Organic LETTERS

Letter

pubs.acs.org/OrgLett

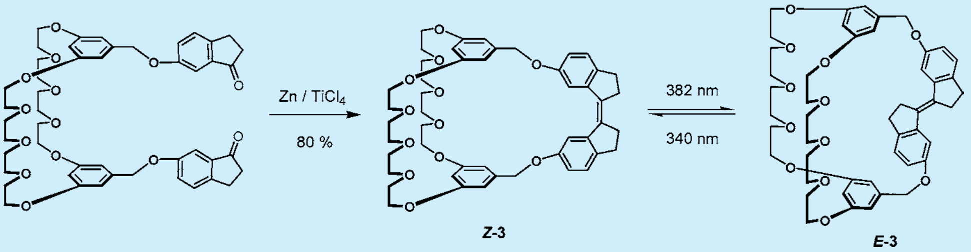
Synthesis of a Photoresponsive Cryptand and Its Complexations with Paraquat and 2,7-Diazapyrenium

Jiang-Fei Xu,[†,‡] Yu-Zhe Chen,[†] Li-Zhu Wu,[†] Chen-Ho Tung,[†] and Qing-Zheng Yang*,[†]

[†]Key Laboratory of Photochemical Conversion and Optoelectronic Materials, Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing 100190, P. R. China

[‡]University of the Chinese Academy of Sciences, Beijing 100049, P. R. China

Supporting Information

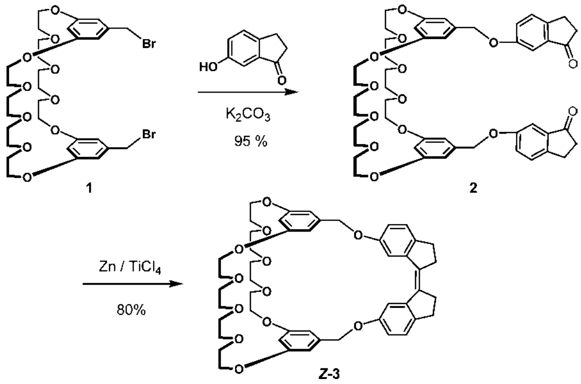


ABSTRACT: A McMurry coupling reaction was used for the efficient synthesis of a bis(*m*-phenylene)-32-crown-10 based cryptand *Z*-**3** with high yield. This photoresponsive cryptand formed host–guest complexes with paraquat derivative **4** and 2,7-diazapyrenium derivative **5**. *Z*-**3**, and *E*-**3** exhibited similar binding affinity to the small guest **4**, while dramatic changes were observed in the binding affinity to the large guest **5**.

Crown ethers are a prototypical and seminal class of hosts that have played a significant role in the emerging field of supramolecular chemistry. The host–guest interaction between crown ethers and guest molecules such as the paraquat (*N*,*N*′-dimethyl-4,4′-bipyridinium) dication is an important secondary interaction for the construction of supramolecular systems.[1] Threaded structures such as pseudorotaxanes, rotaxanes, catenanes, and supramolecular polymers have been prepared by using the host–guest complexation of crown ethers and their complementary guest molecules.[2] However, the binding constants of the crown ethers with paraquat derivatives are on the order of 10^2–10^3 M^{-1},[3a] which are not large enough for the efficient preparation of threaded structures and construction of supramolecular polymers with high molecular weight. To improve the complexation for guest molecules, crown ether-based cryptands have been designed. Cryptands are bicyclic ligands that complex with guest molecules with several orders of magnitude higher association constants than those of the corresponding crown ethers.[3b] Such high binding affinities for cryptands are generally due to the preorganization of the hosts during the association process and the contribution of binding sites on the third arm. Since Gibson et al. reported a bis(*m*-phenylene)-32-crown-10 (BMP32C10)-based cryptand in 1999 that exhibited a 100-fold increase in association constant for paraquat relative to simple crown ether BMP32C10,[3a] impressive progress has been made in the study of crown ether derived cryptands.[3] A series of BMP32C10-based cryptands with different third arms were reported by Gibson and Huang et al.[3b,4] The syntheses of the cryptands were accomplished by introduction of the third arms to crown ethers using the pseudo high dilution technique.[4a] However, the pseudo high dilution technique for macrocyclization was time-consuming, and the yields of cryptands were low (generally lower than 50%). It is highly desirable to develop a method for the syntheses of cryptands with high yield.

