluorescence intensity vs concentration of γ-CD measured at 485 nm (▲) and 405 nm (Δ).

complex of **2c** and γ-CD with 1:1 molar ratio. The HRMS spectrum of the mixture of **2c** and γ-CD in water showed an obvious molecular ion peak (2597.0797) of **2c**-γ-CD (calculated 2597.0762 (M + Na)), demonstrating the possibility of a 1:1 complex (Supplementary Figure S18).

The **2c**-γ-CD complex was further corroborated by ^{1}H NMR spectrum (Figure 4). The ^{1}H NMR titration of **2c** by γ-CD

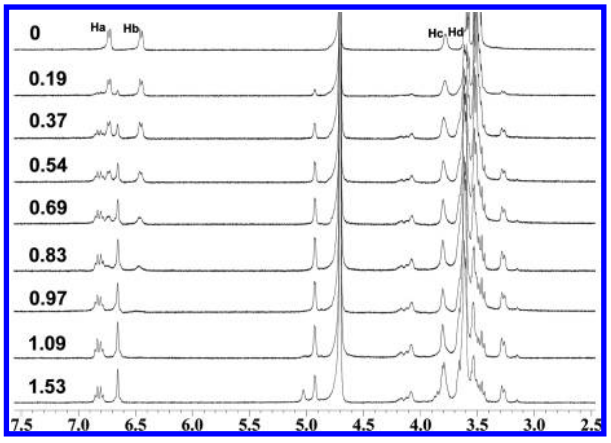


Figure 4. Change of ^{1}H NMR spectra of **2c** with γ-CD in D_2O. [**2c**] = 2.0 mM. The number over the spectrum is the molar ratio of γ-CD vs **2c**.

disclosed that two pairs of new doublets (6.84, 6.79 and 6.66, 6.64 ppm) that were ascribed to aromatic protons appeared and became stronger, while one pair of doublets (6.73 ppm, 6.45 ppm) from aromatic protons of free **2c** decreased gradually with addition of γ-CD. After a 1:1 molar ratio of γ-CD vs **2c**, this pair of doublets from free **2c** completely disappeared and the two pairs of new doublets did not grow further. This unambiguously demonstrated that the **2c**-γ-CD complex with a 1:1 binding ratio was produced. During the titration, all signals of both free **2c** and the complex had no shift, indicating no distinct interaction between free **2c** and the complex. The pair of doublets at 6.66 and 6.64 ppm, which seemed to be a singlet snuggled by one tiny peak at each side, should be ascribed to the protons of one phenyl ring, and the pair of doublets at 6.84 and 6.79 ppm should result from another phenyl ring, just like the pair of doublets for free **2c**. Therefore, the **2c**-γ-CD complex had two sets of phenyl signals with a big downfield shift compared to free **2c** which had only one set of phenyl signals, hinting that all four phenyl rings of the TPE unit were no longer the same but divided into two groups. Probably, two

dx.doi.org/10.1021/ol500638c | Org. Lett. 2014, 16, 2170−2173

phenyl rings completely inserted into the cavity of γ-CD, while the other two phenyl rings were partially included by γ-CD. The ^{1}H NMR titration of γ-CD with **2c** (Supplementary Figures S19 and S20) also confirmed the formation of a **2c**-γ-CD complex. Since the concentration of the complex, free **2c**, and γ-CD at equilibrium could be directly measured from the ^{1}H NMR spectra, the associated constant of the complex could be calculated by using the thermodynamic equilibrium equation to be 1.22 (±0.21) × 10^4 M^{-1}, which is a large value.

In the 2D NOESY spectrum of the **2c** and γ-CD mixture, the triplet peak of the **2c**-γ-CD complex at 3.45 ppm should be ascribed to the proton H_2 of γ-CD since it had a strong cross-peak with H_1 of γ-CD. The new proton signals as a doublet at 3.26 ppm, which was at the upmost field of all the signals, was correlated with the proton H_2 of γ-CD. Therefore, this signal should belong to proton H_3 of γ-CD since H_3 and H_2 were in a neighboring position. These two protons have been reported to have a strong NOE, although they are in a *trans* position.[16] Now the proton H_3 had a strong cross-peak with the aromatic protons of **2c**, indicating that **2c** was encapsulated into the cavity of γ-CD by its two phenyl rings from the wide rim of γ-CD because the proton H_3 is near to the wide rim and points to the inside of the γ-CD cavity. In addition, the NOE of H_3 with the aromatic proton H_a was stronger than that with the aromatic proton H_b, further demonstrating that the phenyl ring deeply inserted into the cavity until H_a was nearer to it than H_b. Due to the strong shielding role from the encapsulated phenyl ring, the proton H_3 of the complex displayed the most obvious upfield shift compared with that of the free γ-CD.

