JOC The Journal of Organic Chemistry

Article

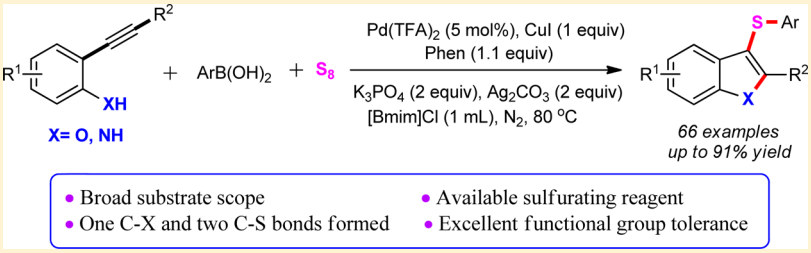
pubs.acs.org/joc

Assembly of 3-Sulfenylbenzofurans and 3-Sulfenylindoles by Palladium-Catalyzed Cascade Annulation/Arylthiolation Reaction

Jianxiao Li,[†] Chunsheng Li,[†] Shaorong Yang,[†] Yanni An,[†] Wanqing Wu,*[,†,‡] and Huanfeng Jiang*[,†]

[†]School of Chemistry and Chemical Engineering and [‡]State Key Laboratory of Luminescent Materials and Devices, South China University of Technology, Guangzhou 510640, China

Supporting Information



ABSTRACT: A novel and efficient palladium-catalyzed cascade annulation/arylthiolation reaction has been developed to afford functionalized 3-sulfenylbenzofuran and 3-sulfenylindole derivatives in moderate to good yields from readily available 2-alkynylphenols and 2-alkynylamines in ionic liquids. This protocol provides a valuable synthetic tool for the assembly of a wide range of 3-sulfenylbenzofuran and 3-sulfenylindole derivatives with high atom- and step-economy and exceptional functional group tolerance. Moreover, the employment of ionic liquids under mild reaction conditions makes this transformation green and practical. Furthermore, this approach enriched current C−S bond formation chemistry, making a valuable and practical method in synthetic and medicinal chemistry.

INTRODUCTION

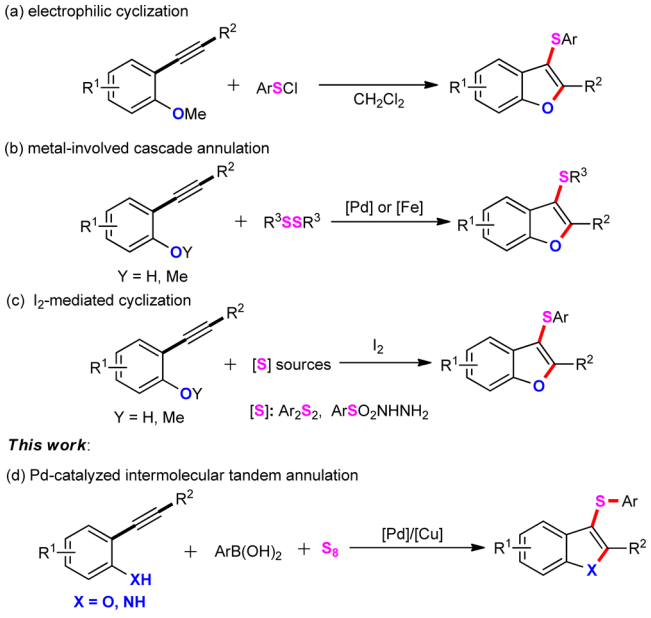
The development of general and efficient methods for the assembly of new chemical bonds is fundamental for vibrant fields in both academic and industrial processes.[1] Prominently, transition metal-catalyzed transformations have emerged as a powerful tool for the efficient construction of carbon−heteroatom bonds and, hence, have become the most attractive and versatile methods in contemporary organic synthesis.[2] In this regard, as one of the most important carbon−heteroatom bonds in organic chemistry, C−S bonds are frequently found in many important pharmaceuticals and biologically active natural compounds.[3] In recent years, many representative methods have been developed for constructing C−S bonds. Generically, three strategies are typically employed: (i) coupling of vinyl/aryl halides with sulfenylating sources, such as thiols, sulfonyl chlorides, disulfides, and other activated sulfurating reagents;[4] (ii) coupling of alkyl- and aryllithium or Grignard reagents with diphenyldisulfides, thiosulfonates, and sulfur;[5] and (iii) direct arylthiolation of C−H bonds with sulfurating reagents.[6] Despite these significant advances, all of these elegant developments suffer from certain limitations, such as prefunctionalized reactants, stringent reaction conditions, or toxic and unstable sulfur sources, which lower the synthetic efficiency and generality. As a consequence, the development of efficient and atom economical synthetic methods for the rapid and straightforward construction of C−S bonds is still highly desirable.

In addition, among the family of benzofurans, 2,3-difunctionalized benzofurans are attractive synthetic targets because of their remarkable biological activities and potential for becoming pharmaceuticals,[7] prompting the development of many efficient synthetic methods for constructing this scaffold.[8] However, the straightforward synthesis of 2-substituted 3-sulfenylbenzofurans from readily accessible starting materials has been scarcely explored. Recent achievements for the construction of 3-sulfenylbenzofuran scaffolds mainly include (i) electrophilic cyclization of 2-alkynylphenol derivatives with sulfurating reagents (Scheme 1a),[9] (ii) metal-involved cascade annulation of 2-alkynylphenol derivatives with disulfides (Scheme 1b),[10] and (iii) I_2-mediated cyclization of 2-alkynylanisoles with sulfurating reagents (Scheme 1c).[11] Nevertheless, these approaches require foul-smelling, toxic, and unstable sulfur sources as starting materials. From the viewpoint of synthetic simplicity as well as a new practical and environmentally benign process, the synthesis of 3-sulfenylbenzofurans via a transition metal-catalyzed cascade annulation reaction would be an ideal strategy. More recently, we reported an efficient and ecofriendly method for the construction of 2,3-difunctionalized benzofuran derivatives in moderate to good yields from readily available 2-alkynylphenols in ionic liquids.[12] Inspired by the aforementioned background and our long-standing interest in Pd-catalyzed cross-coupling reactions in

Received: January 24, 2016
Published: March 15, 2016

DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

Scheme 1. Representative Strategies for the Synthesis of 3-Sulfenylbenzofurans



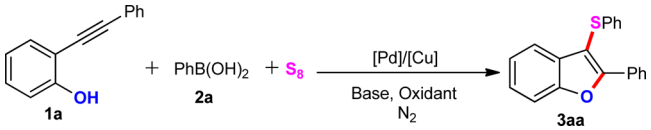
ionic liquids,[13] herein we disclose an efficient and concise route for the synthesis of 3-sulfenylbenzofurans and 3-sulfenylindoles via nucleopalladation triggering an intermolecular cascade reaction in ionic liquids (Scheme 1d).

RESULTS AND DISCUSSION

To begin our investigation, 2-(phenylethynyl)phenol (**1a**), phenylboronic acid (**2a**), and elemental sulfur (S_8) were selected as a model system to screen the optimal conditions, and the results are summarized in Table 1. First, with the combination of $Pd(OAc)_2$ (5 mol %), CuI (1 equiv), Phen (1.1 equiv), BQ (2 equiv), and K_2CO_3 (2 equiv) in [Bmim]Cl (1 mL)[14] at 80 °C for 8 h, the desired sulfenylation product **3aa** was obtained in 27% GC yield (Table 1, entry 1). Further exploration of oxidants in the model reaction indicated that Ag_2CO_3 was superior to others (entries 1−4). Among the examination of palladium catalysts, other palladium catalysts, including $Pd(OAc)_2$, PdI_2, $PdCl_2$, $Pd(PhCN)_2Cl_2$, and $[Pd(n^3\text{-}C_3H_5)Cl]_2$, were inferior to $Pd(TFA)_2$ (entries 4−9). Subsequently, different copper salts were examined, including CuCl, CuBr, CuCN, and CuI, and CuI was the most effective catalyst for this transformation (entry 5). Except for K_3PO_4, other bases, including K_2CO_3, KF, Cs_2CO_3, Et_3N, and CsF, showed low efficiencies (entries 5, 14−18). Finally, the reaction without the use of a metal salt was found to be ineffective (entries 20 and 21).

After establishing the optimized reaction conditions, the generality and substrate scope of 2-alkynylphenol derivatives were investigated (Scheme 2). Gratifyingly, both electron-donating and -withdrawing substituents on the phenyl ring afforded the desired products in good yields (**3aa**−**3am**). Additionally, this transformation could be successfully extended to 2,4- and 3,4-disubstituted 2-alkynylphenols, furnishing the corresponding 3-sulfenylbenzofuran derivatives **3aj** and **3ak** in 83 and 73% yields, respectively. More bulky substrates, such as 2-((4′-propyl-[1,1′-biphenyl]-4-yl)ethynyl)phenol (**1l**) and 2-((4-(4-ethylcyclohexyl)phenyl)ethynyl)phenol (**1m**), also efficiently reacted with **2a** and gave the products **3al** and **3am** in

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	CuX	oxidant	base	conversion (%)[b]
1	$Pd(OAc)_2$	CuI	BQ	K_2CO_3	27
2	$Pd(OAc)_2$	CuI	DDQ	K_2CO_3	trace
3	$Pd(OAc)_2$	CuI	$AgNO_3$	K_2CO_3	46
4	$Pd(OAc)_2$	CuI	Ag_2CO_3	K_2CO_3	56
5	$Pd(TFA)_2$	CuI	Ag_2CO_3	K_2CO_3	78
6	PdI_2	CuI	Ag_2CO_3	K_2CO_3	23
7	$PdCl_2$	CuI	Ag_2CO_3	K_2CO_3	64
8	$Pd(PhCN)_2Cl_2$	CuI	Ag_2CO_3	K_2CO_3	34
9	$[Pd(n^3\text{-}C_3H_5)Cl]_2$	CuI	Ag_2CO_3	K_2CO_3	9
10	$Pd(TFA)_2$		Ag_2CO_3	K_2CO_3	
11	$Pd(TFA)_2$	CuCl	Ag_2CO_3	K_2CO_3	27
12	$Pd(TFA)_2$	CuBr	Ag_2CO_3	K_2CO_3	38
13	$Pd(TFA)_2$	CuCN	Ag_2CO_3	K_2CO_3	trace
14	$Pd(TFA)_2$	CuI	Ag_2CO_3	K_3PO_4	95(90)
15	$Pd(TFA)_2$	CuI	Ag_2CO_3	KF	65
16	$Pd(TFA)_2$	CuI	Ag_2CO_3	Cs_2CO_3	79
17	$Pd(TFA)_2$	CuI	Ag_2CO_3	Et_3N	28
18	$Pd(TFA)_2$	CuI	Ag_2CO_3	CsF	69
19[c]	$Pd(TFA)_2$	CuI	Ag_2CO_3	K_3PO_4	94
20		CuI	Ag_2CO_3	K_3PO_4	
21	$Pd(TFA)_2$		Ag_2CO_3	K_3PO_4	

[a]Reactions were performed with **1a** (0.10 mmol), **2a** (0.15 mmol), S_8 (0.30 mmol), catalyst (5 mol %), CuX (0.20 mmol), Phen (1,10-phenanthroline, 0.22 mmol), oxidant (0.2 mmol), base (0.2 mmol), and [Bmim]Cl (1-butyl-3-methylimidazolium chloride, 1 mL) at 80 °C for 8 h. BQ = 1,4-benzoquinone. [b]Determined by GC using dodecane as the internal standard. The value in parentheses is the yield of isolated product. [c]At 100 °C.

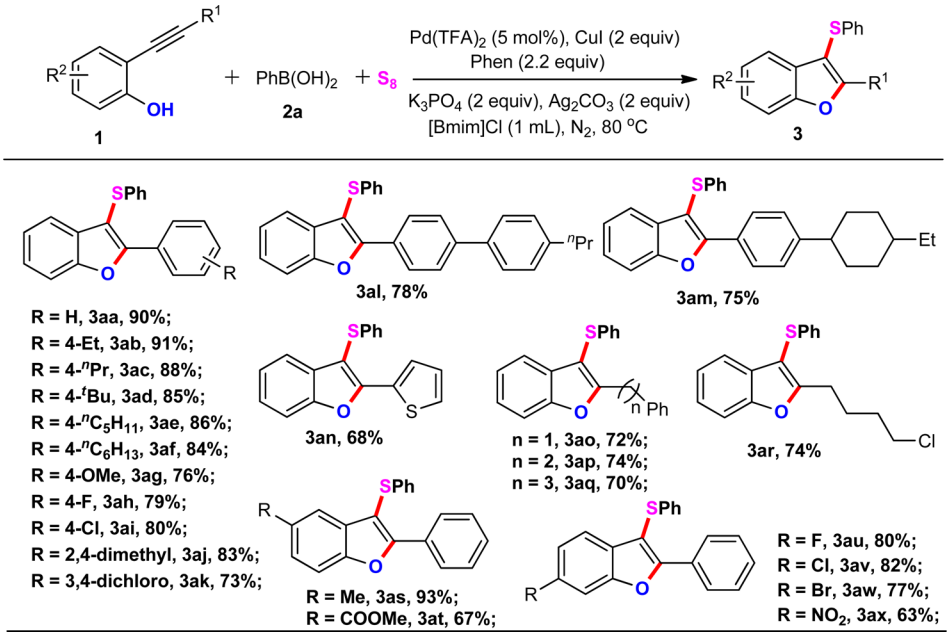
78 and 75% yields, respectively. Importantly, an impressive feature of the current cascade annulation/arylthiolation reaction is its high tolerance for functional groups. For instance, the 2-alkynylphenols containing a thienyl group underwent the cascade reaction to give the corresponding product **3an** in 68% yield. Notably, 2-alkynylphenols **1** with alkyl groups attached on the triple bond proceeded smoothly to give the products **3** in moderate to good yields (**3ao**−**3ar**). Delightfully, various substituted 2-alkynylphenols with electron-donating groups (Me) and weakly or moderately electron-withdrawing groups (F, Cl, Br, COOMe, NO_2) afforded the corresponding 3-sulfenylbenzofuran derivatives **3as**−**3ax** in moderate to excellent yields.

