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Article

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Copper-Catalyzed Three-Component Reaction for Regioselective Aryl- and Heteroarylselenation of Indoles Using Selenium Powder

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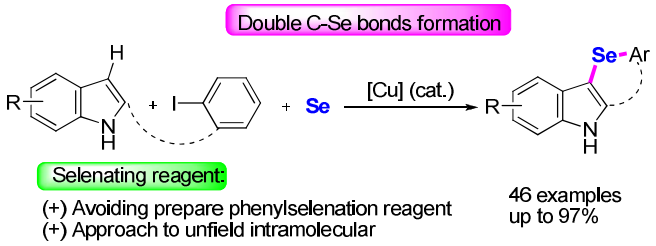


ABSTRACT: A new and efficient copper-catalyzed C_3-aryl- and heteroarylselenation of indoles employing selenium powder is developed. The advantages of this chemistry involve the use of cheap selenating reagents, the tolerance of a variety of functional groups and the practicality. In addition, this protocol has been further elaborated in an intramolecular phenylselenation of (hetero) aryl C-H bond to construct an important motif of benzoselenopheno [3,2-b]indole.The preliminary mechanism study suggests that the reaction starts with a Ullman-type selenation between aryl iodides and selenium, followed by an oxidative cross-coupling with indole. The utility of this method has been demonstrated in an efficient gram-scale synthesis and an application to the synthesis of tubulin polymerization inhibitor.

INTRODUCTION

Selective C-Se bond formation is of great importance in modern organic synthesis, since the selenium-containg architectures are prevalent in a diverse of drug candidates, biologically active compounds, and functional organic materials.[1] Considering the significance of organoselenium

compounds, especially the 3-selenylindoles[2] display the biological activity of antitumor activity[3] and as inhibitor of tubulin polymerization.[4] Therefore, the development of a new synthetic route for the introduction of stable, economical selenium reagent into organic skeleton would be significant synthetic value.

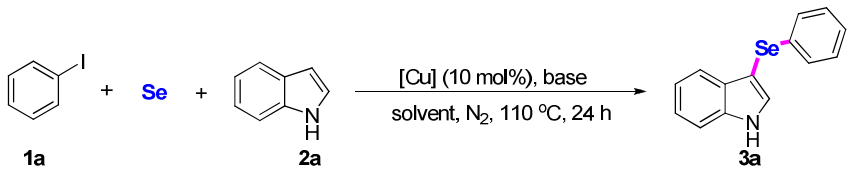
In recent years, transition-metal catalyzed cross-coupling reactions have become the most important methdology for the construction of C-Se bonds.[5] On the basis of selenium source, there are two general methods for the construction of C-Se bonds to synthesize diaryl selenides. The first approach is involved the transition-metal catalyzed cross-coupling reaction between prefunctionalized aryl substrates with nucleophilic organoselenium reagents (selenol,[6] $ArSeSnR_3$,[7] diselenides[8]) under basic condtions. Wheras arylselenols have been used as the original material to prepare these phenylselenation reagent.[6] Most arylselenols suffer from the trouble handling because of unpleasant odors and instability, which hamper their applications in pharmaceutical industry. Recently, the direct transformation phenyselenation of inert C-H bond with diaryl selenides has emerged as comprising and complementary routes.[9] However, most of these works are highly problematic due to the loss of one equivalent of PhSe- as waste, requiring external copper or silver salts as oxidant. The second newborn avenue is transition-metal catalyzed C–Se bond formation using the elemental selenium as selenating reagent, which is mainly limit to afford symmetrical diaryl selenides.[10] The use of selenium powder, which is commercial available, stable and easy-to-handle, as a cross-coupling partner to construct C-Se bond is a more straightforward and attractive alternative. However, the relative reports of the activation selenium element are scarce.[11] This is presumably due to the affinity of selenium to transition metal, and easily form the stability transition-metal selenium clusters,[12] which attenuate the activity of catalysts. From these

wonderful advancing achievements, it is thereby envisioned that a single Se atom to bridge two cross-coupling partners of Csp^2-X and Csp^2-H strategy under transition-metal catalyzed might be more practical and economical. Such a method would receive a considerable attention for designing counterintuitive synthetic strategies that are unattainable by other means, such as intramolecular phenylselenation of (hetero)arene C-H bond. Herein we report a new and efficient copper-catalyzed C_3-phenylselenation of indoles through double C−Se bonds formation, using (hetero) aryl iodides, elemental selenium and indoles as reactants.

To achieve the copper-catalyzed arylselenation of indole with selenium powder and aryl iodides, the following issues need to be considered: (i) Free (NH) indole has three accessible reaction positions,[13] in order to access the highly regioselectivity, the catalyst system for the C-arylselenation of indoles should avoid to produce N-arylation of indole under the reaction conditions;[14] (ii) The cleavage of the acidic N-H of indole usually requires basic conditions to enable the nucleophilicity of C3 posiiton; Otherwise, if the C-H bond of indole cleavage is relatively slow, the symmetrical diaryl diselenides would formed from aryl iodides with elemental selenium by copper-catalyed. Based on these considerations, the strategy to solve these problems are to develop robust conditions that could match the rate of copper-catalyzed selenation of aryl iodides with elemental selenium and the rate of transmetalation of indole-metal intermediate species,[15] to suppress the undesired side-reactions including the homo-coupling of PhSeCu species.

RESULTS AND DISCUSSION

Table 1. Reaction Optimization[a]



1a 2a 3a

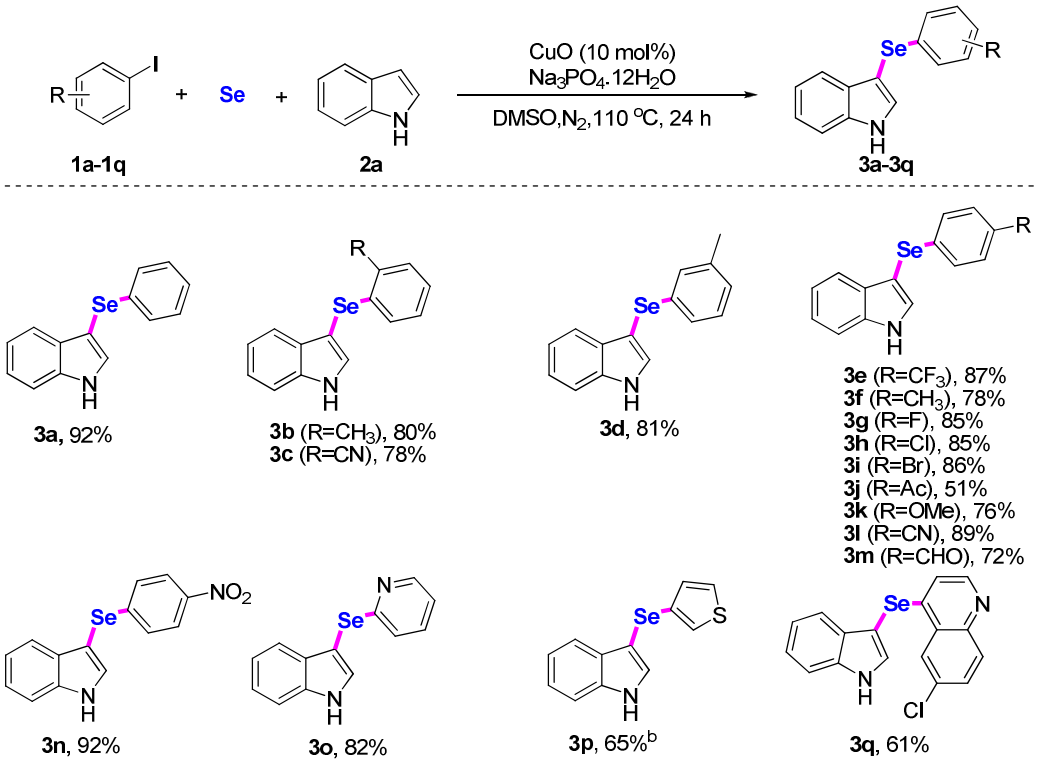
entry	[Cu]	base	solvent	Yield (%)[b]
1	CuI	$Na_3PO_4.12H_2O$	DMF	35
2	CuI	$Na_3PO_4.12H_2O$	Toluene	none
3	CuI	$Na_3PO_4.12H_2O$	1,4-Dioxane	none
4	CuI	$Na_3PO_4.12H_2O$	CH_3CN	none
5	CuI	$Na_3PO_4.12H_2O$	DMSO	60
6	$CuBr_2$	$Na_3PO_4.12H_2O$	DMSO	56
7	$CuCl_2$	$Na_3PO_4.12H_2O$	DMSO	59
8	$Cu(OAc)_2$	$Na_3PO_4.12H_2O$	DMSO	64
9	CuO	$Na_3PO_4.12H_2O$	DMSO	92
10	CuO	Na_2CO_3	DMSO	75
11	CuO	K_2CO_3	DMSO	79
12	CuO	NaOAc	DMSO	42
13	CuO	K_3PO_4	DMSO	50
14[c]	CuO	$Na_3PO_4.12H_2O$	DMSO	31
15[d]	CuO	$Na_3PO_4.12H_2O$	DMSO	54
16		$Na_3PO_4.12H_2O$	DMSO	0

