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Palladium-Catalyzed Carbonylation of 2-Haloselenophenes: Synthesis of Selenophene-2-carboxamides, Selenophene-2,5-dicarboxamides and *N*,*N*′-Bridged Selenophene-2-carboxamides

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Keywords: Selenophene / Carbonylation / Palladium / Amides / Carbon monoxide

We present herein our results on the palladium-catalyzed carbonylation of 2-haloselenophene and amines, under carbon monoxide atmosphere, giving a new route to prepare selenophene-2-carboxamides, selenophene-2,5-dicarboxamides and *N*,*N*′-bridged selenophene-2-carboxamides in good yields. The reaction proceeded cleanly under mild conditions, using a simple apparatus and procedure, and in the absence of high pressure of carbon monoxide.

Introduction

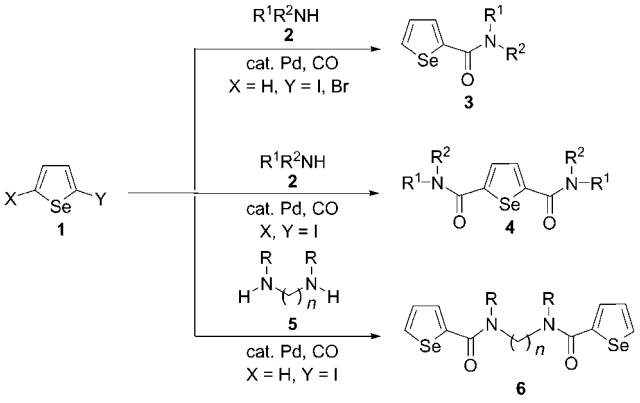
The palladium-catalyzed carbonylation of aryl and heteroaryl halides in the presence of carbon monoxide is one of the most versatile and convenient methods for the preparation of aromatic and heteroaromatic carbonyl compounds, including key intermediates in natural products synthesis.[1] The procedure usually tolerates a wide range of functionality, and has been employed for the synthesis of many biologically active molecules.[2] This method is a convenient but underdeveloped synthetic route to a number of common functional groups, including amides, esters, lactams and lactones.[3] Carbonylation reactions are usually carried out at high pressures using carbon monoxide gas in the presence of a palladium catalyst, and can take many hours to reach completion. The rates of these reactions are dependent on several factors, including aryl halide species, the nature of the catalyst, the nucleophilic species and the pressure and temperature of the system. The rates of the catalytic cycle can be enhanced by using high pressure reactors; however, such reactors are inherently expensive and require special safety precautions.

Recently, we described the carbon–nitrogen bond formation via a coupling reaction of 2-iodo-selenophene catalyzed by Cu^{I} in the presence of a base and an inexpensive ligand, and established the first route to obtain 2-nitrogen-selenophene derivatives in good yields.[4]

Chalcogenide compounds have found wide utility in organic synthesis because of their effects on an extraordinary number of very different reactions, including many carbon–carbon bond formations,[5] under relatively mild reaction conditions. In addition, they have become attractive synthetic targets because of their chemo-, regio-, and stereoselective reactions,[6] used with a wide variety of functional groups, thus avoiding protection group chemistry and accessing molecules with useful biological activities.[7]

To the best of our knowledge, there are no reports on the use of halogenated selenophenes as electrophilic substrates for palladium-catalyzed carbonylative cross-coupling reactions to form amides.

In this context, we have examined a procedure to prepare selenophenecarboxamide derivatives by the carbonylation of haloselenophenes with amines in the presence of palladium catalyst, using a simple apparatus and procedure, and in the absence of high pressure of carbon monoxide (Scheme 1).



Scheme 1. General scheme.

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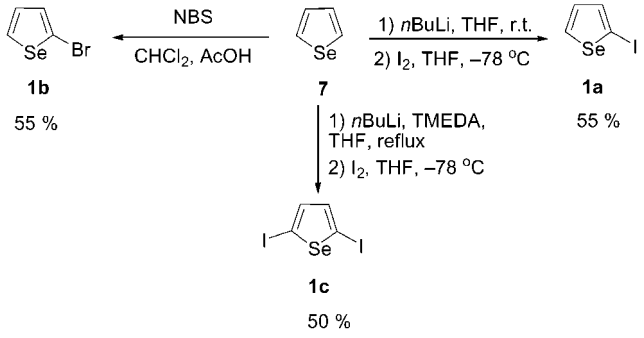
Results and Discussion

The starting 2-iodoselenophene **1a** was readily available through the metalation of selenophene **7**[8] with *n*-butyllithium to give 2-(lithium)selenophene derivatives. The treatment of 2-(lithium)selenophene with iodine leads to the formation of 2-iodoselenophene.[9] 2,5-Diiodoselenophene (**1c**) was prepared by the dimetalation of selenophene with 2 equiv. of *n*-butyllithium, in the presence of TMEDA, followed by reaction with iodine.[10] Conversely, 2-bromoselenophene (**1b**) was prepared via bromination of selenophene with NBS in a mixture of CH_2Cl_2 and AcOH[11] (Scheme 2).

