Organic LETTERS

Letter

pubs.acs.org/OrgLett

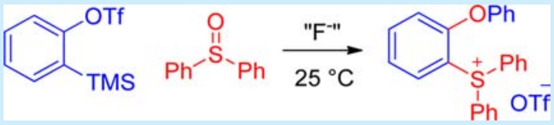
Synthesis of *o*-Aryloxy Triarylsulfonium Salts via Aryne Insertion into Diaryl Sulfoxides

Xiaojin Li,[†] Yan Sun,[†] Xin Huang,[†] Lei Zhang,[†] Lichun Kong,[†] and Bo Peng*[,†,‡]

[†]Department of Chemistry, Zhejiang Normal University, 688 Yingbin Road, Jinhua 321004, China
[‡]State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116024, China

Supporting Information

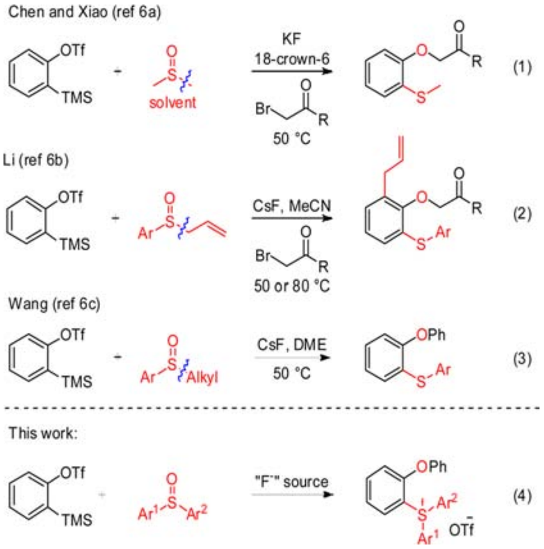
ABSTRACT: The aryne insertion into "S═O" bond has been validated recently. This technology is elusively applied to the synthesis of thioethers. In contrast to the reported cases, the reaction described furnished *o*-aryloxy triarylsulfonium salts, in lieu of thioethers, in good to excellent yields. The reaction is also featured by its exquisite regioselectivity, broad substrate scope, and mild conditions (25 °C). Preliminary mechanistic studies suggest that the reaction probably proceeds in a sequential [2 + 2] cycloaddtion/*O*-arylation/protonation pathway.



Arynes are a prominent class of transient electrophilic species. The high strain and low-lying LUMO enable them to interact with a wide array of charged or neutral nucleophiles.[1] As a consequence, arynes have been widely employed in the synthesis of natural products and bioactive compounds.[2] Among numerous aryne transformations, the insertion of aryne into σ bonds or π bonds has received considerable attention from the synthetic community since this reaction mode can directly enhance the complexity of arenes by producing multisubstituted arenes in a single transformation.[3−5] In particular, the splitting of heteroatom−heteroatom bonds such as "S═O", "N═O", "S═N", "P═N", "P−N", "P−O", etc. by arynes has also been validated and significantly advanced in recent years.[6] For example, Xiao and Chen disclosed the first case of aryne insertion into the "S═O" bond of sulfoxide (DMSO) (Scheme 1, eq 1).[6a] In their study, a series of 1,2-O,S-disubstituted arenes were assembled from three components including arynes, DMSO, and α-bromo carbonyl compounds. Most recently, Li and co-workers creatively merged the aryne insertion technology and Claisen rearrangement process and developed a mechanistic novel aryne 1,2,3-trifunctionalization reaction (Scheme 1, eq 2).[6b] In addition, Wang and co-workers found that the reaction between arynes and sulfoxides could also take place in absence of α-bromo carbonyl compounds to produce *o*-aryloxy diaryl sulfides (Scheme 1, eq 3).[6c] Their further studies successfully applied the released alkyl group for the epoxidation of carbonyl compounds.[6d] Interestingly, all of these transformations experienced a dealkylation process, thus delivering thioethers as the sole products. This is probably due to the vulnerability of the S−C(alkyl) bond in the in situ generated aryl alkyl sulfonium intermediate.[7]

In addition, triarylsulfonium salts are a unique class of S(IV) compounds. Their well-known capability of delivering protons under UV conditions has allowed them to be superior photoinitiators in polymerization reactions[8] and lithographic processes.[9,10] In addition, they can also be harnessed as aryl sources in versatile organic transformations.[11] Therefore, the mild and selective synthesis of triarylsulfonium salts is highly desirable.[12]

