JOC Article

Palladium-Catalyzed Suzuki Cross-Coupling of 2-Haloselenophenes: Synthesis of 2-Arylselenophenes, 2,5-Diarylselenophenes, and 2-Arylselenophenyl Ketones

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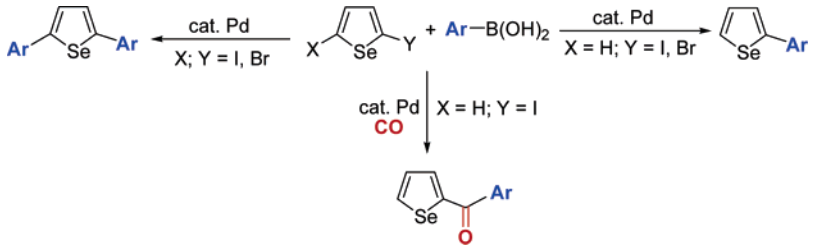

We present herein our results on the Suzuki coupling reaction of 2-haloselenophenes with boronic acids catalyzed by palladium salt and describe a new route established to prepare 2-arylselenophenes and 2,5-diarylselenophenes in good yields. The reaction proceeded cleanly under mild conditions and was performed with aryl boronic acids bearing electron-withdrawing, electron-donating, and neutral substituents, in the presence of $Pd(OAc)_2$, K_2CO_3/H_2O in DME. In addition, by this protocol unsymmetrical aryl ketones were also obtained from 2-iodoselenophene and boronic acids via a carbonylative process.

Introduction

In the past decade, there have been developments in palladium-catalyzed coupling systems as a consequence of great interest in the development of coupling substrates that are more economic, more easily accessible, and reactive even under mild conditions. In this way, the palladium-catalyzed cross-coupling reactions of aryl halides or triflates with boronic acids, commonly referred to as Suzuki reactions, are a powerful, versatile, and popular tool for selective construction of carbon−carbon bonds.[1] The palladium-catalyzed Suzuki cross-coupling reaction of aryl halides with boronic acids and esters has become a common and convenient synthetic method in organic chemistry for biaryl compounds.[2] Many examples of Suzuki coupling reactions between heterocyclic halides and phenyl boronic acids that have appeared in the literature over the past two decades,[3] being the key stage in the synthesis of many currently interesting heterocycle-incorporated compounds, have proved to proceed generally and effectively.[4] More recently, significant advances have been made in the use of organoboron reagents as coupling partners in a number of palladium-mediated carbon−carbon bond formation. Among them, the use of potassium organotrifluoroborates, as the organoboron coupling partner, has some advantages in comparison to boronic acids and boronic esters, such as being more nucleophilic, stable in the air, crystalline as solids, and easily prepared.[5]

Organoselenium compounds have become attractive synthetic targets because of their chemo-, regio-, and stereoselective reactions and their useful biologic activities.[6] Furthermore,

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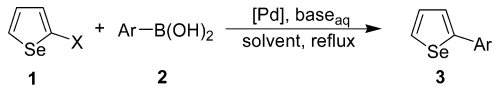
SCHEME 1



organoselenium compounds can usually be used with a wide variety of functional groups, thus avoiding protection group chemistry.[7] Organoselenium chemistry developed rapidly, mainly in the area of selenocarbohydrates, selenoamino acids, and selenopeptides. The selenium group can be introduced in an organic substrate via both nucleophile and electrophile reagents. After being introduced in an organic substrate, the organoselenium group can easily be removed by selenoxide syn elimination[8] and [2,3] sigmatropic rearrangement.[9] In addition, the carbon−selenium bond can also be replaced by a carbon−hydrogen,[10] carbon−halogen,[11] carbon−lithium,[12] or carbon−carbon bond.[13]

Our continuing interest in the synthesis[14] and applications[15] of organochalcogenides in organic synthesis prompted us to examine a procedure to prepare 2-arylselenophenes by the boronic acid coupling reaction with 2-haloselenophene in the presence of palladium salt (Scheme 1).

Results and Discussion

The starting 2-iodoselenophene **1a** was readily available by using the metalation of selenophene[16] **4** with *n*-butyllithium to give 2-(lithium)selenophene derivatives. The treatment of 2-(lithium)selenophene with iodine led to the formation of 2-iodoselenophene **1a**, isolated in 60% yield after purification (Scheme 2).[17] The 2-bromoselenophene **1b** was prepared by the bromination of selenophene **4** with NBS in a mixture of CH_2Cl_2 and AcOH in 62% yield (Scheme 2).[18]