[a]Reaction condition: 0.2 mmol iodobenzene, 0.6 mmol Se, 0.5 mmol indole, 0.02 mmol [Cu], 0.8 mmol base, 2 mL solvent, N_2, 110 ℃, 24 h. [b]Isolated yield. [c]Under O_2. [d]Under air.

The project began with the study on the reaction between iodobenzene (**1a**) and indole (**2a**). After initial optimizations, it was found that **2a** was transformed into the desired C3-arylsenelonation product (**3a)** in 35% isolated yield (entry 1), along with a small amount of the diphenyl diselenide byproduct (Table 1, entry 1). Among the several solvents examined, DMSO was the optimal solvent, afforded the product in 60 % isolated yield (entry 5), and the reaction became sluggish when solvents like toluene, 1, 4-dioxane and CH_3CN were used (entries 2-4). Among various copper salts tested, the best result was obtained with CuO, providing the product in 92% yield (entries 9). And then, we screened an array of bases; the use of Na_2CO_3 and NaOAc gave slightly lower yields (entries 10-13). N_2 atmosphere is essential for this reaction, and when the reaction

was conducted under O_2 or air, decreased the yield of the reaction (entries 14, 15). This would be due to the reasons that O_2 could intercept the catalytic intermediate in the process, and indole is not stable under high O_2 concentration. A control experiment showed that the copper catalyst is essential for this transformation since no coupling product was obtained in the absence of copper (entry 16). Of particular note, in all cases, the reaction show excellent regioselectivity and no 2-arylselenolation of indoles or N-aryl indoles byproducts were observed from analysis of the crude reactions mixtures.

Scheme 1. Aryl iodides Scope[a]

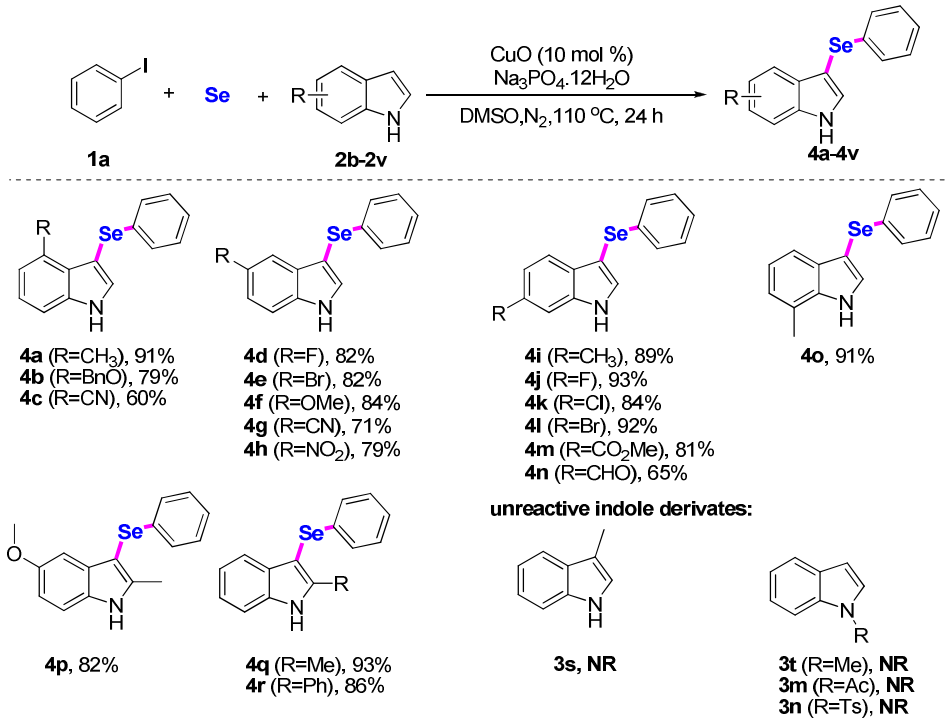


[a]Reaction conditions: aryl iodides (0.2 mmol), Se_8 (0.6 mmol), indole (0.5 mmol), CuO (0.02 mmol), $Na_3PO_4{\cdot}12H_2O$ (0.8 mmol), DMSO (2 mL), 110 °C, 24 h, N_2, isolated yields. [b]CuO (20 mol %).

With the optimal conditions in hand, the scope of the substrates was explored. A wide range