Subsequently, for further demonstrating the synthetic potential of this method, various arylboronic acid derivatives were introduced to this cascade reaction (Scheme 3). Various substituents of arylboronic acid, such as methyl, methoxyl, halo, and nitro groups were tolerated well, allowing the generation of a range of 3-sulfenylbenzofuran derivatives in moderate yields (**3ba**−**3bh**).

As mentioned previously, 3-sulfenylindoles could be synthesized by 2-alkynylanilines with disulfides.[15] Gratifyingly, 3-sulfenylindoles could also be constructed via the cascade annulation/arylthiolation of 2-(phenylethynyl)aniline derivatives with phenylboronic acid **2a**. As illustrated in Scheme 4,

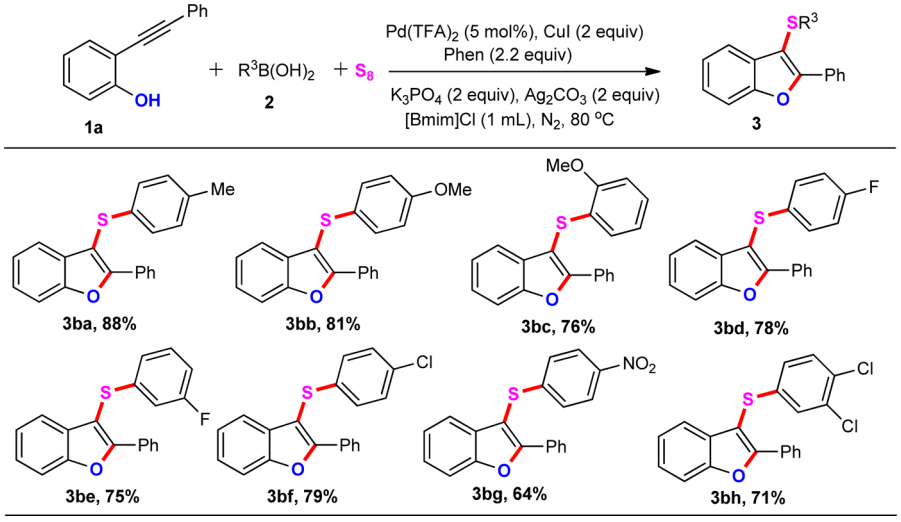
DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

Scheme 2. Cascade Annulation/Arylthiolation of 2a with Various 2-Alkynylphenols[a]



[a]Reaction conditions: **1** (0.20 mmol), **2a** (0.4 mmol), S_8 (0.60 mmol), $Pd(TFA)_2$ (5 mol %), CuI (0.40 mmol), Phen (0.44 mmol), Ag_2CO_3 (0.4 mmol), K_3PO_4 (0.4 mmol), and [Bmim]Cl (1 mL) at 80 °C for 8 h; yields refer to isolated yield.

Scheme 3. Cascade Annulation/Arylthiolation of 1a with Various Arylboronic Acid Derivatives[a]



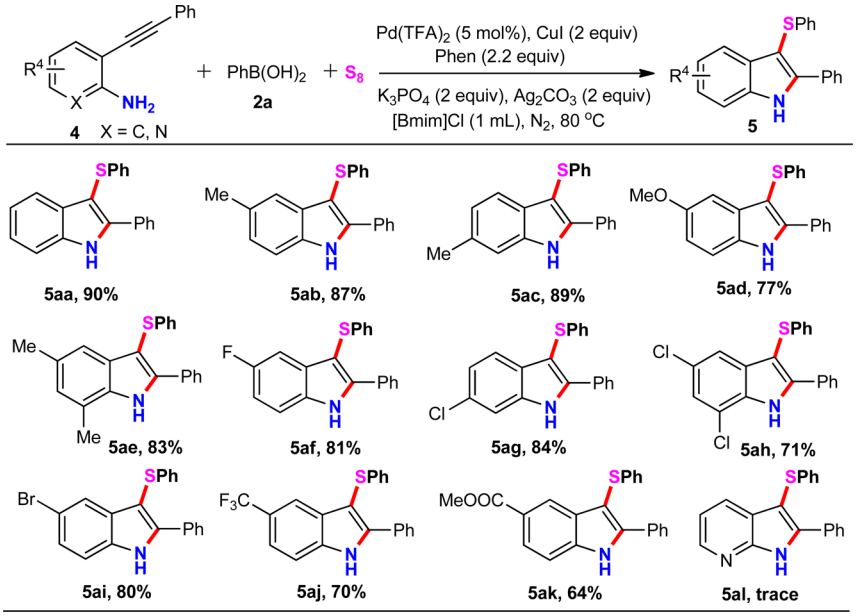
[a]Reaction conditions: **1a** (0.20 mmol), **2** (0.4 mmol), S_8 (0.60 mmol), $Pd(TFA)_2$ (5 mol %), CuI (0.40 mmol), Phen (0.44 mmol), Ag_2CO_3 (0.4 mmol), K_3PO_4 (0.4 mmol), and [Bmim]Cl (1 mL) at 80 °C for 8 h; yields refer to isolated yield.

anilines with electron-rich substituents (Me, OMe) or electron-poor substituents (F, Cl, Br, CF_3, COOMe) all gave the desired products in satisfactory yields (**5aa**−**5ak**). Moreover, substitution position of the aromatic ring had just a slight impact (**5ab**, **5ac**, and **5ae**). These results showed that this new transformation was tolerant toward the electronic and steric effects of the aromatic ring. However, when 3-(phenylethynyl)-pyridin-2-amine (**4l**) was subjected to the standard reaction conditions, only a trace amount of the desired product **5al** was detected by GC-MS.

For exploring the generality and scope of this method further, a wide array of 2-alkynylamines were examined, and the results are summarized in Scheme 5. A range of functional groups on the arylalkynyl moiety, including *p*-Me, *p*-OMe, and *p*-Cl, was tolerated under the standard reaction conditions (**5ba**−**5bc**). Unfortunately, only trace desired product was detected by GC-MS when 2-((4-nitrophenyl)ethynyl)aniline (**4b**) was used as the substrate. Furthermore, 2-alkynylamines **4** with alkyl groups attached on the triple bond also proceeded well to give products **5** in moderate to good yields (**5be**−**5bo**). Gratifyingly, the substrates containing three-, five- or six-membered-ring-substituted 2-alkynylamines proceeded smoothly under the optimized conditions to afford the corresponding products in high yields (**5be**−**5bi**). It is noteworthy that, with the carbon chain of alkyl groups extended, the 3-sulfenylindole derivatives **5bj**−**5bo** were successfully obtained in good to excellent yields. Notably, 2-alkynylamines containing vinyl or thienyl groups were well-

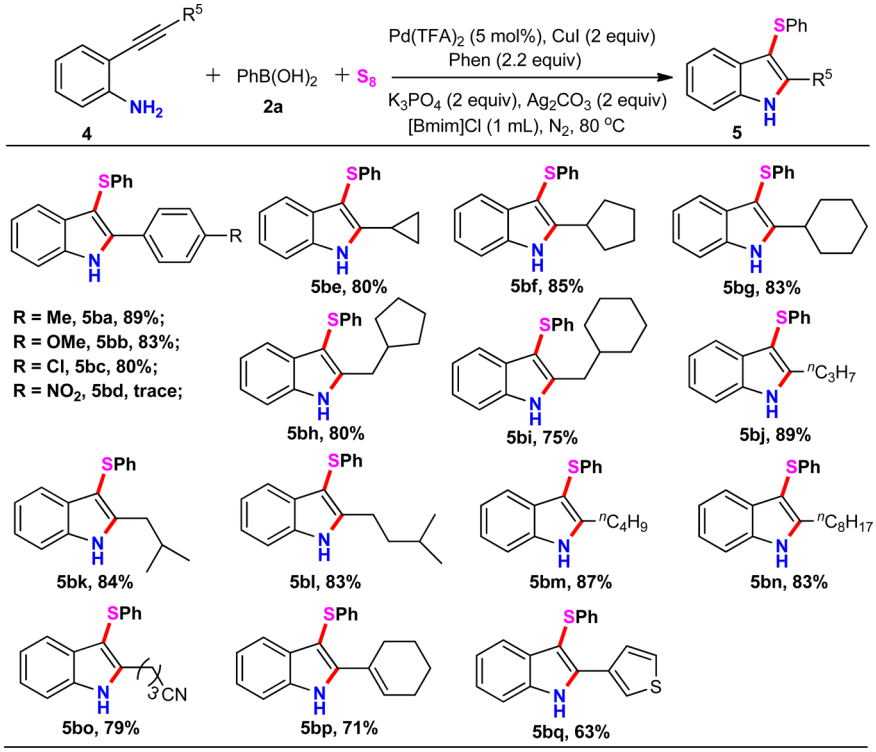
DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

Scheme 4. Substrate Scope of 2-Alkynyl Arylamines[a]



[a]Reaction conditions: **4** (0.20 mmol), **2a** (0.4 mmol), S_8 (0.60 mmol), $Pd(TFA)_2$ (5 mol %), CuI (0.40 mmol), Phen (0.44 mmol), Ag_2CO_3 (0.4 mmol), K_3PO_4 (0.4 mmol), and [Bmim]Cl (1 mL) at 80 °C for 8 h; yields refer to isolated yield.

Scheme 5. Substrate Scope of 2-Alkynyl Arylamines[a]



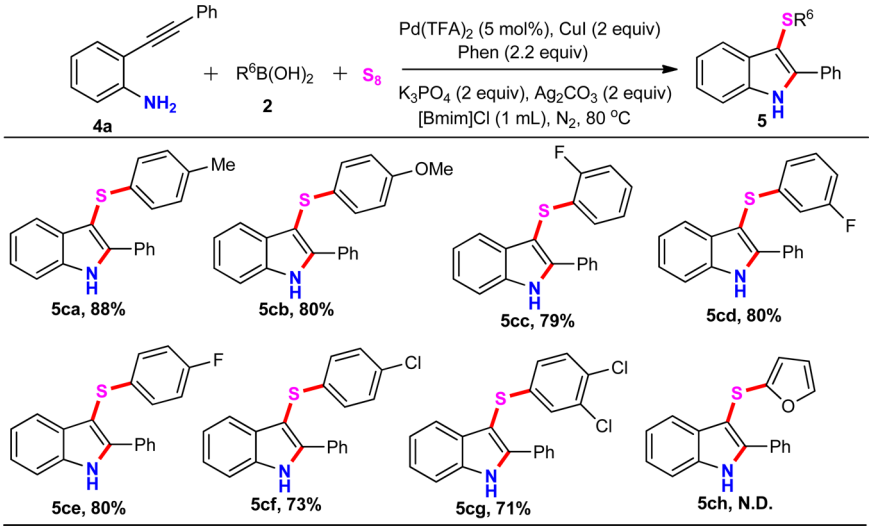
[a]Reaction conditions: **4** (0.20 mmol), **2a** (0.4 mmol), S_8 (0.60 mmol), $Pd(TFA)_2$ (5 mol %), CuI (0.40 mmol), Phen (0.44 mmol), Ag_2CO_3 (0.4 mmol), K_3PO_4 (0.4 mmol), and [Bmim]Cl (1 mL) at 80 °C for 8 h; yields refer to isolated yield.

tolerated and afforded desired products **5bp** and **5bq** in 71 and 63% yields, respectively.

To extend the applicability of our reaction, we then evaluated the compatibility of various arylboronic acids in this transformation (Scheme 6). Under the standard reaction conditions, various arylboronic acid derivatives with *p*-Me, *p*-MeO, *p*-F, *m*-F, *o*-F, and *p*-Cl substituents were explored. These functional groups were compatible with the current procedure and afforded the corresponding 3-sulfenylindole derivatives **5ca**–**5cg** in 71–88% yields. Unfortunately, the coupling reactions between 2-(phenylethynyl)aniline (**4a**) and furan-2-ylboronic acid (**2h**) failed to give the desired product.

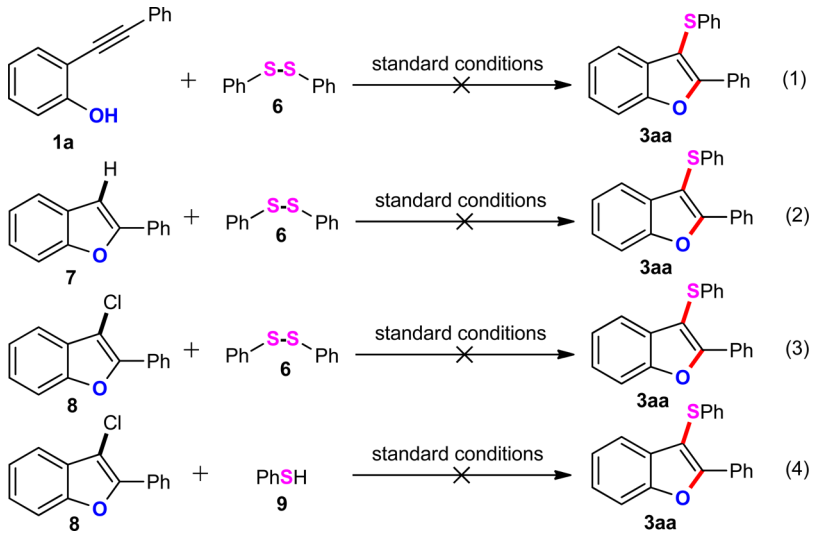
DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875–2887

Scheme 6. Substrate Scope of Various Arylboronic Acid Derivatives[a]



[a]Reaction conditions: **4a** (0.20 mmol), **2** (0.4 mmol), S_8 (0.60 mmol), $Pd(TFA)_2$ (5 mol %), CuI (0.40 mmol), Phen (0.44 mmol), Ag_2CO_3 (0.4 mmol), K_3PO_4 (0.4 mmol), and [Bmim]Cl (1 mL) at 80 °C for 8 h; yields refer to isolated yield.

