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One-Pot Four-Component Assembling for Selenoureas

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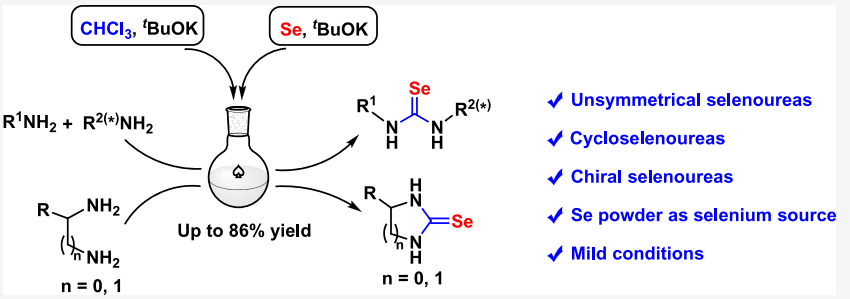

ABSTRACT: An efficient and practical method for the straightforward construction of unsymmetrical selenoureas and cycloselenoureas via the combination of selenium powder, chloroform, and two different amines was comprehensively achieved in one-pot with only the assistance of a base under mild conditions. Thirty-three new structures of unsymmetrical selenoureas including three chiral examples and eight cycloselenoureas were achieved. 1,1-Dimethyl-3-phenylselenourea **II**, which shows good fungicidal activity, was practically synthesized through this protocol in gram-scale. Isoselenocyanate was further confirmed as a key intermediate by control experiment.

INTRODUCTION

Selenoureas are a prevalent motif in the fields of bioorganic and pharmaceutical chemistry.[1,2] Recent studies demonstrated that selenoureas were excellent antioxidant agents *in vitro* showing relevant activities in the scavenging of free radicals and peroxides such as phenolic selenourea **I**.[1c] 1,1-Dimethyl-3-phenylselenourea **II** shows fungicidal activity against most fungi.[1d] Meanwhile, piperidine-1-carboselenoamide **III** exhibits inhibitory effects on tyrosinase activity.[1f] Selenoureas **IV** and **V** possess jack bean urease inhibition.[1g] Furthermore, selenoureas can be used as ligands for biologically active metal complexes[3] such as complex **VI** displaying superior antitumor effect (Figure 1).[3b] In addition, they are widely applied for the synthesis of selenium-containing heterocycles[4] such as selenazole[4a] and selenazine,[4d] essential for drug discovery.

The general synthesis of selenoureas is the reaction of isoselenocyanates with amines.[5] However, the formation of isoselenocyanates needs the utility of highly toxic and environmentally unfriendly triphosgene or potassium selenocyanate (Scheme 1, route 1). Other methods scarcely avoid the employment of unstable LiAlHSeH,[6] toxic and smelly isocyanide,[7] high tempertature,[8] and so on.[9] Therefore, development of an efficient and environmentally benign approach for the synthesis of selenoureas is of great significance. With our continuing effort on the organosulfur chemistry with ecofriendly concept,[10] we have developed an efficient and practical methodology for the synthesis of thiocarbamides and oxazolidinethiones under mild conditions by the combination of sulfur powder, chloroform, and amines

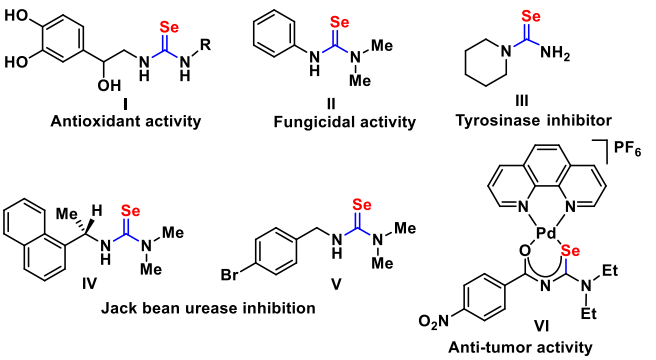

Figure 1. Representative selenoureas.

in the presence of a base.[11] Although sulfur and selenium are in the same group in the periodic table, selenourea has never been achieved by this method. Compared to nonmetallic element sulfur, selenium is a semimetallic element. Due to its lower electronegativity (Se: 2.55 *vs* S: 2.58),[12] larger atomic radius (Se: 1.17 Å *vs* S: 1.02 Å),[13] and higher polarizability (Se: 3.8 Å *vs* S: 2.9 Å),[14] the bond dissociation enthalpies of C═Se is

