Organic LETTERS

Letter

pubs.acs.org/OrgLett

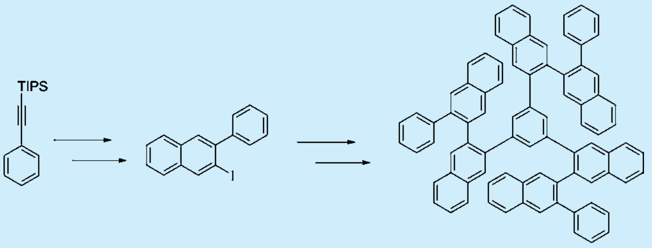
# Rapid Synthesis of Crowded Aromatic Architectures from Silyl Acetylenes

Samuel J. Hein, Hasan Arslan, Ivan Keresztes, and William R. Dichtel*

Department of Chemistry and Chemical Biology, Cornell University, Ithaca, New York 14853-1301, United States

S *Supporting Information*

**ABSTRACT:** Congested aromatic systems were prepared by benzannulating silyl-protected arylacetylenes. The silyl groups may be retained in the naphthalene products and transformed into iodides in high yield. The desirable attributes of this strategy, particularly its remarkable tolerance of sterically hindered alkynes, are showcased in the efficient synthesis of a congested, branched oligo(naphthalene). As such, benzannulations of diaryl and silyl-protected acetylenes show outstanding promise for accessing new aromatic architectures.

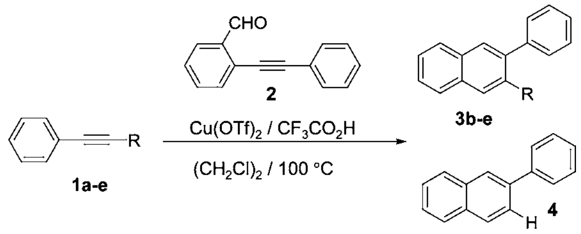


Extended aromatic structures have attracted intense interest for organic optoelectronic devices, including photovoltaics[1] and field effect transistors,[2] as well as for accessing porous polymers.[3] Improved synthetic approaches have provided increasingly elaborate systems, such as poly(*o*-arylenes),[4] contorted hexabenzocoronenes (HBCs),[5] and cyclo(*p*-phenylenes).[6] These architectures exemplify the diverse structural landscape available for fundamental and applied studies. For example, oligo(*o*-phenylenes) exhibit specific helical conformations[7] and spectral properties that arise from either fully extended or coiled conformations,[8] but this structural motif was virtually unexplored[9] until cross-coupling conditions tolerant of their steric hindrance were identified. We recently adapted a benzannulation reaction first reported by Yamamoto[10] to prepare congested aromatic systems containing 2,3-diarylnaphthalene functionalities. This reaction is the first cycloaddition capable of modifying the relatively unreactive alkynes along the backbone of a poly(phenylene ethynylene) (PPE).[11] It also tolerates sterically demanding aryl substituents on the alkynes, as demonstrated by its use in recent syntheses of contorted HBCs[12] and a (6,6) carbon nanotube segment precursor.[13] Furthermore, $^{13}$C-labeled and fluorine-substituted cycloaddition partners proved that the benzannulation reaction proceeds regioselectively for most diarylacetylene substrates.[11,14] This feature will facilitate the synthesis of low-symmetry products as single regioisomers.

Here we integrate the benzannulation reaction into a general strategy to produce larger aromatic systems by expanding its utility to silyl-protected acetylenes. Only a limited number of these substrates have been explored in benzannulation reactions,[15] and they are unreported as substrates for the $Cu(OTf)_2$ or $ZnCl_2$-mediated reactions described below. A broad range of silyl protecting groups is tolerated, including bulky triisopropyl (TIPS) and *tert*-butyldimethyl silyl (TBS) acetylenes. Under typical benzannulation conditions, these groups are protodesilylated to provide the corresponding 2-arylnaphthalene. We modified the reaction conditions to retain the silyl group, such that they may be transformed to iodides and derivatized using cross-coupling reactions. We apply this method iteratively to access a branched oligo(naphthalene) product so hindered that it exhibits restricted bond rotations at 140 °C in tetrachloroethane. This compound demonstrates both the utility of silyl-substituted naphthalene synthons and the remarkable ability of the benzannulation reaction to modify hindered alkynes.