Scheme 7. Control Experiments

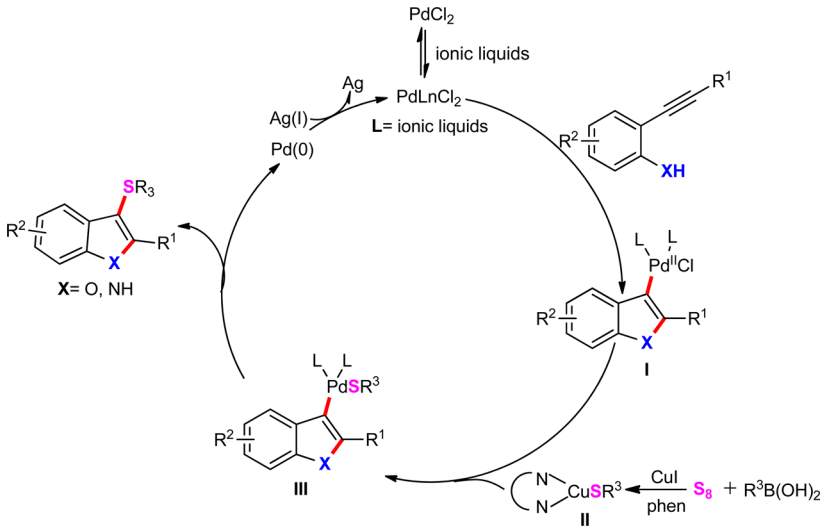


To investigate the mechanism of the cascade arylthiolation, we performed several controlled experiments (Scheme 7). Under the standard conditions, the reaction of **1a** with 1,2-diphenyldisulfane (**6**) did not give the desired 2-phenyl-3-(phenylthio)benzofuran (**3aa**) (Scheme 7, eq 1). Furthermore, when 2-phenylbenzofuran (**7**) and disulfide (**6**) were allowed to react under the standard conditions, the same result was also obtained, and no desired product was detected (Scheme 7, eq 2). In addition, the control experiment of potential intermediate 3-chloro-2-phenylbenzofuran (**8**) with disulfide (**6**) also was investigated by following the current procedure, and the result showed that no target product **3aa** was observed by GC-MS analysis (Scheme 7, eq 3).[10a] All of these observations indicated that disulfide (**6**), 2-phenylbenzofuran (**7**), and 3-chloro-2-phenylbenzofuran (**8**) were not involved in this chemical process. Finally, when 3-chloro-2-phenylbenzofuran (**8**) was employed to react with thiophenol (**9**) under the standard conditions, no reaction occurred at all, which further suggested that the reaction did not proceed via a chlorocyclization process (Scheme 7, eq 4).

On the basis of the above results and the reported mechanism, a tentative mechanism is proposed in Scheme 8. Initially, a Pd complex is formed in situ in ionic liquids.[12,13] Then, nucleopalladation of 2-alkynylphenols or 2-alkynylamines affords vinyl palladium intermediate **I**.[16] Simultaneously, organocopper thiolate complex **II** is generated in situ from the reaction of elemental sulfur (S_8) with aryl boronic acid in the presence of CuI complex.[17] Subsequently, intermediate **I** undergoes the transmetalation process with organocopper thiolate complex **II** to provide intermediate **III**. Finally, a reductive elimination gives the target product. It is noteworthy that a silver mirror reaction is observed after the reaction is finished.[18] Hence, the resulting palladium(0) is additionally oxidized to palladium(II) to complete this catalytic cycle.

DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

Scheme 8. Proposed Mechanism



CONCLUSIONS

In conclusion, we have successfully accomplished an attractive strategy for direct assembly of 3-sulfenylbenzofurans and 3-sulfenylindoles via palladium- and copper-catalyzed cascade annulation/arylthiolation of 2-alkynylphenols or 2-alkynylamines with arylboronic acid and S_8 in ionic liquids. This observation provides a novel route for directly accessing 3-sulfenylbenzofurans and 3-sulfenylindoles in good to excellent yields and good functional group tolerance with high atom efficiency. Further investigation of the reaction mechanism as well as synthetic potential applications of this protocol is currently under way.

EXPERIMENTAL SECTION

General Methods. Melting points were measured by a melting point instrument and were uncorrected. ^{1}H and ^{13}C NMR spectra were recorded using a 400 MHz NMR spectrometer. The chemical shifts were referenced to signals at 7.24 and 77.0 ppm, respectively, and chloroform was used as a solvent with TMS as the internal standard. IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with an infrared spectrometer. GC-MS was obtained using electron ionization. The data of HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). TLC was performed by using commercially available 100−400 mesh silica gel plates (GF_{254}). Unless otherwise noted, all purchased chemicals were used without further purification. The 2-alkynylphenols and 2-alkynylamines were prepared according to the literature.[19]

General Procedure for Cascade Annulation/Arylthiolation. $Pd(TFA)_2$ (5 mol %) and [Bmim]Cl (1 mL) were combined in an Schlenk tube equipped with a stir-bar and stirred at room temperature for 10 min. A balloon filled with N_2 was connected to the Schlenk tube via the side tube and purged 3 times. Then, **1** (0.20 mmol), **2** (0.4 mmol), S_8 (0.60 mmol), CuI (0.40 mmol), Phen (0.44 mmol), Ag_2CO_3 (0.4 mmol), and K_3PO_4 (0.4 mmol) were quickly added to the tube under N_2 atmosphere and stirred at 80 °C for 8 h. After the reaction was completed, the N_2 gas was released carefully, and the reaction was quenched by water and extracted with CH_2Cl_2 three times. The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under vacuum. The desired products were obtained in the corresponding yields after purification by flash chromatography on silica gel with hexanes/ethyl acetate. Compounds **3ab**−**3af**, **3ah**, **3aj**−**3am**, **3ao**−**3ar**, **3at**, **3au**, **3aw**, **3ax**, **3bc**, **3bh**, **5ac**−**5ak**, **5bc**−**5bp**, **5cc**, **5cd**, and **5cg** are all new compounds.

*2-Phenyl-3-(phenylthio)benzofuran (**3aa**).*[10a] Yield of 90% (54.4 mg) as a white solid; mp 64.3−65.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.0 Hz, 1H), 7.50−7.38 (m, 4H), 7.32 (t, J = 7.6 Hz, 1H), 7.25−7.15 (m, 5H), 7.13−7.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 154.0, 136.2, 130.8, 129.8, 129.4, 129.1, 128.6, 127.4, 126.6, 125.6, 125.3, 123.5, 120.4, 111.4, 104.7 ppm; ν_{max} (KBr, cm^{-1}) 3040, 2935, 1630, 1444, 1410, 1032, 687; MS (EI) m/z 105, 165, 197, 225, 273, 302; HRMS-ESI (m/z) calcd for $C_{20}H_{14}NaOS$ $[M + Na]^+$ 325.0658, found 325.0654.

*2-(4-Ethylphenyl)-3-(phenylthio)benzofuran (**3ab**).* Yield of 91% (60.1 mg) as a yellow solid; mp 69.8−70.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.29 (dd, J = 17.6, 7.6 Hz, 3H), 7.22−7.13 (m, 5H), 7.12−7.04 (m, 1H), 2.67 (q, J = 7.2 Hz, 2H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 153.9, 145.9, 136.4, 131.0, 129.1, 128.2, 127.5, 127.3, 126.5, 125.5, 125.1, 123.4, 120.3, 111.3, 103.9, 28.8, 15.3 ppm; ν_{max} (KBr, cm^{-1}) 3045, 2932, 1633, 1441, 1415, 1023, 683; MS (EI) m/z 133, 165, 193, 225, 268, 301, 330; HRMS-ESI (m/z) calcd for $C_{22}H_{18}NaOS$ $[M + Na]^+$ 353.0971, found 353.0977.

*3-(Phenylthio)-2-(4-propylphenyl)benzofuran (**3ac**).* Yield of 88% (60.5 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 7.2 Hz, 1H), 7.24 (d, J = 8.0 Hz, 2H), 7.21−7.13 (m, 5H), 7.10−7.03 (m, 1H), 2.60 (t, J = 7.6 Hz, 2H), 1.72−1.58 (m, 2H), 0.94 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 153.9, 144.4, 136.5, 131.0, 129.1, 128.7, 127.4, 127.3, 126.6, 125.5, 125.1, 123.4, 120.3, 111.3, 103.9, 38.0, 24.4, 13.9 ppm; ν_{max} (KBr, cm^{-1}) 3048, 2933, 1631, 1445, 1408, 1022, 687; MS (EI) m/z 105, 165, 178, 224, 282, 315, 344; HRMS-ESI (m/z) calcd for $C_{23}H_{20}NaOS$ $[M + Na]^+$ 367.1127, found 367.1135.

*2-(4-(tert-Butyl)phenyl)-3-(phenylthio)benzofuran (**3ad**).* Yield of 85% (60.8 mg) as a yellow solid; mp 108.9−110.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 7.6 Hz, 2H),

DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

7.55 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 7.6 Hz, 3H), 7.32 (t, J = 7.6 Hz, 1H), 7.23−7.16 (m, 5H), 7.12−7.07 (m, 1H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 153.9, 152.7, 136.4, 130.9, 129.0, 127.2, 127.0, 126.4, 125.6, 125.4, 125.0, 123.4, 120.3, 111.3, 103.9, 34.8, 31.2 ppm; ν_{max} (KBr, cm^{-1}) 3050, 2936, 1638, 1446, 1412, 1029, 686; MS (EI) m/z 115, 156, 189, 234, 315, 343, 358; HRMS-ESI (m/z) calcd for $C_{24}H_{22}NaOS$ [M + Na]$^+$ 381.1284, found 381.1289.

*2-(4-Pentylphenyl)-3-(phenylthio)benzofuran (**3ae**).* Yield of 86% (63.9 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 7.2 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.2 Hz, 1H), 7.30 (d, J = 7.2 Hz, 1H), 7.24 (d, J = 7.6 Hz, 2H), 7.21−7.12 (m, 5H), 7.11−7.04 (m, 1H), 2.62 (t, J = 7.2 Hz, 2H), 1.69−1.56 (m, 2H), 1.39−1.27 (m, 4H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 154.0, 144.7, 136.5, 131.0, 129.1, 128.7, 127.4, 127.3, 126.5, 125.5, 125.1, 123.4, 120.3, 111.3, 103.9, 35.9, 31.5, 30.9, 22.6, 14.1 ppm; ν_{max} (KBr, cm^{-1}) 3048, 2926, 1636, 1448, 1410, 1028, 684; MS (EI) m/z 105, 139, 165, 178, 282, 315, 340, 372; HRMS-ESI (m/z) calcd for $C_{25}H_{24}NaOS$ [M + Na]$^+$ 395.1440, found 395.1447.

*2-(4-Hexylphenyl)-3-(phenylthio)benzofuran (**3af**).* Yield of 84% (64.8 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 7.2 Hz, 1H), 7.24 (d, J = 8.0 Hz, 2H), 7.22−7.12 (m, 5H), 7.11−7.04 (m, 1H), 2.62 (t, J = 7.6 Hz, 2H), 1.61 (dd, J = 13.6, 6.8 Hz, 2H), 1.35−1.25 (m, 6H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 153.9, 144.7, 136.4, 131.0, 129.1, 128.7, 127.4, 127.3, 126.5, 125.5, 125.1, 123.4, 120.3, 111.3, 103.8, 35.9, 31.8, 31.2, 29.0, 22.6, 14.1 ppm; ν_{max} (KBr, cm^{-1}) 3046, 2932, 1630, 1445, 1416, 1022, 684; MS (EI) m/z 105, 165, 224, 315, 354, 386; HRMS-ESI (m/z) calcd for $C_{26}H_{26}NaOS$ [M + Na]$^+$ 409.1597, found 409.1597.

*2-(4-Methoxyphenyl)-3-(phenylthio)benzofuran (**3ag**).*[10a] Yield of 76% (50.5 mg) as a yellow solid; mp 76.0−77.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.8 Hz, 2H), 7.52 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.21−7.14 (m, 5H), 7.11−7.04 (m, 1H), 6.94 (d, J = 8.8 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 157.9, 153.8, 136.5, 131.1, 129.1, 129.0, 126.4, 125.5, 124.9, 123.4, 122.5, 120.1, 114.1, 111.2, 102.7, 55.4 ppm; ν_{max} (KBr, cm^{-1}) 3048, 2938, 1636, 1442, 1411, 1028, 688; MS (EI) m/z 108, 152, 193, 227, 271, 317, 332; HRMS-ESI (m/z) calcd for $C_{21}H_{16}NaO_2S$ [M + Na]$^+$ 355.0763, found 355.0770.