Scheme 1. Reactions of Aryne with Sulfoxides

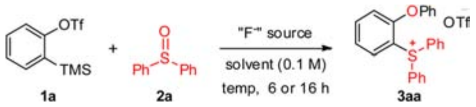


Inspired by the recent progress in the aryne insertion reactions (eq 1−3), we envisioned that the triarylsulfonium salts, instead of reported thioethers, might be achieved by simply treating diaryl sulfoxides with arynes (eq 4). It can be expected that the established stability[11,12] of triarylsulfonium salts may impede their further conversion to thioethers. To verify this hypothesis, we commenced the study by use of Kobayashi precursor **1a** and diphenyl sulfoxide **2a** under ambient temperature (25 °C) (Table 1, entry 1). To our delight, the expected triarylsulfonium **3aa** was directly attained in a good yield (74% NMR yield) in our first trial. The structure of **3aa** was also confirmed unambiguously

Received: December 23, 2016
Published: February 3, 2017

DOI: 10.1021/acs.orglett.6b03840
Org. Lett. 2017, 19, 838−841

Table 1. Optimization of Reaction Conditions



entry	"F⁻" source	solvent	temp (°C)	yield[b] (%)
1	CsF	MeCN	25	74
2	KF/18-crown-6	THF	25	33
3	CsF	DME	25	16
4	CsF	THF	25	14
5	CsF	1,4-dioxane	25	0[c]
6	CsF	MeCN	0	23
7	CsF	MeCN	50	68
8	CsF	MeCN	25	87[d]

[a] Unless otherwise noted, reactions were perfomed with **1a** (0.3 mmol), diphenyl sulfoxide **2a** (0.3 mmol), and "F⁻" source (0.6 mmol) for 6 h. [b] NMR yield (mesitylene as the internal standard). [c] **1a** mostly deteriorated. [d] Reaction time was 16 h.

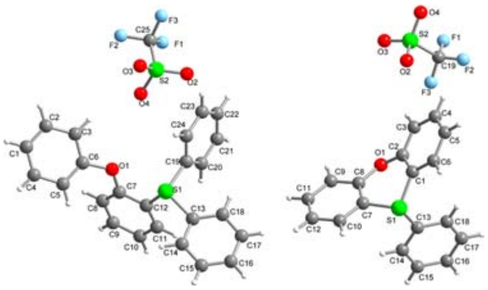
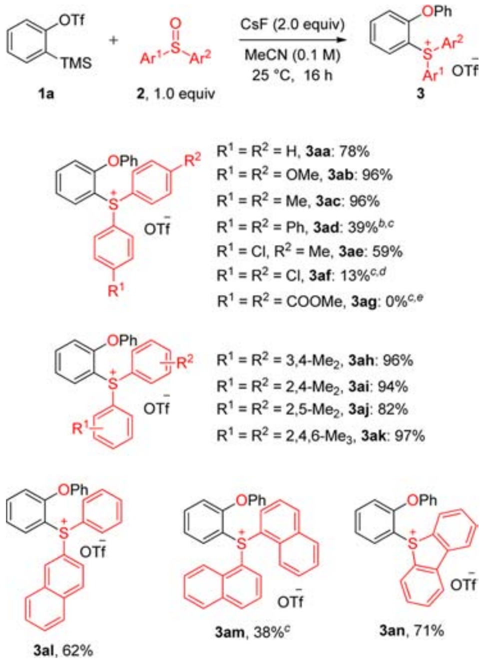


Figure 1. X-ray structure of products **3aa** (left) and **4** (right).

by single-crystal X-ray diffraction (Figure 1, left). As anticipated, triarylsulfonium **3aa** remained intact from the reaction and usual workup process (silica chromatography). After thoroughly varying the reaction conditions ("F⁻" sources, solvents, temperatures, and reaction times) (entries 2–8), we found that simply prolonging the reaction time from 6 to 16 h achieved the best yield (87% NMR yield) (entry 8).[13,14]