The ^{13}C NMR spectrum of the **2c**-γ-CD complex disclosed that four carbon peaks of the four phenyl rings in free **2c** changed into eight carbon peaks in the complex (each carbon peak was divided into two peaks) (Supplementary Figure S22), indicating that one set of phenyl rings in free **2c** became into two sets of ones in the complex, which was in line with ^{1}H NMR test. However, the carbon signal from the double bond was still one peak rather than two peaks, demonstrating that the two carbons of the double bond were still the same in the complex. Therefore, **2c** was included into the cavity of γ-CD along a direction of two phenyl rings at different carbons of the double bond rather than at the same carbon (Figure 5, **2c**-γ-CD). In this including way, all four phenyl rings could go into the cavity of γ-CD due to a 0.79 nm depth of the cavity,[14] so that they all had cross-peaks with H_3 of γ-CD in 2D NOESY spectrum. Due to the restriction of the phenyl ring rotations, the monomer emission of **2c** significantly increased. In addition, the absorbance maximum wavelength (312 nm) of the **2c**-γ-CD complex was less by 5 nm than that (317 nm) of **2c** in water (Supplementary Figure S23), also demonstrating that the phenyl rings were confined in the cavity of γ-CD and a more twisted propeller conformation of the TPE unit was produced.

As expected, the aggregate emission increased while the monomer emission decreased with the potassium salt of ursodeoxycholic acid (here abbreviated as cholate), a kind of clinical drug for dissolving gallstones that can be easily included by γ-CD (Figure 6).[17] A distinct color change from blue to green, which was inverse to the color change when **2c** and γ-CD were mixed, could be seen under a 365 nm lamp after 2−3 equiv of the cholate was added (Figure 2). At 437 nm, a clear isoemissive point was observed, indicating the dissociation of the **2c**-γ-CD complex and the formation of a new complex. The **2a**-γ-CD and **2b**-γ-CD complexes also had a similar change

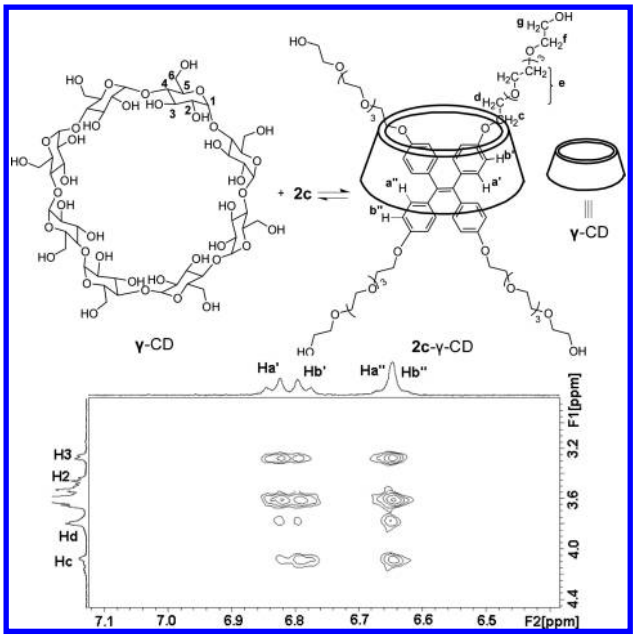


Figure 5. Schematic structure of **2c**-γ-CD inclusion complex and its partial 2D NOESY spectrum in D_2O. [**2c**] = [γ-CD] = 2 mM.

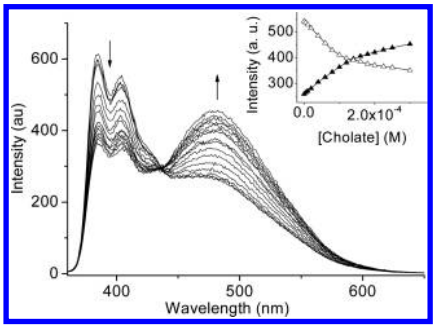


Figure 6. Change of fluorescence spectra of **2c**-γ-CD complex with the cholate in water. λ_{ex} = 330 nm, ex/em slits = 5/5 nm. [**2c**] = [γ-CD] = 5.0 × 10^{-5} M. Inset, curves of intensity vs the cholate concentration measured at 485 nm (▲) and 405 nm (Δ).

with the cholate (Supplementary Figure S24). This result further confirmed the monomer emission and the aggregate emission of **2**.