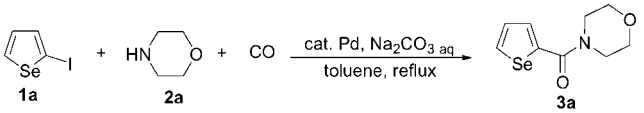


Scheme 2. Starting materials synthesis.

Since our initial studies have focused on the development of an optimum set of reaction conditions, the carbonylation reaction of 2-iodoselenophene with an amine was examined to optimize the reaction conditions. Thus, 2-iodoselenophene (**1a**) (0.5 mmol), morpholine (**2a**) (0.8 mmol), and aqueous Na_2CO_3 (2.2 mmol, 2 M) in toluene (3 mL) were treated with different palladium catalysts in the presence of carbon monoxide (1 atm) under reflux with different reaction times (Table 1). As shown in Table 1, palladium catalysts such as $PdCl_2(PPh_3)_2$, $Pd(OAc)_2$ and $PdCl_2$ exhibited the lowest catalyst activity in this reaction (Table 1, entries 1–3). However, with 10 mol-% of $Pd(PPh_3)_4$, the reaction was completed in a short reaction time (2 h), and an excellent yield of product was obtained (92%) (Table 1, entry 4). It is relevant to note that when the amount of catalyst was reduced from 10 to 5 mol-%, a notable decrease in the yields was observed, even under reflux and long reaction times (Table 1, entries 5–7). No reaction occurred in absence of palladium catalyst even after 72 h.

We also observed that the nature of the base was critical for the success of the carbonylation. The reaction of 2-iodoselenophene **1a** (0.5 mmol) with morpholine **2a** (0.8 mmol) and $Pd(PPh_3)_4$ (10 mol-%) in toluene, under carbon monoxide atmosphere, was refluxed with different bases as shown in Table 2. The results showed that K_2CO_3 and KOH afforded unsatisfactory yields (Table 2, entries 1 and 2), while the organic base, Et_3N, in the absence of H_2O, led to a moderate yield of the carbonylation product (Table 2, entry 3). When an aqueous solution of Cs_2CO_3 was used, the desired amide was obtained in good yield (Table 2, entry 4). Due to the high cost of Cs_2CO_3, we turned our attention to the study of the other bases. When the reaction was carried out with K_3PO_4, the carbonylation product also was formed in good yield (Table 2, entry 5). To our satisfaction, the use of an aqueous solution of Na_2CO_3, an inexpensive base, resulted in the carbonylation product in 92% yield (Table 2, entry 6).

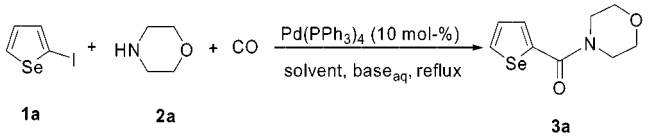
Table 1. Effects of palladium catalyst on the carbonylation reaction of **1a** and **2a**.



Entry	Palladium catalyst (mol-%)	Time/h	% Yield[a]
1	$PdCl_2(PPh_3)_2$ (10)	12	31
2	$Pd(OAc)_2$ (10)	12	15
3	$PdCl_2$ (10)	12	20
4	$Pd(PPh_3)_4$ (10)	2	92
5	$Pd(PPh_3)_4$ (7.5)	12	45
6	$Pd(PPh_3)_4$ (5)	2	15
7	$Pd(PPh_3)_4$ (5)	12	33

[a] Yields correspond to reactions performed using 2-iodoselenophene (0.5 mmol), morpholine (0.8 mmol), Na_2CO_3 (2.2 mmol) in H_2O (1.1 mL) in toluene (3 mL) with different palladium catalysts.

Table 2. Study of base and solvent effects on the carbonylation reaction of **1a** in the presence of **2a**.

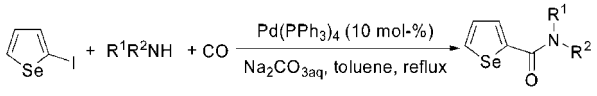


Entry	Solvent	Base	Time/h	% Yield[a]
1	toluene	K_2CO_3	12	43
2	toluene	KOH	12	22
3	toluene	Et_3N[b]	12	67
4	toluene	Cs_2CO_3	12	69
5	toluene	K_3PO_4	2	75
6	toluene	Na_2CO_3	2	92
7	DME	Na_2CO_3	12	59
8	DMF	Na_2CO_3	24	30
9	THF	Na_2CO_3	24	15
10	H_2O	Na_2CO_3	24	12
11	DMSO	Na_2CO_3	24	25
12	1,4-dioxane	Na_2CO_3	24	26

