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Synthesis of Functionalized Triphenylenes via a Traceless Directing Group Strategy

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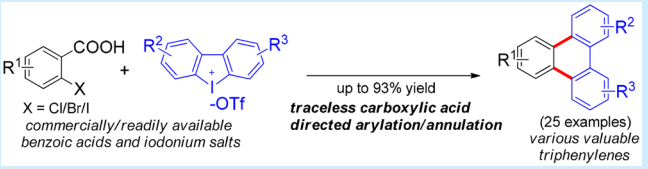
Supporting Information

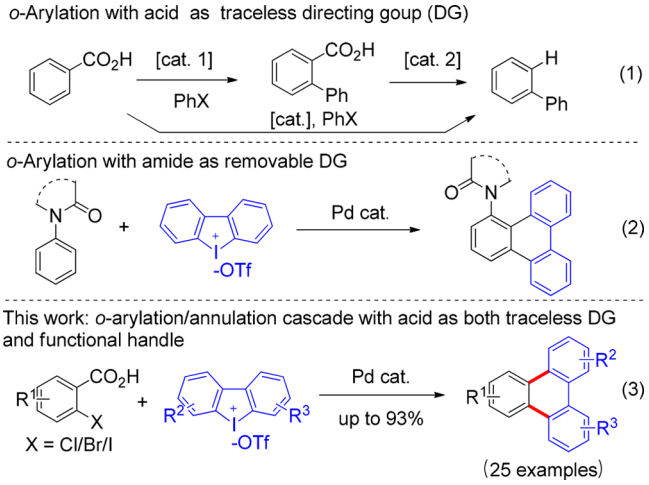
ABSTRACT: A novel ligand-free Pd-catalyzed cascade reaction between *o*-chlorobenzoic acids and cyclic diaryliodonium salts is reported. This one-pot procedure involves a carboxylic acid directed *o*-arylation followed by intramolecular decarboxylative annulation affording various valuable triphenylenes, which can be further transformed into diversified building blocks for material chemistry. For the first time, it was shown that an aromatic halide can react with diaryliodonium salts under the direction of carboxylic acid functionality. It was also demonstrated that the carboxylic acid could be employed as both a traceless directing group and functional handle for the atom- and step-economical one-pot double cross-coupling annulation reaction with cyclic diaryliodonium salts as the π-extending agents.



The use of abundant and diversified carboxylic acids for transition-metal catalyzed reactions is a fast growing area of research.[1] Pioneering work has well established the fact that the carboxylic acid functionality could be employed as either a functional handle to undergo *ipso*-decarboxylative cross-coupling reactions[2] or a removable/traceless directing group for *ortho* arene functionalization,[3] which requires no significant prefunctionalization and proceeds under catalytic conditions leading to dramatically streamlined syntheses of functionalized poly(hetero)aromatic compounds. Even though the possibilities encompassed by the traceless carboxylic acid directing group strategy are immense,[4] only a few classes of transformations on a small range of substrates have been explored to date.[5] Furthermore, in those examples, the carboxylic acid functionalities were simply removed via protodecarboxylation in situ or by another extra step,[5] and had not been employed as functional handles for further decarboxylative cross-coupling reactions (Scheme 1, eq 1).

Polycyclic aromatic hydrocarbons (PAHs), regarded as segments of infinite two-dimensional graphene, have been extensively exploited as potential candidates for optoelectronic devices and π-conjugated functional materials.[6] Among these, triphenylenes are the most often synthesized, by either aryne-based[7] or nonaryne-based[8] approaches, which however still suffer from different drawbacks, such as harsh conditions or limited substrate scopes, etc. Recently, Park and Hong reported a novel triphenylene synthesis by multiple C−H bond activations.[9] In this example, the amide functionality was employed as the directing group and remained in the triphenylenes after the reaction, thus limiting the structural diversity of the final products (Scheme 1, eq 2). Although the amide directing group can be removed, it does require extra steps and resources. This limitation can be overcome by employing traceless directing groups such as carboxylic acid functionality, which can be easily detached from the products in situ.[5]