With the optimized conditions in hand, we then investigated the scope of diaryl sulfoxides **2**. As depicted in Scheme 2, a wide range of diaryl sulfoxides are compatible in this transformation. The desired *o*-aryloxy triarylsulfonium salts (**3aa–an**) were obtained generally in synthetic useful yields. It is worthy of note that the reaction is highly sensitive to the electronic nature of diaryl sulfoxides. It appears that electron-donating groups (−OMe, Me) (**2b** and **2c**) surpassed the electron-withdrawing groups (−Ph and −Cl) (**2d** and **2f**). The desired *o*-triarylsulfonium salts **3ab** and **3ac** were obtained in excellent yields (96%). In contrast, **2d** and **2f** exhibited less reactivity and afforded much lower yields of **3ad** and **3af** (39% and 13%, respectively). Notably, benzyne precursor **1a** decomposed after the reactions. Similar to **2d** and **2f**, diaryl sulfoxide **2g** bearing an electron-withdrawing ester group also proved unsuitable for the reaction as no desired **3ag** could be obtained. Substrates with electron-donating groups, regardless of the substitution positions (*o*-, *m*-, *p*-), gave rise to the *o*-aryloxy triarylsulfonium salts **3ah–ak** in good to excellent yields (82–97% yields). Remarkably, stereohindered diaryl sulfoxide **2k** still achieved **3ak** in nearly quantitative yield (97%). The high efficiency in producing **3ai**, **3aj**, and **3ak** demonstrated that steric hindrance did not exert any appreciable influence upon the reaction. Besides the diphenyl sulfoxides, naphthyl sulfoxides (**2l** and **2m**) were also proven

Scheme 2. Substrate Scope of Aryl Sulfoxides



[a] Reactions were performed on 0.3 mmol scale. [b] 51% of **2d** was recovered. [c] **1a** decomposed after the reaction. [d] 57% of **2f** was recovered. [e] 85% of **2g** was recovered.

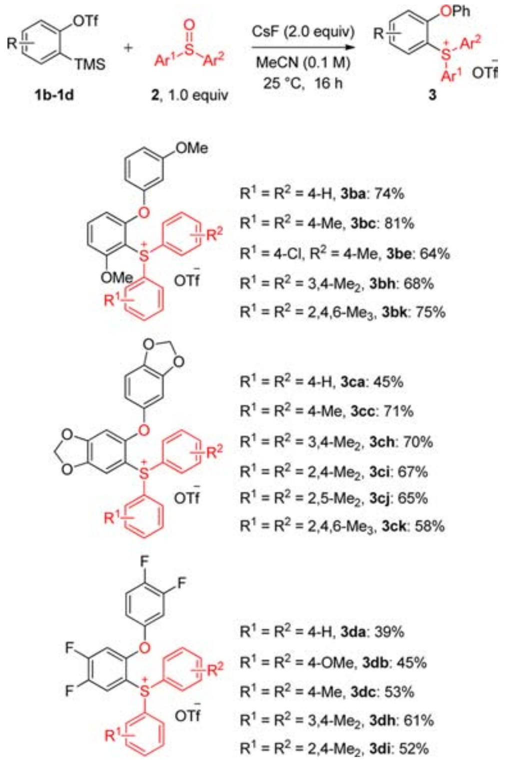
suitable for the reaction, albeit furnishing the corresponding triarylsulfonium salts **3al** and **3am** in modest yields (62% and 38% yields, respectively). Gratifyingly, the reaction could also be applied to the biaryl sulfoxide **2n**. The corresponding triarylsulfonium **3an** was produced in a synthetic useful yield (71%).

Inspired by the results in hand, we moved to the aryl/heteroaryl sulfoxides **2o** and **2p** (Scheme 3). Surprisingly, in place of the expected **3ao** and **3ap**, triarylsulfonium **4** was obtained in modest yields (52% and 62%, respectively). The structure of **4** was also confirmed by single-crystal X-ray diffraction (Figure 1, right). This result might be rationalized by an intramolecular nucleophilic substitution of a thiophene group by a phenyl group, simultaneously releasing the thiophene moiety in **2o** or **2p**.[15]

Scheme 3. Reactions of 2n and 2o with 1a under Optimal Conditions

Afterward, an array of benzyne precursors (**1b–d**) were assessed under the optimized reaction conditions (Scheme 4). Regardless of coupling partners (diaryl sulfoxides), reactions of **1b** and **1c** provided the desired *o*-aryloxy triarylsulfoniums in modest to good yields (from 45% to 81%) as shown in Scheme 4. The stereohindered diaryl sulfoxide **2k** smoothly underwent reactions with **1b** and **1c**, affording **3bk** and **3ck**, respectively, in synthetically useful yields. These results are in line with the aforementioned facile formation of **3ak**, once again indicating that the reaction is not stereosensitive. In view of the significant importance of fluoro-containing compounds,[16] the electron-