In conclusion, it was found for the first time that neutral amphiphilic TPE derivatives with AIE effect could selectively insert into the cavity of γ-CD by its TPE unit and form a stable inclusion complex. After the TPE fluorogen was confined in the cavity, the monomer emission at the short wavelength increased while the AIE effect at the long wavelength had a significant attenuation due to deaggregation by the host compound. This finding provided a new insight into the fluorescence of AIE compounds.

■ ASSOCIATED CONTENT

Supporting Information

Synthetic and experimental details, DLS diagrams, and additional spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

dx.doi.org/10.1021/ol500638c | *Org. Lett.* 2014, 16, 2170−2173

AUTHOR INFORMATION

Corresponding Author

*E-mail: zyansong@hotmail.com.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors thank National Natural Science Foundation of China (21072067) for financial support and thank the Analytical and Testing Centre at Huazhong University of Science and Technology for measurement.

REFERENCES

(1) (a) Hong, Y.; Lam, J. W. Y.; Tang, B. Z. *Chem. Soc. Rev.* **2011**, *40*, 5361−5388. (b) Hong, Y.; Lam, J. W. Y.; Tang, B. Z. *Chem. Commun.* **2009**, 4332−4353. (c) Ding, D.; Li, K.; Liu, B.; Tang, B. Z. *Acc. Chem. Res.* **2013**, *46*, 2441−2453. (d) Wang, M.; Zhang, G.; Zhang, D.; Zhu, D.; Tang, B. Z. *J. Mater. Chem.* **2010**, *20*, 1858−1867.

(2) (a) Luo, J.; Xie, Z.; Lam, J. W. Y.; Cheng, L.; Chen, H.; Qiu, C.; Kwok, H. S.; Zhan, X.; Liu, Y.; Zhu, D.; Tang, B. Z. *Chem. Commun.* **2001**, 1740−1741. (b) Tang, B. Z.; Zhan, X.; Yu, G.; Lee, P. P. S.; Liu, Y.; Zhu, D. *J. Mater. Chem.* **2001**, *11*, 974−2978.

(3) (a) Ren, Y.; Lam, J. W. Y.; Dong, Y.; Tang, B. Z.; Wong, K. S. *J. Phys. Chem. B* **2005**, *109*, 1135−1140. (b) Qian, Y.; Cai, M.-M.; Xie, L.-H.; Yang, G.-Q.; Wu, S.-K.; Huang, W. *ChemPhysChem* **2011**, *12*, 397−404.

(4) (a) Liu, Y.; Tao, X.; Wang, F.; Dang, X.; Zou, D.; Ren, Y.; Jiang, M. *J. Phys. Chem. C* **2008**, *112*, 3975−3981. (b) Yang, M.; Xu, D.; Xi, W.; Wang, L.; Zheng, J.; Huang, J.; Zhang, J.; Zhou, H.; Wu, J.; Tian, Y. *J. Org. Chem.* **2013**, *78*, 10344−10359. (c) An, B.-K.; Lee, D.-S.; Lee, J.-S.; Park, Y.-S.; Song, H.-S.; Park, S. Y. *J. Am. Chem. Soc.* **2004**, *126*, 10232−10233. (d) Cai, M.; Gao, Z.; Zhou, X.; Wang, X.; Chen, S.; Zhao, Y.; Qian, Y.; Shi, N.; Mi, B.; Xie, L.; Huang, W. *Phys. Chem. Chem. Phys.* **2012**, *14*, 5289−5296. (e) Gao, B.-R.; Wang, H.-Y.; Hao, Y.-W.; Fu, L.-M.; Fang, H.-H.; Jiang, Y.; Wang, L.; Chen, Q.-D.; Xia, H.; Pan, L.-Y.; Ma, Y.-G.; Sun, H.-B. *J. Phys. Chem. B* **2010**, *114*, 128−134. (f) Xie, Z.; Yang, B.; Xie, W.; Liu, L.; Shen, F.; Wang, H.; Yang, X.; Wang, Z.; Li, Y.; Hanif, M.; Yang, G.; Ye, L.; Ma, Y. *J. Phys. Chem. B* **2006**, *110*, 20993−21000. (g) Ren, Yi; Kan, W.; Henderson, M. A.; Bomben, P. G.; Berlinguette, C. P.; Thangadurai, V.; Baumgartner, T. *J. Am. Chem. Soc.* **2011**, *133*, 17014−17026. (h) Xie, Z.; Yang, B.; Li, F.; Cheng, G.; Liu, L.; Yang, G.; Xu, H.; Ye, L.; Hanif, M.; Liu, S.; Ma, D.; Ma, Y. *J. Am. Chem. Soc.* **2005**, *127*, 14152−14153. (i) Li, D.-M.; Zheng, Y.-S. *J. Org. Chem.* **2011**, *76*, 1100−1108.