We first evaluated the benzannulation of phenylacetylenes protected by silyl groups that differ in size and relative stability. Typical reaction conditions include excess $CF_3CO_2H$ (10 equiv per alkyne) because its conjugate base is thought to promote the

**Table 1. Benzannulation of Silyl-Protected Phenylacetylenes Using Reduced Equivalents of $CF_3CO_2H$ Retains Silyl Groups Larger than TMS in the Naphthalene Products 3b−e**



Conditions: **1** (0.100 g), **2** (2 equiv), $Cu(OTf)_2$ (0.05 equiv), $CF_3CO_2H$ (1 equiv), $C_2H_4Cl_2$, 100 °C, 30 min

| substrate | R | isolated yield (%) 3 | isolated yield (%) 4 |
|---|---|---|---|
| **1a** | $Si(Me)_3$ | none | 40 |
| **1b** | $Si(Et)_3$ | 67 | none |
| **1c** | Si-*t*-Bu$(Me)_2$ | 85 | none |
| **1d** | Si(*i*-Pr)$_3$ | 89 | none |
| **1e** | $SiPh(Me)_2$ | 78 | none |

**Received:** June 27, 2014
**Published:** August 27, 2014

dx.doi.org/10.1021/ol501874s | *Org. Lett.* 2014, 16, 4416−4419

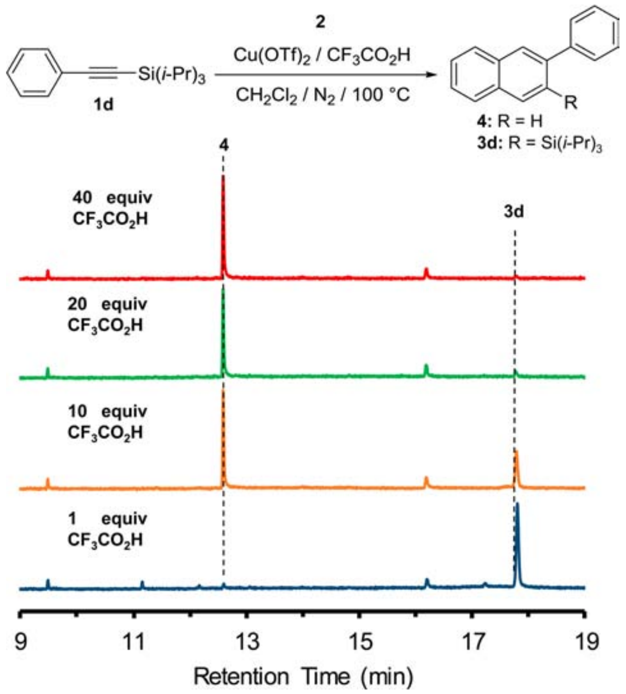
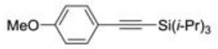
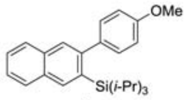
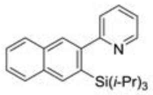
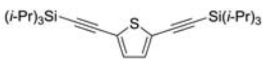
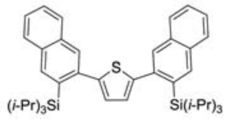
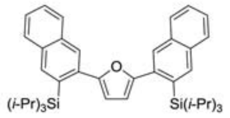
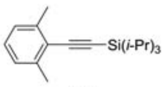
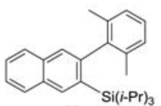


**Figure 1.** Partial GC/MS total ion count chromatograms of the crude reaction mixtures for the benzannulation of **1d** in the presence of varying [CF$_3$CO$_2$H]. The TIPS group is retained in the presence of 1 equiv of CF$_3$CO$_2$H. Partial protodesilylation occurs with 10 equiv of CF$_3$CO$_2$H to provide **4**, which is the dominant product when either 20 or 40 equiv of the acid are employed.