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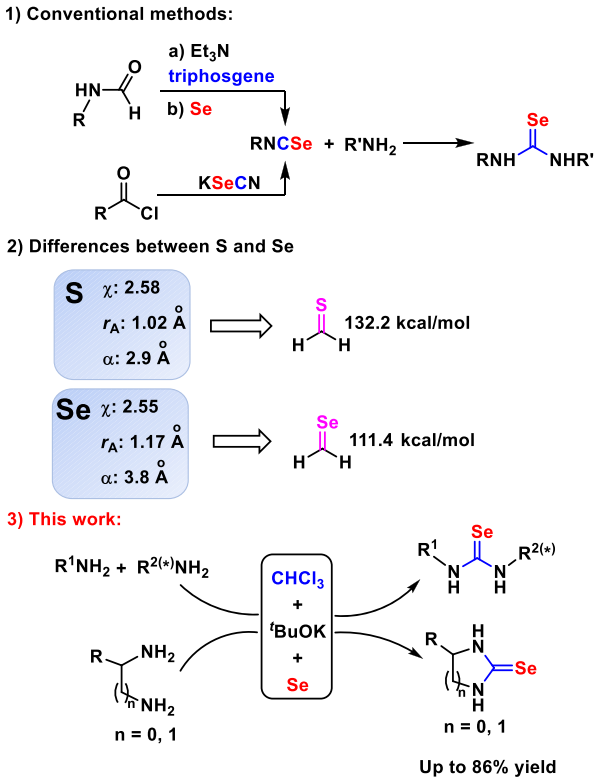
Scheme 1. Synthesis of Selenoureas and Differences between S and Se

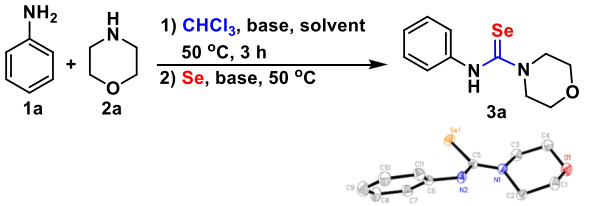


about 20 kcal/mol lower than that of C═S (Scheme 1, route 2).[15] Therefore, selenoureas are less stable and more difficult to synthesize than thiocarbamides. Moreover, in comparison to other selenium sources, selenium powder is hypotoxic and readily available, which makes it an ideal source to construct selenoureas. Herein, we report an efficient method for the synthesis of selenoureas by one-pot, four-component reactions using selenium powder, chloroform, and amines under mild conditions.

RESULTS AND DISCUSSION

At the outset of this investigation, the reactions were first carried out using aniline **1a**, chloroform, potassium *tert*-butoxide in the mixture solvent of *tert*-butyl alcohol/1,4-dioxane at 50 °C for 3 h, and then the extra potassium *tert*-butoxide, selenium powder and morpholine **2a** were added and the mixture was further stirred at 50 °C for 8 h, selenourea **3a** was obtained in 63% yield (Table 1, entry 1). The structure of **3a** was further confirmed through X-ray crystallographic analysis.[16] Inferior results were obtained when other bases such as potassium hydroxide, sodium hydroxide, and sodium *tert*-butoxide were used (Table 1, entries 2, 4, and 6). In addition, no desired product can be detected when weak bases such as potassium carbonate and lithium hydroxide were added (Table 1, entries 3 and 5). When no extra potassium *tert*-butoxide was added in the second step, the yield drastically decreased from 63 to 39%, which indicated that the addition of extra potassium *tert*-butoxide in the second step was beneficial. Using potassium *tert*-butoxide as the base, a variety of solvents were then tested (Table 1, entries 7−14). It was found that solvents affected the reactions significantly. For instance, a similar good yield was observed when the combination of isopropanol/1,4-dioxane was used (Table 1, entry 11). In the