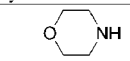
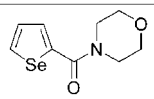
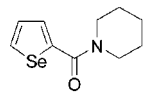
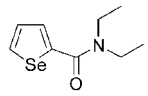
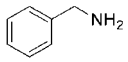
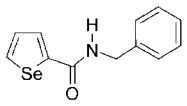
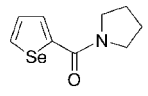
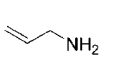
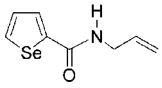
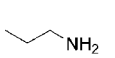
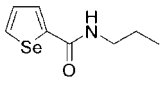
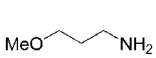
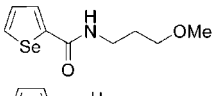
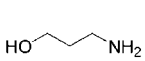
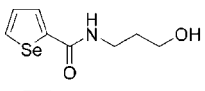
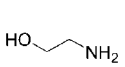
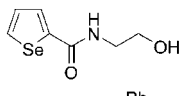
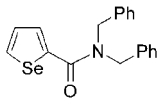
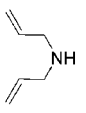
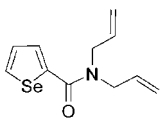
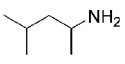
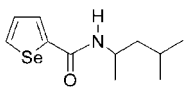
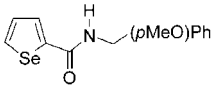
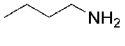
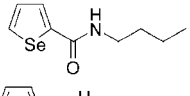
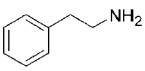
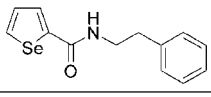
[a] Yields correspond to reactions performed using 2-iodoselenophene (0.5 mmol), morpholine (0.8 mmol), $Pd(PPh_3)_4$ (10 mol-%), basic solution (2.2 mmol) in H_2O (1.1 mL) with different solvents (3 mL). [b] Dry Et_3N instead of an aqueous solution was used.

Regarding the influence of the solvent in this carbonylation reaction, optimal results were achieved using toluene (Table 2, entry 6). By using DME (Table 2, entry 7), a moderate yield was obtained, while other solvents such as DMF, THF, H_2O, DMSO and 1,4-dioxane (Table 2, entries 8–12) furnished a small amount of the desired product. Thus, careful analysis of the optimized reactions revealed that the optimum conditions for this carbonylation reaction procedure corresponded to those of Table 1; entry 4. Using

Table 3. Synthesis of selenophene-2-carboxamides **3** by aminocarbonylation of 2-iodoselenophene.



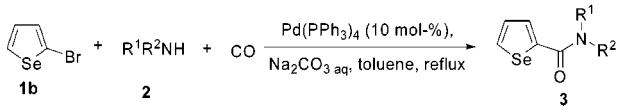
1a **2** **3**

Entry	R^1R^2NH	Product		% Yield[a]
1			**3a**	92
2			**3b**	81
3			**3c**	57
4			**3d**	77
5			**3e**	72
6			**3f**	75
7			**3g**	83
8			**3h**	84
9			**3i**	74
10			**3j**	71
11			**3k**	57
12			**3l**	54
13			**3m**	69
14	(*p*MeO)PhNH$_2$		**3n**	73
15			**3o**	78
16			**3p**	77

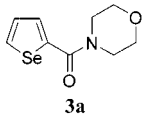
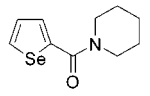
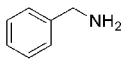
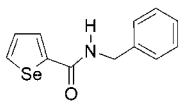
[a] Yields correspond to reactions performed using 2-iodoselenophene (0.5 mmol), amines (0.8 mmol), $Pd(PPh_3)_4$ (10 mol-%), and aqueous Na_2CO_3 (2.2 mmol, 2 M) in toluene (3 mL).

these conditions, we were able to prepare morpholino(selenophen-2-yl)methanone (**3a**) in 92% yield. To demonstrate the efficiency of this reaction, we explored the generality of

Table 4. Synthesis of selenophene-2-carboxamides **3** by aminocarbonylation of 2-bromoselenophene.



1b **2** **3**

Entry	R^1R^2NH	Product		% Yield[a]
1			**3a**	75
2			**3b**	70
3			**3d**	60
4			**3e**	71
5			**3f**	57
6			**3h**	64
7			**3i**	53
8			**3l**	47
9			**3m**	50
10	(*p*MeO)PhNH$_2$		**3n**	69

[a] Yields correspond to reactions performed using 2-bromoselenophene (0.5 mmol), amines (0.8 mmol), $Pd(PPh_3)_4$ (10 mol-%), and aqueous Na_2CO_3 (2.2 mmol, 2 M) in toluene (3 mL).

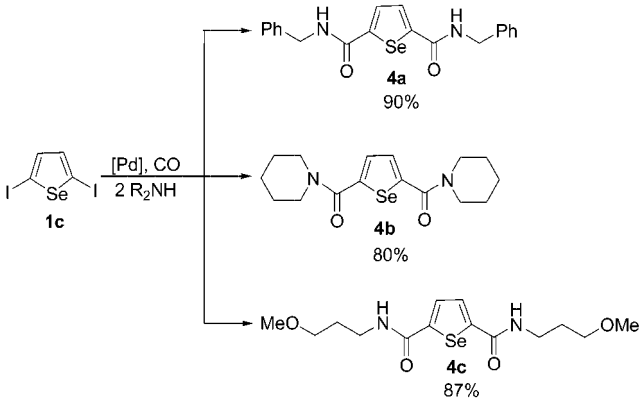
our method, extending the conditions to other amines; the results are summarized in Table 3.