**Table 2. Benzannulation of Various TIPS-Protected Acetylenes**[a]

| alkyne | product | isolated yield (%) |
|---|---|---|
| <br>**5** | <br>**6** | 69% |
| <br>**7** | <br>**8** | no conversion |
| <br>**9** | <br>**10** | 45% |
| <br>**11** | <br>**12** | 58% |
| <br>**13** | <br>**14** | 78% |

[a] Alkyne: (0.05 g) 2: (2 equiv), Cu(OTf)$_2$: (0.05 equiv), CF$_3$CO$_2$H: (1 equiv), 30 min, 100 °C.

formation of naphthalenes over naphthyl ketone side products.[10] These conditions provide desilylated 2-phenylnaphthalene **4** as the major or only benzannulation product for various silyl-protected phenylacetylenes, even for relatively robust TIPS, TBS, and dimethylphenylsilyl (DMPS) groups. In contrast, reducing the initial concentration of CF$_3$CO$_2$H (1 equiv per alkyne), provides nearly complete retention of the silyl eithers in naphthalene products **3b**–**e** (Table 1). After an aqueous workup and purification by flash chromatography, **3b**–**e** were isolated in good to excellent yields.

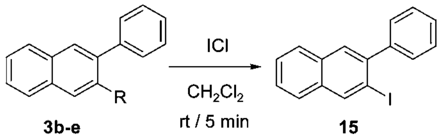
Substrates **1b** and **1c** provided only small amounts of protodesilylated product **4**, as observed by GC/MS, whose identity was confirmed by comparison to an independently prepared sample. No evidence for the formation of **4** was observed for larger substrates **1d** and **1e**. In contrast, the TMS group was unstable to even 1 equiv of CF$_3$CO$_2$H, and **4** was the only observed benzannulation product. Alternative benzannulation conditions[16] employ ZnCl$_2$ without added Brønsted acids but are less active than the Cu(OTf)$_2$/CF$_3$CO$_2$H conditions. Compound **1a** was smoothly benzannulated in the presence of ZnCl$_2$ to provide **3a** in good isolated yield (75%), alongside trace amounts of **4**. Collectively, these experiments indicate that the Cu-catalyzed benzannulation reaction proceeds efficiently for silyl-protected alkynes and that silyl groups larger than TMS are stable to the modified reaction conditions. TMS groups are tolerated under alternative ZnCl$_2$-catalyzed conditions that do not employ stoichiometric CF$_3$CO$_2$H.

It will often be desirable to retain the silyl group to direct further functionalization at the 2-position of the naphthalene product (see below). However, some synthetic routes will employ a silyl protecting group that should not be retained after benzannulation. Even the large TIPS group may be removed during the benzannulation reaction by using increased [CF$_3$CO$_2$H]. GC/MS analysis of crude reaction mixtures of the benzannulation of **1d** that employed up to 20 equiv of CF$_3$CO$_2$H provided mixtures of **3d** and **4** (Figure 1), whereas **4** was formed exclusively at higher [CF$_3$CO$_2$H] (40 equiv) without introducing additional side products. These experiments indicate that robust silyl protecting groups may be retained or removed in situ by adjusting the initial quantities of acid.

The substrate scope of the benzannulation reaction was expanded beyond phenylacetylene by evaluating a series of aromatic systems containing TIPS-protected acetylenes (Table 2). An alkyne with an electron-rich aromatic system, such as the methoxy substituted derivative **5**, is well tolerated. Electron-withdrawing aromatic systems, such as pyridine derivate **7**, which is likely to be protonated under the reaction conditions, are poor substrates. Common electron-rich heterocycles, such as thiophenes and furans, are tolerated, as demonstrated by the acceptable isolated yields for the double benzannulations of **9** and **11**, respectively. Naphthalene-substituted derivatives of thiophenes and furans are relatively unexplored, and naphthalene-substituted oligothiophenes were recently shown to form nanofibers on mica.[17] Finally, substrate **13**, which features an alkyne flanked by bulky 2,6-dimethylphenyl and TIPS substituents, is benzannulated in good yield, further highlighting the remarkable tolerance of this reaction to sterically crowded substrates.