SCHEME 2

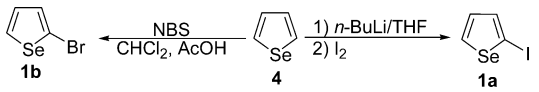
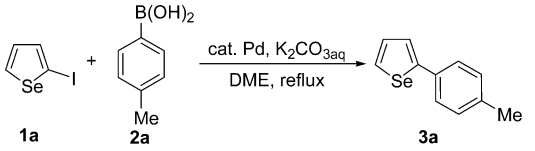


TABLE 1. Effects of Palladium Catalysts on Cross-Coupling of 1a and 2a



entry	palladium catalyst (mol %)	time (h)	yield (%)
1	$PdCl_2(PPh_3)_2$ (5)	1.5	70
2	$Pd(PPh_3)_4$ (5)	1	65
3	$PdCl_2$ (5)	2	84
4	$Pd(OAc)_2$ (5)	1	94
5	$Pd(OAc)_2$ (3)	1	95
6	$Pd(OAc)_2$ (1)	1	68

Since our initial studies have focused on the development of an optimum set of reaction conditions, the coupling reaction of boronic acid with 2-iodoselenophene was examined to optimize the reaction conditions. In this way, 2-iodoselenophene **1a** (0.5 mmol) and *p*-tolylboronic acid (0.7 mmol) in DME were treated at room temperature with different palladium catalysts. After 30 min at this temperature, a solution of K_2CO_3 (2.4 mmol) in H_2O (1.2 mL) was added and the mixture was refluxed for different reaction times (Table 1).

As shown in Table 1, palladium catalysts such as $PdCl_2$, $PdCl_2(PPh_3)_2$, and $Pd(PPh_3)_4$ exhibit moderate to good catalytic activity in this reaction (Table 1, entries 1−3). However, with 3 mol % of $Pd(OAc)_2$ (Table 1, entry 5), the reaction was completed in a short time (1 h) and an excellent yield of product was obtained (95%). It is intriguing that the reaction proceeds much better with Pd(II) than with a Pd(0), but it is reasonable since the reduction of Pd(II) can occur with the boronic acid. It is important to note that when the amount of catalyst is reduced from 3 to 1 mol % a decrease in the yield was observed (Table 1, entries 5 and 6), while the increase from 3 to 5 mol % did not improve the yield (Table 1, entries 4 and 5). The catalytic study also showed that in the absence of palladium catalyst there was no reaction even after the reaction mixture was stirred for 72 h.

We also observed that the nature of the base was critical for the success of the coupling. The reaction of 2-iodoselenophene **1a** (0.5 mmol) with *p*-tolylboronic acid (0.7 mmol) and $Pd(OAc)_2$ (3 mol %) in DME was refluxed with different bases as shown in Table 2. The use of AcOK, AcOLi, and *t*-$BuCO_2$-

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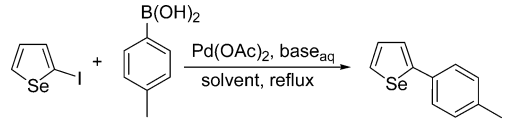
TABLE 2. Study of Base and Solvent Effects on Cross-Coupling Reaction



1a 2a 3a

entry	solvent	base	time (h)	yield (%)
1	DME	AcOK	24	18
2	DME	AcOLi	24	19
3	DME	*t*-$BuCO_2Li$	24	38
4	DME	Cs_2CO_3	12	84
5	DME	Na_2CO_3	24	61
6	DME	KOH	1	90
7	DME	K_3PO_4	1	87
8	DME	K_2CO_3	1	95
9	1,4-dioxane	K_2CO_3	2	38
10	THF	K_2CO_3	12	35
11	toluene	K_2CO_3	1	28
12	H_2O	K_2CO_3	24	46
13	DMF	K_2CO_3	1	75

Li afforded unsatisfactory yields (Table 2, entries 1−3), while an aqueous solution of Cs_2CO_3 (Table 2, entry 4) led to a high yield of the cross-coupling product. Due to the high cost of Cs_2CO_3, we turned our attention to the study of other bases. When the reaction was carried out with inorganic bases such as Na_2CO_3, KOH, and K_3PO_4, the coupling product was obtained in moderate to good yields (Table 2, entries 5−7). To our satisfaction, the use of an aqueous solution of K_2CO_3, an inexpensive base, resulted in the coupled product in 95% yield. Another interesting aspect of this reaction is that when dry bases were used in place of an aqueous solution only a trace amount of product was obtained.

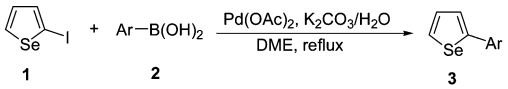
Regarding the influence of the solvent in this coupling reaction, optimal results were achieved using DME (Table 2, entry 8). By using DMF (Table 2, entry 13) moderate yield was obtained, while other solvents such as 1,4-dioxane, THF, toluene, and H_2O (Table 2, entries 9−12) furnished a small amount of the desired arylated product.