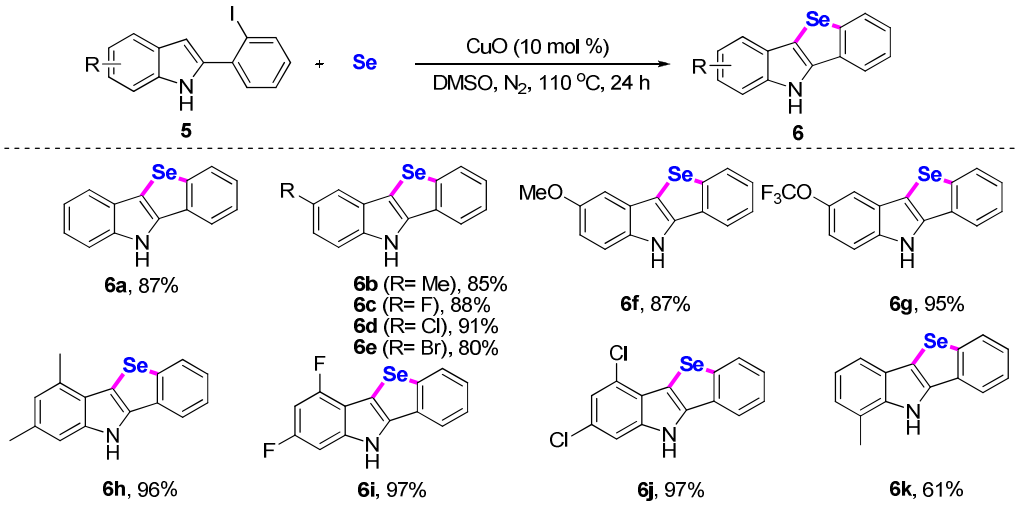
of aryl iodides were employed and the reaction generally proceeded smoothly, afforded the corresponding products in good to excellent yields (Scheme 1). When iodobenzenes bearing a variety of electron-donating groups, such as methyl (**3b**), methoxy (**3k**), and trifluoromethyl (**3e**), the reactions reacted smoothly and good yields were obtained. The reaction of iodobenzene bearing electron-withdrawing groups such as fluoro (**3g**), chloro (**3h**), bromo (**3i**), acetyl (**3j**), aldehyde (**3m**), and nitro(**3n**) gave the corresponding products in moderate to excellent yields. The compatibility of these functional groups in this reaction provided an opportunity for further elaboration to achieve more complex products. It was noteworthy that steric hindrance did not have great effect on the reaction, for example, when methyl substitute located on the C-2, C-3, C-4 position of benzene iodide, similar yields (**3b**, **3d**, **3f**) were observed. It was remarkable that heterocyclic iodides, such as pyridine, thiophene and quinoline also provided the corresponding products (**3o**, **3p**, **3q**) in good yields.

Scheme 2. Indoles Scope



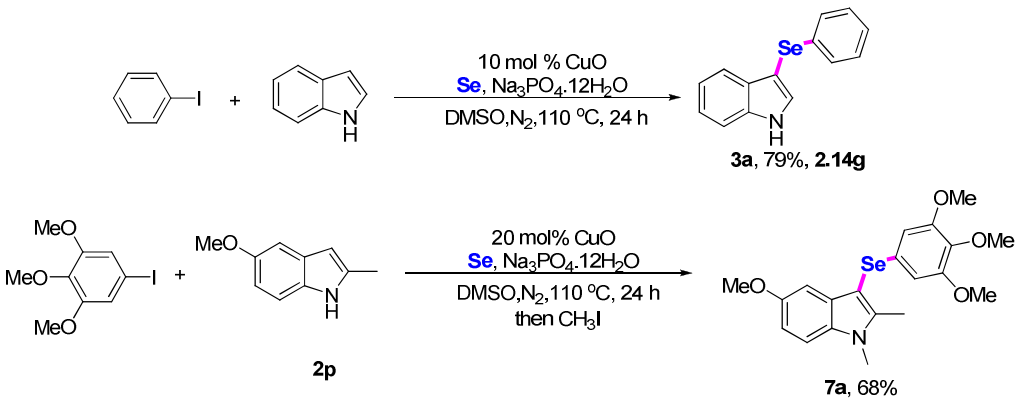
Furthermore, a diverse of substituted indoles were subjected to the optimal reaction conditions to explore the scope and generality of this reaction (Scheme 2). A variety of functional groups on the benzene ring of indoles were compatible, such as methyl(**4a**, **4i**, **4o**), fluoride(**4d**, **4j**), chloride(**4k**), bromide(**4e**, **4l**), methoxy (**4b**, **4f**, **4p**) and nitro(**4h**), which had little effect on the reactivity and the regioselectivity of reactions. When the introduction of the methyl and phenyl occupied at the C2 of indole, the corresponding products were obtained (**4p**, **4q**, **4r**) in good yields. The free NH group of indole was found to play a critical role, the more nucleophilic 1-methylindole (**3s**) and electron-poor N-Ac(**3m**) and N-Ts (**3n**) of indole did not undergo the copper-mediated arylselenation reaction. To investigate whether arylselenation for other heterocyclic compounds such as functionalized pyrroles、 benzofuranes、thianaphthene and benzimidazole under current reaction condition, however, only slight decomposition of the starting materials without the expected products. Based on these experiments result, it's perhaps that the relative stability of C3 nucleophilicity of indole was critical successful for this reaction.

Scheme 3. Intramolecular C-Se Bond Formation



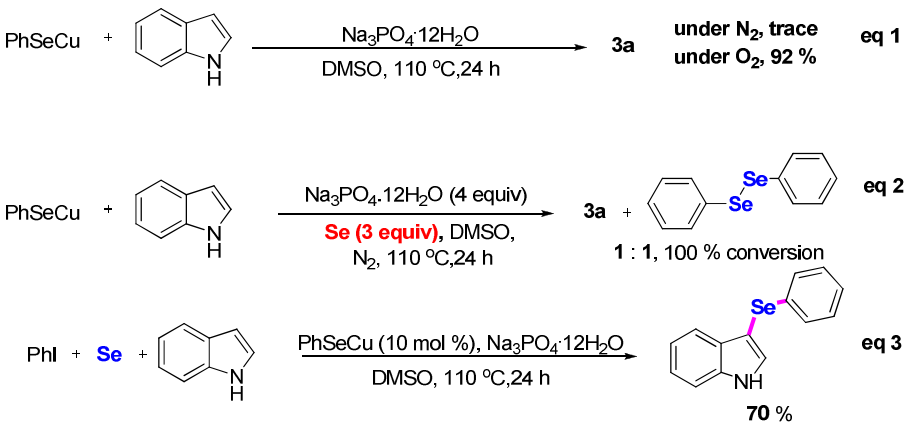
Next, the synthetic method was extended to intramolecular C-Se bond formation, providing a straightforward pathway to synthesize Benzoselenopheno[3,2-b]indole. As shown in Scheme 3, the cyclization starting substrates could be easily prepared by use of Fischer indole synthesis approach. Overall, good to excellent yields of **6** were obtained, and various substituents on the indole ring showed nonbiased to the efficiency of the reactions. A variety of functional groups such as electron-donating groups methyl(**6b, 6k**), methoxy (**6f**), trifluoromethoxy (**6g**), and electron-withdrawing groups fluoride(**6c**), chloride(**6d**), and bromide(**6e**) were compatible. Disubstituted on benzene ring of Benzoselenopheno[3,2-b]indole could also be obtained (**6h**, **6i**, **6j**). These results highlight the generality of the new method. The products of intramolecular reactions also could be potential compounds for electronic materials.[16]

Scheme 4. Gram-Scale Synthesis and Application



The utility of this new method was further demonstrated by an efficient gram-scale synthesis and an application to the synthesis of an important inhibitor (Scheme 4). The copper-catalyzed double C-Se bond formation produced the proudct **3a** in 79% yield as 2.14 gram under standard reaction conditions. Inaddition, application of the new method in a two-step synthesis of 3-(3, 4, 5-Trimethoxyphenylselenyl)-methyl-indole[4] was achieved, a reported efficient inhibitor in the tubulin polymerization and disrupt tubulin microtubule dynamics. Subsequent methylation treated with CH_3I afforded the target product in 68% overall yield.