Scheme 1. *O*-Arylation of Arenes via Directing Group Strategy



In continuation of our research interest in decarboxylative cross-coupling reactions[10] and cyclic diaryliodonium salt chemistry,[11−13] we would like to develop a novel and efficient method for the synthesis of various asymmetrical triphenylenes and their *N*-incorporated derivatives in an atom- and step-economical way[14] by employing the carboxylic acids as both traceless directing groups and functional handles, together with

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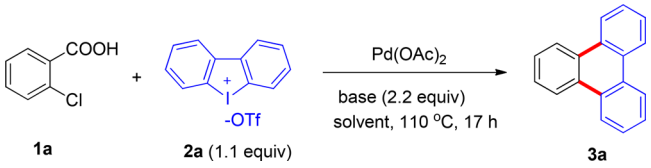
the cyclic diaryliodonium salts as the 1,4-dimetal equivalents for the double cross-coupling reactions (Scheme 1, eq 3). However, there are some problems to be solved. First, to our knowledge there is no report on the cross-coupling between the aromatic halides and diaryliodonium salts. Second, the carboxylic acid functionality might react with the cyclic diaryliodonium salt straightway via either *o*-arylation[13d,15] or decarboxylative arylation.[16] Third, even if the first carboxylic acid directed *o*-arylation step takes place successfully, the in situ protodecarboxylation[5] might occur to give the acyclic coupling compound as the final product, without the desired triphenylene product being formed from the intramolecular decarboxylative annulation.

We initiated the investigation by performing the reaction of the commercially available *o*-chloro benzoic acid **1a** with cyclic diaryliodonium salt **2a** under transition metal (TM) catalyzed conditions (Table 1).

Table 1. Reaction Optimization[a]



1a **2a** (1.1 equiv) **3a**

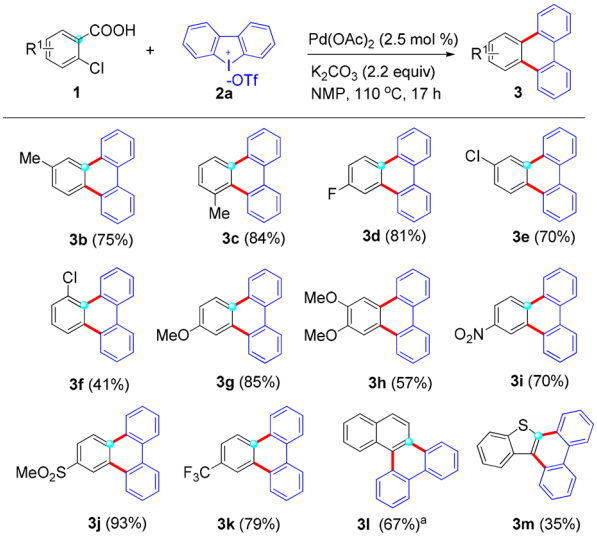
entry	$Pd(OAc)_2$ (mol %)	base	solvent[b]	yield (%)[c]
1[d]	10	$NaHCO_3$	DMF	30
2[d]	10	K_3PO_4	DMF	46
3[d]	10	Na_2CO_3	DMF	57
4[d]	10	K_2CO_3	DMF	66
5	10	K_2CO_3	DMF	67
6	—	K_2CO_3	DMF	—
7	10	K_2CO_3	DMA	58
8	10	K_2CO_3	DMSO	58
9	10	K_2CO_3	^{i}PrOH	—
10	10	K_2CO_3	DCE	—
11	10	K_2CO_3	NMP	74
12[e]	10	K_2CO_3	NMP	68
13[f]	10	K_2CO_3	NMP	69
14	5	K_2CO_3	NMP	74
15	2.5	K_2CO_3	NMP	81

[a]0.5 mmol scale. [b]Anhydrous solvent. [c]Isolated yields. [d]PPh_3 (20 mol %) was added. [e]Salt **2a** (0.8 equiv). [f]Salt **2a** (1.5 or 2.0 equiv).