Thus, the careful analysis of the optimized reactions revealed that the optimum conditions for this cross-coupling procedure were the addition of a solution of 2-iodoselenophene **1a** (0.5 mmol) in DME (5 mL) to a mixture of $Pd(OAc)_2$ (3 mol %) and *p*-tolylboronic acid (0.7 mmol) at room temperature. After 30 min at this temperature, a solution of K_2CO_3 (2.4 mmol) in H_2O (1.2 mL) was added and the mixture was refluxed for 1 h. Using this reaction condition, we were able to prepare 2-*p*-tolylselenophene **3a** in 95% yield. To demonstrate the efficiency of this reaction, we explored the generality of our method extending the conditions to other boronic acids; the results are summarized in Table 3.

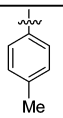
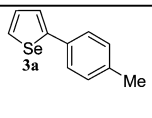
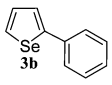
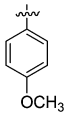
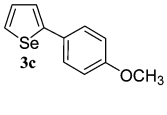
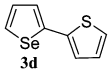
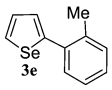
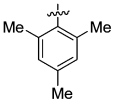
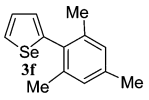
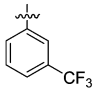
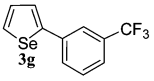
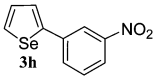
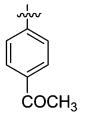
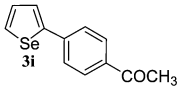
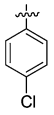
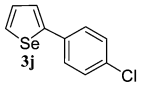
Inspections of Table 3 show that the reaction worked well for a variety of boronic acids. Satisfactorily, all boronic acids tested were effective, although poor yields were observed in more hindered boronic acids (Table 3, entries 5 and 6).

Next, we extended our standard catalytic system, used to the coupling reaction described in Table 3, to the reaction of 2-bromoselenophene **1b** with boronic acids, but unfortunately, the system gave lower yields than the corresponding iodides **1a** (Table 4, entry 4). Then, we focused our attention to find a new catalytic system that could deliver the product of the reaction between 2-bromoselenophene and boronic acid in acceptable yields. Toward this end, we used a variety of

TABLE 3. Coupling Products Obtained Using 2-Iodoselenophene with Boronic Acids

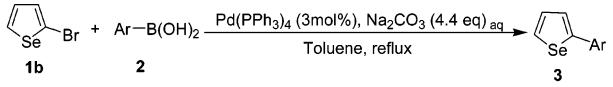


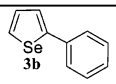
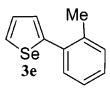
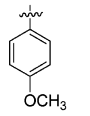
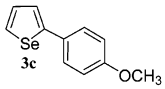
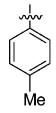
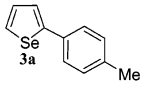
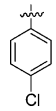
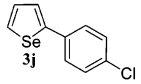
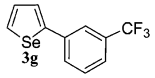
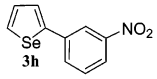
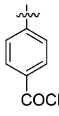
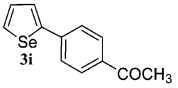
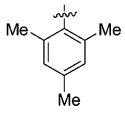
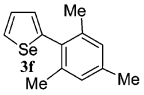
1 2 3

Entry	Ar	Product	Time (h)	Yield (%)
1			1	95
2			1	77
3			1	83
4			1	80
5			24	55
6			48	32
7			1	72
8			24	65
9			24	76
10			1	94

catalysts, solvents, and bases. After a series of experiments, we found that when the catalytic system was changed to $Pd(PPh_3)_4$ (3 mol %), using toluene as solvent and changing the base to Na_2CO_3, the yield was greatly improved (Table 4, entry 4). Thus, the careful analysis of the optimized reactions revealed that the optimum conditions for this cross-coupling reaction were the

TABLE 4. Coupling Product Using 2-Bromoselenophene and Boronic Acids

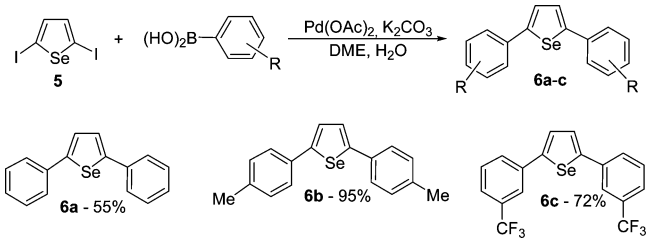


Entry	Ar	Product	Time (h)	Yield (%)
1		 3b	48	69
2		 3e	72	20
3		 3c	72	81
4		 3a	24	85(25)[a]
5		 3j	48	70
6		 3g	48	69
7		 3h	24	74
8		 3i	24	79
9		 3f	48	10