Herein, we report the synthesis of BMP32C10-based cryptand *Z*-**3** by using a McMurry coupling reaction for the macrocyclization step with a high yield of 80% (Scheme 1). McMurry coupling reaction, the reductive coupling of carbonyl compounds to produce olefins through low valent titanium, has acquired great attention in organic synthesis.[5] Various cyclo-

Scheme 1. Synthesis of Cryptand *Z*-3



Received: November 19, 2013
Published: January 30, 2014

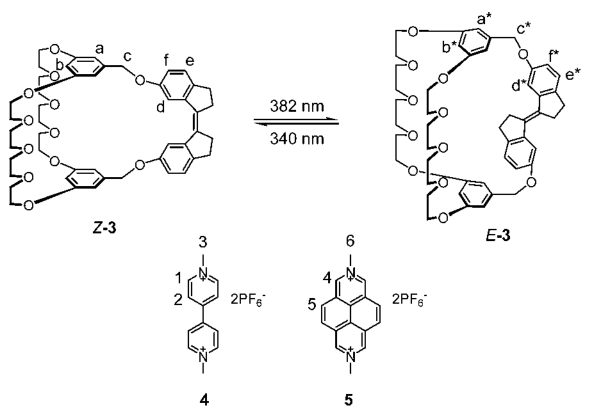
dx.doi.org/10.1021/ol403343s | *Org. Lett.* 2014, 16, 684–687

alkenes have been synthesized by intramolecular couplings of dicarbonyl compounds in good yields. In our work, the intramolecular McMurry coupling of the two indanone units in compound **2** yields the *Z*-stiff stilbene (1,1-biindane) unit, which acts as the third arm of the cryptand. It is noteworthy that the stiff stilbene is a chromophore that undergoes photoisomerization upon light irradiation.[6] Thus, compound *Z*-**3** is actually a photoresponsive cryptand of which the configuration and the cavity size can be changed by the photocontrolled *Z*/*E* isomerization of the stiff stilbene moiety. We were interested if the change of configuration and cavity size can influence the binding ability of cryptand with guest molecules.

Synthesis of the stiff stilbene-containing cryptand *Z*-**3** is shown in Scheme 1. Bis(5-bromomethyl-*m*-phenylene)-32-crown-10 (compound **1**) was prepared according to literature procedure and was readily converted into compound **2** with the commercially available 6-hydroxy-1-indanone in acetone in almost quantitative yield (95%). The resulting dicarbonyl compound **2** was converted into cryptand *Z*-**3** via McMurry coupling. The $TiCl_4$−Zn system was used for the coupling reaction.[7] $TiCl_4$ and 2 molar equiv of Zn dust in THF was refluxed for 2 h to yield a slurry of the low valent titanium reagent. The THF solution of compound **2** was added to the above refluxing mixture over a period of 1 h via a syringe pump under N_2 atmosphere. After the addition was completed, the reflux was continued for 0.5 h. The resulting crude product was purified by column chromatography to give the cryptand *Z*-**3** as a yellow powder (80%). The overall yield of cryptand *Z*-**3** was 76% based on compound **1** (two steps), which was significantly higher than that of the traditional pseudo high dilution technique.[3a,4] It is noteworthy that no *E*-**3** was formed in our intramolecular McMurry coupling reaction, possibly because the formation of strained *E*-macrocycle is unfavorable.

The stiff stilbene unit in cryptand *Z*-**3** could photoisomerize to structurally distinct *E*-isomers upon UV light irradiation (Scheme 2). The *Z*- and *E*-isomers of stiff stilbene are both thermostable since they are separated by an activation barrier of about 43 kcal mol^{-1}.[8] The stability of stiff stilbene offers considerable advantages as a chromophore for photoresponsive supramolecular systems over the commonly used azobenzenes. As we know the *Z*-isomer of azobenzene and its derivatives show poor thermostability and very short half-life at room temperature.[9] In our previous work, we reported photoresponsive supramolecular polymers composed of quadruply hydrogen-bonded monomers of stiff stilbene with two ureidopyrimidinone (UPy) moieties.[10] It was found that the self-assembly behavior and physical properties of the supramolecular polymers can be regulated by photoisomeirization of stiff stilbene. Therefore, we speculate that photoisomerization of the stiff stilbene contained in cryptand **3** may influence the host−guest complexation behavior of **3** with guest molecules.