*2-(4-Fluorophenyl)-3-(phenylthio)benzofuran (**3ah**).* Yield of 79% (50.6 mg) as a white solid; mp 68.5−69.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26−8.17 (m, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.24−7.16 (m, 5H), 7.12 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (d, J = 249.4 Hz), 156.6, 153.9, 136.0, 130.8, 129.4 (d, J = 8.0 Hz), 129.1, 126.5, 126.1 (d, J = 3.3 Hz), 125.7, 125.3, 123.6, 120.4, 115.7 (d, J = 21.6 Hz), 111.3, 104.4 ppm; ν_{max} (KBr, cm^{-1}) 3049, 1628, 1437, 1402, 1028, 687; MS (EI) m/z 105, 165, 197, 215, 291, 320; HRMS-ESI (m/z) calcd for $C_{20}H_{13}FNaOS$ [M + Na]$^+$ 343.0563, found 343.0558.

*2-(4-Chlorophenyl)-3-(phenylthio)benzofuran (**3ai**).*[11b] Yield of 80% (53.7 mg) as a white solid; mp 77.6−78.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 7.2 Hz, 2H), 7.55 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.41 (d, J = 7.2 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.23−7.16 (m, 5H), 7.14−7.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 153.9, 135.8, 135.4, 130.7, 129.1, 128.9, 128.6, 128.3, 126.6, 125.7, 125.5, 123.6, 120.5, 111.4, 105.4 ppm; ν_{max} (KBr, cm^{-1}) 3046, 2938, 1622, 1436, 1408, 1022, 680; MS (EI) m/z 105, 139, 163, 224, 268, 307, 336; HRMS-ESI (m/z) calcd for $C_{20}H_{13}ClNaOS$ [M + Na]$^+$ 359.0268, found 359.0267.

*2-(2,4-Dimethylphenyl)-3-(phenylthio)benzofuran (**3aj**).* Yield of 83% (54.8 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 7.6 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.24 (d, J = 7.6 Hz, 1H), 7.21−7.08 (m, 6H), 7.05 (d, J = 7.6 Hz, 1H), 2.38 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 154.5, 140.0, 138.0, 136.6, 131.5, 130.9, 129.7, 128.9, 126.6, 126.3, 126.0, 125.3, 124.8, 123.3, 120.4, 111.5, 106.3, 21.3, 20.5 ppm; ν_{max} (KBr, cm^{-1}) 3043, 2935, 1626, 1438, 1408, 1360, 1030, 690; MS (EI) m/z 115, 165, 221, 269, 297, 330; HRMS-ESI (m/z) calcd for $C_{22}H_{18}NaOS$ [M + Na]$^+$ 353.0971, found 353.0973.

*2-(3,4-Dichlorophenyl)-3-(phenylthio)benzofuran (**3ak**).* Yield of 73% (54.0 mg) as a yellow solid; mp 116.6−117.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.23−7.16 (m, 5H), 7.15−7.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 154.0, 135.4, 133.3, 133.0, 130.6, 129.7, 129.2, 128.9, 127.0, 126.3, 126.0, 125.9, 123.8, 120.7, 111.4, 106.8 ppm; ν_{max} (KBr, cm^{-1}) 3036, 1627, 1442, 1410, 1026, 687; MS (EI) m/z 105, 163, 197, 225, 258, 302, 341, 370; HRMS-ESI (m/z) calcd for $C_{20}H_{12}Cl_2NaOS$ [M + Na]$^+$ 392.9878, found 392.9877.

*3-(Phenylthio)-2-(4′-propyl-[1,1′-biphenyl]-4-yl)-benzofuran (**3al**).* Yield of 78% (65.5 mg) as a yellow solid; mp 113.9−114.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 8.0 Hz, 2H), 7.55 (t, J = 8.0 Hz, 3H), 7.49 (d, J = 7.6 Hz, 1H), 7.34 (d, J = 7.6 Hz, 1H), 7.30−7.16 (m, 7H), 7.14−7.07 (m, 1H), 2.63 (t, J = 7.6 Hz, 2H), 1.84−1.58 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 154.0, 142.4, 142.0, 137.7, 136.3, 131.0, 129.1, 129.0, 128.4, 127.7, 127.0, 126.9, 126.6, 125.6, 125.3, 123.5, 120.4, 111.3, 104.7, 37.7, 24.5, 13.9 ppm; ν_{max} (KBr, cm^{-1}) 3046, 2933, 1626, 1445, 1408, 1400, 1024, 688; HRMS-ESI (m/z) calcd for $C_{29}H_{24}NaOS$ [M + Na]$^+$ 443.1440, found 443.1449.

*2-(4-(4-Ethylcyclohexyl)phenyl)-3-(phenylthio)benzofuran (**3am**).* Yield of 75% (61.8 mg) as a yellow solid; mp 63.3−64.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.31−7.25 (m, 3H), 7.23−7.14 (m, 5H), 7.12−7.04 (m, 1H), 2.49 (t, J = 12.0 Hz, 1H), 1.89 (t, J = 11.6 Hz, 4H), 1.45 (dd, J = 23.2, 11.6 Hz, 2H), 1.26 (dt, J = 13.2, 6.6 Hz, 3H), 1.04 (dd, J = 23.2, 11.2 Hz, 2H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 153.9, 149.6, 136.5, 131.0, 129.1, 127.5, 127.4, 127.1, 126.5, 125.5, 125.1, 123.4, 120.3, 111.3, 103.8, 44.6, 39.1, 34.2, 33.1, 30.0, 11.5 ppm; ν_{max} (KBr, cm^{-1}) 3044, 2932, 1628, 1446, 1418, 1406, 1022, 686; HRMS-ESI (m/z) calcd for $C_{28}H_{28}NaOS$ [M + Na]$^+$ 435.1753, found 435.1759.

*3-(Phenylthio)-2-(thiophen-2-yl)benzofuran (**3an**).*[10a] Yield of 68% (50.5 mg) as a yellow solid; mp 123.2−124.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 3.6 Hz, 1H), 7.49 (dd, J = 17.2, 8.0 Hz, 2H), 7.39 (d, J = 4.0 Hz, 1H), 7.31−7.28 (m, 1H), 7.24−7.16 (m, 5H), 7.12−7.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 153.9, 135.8, 131.3, 130.7, 129.1, 128.2, 127.6, 127.5, 126.9, 125.8, 125.3, 123.7, 120.1, 111.3, 103.7 ppm; ν_{max} (KBr, cm^{-1}) 3038, 2934, 1628, 1448, 1410, 1032, 692; MS (EI) m/z 127, 171, 203, 247, 275, 308; HRMS-ESI (m/z) calcd for $C_{18}H_{12}NaOS_2$ [M + Na]$^+$ 331.0222, found 331.0220.

DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

*2-Benzyl-3-(phenylthio)benzofuran (**3ao**).* Yield of 72% (45.5 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, J = 6.4 Hz, 2H), 7.30−7.22 (m, 5H), 7.20−7.02 (m, 7H), 4.27 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 154.6, 137.0, 136.6, 129.4, 129.0, 128.9, 128.7, 126.8, 126.7, 125.5, 124.6, 123.3, 120.1, 111.4, 105.6, 33.0 ppm; ν_{max} (KBr, cm^{-1}) 3046, 2935, 1630, 1447, 1405, 1020, 688; MS (EI) m/z 152, 178, 207, 239, 283, 316; HRMS-ESI (m/z) calcd for $C_{21}H_{16}NaOS$ [M + Na]$^+$ 339.0814, found 339.0819.

*2-Phenethyl-3-(phenylthio)benzofuran (**3ap**).* Yield of 74% (48.8 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.4 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.39−7.27 (m, 4H), 7.22 (dd, J = 17.6, 7.2 Hz, 5H), 7.14 (d, J = 6.4 Hz, 1H), 7.08 (d, J = 7.6 Hz, 2H), 3.33 (t, J = 7.6 Hz, 2H), 3.14 (t, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.50, 154.4, 140.5, 136.6, 129.5, 128.9, 128.5, 128.4, 126.7, 126.3, 125.4, 124.4, 123.2, 119.9, 111.2, 105.5, 34.1, 28.7 ppm; ν_{max} (KBr, cm^{-1}) 3049, 2933, 1635, 1448, 1405, 1026, 687; MS (EI) m/z 121, 165, 178, 211, 239, 296, 330; HRMS-ESI (m/z) calcd for $C_{22}H_{18}NaOS$ [M + Na]$^+$ 353.0971, found 353.0972.

*2-(3-Phenylpropyl)-3-(phenylthio)benzofuran (**3aq**).* Yield of 70% (48.2 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.26 (dd, J = 15.2, 6.8 Hz, 4H), 7.21−7.05 (m, 8H), 2.98 (t, J = 7.2 Hz, 2H), 2.67 (t, J = 7.6 Hz, 2H), 2.23−1.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 154.4, 141.6, 136.9, 129.6, 128.9, 128.4, 128.3, 126.5, 125.9, 125.4, 124.3, 123.2, 119.8, 111.1, 104.7, 35.3, 29.6, 26.3 ppm; ν_{max} (KBr, cm^{-1}) 3048, 2936, 1631, 1449, 1403, 1022, 689; MS (EI) m/z 115, 131, 178, 239, 281, 309, 344; HRMS-ESI (m/z) calcd for $C_{23}H_{20}NaOS$ [M + Na]$^+$ 367.1127, found 367.1127.

*2-(4-Chlorobutyl)-3-(phenylthio)benzofuran (**3ar**).* Yield of 70% (48.2 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.18 (dd, J = 12.8, 7.2 Hz, 3H), 7.09 (dd, J = 13.0, 6.8 Hz, 3H), 3.50 (t, J = 6.4 Hz, 2H), 2.97 (t, J = 7.2 Hz, 2H), 2.01−1.84 (m, 2H), 1.85−1.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 154.4, 136.8, 129.5, 129.0, 126.5, 125.5, 124.4, 123.3, 119.9, 111.2, 105.2, 44.4, 31.8, 25.8, 25.3 ppm; ν_{max} (KBr, cm^{-1}) 3046, 2936, 1636, 1452, 1400, 1024, 687; MS (EI) m/z 115, 152, 178, 221, 281, 316; HRMS-ESI (m/z) calcd for $C_{18}H_{17}ClNaOS$ [M + Na]$^+$ 339.0581, found 339.0581.

*5-Methyl-2-phenyl-3-(phenylthio)benzofuran (**3as**).*[10a] Yield of 93% (58.8 mg) as a white solid; mp 76.5−77.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 13.6 Hz, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.31 (t, J = 6.6 Hz, 2H), 7.23−7.13 (m, 6H), 7.12−7.03 (m, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 154.0, 138.3, 136.3, 130.9, 130.3, 129.8, 128.5, 126.8, 125.6, 125.2, 124.7, 123.5, 120.4, 111.3, 104.7, 21.6 ppm; ν_{max} (KBr, cm^{-1}) 3043, 2928, 1633, 1445, 1415, 1026, 680; MS (EI) m/z 105, 119, 178, 225, 284, 301, 316; HRMS-ESI (m/z) calcd for $C_{21}H_{16}NaOS$ [M + Na]$^+$ 339.0814, found 339.0818.

*Methyl-2-phenyl-3-(phenylthio)benzofuran-5-carboxylate (**3at**).* Yield of 67% (48.2 mg) as a yellow solid; mp 116.5−117.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26−8.20 (m, 3H), 8.07 (dd, J = 8.8, 1.6 Hz, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.48−7.40 (m, 3H), 7.23−7.17 (m, 4H), 7.15−7.09 (m, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 159.0, 156.5, 135.8, 131.1, 129.9, 129.3, 129.2, 128.7, 127.5, 127.1, 126.6, 126.0, 125.8, 122.7, 111.3, 105.3, 52.1 ppm; ν_{max} (KBr, cm^{-1}) 3026, 2928, 1722, 1445, 1408, 1236, 1094, 690; MS (EI) m/z 105, 164, 224, 283, 329, 360; HRMS-ESI (m/z) calcd for $C_{22}H_{16}NaO_3S$ [M + Na]$^+$ 383.0712, found 383.0715

*6-Fluoro-2-phenyl-3-(phenylthio)benzofuran (**3au**).* Yield of 80% (51.2 mg) as a white solid; mp 83.7−84.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 7.6 Hz, 2H), 7.52−7.35 (m, 4H), 7.23−7.16 (m, 4H), 7.12 (d, J = 6.4 Hz, 2H), 7.02 (t, J = 9.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7 (d, J = 238.7 Hz), 159.3, 150.1, 132.1, 159.7 (d, J = 10.4 Hz), 129.7, 129.5, 129.2, 128.7, 127.5, 126.7, 125.8, 113.1 (d, J = 26.4 Hz), 112.1 (d, J = 9.4 Hz), 106.1 (d, J = 25.4 Hz), 105.0 (d, J = 4.0 Hz) ppm; ν_{max} (KBr, cm^{-1}) 3048, 1633, 1450, 1403, 1022, 685; MS (EI) m/z 105, 183, 215, 243, 287, 320; HRMS-ESI (m/z) calcd for $C_{20}H_{13}FNaOS$ [M + Na]$^+$ 343.0563, found 343.0564.