[a] Yields in parentheses correspond to reactions performed in $Pd(OAc)_2$ (3 mol %), K_2CO_3 (2.4 mmol) in H_2O (1.2 mL) and DME (5 mL).

addition of $Pd(PPh_3)_4$ (3 mol %) to a mixture of 2-bromoselenophene **1b** (0.5 mmol) and boronic acids (0.75 mmol) in toluene (3.5 mL). After that, a solution of Na_2CO_3 (2.2 mmol) in H_2O (1.2 mL) was added and the mixture was refluxed. To demonstrate the efficiency of this reaction, we extended the conditions to other boronic acids (Table 4). In general, all of the reactions proceeded smoothly with good yields. Most importantly, the coupling turned out to be general with respect to a diverse array of functionality. The reaction showed compatibility with ketone, nitro, ester, and halogen groups. A closer inspection of the results revealed that the reaction is sensitive to the steric effect of the aromatic ring attached in the boronic acid. For example, boronic acid bearing a Me substituent at the ortho position gave worse yield than no substituted boronic acid (Table 4, entries 2 and 1, respectively).

SCHEME 3



After that, the possibility of generating 2,5-diarylselenophenes was also investigated. As illustrated in Scheme 3, the cross-coupling reaction of 2,5-diiodoselenophene **5**[19] and boronic acids, under the same reaction conditions described for 2-iodoselenophene, led to the substituted diaryl selenophene derivatives **6a**−**c** in good yields (Scheme 3). We investigated the optimum conditions and found that it was only necessary to change the boronic acid amount from 0.7 to 1.4 equiv to give the dual Suzuki coupling with 2,5-diiodoselenophene.

Having optimized the reaction conditions for direct coupling of 2-iodoselenophene or 2-bromoselenophene with boronic acids, we turned our attention to carbonylative cross-coupling reactions using 2-iodoselenophene, boronic acids, and carbon monoxide (Table 5).

Palladium-catalyzed carbonylative cross-coupling is an attractive approach to the formation of unsymmetrically substituted biaryl ketones.[20] Aryl halides with various coupling partners have found success, including stannanes,[21] magnesium,[22] aluminum,[23] silanes,[24] and boronic acids.[25] Drawbacks to this approach often involve significant amounts of biaryl coupled products, the result of coupling without carbon monoxide insertion. The forms of the palladium catalysts, ligands, bases, additives, solvents, and temperature have been reported to have an effect on the amount of ketone versus biaryl formed. To the best of our knowledge, however, no carbonylative cross-coupling reaction using 2-haloselenophene as substrate, to prepare unsymmetrical ketones, has been described thus far. Thus, the standard reaction condition applied to direct coupling of 2-bromoselenophene with boronic acids was also tested for the carbonylative process. Accordingly, the treatment of 2-iodoselenophene (0.5 mmol) with organoboronic acids (0.75 mmol)

(19) 2,5-Diiodoselenophene was prepared according to Zeni, G.; Nogueira, C. W.; Silva, D. O.; Menezes, P. H.; Braga, A. L.; Stefani, H. A.; Rocha, J. B. T. *Tetrahedron Lett.* **2003**, *44*, 685−688, using I_2 instead of Te^0.

(20) Schoenberg, I.; Bartoletti, I.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3318−3326.

(21) (a) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc*. **1988**, *110*, 1557−1565. (b) Kang, S.-K.; Yamaguchi, T.; Kim, T.-H.; Ho, P.-S. *J. Org. Chem.* **1996**, *61*, 9082−9083. (c) Morera, E.; Ortar, G. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1815−1818. (d) Ceccarelli, S.; Piarulli, U.; Gennari, C. *J. Org. Chem.* **2000**, *65*, 6254−6256.

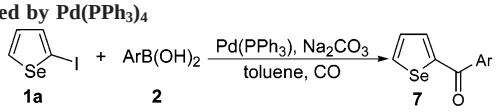
(22) Yamamoto, M.; Kohara, T.; Yamamoto, A. *Chem. Lett.* **1976**, 1217−1220.

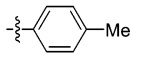
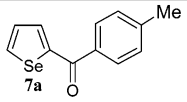
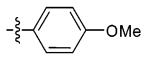
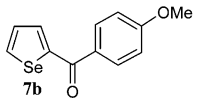
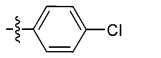
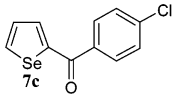
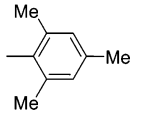
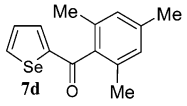
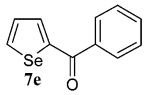
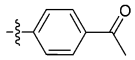
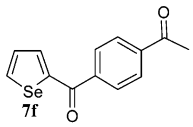
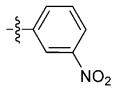
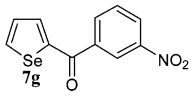
(23) Bumagin, N. A.; Ponomaryov, A. B.; Beletskaya, I. P. *Tetrahedron Lett.* **1985**, *26*, 4819−4822.