The benzannulation of these model silyl-protected phenylacetylene substrates provides naphthalene building blocks with variable silyl and aryl groups at the 2- and 3-positions, respectively. Although new C–C bonds may be formed at silyl sites directly under Hiyama cross-coupling conditions,[18] we explored converting the silyl group to a halide to take advantage

**Table 3. Iodization/Protodesilylation of Each Silyl Naphthalane**

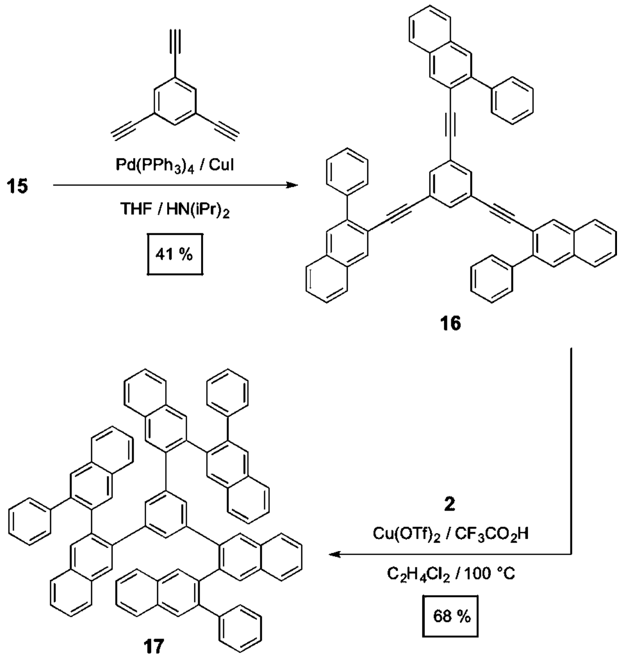


| entry | 3 | R | isolated yields (%) |
|---|---|---|---|
| 1 | **3b** | $Si(Et)_3$ | 90 |
| 2 | **3c** | Si-*t*-Bu$(Me)_2$ | 93 |
| 3 | **3d** | Si(*i*-Pr)$_3$ | 92 |
| 4 | **3e** | $SiPh(Me)_2$ | none |

of a full range of available transition metal-catalyzed C−C, C−N, C−O, and C−F bond-forming reactions. Silyl groups of each of the isolated naphthalenes **3b−d** underwent rapid and quantitative conversion to 2-iodo-3-phenylnaphthalene **15** upon treatment with ICl in $CH_2Cl_2$ (Table 3). The reaction proceeded to completion after only 5 min at rt, in contrast to previous reports that employed longer reaction times and elevated temperatures.[19] The DMPS naphthalene **3e** is incompatible with this procedure, as desilylated product **4**, iodobenzene, and unidentified chlorinated products were observed by GC/MS instead of **15** (see Figure S43, Supporting Information). These observations indicate that triethylsilyl (TES), TBS, and TIPS groups are readily converted to aryl iodide substrates, which readily undergo many C−C bond-forming reactions.

1,2-Diaryl linkages are quite sterically hindered, which made oligo- and poly(*o*-phenylenes) essentially unstudied prior to recent pioneering reports by Hartley[20] and Aida.[21] This substitution pattern also figures prominently in the bottom-up synthesis of graphene nanoribbons (GNRs) and other carbon nanostructures.[22] The outstanding efficiency and steric tolerance of the benzannulation reaction, combined with the synthetic versatility of halogenated naphthalenes derived from silyl acetylenes, suggests a new strategy to access highly crowded aromatic architectures. To explore this possibility, **15** was joined to 1,3,5-triethynyl benzene under Sonogashira cross-coupling conditions to provide the trialkyne **16**. Its internal alkynes remain accessible for another benzannulation reaction, providing oligo(arylene) **17**, in which each aromatic subunit is a part of at least one *o*-aryl linkage (Scheme 1). Compound **17** was characterized using high-resolution mass spectrometry, variable-temperature 1D and 2D NMR spectroscopy, and UV/vis and photoemission spectroscopies.