*6-Chloro-2-phenyl-3-(phenylthio)benzofuran (**3av**).*[10a] Yield of 82% (55.1 mg) as a yellow solid; mp 106.5−108.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 7.2 Hz, 2H), 7.54 (s, 1H), 7.47−7.31 (m, 4H), 7.20−7.13 (m, 5H), 7.12−7.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 154.0, 135.8, 131.1, 129.7, 129.6, 129.4, 129.2, 128.7, 127.4, 126.8, 125.8, 124.3, 121.0, 112.0, 104.9 ppm; ν_{max} (KBr, cm^{-1}) 3036, 2936, 1638, 1441, 1413, 1035, 688; MS (EI) m/z 105, 163, 224, 259, 301, 336; HRMS-ESI (m/z) calcd for $C_{20}H_{13}ClNaOS$ [M + Na]$^+$ 359.0268, found 359.0273.

*6-Bromo-2-phenyl-3-(phenylthio)benzofuran (**3aw**).* Yield of 77% (58.5 mg) as a yellow solid; mp 118.2−119.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 7.2 Hz, 2H), 7.70 (s, 1H), 7.40 (dq, J = 14.0, 6.8 Hz, 3H), 7.34−7.25 (m, 2H), 7.20−7.13 (m, 4H), 7.12−7.05 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 154.2, 135.7, 130.0, 129.7, 129.4, 129.2, 128.7, 127.4, 127.0, 126.8, 125.8, 121.4, 118.6, 114.9, 105.0 ppm; ν_{max} (KBr, cm^{-1}) 3036, 1632, 1455, 1413, 1024, 689; MS (EI) m/z 105, 163, 195, 224, 268, 301, 353, 380; HRMS-ESI (m/z) calcd for $C_{20}H_{13}BrNaOS$ [M + Na]$^+$ 402.9763, found 402.9759.

*6-Nitro-2-phenyl-3-(phenylthio)benzofuran (**3ax**).* Yield of 63% (43.7 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 6.8 Hz, 2H), 8.04 (s, 1H), 7.92 (dd, J = 8.0, 1.2 Hz, 1H), 7.59 (d, J = 8.2 Hz, 1H), 7.50−7.36 (m, 6H), 7.35−7.30 (m, 1H), 7.25 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 154.1, 148.8, 139.4, 131.7, 129.9, 129.8, 128.8, 127.4, 125.8, 123.9, 120.9, 120.4, 119.9, 111.7, 102.7 ppm; ν_{max} (KBr, cm^{-1}) 3034, 1636, 1425, 1406, 1028, 684; MS (EI) m/z 105, 165, 197, 268, 300, 347; HRMS-ESI (m/z) calcd for $C_{20}H_{13}NNaO_3S$ [M + Na]$^+$ 370.0508, found 370.0504.

*2-Phenyl-3-(p-tolylthio)benzofuran (**3ba**).*[10a] Yield of 88% (55.6 mg) as a yellow solid; mp 70.0−71.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.41 (t, J = 7.2 Hz, 2H), 7.35 (d, J = 6.8 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.19 (d, J = 7.6 Hz, 1H), 7.10 (d, J = 7.6 Hz, 2H), 6.97 (d, J = 7.6 Hz, 2H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 154.0, 135.6, 132.6, 131.1, 123.0, 129.9, 129.4, 128.7, 127.5, 127.0, 125.3, 123.5, 120.6, 111.4, 105.4, 21.0 ppm; ν_{max} (KBr, cm^{-1}) 3042, 2936, 1637, 1448, 1410, 1028, 681; MS (EI) m/z 119, 165, 207, 239, 283, 301, 316; HRMS-ESI (m/z) calcd for $C_{21}H_{16}NaOS$ [M + Na]$^+$ 339.0814, found 339.0818.

*3-((4-Methoxyphenyl)thio)-2-phenylbenzofuran (**3bb**).*[10a] Yield of 81% (53.8 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.6 Hz, 1H), 7.79 (s, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.38−7.27 (m, 2H), 7.22−7.14 (m, 5H), 7.09 (dt, J = 8.0, 4.8 Hz, 1H), 6.93 (dd, J = 8.0, 1.6 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 157.3, 153.9, 136.2, 130.9, 129.7, 129.1, 126.6, 125.6, 125.4, 123.6, 120.5, 119.9, 115.8, 112.4, 111.4, 105.0, 55.3 ppm;

DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

ν_{max} (KBr, cm^{-1}) 3034, 2927, 1626, 1444, 1413, 1012, 692; MS (EI) m/z 113, 152, 225, 271, 299, 332; HRMS-ESI (m/z) calcd for $C_{21}H_{16}NaO_2S$ $[M + Na]^+$ 355.0763, found 355.0763.

3-((2-Methoxyphenyl)thio)-2-phenylbenzofuran (**3bc**). Yield of 76% (50.5 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 8.0 Hz, 1H), 7.49−7.41 (m, 3H), 7.38 (d, J = 7.2 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.19 (dd, J = 7.0, 6.4 Hz, 3H), 6.74 (d, J = 8.4 Hz, 2H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 156.7, 153.9, 130.9, 123.0, 129.3, 129.3, 128.6, 127.4, 126.5, 125.2, 123.4, 120.5, 114.9, 111.3, 106.5, 55.3 ppm; ν_{max} (KBr, cm^{-1}) 3028, 2920, 1636, 1451, 1411, 1026, 689; MS (EI) m/z 105, 139, 165, 227, 255, 299, 317, 332; HRMS-ESI (m/z) calcd for $C_{21}H_{16}NaO_2S$ $[M + Na]^+$ 355.0763, found 355.0770.

3-((4-Fluorophenyl)thio)-2-phenylbenzofuran (**3bd**).[10a] Yield of 78% (49.9 mg) as a yellow solid; mp 55.0−56.7 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 7.2 Hz, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 7.2 Hz, 3H), 7.39 (d, J = 7.2 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.22−7.13 (m, 3H), 6.89 (t, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (d, J = 243.9 Hz), 157.3, 154.0, 131.1 (d, J = 3.2 Hz), 130.7, 129.8, 129.5, 128.8 (d, J = 8.2 Hz), 128.6, 127.4, 125.4, 123.6, 120.3, 116.2 (d, J = 21.0 Hz), 111.4, 105.3 ppm; ν_{max} (KBr, cm^{-1}) 3038, 2934, 1636, 1443, 1414, 1026, 687; MS (EI) m/z 105, 165, 197, 243, 291, 320; HRMS-ESI (m/z) calcd for $C_{20}H_{13}FNaOS$ $[M + Na]^+$ 343.0563, found 343.0562.

3-((3-Fluorophenyl)thio)-2-phenylbenzofuran (**3be**).[10a] Yield of 75% (48.0 mg) as a white solid; mp 65.4−67.2 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 7.2 Hz, 2H), 7.56 (d, J = 8.4 Hz, 1H), 7.51−7.29 (m, 5H), 7.24 (d, J = 7.2 Hz, 1H), 7.13 (dd, J = 14.4, 7.2 Hz, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.86 (d, J = 9.2 Hz, 1H), 6.77 (t, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2 (d, J = 246.8 Hz), 157.9, 154.0, 138.9, 138.8, 130.6, 130.4 (d, J = 8.5 Hz), 129.6 (d, J = 3.9 Hz), 128.7, 127.5, 125.5, 123.7, 121.9 (d, J = 2.8 Hz), 120.3, 113.3 (d, J = 24.0 Hz), 112.5 (d, J = 21.3 Hz), 111.5, 103.8 ppm; ν_{max} (KBr, cm^{-1}) 3026, 2934, 1638, 1445, 1408, 1026, 686; MS (EI) m/z 105, 165, 197, 243, 291, 320; HRMS-ESI (m/z) calcd for $C_{20}H_{13}FNaOS$ $[M + Na]^+$ 343.0563, found 343.0563.

3-((4-Chlorophenyl)thio)-2-phenylbenzofuran (**3bf**).[10a] Yield of 79% (53.1 mg) as a white solid; mp 80.5−81.8 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 7.2 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.47−7.35 (m, 4H), 7.30 (t, J = 7.6 Hz, 1H), 7.21 (d, J = 7.6 Hz, 1H), 7.10 (q, J = 8.8 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 154.1, 134.8, 131.6, 130.6, 129.7, 129.6, 129.3, 128.7, 127.9, 127.5, 125.5, 123.7, 120.3, 111.5, 104.3 ppm; ν_{max} (KBr, cm^{-1}) 3038, 2930, 1634, 1445, 1411, 1026, 686; MS (EI) m/z 105, 165, 197, 268, 301, 336; HRMS-ESI (m/z) calcd for $C_{20}H_{13}ClNaOS$ $[M + Na]^+$ 359.0268, found 359.0273.

3-((4-Nitrophenyl)thio)-2-phenylbenzofuran (**3bg**).[9] Yield of 64% (44.3 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 7.6 Hz, 2H), 8.04 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.0 Hz, 1H), 7.48−7.36 (m, 5H), 7.25 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 154.1, 146.2, 145.5, 130.0, 129.2, 128.8, 127.4, 125.8, 125.8, 124.3, 123.9, 119.9, 111.7, 102.1 ppm; ν_{max} (KBr, cm^{-1}) 3046, 2936, 1634, 1444, 1412, 1032, 680; MS (EI) m/z 105, 165, 197, 225, 268, 301, 347; HRMS-ESI (m/z) calcd for $C_{20}H_{13}NNaO_3S$ $[M + Na]^+$ 370.0508, found 370.0503.

3-((3,4-Dichlorophenyl)thio)-2-phenylbenzofuran (**3bh**). Yield of 71% (53.1 mg) as a white solid; mp 119.7−121.1 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 7.2 Hz, 2H), 7.57 (d, J = 8.0 Hz, 1H), 7.50−7.39 (m, 4H), 7.36 (t, J = 7.6 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.07 (s, 1H), 7.01 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 154.0, 140.3, 135.6, 130.2, 129.9, 129.4, 128.8, 127.5, 125.8, 125.7, 124.1, 123.9, 120.0, 111.6, 102.6 ppm; ν_{max} (KBr, cm^{-1}) 3034, 1635, 1456, 1415, 1024, 687; MS (EI) m/z 105, 165, 197, 225, 271, 293, 341, 370; HRMS-ESI (m/z) calcd for $C_{20}H_{12}Cl_2NaOS$ $[M + Na]^+$ 392.9878, found 392.9876.

2-Phenyl-3-(phenylthio)-1H-indole (**5aa**).[15a] Yield of 90% (54.2 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.72 (d, J = 7.6 Hz, 2H), 7.62 (d, J = 7.6 Hz, 1H), 7.37 (dt, J = 21.2, 6.8 Hz, 4H), 7.25 (t, J = 7.6 Hz, 1H), 7.13 (dt, J = 15.6, 7.2 Hz, 5H), 7.03 (t, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 139.3, 135.9, 131.5, 131.2, 128.8, 128.8, 128.7, 128.2, 125.6, 124.7, 123.4, 121.2, 120.0, 111.2, 99.5 ppm; ν_{max} (KBr, cm^{-1}) 3028, 2936, 1626, 1443, 1410, 1022, 685; MS (EI) m/z 121, 165, 197, 223, 268, 301.

5-Methyl-2-phenyl-3-(phenylthio)-1H-indole (**5ab**).[15a] Yield of 87% (54.8 mg) as a yellow solid; mp 116.8−118.2 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.45−7.32 (m, 4H), 7.29 (d, J = 8.4 Hz, 1H), 7.14 (t, J = 7.2 Hz, 2H), 7.11−7.00 (m, 4H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 139.6, 134.2, 131.6, 130.7, 128.9, 128.8, 128.6, 128.1, 125.5, 125.1, 124.6, 119.5, 110.9, 98.7, 21.5 ppm; ν_{max} (KBr, cm^{-1}) 3034, 2934, 1624, 1446, 1413, 1025, 689; MS (EI) m/z 121, 165, 204, 223, 238, 267, 282, 315; HRMS-ESI (m/z) calcd for $C_{21}H_{17}NNaS$ $[M + Na]^+$ 338.0974, found 338.0969.

6-Methyl-2-phenyl-3-(phenylthio)-1H-indole (**5ac**). Yield of 89% (56.1 mg) as a yellow solid; mp 129.7−130.7 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.69 (d, J = 7.2 Hz, 2H), 7.46−7.32 (m, 4H), 7.28 (d, J = 8.0 Hz, 1H), 7.14 (t, J = 7.6 Hz, 2H), 7.11−6.99 (m, 5H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 139.6, 134.2, 131.6, 130.7, 128.8, 128.8, 128.6, 128.1, 125.5, 125.1, 124.6, 119.5, 110.9, 98.6, 21.5 ppm; ν_{max} (KBr, cm^{-1}) 3370, 2938, 1618, 1447, 1406, 1340, 675; MS (EI) m/z 128, 151, 178, 242, 257, 315; HRMS-ESI (m/z) calcd for $C_{21}H_{17}NNaS$ $[M + Na]^+$ 338.0974, found 338.0980.

5-Methoxy-2-phenyl-3-(phenylthio)-1H-indole (**5ad**). Yield of 77% (50.9 mg) as a yellow solid; mp 145.2−146.4 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.68 (d, J = 7.6 Hz, 2H), 7.41−7.30 (m, 3H), 7.26 (d, J = 8.4 Hz, 1H), 7.18−6.99 (m, 6H), 6.89 (d, J = 8.8 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 142.7, 139.3, 132.2, 131.5, 130.8, 128.9, 128.8, 128.6, 128.1, 125.5, 124.7, 113.8, 112.2, 101.2, 98.9, 55.8 ppm; ν_{max} (KBr, cm^{-1}) 3356, 2936, 1616, 1445, 1408, 1333, 676; MS (EI) m/z 107, 152, 183, 199, 277, 331; HRMS-ESI (m/z) calcd for $C_{21}H_{17}NNaOS$ $[M + Na]^+$ 354.0923, found 354.0928.