After intensive screening of the catalytic systems (see Supporting Information), we are pleased to find the desired triphenylene **3a** could be obtained in 30% yield with $Pd(OAc)_2$ (10 mol %) as the catalyst, PPh_3 (20 mol %) as the ligand, and $NaHCO_3$ (2.2 equiv) as the base in DMF at 110 °C for 17 h (Table 1, entry 1). Next a base screening was carried out to optimize the yield (Table 1, entries 1−4), and it was found that the yield could be improved to 66% with K_2CO_3 as the base (Table 1, entry 4). The blank experiment showed that the reaction was still equally effective without the ligand (Table 1, entry 5). However, the control experiment run in the absence of the Pd catalyst was negative (Table 1, entry 6). The impact of the solvent was then investigated (Table 1, entries 7−11), and the product was isolated in 74% yield when NMP was used as the solvent (Table 1, entries 11). Fine tuning of the salt-to-acid ratio (Table 1, entries 12−13) and amount of the catalyst (Table 1, entries 14−15) provided the optimized product yield of 81% (Table, entry 15).

With the optimum conditions in hand, we next examined the scope of this novel acid directed *ortho*-arylation/decarboxylative annulation sequence using a range of commercially available *o*-chloro(hetero)aromatic acid derivatives (Table 2). Yields were

Table 2. Acid Substrate Scope



generally moderate to good for benzoic acids with simple alkyl substituents (**3b−c**). For the substrates with more than one chloro substituent on the aromatic ring, only one of the chlorines ortho to the carboxylic acid was reacted (**3d−f**), which demonstrated the essential directing effect of the acid functionality. The substrates with either electron-donating or -withdrawing groups were effective for the reaction (**3g−k**). Except in the case of the phenyl chloride, the 1-bomo-2-naphthoic acid also reacted well to give the benzo[*g*]chrysene **3l** in 67% yield. However, the 3-chlorobenzothiophene-2-carboxylic acid only afforded the benzo[*b*]phenanthro[9,10-*d*]thiophene **3m** in 35% yield probably due to catalyst poisoning by sulfur.

To fully establish the scopes of this one-pot annulation process, a range of substituted cyclic diaryliodonium salts were prepared according to Olofsson's method and subjected to the optimized reaction protocol with *ortho*-chloro benzoic acid derivatives (Table 3).[17] Initially we tested the reactions of symmetrical cyclic diaryliodonium salts with 2-chlorobenzoic acid or 2-chloro-5-substitutedbenzoic acids (**4a−f**), which afforded the corresponding products in moderate to good yields. Next, a series of unsymmetrical cyclic diaryliodonium salts were examined (**3d**, **4g−k**). It was found that both electron-donating and -withdrawing substituents on diaryliodonium salts were tolerated, although the yield was decreased when the unsymmetrical diaryliodonium salt with a strong electron-rich substituent was employed (**4j**).

In order to gain insight into this novel annulation process, we carried out the following control experiments (Scheme 2). First, when the *ortho*-chloro benzoic acid **1a** was reacted under the optimum conditions alone without the presence of cyclic diaryliodonium salts, the triphenylene product **3a** did not form at all. Furthermore, no cyclized product **5** was obtained by reacting the *ortho*-chloro benzoic acid **1a** with 2-methylfuran (Scheme 2, eq 4), which showed that a benzyne mechanism as described by Larock for the synthesis of triphenylene did not involve our annulation reaction.[7b] Except in the case of the *o*-