**Scheme 1**



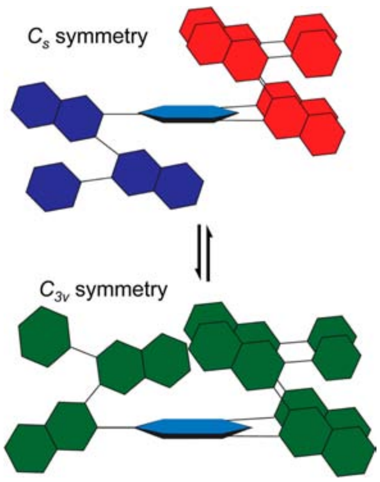


**Figure 2.** Schematic depiction of the major $C_s$ symmetric conformer and minor $C_{3v}$ conformer of compound **17**. A more complete description of its conformational behavior is provided in the Supporting Information.

The $^1H$ and $^{13}C$ NMR spectra of **17** indicate that the *o*-aryl linkages of **17** restrict the C−C bond rotation around the central trisubstituted benzene ring, even at elevated temperature. At rt, its $^1H$ and $^{13}C$ NMR spectra exhibit 48 and 46 resonances, respectively, corresponding to a mixture of conformers undergoing slow exchange with respect to each measurement (see Figures S34−35, Supporting Information). The major conformation exhibits $C_s$ symmetry, in which one of the oligo(aryl) substituents on the central benzene ring is *anti* with respect to the other two (Figure 2). When rotation about the inner C−C bonds is slow on the NMR time scale, the hydrogens of the central benzene ring appear as two distinct singlets that integrate in a 2:1 ratio. A minor conformation with $C_{3v}$ symmetry, in which the three oligo(aryl) substituents are *syn*, is also observed. These hindered bond rotations that persist at elevated temperature demonstrate the extreme steric hindrance of **17** and highlight the ability of the benzannulation reaction to modify congested aromatic systems.

In conclusion, we have broadened the scope of the benzannulation reaction to silyl-protected phenylacetylenes. By varying the acid concentration, the silyl groups may either be removed or retained in the resulting phenylnaphthalene products. The reaction tolerates electron-donating substitutents and electron-rich heterocycles. When the silyl group is retained, it may be transformed to an iodide under mild conditions to enable further elaboration using various transition-metal-catalyzed cross-coupling reactions. We demonstrate the utility of these transformations in the iterative synthesis of a highly congested aromatic system that exhibits restricted C−C bond rotations, even at elevated temperatures. These results, combined with the excellent regioselectivity of the benzannulation reaction, provide a powerful means to access sterically hindered aromatic architectures.

## ■ ASSOCIATED CONTENT

### Supporting Information

Experimental procedures and characterization data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION

### Corresponding Author

*E-mail: wdichtel@cornell.edu.

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

This work was supported by the Beckman Young Investigator Program of the Arnold and Mabel Beckman Foundation, the NSF (CHE-1124754), the Doctoral New Investigator Program of the ACS Petroleum Research Fund (52019-DNI7), a Sloan Research Fellowship from the Alfred P. Sloan Foundation, and a Camille Dreyfus Teacher-Scholar Award from the Camille and Henry Dreyfus Foundation.