Table 1. Optimization for the Reaction Conditions



entry[a]	base	solvent	yield (%)[b]
1	^{t}BuOK	^{t}BuOH/1,4-dioxane	63
2	KOH	^{t}BuOH/1,4-dioxane	33
3	K_2CO_3	^{t}BuOH/1,4-dioxane	NR
4	NaOH	^{t}BuOH/1,4-dioxane	25
5	LiOH· H_2O	^{t}BuOH/1,4-dioxane	NR
6	^{t}BuONa	^{t}BuOH/1,4-dioxane	35
7	^{t}BuOK	^{t}BuOH/1,4-dioxane	16
8	^{t}BuOK	EtOH/1,4-dioxane	42
9	^{t}BuOK	^{n}PrOH/1,4-dioxane	48
10	^{t}BuOK	^{n}BuOH/1,4-dioxane	47
11	^{t}BuOK	^{i}PrOH/1,4-dioxane	61
12	^{t}BuOK	^{t}BuOH/THF	51
13	^{t}BuOK	1,4-dioxane	33
14	^{t}BuOK	^{t}BuOH	39
15[c]	^{t}BuOK	^{t}BuOH/1,4-dioxane	61
16[d]	^{t}BuOK	^{t}BuOH/1,4-dioxane	32
17[e]	^{t}BuOK	^{t}BuOH/1,4-dioxane	74

[a]Otherwise specified, all reactions were first carried out under N_2 using **1a** (1.2 mmol), $CHCl_3$ (6.0 mmol), and a base (3.6 mmol) in the mixture solvent (1.2/1.2 mL) or single solvent (2.4 mL) at 50 °C for 3 h, and then **2a** (0.6 mmol), Se (1.8 mmol), and the same base (1.2 mmol) were added, and the mixture was further stirred under N_2 at 50 °C for 8 h. [b]Isolated yields. [c]Se (2.4 mmol). [d]Se (1.2 mmol). [e]The second step was performed for 5 h.

presence of other solvents such as the combination of ethanol/1,4-dioxane, propanol/1,4-dioxane, butanol/1,4-dioxane, and *tert*-butyl alcohol/tetrahydrofuran, moderate yields were afforded (Table 1, entries 8−10 and 12). Somewhat lower yields were obtained when the combination of methanol/1,4-dioxane or single 1,4-dioxane and *tert*-butyl alcohol were applied (Table 1, entries 7, 13, and 14). Elevating the amount of selenium powder to 4.0 equiv almost did not affect the reaction (Table 1, entries 1 *vs* 15), while when that of selenium powder decreased to 2.0 equiv, the yield dramatically declined to 32% (Table 1, entries 1 *vs* 16). Further studies showed that properly reducing the reaction time of the second step is beneficial to the reaction to some extent, and the best yield was achieved when the reaction time was reduced to 5 h (Table 1, entry 17). Finally, it was found that both steps carried out at 50 °C were required to achieve satisfactory results. Either the one step was carried out at 50 °C and another at room temperature, or both steps were performed at room temperature, the yields dramatically decreased to 28−44%.

Once the optimal conditions were established, the synthesis of selenoureas by this methodology using morpholine as one of the reaction partners was examined. As shown in Table 2, all reactions took place smoothly to furnish the desired selenoureas **3** in moderate to good yields. Substituents on the phenyl rings of anilines **1** have some effect on the reactions. For example, the best yield was achieved when the methoxy group was attached on the *ortho*-position (**3e**), followed by the