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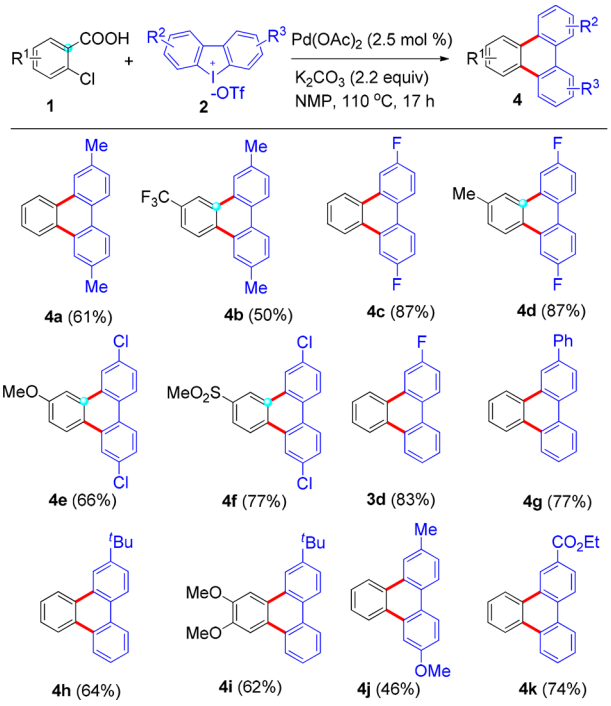
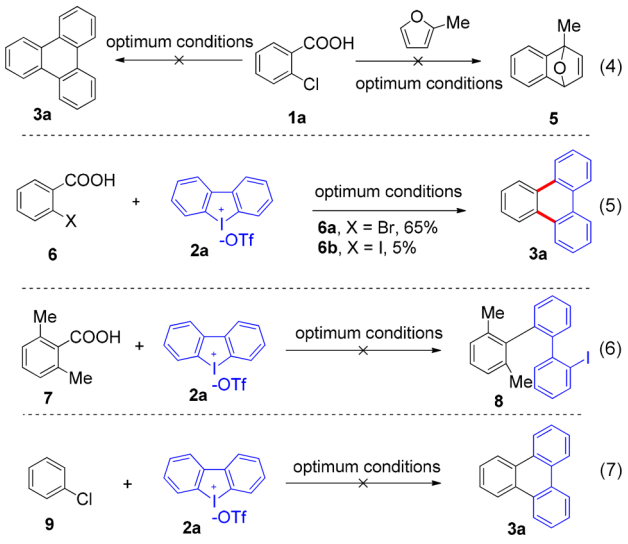
Table 3. Cyclic Diaryliodonium Salt Scope



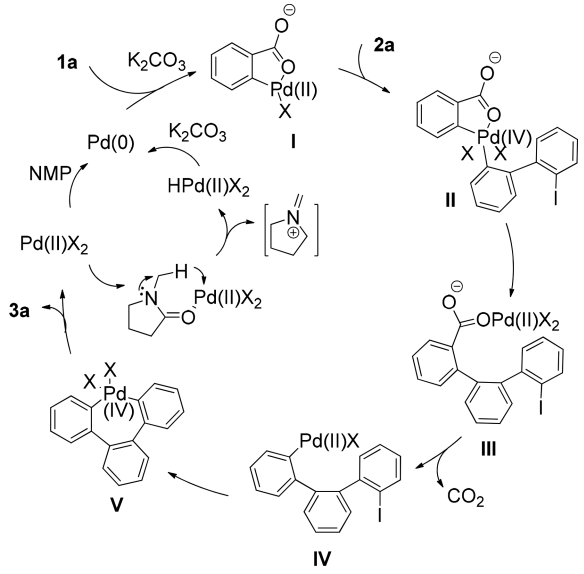
Scheme 2. Control Experiments



chlorobenzoic acid **1a**, the *o*-bromobenzoic acid **6** also reacted well giving the triphenylene **3a** in 65% yield (Scheme 2, eq 5). However, under the above optimum conditions the *o*-iodobenzoic acid **6b** only afforded the desired product **3a** in poor yield (unoptimized). By reacting the 2,6-dimethylbenzoic acid **7** with the cyclic diaryliodonium salt **2a** under the optimum conditions (Scheme 2, eq 6), the decarboxylative arylated product **8** was not obtained, which indicated that our reaction requires a synergistic effect of both carboxylic acid and *ortho*-chlorine. Finally, it was found that no reaction took place between chlorobenzene **9** and diaryliodonium salt **2a** under the optimum conditions (Scheme 2, eq 7), which demonstrates the essential directing effect of carboxylic acid.

Based on the above experiments and previous literature,[8d,18] an acid directed *ortho*-arylation followed by an intramolecular decarboxylative arylation/cyclization pathway might operate in our annulation reaction (Scheme 3). First, a five-membered

Scheme 3. Proposed Reaction Pathway



Pd(II) complex **I** might be formed from the *ortho*-chlorobenzoic acid **1a**, which then attacks the cyclic diaryliodonium salt **2a** to give the Pd (IV) complex **II**. A reductive elimination followed by decarboxylation affords the Pd coordinated polyphenyl iodide **IV** which can be cyclized to give the seven-membered Pd(IV) complex **V**. Finally, a reductive elimination releases the triphenylene product **3a** and Pd(OTf)I, which could be reduced under the reaction conditions to give the Pd(0) catalyst for the next catalytic cycle.[19]