Thus, careful analysis of the optimized reactions revealed that the optimum conditions for this carbonylation reaction procedure were the addition of a solution of 2-iodoselenophene **1a** (0.5 mmol) in toluene to the catalyst precursor $Pd(PPh_3)_4$ (10 mol-%). The amine **2a** (0.8 mmol) was added next, followed by the addition of a solution of Na_2CO_3 (2.2 mmol) in H_2O (1.1 mL). The mixture was refluxed for 2 h. Using this procedure, we were able to prepare morpholino(selenophen-2-yl)methanone **3a** in 92% yield. To demonstrate the efficiency of this reaction, we explored the method by extending these conditions to other amines; the results are summarized in Table 3.

Table 3 shows that the reaction worked well for a variety of amines. All amines tested were effective, although poor yields were observed in more hindered amines (Table 3, entries 3, 11 and 12). Most importantly, the carbonylation turned out to be general with respect to a diverse array of functionality. The reaction not only showed compatibility with methoxy and hydroxy groups (Table 3, entries 8–10), but also did not provide ester derivative formation from alcohol carbonylation (Table 3, entries 9 and 10).

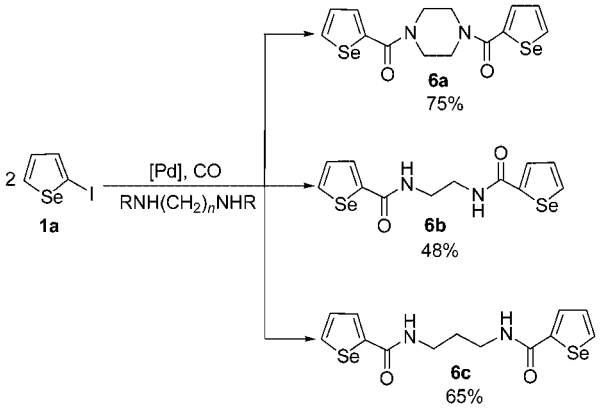
Next, we extended our standard catalyst system, used in the carbonylation reaction described in Table 3, to the reaction of 2-bromoselenophene (**1b**) with some selected amines. Fortunately, all of the reactions proceeded smoothly and with good yields. The results are summarized in Table 4. As expected, the 2-iodoselenophene gave the products in higher yields than 2-bromoselenophene (Table 3).

The possibility of generating selenophene-2,5-dicarboxamides was also investigated starting from 2,5-diiodoselenophene (**1c**). As illustrated in Scheme 3, the carbonylation reaction of **1c** (0.5 mmol) and amines, under the same conditions described for 2-iodoselenophene in Table 3, but with 1.6 mmol of amine rather than 0.8, led to selenophene-2,5-dicarboxamide derivatives **4a**–**c** in excellent yields (Scheme 3).



Scheme 3. Carbonylation reaction using 2,5-diiodoselenophene (**1c**) and amines.

Further, we to explored the carbonylation reaction using 2 equiv. of 2-iodoselenophene (**1a**) and 1 equiv. of a diamine **5** under the same conditions used in Table 3. Thus, 2-iodoselenophene (1.0 mmol) and diamine (0.8 mmol) in toluene (5 mL), in the presence of $Pd(PPh_3)_4$ (10 mol-%) and Na_2CO_3 (4.4 mmol) in H_2O (2.2 mL) were refluxed for 12 h. We were pleased to observe formation of *N*,*N*′-bridged selenophene-2-carboxamides **6a**–**c** in good yields (Scheme 4).



Scheme 4. *N*,*N*′-Bridged selenophene-2-carboxamides **6a**–**c** formed by the carbonylation reaction of 2-iodoselenophene (**1a**) and diamines.

Conclusions

In summary, we have explored the carbonylation reaction of haloselenophenes with amines catalyzed by palladium and established a new route to prepare selenophene-2-carboxamides in good yields. The reaction proceeded cleanly under mild conditions and was performed with primary and secondary amines in the presence of $Pd(PPh_3)_4$ and aqueous Na_2CO_3 in toluene. In addition, by this protocol, selenophene-2,5-dicarboxamides were also obtained in good yields from 2,5-diiodoselenophene. Conversely, using this method, we were able to prepare *N*,*N*′-bridged selenophene-2-carboxamides by a simple stoichiometric control of 2-iodoselenophene and a diamine.