(24) Hatanaka, Y.; Fukushima, S.; Hiyama, T. *Tetrahedron* **1992**, *48*, 2113−2119.

(25) (a) Langstrom, B.; Ishiyama, T.; Kizaki, H.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1993**, *34*, 7595−7598. (b) Rahman, O.; Llop, J. Langström, B. *Eur. J. Org. Chem.* **2004**, *2004*, 2674−2678. (c) Ishiyama, T.; Kizaki, H.; Hayashi, T.; Suzuki, A.; Miyaura, N. *J. Org. Chem*. **1998**, *63*, 4726−4731.

TABLE 5. Carbonylative Coupling of 1a with 2 to Give 7 Catalyzed by $Pd(PPh_3)_4$



Entry	Ar	Product	Yield (%)
1			81
2			80
3			69
4			53
5			42
6			10
7			-

in the presence of $Pd(PPh_3)_4$ (3 mol %), a solution of Na_2CO_3 (2.2 mmol) in H_2O (1.2 mL) under carbon monoxide atmosphere (balloon), and toluene (3 mL) at 110 °C for 12 h afforded unsymmetrical ketones. The scope and limitations of this carbonylative cross-coupling process are summarized in Table 5.

The presence of different functional groups is compatible with the carbonylation reaction. It is noteworthy that the reaction is sensitive to the electronic nature of functional groups present in the aromatic ring of boric acids, since the reactions with boronic acids bearing a neutral and an electron-rich group gave the desired product in good yields (Table 5, entries 1−3). However, aryl boronic acids bearing strong electron-withdrawing groups in the aromatic ring (Table 5, entries 6 and 7) did not give the carbonylative products; in this case, only significant amounts of the direct coupling products were observed. When we performed this reaction with hindered boronic acid, the carbonylation product was obtained in moderate yield (Table 5, entry 4). Differentiation in the reactivity between chlorine and boron atoms of boronic acids can be seen by coupling of 4-chlorophenylboronic acid with 2-iodoselenophene to provide only the ketone in 69% yield, without any Ullmann-type reaction product observed (Table 5, entry 3). To the best of our knowledge, aryl chloride could react with boronic acids to afford biaryl products using palladium catalysts.[26] In our case, the chlorine substituent was not affected.

Conclusion

In summary, we have explored the carbon−carbon bond formation via Suzuki coupling reaction of 2-haloselenophenes with boronic acids catalyzed by palladium salt and established a new route to prepare 2-arylselenophenes in good yields. The reaction proceeded cleanly under mild reaction conditions and was performed with aryl boronic acids bearing electron-withdrawing, electron-donating, and neutral substituents, in the presence of $Pd(OAc)_2$ and K_2CO_3/H_2O in DME. In addition, by this protocol unsymmetrical aryl ketones were also obtained from 2-iodoselenophene and boronic acids via a carbonylative process. The pharmacological activities of these compounds are under study in our laboratory. Analysis of the ^1H and ^{13}C NMR spectra showed that all the obtained products presented data in full agreement with their assigned structures.

Experimental Section

General Procedure for the Preparation of the Arylselenophenes from 2-Iodoselenophene. The solution of 2-iodoselenophene (0.128 g, 0.5 mmol) in DME (5 mL) was added to $Pd(OAc)_2$ (0,003 g, 3 mol %) and boronic acid (0.7 mmol), under argon. The resulting solution was stirred for 30 min at room temperature. After this time, a solution of K_2CO_3 (2.4 mmol, 0.309 g) in H_2O (1.2 mL) was added. The mixture was then heated at reflux for the time indicated in Table 3, cooled to room temperature, diluted with dichloromethane (20 mL), and washed with brine (2 × 20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane/ethyl acetate (95:5) or hexane.

2-Phenylselenophene (3b). Yield: 0.079 g (77%). ^1H NMR: $CDCl_3$, 400 MHz, δ (ppm): 7.89 (d, J = 5.55 Hz, 1H), 7.53 (d, J = 7.75 Hz, 2H), 7.42 (d, J = 4.10 Hz, 1H), 7.34−7.30 (m, 3H), 7.27−7.24 (m, 1H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 150.8, 136.4, 130.5, 129.9, 128.8, 127.5, 126.3, 125.2. MS (EI, 70 eV) *m*/*z* (relative intensity): 210 (25), 208 (99), 128 (100), 115 (38), 102 (35). HRMS Calcd for $C_{10}H_8Se$: 207.9791. Found: 207.9796.