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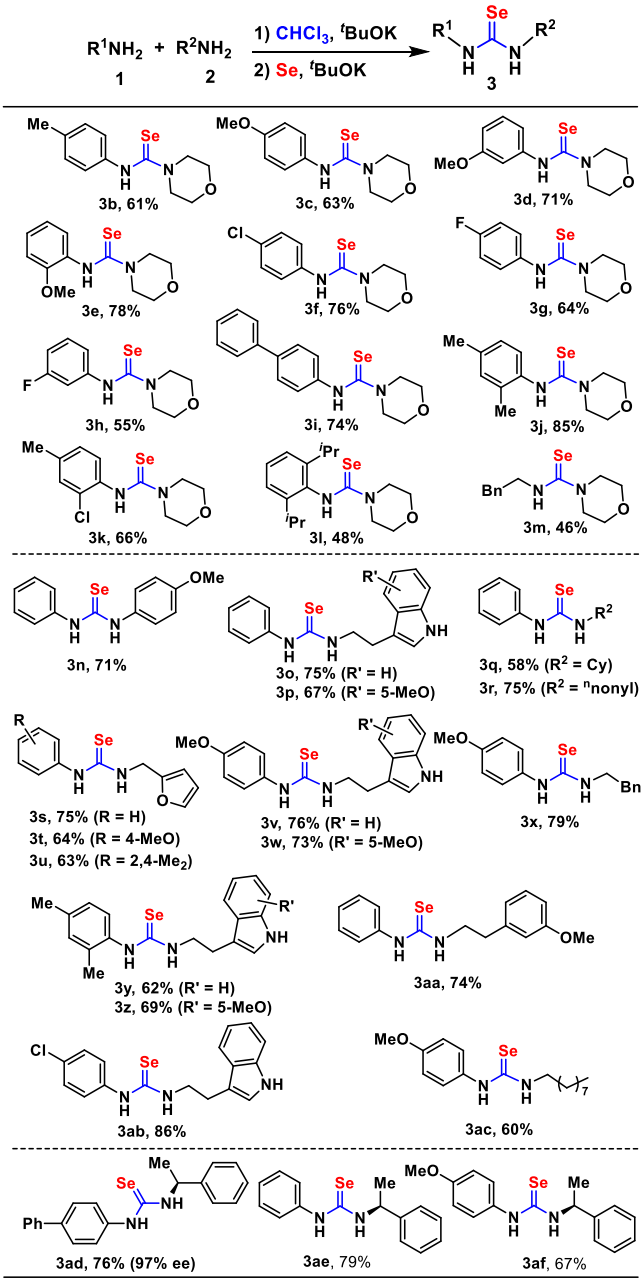
Table 2. Synthesis of Selenoureas Using Various Amines[a]

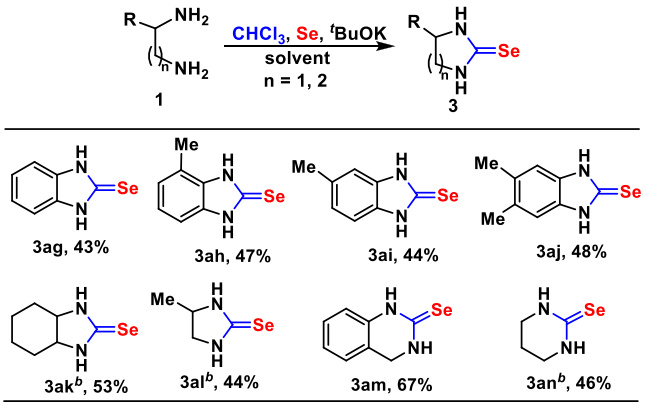


[a]Under N_2, all reactions were carried out using 1 (1.2 mmol), $CHCl_3$ (6 mmol), and ^{t}BuOK (3.6 mmol) in ^{t}BuOH/1,4-dioxane (1.2/1.2 mL) at 50 °C for 3 h; then **2** (0.6 mmol), Se (1.8 mmol), and ^{t}BuOK (1.2 mmol) were added, and the mixture was further stirred at 50 °C for 5 h. Isolated yields.

the limitation and scope of the methodology. Through the reactions using various amines **1** and **2**, the desired selenoureas **3** were also obtained in moderate-to-good yields in all cases. The substrates examined showed that substituents on both amines affected the reactions to some extent. For instance, aniline **1** possessing an electron-rich group on the phenyl ring gave inferior yield than that possessing electron-neutral one (**3s** and **3t**). In some cases, anilines **1** bearing both electron-rich and -neutral groups on the phenyl rings gave similar results (**3o** and **3v**), while that having electron-poor group gave the best yield (**3ab**). For the reactions of tryptamines, sometimes, similar good yields can be achieved when an electron-rich or -neutral group was attached on the phenyl ring (**3v** and **3w**), while in other cases, inferior yields were found for the one having electron-rich group on the phenyl ring (**3o** and **3p**), or the opposite results were given (**3y** and **3z**), according to the other counterparts involved. When (*S*)-1-phenylethan-1-amine was used as one of the reaction partners, chiral selenoureas **3ad**–**3af** were achieved, which may be potential organocatalysts in asymmetric synthesis. All reactions performed well to give the corresponding products in good yields, with the *ee* values retained under such reaction conditions (see the Supporting Information for the details).

The synthesis of cycloselenoureas **3** by the intramolecular reaction was also performed. As shown in Table 3, the corresponding five- and six-membered cycloselenoureas **3ag**–**3an** were obtained in moderate yields.