Scheme 2. Photoisomerization of Cryptand 3 and the Structures of Paraquat Derivative 4 and 2,7-Diazapyrenium Derivative 5



Irradiation of *Z*-**3** at 382 nm yielded *E*-**3** in nearly quantitative yield (~ 98%), as determined by ^{1}H NMR spectroscopy. It is noteworthy that the photoisomerization can still take place in the presence of electron-deficient guests **4** and **5** (Supplementary Figures S9, S10). Unlike common alkenes whose *Z*- and *E*-isomers are difficult to identify by TLC and separate by column chromatography, *Z*-**3** and *E*-**3** show considerable differences on TLC. The R_f values of *Z*-**3** and *E*-**3** were 0.54 and 0.68, respectively (TLC, dichloromethane/methanol = 100:5 v/v). Such great differences in the polarities confirm the distinct configuration of crown ether moieties in the cryptand for *Z*-**3** and *E*-**3**. As we know, configurations of host molecules show important influence on the binding behaviors with guest molecules.[11] Thus, the host−guest complexations of *Z* and *E* cryptand **3** with different guests (paraquat derivative **4** and 2,7-diazapyrenium derivative **5**) were studied.

The complexation of **3** with paraquat derivative **4** was studied by UV−vis spectroscopy, mass spectrometry, and ^{1}H NMR spectroscopy. Equimolar acetonitrile solutions of *Z* and *E* cryptands with paraquat **4** are light yellow due to the formation of a charge transfer complex between the electron-rich aromatic rings of the cryptands and the electron-poor pyridinium rings of the guest **4**. Job plots based on UV−vis spectroscopy absorbance data demonstrated that the two complexes were of 1:1 stoichiometry in solution, which was further confirmed by high resolution electrospray ionization mass spectrometry (HR-ESI-MS): *m*/*z* 1155.45834 for $[Z\text{-}\mathbf{3}\supset\mathbf{4} - PF_6]^+$, *m*/*z* 505.24616 for $[Z\text{-}\mathbf{3}\supset\mathbf{4} - 2PF_6]^{2+}$, *m*/*z* 1155.45940 for $[E\text{-}\mathbf{3}\supset\mathbf{4} - PF_6]^+$, and *m*/*z* 505.24652 for $[E\text{-}\mathbf{3}\supset\mathbf{4} - 2PF_6]^{2+}$. We also obtained single crystals of the complex *E*-**3**⊃**4** with 1:1 stoichiometry by the vapor diffusion method. The complex is stabilized by hydrogen-bonding, charge-transfer, and edge-to-face π-stacking interactions. The crystal structure shows that seven hydrogen bonds are formed between four hydrogen atoms of **4** and five oxygen atoms on *E*-**3**. Two α-pyridinium hydrogen atoms (**b**, **c**, **d**, **e**, and **f**) and two *N*-methyl hydrogen atoms (**a** and **g**) are involved in these hydrogen-bonding interactions (Figure 1). It is interesting that aromatic edge-to-face π-stacking interactions (**h** and **i**) between the pyridinium rings of **4** and the stiff stilbene moieties of *E*-**3** are observed in the solid state (Figure 1), suggesting that the presence of *E*-stiff stilbene further stabilizes the complex *E*-**3**⊃**4**.

As shown in Figure 2, when 1.10 equiv of **4** was added into *Z*-**3**, the signals of H_a and H_b, the protons on the electron-rich aromatic rings of *Z*-**3**, shifted upfield 0.236 and 0.189 ppm, respectively. By comparison, the signals of H_{a*} and H_{b*} on *E*-**3** shifted upfield 0.071 and 0.225 ppm, respectively, upon addition of 1.10 equiv of **4**. The association constants (K_a) of *Z*-**3**⊃**4** and *E*-**3**⊃**4** were determined to be 750 ± 28 and 570 ± 13 M^{-1} in acetonitrile, respectively, by fitting the chemical shift changes of protons on the host **3** as a function of the initial concentration of guest **4**.