2-*p*-Tolylselenophene (3a). Yield: 0.104 g (95%). ^1H NMR: $CDCl_3$, 400 MHz, δ (ppm): 7.87 (d, J = 5.55 Hz, 1H), 7.44 (d, J = 8.04 Hz, 2H), 7.39 (d, J = 3.51 Hz, 1H), 7.29−7.26 (m, 1H), 7.14 (d, J = 8.04 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 150.9, 137.4, 133.7, 130.5, 129.5, 129.3, 126.3, 124.7, 21.1. MS (EI, 70 eV) *m*/*z* (relative intensity): 224 (22), 222 (96), 182 (56), 167 (31), 141 (100), 115 (68). HRMS Calcd for $C_{11}H_{10}Se$: 221.9948. Found: 221.9953.

2-(4-Methoxyphenyl)selenophene (3c). Yield: 0.098 g (83%). ^1H NMR: $CDCl_3$, 400 MHz, δ (ppm): 7.84 (d, J = 5.55 Hz, 1H), 7.47 (d, J = 8.77 Hz, 2H), 7.32 (d, J = 3.65 Hz, 1H), 7.28−7.26 (m, 1H), 6.88 (d, J = 8.77 Hz, 2H), 3.81 (s, 3H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 159.3, 150.7, 130.5, 129.3, 128.7, 127.6, 124.1, 114.3, 55.3. MS (EI, 70 eV) *m*/*z* (relative intensity): 240 (17), 238 (100), 223 (90), 195 (4), 115 (88). HRMS Calcd for $C_{11}H_{10}OSe$: 237.9897. Found: 237.9903.

2-(Selenophen-2-yl)thiophene (3d). Yield: 0.085 g (80%). ^1H NMR: $CDCl_3$, 400 MHz, δ (ppm): 7.85 (d, J = 5.55 Hz, 1H), 7.31 (d, J = 3.65 Hz, 1H), 7.25−7.19 (m, 2H), 7.12 (d, J = 3.65

(26) (a) Arvela, R. K.; Leadbeater, N. E. *Org. Lett.* **2005**, *7*, 2101−2104. (b) LeBlond, C. R.; Andrews, A. T.; Sowa, J. R.; Sun, Y. *Org. Lett.* **2001**, *3*, 1555−1557.

Hz, 1H), 7.00−6.98 (m, 1H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 130.2, 129.7, 129.5, 127.8, 126.7, 125.9, 124.5, 124.4. MS (EI, 70 eV) *m*/*z* (relative intensity): 214 (85), 134 (100), 121 (10), 108 (20), 89 (23). HRMS Calcd for C_8H_6SSe: 213.9355. Found: 213.9361.

2-*o*-Tolylselenophene (3e). Yield: 0.060 g (55%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 8.02 (d, J = 5.55 Hz, 1H), 7.39−7.37 (m, 1H), 7.33−7.31 (m, 1H), 7.26−7.18 (m, 4H), 2.41 (s, 3H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 149.4, 136.3, 135.7, 130.7, 130.6, 130.5, 129.6, 128.6, 127.7, 125.8, 29.7. HRMS Calcd for $C_{11}H_{10}Se$: 221.9948. Found: 221.9955.

2-Mesitylselenophene (3f). Yield: 0.039 g (32%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 8.04 (d, J = 5.55 Hz, 1H), 7.31−7.29 (m, 1H), 6.93−6.92 (m, 3H), 2.31 (s, 3H), 2.14 (s, 6H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 148.1, 137.6, 133.1, 130.9, 130.2, 129.5, 128.6, 128.1, 21.0, 20.8. MS (EI, 70 eV) *m*/*z* (relative intensity): 252 (14), 250 (74), 235 (32), 169 (100), 155 (41), 128 (29), 115 (26). HRMS Calcd for $C_{13}H_{14}Se$: 250.0261. Found: 250.0266.

2-(3-(Trifluoromethyl)phenyl)selenophene (3g). Yield: 0.099 g (72%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 7.98 (d, J = 5.55 Hz, 1H), 7.78 (s, 1H), 7.69 (d, J = 7.75 Hz, 1H), 7.58−7.43 (m, 2H), 7.45 (t, J = 7.75 Hz, 1H), 7.33−7.31 (m, 1H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 148.9, 137.2, 131.5 (q, J = 32.53 Hz), 131.2, 130.7, 129.6, 129.4, 126.4, 124.0 (q, J = 3.53 Hz), 123.9 (q, J = 272,68 Hz), 122.9 (q, J = 3.53 Hz). MS (EI, 70 eV) *m*/*z* (relative intensity): 276 (100), 196 (48), 175 (13), 146 (23), 126 (10), 115 (11). HRMS Calcd for $C_{11}H_7F_3Se$: 275.9665. Found: 275.9671.