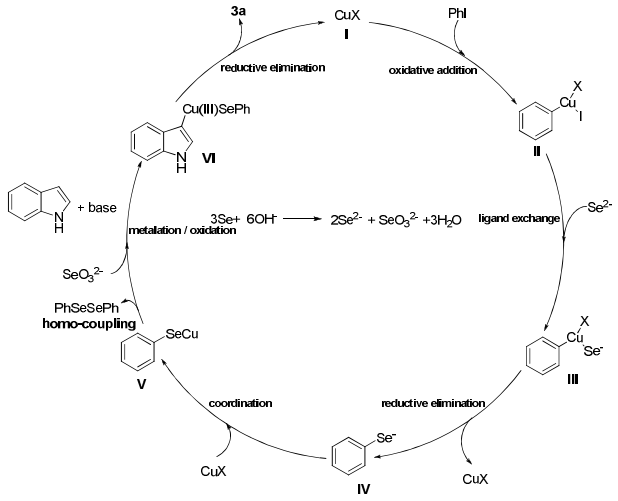
Scheme 5. Preliminary mechanism investigation



To understand the reaction mechanism, controll experiments were conducted (Scheme 5). First, a stoichiometric reaction of PhSeCu with simple indole under N_2 atmosphere did not promote the reaction, but the desired product **3a** was obtained in 92% isolated yield under O_2

atmosphere. The lack of reactivity with PhSeCu under N_2 indicated that the C-Se bond formation of indole probably proceeded through the oxidative cross-coupling pathway. An interesting phenomenon was observed, however, when adding 3 equivalent of selenium powder under N_2 atmosphere, 3-phenyselenation of indole **3a** and the byproduct diphenyl selenide were obtained in a 1:1 ratio and the PhSeCu went to full conversion (**eq 2**); these experiments could explain the transformation needs an excess amount of element Se. Secondly, As shown in **eq 3**, it suggested that PhSeCu may be a chemical competent intermediate produced in situ during the catalytic cycle. It could also rationalize why a small amount of diphenyl diselenides were detected in the reaction. Finally, when the radical inhibitor TEMPO was added to the reaction conditions, product **3a** was still obtained in **91**% yield, which in turn suggested that a radical-involved mechanism could be ruled out.

Scheme 6. Proposed Catalytic Cycle



On the basis of above observations and related literatures,[17] a plausible mechanism for the reaction is proposed (Scheme 6). It is well-known that selenium readily transformed to selenide anion and selenite in the presence of a base.[18] A proposed catalytic cycle could start with an oxidative addition of iodobenzene with CuX, followed by ligand exchange with Se^{2-} to generate

the intermediate (III). Then, reductive elimination of (III) will generate the arylselenium anion(IV), which reacts with CuX to form the PhSeCu(V) species. Then, base assisted metalation of indole with PhSeCu led to (VI) through selenite instantaneous oxidation, followed by immediate reductive eliminaton to provide the desired product and regenerate the CuX catalyst. At this stage, the accurate role of elemental selenium is vague, but indeed participates in the oxidation step according to the above experimental results.

In summary, we have developed a new and efficient copper catalyzed three-component reaction for the selective synthesis of unsymmetrical diphenyl selenides. Commercial available, stable, easy-to-handle elemental selenium was used as selenating reagent. In addition, both intermolecular and intramolecular reactions were achieved to set linear or cyclic selenating system. Moreover, good to excellent yields were obtained and the reaction can tolerate a wide scope of functional groups. Furthermore, early mechanism study suggests that copper-catalyzed direct double C-Se bonds formation proceeds through Ullman-type selenation of aryl iodides and selenium and consequential oxidative cross-coupling with indole. Further studies on the reaction mechanism and the development of new strategies of selective selenation transformations are underway in our laboratory.

EXPERIMENTAL SECTION

General Remarks. ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz) and ^{19}F NMR (470 MHz) spectra were recorded in DMSO-*d6* solutions using 500 MHz spectrometer. High-resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometer. All reactions were conducted using standard Schlenk techniques. Column chromatography was performed using EM silica gel 60 (300−400 mesh). Copies of their ^{1}H NMR and ^{13}C NMR spectra are provided. 2-(2-iodophenyl)-1H-indole[19],

2-(2-iodophenyl)-5-methyl-1H-indole[19], 5-fluoro-2-(2-iodophenyl)-1H-indole[19], 5-chloro-2-(2-iodophenyl)-1H-indole[19], 5-bromo-2-(2-iodophenyl)-1H-indole[19], 2-(2-iodophenyl)-5-methoxy -1H-indole[19], 2-(2-iodophenyl)-5-(trifluoromethoxy)-1H-indole[19], 2-(2-iodophenyl)-4,6-dimethyl -1H-indole[19],4,6-difluoro-2-(2-iodophenyl)-1H-indole[19], 4,6-dichloro-2-(2-iodophenyl) -1H-indole[19], 2-(2-iodophenyl)-7-methyl-1H-indole[19] and PhSeCu[20] were prepared according to the reported procedures. ^{1}H and ^{13}C spectra of known compounds were in accordance with those described in the literatures.

Procedure for Intermolecular Phenylselenation of Indole Reactions: To a 10 mL Schlenk tube equipped with a stir bar was added aryl iodide 1 (0.2 mmol), indole 2 (0.5 mmol), Se (47.4 mg, 0.6 mmol), CuO (10 mol %), $Na_3PO_4.12H_2O$ (0.8 mmol) in DMSO (2 mL). The tube was evacuated and refilled with N_2 three times. The reaction mixture was stirred at 110 ^{o}C for 24 h. After cooling down, the reaction mixture was diluted with 10 mL of ethyl ether, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (20 mL). The filtrate was washed with water (3×15 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

Procedure for Intramolecular Phenylselenation of Indole Reactions: To a 10 mL Schlenk tube equipped with a stir bar was added substrate 5 (0.2 mmol), Se (47.4 mg, 0.6 mmol), CuO (10 mol %), $Na_3PO_4.12H_2O$ (0.8 mmol) in DMSO (2 mL). The tube was evacuated and refilled with N_2 three times. The reaction mixture was stirred at 110 ^{o}C for 24 h. After cooling down, the reaction mixture was diluted with 10 mL of ethyl ether, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (20 mL). The filtrate was

washed with water (3×15 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

Preliminary Mechanism Investigation: Two 10 mL of Schlenk tubes equipped with a stir bar were added with PhSeCu (0.2 mmol), indole (0.5 mmol), $Na_3PO_4{\cdot}12H_2O$ (0.8 mmol) in DMSO (2 mL). In the first tube, The tube was evacuated and refilled N_2 three times. In the other tube, The tube was fitted with a rubber septum, and then it was evacuated and refilled with O_2 three times. These reactions mixture were stirred at 110 ^oC for 24 h (see Scheme 5, eq 1). To a 10 mL Schlenk tube equipped with a stir bar was added PhSeCu (0.2 mmol), Se (31.6 mg, 0.4 mmol), indole (0.5 mmol), $Na_3PO_4.12H_2O$ (0.8 mmol) in DMSO (2 mL). The tube was evacuated and refilled with N_2 three times. The reaction mixture was stirred at 110 ^oC for 24 h(see Scheme 5, eq 2). To a 10 mL Schlenk tube equipped with a stir bar was added aryl iodide **1** (0.2 mmol), indole **2** (0.5 mmol), Se (47.4 mg, 0.6 mmol), PhSeCu (10 mol %), $Na_3PO_4.12H_2O$ (0.8 mmol) in DMSO (2 mL). The tube was evacuated and refilled with N_2 three times. The reaction mixture was stirred at 110 ^oC for 24 h(see Scheme 5, eq 3). After cooling down, the reaction mixture was diluted with 10 mL of ethyl ether, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (20 mL). The filtrate was washed with water (3×15 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