Experimental Section

General: Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained at 200 MHz with a DPX-200 NMR spectrometer or at 400 MHz with a DPX-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$ or tetramethylsilane (TMS) as the external reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (J) in Hertz and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained either at 50 MHz with a DPX-200 NMR spectrometer or at 100 MHz with a DPX-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$. High resolution mass spectra were recorded with a MS50TC double focusing

magnetic sector mass spectrometer using EI at 70 eV. Column chromatography was performed using silica gel (230–400 mesh) following the methods described by Still.[12] Thin-layer chromatography (TLC) was performed using silica gel GF_{254}, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine vapour or acidic vanillin. Most reactions were monitored by TLC for disappearance of starting material. All solvents were ACS or HPLC grade unless otherwise noted. Air- and moisture-sensitive reactions were conducted in flame-dried or oven-dried glassware equipped with tightly fitted rubber septa under a positive atmosphere of dry nitrogen or argon. Reagents and solvents were handled using standard syringe techniques. Temperatures above room temperature were maintained by use of a mineral oil bath with an electrically heated coil connected to a Variac controller.

Typical Procedure for Carbonylation of 2-Haloselenophene 1 and Amines: A dried Schlenk flask containing $Pd(PPh_3)_4$ (0.056 g, 10 mol-%) was evacuated and connected to an atmosphere of argon. 2-Haloselenophene **1** (0.5 mmol), toluene (3 mL), amine **2** (0.8 mmol) and Na_2CO_3 (0.243 g, 2.2 mmol) in H_2O (1.1 mL) were added. After removal of argon atmosphere by bubbling CO through the reaction medium, the system was purged with CO using a balloon. The mixture was stirred at 110 °C under carbon monoxide atmosphere (balloon) for 2–12 h. The resulting mixture was quenched by addition of H_2O (10 mL) and then extracted with EtOAc (3 × 10 mL). The combined organic extracts was dried with $MgSO_4$, filtered, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (EtOAc/hexane, 30:70).

Morpholino(selenophen-2-yl)methanone (3a): Yield 0.112 g (92%). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.19 (d, J = 5.55 Hz, 1 H), 7.46 (d, J = 3.50 Hz, 1 H), 7.31 (dd, J = 3.50, 5.55 Hz, 1 H), 3.78–3.70 (m, 8 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.9, 142.7, 134.6, 130.5, 129.1, 66.7, 45.7 ppm. MS (EI, 70 eV): m/z (%) = 244 (100), 158 (54), 129 (71), 114 (35). HRMS: calcd. for $C_9H_{11}NO_2Se$ 244.9955; found 244.9960.

Piperidin-1-yl(selenophen-2-yl)methanone (3b): Yield (Hal = I) 0.91 g (75%), (Hal = Br) 0.84 g (70%). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.4 (d, J = 5.55 Hz, 1 H), 7.46 (d, J = 3.82 Hz, 1 H), 7.29 (dd, J = 3.82, 5.55 Hz, 1 H), 3.68–3.63 (m, 4 H), 1.66–1.61 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.7, 143.7, 133.7, 129.8, 128.9, 46.7, 26.0, 24.4 ppm. MS (EI, 70 eV): m/z (%) = 242 (100), 258 (63), 157 (53), 129 (76), 83 (35). HRMS: calcd. for $C_{10}H_{13}NOSe$ 243.0162; found 243.0176.

***N*,*N*-Diethylselenophene-2-carboxamide (3c):** Yield 0.065 g (57%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (dd, J = 1.02, 5.55 Hz, 1 H), 7.48 (dd, J = 1.02, 3.82 Hz, 1 H), 7.30 (dd, J = 3.55, 5.55 Hz, 1 H), 3.58 (q, J = 7.05 Hz, 4 H), 1.27 (t, J = 7.05 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.1, 144.7, 133.9, 129.3, 129.1, 42.0, 13.5 ppm. MS (EI, 70 eV): m/z (%) = 230 (100), 200 (29), 157 (31), 129 (76), 99 (31) ppm. HRMS: calcd. for $C_9H_{13}NOSe$ 231.0162; found 231.0159.

***N*-Benzylselenophene-2-carboxamide (3d):** Yield (Hal = I) 0.105 g (77%), (Hal = Br) 0.081 g (60%). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.18 (d, J = 5.55 Hz, 1 H), 7.68 (d, J = 3.82 Hz, 1 H), 7.31–7.28 (m, 6 H), 6.63 (s, 1 H), 4.54 (d, J = 5.73 Hz, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.0, 145.5, 138.0, 136.2, 130.0, 128. 6, 127.8, 127.5, 44.0 ppm. MS (EI, 70 eV): m/z (%) = 264 (100), 173 (34), 157 (83), 129 (89), 105 (32), 81 (21). HRMS: calcd. for $C_{12}H_{11}NOSe$ 265.0006; found 265.0010.

Pyrrolidin-1-yl(selenophen-2-yl)methanone (3e): Yield (Hal = I) 0.082 g (72%), (Hal = Br) 0.080 g (71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.19 (d, J = 5.55 Hz, 1 H), 7.69 (d, J = 3.60 Hz, 1 H), 7.34–7.24 (m, 1 H), 3.74–3.65 (m, 4 H), 1.98–1.94 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.9, 146.3, 135.4, 131.0, 129.7, 48.9, 47.3, 26.6, 23.9 ppm. MS (EI, 70 eV): m/z (%) = 228 (100), 157 (55), 128 (44), 87 (21), 70 (17). HRMS: calcd. for $C_9H_{11}NOSe$ 229.0006; found 229.0002.