5,7-Dimethyl-2-phenyl-3-(phenylthio)-1H-indole (**5ae**). Yield of 83% (54.6 mg) as a yellow solid; mp 156.1−157.7 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.73 (d, J = 7.6 Hz, 2H), 7.40 (t, J = 7.2 Hz, 2H), 7.35 (d, J = 7.2 Hz, 1H), 7.27 (s, 1H), 7.17−7.08 (m, 4H), 7.03 (t, J = 6.8 Hz, 1H), 6.90 (s, 1H), 2.50 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 139.6, 133.7, 131.7, 131.2, 130.9, 128.8, 128.7, 128.6, 128.2, 125.8, 125.5, 124.5, 120.0, 117.2, 99.2, 21.5, 16.4 ppm; ν_{max} (KBr, cm^{-1}) 3360, 2932, 1628, 1450, 1332, 682; MS (EI) m/z 115, 150, 237, 281, 296, 313, 329; HRMS-ESI (m/z) calcd for $C_{22}H_{19}NNaS$ $[M + Na]^+$ 352.1130, found 352.1137.

5-Fluoro-2-phenyl-3-(phenylthio)-1H-indole (**5af**). Yield of 81% (51.6 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ

DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

8.40 (s, 1H), 7.62 (d, J = 7.2 Hz, 2H), 7.29 (dd, J = 16.0, 7.6 Hz, 3H), 7.24−7.14 (m, 2H), 7.06 (t, J = 7.2 Hz, 2H), 6.96 (dd, J = 14.8, 7.6 Hz, 3H), 6.88 (t, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8 (d, J = 235.7 Hz), 143.8, 138.8, 132.2 (d, J = 2.5 Hz), 132.1, 129.0, 128.9, 128.8, 128.1, 125.7, 124.9, 112.1 (d, J = 9.4 Hz), 111.8 (d, J = 26.4 Hz), 105.0 (d, J = 24.1 Hz), 99.6 (d, J = 4.5 Hz) ppm; ν_{max} (KBr, cm^{-1}) 3357, 2936, 1625, 1456, 1338, 689; MS (EI) m/z 139, 183, 215, 241, 285, 304, 319; HRMS-ESI (m/z) calcd for $C_{20}H_{14}FNNaS$ [M + Na]$^+$ 342.0723, found 342.0718.

6-Chloro-2-phenyl-3-(phenylthio)-1H-indole (**5ag**). Yield of 84% (56.3 mg) as a yellow solid; mp 114.7−115.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.71 (d, J = 7.2 Hz, 2H), 7.50 (d, J = 8.4 Hz, 1H), 7.46−7.32 (m, 4H), 7.17−7.10 (m, 3H), 7.08−7.01 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 138.8, 136.2, 131.0, 129.8, 129.2, 129.0, 128.9, 128.8, 128.1, 125.7, 124.9, 121.9, 120.9, 111.2, 99.9 ppm; ν_{max} (KBr, cm^{-1}) 3368, 2931, 1623, 1456, 1348, 686; MS (EI) m/z 121, 150, 223, 267, 300, 335; HRMS-ESI (m/z) calcd for $C_{20}H_{14}ClNNaS$ [M + Na]$^+$ 358.0428, found 358.0432.

5,7-Dichloro-2-phenyl-3-(phenylthio)-1H-indole (**5ah**). Yield of 71% (52.4 mg) as a yellow solid; mp 116.9−118.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.75 (d, J = 7.2 Hz, 2H), 7.51 (s, 1H), 7.47−7.36 (m, 3H), 7.25 (s, 1H), 7.17 (t, J = 7.6 Hz, 2H), 7.06 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 138.3, 133.2, 131.7, 130.5, 129.4, 129.0, 128.9, 128.2, 127.1, 125.7, 125.1, 122.9, 118.3, 117.0, 100.7 ppm; ν_{max} (KBr, cm^{-1}) 3320, 2948, 1636, 1458, 1366, 687; MS (EI) m/z 150, 257, 301, 337, 369; HRMS-ESI (m/z) calcd for $C_{20}H_{13}Cl_2NNaS$ [M + Na]$^+$ 392.0038, found 392.0037.

5-Bromo-2-phenyl-3-(phenylthio)-1H-indole (**5ai**). Yield of 80% (60.9 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.69 (s, 1H), 7.64 (d, J = 6.8 Hz, 2H), 7.32 (dd, J = 15.6, 7.2 Hz, 3H), 7.25 (d, J = 8.8 Hz, 1H), 7.20 (d, J = 8.4 Hz, 1H), 7.08 (t, J = 7.2 Hz, 2H), 6.98 (d, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 138.8, 134.5, 133.1, 130.9, 129.1, 128.9, 128.8, 128.1, 126.4, 125.6, 124.9, 122.5, 114.7, 112.7, 99.2 ppm; ν_{max} (KBr, cm^{-1}) 3408, 2954, 1630, 1449, 1346, 689; MS (EI) m/z 121, 150, 190, 223, 267, 300, 347, 381; HRMS-ESI (m/z) calcd for $C_{20}H_{14}BrNNaS$ [M + Na]$^+$ 401.9923, found 401.9927.

2-Phenyl-3-(phenylthio)-5-(trifluoromethyl)-1H-indole (**5aj**). Yield of 70% (51.7 mg) as a yellow solid; mp 247.4−248.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.94 (s, 1H), 7.72 (d, J = 7.2 Hz, 2H), 7.47 (s, 2H), 7.43−7.32 (m, 3H), 7.15 (t, J = 7.2 Hz, 2H), 7.11−7.00 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 138.6, 137.2, 130.9, 130.7, 129.2, 129.0, 128.9, 128.2, 125.7, 125.0, 123.6 (q, J = 41.6 Hz), 120.2 (q, J = 3.4 Hz), 111.7 (q, J = 4.0 Hz), 111.6, 100.7 ppm; ν_{max} (KBr, cm^{-1}) 3396, 2938, 1628, 1454, 1370, 681; MS (EI) m/z 121, 150, 188, 267, 337, 369; HRMS-ESI (m/z) calcd for $C_{21}H_{14}F_3NNaS$ [M + Na]$^+$ 392.0691, found 392.0697.

Methyl-2-phenyl-3-(phenylthio)-1H-indole-5-carboxylate (**5ak**). Yield of 64% (45.9 mg) as a yellow solid; mp 253.5−253.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 7.2 Hz, 2H), 7.44 (dd, J = 19.6, 12.0 Hz, 4H), 7.17 (t, J = 7.2 Hz, 2H), 7.08 (d, J = 7.2 Hz, 3H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 143.5, 138.9, 138.4, 131.0, 130.9, 129.1, 128.9, 128.8, 128.1, 125.6, 124.9, 124.8, 123.5, 122.7, 110.9, 51.9 ppm; ν_{max} (KBr, cm^{-1}) 3361, 2942, 1626, 1443, 1326, 685; MS (EI) m/z 121, 163, 223, 267, 299, 327, 359; HRMS-ESI (m/z) calcd for $C_{22}H_{17}NNaO_2S$ [M + Na]$^+$ 382.0872, found 382.0872.

3-(Phenylthio)-2-(p-tolyl)-1H-indole (**5ba**).[15b] Yield of 89% (56.1 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.61 (d, J = 7.2 Hz, 3H), 7.38 (d, J = 8.0 Hz, 1H), 7.21 (t, J = 9.2 Hz, 3H), 7.16−7.06 (m, 5H), 7.01 (t, J = 6.4 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 139.4, 138.8, 135.8, 131.3, 129.5, 128.8, 128.6, 128.0, 125.6, 124.6, 123.2, 121.1, 119.9, 111.1, 99.0, 21.4 ppm; ν_{max} (KBr, cm^{-1}) 3038, 2936, 1623, 1440, 1412, 1034, 686; MS (EI) m/z 121, 150, 204, 238, 267, 283, 315; HRMS-ESI (m/z) calcd for $C_{21}H_{17}NNaS$ [M + Na]$^+$ 338.0974, found 338.0973.

2-(4-Methoxyphenyl)-3-(phenylthio)-1H-indole (**5bb**).[15b] Yield of 83% (54.9 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.71−7.56 (m, 3H), 7.36 (d, J = 8.0 Hz, 1H), 7.21 (d, J = 7.6 Hz, 1H), 7.19−7.04 (m, 5H), 7.02 (t, J = 6.8 Hz, 1H), 6.90 (d, J = 8.0 Hz, 2H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 142.2, 139.5, 135.8, 131.4, 129.5, 128.9, 125.6, 124.6, 123.9, 123.1, 121.1, 119.8, 114.3, 111.1, 98.4, 55.4 ppm; ν_{max} (KBr, cm^{-1}) 3034, 2936, 1633, 1442, 1410, 1023, 684; MS (EI) m/z 120, 165, 223, 254, 299, 316, 331; HRMS-ESI (m/z) calcd for $C_{21}H_{17}NNaOS$ [M + Na]$^+$ 354.0923, found 354.0926.

2-(4-Chlorophenyl)-3-(phenylthio)-1H-indole (**5bc**). Yield of 80% (53.6 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.64 (dd, J = 15.2, 7.6 Hz, 3H), 7.40 (dd, J = 17.0, 8.0 Hz, 3H), 7.27 (t, J = 7.6 Hz, 1H), 7.16 (dd, J = 14.2, 7.2 Hz, 3H), 7.05 (dd, J = 14.8, 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 138.9, 135.9, 134.8, 131.2, 129.9, 129.3, 129.0, 128.9, 125.6, 124.8, 123.7, 121.4, 120.1, 111.2, 100.2 ppm; ν_{max} (KBr, cm^{-1}) 3327, 2923, 1624, 1448, 1320, 688; MS (EI) m/z 121, 150, 190, 223, 267, 303, 335; HRMS-ESI (m/z) calcd for $C_{20}H_{14}ClNNaS$ [M + Na]$^+$ 358.0428, found 358.0434.

2-Cyclopropyl-3-(phenylthio)-1H-indole (**5be**). Yield of 80% (42.4 mg) as a yellow solid; mp 97.1−98.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.25 (d, J = 7.6 Hz, 1H), 7.17−7.05 (m, 6H), 7.01 (t, J = 6.8 Hz, 1H), 2.40−2.26 (m, 1H), 1.01 (d, J = 8.0 Hz, 2H), 0.84 (d, J = 4.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 139.6, 135.0, 130.8, 128.7, 125.6, 124.6, 122.2, 120.8, 118.7, 110.8, 99.4, 8.3, 7.9 ppm; ν_{max} (KBr, cm^{-1}) 3371, 2929, 1626, 1445, 1325, 683; MS (EI) m/z 129, 155, 188, 217, 265; HRMS-ESI (m/z) calcd for $C_{17}H_{15}NNaS$ [M + Na]$^+$ 288.0817, found 288.0822.

2-Cyclopentyl-3-(phenylthio)-1H-indole (**5bf**). Yield of 85% (49.8 mg) as a yellow solid; mp 73.4−74.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.54 (d, J = 7.2 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.18−7.07 (m, 4H), 7.06−6.94 (m, 3H), 3.57 (dd, J = 16.4, 8.0 Hz, 1H), 2.15−1.98 (m, 2H), 1.87−1.74 (m, 2H), 1.70−1.56 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 139.8, 135.5, 130.5, 128.7, 125.5, 124.5, 122.2, 120.8, 119.0, 110.9, 98.4, 37.3, 33.4, 25.8 ppm; ν_{max} (KBr, cm^{-1}) 3367, 2923, 1627, 1444, 1329, 684; MS (EI) m/z 108, 130, 155, 225, 260, 293; HRMS-ESI (m/z) calcd for $C_{19}H_{19}NNaS$ [M + Na]$^+$ 316.1130, found 316.1132.

2-Cyclohexyl-3-(phenylthio)-1H-indole (**5bg**). Yield of 83% (50.9 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.22−7.07 (m, 4H), 7.02 (dd, J = 14.4, 7.2 Hz, 3H), 3.19 (t, J = 10.8 Hz, 1H), 1.89 (d, J = 11.6 Hz, 2H), 1.84−1.68 (m, 3H), 1.43 (dt, J = 22.8, 12.4 Hz, 4H), 1.28−1.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 139.7, 135.4, 130.3, 128.7, 125.5, 124.5, 122.2, 120.7, 119.2, 110.9, 97.4, 36.0, 32.9, 26.4, 26.0

DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

ppm; ν_{max} (KBr, cm^{-1}) 3346, 2935, 1633, 1442, 1325, 686; MS (EI) m/z 130, 155, 225, 274, 307; HRMS-ESI (m/z) calcd for $C_{20}H_{21}NNaS$ $[M + Na]^+$ 330.1287, found 330.1288.

2-(Cyclopentylmethyl)-3-(phenylthio)-1H-indole (**5bh**). Yield of 80% (49.1 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.18 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 7.2 Hz, 3H), 7.08−6.88 (m, 3H), 2.88 (d, J = 7.6 Hz, 2H), 2.15 (dt, J = 15.2, 7.6 Hz, 1H), 1.80−1.64 (m, 2H), 1.64−1.57 (m, 2H), 1.55−1.41 (m, 2H), 1.24−1.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 139.6, 135.6, 130.2, 128.7, 125.5, 124.5, 122.2, 120.7, 119.2, 110.8, 99.1, 40.4, 32.7, 32.3, 24.9 ppm; ν_{max} (KBr, cm^{-1}) 3352, 2928, 1617, 1438, 1326, 685; MS (EI) m/z 130, 204, 238, 274, 307; HRMS-ESI (m/z) calcd for $C_{20}H_{21}NNaS$ $[M + Na]^+$ 330.1287, found 330.1291.