Table 3. Synthesis of Cycloselenoureas by Intramolecular Reaction[a]



[a]Under N_2, all reactions were carried out using **1** (0.9 mmol), Se (2.7 mmol), and ^{t}BuOK (4.05 mmol) in ^{i}PrOH/1,4-dioxane (1.5/1.5 mL); then $CHCl_3$ (9 mmol) was added dropwise at 0 °C, and the mixture was heated to 50 °C for 16 h. Isolated yields. [b]2-Ethoxyethanol/1,4-dioxane (1.5/1.5 mL) was used as the solvent.

meta-substituted one (**3d**), and the lowest yield was observed when the methoxy group was attached on the *para*-position (**3c**). Sterically hindered substituents on the phenyl rings of anilines also affected the reactions to some extent. For instance, the best yield was given when 2,4-dimethylaniline was used as the substrate (**3j**). Only 48% yield of the desired product **3l** was afforded when 2,6-di-isopropylaniline was used. Compared to anilines, alkyl amine, such as 2-phenylethan-1-amine, gave the desired product **3m** in a somewhat lower yield.

Encouraged by the above results, a range of amines were then subjected to the optimal conditions to further examine

As can be seen from Tables 1–3, comparted to their sulfur analogues,[11] relatively lower yields were observed for the formation of selenoureas, implying the difficulty for the synthesis of such compounds by this methodology. It should be also noted here that the selenoureas are labile to decompose in the reaction system, and they should be isolated by flash column chromatography as soon as possible once the reaction was completed.

Finally, 1,1-dimethyl-3-phenylselenourea **II**, which has good fungicidal activity against most fungi, was efficiently synthesized in an excellent yield of 82% (1.87 g) with aniline and a

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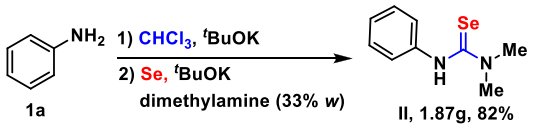
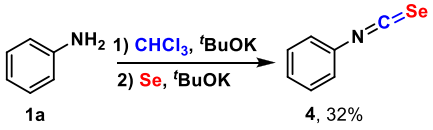
33% aqueous solution of dimethylamine as the starting materials (Scheme 2).

Scheme 2. Gram-Scale Synthesis of 1,1-Dimethyl-3-phenyl Selenourea II



To better understand this reaction process, aniline **1a**, chloroform, and potassium *tert*-butoxide were first stirred in *tert*-butyl alcohol/1,4-dioxane at 50 °C for 3 h; then Se and potassium *tert*-butoxide were added. Finally, phenylisoselenocyanate **4**, which is important material for selenoureas, was obtained in 32% yield, demonstrating that isoselenocyanate could be formed in the reaction (Scheme 3).

Scheme 3. Control Experiment



CONCLUSIONS

In conclusion, an efficient and practical methodology for the synthesis of selenoureas has been developed via a one-pot, four-component reaction. By the combination of various amines **1** and **2**, a series of selenoureas were achieved in moderate-to-good yields under a mild condition. In addition, chiral selenoureas can also be achieved with the *ee* values kept untouched through this method, which will thus display their potential application in asymmetric catalysis. Further studies on the application of such selenoureas are underway in this laboratory.

EXPERIMENTAL SECTION

General Remarks. Melting points are uncorrected. NMR spectra were recorded at 500 or 400 MHz (for ^{1}H NMR) and 125 MHz (for ^{13}C NMR), respectively. ^{1}H and ^{13}C NMR spectra recorded in $CDCl_3$ or DMSO-d_6 solutions were referenced to TMS (0.00 ppm) and the residual solvent peak (77.0 ppm) or (39.5 ppm), respectively. *J*-values are in Hz. Organic solvents used were dried by standard methods. The mass analyzer type for the high-resolution mass spectra is Q-TOF. Other commercially obtained reagents were used without further purification. Flash column chromatography was performed on silica gel.