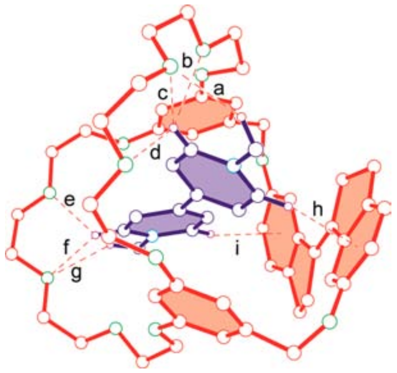


Figure 1. Ball and stick view of the X-ray crystal structure of *E*-**3**$\supset$**4**. Host *E*-**3** is red, guest **4** is blue, hydrogens are purple, oxygens are green, and nitrogens are sky blue. PF_6^- counterions, solvent molecules, and hydrogens except the ones involved in hydrogen bonding between *E*-**3** and **4** were omitted for clarity. Hydrogen bond parameters are as follows: H···O distance (Å), C···O distance (Å), C−H···O angle (deg): **a**, 2.35, 3.23, 150; **b**, 2.54, 2.88, 101; **c**, 2.39, 3.24, 150; **d**, 2.55, 3.09, 146; **e**, 2.38, 3.07, 129; **f**, 2.46, 3.29, 145; **k**, 2.53, 3.30, 136. The edge-to-face π-stacking interactions **h** and **i** are defined by H···phenyl centroid distances (Å) of 2.36 and 2.48 and C···centroid distances (Å) of 3.27 and 3.14, respectively.[12]

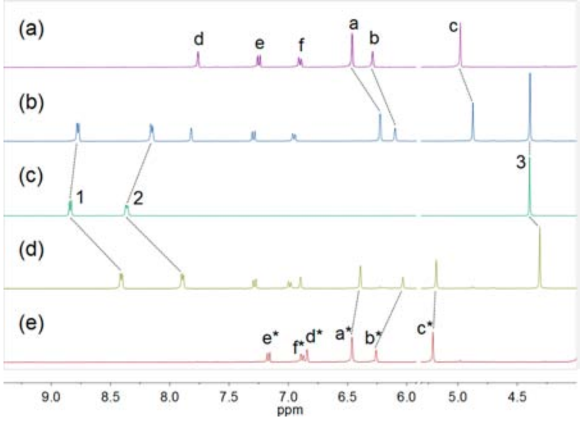


Figure 2. Partial ^{1}H NMR spectra (400 MHz, MeCN-d_3) of (a) *Z*-**3**, (b) a mixture of 2.00 mM *Z*-**3** and 2.20 mM **4**, (c) **4**, (d) a mixture of 2.00 mM *E*-**3** and 2.20 mM **4**, and (e) *E*-**3**.