2-(Cyclohexylmethyl)-3-(phenylthio)-1H-indole (**5bi**). Yield of 75% (48.2 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.17 (t, J = 8.0 Hz, 1H), 7.10 (q, J = 6.8 Hz, 3H), 7.01 (dd, J = 14.0, 7.2 Hz, 3H), 2.75 (d, J = 6.8 Hz, 2H), 1.70−1.53 (m, 7H), 1.16−1.06 (m, 3H), 1.01−0.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 139.6, 135.5, 130.3, 128.7, 125.6, 124.5, 122.2, 120.7, 119.2, 110.8, 99.7, 38.6, 34.3, 33.2, 26.3, 26.1 ppm; ν_{max} (KBr, cm^{-1}) 3346, 2932, 1627, 1447, 1323, 687; MS (EI) m/z 130, 178, 204, 238, 288, 321; HRMS-ESI (m/z) calcd for $C_{21}H_{23}NNaS$ $[M + Na]^+$ 344.1443, found 344.1448.

3-(Phenylthio)-2-propyl-1H-indole (**5bj**). Yield of 89% (47.5 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 7.15−7.07 (m, 3H), 7.06−6.98 (m, 3H), 2.85 (t, J = 7.2 Hz, 2H), 1.78−1.53 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 139.6, 135.5, 130.3, 128.7, 125.5, 124.5, 122.2, 120.7, 119.1, 110.8, 99.1, 28.5, 22.9, 13.9 ppm; ν_{max} (KBr, cm^{-1}) 3368, 2946, 2848, 1603, 1445, 1313, 1243, 685; MS (EI) m/z 130, 178, 205, 238, 267; HRMS-ESI (m/z) calcd for $C_{17}H_{17}NNaS$ $[M + Na]^+$ 290.0974, found 290.0975.

2-Isobutyl-3-(phenylthio)-1H-indole (**5bk**). Yield of 84% (47.2 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.18 (t, J = 7.5 Hz, 1H), 7.11 (dd, J = 9.6, 4.4 Hz, 3H), 7.01 (dd, J = 14.8, 7.6 Hz, 3H), 2.74 (d, J = 7.2 Hz, 2H), 1.97 (td, J = 13.2, 6.8 Hz, 1H), 0.90 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 139.5, 135.6, 130.3, 128.7, 125.5, 124.5, 122.3, 120.7, 119.2, 110.9, 99.6, 35.6, 29.3, 22.6 ppm; ν_{max} (KBr, cm^{-1}) 3362, 2944, 2849, 1606, 1446, 1320, 1244, 687; MS (EI) m/z 102, 130, 178, 204, 238, 281; HRMS-ESI (m/z) calcd for $C_{18}H_{19}NNaS$ $[M + Na]^+$ 304.1130, found 304.1128.

2-Isopentyl-3-(phenylthio)-1H-indole (**5bl**). Yield of 83% (48.9 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.18 (d, J = 6.8 Hz, 1H), 7.14−7.07 (m, 3H), 7.01 (dd, J = 14.8, 7.6 Hz, 3H), 2.97−2.78 (m, 2H), 1.62−1.41 (m, 3H), 0.87 (d, J = 5.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 139.6, 135.6, 130.4, 128.7, 125.6, 124.5, 122.2, 120.7, 119.1, 110.8, 98.9, 38.6, 27.8, 24.4, 22.4 ppm; ν_{max} (KBr, cm^{-1}) 3372, 2948, 2846, 1623, 1442, 1323, 1245, 688; MS (EI) m/z 77, 130, 162, 206, 238, 295; HRMS-ESI (m/z) calcd for $C_{19}H_{21}NNaS$ $[M + Na]^+$ 318.1287, found 318.1291.

2-Butyl-3-(phenylthio)-1H-indole (**5bm**). Yield of 87% (48.9 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.11 (q, J = 6.8 Hz, 3H), 7.02 (dd, J = 12.8, 7.2 Hz, 3H), 2.88 (t, J = 7.6 Hz, 2H), 1.84−1.41 (m, 2H), 1.33 (dq, J = 14.2, 7.2 Hz, 2H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.5, 139.6, 135.5, 130.3, 128.7, 125.5, 124.5, 122.2, 120.7, 119.1, 110.8, 98.9, 31.7, 26.2, 22.4, 13.8 ppm; ν_{max} (KBr, cm^{-1}) 3365, 2928, 2851, 1622, 1448, 1316, 1243, 686; MS (EI) m/z 130, 172, 206, 238, 281; HRMS-ESI (m/z) calcd for $C_{18}H_{19}NNaS$ $[M + Na]^+$ 304.1130, found 304.1126.

2-Octyl-3-(phenylthio)-1H-indole (**5bn**). Yield of 83% (55.9 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 6.8 Hz, 3H), 7.02 (dd, J = 12.4, 7.6 Hz, 3H), 2.87 (t, J = 7.6 Hz, 2H), 1.62 (dd, J = 14.0, 7.2 Hz, 2H), 1.36−1.15 (m, 12H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 139.6, 135.5, 130.4, 128.7, 125.5, 124.5, 122.2, 120.7, 119.1, 110.8, 98.9, 31.9, 29.6, 29.3, 29.3, 29.2, 26.5, 22.7, 14.1 ppm; ν_{max} (KBr, cm^{-1}) 3343, 2964, 1628, 1436, 1324, 1246, 683; MS (EI) m/z 130, 206, 238, 304, 337; HRMS-ESI (m/z) calcd for $C_{22}H_{27}NNaS$ $[M + Na]^+$ 360.1756, found 360.1763.

4-(3-(Phenylthio)-1H-indol-2-yl)butanenitrile (**5bo**). Yield of 79% (47.5 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.23 (d, J = 5.6 Hz, 1H), 7.14 (t, J = 7.6 Hz, 3H), 7.03 (t, J = 9.0 Hz, 3H), 3.04 (t, J = 7.2 Hz, 2H), 2.28 (t, J = 6.8 Hz, 2H), 2.12−1.77 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 139.1, 135.6, 130.2, 128.8, 125.1, 124.8, 122.8, 121.1, 119.4, 119.2, 111.1, 100.2, 25.5, 25.4, 16.5 ppm; ν_{max} (KBr, cm^{-1}) 3408, 2946, 1723, 1633, 1442, 1320, 680; MS (EI) m/z 130, 205, 238, 259, 292; HRMS-ESI (m/z) calcd for $C_{18}H_{16}N_2NaS$ $[M + Na]^+$ 315.0926, found 315.0929.

2-(Cyclohex-1-en-1-yl)-3-(phenylthio)-1H-indole (**5bp**). Yield of 71% (47.5 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.24−6.92 (m, 8H), 6.35 (s, 1H), 2.61−2.52 (m, 2H), 2.24−2.17 (m, 2H), 1.77−1.70 (m, 2H), 1.68−1.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 139.7, 135.0, 131.3, 130.2, 129.3, 128.7, 125.5, 124.4, 122.7, 120.8, 119.5, 110.8, 97.8, 27.4, 25.7, 22.6, 21.8 ppm; ν_{max} (KBr, cm^{-1}) 3428, 2942, 1633, 1610, 1444, 1323, 683; MS (EI) m/z 115, 154, 195, 228, 272, 305; HRMS-ESI (m/z) calcd for $C_{20}H_{19}NNaS$ $[M + Na]^+$ 328.1130, found 328.1134.

3-(Phenylthio)-2-(thiophen-3-yl)-1H-indole (**5bq**).[15a] Yield of 63% (47.5 mg) as a brown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.76 (s, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.55 (d, J = 4.8 Hz, 1H), 7.44−7.29 (m, 2H), 7.24−7.19 (m, 1H), 7.12 (dt, J = 14.8, 7.6 Hz, 5H), 7.02 (t, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 137.8, 135.6, 132.1, 131.3, 128.9, 126.5, 126.3, 125.7, 124.8, 123.8, 123.4, 121.3, 119.8, 111.1, 99.1 ppm; ν_{max} (KBr, cm^{-1}) 3346, 2938, 1630, 1446, 1410, 688; MS (EI) m/z 120, 136, 186, 229, 274, 307; HRMS-ESI (m/z) calcd for $C_{18}H_{13}NNaS_2$ $[M + Na]^+$ 330.0382, found 330.0389.

2-Phenyl-3-(p-tolylthio)-1H-indole (**5ca**).[15a] Yield of 88% (55.4 mg) as a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.73 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 7.6 Hz, 1H), 7.46−7.32 (m, 4H), 7.24 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 7.2 Hz, 1H), 6.97 (dd, J = 19.6, 8.0 Hz, 4H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 135.8, 135.6, 134.4, 131.5, 131.3, 129.7, 128.8, 128.7, 128.2, 125.8, 123.3, 121.2, 120.1, 111.2, 99.9, 20.9 ppm; ν_{max} (KBr, cm^{-1}) 3336, 2934, 1628, 1442, 1413, 687; MS (EI) m/z 121, 165, 223, 267, 283, 315; HRMS-ESI (m/z) calcd for $C_{21}H_{17}NNaS$ $[M + Na]^+$ 338.0974, found 338.0979.

DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

*3-((4-Methoxyphenyl)thio)-2-phenyl-1H-indole (**5cb**).*[15a] Yield of 80% (53.0 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.75 (d, J = 7.6 Hz, 2H), 7.64 (d, J = 7.6 Hz, 1H), 7.49−7.33 (m, 4H), 7.23 (d, J = 6.4 Hz, 1H), 7.15 (t, J = 7.2 Hz, 1H), 7.05 (d, J = 8.4 Hz, 2H), 6.71 (d, J = 8.4 Hz, 2H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 141.6, 135.8, 131.6, 131.2, 129.8, 128.7, 128.6, 128.2, 127.8, 123.3, 121.1, 120.0, 114.6, 111.2, 100.9, 55.3 ppm; ν_{max} (KBr, cm^{-1}) 3338, 2936, 1630, 1446, 1411, 688; MS (EI) m/z 139, 155, 207, 281, 310, 331; HRMS-ESI (m/z) calcd for $C_{21}H_{17}NNaOS$ $[M + Na]^+$ 354.0923, found 354.0929.

*3-((2-Fluorophenyl)thio)-2-phenyl-1H-indole (**5cc**).* Yield of 79% (50.4 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.61 (d, J = 8.0 Hz, 1H), 7.37 (dt, J = 14.2, 7.2 Hz, 4H), 7.25 (t, J = 7.6 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 7.05−6.93 (m, 2H), 6.79 (dd, J = 9.6, 6.0 Hz, 1H), 6.71 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1 (d, J = 242.0 Hz), 142.6, 135.9, 131.2, 131.1, 128.9, 128.2, 127.4 (d, J = 2.5 Hz), 126.5, 126.4, 126.0 (d, J = 7.2 Hz), 124.5 (d, J = 3.2 Hz), 123.5, 121.3, 119.9, 115.1 (d, J = 20.8 Hz), 111.3, 97.1 ppm; ν_{max} (KBr, cm^{-1}) 3348, 2924, 1630, 1439, 1325, 686; MS (EI) m/z 121, 165, 196, 287, 319; HRMS-ESI (m/z) calcd for $C_{20}H_{14}FNNaS$ $[M + Na]^+$ 342.0723, found 342.0729.

*3-((3-Fluorophenyl)thio)-2-phenyl-1H-indole (**5cd**).* Yield of 80% (51.0 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.61 (d, J = 8.0 Hz, 1H), 7.48−7.32 (m, 4H), 7.26 (t, J = 7.6 Hz, 1H), 7.17 (t, J = 7.6 Hz, 1H), 7.09 (dd, J = 14.2, 7.6 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 6.72 (dd, J = 15.6, 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (d, J = 245.8 Hz), 142.3, 142.0 (d, J = 7.3 Hz), 135.9, 131.2, 130.9, 130.1 (d, J = 8.5 Hz), 128.9, 128.8, 128.1, 123.6, 121.4, 121.1 (d, J = 2.8 Hz), 119.8, 112.4 (d, J = 23.9 Hz), 111.6 (d, J = 21.4 Hz), 111.3, 98.6 ppm; ν_{max} (KBr, cm^{-1}) 3336, 2934, 1627, 1442, 1324, 686; MS (EI) m/z 121, 165, 196, 242, 287, 319; HRMS-ESI (m/z) calcd for $C_{20}H_{14}FNNaS$ $[M + Na]^+$ 342.0723, found 342.0729.

*3-((4-Fluorophenyl)thio)-2-phenyl-1H-indole (**5ce**).*[15a] Yield of 80% (51.0 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.72 (d, J = 7.2 Hz, 2H), 7.61 (d, J = 7.6 Hz, 1H), 7.39 (dq, J = 14.4, 7.2 Hz, 4H), 7.26 (t, J = 7.6 Hz, 1H), 7.16 (t, J = 7.6 Hz, 1H), 7.04 (dd, J = 8.8, 5.2 Hz, 2H), 6.84 (t, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8 (d, J = 242.2 Hz), 141.9, 135.8, 134.1 (d, J = 3.0 Hz), 131.4, 131.0, 128.9, 128.8, 128.2, 127.5 (d, J = 7.7 Hz), 123.5, 121.3, 119.8, 116.6 (d, J = 21.9 Hz), 111.3, 99.9 ppm; ν_{max} (KBr, cm^{-1}) 3334, 2932, 1628, 1446, 1328, 689; MS (EI) m/z 121, 165, 196, 223, 287, 319; HRMS-ESI (m/z) calcd for $C_{20}H_{14}FNNaS$ $[M + Na]^+$ 342.0723, found 342.0726.