2-(3-Nitrophenyl)selenophene (3h). Yield: 0.081 g (65%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 8.38 (s, 1H), 8.10 (d, J = 7.89 Hz, 1H), 8.04 (d, J = 5.55 Hz, 1H), 7.83 (d, J = 7.60 Hz, 1H), 7.57 (d, J = 3.51 Hz, 1H), 7.52 (t, J = 8.04 Hz, 1H), 7.37−7.34 (m, 1H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 167.7, 147.6, 138.1, 132.3, 131.9, 130.8, 129.8, 127.1, 121.9, 120.7. MS (EI, 70 eV) *m*/*z* (relative intensity): 253 (9), 207 (7), 127 (14), 115 (100). HRMS Calcd for $C_{10}H_7NO_2Se$: 252.9642. Found: 252.9648.

1-(4-(Selenophen-2-yl)phenyl)ethanone (3i). Yield: 0.094 g (76%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 8.02 (d, J = 5.55 Hz, 1H), 7.93 (d, J = 8.33 Hz, 2H), 7.62 (d, J = 8.33 Hz, 2H), 7.58 (d, J = 3.51 Hz, 1H), 7.35−7.33 (m, 1H), 2.59 (s, 3H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 197.2, 149.2, 140.7, 135.8, 131.8, 130.8, 129.1, 126.8, 126.1, 26.5. MS (EI, 70 eV) *m*/*z* (relative intensity): 250 (9), 235 (100), 207 (5), 126 (25), 115 (99). HRMS Calcd for $C_{12}H_{10}OSe$: 249.9897. Found: 249.9905.

2-(4-Chlorophenyl)selenophene (3j). Yield: 0.113 g (94%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 7.91 (d, J = 5.55 Hz, 1H), 7.44 (d, J = 8.33 Hz, 2H), 7.42−7.38 (m, 1H), 7.30−7.27 (m, 3H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 149.3, 134.9, 130.6, 130.4, 128.9, 128.1, 127.5, 125.6. MS (EI, 70 eV) *m*/*z* (relative intensity): 244 (6), 242 (100), 162 (69), 126 (26), 115 (27). HRMS Calcd for $C_{10}H_7ClSe$: 241.9401. Found: 241.9407.

General Procedure for the Preparation of the Bis-arylselenophene from 2,5-Diiodoselenophene. The solution of 2,5-diiodoselenophene (0.096 g, 0.25 mmol) in DME (5 mL) was added, under argon, to a mixture of $Pd(OAc)_2$ (0.003 g, 6 mol %) and boronic acid (0.7 mmol). The resulting solution was stirred for 30 min at room temperature. After this time, the solution was added to the solution of K_2CO_3 (2.4 mmol, 0.309 g) in H_2O (1.2 mL). The mixture was then heated at reflux for the time indicated in Scheme 3, cooled to room temperature, diluted with dichloromethane (20 mL), and washed with brine (2 × 20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane/ethyl acetate (95:5) or hexane.

2,5-Bis-*p*-tolylselenophene (6b). Yield: 0.148 g (95%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 7.44 (d, J = 7.65 Hz, 4H), 7.36 (s, 2H), 7.14 (d, J = 7.61 Hz, 4H), 2.34 (s, 6H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 149.4, 137.4, 133.7, 129.6, 125.9, 125.6, 21.1. MS (EI, 70 eV) *m*/*z* (relative intensity): 312 (100), 309 (26), 215 (26), 154 (20), 115 (27), 101 (10), 89 (7). HRMS Calcd for $C_{18}H_{16}Se$: 312.0417. Found: 312.0424.

2,5-Bis-(3-(trifluoromethyl)phenyl)selenophene (6c). Yield: 0.151 g (72%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 7.80 (s, 2H), 7.71 (d, J = 7.64 Hz, 2H), 7.57−7.49 (m, 6H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 149.0, 136.8, 131.5 (q, J = 32.53 Hz), 129.5, 129.3, 127.4, 124.3 (q, J = 3.53 Hz), 123.9 (q, J = 272.68 Hz), 122.6 (q, J = 3.53 Hz). MS (EI, 70 eV) *m*/*z* (relative intensity): 420 (100), 418 (48), 340 (13), 270 (16), 210 (16). HRMS Calcd for $C_{18}H_{10}F_6Se$: 419.9852. Found: 419.9858.

2,5-Bis-phenylselenophene (6a). Yield: 0.078 g (55%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 7.56 (d, J = 7.60 Hz, 4H), 7.44 (s, 2H), 7.38−7.23 (m, 6H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 149.9, 136.4, 128.9, 127.6, 126.2, 126.1. MS (EI, 70 eV) *m*/*z* (relative intensity): 284 (100), 280 (22), 203 (53), 142 (14), 101 (30). HRMS Calcd for $C_{16}H_{12}Se$: 284.0104. Found: 284.0110.