General Procedure for the Synthesis of Selenoureas. Under a N_2 atmosphere, amine **1** (1.2 mmol, 2.0 equiv), ^{t}BuOK (403.2 mg, 3.6 mmol, 6.0 equiv), $CHCl_3$ (0.48 mL, 6 mmol, 10 equiv), and ^{t}BuOH/1,4-dixoane (1.2/1.2 mL) were added into a Schlenk reaction tube. The mixture was stirred at 50 °C in a heating mantle for 3 h. Then, also under a N_2 atmosphere, Se (142.1 mg, 1.8 mmol, 3.0 equiv), ^{t}BuOK (134.4 mg, 1.2 mmol, 2.0 equiv), and amine **2** (0.6 mmol) were added to the reaction mixture and stirred at the same temperature for 5 h. After the reaction was finished, saturated aq. NH_4Cl was added and the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel to give the pure products **3a**-**3af**.

General Procedure for the Synthesis of Cycloselenoureas. Under a N_2 atmosphere, diamine **1** (0.9 mmol), ^{t}BuOK (453.6 mg, 4.05 mmol, 4.5 equiv), Se (213.2 mg, 2.7 mmol, 3.0 equiv), and ^{i}PrOH (or 2-ethoxyethanol)/1,4-dixoane (1.5/1.5 mL) were added into a Schlenk reaction tube at room temperature. Then, under 0 °C, $CHCl_3$ (0.72 mL, 9 mmol, 10.0 equiv) was added dropwise. The mixture was stirred at 50 °C in a heating mantle for 16 h. After it was cooled to room temperature, saturated aq. NH_4Cl was added and the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel to give the pure products **3ag**−**3an**.

General Procedure for the Synthesis of Phenyl Isoselenocyanate. Under a N_2 atmosphere, aniline **1a** (109.5 μL, 1.2 mmol), ^{t}BuOK (403.2 mg, 3.6 mmol, 3.0 equiv), $CHCl_3$ (0.48 mL, 6 mmol, 5.0 equiv), and ^{t}BuOH/1,4-dixoane (1.2/1.2 mL) were added into a Schlenk reaction tube. The mixture was stirred at 50 °C in a heating mantle for 3 h. Then, also under a N_2 atmosphere, Se (142.1 mg, 1.8 mmol, 1.5 equiv) and ^{t}BuOK (134.4 mg, 1.2 mmol) were added to the reaction mixture and it was stirred at the same temperature for another 5 h. After it was cooled to room temperature, saturated aq. NH_4Cl was added and the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel to give the pure products **4**.

Compound ***3a***.[17] Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (119.5 mg, 74%). mp 150.5 °C (decomposed). ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.35 (t, J = 7.5 Hz, 2H), 7.26 (s, 1H), 7.18 (d, J = 7.5 Hz, 1H), 7.14 (t, J = 7.5 Hz, 2H), 3.82 (t, J = 5.0 Hz, 4H), 3.73 (t, J = 5.0 Hz, 4H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 184.0, 140.0, 129.4, 125.7, 122.8, 66.0, 52.1. IR (neat) 3386, 3041, 2852, 2226, 1738, 1525, 1330, 1221, 1109, 1023, 860, 751 cm^{-1}. MS (ESI) 293 [M + Na$^+$]. HRMS (ESI) calcd for $C_{11}H_{14}N_2NaOSe$ [M + Na$^+$] 293.0164; found 293.0166.

Compound ***3b***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as white solid (103.7 mg, 61%). mp 163.1−163.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.75 (s, 1H), 7.14 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 8.0 Hz, 2H), 3.84 (s, 4H), 3.72 (t, J = 4.0 Hz, 4H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 183.9, 137.5, 135.8, 130.0, 123.3, 66.0, 51.9, 20.9. IR (neat) 3195, 3026, 2914, 2857, 1883, 1590, 1526, 1418, 1325, 1214, 1118, 1026, 940, 863, 806, 704 cm^{-1}. MS (ESI) 285 [M + H$^+$]. HRMS (ESI) calcd for $C_{12}H_{17}N_2OSe$ [M + H$^+$] 285.0501; found 285.0501.

Compound ***3c***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (113.1 mg, 63%). mp 221.3−221.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.69 (s, 1H), 7.07 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 3.86 (t, J = 4.4 Hz, 4H), 3.80 (s, 3H), 3.72 (t, J = 4.4 Hz, 4H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 184.0, 157.8, 133.1, 125.7, 114.5, 66.0, 55.4, 51.5. IR (neat) 3373, 3155, 3012, 2845, 1876, 1535, 1429, 1332, 1249, 1113, 1029, 936, 826 cm^{-1}. MS (ESI) 301 [M + H$^+$]. HRMS (ESI) calcd for $C_{12}H_{17}N_2O_2Se$ [M + H$^+$] 301.0450; found 301.0443.