Compared with their all-hydrocarbon analogues, *N*-incorporated triphenylenes which exhibit unprecedented chemical and physical properties have been far less studied because of their limited accessibility.[20] By reacting 5-amino-2-chlorobenzoic acid **10** with cyclic diaryliodonium salt **2a** under optimum conditions at 110 °C, interestingly the carbazolyl substituted triphenylene **11** was obtained in 33% yield, which can be used as an organic electronic device.[21] By conducting the reaction at 145 °C in the presence of 2.5 equiv amounts of diaryliodoniym salt **2a**, the yield of compound **11** could be improved to 81% (Scheme 4, eq 8). However, if 6-amino-2-chlorobenzoic acid **12** was treated with cyclic diaryliodonium salt **2a** under the optimum conditions at 110 °C, the 1-amino triphenylene **13** was obtained in 46% yield along with 10% *N*-arylated triphenylene **14** (Scheme 4, eq 9), which did not cyclize to form the carbazole probably due to the nearby steric hindrance. By conducting the reaction at 145 °C in the presence of 2.5 equiv amounts of diaryliodoniym salt **2a**, the yield of compound **13** could be improved to 65%. To demonstrate the applicability of our novel triphenylene synthetic method, we managed to convert the substituted triphenylene **13** to different *N*-incorporated PAHs successfully. After a simple protection, the *N*-substituted triphenylene **15** was obtained which could be applied to a field-effect transistor sensor for rapid, sensitive, and reversible alcohol vapor detection (Scheme 4, eq 9).[9] The *N*-substituted triphenylene **15** could be cyclized to give the polycyclic product **16**, with possibly improved physicochemical properties for applications as organic electronics.[20] Treated

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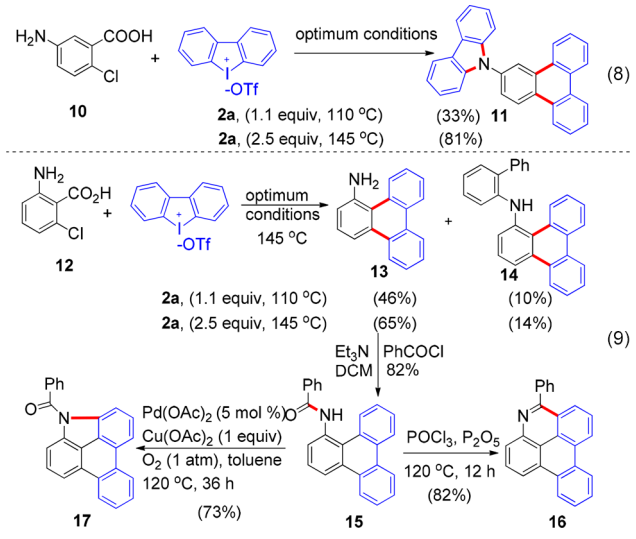
Scheme 4. Synthesis of Amino Substituted Triphenylenes and Further Transformations into *N*-Incorporated PAHs



compound **15** with Pd-catalyzed conditions afforded the 4-substituted naphtho[1,2,3,4-*def*]carbazole **17** in 73% yield, which could be applied for the synthesis of an azafullerene-based organic solar cell.[22] In addition, according to Shao's two-step procedure the triphenylene frameworks could be converted to trichalcogenasumanenes, a new buckybowl system with interesting features for coordination chemistry as well as electronic materials.[23]

In summary, we have developed a general and efficient one-pot procedure for the synthesis of functionalized triphenylenes from readily available starting materials. The valuable triphenylenes can be further transformed into diversified building blocks for material chemistry. For the first time, we showed that aromatic halide can react with diaryliodonium salts under the direction of carboxylic acid. The key for this novel method is the unprecedented employment of carboxylic acid as both a traceless directing group and functional handle, together with the cyclic diaryliodonium salts as the 1,4-dimetal equivalents for the one-pot double cross-coupling reaction.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b00071.

Experimental procedures and spectroscopic characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For reviews, see: (a) Baudoin, O. *Angew. Chem., Int. Ed.* **2007**, *46*, 1373−1375. (b) Bonesi, S. M.; Fagnoni, M.; Albini, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 10022−10025. (c) Goossen, L. J.; Rodriguez, N.; Goossen, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 3100−3120.