Characterization Data of Compounds 3, 4, 6, 7a:

3-(phenylseleno)-1H-indole(**3a**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a white solid (50.2 mg, 92 % yield). The ^1H, ^{13}C NMR spectra

were in accordance with those described in the literature.[21]

3-(o-tolylseleno)-1H-indole(**3b**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a white solid (45.6 mg, 80 % yield). The ^{1}H, ^{13}C NMR spectra were in accordance with those described in the literature.[22]

2-((1H-indol-3-yl)seleno)benzonitrile (**3c**) Following the general procedure, 0.04 mmol CuO, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (46.6 mg, 78 % yield), mp 103-105 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.85 (s, 1H), 7.84 (d, J = 2.5 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.29 (t, J = 7.5 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 139.1, 136.7, 133.6, 133.6, 133.5, 129.1, 128.7, 126.3, 122.2, 120.4, 118.6, 117.3, 112.3, 110.8, 93.0. HRMS (EI, 70 eV) calcd for $C_{15}H_{10}N_2Se$ [M^+]: 298.0009, found 298.0013.

3-(m-tolylseleno)-1H-indole (**3d**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown viscous oil(46.3 mg, 81 % yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.67 (s, 1H), 7.73 (d, J = 2.5 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.08-7.02 (m, 3H), 6.91 (d, J = 7.5 Hz, 2H), 2.16 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 138.3, 136.6, 133.5, 132.7, 129.5, 128.9, 128.6, 126.4, 125.3, 121.9, 120.0, 119.0, 112.1, 95.1, 20.8. HRMS (EI, 70 eV) calcd for $C_{15}H_{13}NSe$ [M^+]: 287.0213, found 287.0214.

3-((4-(trifluoromethyl)phenyl)seleno)-1H-indole (**3e**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellowish solid (59.1 mg, 87 % yield), mp 123−124 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.79 (s, 1H), 7.80 (s, 1H), 7.53-7.49 (m, 3H), 7.38 (d, J = 7.5 Hz, 1H), 7.31 (d, J = 7.5 Hz, 2H), 7.20 (t, J = 7.0 Hz, 1H), 7.08 (t, J = 7.0 Hz, 1H).

^{13}C NMR (125 MHz, DMSO) δ 140.4, 136.7, 133.3, 129.2, 128.0, 126.0 (d, J_F = 31.3 Hz), 125.6 (q, J_F = 5.0 Hz), 124.3 (d, J_F = 270.0 Hz), 122.2, 120.3, 118.8, 112.3, 93.7. ^{19}F NMR (470 MHz, DMSO-d_6): δ -60.86 (s, 3F). HRMS (ESI) calcd for $C_{15}H_{10}F_3NSe$ $[M+Na]^+$: 363.9823, found 363.9827.

3-(p-tolylseleno)-1H-indole (**3f**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a white solid (44.6 mg, 78 % yield). The ^{1}H, ^{13}C NMR spectra were in accordance with those described in the literature.[21]

3-((4-fluorophenyl)seleno)-1H-indole (**3g**) Following the general procedure, 0.04 mmol CuO, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (49.3 mg, 85 % yield), mp 135−136 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.68 (s, 1H), 7.74 (s, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.22 – 7.16 (m, 3H), 7.09-7.02 (m, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.8 (d, J_F = 241.3 Hz), 136.6, 132.7, 130.3 (d, J_F = 7.5 Hz), 129.30, 128.4 (d, J_F = 3.8 Hz), 122.0, 120.1, 118.9, 116.1 (d, J_F = 22.5 Hz), 112.1, 95.4. ^{19}F NMR (470 MHz, DMSO-d_6): δ -117.40 (s, 1F). HRMS (EI, 70 eV) calcd for $C_{14}H_{10}FNSe$ $[M^+]$: 290.9962, found 290.9962.

3-((4-chlorophenyl)seleno)-1H-indole (**3h**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a white solid (52.4 mg, 85 % yield). The ^{1}H, ^{13}C NMR spectra were in accordance with those described in the literature.[21]

3-((4-bromophenyl)seleno)-1H-indole (**3i**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (60.6 mg, 86 % yield), mp 131-135 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.73 (s, 1H), 7.76 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.39-7.34 (m, 3H), 7.18 (t, J = 7.5 Hz, 1H), 7.09-7.06 (m, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 136.6, 133.3, 132.9, 131.8, 130.0, 129.2, 122.1, 120.1, 118.8, 118.6, 112.2, 94.5. HRMS (EI, 70 eV) calcd for

$C_{14}H_{10}BrNSe$ [M^+]: 350.9162, found 350.9162.

1-(4-((1H-indol-3-yl)seleno)phenyl)ethan-1-one (**3j**) Following the general procedure, 0.04 mmol CuO, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellow solid (32.1 mg, 51 % yield), mp 139-141 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.78 (s, 1H), 7.79 (d, J = 2.5 Hz, 1H), 7.73 (d, J = 8.5 Hz, 2H), 7.52 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.24 – 7.18 (m, 3H), 7.09 – 7.06 (m, 1H), 2.47 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 197.0, 141.6, 136.7, 134.1, 133.1, 129.2, 128.7, 127.3, 122.1, 120.2, 118.8, 112.2, 93.8, 26.4. HRMS (EI, 70 eV) calcd for $C_{16}H_{13}NOSe$ [M^+]: 315.0162, found 315.0168.

3-((4-methoxyphenyl)seleno)-1H-indole (**3k**) Following the general procedure, 0.04 mmol CuO, using 7:1 petroleum ether-EtOAc as the eluant afforded a white solid (45.9 mg, 76 % yield) , mp 113−115 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.58 (s, 1H), 7.69 (s, 1H), 7.45 (t, J = 8.0 Hz, 2H), 7.20 – 7.14 (m, 7.4 Hz, 3H), 7.06 (t, J = 7.0 Hz, 1H), 6.78 (d, J = 7.5 Hz, 2H), 3.66 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.9 , 136.5 , 132.1 , 130.7, 129.4 , 123.0 , 121.8, 119.8 , 119.0 , 114.8 , 111.9 , 96.5 , 55.0. HRMS (EI, 70 eV) calcd for $C_{15}H_{13}NOSe$ [M^+]: 303.0162, found 303.0159.

4-((1H-indol-3-yl)seleno)benzonitrile (**3l**) Following the general procedure, 0.04 mmol CuO, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown liquid (52.9 mg, 89 % yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.83 (s, 1H), 7.80 (s, 1H), 7.58 (d, J = 7.5 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.21 (t, J = 7.5 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 142.5, 136.7, 133.4, 132.4, 129.1, 128.0, 122.3, 120.4, 118.9, 118.7, 112.3, 107.7, 93.3. HRMS (EI, 70 eV) calcd for $C_{15}H_{10}N_2Se$ [M^+]: 298.0009, found 298.0008.

4-((1H-indol-3-yl)seleno)benzaldehyde (**3m**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellow solid (43.1 mg, 72 % yield), mp 143−145 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.81 (s, 1H), 9.85 (s, 1H), 7.80 (d, J = 2.5 Hz, 1H), 7.67 (d, J = 8.0, 2H), 7.52 (d, J = 8.0 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.20 (t, J = 7.5 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.1, 143.9, 136.7, 133.7, 133.3, 129.9, 129.2, 127.6, 122.2, 120.3, 118.8, 112.3, 93.5. HRMS (ESI) calcd for $C_{15}H_{11}NOSe$ $[M+H]^+$: 302.0079, found 302.0080.