*3-((4-Chlorophenyl)thio)-2-phenyl-1H-indole (**5cf**).*[15a] Yield of 73% (48.9 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.47−7.34 (m, 4H), 7.27−7.21 (m, 1H), 7.17 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 137.9, 135.9, 131.3, 130.9, 130.4, 128.9, 128.8, 128.6, 128.1, 126.8, 123.5, 121.4, 119.8, 111.3, 99.0 ppm; ν_{max} (KBr, cm^{-1}) 3330, 2934, 1626, 1448, 1324, 680; MS (EI) m/z 121, 150, 223, 267, 303, 335; HRMS-ESI (m/z) calcd for $C_{20}H_{14}ClNNaS$ $[M + Na]^+$ 358.0428, found 358.0432.

*3-((3,4-Dichlorophenyl)thio)-2-phenyl-1H-indole (**5cg**).* Yield of 71% (52.4 mg) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.69 (d, J = 7.6 Hz, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.50−7.36 (m, 4H), 7.29 (t, J = 7.6 Hz, 1H), 7.24−7.19 (m, 1H), 7.02 (s, 1H), 6.92 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 142.6, 135.9, 135.3, 131.0, 130.7, 129.1, 128.9, 128.1, 124.9, 123.7, 123.4, 121.6, 119.6, 111.4, 97.4 ppm; ν_{max} (KBr, cm^{-1}) 3328, 2924, 1624, 1446, 1328, 687; MS (EI) m/z 107, 142, 177, 286, 321, 369; HRMS-ESI (m/z) calcd for $C_{20}H_{13}Cl_2NNaS$ $[M + Na]^+$ 392.0038, found 392.0043.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00162.

Copies of ^{1}H and ^{13}C NMR spectra for compounds **3** and **5** (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*Fax: (+86) 20-8711-2906. E-mail: cewuwq@scut.edu.cn.
*E-mail: jianghf@scut.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the National Natural Science Foundation of China (21490572, 2147205, and 21502055), the Fundamental Research Funds for the Central Universities (2015ZY001 and 2015ZM150), and the China Postdoctoral Science Foundation (2015M572303) for financial support.

■ REFERENCES

(1) For selected reviews, see: (a) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890−931. (b) Sheldon, R. A. *Chem. Soc. Rev.* **2012**, *41*, 1437−1451. (c) Gulevich, A. V.; Dudnik, A. S.; Chernyak, N.; Gevorgyan, V. *Chem. Rev.* **2013**, *113*, 3084−3213. (d) Chen, F.; Wang, T.; Jiao, N. *Chem. Rev.* **2014**, *114*, 8613−8661. (e) Huang, L.; Arndt, M.; Gooβen, K.; Heydt, H.; Gooβen, L. J. *Chem. Rev.* **2015**, *115*, 2596−2697.

(2) For selected reviews, see: (a) *Transition Metals for Organic Synthesis*; Beller, M. Bolm, C., Eds.; Wiley-VCH: Weinheim, Germany, 2004. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2006**, *106*, 4644−4680. (c) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134−7186. (d) Patil, N. T.; Yamamoto, Y. *Chem. Rev.* **2008**, *108*, 3395−3442. (e) Li, B.-J.; Shi, Z.-J. *Chem. Soc. Rev.* **2012**, *41*, 5588−5598. (f) Huang, H.; Ji, X.; Wu, W.; Jiang, H. *Chem. Soc. Rev.* **2015**, *44*, 1155−1171.

(3) For selected examples, see: (a) Liu, L.; Stelmach, J. E.; Natarajan, S. R.; Chen, M.-H.; Singh, S. B.; Schwartz, C. D.; Fitzgerald, C. E.; O'Keefe, S. J.; Zaller, D. M.; Schmatz, D. M.; Doherty, J. B. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3979−3982. (b) Gangjee, A.; Zeng, Y.; Talreja, T.; McGuire, J. J.; Kisliuk, R. L.; Queener, S. F. *J. Med. Chem.* **2007**, *50*, 3046−3053. (c) Stump, B.; Eberle, C.; Kaiser, M.; Brun, R.; Krauth-Siegel, R. L.; Diederich, F. *Org. Biomol. Chem.* **2008**, *6*, 3935−3947. (d) Blair, L. M.; Sperry, J. *J. Nat. Prod.* **2013**, *76*, 794−812. (e) Wilson, A. J.; Kerns, J. K.; Callahan, J. F.; Moody, C. J. *J. Med. Chem.* **2013**, *56*, 7463−7476.

(4) For recent representative examples, see: (a) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790−6791. (b) Zhao, X.; Dimitrijevic, E.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 3466−3467. (c) Martinek, M.; Korf, M.; Srogl, J. *Chem. Commun.* **2010**, *46*, 4387−4389. (d) Sahoo, S. K.; Banerjee, A.; Chakraborty, S.; Patel, B. K. *ACS Catal.* **2012**, *2*, 544−551. (e) Wu, Z.; Song, H.; Cui, X.; Pi, C.; Du, W.; Wu, Y. *Org. Lett.* **2013**, *15*, 1270−1273. (f) Timpa, S. D.; Pell, C. J.; Ozerov, O. V. *J. Am. Chem. Soc.* **2014**, *136*, 14772−14779. (g) Mao, J.; Jia, T.; Frensch, G.; Walsh, P. J. *Org. Lett.* **2014**, *16*, 5304−5307.

DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887

(5) (a) Ham, J.; Yang, I.; Kang, H. *J. Org. Chem.* **2004**, *69*, 3236−3239. (b) Stoll, A. H.; Krasovskiy, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 606−609. (c) Kumar, S.; Singh, H. B.; Wolmershäuser, G. *Organometallics* **2006**, *25*, 382−393. (d) Cheng, J.-H.; Ramesh, C.; Kao, H.-L.; Wang, Y.-J.; Chan, C.-C.; Lee, C.-F. *J. Org. Chem.* **2012**, *77*, 10369−10374. (e) Yonova, I. M.; Osborne, C. A.; Morrissette, N. S.; Jarvo, E. R. *J. Org. Chem.* **2014**, *79*, 1947−1953.

(6) For recent representative examples, see: (a) Dai, C.; Xu, Z.; Huang, F.; Yu, Z.; Gao, Y.-F. *J. Org. Chem.* **2012**, *77*, 4414−4419. (b) Yang, F. L.; Tian, S. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 4929−4932. (c) Li, X.; Xu, Y.; Wu, W.; Jiang, C.; Qi, C.; Jiang, H. *Chem. - Eur. J.* **2014**, *20*, 7911−7915. (d) Xiao, F.; Xie, H.; Liu, S.; Deng, G. J. *Adv. Synth. Catal.* **2014**, *356*, 364−368. (e) Ravi, C.; Mohan, D. C.; Adimurthy, S. *Org. Lett.* **2014**, *16*, 2978−2981. (f) Hiebel, M.-A.; Berteina-Raboin, S. *Green Chem.* **2015**, *17*, 937−944. (g) Zhang, G.; Liu, C.; Yi, H.; Meng, Q.; Bian, C.; Chen, H.; Jian, J.-X.; Wu, L.-Z.; Lei, A. *J. Am. Chem. Soc.* **2015**, *137*, 9273−9280.

(7) For selected examples, see: (a) Durani, N.; Jain, R.; Saeed, A.; Dikshit, D. K.; Durani, S.; Kapil, R. S. *J. Med. Chem.* **1989**, *32*, 1700−1707. (b) Ohno, M.; Miyamoto, M.; Hoshi, K.; Takeda, T.; Yamada, N.; Ohtake, A. *J. Med. Chem.* **2005**, *48*, 5279−5294. (c) He, Y.; Xu, J.; Yu, Z.-H.; Gunawan, A. M.; Wu, L.; Wang, L.; Zhang, Z.-Y. *J. Med. Chem.* **2013**, *56*, 832−842.

(8) For selected examples, see: (a) Carrër, A.; Brinet, D.; Florent, J.-C.; Rousselle, P.; Bertounesque, E. *J. Org. Chem.* **2012**, *77*, 1316−1327. (b) Kuram, M. R.; Bhanuchandra, M.; Sahoo, A. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 4607−4612. (c) Liu, G.; Shen, Y.; Zhou, Z.; Lu, X. *Angew. Chem., Int. Ed.* **2013**, *52*, 6033−6037. (d) Han, Z.; Zhang, L.; Li, Z.; Fan, R. *Angew. Chem., Int. Ed.* **2014**, *53*, 6805−6809. (e) Lee, J. H.; Kim, M.; Kim, I. *J. Org. Chem.* **2014**, *79*, 6153−6163. (f) Murakami, K.; Yorimitsu, H.; Osuka, A. *Angew. Chem., Int. Ed.* **2014**, *53*, 7510−7513. (g) Yuan, W.; Ma, S. *Org. Lett.* **2014**, *16*, 193−195.

(9) Yue, D.; Yao, T.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 10292−10296.

(10) (a) Du, H. A.; Zhang, X. G.; Tang, R. Y.; Li, J. H. *J. Org. Chem.* **2009**, *74*, 7844−7848. (b) Gay, R. M.; Manarin, F.; Schneider, C. C.; Barancelli, D. A.; Costa, M. D.; Zeni, G. *J. Org. Chem.* **2010**, *75*, 5701−5706.

(11) (a) Xu, M.; Zhang, X. H.; Zhong, P. *Tetrahedron Lett.* **2011**, *52*, 6800−6804. (b) Han, J. S.; Shao, Y. L.; Zhang, X. H.; Zhong, P. *Phosphorus, Sulfur Silicon Relat. Elem.* **2013**, *188*, 1599−1610. (c) Zhao, X.; Zhang, L.; Lu, X.; Li, T.; Lu, K. *J. Org. Chem.* **2015**, *80*, 2918−2924.

(12) Li, J.; Zhu, Z.; Yang, S.; Zhang, Z.; Wu, W.; Jiang, H. *J. Org. Chem.* **2015**, *80*, 3870−3879.

(13) (a) Yang, S.-R.; Jiang, H.-F.; Li, Y.-Q.; Chen, H.-J.; Luo, W.; Xu, Y.-B. *Tetrahedron* **2008**, *64*, 2930−2937. (b) Li, J.; Yang, S.; Huang, L.; Chen, H.; Jiang, H. *RSC Adv.* **2013**, *3*, 11529−11532. (c) Li, J.; Yang, S.; Jiang, H.; Wu, W.; Zhao, J. *J. Org. Chem.* **2013**, *78*, 12477−12486. (d) Li, J.; Yang, S.; Wu, W.; Qi, C.; Deng, Z.; Jiang, H. *Tetrahedron* **2014**, *70*, 1516−1523. (e) Li, J.; Yang, S.; Wu, W.; Jiang, H. *Chem. Commun.* **2014**, *50*, 1381−1383. (f) Li, J.; Yang, W.; Yang, S.; Huang, L.; Wu, W.; Sun, Y.; Jiang, H. *Angew. Chem., Int. Ed.* **2014**, *53*, 7219−7222. (g) Wu, W.; Jiang, H. *Acc. Chem. Res.* **2014**, *47*, 2483−2504.

(14) For details of optimization of the reaction solvents, see the Supporting Information.

(15) (a) Guo, Y.-J.; Tang, R.-Y.; Li, J.-H.; Zhong, P.; Zhang, X.-G. *Adv. Synth. Catal.* **2009**, *351*, 2615−2618. (b) Li, Z.; Hong, L.; Liu, R.; Shen, J.; Zhou, X. *Tetrahedron Lett.* **2011**, *52*, 1343−1347. (c) Tao, L.-M.; Liu, W.-Q.; Zhou, Y.; Li, A.-T. *J. Chem. Res.* **2012**, *36*, 644−646.

(16) (a) Chaplin, J. H.; Flynn, B. L. *Chem. Commun.* **2001**, 1594−1595. (b) Nakamura, M.; Ilies, L.; Otsubo, S.; Nakamura, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 944−947. (c) Zhou, R.; Wang, W.; Jiang, Z.; Wang, K.; Zheng, X.; Fu, H.; Chen, H.; Li, R. *Chem. Commun.* **2014**, *50*, 6023−6026.

(17) (a) Posner, G. H.; Brunelle, D. J.; Sinoway, L. *Synthesis* **1974**, *1974*, 662−663. (b) Helton, M. E.; Chen, P.; Paul, P. P.; TyeKlar, Z.; Sommer, R. D.; Zakharov, L. N.; Rheingold, A. L.; Solomon, E. I.; Karlin, K. D. *J. Am. Chem. Soc.* **2003**, *125*, 1160−1161. (c) Chu, L.; Qing, F. L. *Org. Lett.* **2010**, *12*, 5060−5063. (d) Senecal, T. D.; Parsons, A. T.; Buchwald, S. L. *J. Org. Chem.* **2011**, *76*, 1174−1176. (e) Chen, C.; Xie, Y.; Chu, L.; Wang, R.-W.; Zhang, X.; Qing, F.-L. *Angew. Chem., Int. Ed.* **2012**, *51*, 2492−2495.

(18) Stuart, D. R.; Villemure, E.; Fagnou, K. *J. Am. Chem. Soc.* **2007**, *129*, 12072−12073.

(19) Martínez, C.; Álvarez, R.; Aurrecoechea, J. M. *Org. Lett.* **2009**, *11*, 1083−1086.

DOI: 10.1021/acs.joc.6b00162
J. Org. Chem. 2016, 81, 2875−2887