Scheme 4. Substrate Scope of Benzyne Precursors

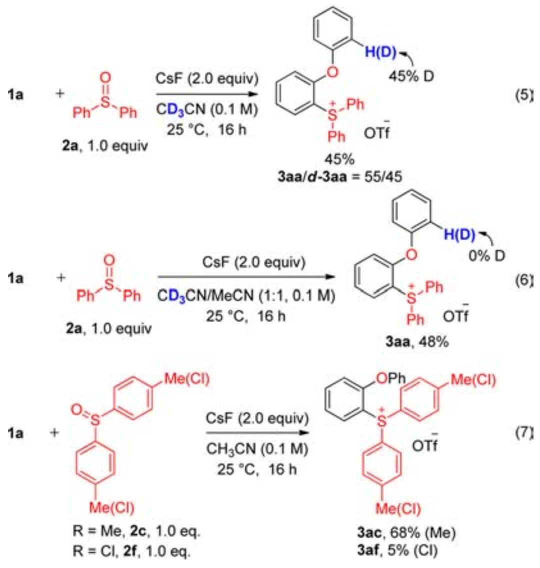


[a] Reactions were performed on 0.3 mmol scale.

poor 3,4-difluorobenzyne precursor (**1d**) was also examined. Pleasantly, various fluoro-containing triarylsulfonium salts were furnished by this method, albeit in modest yields (from 39% to 61%).

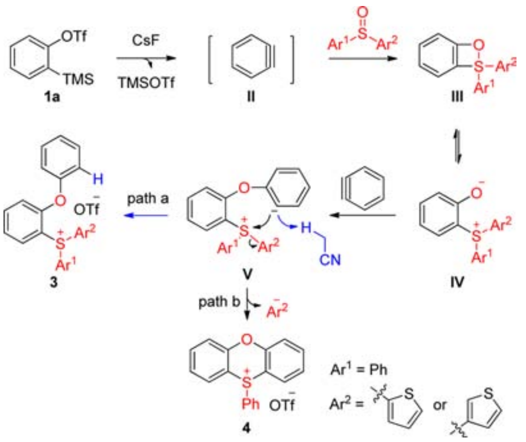
To probe the mechanism of the reaction, the labeling and control experiments were performed (Scheme 5). When the reaction of **1a** with **2a** was conducted in CD$_3$CN, a mixture of **3aa** and **d-3aa** was obtained in a ratio of 55/45 (**3aa**/**d-3aa**) (Scheme 3, eq 5). The deuterium atom in CD$_3$CN was introduced to the phenoxyl group of **3aa** in its *ortho* position. The corresponding proton from unlabeled-**3aa** might be contributed by the small amount of MeCN (CD$_3$CN, Isotopic Enrichment, 99.8%) or a trace amount of water. Using a mixture of MeCN/CD$_3$CN (1/1) as solvent exclusively led to the formation of **3aa** (eq 6). These results suggest that the protonation occurred at the *ortho* position of phenoxyl group should be a rate-determining step in the reaction. Furthermore, a controlled reaction of **1a** with a mixture of **2c** and **2f** (1/1) was performed (eq 7). Consistent with the previous findings (Scheme 2, **3ac** vs **3af**), benzyne preferentially reacts with the electron-rich aryl sulfoxide **2c**.

Scheme 5. Labeling and Control Experiments



With the obtained results in hand, we tentatively proposed a mechanism for the transformation (Scheme 6).[6a−d] First, Kobayashi precursor **II** is formed by treating **1a** with CsF. Then a rapid [2 + 2] cycloaddtion of diaryl sulfoxide **2** to benzyne affords the intermediate **III**. The ring strain in the four-membered ring of **III** allows for its ring opening to furnish the 1,4-zwitterionic intermediate **IV**. The oxygen anion of **IV** traps another benzyne to give the sulfonium intermediate **V**. The phenyl anion of **V** is quenched by acetonitrile or other proton sources to produce the final product **3** (path a). Instead of path a, the intermediate **V** from the aryl/heteroaryl sulfoxides **2o** and **2p** may undergo an intramolecular nucleophilic substitution, leading to triarylsulfonium **4** (path b). Path b is also supported by the fact that the released thiophene moiety was determined by GC−MS.[15]