3-((4-nitrophenyl)seleno)-1H-indole (**3n**) Following the general procedure, 0.04 mmol CuO, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (58.3 mg, 92 % yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.86 (s, 1H), 8.00 (d, J = 8.5 Hz, 2H), 7.82 (s, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.37-7.33 (m, 3H), 7.21 (t, J = 7.5 Hz, 1H), 7.09 (t, J = 7.0 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 145.5, 145.3, 136.7, 133.4, 129.1, 127.8, 123.8, 122.3, 120.4, 118.7, 112.3, 93.2. HRMS (EI, 70 eV) calcd for $C_{14}H_{10}N_2O_2Se$ $[M^+]$: 317.9907, found 317.9912.

3-(pyridin-2-ylseleno)-1H-indole (**3o**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a white solid (44.8 mg, 82 % yield), mp 103−104 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.75 (s, 1H), 8.37 (s, 1H), 7.76 (s, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.44 – 7.40 (m, 2H), 7.20 (t, J = 7.0 Hz, 1H), 7.10 - 7.08 (m, 2H), 6.70 (d, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.2, 149.5, 136.9, 136.7, 133.1, 129.3, 122.1, 121.9, 120.2 (2C), 118.9, 112.2, 94.5. HRMS (ESI) calcd for $C_{13}H_{10}N_2Se$ $[M+H]^+$: 275.0082, found 275.0088.

3-(thiophen-3-ylseleno)-1H-indole (**3p**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellow viscous oil (36.1 mg, 65 % yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.58 (s, 1H), 7.70 (t, J = 2.0 Hz, 1H), 7.53 – 7.42 (m, 3H), 7.23 – 7.12 (m,

2H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 5.0 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 136.4, 131.8, 129.7, 129.3, 127.0 , 126.1, 123.0, 121.9, 119.86 , 119.0, 112.0, 96.2. HRMS (ESI) calcd for $C_{12}H_9NSSe$ $[M+H]^+$: 279.9694, found 279.9704.

4-((1H-indol-3-yl)seleno)-7-chloroquinoline (**3q**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellow solid (43.6 mg, 61 % yield), mp 176−177 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.94 (s, 1H), 8.45 (d, *J* = 4.0 Hz, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 8.08 (s, 1H), 7.89 (s, 1H), 7.75 (d, *J* = 8.5 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 4.0 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 150.7, 147.6, 146.6, 136.9, 134.4, 133.9, 129.1, 128.2, 127.5, 126.7, 125.7, 122.3, 120.5, 120.2, 118.7, 112.4, 91.3. HRMS (ESI) calcd for $C_{17}H_{11}ClN_2Se$ $[M+H]^+$: 358.9849, found 358.9864.

4-methyl-3-(phenylseleno)-1H-indole (**4a**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (52.2 mg, 91 % yield), mp 141-142 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.66 (s, 1H), 7.66 (d, *J* = 2.5 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.20 – 7.09 (m, 5H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 7.0 Hz, 1H), 2.57 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 137.1, 136.1, 133.8, 130.1, 129.1, 127.5, 126.7, 125.3, 122.0, 121.5, 110.2, 93.8, 18.4. HRMS (EI, 70 eV) calcd for $C_{15}H_{13}NSe$ $[M^+]$: 287.0213, found 287.0215.

4-(benzyloxy)-3-(phenylseleno)-1H-indole (**4b**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a atropurpureus liquid (59.8 mg, 79 % yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.61 (s, 1H), 7.49 (d, *J* = 2.5 Hz, 1H), 7.29 – 7.27 (m, 2H), 7.25 – 7.21 (m, 3H), 7.20 – 7.15 (m, 4H), 7.11 – 7.04 (m, 3H), 6.61 (d, *J* = 7.5 Hz, 1H), 5.07 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.6, 138.7, 137.3, 135.5, 131.8, 128.8, 128.2, 127.9, 127.1, 126.8,

125.2, 122.7, 118.6, 105.4, 101.7, 93.0, 68.8. HRMS (EI, 70 eV) calcd for $C_{21}H_{17}NOSe$ [M^+]: 379.0475, found 379.0478.

3-(phenylseleno)-1H-indole-4-carbonitrile (**4c**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellow solid (35.7 mg, 60 % yield). The ^1H, ^{13}C NMR spectra were in accordance with those described in the literature. [22]

5-fluoro-3-(phenylseleno)-1H-indole (**4d**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (47.5 mg, 82 % yield), mp 126-128 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 11.81 (s, 1H), 7.82 (s, 1H), 7.52 – 7.48 (m, 1H), 7.19 – 7.00 (m, 7H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.6 (d, J_F = 231.3 Hz), 134.8, 133.3 (d, J_F = 11.3 Hz) , 130.2 (d, J_F = 10.0 Hz), 129.1, 128.2, 125.7, 113.4 (d, J_F = 8.8 Hz), 110.3 (d, J_F = 26.3 Hz), 103.6 (d, J_F = 23.8 Hz), 95.1. ^{19}F NMR (470 MHz, DMSO-d_6): δ -123.42 (s, 1F). HRMS (EI, 70 eV) calcd for $C_{14}H_{10}FNSe$ [M^+]: 290.9962, found 290.9969.

5-bromo-3-(phenylseleno)-1H-indole (**4e**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (57.6 mg, 82 % yield). The 1H, 13C NMR spectra were in accordance with those described in the literature.[21]

5-methoxy-3-(phenylseleno)-1H-indole (**4f**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown viscous oil (50.7 mg, 84 % yield). The ^1H, ^{13}C NMR spectra were in accordance with those described in the literature.[21]

3-(phenylseleno)-1H-indole-5-carbonitrile (**4g**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (42.2 mg, 71 % yield), mp 141-143 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 12.23 (s, 1H), 7.98 (s, 1H), 7.83 (s, 1H), 7.67 (d, J = 8.5 Hz, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.20 – 7.14 (m, 5H). ^{13}C NMR (125 MHz, DMSO-d_6) δ

138.6, 135.5, 132.8, 129.4, 129.2, 128.5, 126.0, 124.8, 124.3, 120.2, 113.6, 102.3, 96.5. HRMS (EI, 70 eV) calcd for $C_{15}H_{10}N_2Se$ [M^+]: 298.0009, found 298.0014.

5-nitro-3-(phenylseleno)-1H-indole (**4h**) Following the general procedure,0.04 mmol Cu, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellow solid (50.1 mg, 79 % yield), mp 141-143 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.39 (s, 1H), 8.29 (s, 1H), 8.08 (d, J = 11.5 Hz, 2H), 7.69 (d, J = 8.5 Hz, 1H), 7.23 – 7.14 (m, 5H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 141.5, 139.9, 136.7, 132.6, 129.2, 129.1, 128.5, 126.0, 117.3, 115.6, 112.8, 98.1. HRMS (EI, 70 eV) calcd for $C_{14}H_{10}N_2O_2Se$ [M^+]: 317.9907, found 317.9915.