The association constants of *Z*-**3**$\supset$**4** and *E*-**3**$\supset$**4** were quite similar. This result was different from our expectations that configuration change could modulate the affinity of host−guest interactions. A possible explanation for the similar complexation behaviors of *Z*-**3** and *E*-**3** with **4** is that the size of guest **4** was too small to fit the cavities of cryptand **3**, so it is hard to form compact host−guest complexes. To confirm our speculations, we studied the host−guest complexation of cryptand **3** with a large guest **5**, *N*,*N*′-dimethyl-2,7-diazapyrenium (DAP) salt. Job plots based on UV−vis spectroscopy absorbance data in acetonitrile demonstrated that the complexes of *Z*-**3**$\supset$**5** and *E*-**3**$\supset$**5** were of 1:1 stoichiometry in solution. HR-ESI-MS experiments further demonstrated the formation of 1:1 complexes between *Z*-**3** and **5**, and *E*-**3** and **5**, respectively. ^{1}H NMR spectrum of an equivalent mixture of *Z*-**3** and **5** shows that the chemical shifts of H_a and H_b on *Z*-**3** changed dramatically after complexation (Figure 3). Signals of H_a and H_b shifted upfield 0.548 and 1.343 ppm, respectively. Such large chemical shift changes indicated that strong π-donor/π-acceptor interactions exist between *Z*-**3** and **5**. The association constant for the complexation between *Z*-**3** and **5** was determined to be 3.26 ($\pm$0.55) $\times$ 10^3 M^{-1}, which is significantly larger than that of the complexation between *Z*-**3** and **4**. On the other hand, the signals of H_{a*} and H_{b*} on *E*-**3** shifted upfield 0.089 and 0.773 ppm, respectively, when 1.00 equiv of **5** was added. The K_a of *E*-**3**$\supset$**5** was determined to be 227 ± 40 M^{-1}. Remarkable change was observed between host−guest complexations of *Z*-**3**$\supset$**5** and *E*-**3**$\supset$**5**; the K_a of *Z*-**3**$\supset$**5** was about 14 times higher than that of *E*-**3**$\supset$**5**. This result may be explained by the fact that the large cavity size of *Z*-**3** would enable the formation of compact and well-stacked host−guest complex between *Z*-**3** and a large guest **5**. *E*-**3** may have a smaller cavity than *Z*-**3**, resulting in the weaker interaction between *E*-**3** and **5** compared to that of *E*-**3** and **4**. The host−guest complexations of *Z*-**3**$\supset$**5** and *E*-**3**$\supset$**5** were further studied by 2D NOESY. In the 2D NOESY spectrum of a mixture of *Z*-**3** and **5**, protons on guest **5** have strong NOE correlation signals with the protons on the ether chains, phenyl rings, and stiff stilbenes of host *Z*-**3** (Supplementary Figure S26), indicating the formation of inclusion complexes between *Z*-**3** and **5**. On the other hand, the protons on guest **5** only show some weak NOE correlation signals with the protons on the ether chains of *E*-**3** (Supplementary Figure S27), which confirmed the weak complexation between *E*-**3** and **5**.

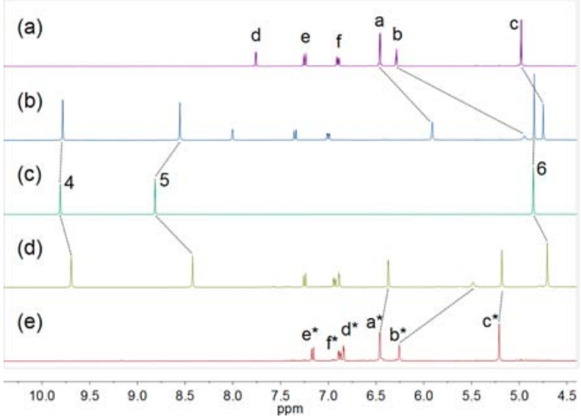


Figure 3. Partial ^{1}H NMR spectra (400 MHz, MeCN-d_3) of (a) *Z*-**3**, (b) a mixture of 2.00 mM *Z*-**3** and 2.00 mM **5**, (c) **5**, (d) a mixture of 2.00 mM *E*-**3** and 2.00 mM **5**, and (e) *E*-**3**.

In conclusion, we introduced an efficient method to synthesize crown ether based cryptands by using a McMurry coupling reaction for the macrocyclization and formation of the third arm of cryptand. We have synthesized a BMP32C10-based cryptand *Z*-**3** by this method with high yield (overall yield 76%, two steps). The photoresponsive cryptand **3** formed host−guest complexes with paraquat derivative **4** and DAP derivative **5**. *Z*-**3** and *E*-**3** exhibited similar binding affinity to the small guest **4**, while dramatic changes were observed in the binding affinity to the large guest **5**. Our studies provided an efficient synthesis of a photoresponsive cryptand. A McMurry coupling reaction would be useful for the synthesis of macrocycles as building blocks to construct photoresponsive self-assembly systems.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details, synthesis of compounds, ^{1}H NMR spectra, ^{13}C NMR spectra, and HR-ESI-MS of compounds;

Job plots for the host−guest complexes; HR-ESI-MS of the host−guest complexes; determination of the association constants, X-ray crystal data of *E*-**3**⊃**4** including cif file; and other materials. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: qzyang@mail.ipc.ac.cn.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was financially supported by the 973 Program (2013CB933800, 2013CB834505), National Natural Science Foundation of China (21072202, 21222210, 91027041), and the Chinese Academy of Sciences (100 Talents Program).