Scheme 6. Possible Mechanism



In conclusion, we have developed a facile method for the synthesis of *o*-aryloxy triarylsulfonium salts by simply treating benzyne with diaryl sulfoxides. This reaction can be performed under mild conditions provides a wide range of triarylsulfonium compounds in good to excellent yields. Electron-rich diaryl sulfoxides were found to be more reactive than the electron-poor ones. The bulky aryl sulfoxides **2i** and **2k** are nicely tolerated in the reaction. Preliminary mechanistic studies suggest that a sequential [2 + 2] cycloaddition/*O*-arylation/protonation process might be involved in the reaction. Further applications of the obtained *o*-aryloxy triarylsulfonium salts are ongoing in our group.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03840.

Experimental procedures and characterization data (PDF)
X-ray data for **3aa** (CIF)

X-ray data for **4** (CIF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: pengbo@zjnu.cn.

ORCID

Bo Peng: 0000-0002-8237-6698

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work is supported by Zhejiang Normal University, the National Natural Science Foundation of China (Grant No. 21502171), and the State Key Laboratory of Fine Chemicals (KF 1512).

REFERENCES

(1) (a) Yoshida, S.; Hosoya, T. *Chem. Lett.* **2015**, *44*, 1450. (b) Dubrovskiy, A. V.; Markina, N. A.; Larock, R. C. *Org. Biomol. Chem.* **2013**, *11*, 191. (c) Wu, C.; Shi, F. *Asian J. Org. Chem.* **2013**, *2*, 116. (d) Bhunia, A.; Yetra, S. R.; Biju, A. T. *Chem. Soc. Rev.* **2012**, *41*, 3140. (e) Sanz, R. *Org. Prep. Proced. Int.* **2008**, *40*, 215. (f) Wenk, H. H.; Winkler, M.; Sander, W. *Angew. Chem., Int. Ed.* **2003**, *42*, 502.

(2) (a) Goetz, A. E.; Shah, T. K.; Garg, N. K. *Chem. Commun.* **2015**, *51*, 34. (b) Gampe, C. M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3766. (c) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**, *112*, 3550. (d) Pellissier, H.; Santelli, M. *Tetrahedron* **2003**, *59*, 701.

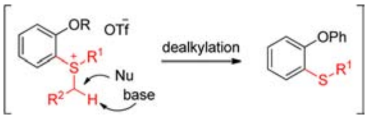
(3) For selected reviews, see: (a) Peña, D.; Pérez, D.; Guitián, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 3579. (b) Okuma, K. *Heterocycles* **2012**, *85*, 515. (c) Yoshida, H.; Takaki, K. *Synlett* **2012**, *23*, 1725. (d) Yoshioka, E.; Miyabe, H. *Tetrahedron* **2012**, *68*, 179. (e) Miyabe, H. *Curr. Org. Chem.* **2015**, *19*, 1222.

(4) For recent examples of aryne insertion into σ bonds, see: (a) Wright, A. C.; Haley, C. K.; Lapointe, G.; Stoltz, B. M. *Org. Lett.* **2016**, *18*, 2793. (b) Rao, B.; Tang, J.; Zeng, X. *Org. Lett.* **2016**, *18*, 1678. (c) Samineni, R.; Srihari, P.; Mehta, G. *Org. Lett.* **2016**, *18*, 2832. (d) Pawliczek, M.; Garve, L. K. B.; Werz, D. B. *Org. Lett.* **2015**, *17*, 1716. (e) Rao, B.; Zeng, X. *Org. Lett.* **2014**, *16*, 314. (f) Fang, Y.; Rogness, D. C.; Larock, R. C.; Shi, F. *J. Org. Chem.* **2012**, *77*, 6262. (g) Łaczkowski, K. Z.; García, D.; Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Org. Lett.* **2011**, *13*, 960.