## ■ REFERENCES

(1) (a) Chang, Y. J.; Chow, T. J. *J. Mater. Chem.* **2011**, *21*, 9523. (b) Shin, R. Y. C.; Sonar, P.; Siew, P. S.; Chen, Z. K.; Sellinger, A. *J. Org. Chem.* **2009**, *74*, 3293−3298. (c) Liu, X.; Sun, Y.; Hsu, B. B. Y.; Lorbach, A.; Qi, L.; Heeger, A. J.; Bazan, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 5697−5708. (d) Takimiya, K.; Osaka, I.; Mori, T.; Nakano, M. *Acc. Chem. Res.* **2014**, *47*, 1493−1502. (e) Schipper, D. J.; Moh, L. C. H.; Müller, P.; Swager, T. M. *Angew. Chem., Int. Ed.* **2014**, *126*, 5957−5961.

(2) (a) Xiao, S.; Kang, S. J.; Wu, Y.; Ahn, S.; Kim, J. B.; Loo, Y. L.; Siegrist, T.; Steigerwald, M. L.; Li, H.; Nuckolls, C. *Chem. Sci.* **2013**, *4*, 2018−2023. (b) Niimi, K.; Shinamura, S.; Osaka, I.; Miyazaki, E.; Takimiya, K. *J. Am. Chem. Soc.* **2011**, *133*, 8732−8739. (c) Jia, H. P.; Liu, S. X.; Sanguinet, L.; Levillain, E.; Decurtins, S. *J. Org. Chem.* **2009**, *74*, 5727−5729.

(3) (a) Vermeulen, N.; Karagiaridi, O.; Sarjeant, A. A.; Stern, C. L.; Hupp, J. T.; Farha, O. K.; Stoddart, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 14916−14919. (b) Modak, A.; Nandi, M.; Mondal, J.; Bhaumik, A. *Chem. Commun.* **2012**, *48*, 248−250. (c) Liu, J.; Yee, K.-K.; Lo, K. K. W.; Zhang, K. Y.; To, W. P.; Che, C.-M.; Xu, Z. *J. Am. Chem. Soc.* **2014**, *136*, 2818−2824. (d) Zhang, P.; Weng, Z.; Guo, J.; Wang, C. *Chem. Mater.* **2011**, *23*, 5243−5249.

(4) (a) Ito, S.; Takahashi, K.; Nozaki, K. *J. Am. Chem. Soc.* **2014**, *136*, 7547−7550. (b) Blake, A. J.; Cooke, P. A.; Doyle, K. J.; Gair, S.; Simpkins, N. S. *Tetrahedron Lett.* **1998**, *39*, 9093−9096.

(5) (a) Golling, F. E.; Quernheim, M.; Wagner, M.; Nishiuchi, T.; Müllen, K. *Angew. Chem., Int. Ed.* **2014**, *53*, 1525−1528. (b) Zhang, Q.; Peng, H.; Zhang, G.; Lu, Q.; Chang, J.; Dong, Y.; Shi, X.; Wei, J. *J. Am. Chem. Soc.* **2014**, *136*, 5057−5064. (c) Dou, X.; Yang, X.; Bodwell, G. J.; Wagner, M.; Enkelmann, V.; Mu, K. *Org. Lett.* **2007**, *9*, 2485−2488. (d) Feng, X.; Wu, J.; Ai, M.; Pisula, W.; Zhi, L.; Rabe, J. P.; Müllen, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 3033−3036.

(6) Nishiuchi, T.; Feng, X.; Enkelmann, V.; Wagner, M.; Müllen, K. *Chemistry* **2012**, *18*, 16621−16625.

(7) Mathew, S. M.; Engle, J. T.; Ziegler, C. J.; Hartley, C. S. *J. Am. Chem. Soc.* **2013**, *135*, 6714−6722.

(8) (a) Mathew, S. M.; Hartley, C. S. *Macromolecules* **2011**, *44*, 8425−8432. (b) He, J.; Crase, J. L.; Wadumethrige, S. H.; Thakur, K.; Dai, L.; Zou, S.; Rathore, R.; Hartley, C. S. *J. Am. Chem. Soc.* **2010**, *132*, 13848−13857.