6-methyl-3-(phenylseleno)-1H-indole (**4i**)

Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellow solid (51.0 mg, 89 % yield), mp 140−143 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.52 (s, 1H), 7.63 (s, 1H), 7.27 (d, J = 5.5 Hz, 2H), 7.17 – 7.09 (m, 5H), 6.89 (d, J = 8.0 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 137.0, 133.8, 132.0, 131.2, 129.0, 128.0, 127.4, 125.5, 121.8, 118.7, 111.8, 94.7, 21.2. HRMS (EI, 70 eV) calcd for $C_{15}H_{13}NSe$ [M^+]: 287.0213, found 287.0216.

6-fluoro-3-(phenylseleno)-1H-indole (**4j**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (53.9 mg, 93 % yield), mp 131-132 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.75 (s, 1H), 7.74 (s, 1H), 7.36 (dd, J = 8.5, 5.0 Hz, 1H), 7.28 (d, J = 9.5 Hz, 1H), 7.16 – 7.10 (m, 5H), 6.94 – 6.91 (m, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.2 , (d, J_F = 233.8 Hz), 136.4 (d, J_F = 13.8 Hz), 133.4 (d, J_F = 12.5 Hz), 129.1, 128.2, 126.2, 125.7, 120.1 (d, J_F = 10.0 Hz), 108.6 (d, J_F = 25 Hz), 98.1 (d, J_F = 26.3 Hz), 95.3. ^{19}F NMR (470 MHz, DMSO-d_6): δ -121.07 (s, 1F). HRMS (EI, 70 eV) calcd for $C_{14}H_{10}FNSe$ [M^+]: 290.9962, found 290.9969.

6-chloro-3-(phenylseleno)-1H-indole (**4k**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (51.6 mg, 84 % yield), mp 127-130 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.82 (s, 1H), 7.79 (s, 1H), 7.55 – 7.54 (m, 1H), 7.40 – 7.38 (m, 1H), 7.18 – 7.07 (m, 6H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 136.9, 133.8, 133.2, 129.0, 128.3, 128.2, 126.7, 125.7, 120.3, 111.7, 95.5. HRMS (EI, 70 eV) calcd for $C_{14}H_{10}ClNSe$ [M^+]: 306.9667, found 306.9672.

6-bromo-3-(phenylseleno)-1H-indole (**4l**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (64.6 mg, 92 % yield), mp 126-127 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.80 (s, 1H), 7.77 (s, 1H), 7.68 (s, 1H), 7.34 (d, J = 8.5 Hz, 1H), 7.21 – 7.10 (m, 6H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 137.5, 133.8, 133.3, 129.1, 128.6, 128.2, 125.7, 123.0, 120.8, 114.8, 114.7, 95.4. HRMS (EI, 70 eV) calcd for $C_{14}H_{10}BrNSe$ [M^+]: 350.9162, found 350.9168.

methyl 3-(phenylseleno)-1H-indole-6-carboxylate (**4m**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a white solid (53.5 mg, 81 % yield), mp 144-146 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.07 (s, 1H), 8.15 (s, 1H), 7.99 (d, J = 2.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.5 Hz, 1H), 7.19 – 7.10 (m, 5H), 3.86 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 166.9, 136.4, 135.9, 133.2, 133.2, 129.1, 128.2, 125.7, 123.2, 120.6, 118.9, 114.0, 95.7, 51.7. HRMS (EI, 70 eV) calcd for $C_{16}H_{13}NO2Se$ [M^+]: 331.0112, found 331.0115.

3-(phenylseleno)-1H-indole-6-carbaldehyde (**4n**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (39.1 mg, 65 % yield), mp 144-147 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.24 (s, 1H), 10.03 (s, 1H), 8.06 (d, J = 10.0 Hz,

2H), 7.61 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.18 – 7.10 (m, 5H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.6, 137.2, 136.1, 134.3, 133.0, 131.1, 129.1, 128.3, 125.8, 119.9, 119.5, 115.9, 96.2. HRMS (EI, 70 eV) calcd for $C_{15}H_{11}NOSe$ [M^+]: 301.0006, found 301.0013.

7-methyl-3-(phenylseleno)-1H-indole (**4o**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown liquid (52.1 mg, 91 % yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.71 (s, 1H), 7.75 (d, J = 2.5 Hz, 1H), 7.30 – 7.28 (m, 1H), 7.19 – 7.13 (m, 4H), 7.08 (t, J = 7.0 Hz, 1H), 6.99 (d, J = 6.5 Hz, 2H), 2.54 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 136.1, 133.8, 132.3, 129.3, 128.9, 128.1, 125.4, 122.5, 121.3, 120.1, 116.6, 95.5, 16.6. HRMS (EI, 70 eV) calcd for $C_{15}H_{13}NSe$ [M^+]: 287.0213, found 287.0208.

5-methoxy-2-methyl-3-(phenylseleno)-1H-indole (**4p**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellow liquid (51.9 mg, 82 % yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.48 (s, 1H), 7.27 (d, J = 9.0 Hz, 1H), 7.18 – 7.15 (m, 2H), 7.11 – 7.08 (m, 3H), 6.80 (d, J = 2.5 Hz, 1H), 6.74 (dd, J = 9.0, 2.5 Hz, 1H), 3.69 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 154.1, 142.2, 133.7, 131.4, 130.9, 129.1, 127.8, 125.4, 111.9, 110.8, 100.6, 93.3, 55.3, 12.7. HRMS (EI, 70 eV) calcd for $C_{16}H_{15}NOSe$ [M^+]: 317.0319, found 317.0319.

2-methyl-3-(phenylseleno)-1H-indole (**4q**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a white solid (53.1 mg, 93 % yield). The ^{1}H, ^{13}C NMR spectra were in accordance with those described in the literature.[21]

2-phenyl-3-(phenylseleno)-1H-indole (**4r**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a yellow viscous oil (59.9 mg, 86 % yield). The ^{1}H, ^{13}C NMR spectra were in accordance with those described in the literature.[21]

1-H-benzo[4,5]selenopheno[3,2-b]indole (**6a**)Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (47.0 mg, 87 % yield), mp 232-234 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.15 (s, 1H), 8.09 (t, J = 7.5 Hz, 2H), 7.76 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 7.25 (t, J = 7.0 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 141.7, 139.8, 139.0, 129.2, 127.6, 124.9, 124.4, 124.3, 122.6, 121.4, 119.3, 119.3, 112.3, 110.9. HRMS (ESI) calcd for $C_{14}H_{10}NSe$ $[M+H]^+$: 271.9973, found 271.9980.

3-methyl-10H-benzo[4,5]selenopheno[3,2-b]indole (**6b**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a dark brown solid (48.3 mg, 85 % yield), mp 239-240 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.02 (s, 1H), 8.09 - 8.04 (m, 2H), 7.53 (s, 1H), 7.49 - 7.45 (m, 2H), 7.29 (t, J = 7.5 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 141.6, 139.1, 138.2, 129.3, 128.0, 127.6, 125.0, 124.5, 124.3, 124.2, 121.3, 118.9, 112.1, 110.4, 21.2. HRMS (ESI) calcd for $C_{15}H_{12}NSe$ $[M+H]^+$: 286.0129, found 286.0119.