(2) For reviews, see: (a) Rodríguez, N.; Goossen, L. J. *Chem. Soc. Rev.* **2011**, *40*, 5030−5048. (b) Shang, R.; Liu, L. *Sci. China: Chem.* **2011**, *54*, 1670−1687. (c) Cornella, J.; Larrosa, I. *Synthesis* **2012**, *44*, 653−676. (d) Wei, Y.; Hu, P.; Zhang, M.; Su, W. *Chem. Rev.* **2017**, *117*, 8864−8907 and references therein.

(3) (a) Cornella, J.; Righi, M.; Larrosa, I. *Angew. Chem., Int. Ed.* **2011**, *50*, 9429−9432. (b) Luo, J.; Preciado, S.; Larrosa, I. *J. Am. Chem. Soc.* **2014**, *136*, 4109−4112. (c) Huang, L.; Hackenberger, D.; Gooßen, L. J. *Angew. Chem., Int. Ed.* **2015**, *54*, 12607−12611. (d) Zhang, Y.; Zhao, H.; Zhang, M.; Su, W. *Angew. Chem., Int. Ed.* **2015**, *54*, 3817−3821. (e) Qin, X.; Sun, D.; You, Q.; Cheng, Y.; Lan, J.; You, J. *Org. Lett.* **2015**, *17*, 1762−1765.

(4) For reviews, see: (a) Rousseau, G.; Breit, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 2450−2494. (b) Zhang, F.; Spring, D. R. *Chem. Soc. Rev.* **2014**, *43*, 6906−6919 and references therein.

(5) Font, M.; Quibell, J. M.; Perry, G. J. P.; Larrosa, I. *Chem. Commun.* **2017**, *53*, 5584−5597.

(6) (a) Watson, M. D.; Fechtenkotter, A.; Mullen, K. *Chem. Rev.* **2001**, *101*, 1267−1300. (b) Boden, N.; Bissell, N.; Clements, J.; Movaghar, B. *Liq. Cryst. Today* **1996**, *6*, 1−4.

(7) (a) Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Angew. Chem., Int. Ed.* **1998**, *37*, 2659−2661. (b) Liu, A.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2005**, *127*, 15716−15717. (c) Jayanth, T. T.; Cheng, C.-H. *Chem. Commun.* **2006**, 894−896. (d) Cant, A. A.; Roberts, L.; Greaney, M. F. *Chem. Commun.* **2010**, *46*, 8671−8673. (e) Pérez, D.; Peña, D.; Guitián, E. *Eur. J. Org. Chem.* **2013**, *2013*, 5981−6013 and references therein.

(8) (a) Nagao, I.; Shimizu, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 7573−7576. (b) Kumar, B.; Strasser, C. E.; King, B. *J. Org. Chem.* **2012**, *77*, 311−316. (c) Iwasaki, M.; Iino, S.; Nishihara, Y. *Org. Lett.* **2013**, *15*, 5326−5329. (d) Iwasaki, M.; Araki, Y.; Nishihara, Y. *J. Org. Chem.* **2017**, *82*, 6242−6258. (e) Wu, Y.; Peng, X.; Luo, B.; Wu, F.; Song, F.; Huang, P.; Wen, S. *Org. Biomol. Chem.* **2014**, *12*, 9777−9780. (f) Iwasaki, M.; Araki, Y.; Iino, S.; Nishihara, Y. *J. Org. Chem.* **2015**, *80*, 9247−9263. (g) Vasu, D.; Yorimitsu, H.; Osuka, A. *Angew. Chem., Int. Ed.* **2015**, *54*, 7162−7166. (h) Ozaki, K.; Kawasumi, K.; Shibata, M.; Ito, H.; Itami, K. *Nat. Commun.* **2015**, *6*, 6251. (i) Ozaki, K.; Matsuoka, W.; Ito, H.; Itami, K. *Org. Lett.* **2017**, *19*, 1930−1933. (j) Matsuoka, W.; Ito, H.; Itami, K. *Angew. Chem., Int. Ed.* **2017**, *56*, 12224−12228. (k) Koga, Y.; Kaneda, T.; Saito, Y.; Murakami, K.; Itami, K. *Science* **2018**, *359*, 435−439.