***N*-Allylselenophene-2-carboxamide (3f):** Yield (Hal = I) 0.080 g (75%), (Hal = Br) 0.060 g (57%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (dd, J = 1.17, 5.55 Hz, 1 H), 7.68 (dd, J = 1.17, 3.82 Hz, 1 H), 7.34 (dd, J = 3.82, 5.55 Hz, 1 H), 6.15 (s, 1 H), 6.02–5.83 (m, 1 H), 5.31–5.22 (m, 1 H), 5.21–5.15 (m, 1 H), 4.05 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.9, 145.6, 136.1, 134.0, 130.0, 129.4, 116.8, 42.4 ppm. MS (EI, 70 eV): m/z (%) = 213 (100), 157 (55), 129 (44), 84 (32). HRMS: calcd. for C_8H_9NOSe 214.9849; found 214.9851.

***N*-Propylselenophene-2-carboxamide (3g):** Yield 0.089 g (83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (dd, J = 1.02, 5.55 Hz, 1 H), 7.66 (dd, J = 1.02, 3.82 Hz, 1 H), 7.33 (dd, J = 3.82, 5.55 Hz, 1 H), 6.19 (s, 1 H), 3.43–3.33 (m, 2 H), 1.64 (sext, J = 7.35 Hz, 2 H), 0.97 (t, J = 7.35 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 146.0, 135.8, 129.9, 129.1, 41.8, 22.8, 11.3 ppm. MS (EI, 70 eV): m/z (%) = 216 (100), 157 (62), 128 (7), 73 (21). HRMS: calcd. for $C_8H_{11}NOSe$ 217.0006; found 217.0002.

***N*-(3-Methoxypropyl)selenophene-2-carboxamide (3h):** Yield (Hal = I) 0.103 g (84%), (Hal = Br) 0.078 g (64%). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.17 (d, J = 5.55 Hz, 1 H), 7.65 (d, J = 3.82 Hz, 1 H), 7.32 (dd, J = 3.82, 5.55 Hz, 1 H), 6.97 (s, 1 H), 3.57 (t, J = 5.55 Hz, 4 H), 3.37 (s, 3 H), 1.86 (q, J = 5.73 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.9, 146.1, 135.5, 129.5, 129.1, 72.2, 58.8, 39.1, 28.7 ppm. MS (EI, 70 eV): m/z (%) = 246 (100), 215 (21), 201 (11), 187 (16), 157 (55), 129 (54), 87 (35). HRMS: calcd. for $C_9H_{13}NO_2Se$ 247.0112; found 247.0117.

***N*-(3-Hydroxypropyl)selenophene-2-carboxamide (3i):** Yield (Hal = I) 0.085 g (74%), (Hal = Br) 0.06 g (53%). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.19 (d, J = 5.55 Hz, 1 H), 7.69 (d, J = 3.89 Hz, 1 H), 7.31 (dd, J = 3.89, 5.55 Hz, 1 H), 6.93 (s, 1 H), 3.71 (t, J = 5.36 Hz, 2 H), 3.62 (m, 2 H), 1.78 (q, J = 5.95 Hz, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 164.1, 145.4, 136.1, 132.0, 130.0, 59.7, 37.2, 32.0 ppm. MS (EI, 70 eV): m/z (%) = 214 (100), 185 (32), 157 (39), 125 (71), 85 (45). HRMS: calcd. for $C_8H_{11}NO_2Se$ 232.9955; found 232.9951.

***N*-(2-Hydroxyethyl)selenophene-2-carboxamide (3j):** Yield 0.067 g (71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (dd, J = 0.88, 5.55 Hz, 1 H), 7.71 (dd, J = 0.88, 3.89 Hz, 1 H), 7.33 (dd, J = 3.89, 5.55 Hz, 1 H), 6.71 (s, 1 H), 3.84–3.79 (m, 2 H), 3.61–3.56 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.2, 145.1, 136.0, 130.1, 130.0, 61.9, 42.8 ppm. MS (EI, 70 eV): m/z (%) = 200 (100), 186 (32), 157 (39), 125 (71), 85 (45). HRMS: calcd. for $C_7H_9NO_2Se$ 218.9799; found 218.9802.

***N*,*N*-Dibenzylselenophene-2-carboxamide (3k):** Yield (Hal = I) 0.100 g (57%), (Hal = Br) 0.082 g (47%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, J = 5.43 Hz, 1 H), 7.46 (d, J = 3.23 Hz, 1 H), 7.38–7.25 (m, 10 H), 7.24 (d, J = 5.55 Hz, 1 H), 4.72 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.3, 144.0, 137.5, 136.5, 135.2, 130.3, 129.5, 128.8, 128.5, 127.9, 127.5, 127.2, 51.4 ppm. MS (EI, 70 eV): m/z (%) = 354 (100), 263 (31), 172 (22), 157 (40), 128 (68), 91 (43), 77 (18). HRMS: calcd. for $C_{19}H_{17}NOSe$ 355.0475; found 355.0471.