(9) The synthesis of poly(*o*-phenyelenes) has also been reported through oxidative polymerizations, but these materials were subsequently shown to contain a significant percentage of defects, see: (a) Kovacic, P.; Uchic, J. T.; Hsu, L.-C. *J. Polym. Sci., Polym. Chem.* **1967**, *5*, 945−964. (b) Kovacic, P.; Ramsey, J. *Polym. Sci. Polym. Chem.* **1969**, *7*, 111−125. (c) Hsing, C.; Jones, M.; Kovacic, P. *J. Polym. Sci., Polym. Chem.* **1981**, *19*, 973−984.

(10) Asao, N.; Nogami, T.; Lee, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 10921−10925.

(11) Arslan, H.; Saathoff, J. D.; Bunck, D. N.; Clancy, P.; Dichtel, W. R. *Angew. Chem., Int. Ed.* **2012**, *51*, 12051−12054.

(12) Arslan, H.; Uribe-Romo, F. J.; Smith, B. J.; Dichtel, W. R. *Chem. Sci.* **2013**, *4*, 3973−3978.

(13) He, Z.; Xu, X.; Zheng, X.; Ming, T.; Miao, Q. *Chem. Sci.* **2013**, *4*, 4525−4531.

(14) Arslan, H.; Walker, K. L.; Dichtel W. R. Manuscript in preparation.

(15) Isogai, Y.; Nawaz Khan, F.; Asao, N. *Tetrahedron* **2009**, *65*, 9575−9582.

(16) Fang, X. L.; Tang, R. Y.; Zhang, X. G.; Zhong, P.; Deng, C. L.; Li, J. H. *J. Organomet. Chem.* **2011**, *696*, 352−356.

(17) Balzer, F.; Schiek, M.; Osadnik, A.; Wallmann, I.; Parisi, J.; Rubahna, H.-C; Lützenb, A. *Phys. Chem. Chem. Phys.* **2014**, *16*, 5747−5754.

(18) (a) Monguchi, Y.; Yanase, T.; Mori, S.; Sajiki, H. *Synthesis* **2012**, *45*, 40−44. (b) Cheng, K.; Wang, C.; Ding, Y.; Song, Q.; Qi, C.; Zhang, X. M. *J. Org. Chem.* **2011**, *76*, 9261−9268.

(19) Mita, T.; Michigami, K.; Sato, Y. *Org. Lett.* **2012**, *14*, 3462−3465.

(20) (a) Hartley, C. S. *J. Org. Chem.* **2011**, *76*, 9188−9191. (b) He, J.; Mathew, S. M.; Cornett, S. D.; Grundy, S. C.; Hartley, C. S. *Org. Biomol. Chem.* **2012**, *10*, 3398−3405.

(21) (a) Ohta, E.; Sato, H.; Ando, S.; Kosaka, A.; Fukushima, T.; Hashizume, D.; Yamasaki, M.; Hasegawa, K.; Muraoka, A.; Ushiyama, H.; Yamashita, K.; Aida, T. *Nat. Chem.* **2011**, *3*, 68−73. (b) Ando, S.; Ohta, E.; Kosaka, A.; Hashizume, D.; Koshino, H.; Fukushima, T.; Aida, T. *J. Am. Chem. Soc.* **2012**, *134*, 11084−11087.

(22) (a) Narita, A.; Feng, X.; Hernandez, Y.; Jensen, S.; Bonn, M.; Yang, H.; Verzhbitskiy, I.; Casiraghi, C.; Hansen, M. R.; Koch, A. H. R.; Fytas, G.; Ivasenko, O.; Li, B.; Mali, K. S.; Balandina, T.; Mahesh, S.; De Feyter, S.; Müllen, K. *Nat. Chem.* **2014**, *6*, 126−132. (b) Schwab, M. G.; Narita, A.; Hernandez, Y.; Balandina, T.; Mali, K. S.; De Feyter, S.; Feng, X.; Müllen, K. *J. Am. Chem. Soc.* **2012**, *134*, 18169−18172.