(5) For recent examples of aryne insertion into π bonds, see: (a) Yoshioka, E.; Nishimura, M.; Nakazawa, T.; Kohtani, S.; Miyabe, H. *J. Org. Chem.* **2015**, *80*, 8464. (b) Yoshioka, E.; Tamenaga, H.; Miyabe, H. *Tetrahedron Lett.* **2014**, *55*, 1402. (c) Li, R.; Wang, X.; Wei, Z.; Wu, C.; Shi, F. *Org. Lett.* **2013**, *15*, 4366. (d) Yoshioka, E.; Kohtani, S.; Miyabe, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 6638. (e) Biswas, K.; Greaney, M. F. *Org. Lett.* **2011**, *13*, 4946. (f) Yoshida, H.; Watanabe, M.; Fukushima, H.; Ohshita, J.; Kunai, A. *Org. Lett.* **2004**, *6*, 4049.

(6) (a) Liu, F.-L.; Chen, J.-R.; Zou, Y.-Q.; Wei, Q.; Xiao, W.-J. *Org. Lett.* **2014**, *16*, 3768. (b) Li, Y.; Qiu, D.; Gu, R.; Wang, J.; Shi, J.; Li, Y. *J. Am. Chem. Soc.* **2016**, *138*, 10814. (c) Li, H.-Y.; Xing, L.-J.; Lou, M.-M.; Wang, H.; Liu, R.-H.; Wang, B. *Org. Lett.* **2015**, *17*, 1098. (d) Lou, M.-M.; Wang, H.; Song, L.; Liu, H.-Y.; Li, Z.-Q.; Guo, X.-S.; Zhang, F.-G; Wang, B. *J. Org. Chem.* **2016**, *81*, 5915. (e) Yoshida, S.; Yano, T.; Misawa, Y.; Sugimura, Y.; Igawa, K.; Shimizu, S.; Tomooka, K.; Hosoya, T. *J. Am. Chem. Soc.* **2015**, *137*, 14071. (f) Lopez-Leonardo, C.; Raja, R.; López-Ortiz, F.; del Águila-Sánchez, M. Á.; Alajarin, M. *Eur. J. Org. Chem.* **2014**, *2014*, 1084. (g) Alajarin, M.; Lopez-Leonardo, C.; Raja, R.; Orenes, R.-A. *Org. Lett.* **2011**, *13*, 5668. (h) Chakrabarty, S.; Chatterjee, I.; Tebben, L.; Studer, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 2968. (i) Chen, Z.; Wang, Q. *Org. Lett.* **2015**, *17*, 6130. (j) Hendrick, C. E.; Wang, Q. *J. Org. Chem.* **2015**, *80*, 1059. (k) Hendrick, C. E.; McDonald, S. L.; Wang, Q. *Org. Lett.* **2013**, *15*, 3444. (l) Yoshida, H.; Yoshida, R.; Takaki, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 8629. (m) Shen, C.; Yang, G.; Zhang, W. *Org. Lett.* **2013**, *15*, 5722. (n) Qi, N.; Zhang, N.; Allu, S. R.; Gao, J.; Guo, J.; He, Y. *Org. Lett.* **2016**, *18*, 6204.

(7) Plausible dealkylation of aryl alkyl sulfonium species:



(8) (a) Barker, I. A.; Dove, A. P. *Chem. Commun.* **2013**, *49*, 1205. (b) Versace, D.-L.; Dubot, P.; Cenedese, P.; Lalevée, J.; Soppera, O.; Malval, J.-P.; Renard, E.; Langlois, V. *Green Chem.* **2012**, *14*, 788. (c) Yoshida, E. *Polymers* **2012**, *4*, 1580. (d) Crivello, J. V. *Silicon* **2009**, *1*, 111. (e) Crivello, J. V. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 3820.

(9) (a) Jang, E.; Kwun, G.; Choi, W.; Lee, H. *Colloids Surf., A* **2008**, *313*, 383. (b) Jeon, S.; Malyarchuk, V.; Rogers, J. A.; Wiederrecht, G. P. *Opt. Express* **2006**, *14*, 2300. (c) Douvas, A.; Argitis, P.; Misiakos, K.; Dimotikali, D.; Petrou, P. S.; Kakabakos, S. E. *Biosens. Bioelectron.* **2002**, *17*, 269. (d) Ito, H. *Jpn. J. Appl. Phys.* **1992**, *31*, 4273.