Compound ***3d***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (127.5 mg, 71%). mp 146.2 °C (decomposed). ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.86 (s, 1H), 7.24 (t, J = 8.0 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 6.64 (d, J = 8.0 Hz, 1H), 6.62 (s, 1H), 3.83 (s, 4H), 3.79 (s, 3H), 3.71 (t, J = 4.5 Hz, 4H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 183.9, 160.4, 141.0, 130.2, 114.7, 110.9, 108.5, 66.0, 55.4, 52.3. IR (neat) 3223, 3052, 2932, 2828, 1586, 1533, 1467, 1412, 1309, 1219, 1112, 1024, 960, 859, 692 cm^{-1}. MS (ESI) 301 [M + H$^+$]. HRMS (ESI) calcd for $C_{12}H_{17}N_2O_2Se$ [M + H$^+$] 301.0450; found 301.0441.

Compound ***3e***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (140.0 mg, 78%). mp 219.9 °C (decomposed). ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.66 (s, 1H), 7.46 (dd, J = 10.0, 1.5 Hz, 1H), 7.13 (td, J = 10.0, 1.5 Hz, 1H), 6.97−6.90 (m, 2H), 3.90 (t, J = 6.0 Hz, 4H), 3.86 (s, 3H), 3.76 (t, J = 6.0 Hz, 4H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 183.3, 150.0, 128.7, 125.7, 122.7, 120.5, 111.0, 66.1, 55.7, 51.6. IR (neat) 3244, 3149, 2918, 2853, 1602, 1526, 1453, 1334, 1322, 1223,

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1110, 1024, 937, 851, 749 cm^{-1}. MS (ESI) 301 [M + H^+]. HRMS (ESI) calcd for $C_{12}H_{17}N_2O_2Se$ [M + H^+] 301.0450; found 301.0460.

Compound ***3f***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as white solid (138.5 mg, 76%). mp 148.0 °C (decomposed). ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.80 (s, 1H), 7.31 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 3.87 (t, J = 4.8 Hz, 4H), 3.74 (t, J = 4.8 Hz, 4H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 184.0, 138.5, 131.3, 129.4, 124.8, 66.0, 51.7. IR (neat) 3183, 2854, 1880, 1593, 1528, 1491, 1421, 1318, 1209, 1114, 1025, 860, 817 cm^{-1}. MS (ESI) 305 [M + H^+]. HRMS (ESI) calcd for $C_{11}H_{14}ClN_2OSe$ [M + H^+] 304.9952; found 304.9950.

Compound ***3g***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as white solid (110.3 mg, 64%). mp 170.9 °C (decomposed). ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.67 (s, 1H), 7.13 (dd, J = 8.8, 4.8 Hz, 2H), 7.05 (t, J = 8.8 Hz, 2H), 3.89 (t, J = 4.0 Hz, 4H), 3.74 (t, J = 4.8 Hz, 4H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 184.2, 160.6 (d, J_{C-F} = 245.0 Hz), 136.1, 126.0 (d, J_{C-F} = 8.75 Hz), 116.1 (d, J_{C-F} = 22.5 Hz), 66.0, 51.4. IR (neat) 3076, 3025, 2909, 1881, 1641, 1552, 1470, 1362, 1199, 1112, 902, 834, 771 cm^{-1}. MS (ESI) 289 [M + H^+]. HRMS (ESI) calcd for $C_{11}H_{14}FN_2OSe$ [M + H^+] 289.0250; found 289.0248.

Compound ***3h***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as white solid (94.8 mg, 55%). mp 143.1 °C (decomposed). ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.85 (s, 1H), 7.30 (dd, J = 15.0, 8.0 Hz, 1H), 6.90−6.81 (m, 3H), 3.86 (s, 4H), 3.74 (t, J = 5.0 Hz, 4H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 184.1, 163.1 (d, J_{C-F} = 245.0 Hz), 141.3 (d, J_{C-F} = 10.0 Hz), 130.6 (d, J_{C-F} = 8.75 Hz), 118.1 (d, J_{C-F} = 2.5 Hz), 112.4 (d, J_{C-F} = 21.25 Hz), 110.9 (d, J_{C-F} = 23.75 Hz), 66.0, 52.2. IR (neat) 3404, 3147, 3005, 2951, 2840, 1613, 1465, 1433, 1361, 1150, 1067, 1021, 919, 784 cm^{-1}. MS (ESI) 289 [M + H^+]. HRMS (ESI) calcd for $C_{11}H_{14}FN_2OSe$ [M + H^+] 289.0250; found 289.0259.