General Procedure for the Synthesis of Diaryl Ketones from 2-Iodoselenophene. A dried Schlenk flask containing $Pd(PPh_3)_4$ (0.017 g, 3 mol %) and boronic acid (0.75 mmol) was evacuated and connected to an atmosphere of argon. 2-Iodoselenophene (0.128 g, 0.5 mmol), toluene (3 mL), and aqueous Na_2CO_3 (1.1 mL of solution 2 M in H_2O, 2.17 mmol) were added. After removal of argon atmosphere, the system was purged with CO three times using a balloon. The mixture was stirred at 110 °C under carbon monoxide atmosphere (balloon) for 12 h. The resulting mixture was quenched by addition of NH_4Cl solution (10 mL) and then extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried with $MgSO_4$, filtered, and evaporated under reduced pressure. The crude products were purified by flash column chromatography (EtOAc/hexane, 20:80).

Selenophen-2-yl(*p*-tolyl)methanone (7a). Yield: 0.101 g (81%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 8.40 (d, J = 5.55 Hz, 1H), 7.83 (d, J = 3.95 Hz, 1H), 7.76 (d, J = 8.04 Hz, 2H), 7.42−7.39 (m, 1H), 7.28 (d, J = 8.04 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 189.0, 150.7, 139.9, 136.8, 130.5, 130.1, 129.3, 129.0, 128.8, 21.5. MS (EI, 70 eV) *m*/*z* (relative intensity): 252 (13), 250 (69), 159 (74), 119 (100), 91 (75). HRMS Calcd for $C_{12}H_{10}OSe$: 249.9897. Found: 249.9904.

(4-Methoxyphenyl)(selenophen-2-yl)methanone (7b). Yield: 0.107 g (80%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 8.38 (d, J = 5.55 Hz, 1H), 7.87 (d, J = 8.77 Hz, 2H), 7.82 (d, J = 3.65 Hz, 1H), 7.41−7.39 (m, 1H), 6.96 (d, J = 8.77 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 187.9, 162.9, 150.7, 139.4, 136.2, 132.0, 131.4, 130.4, 130.2, 55.3. MS (EI, 70 eV) *m*/*z* (relative intensity): 266 (53), 264 (29), 251 (13), 159 (38), 135 (100), 77 (40). HRMS Calcd for $C_{12}H_{10}O_2Se$: 265.9846. Found: 265.9852.

(4-Chlorophenyl)(selenophen-2-yl)methanone (7c). Yield: 0.093 g (69%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 8.45 (d, J = 5.55 Hz, 1H), 7.81−7.77 (m, 3H), 7.45 (d, J = 8.48 Hz, 2H), 7.43−7.40 (m, 1H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 188.0, 149.9, 140.7, 138.4, 137.1, 135.9, 130.7, 130.5, 128.6. MS (EI, 70 eV) *m*/*z* (relative intensity): 270 (52), 159 (100), 139 (40), 111 (42), 75 (38). HRMS Calcd for $C_{11}H_7ClOSe$: 269.9351. Found: 269.9357.

Mesityl(selenophen-2-yl)methanone (7d). Yield: 0.074 g (53%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 8.42 (d, J = 5.55 Hz, 1H), 7.49 (d, J = 3.97 Hz, 1H), 7.33−7.29 (m, 1H), 6.88 (s, 2H), 2.31 (s, 3H), 2.17 (s, 6H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 193.9, 151.4, 141.2, 138.5, 137.4, 134.0, 130.9, 128.2, 128.1, 21.0, 19.2. MS (EI, 70 eV) *m*/*z* (relative intensity): 280 (18), 278 (89), 197 (100), 169 (33), 147 (26), 119 (25), 91 (40). HRMS Calcd for $C_{14}H_{14}OSe$: 278.0210. Found: 278.0216.

Phenyl(selenophen-2-yl)methanone (7e). Yield: 0.049 g (42%). ^{1}H NMR: $CDCl_3$, 400 MHz, δ (ppm): 8.42 (d, J = 5.55 Hz, 1H), 7.84−7.79 (m, 3H), 7.59−7.41 (m, 1H), 7.49−7.41 (m, 3H). ^{13}C NMR: $CDCl_3$, 100 MHz, δ (ppm): 189.3, 150.4, 140.3, 137.3, 132.0, 130.6, 129.9, 129.0, 128.3. MS (EI, 70 eV) *m*/*z* (relative

intensity): 238 (12), 236 (64), 159 (100), 105 (53), 77 (10), 51 (5). HRMS Calcd for $C_{11}H_8OSe$: 235.9740. Found: 235.9744.

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Supporting Information Available: Experimental procedures, additional experimental details for the preparation, and ^{1}H and ^{13}C NMR spectra for all reaction products. This material is available free of charge via the Internet at http://pubs.acs.org.

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