(10) A review on the applications of triarylsulfonium salts: (a) Crivello, J. V. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 4241. For mechanistic studies on the photodecomposition of triarylsulfonium salts, see: (b) Dektar, J. L.; Hacker, N. P. *J. Chem. Soc., Chem. Commun.* **1987**, 1591. (c) Dektar, J. L.; Hacker, N. P. *J. Org. Chem.* **1988**, *53*, 1833.

(11) (a) Donck, S.; Baroudi, A.; Fensterbank, L.; Goddard, J.-P.; Ollivier, C. *Adv. Synth. Catal.* **2013**, *355*, 1477. (b) Mu, L.; Fischer, C. R.; Holland, J. P.; Becaud, J.; Schubiger, P. A.; Schibli, R.; Ametamey, S. M.; Graham, K.; Stellfeld, T.; Dinkelborg, L. M.; Lehmann, L. *Eur. J. Org. Chem.* **2012**, *2012*, 889. (c) Buijsen, P. F. A.; Hacker, N. P. *Tetrahedron Lett.* **1993**, *34*, 1557.

(12) The conventional synthesis of triarylsulfonium salts can be condensed into three types of reactions. For aryl group transfer from diaryliodonium salts to diaryl sulfides, see: (a) Racicot, L.; Kasahara, T.; Ciufolini, M. A. *Org. Lett.* **2014**, *16*, 6382. (b) Yanez, C. O.; Andrade, C. D.; Belfield, K. D. *Chem. Commun.* **2009**, 827. (c) Crivello, J. V.; Lam, J. H. W. *J. Org. Chem.* **1978**, *43*, 3055. For the nucleophilic addition of Grignard reagents to diaryl sulfoxides, see: (d) Imazeki, S.; Sumino, M.; Fukasawa, K.; Ishihara, M.; Akiyama, T. *Synthesis* **2004**, *2004*, 1648. (e) Miller, R. D.; Renaldo, A. F.; Ito, H. *J. Org. Chem.* **1988**, *53*, 5571. (f) Wildi, B. S.; Taylor, S. W.; Potratz, H. A. *J. Am. Chem. Soc.* **1951**, *73*, 1965. For the electrophilic activation of diaryl sulfoxides, see: (g) Yoo, J. B.; Park, S.-W.; Kang, H. N.; Mondkar, H. S.; Sohn, K.; Kim, H.-M.; Kim, K.-B.; Lee, H. *Polymer* **2014**, *55*, 3599. (h) Liu, G.; Mori, S.; Wang, X.; Noritake, S.; Tokunaga, E.; Shibata, N. *New J. Chem.* **2012**, *36*, 1769. (i) Akhtar, S. R.; Crivello, J. V.; Lee, J. L. *J. Org. Chem.* **1990**, *55*, 4222.

(13) In the course of the project, we found the reaction outcome relied heavily on the quality of anhydrous acetonitrile used in the reaction. Therefore, we investigated the influence of water on the reaction. For details, see the Supporting Information. For reported studies of the influence of H_2O in aryne transformations, see: (a) Dhokale, R. A.; Mhaske, S. B. *Org. Lett.* **2016**, *18*, 3010. (b) Feng, M.; Tang, B.; Wang, N.; Xu, H.-X; Jiang, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 14960.

(14) A descriptive example of a large-scale reaction (3 mmol) is provided in the Supporting Information.

(15) To determine the thiophene moiety, D_2O was introduced in the reaction of **2p**. Not surprisingly, deturated thiophene was indeed detected by GC−MS. For details, see the Supporting Information.

(16) (a) Zhou, Y.; Wang, J.; Gu, Z.; Wang, S.; Zhu, W.; Aceña, J. L.; Soloshonok, V. A.; Izawa, K.; Liu, H. *Chem. Rev.* **2016**, *116*, 422. (b) Tirotta, I.; Dichiarante, V.; Pigliacelli, C.; Cavallo, G.; Terraneo, G.; Bombelli, F. B.; Metrangolo, P.; Resnati, G. *Chem. Rev.* **2015**, *115*, 1106. (c) Marsh, E. N. G. *Acc. Chem. Res.* **2014**, *47*, 2878. (d) Chen, H.; Viel, S.; Ziarelli, F.; Peng, L. *Chem. Soc. Rev.* **2013**, *42*, 7971. (e) Berger, R.; Resnati, G.; Metrangolo, P.; Weber, E.; Hulliger, J. *Chem. Soc. Rev.* **2011**, *40*, 3496.