3-fluoro-10H-benzo[4,5]selenopheno[3,2-b]indole (**6c**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a light brown solid (50.7 mg, 88 % yield), mp 238-240 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.26 (s, 1H), 8.11 – 8.07 (m, 2H), 7.65 (d, J = 9.5 Hz, 1H), 7.56 (dd, J = 8.5, 4.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.09 (t, J = 9.0 Hz, 1H). ^{13}C NMR (125 MHz, DMSO) δ 156.8 (d, J_F = 231.3 Hz), 142.1, 140.9, 136.5, 129.0, 127.7, 125.0, 124.8, 124.5 (d, J_F = 11.3 Hz), 121.6, 113.2 (d, J_F = 10.0 Hz), 110.7 (t, J_F = 5.0 Hz), 110.5, 104.5 (d, J_F = 25.0 Hz). ^{19}F NMR (470 MHz, DMSO-d_6): δ -123.9 (s, 1F). HRMS (ESI) calcd for $C_{14}H_9FNSe$ $[M+H]^+$: 289.9879, found 289.9893.

3-chloro-10H-benzo[4,5]selenopheno[3,2-b]indole (**6d**) Following the general procedure, using

7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (55.4 mg, 91 % yield), mp 263-265 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.38 (s, 1H), 8.11 – 8.09 (m, 2H), 7.94 (s, 1H), 7.59 (d, J = 9.0 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.24 (d, J = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 142.3, 140.6, 138.3, 128.9, 127.7, 125.4, 125.1, 124.9, 123.7, 122.4, 121.7, 118.8, 113.7, 110.4. HRMS (ESI) calcd for $C_{14}H_9ClNSe$ $[M+H]^+$: 305.9583, found 305.9585.

3-bromo-10H-benzo[4,5]selenopheno[3,2-b]indole (**6e**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (55.9 mg, 80 % yield), mp 263-264 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.37 (s, 1H), 8.07 – 8.12 (m, 3H), 7.54 (d, J = 8.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.36 – 7.31 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 142.3, 140.4, 138.5, 128.8, 127.7, 126.1, 125.0, 124.9, 124.9, 121.8, 121.6, 114.2, 111.5, 110.2. HRMS (ESI) calcd for $C_{14}H_9BrNSe$ $[M+H]^+$: 349.9078, found 349.9090.

3-methoxy-10H-benzo[4,5]selenopheno[3,2-b]indole (**6f**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (52.3 mg, 87 % yield), mp 214-215 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.98 (s, 1H), 8.07 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.32 (s, 1H), 7.28 (t, J = 7.5 Hz, 1H), 6.89 – 6.87 (m, 1H), 3.81 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.5, 141.6, 139.6, 134.8, 129.4, 127.6, 124.9, 124.6, 124.3, 121.3, 113.0, 112.8, 110.5, 101.2, 55.4. HRMS (ESI) calcd for $C_{15}H_{12}NOSe$ $[M+H]^+$: 302.0079, found 302.0079.

3-(trifluoromethoxy)-10H-benzo[4,5]selenopheno[3,2-b]indole (**6g**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a light brown solid (67.3 mg, 95 % yield), mp 222-223 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.45 (s, 1H), 8.11 (t, J = 8.5 Hz,

2H), 7.93 (s, 1H), 7.66 – 7.63 (m, 1H), 7.50 (t, J = 6.5 Hz, 1H), 7.34 (t, J = 6.5 Hz, 1H), 7.22 (d, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 142.4, 141.7, 141.1, 138.3, 128.9, 127.7, 125.1, 125.0, 124.5, 121.7, 120.5 (q, J_F = 252.5 Hz) , 116.1, 113.2, 112.1, 111.0. ^{19}F NMR (470 MHz, DMSO-d_6): δ -56.9 (s, 3F). HRMS (ESI) calcd for $C_{15}H_9F_3NOSe$ $[M+H]^+$: 355.9796, found 355.9812.

2,4-dimethyl-10H-benzo[4,5]selenopheno[3,2-b]indole (**6h**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a white solid (57.2 mg, 96 % yield), mp 205-206 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.97 (s, 1H), 8.08 (dd, J = 12.0, 8.0 Hz, 2H), 7.48 (t, J = 7.5 Hz, 1H), 7.27 (t, J = 7.5 Hz, 1H), 7.19 (s, 1H), 6.78 (s, 1H), 2.55 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 141.8, 140.1, 137.6, 132.3, 129.2, 127.9 , 127.6, 125.0, 123.8, 122.3, 121.3, 121.2, 110.1, 109.9, 21.5, 18.8. HRMS (ESI) calcd for $C_{16}H_{14}NSe$ $[M+H]^+$: 300.0286, found 300.0276.

2,4-difluoro-10H-benzo[4,5]selenopheno[3,2-b]indole (**6i**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a brown solid (59.4 mg, 97 % yield), mp 197-199 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.65 (s, 1H), 8.13 (dd, J = 16.0, 8.0 Hz, 2H), 7.52 (t, J = 7.5 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.02 (t, J = 10.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.8 (dd, J_F = 11.3, 237.5 Hz), 154.2 (dd, J_F = 16.3, 245.0 Hz), 141.9, 141.3 (dd, J_F = 12.5, 15.0 Hz), 139.5 (d, J_F = 2.5 Hz), 128.5, 127.8, 125.3, 124.8, 121.7, 110.3 (d, J_F = 21.3 Hz), 106.7, 95.5 (dd, J_F = 3.8, 26.3 Hz), 94.8 (dd, J_F = 22.5, 28.8 Hz). ^{19}F NMR (470 MHz, DMSO-d_6): δ -116.8 (s, 1F), 120.2 (s, 1F). HRMS (ESI) calcd for $C_{14}H_8F_2NSe$ $[M+H]^+$: 307.9785, found 307.9788.

2,4-dichloro-10H-benzo[4,5]selenopheno[3,2-b]indole (**6j**) Following the general procedure, using

7:1 petroleum ether-EtOAc as the eluant afforded a yellowish solid (65.8 mg, 97 % yield), mp 218-219 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.70 (s, 1H), 8.15 (t, J = 6.5 Hz, 2H), 7.65 (s, 1H), 7.53 (t, J = 7.0 Hz, 1H), 7.37 (t, J = 7.0 Hz, 1H), 7.33 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 142.5, 140.4, 140.2, 128.3, 127.8, 127.0, 125.3, 125.2, 124.1, 122.0, 121.9, 118.7, 111.3, 109.2. HRMS (ESI) calcd for $C_{14}H_8Cl_2NSe$ $[M+H]^+$: 339.9194, found 339.9185.

1-methyl-10H-benzo[4,5]selenopheno[3,2-b]indole (**6k**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a dark brown solid (34.7 mg, 61 % yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.91 (s, 1H), 8.22 (d, J = 7.5 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 6.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.29 (t, J = 7.5 Hz, 1H), 7.04 (d, J = 7.0 Hz, 2H), 2.59 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 141.6, 139.4, 138.9, 129.5, 127.6, 124.9, 124.3, 124.0, 123.2, 121. 7, 121.6, 119.5, 117.0, 111.5, 17.1. HRMS (ESI) calcd for $C_{15}H_{12}NSe$ $[M+H]^+$: 286.0129, found 286.0119.

5-methoxy-1,2-dimethyl-3-((3,4,5-trimethoxyphenyl)seleno)-1H-indole (**7a**) Following the general procedure, using 7:1 petroleum ether-EtOAc as the eluant afforded a white solid (57.1 mg, 68 % yield). The ^{1}H, ^{13}C NMR spectra were in accordance with those described in the literature.[4]

ASSOCIATED CONTENT

Supporting Information

^{1}H、^{13}C、^{19}F NMR and HRMS spectral data of all compounds reported. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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