(9) Mathew, B. P.; Yang, H. J.; Kim, J.; Lee, B. J.; Kim, Y.-T.; Lee, S.; Lee, C. Y.; Choe, W.; Myung, K.; Park, J.-U.; Hong, S. Y. *Angew. Chem., Int. Ed.* **2017**, *56*, 5007−5011.

(10) (a) Zhang, F.; Greaney, M. F. *Angew. Chem., Int. Ed.* **2010**, *49*, 2768−2771. (b) Zhang, F.; Greaney, M. F. *Org. Lett.* **2010**, *12*, 4745−4747.

(11) For reviews about linear iodonium salts, see: (a) Merritt, E. A.; Olofsson, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 9052−9070. (b) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299−5358. (c) Wang, X.; Studer, A. *Acc. Chem. Res.* **2017**, *50*, 1712−1724 and references therein.

(12) For reviews about cyclic iodonium salts, see: (a) Grushin, V. V. *Chem. Soc. Rev.* **2000**, *29*, 315. (b) Chatterjee, N.; Goswami, A. *Eur. J. Org. Chem.* **2017**, *2017*, 3023−3032.

(13) For very recent work on cyclic diaryliodinum salt chemistry, see: (a) Wang, M.; Wei, J.; Fan, Q.; Jiang, X. *Chem. Commun.* **2017**, *53*, 2918−2921. (b) Peng, X.; Luo, H.; Wu, F.; Zhu, D.; Ganesan, A.; Huang, P.; Wen, S. *Adv. Synth. Catal.* **2017**, *359*, 1152−1156. (c) Xie,

DOI: 10.1021/acs.orglett.8b00071
Org. Lett. XXXX, XXX, XXX−XXX

H.; Ding, M.; Liu, M.; Hu, T. *Org. Lett.* **2017**, *19*, 2600−2603. (d) Xie, H.; Yang, S.; Zhang, C.; Ding, M.; Liu, M.; Guo, J.; Zhang, F. *J. Org. Chem.* **2017**, *82*, 5250−5262.
(14) (a) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 131−163. (b) Zhang, C.; Liu, M.; Ding, M.; Xie, H.; Zhang, F. *Org. Lett.* **2017**, *19*, 3418−3421.
(15) Petersen, T. B.; Khan, R.; Olofsson, B. *Org. Lett.* **2011**, *13*, 3462−3465.
(16) Becht, T.-M.; Drian, C. L. *Org. Lett.* **2008**, *10*, 3161−3164.
(17) Bielawski, M.; Olofsson, B. *Chem. Commun.* **2007**, *24*, 2521−2523.
(18) Wu, Z.; Chen, S.; Hu, C.; Li, Z.; Xiang, H.; Zhou, X. *ChemCatChem* **2013**, *5*, 2839−2842.
(19) Brenda, M.; Knebelkamp, A.; Greiner, A.; Heitz, W. *Synlett* **1991**, *1991*, 809 and references therein..
(20) (a) Wei, J.; Han, B.; Guo, Q.; Shi, X.; Wang, W.; Wei, N. *Angew. Chem., Int. Ed.* **2010**, *49*, 8209−8213. (b) McTiernan, C. D.; Leblanc, X.; Scaiano, J. C. *ACS Catal.* **2017**, *7*, 2171−2175.
(21) Lee, K.-M.; Huh, D.-H.; Ryu, D.-W.; Jung, S.-H.; Chae, M.-Y. Cheil Industries Inc., S. Korea, PCT Int. Appl., 2011152596.
(22) Cambarau, W.; Fritze, U. F.; Viterisi, A.; Palomares, E.; von Delius, M. *Chem. Commun.* **2015**, *51*, 1128−1130.
(23) (a) Amaya, T.; Wang, W.-Z.; Sakane, H.; Hirao, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 403−406. (b) Li, X.; Zhu, Y.; Shao, J.; Wang, B.; Zhang, S.; Shao, Y.; Jin, X.; Yao, X.; Fang, R.; Shao, X. *Angew. Chem., Int. Ed.* **2014**, *53*, 535−538.

DOI: 10.1021/acs.orglett.8b00071
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