***N*,*N*-Diallylselenophene-2-carboxamide (3l):** Yield (Hal = I) 0.068 g (54%), (Hal = Br) 0.062 g (50%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, J = 5.55 Hz, 1 H), 7.58 (d, J = 3.89 Hz, 1 H), 7.29 (dd,

J = 3.89, 5.55 Hz, 1 H), 5.97–5.78 (m, 2 H) 5.29–5.19 (m, 4 H), 4.12–4.10 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.8, 144.0, 134.9, 132.8, 130.2, 129.3, 117.5, 49.9 ppm. MS (EI, 70 eV): *m*/*z* (%) = 254 (100), 228 (31), 201 (34), 157 (58), 129 (50), 96 (54). HRMS: calcd. for $C_{11}H_{13}NOSe$ 255.0162; found 255.0166.

***N*-(1,3-Dimethylbutyl)selenophene-2-carboxamide (3m):** Yield (Hal = I) 0.089 g (69%), (Hal = Br) 0.089 g (69%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 5.55 Hz, 1 H), 7.62 (d, *J* = 3.89 Hz, 1 H), 7.33 (dd, *J* = 3.89, 5.55 Hz, 1 H), 5.75 (s, 1 H), 4.30–4.15 (m, 1 H), 1.76–1.32 (m, 3 H), 1.25–1.20 (m, 3 H), 0.96–0.91 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.3, 146.4, 135.7, 129.9, 128.9, 46.4, 44.2, 25.1, 22.7, 22.5, 21.5 ppm. MS (EI, 70 eV): *m*/*z* (%) = 258 (100), 240 (21), 226 (17), 212 (11), 157 (56), 129 (71), 99 (31). HRMS: calcd. for $C_{11}H_{17}NOSe$ 259.0475; found 259.0479.

***N*-(4-Methoxybenzyl)selenophene-2-carboxamide (3n):** Yield 0.105 g (77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ =8.18 (d, *J* = 5.55 Hz, 1 H), 7.68 (d, *J* = 3.82 Hz, 1 H), 7.31–7.28 (m, 5 H), 6.63 (s, 1 H), 4.54 (d, *J* = 5.73 Hz, 2 H), 3.78 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 145.5, 138.0, 136.2, 130.0, 128.6, 127.8, 127.5, 55.2, 43.6 ppm. MS (EI, 70 eV): *m*/*z* (%) = 294 (100), 173 (49), 129 (82), 121 (12), 107 (19). HRMS: calcd. for $C_{13}H_{13}NO_2Se$ 295.0112; found 295.0116.

***N*-Butylselenophene-2-carboxamide (3o):** Yield 0.089 g (78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (dd, *J* = 1.02, 5.55 Hz, 1 H), 7.70 (dd, *J* = 1.02, 3.96 Hz, 1 H), 7.31 (dd, *J* = 3.96, 5.55 Hz, 1 H), 6.50 (s, 1 H), 3.45–3.35 (m, 2 H), 1.61–1.50 (m, 2 H), 1.43 (q, *J* = 7.35 Hz, 2 H), 0.96 (t, *J* = 7.20 Hz. 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1, 146.1, 135.7, 129.9, 129.1, 39.8, 31.67, 20.0, 13.6 ppm. MS (EI, 70 eV): *m*/*z* (%) = 230 (100), 215 (41), 201 (28), 172 (39), 129 (69), 101 (57). HRMS: calcd. for $C_9H_{13}NOSe$ 231.0162; found 231.0157.

***N*-Phenethylselenophene-2-carboxamide (3p):** Yield 0.107 g (77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (dd, *J* = 1.02, 5.55 Hz, 1 H), 7.58 (dd, *J* = 1.02, 3.96 Hz, 1 H), 7.34–7.16 (m, 6 H), 6.35 (s, 1 H), 3.69–3.49 (m, 2 H), 2.93–2.79 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 145.8, 138.7, 135.9, 129.9, 128.7, 128.6, 126.4, 41.2, 35.6 ppm. MS (EI, 70 eV): *m*/*z* (%) = 278 (100), 187 (72), 173 (44), 158 (39), 129 (76), 91(36). HRMS: calcd. for $C_{13}H_{13}NOSe$ 279.0162; found 279.0166.

Typical Procedure for Carbonylation of 2,5-Diiodoselenophene and Amines: A dried Schlenk flask containing $Pd(PPh_3)_4$ (0.112 g, 20 mol-%) was evacuated and connected to an atmosphere of argon. 2,5-Diiodoselenophene (**1c**) (0.5 mmol), toluene (5 mL), amines **2** (1.6 mmol) and Na_2CO_3 (0.486 g, 4.4 mmol) in H_2O (2.2 mL) were added. After removal of argon atmosphere by bubbling CO into the reaction medium, the system was purged with CO 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 H_2O (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 product was purified by flash column chromatography (EtOAc/hexane, 40:70).