REFERENCES

(1) (a) Allwood, B. L.; Spencer, N.; Shahriari-Zavareh, H.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1058. (b) Stoddart, F. *Chem. Br.* **1991**, 714. (c) Raymo, F. M.; Stoddart, J. F. *Chem. Rev.* **1999**, *99*, 1643. (d) Zheng, B.; Wang, F.; Dong, S.; Huang, F. *Chem. Soc. Rev.* **2012**, *41*, 1621.

(2) (a) Cantrill, S. J.; Pease, A. R.; Stoddart, J. F. *J. Chem. Soc., Dalton Trans.* **2000**, 3715. (b) Kim, K. *Chem. Soc. Rev.* **2002**, *31*, 96. (c) Sauvage, J.-P. *Chem. Commun.* **2005**, 1507. (d) Huang, F.; Gibson, H. W. *Prog. Polym. Sci.* **2005**, *30*, 982. (e) Zhu, X.-Z.; Chen, C.-F. *J. Am. Chem. Soc.* **2005**, *127*, 13158. (f) Zhang, C.; Li, S.; Zhang, J.; Zhu, K.; Li, N.; Huang, F. *Org. Lett.* **2007**, *9*, 5553. (g) Chiu, C.-W.; Lai, C.-C.; Chiu, S.-H. *J. Am. Chem. Soc.* **2007**, *129*, 3500. (h) Wang, F.; Han, C.; He, C.; Zhou, Q.; Zhang, J.; Wang, C.; Li, N.; Huang, F. *J. Am. Chem. Soc.* **2008**, *130*, 11254. (i) Zhu, K.; Li, S.; Wang, F.; Huang, F. *J. Org. Chem.* **2009**, *74*, 1322. (j) Wang, F.; Zheng, B.; Zhu, K.; Zhou, Q.; Zhai, C.; Li, S.; Li, N.; Huang, F. *Chem. Commun.* **2009**, 4375. (k) Lin, T.-C.; Lai, C.-C.; Chiu, S.-H. *Org. Lett.* **2009**, *11*, 613. (l) Guo, J.-B.; Jiang, Y.; Chen, C.-F. *Org. Lett.* **2010**, *12*, 5764. (m) Yan, X.; Zhou, M.; Chen, J.; Chi, X.; Dong, S.; Zhang, M.; Ding, X.; Yu, Y.; Shao, S.; Huang, F. *Chem. Commun.* **2011**, *47*, 7086. (n) Dong, S.; Luo, Y.; Yan, X.; Zheng, B.; Ding, X.; Yu, Y.; Ma, Z.; Zhao, Q.; Huang, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 1905. (o) Guo, J.-B.; Han, Y.; Cao, J.; Chen, C.-F. *Org. Lett.* **2011**, *13*, 5688. (p) Yan, X.; Xu, D.; Chi, X.; Chen, J.; Dong, S.; Ding, X.; Yu, Y.; Huang, F. *Adv. Mater.* **2012**, *24*, 362. (q) You, Y.-C.; Tzeng, M.-C.; Lai, C.-C.; Chiu, S.-H. *Org. Lett.* **2012**, *14*, 1046. (r) Zhang, M.; Xu, D.; Yan, X.; Chen, J.; Dong, S.; Zheng, B.; Huang, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 7011. (s) Yan, X.; Wang, F.; Zheng, B.; Huang, F. *Chem. Soc. Rev.* **2012**, *41*, 6042. (t) Ji, X.; Yao, Y.; Li, J.; Yan, X.; Huang, F. *J. Am. Chem. Soc.* **2013**, *135*, 74.