(5) Zhao, Z.; He, B.; Nie, H.; Chen, B.; Lu, P.; Qin, A.; Tang, B. Z. *Chem. Commun.* **2014**, *50*, 1131−1133.

(6) (a) Hong, Y.; Häußler, M.; Lam, J. W. Y.; Li, Z.; Sin, K. K.; Dong, Y.; Tong, H.; Liu, J.; Qin, A.; Renneberg, R.; Tang, B. Z. *Chem.—Eur. J.* **2008**, *14*, 6428−6437. (b) Wang, M.; Zhang, D.; Zhang, G.; Tang, Y.; Wang, S.; Zhu, D. *Anal. Chem.* **2008**, *80*, 6443−6448. (c) Hong, Y.; Xiong, H.; Lam, J. W. Y.; Häußler, M.; Liu, J.; Yu, Y.; Zhong, Y.; Sung, H. H. Y.; Williams, I. D.; Wong, K. S.; Tang, B. Z. *Chem.—Eur. J.* **2010**, *16*, 1232−1245.

(7) (a) Wang, F.; Wen, J.; Huang, L.; Huang, J.; Ouyang, J. *Chem. Commun.* **2012**, *48*, 7395−7397. (b) Xu, X.; Huang, J.; Li, J.; Yan, J.; Qin, J.; Li, Z. *Chem. Commun.* **2011**, *47*, 12385−12387.

(8) (a) Hong, Y.; Meng, L.; Chen, S.; Leung, C. W. T.; Da, L.; Faisal, M.; Manzano, D.-A. S.; Liu, J.; Lam, J. W. Y.; Huang, X.; Tang, B. Z. *J. Am. Chem. Soc.* **2012**, *134*, 1680−1689. (b) Yang, W.; Wong, Y.; Ng, O. T. W.; Bai, L.-P.; Kwong, D. W. J.; Ke, Y.; Jiang, Z.-H.; Li, H.-W.; Yung, K. K. L.; Wong, M. S. *Angew. Chem., Int. Ed.* **2012**, *51*, 1804−1810.

(9) (a) Bhongale, C. J.; Hsu, C.-S. *Angew. Chem., Int. Ed.* **2006**, *45*, 1404−1408. (b) Li, D.; Yu, J.; Xu, R. *Chem. Commun.* **2011**, *47*, 11077−11079.

(10) Douhal, A. Cyclodextrin Materials Photochemistry. In *Photophysics and Photobiology*, 1st ed.; Elsevier: Amsterdam, 2006.

(11) (a) Hu, X.-M.; Chen, Q.; Wang, J.-X.; Cheng, Q.-Y.; Yan, C.-G.; Cao, J.; He, Y.-J.; Han, B.-H. *Chem.—Asian J.* **2011**, *6*, 2376−2381. (b) Li, C.; Wu, T.; Hong, C.; Zhang, G.; Liu, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 455−459.

(12) (a) Arnaud, A.; Belleney, J.; Boué, F.; Bouteiller, L.; Carrot, G.; Wintgens, V. *Angew. Chem., Int. Ed.* **2004**, *43*, 1718−1721. (b) Zhang, X.; Chen, Z.; Würthner, F. *J. Am. Chem. Soc.* **2007**, *129*, 4886−4887. (c) Görl, D.; Zhang, X.; Würthner, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 2−23.

(13) Kohmoto, S.; Tsuyuki, R.; Hara, Y.; Kaji, A.; Takahashi, M.; Kishikawa, K. *Chem. Commun.* **2011**, *47*, 9158−9160.

(14) Szejtli, J. *Chem. Rev.* **1998**, *98*, 1743−1754.

(15) (a) Song, S.; Zheng, Y.-S. *Org. Lett.* **2013**, *15*, 820−823. (b) Tong, H.; Hong, Y.; Dong, Y.; Ha1ussler, M.; Li, Z.; Lam, J. W. Y.; Dong, Y.; Sung, H. H.-Y.; Williams, I. D.; Tang, B. Z. *J. Phys. Chem. B* **2007**, *111*, 11817−11823.

(16) Ivanov, P. M.; Salvatierra, D.; Jaime, C. *J. Org. Chem.* **1996**, *61*, 7012−7017.

(17) Ueno, A. *Anal. Chem.* **1990**, *62*, 2461−2466.