***N*^{2},*N*^{5}-Dibenzylselenophene-2,5-dicarboxamide (4a):** Yield 0.165 g (90%). ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 7.33–7.20 (m, 12 H), 6.64 (s, 2 H), 4.25 (d, *J* = 5.89 Hz, 4 H) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 160.0, 153.0, 140.8, 128.1, 127.3, 126.9, 126.4, 42.9 ppm. MS (EI, 70 eV): *m*/*z* (%) = 397(100), 306 (43), 215 (38), 172 (32), 129 (82), 91 (54). HRMS: calcd. for $C_{20}H_{18}N_2O_2Se$ 398.0533; found 398.0537.

***N*^{2},*N*^{5}-Dipiperidylselenopheno-2,5-dicarboxamide (4b):** Yield 0.141 g (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (s, 2 H), 3.67–3.62 (m, 8 H), 1.65–1.60 (m, 12 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1, 145.9, 132.0, 46.3, 43.3, 25.9, 24.3 ppm. MS (EI, 70 eV): *m*/*z* (%) = 353 (100), 241 (64), 129 (71), 112 (53). HRMS: calcd. for $C_{16}H_{22}N_2O_2Se$ 354.0846; found 354.0851.

***N*^{2},*N*^{5}-Bis(3-methoxypropyl)selenophene-2,5-dicarboxamide (4c):** Yield 0.157 g (87%). ^{1}H NMR: 400 MHz, [D_6]DMSO): δ = 8.54–8.52 (m, 2 H), 7.89 (s, 2 H), 3.37–3.34 (m, 4 H), 3.32 (s, 6 H), 3.28–3.23 (m, 4 H), 1.76–1.70 (m, 4 H) ppm. ^{13}C NMR (100 MHz, [D_6]-DMSO): δ = 161.7, 150.2, 130.0, 69.4, 57.8, 36.5, 29.0 ppm. MS (EI, 70 eV): *m*/*z* (%) = 361 (100), 330 (27), 299 (33), 271 (12), 243 (41), 216 (52), 129 (75). HRMS: calcd. for $C_{14}H_{22}N_2O_4Se$ 362.0745; found 362.0741.

Typical Procedure for Carbonylation of 2-Iodoselenophene and Diamines: A dried Schlenk flask containing $Pd(PPh_3)_4$ (0.112 g, 10 mol-%) was evacuated and connected to an atmosphere of argon. 2-Iodoselenophene (**1a**) (0.256 g, 1.0 mmol), toluene (5 mL), diamines **5** (0.8 mmol) and Na_2CO_3 (0.486 g, 4.4 mmol) in H_2O (2.2 mL) were added. After removal of argon atmosphere by bubbling CO into the reaction medium, the system was purged with CO 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 H_2O (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 product was purified by flash column chromatography (EtOAc/hexane, 40:70).

1,4-Bis[(selenophene-2-yl)carbonyl]piperidine (6a): Yield 0.150 g (75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 5.55 Hz, 2 H), 7.49 (d, *J* = 3.78 Hz, 2 H), 7.33 (dd, *J* = 3.78, 5.55 Hz, 2 H), 3.82 (m, 8 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.1, 142.5, 135.0, 131.9, 131.8, 130.8, 129.2, 128.4, 128.3, 45.2, 42.6 ppm. MS (EI, 70 eV): *m*/*z* (%) = 400 (100), 271 (46), 157 (25), 144 (59), 129 (72). HRMS: calcd. for $C_{14}H_{14}N_2O_2Se_2$ 401.9386; found 401.9383.

***N*,*N*′-(Ethane-2,1-diyl)bis(selenophene-2-carboxamide) (6b):** Yield 0.089 g (48%). ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 8.83 (s, 2 H), 8.59 (dd, *J* = 1.08, 5.55 Hz, 2 H), 8.14 (dd, *J* = 1.08, 3.87 Hz, 2 H), 7.60 (dd, *J* = 3.87, 5.55 Hz, 2 H), 3.60–3.59 (m, 4 H) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 162.5, 146.6, 136.3, 131.3, 128.5, 40.7 ppm. MS (EI, 70 eV): *m*/*z* (%) = 187 (100), 158 (39), 129 (74). HRMS: calcd. for $C_{12}H_{12}N_2O_2Se_2$ 375.9229; found 375.9296.

***N*,*N*′-(Propane-3,1-diyl)bis(selenophene-2-carboxamide) (6c):** Yield 0.126 g (65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 5.43 Hz, 2 H), 7.86 (d, *J* = 3.82 Hz, 2 H), 7.29 (dd, *J* = 3.82, 5.43 Hz, 2 H), 3.46 (q, *J* = 6.17 Hz, 4 H), 1.77–1.66 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.9, 145.9, 131.8, 128.6, 36.2, 29.6 ppm. MS (EI, 70 eV): *m*/*z* (%) = 389 (100), 261 (62), 218 (31), 176 (54), 129 (61). HRMS: calcd. for $C_{13}H_{14}N_2O_2Se_2$ 389.9386; found 389.9382.

Supporting Information (see also the footnote on the first page of this article): Spectroscopic data for **3a**–**p** described in Table 3, **4a**–**c** and **6a**–**c** related in Schemes 3 and 4, respectively.

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