(3) (a) Bryant, W. S.; Jones, J. W.; Mason, P. E.; Guzei, I. A.; Rheingold, A. L.; Nagvekar, D. S.; Gibson, H. W. *Org. Lett.* **1999**, *1*, 1001. (b) Zhang, M.; Zhu, K.; Huang, F. *Chem. Commun.* **2010**, *46*, 8131. (c) Huang, F.; Zhou, L.; Jones, J. W.; Gibson, H. W.; Ashraf-Khorassani, M. *Chem. Commun.* **2004**, 2670. (d) Huang, F.; Switek, K. A.; Gibson, H. W. *Chem. Commun.* **2005**, 3655. (e) Wang, F.; Zhang, J.; Ding, X.; Dong, S.; Liu, M.; Zheng, B.; Li, S.; Wu, L.; Yu, Y.; Gibson, H. W.; Huang, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 1090. (f) Liu, M.; Li, S.; Hu, M.; Wang, F.; Huang, F. *Org. Lett.* **2010**, *12*, 760. (g) Yan, X.; Wei, P.; Zhang, M.; Chi, X.; Liu, J.; Huang, F. *Org. Lett.* **2011**, *13*, 6370. (h) Niu, Z.; Huang, F.; Gibson, H. W. *J. Am. Chem. Soc.* **2011**, *133*, 2836. (i) Yan, X.; Wei, P.; Xia, B.; Huang, F.; Zhou, Q. *Chem. Commun.* **2012**, *48*, 4968. (j) Li, J.; Wei, P.; Wu, X.; Xue, M.; Yan, X.; Zhou, Q. *RSC Adv.* **2013**, *3*, 21289.

(4) (a) Huang, F.; Switek, K. A.; Zakharov, L. N.; Fronczek, F. R.; Slebodnick, C.; Lam, M.; Golen, J. A.; Bryant, W. S.; Mason, P. E.; Rheingold, A. L.; Ashraf-Khorassani, M.; Gibson, H. W. *J. Org. Chem.* **2005**, *70*, 3231. (b) Li, S.; Liu, M.; Zheng, B.; Zhu, K.; Wang, F.; Li, N.; Zhao, X.-L.; Huang, F. *Org. Lett.* **2009**, *11*, 3350. (c) Liu, M.; Yan, X.; Hu, M.; Chen, X.; Zhang, M.; Zheng, B.; Hu, X.; Shao, S.; Huang, F. *Org. Lett.* **2010**, *12*, 2558. (d) Ji, X.; Zhang, M.; Yan, X.; Li, J.; Huang, F. *Chem. Commun.* **2013**, *49*, 1178. (e) Li, J.; Wei, P.; Wu, X.; Xue, M.; Yan, X. *Org. Lett.* **2013**, *15*, 4984.

(5) (a) McMurry, J. E.; Felming, M. P. *J. Am. Chem. Soc.* **1974**, *96*, 4708. (b) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513.

(6) (a) Yang, Q.-Z.; Huang, Z.; Kucharski, T. J.; Khvostichenko, D.; Chen, J.; Boulatov, R. *Nat. Nanotechnol.* **2009**, *4*, 302. (b) Huang, Z.; Yang, Q.-Z.; Khvostichenko, D.; Kucharski, T. J.; Chen, J.; Boulatov, R. *J. Am. Chem. Soc.* **2009**, *131*, 1407.

(7) Duan, X.-F.; Zeng, J.; Lu, J.-W.; Zhang, Z.-B. *J. Org. Chem.* **2006**, *71*, 9873.

(8) Kucharski, T. J.; Boulatov, R. *J. Mater. Chem.* **2011**, *21*, 8237.

(9) (a) Beharry, A. A.; Sadovski, O.; Woolley, G. A. *J. Am. Chem. Soc.* **2011**, *133*, 19684. (b) Bleger, D.; Schwarz, J.; Brouwer, A. M.; Hecht, S. *J. Am. Chem. Soc.* **2012**, *134*, 20597.

(10) Xu, J.-F.; Chen, Y.-Z.; Wu, D.; Wu, L.-Z.; Tung, C.-H.; Yang, Q.-Z. *Angew. Chem., Int. Ed.* **2013**, *52*, 9738.

(11) Yan, X.; Li, Z.; Wei, P.; Huang, F. *Org. Lett.* **2013**, *15*, 534.

(12) CCDC 972086.