Compound ***3i***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (153.3 mg, 74%). mp 297.4 °C (decomposed). ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.91 (s, 1H), 7.57−7.55 (m, 4H), 7.44 (t, J = 7.2 Hz, 2H), 7.35 (t, J = 7.2 Hz, 1H), 7.16 (d, J = 8.4 Hz, 2H), 3.88 (t, J = 4.8 Hz, 4H), 3.74 (t, J = 4.8 Hz, 4H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 183.8, 139.9, 139.1, 138.5, 128.8, 127.9, 127.4, 126.8, 123.1, 66.0, 52.0. IR (neat) 3284, 3051, 2939, 1573, 1509, 1404, 1344, 1253, 1183, 1102, 1006, 850 cm^{-1}. MS (ESI) 347 [M + H^+]. HRMS (ESI) calcd for $C_{17}H_{19}N_2OSe$ [M + H^+] 347.0658; found 347.0657.

Compound ***3j***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (151.6 mg, 85%). mp 156.3 °C (decomposed). ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.40 (s, 1H), 7.04 (s, 1H), 7.00 (d, J = 8.4 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 3.81 (t, J = 4.4 Hz, 4H), 3.71 (t, J = 4.4 Hz, 4H), 2.30 (s, 3H), 2.22 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 184.2, 136.7, 136.3, 132.4, 131.8, 127.6, 125.2, 66.0, 51.6, 20.9, 18.0. IR (neat) 3202, 2962, 2924, 2852, 1730, 1675, 1525, 1460, 1378, 1321, 1205, 1115, 1025, 856, 807 cm^{-1}. MS (ESI) 299 [M + H^+]. HRMS (ESI) calcd for $C_{13}H_{19}N_2OSe$ [M + H^+] 299.0657; found 299.0659.

Compound ***3k***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (125.8 mg, 66%). mp 140.0 °C (decomposed). ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.42 (s, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.24 (s, 1H), 7.08 (d, J = 8.0 Hz, 1H), 3.91 (s, 4H), 3.76 (t, J = 5.0 Hz, 4H), 2.33 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 183.9, 137.4, 134.3, 130.2, 128.1, 127.4, 126.1, 66.0, 51.3, 20.8. IR (neat) 3120, 2915, 2857, 1525, 1421, 1319, 1220, 1117, 1028, 937, 811 cm^{-1}. MS (ESI) 319 [M + H^+]. HRMS (ESI) calcd for $C_{12}H_{16}ClN_2OSe$ [M + H^+] 319.0108; found 319.0099.

Compound ***3l***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as white solid (101.8 mg, 48%). mp 197.9 °C (decomposed). ^1H NMR (500 MHz, DMSO-d_6) δ 9.14 (s, 1H), 7.25 (t, J = 7.5 Hz, 1H), 7.13 (d, J = 7.5 Hz, 2H), 4.05 (s, 4H), 3.66 (s, 4H), 2.97 (hept, J = 6.5 Hz, 2H), 1.21 (d, J = 6.5 Hz, 6H), 1.12 (d, J = 6.5 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 182.4, 146.0, 136.4, 127.4, 122.9, 65.9, 50.1, 28.0, 23.9, 23.1. IR (neat) 3227, 2955, 2864, 1955, 1741, 1591, 1525, 1392, 1323, 1214, 1120, 1027, 940, 805 cm^{-1}. MS (ESI) 355 [M + H^+]. HRMS (ESI) calcd for $C_{17}H_{27}N_2OSe$ [M + H^+] 355.1284; found 355.1291.

Compound ***3m***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as white solid (82.1 mg, 46%). mp 112.1 °C (decomposed). ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 7.33 (t, J = 7.2 Hz, 2H), 7.25−7.22 (m, 3H), 5.68 (br, 1H), 4.07 (dd, J = 12.0, 6.8 Hz, 2H), 3.77 (dd, J = 9.2, 4.0 Hz, 4H), 3.70 (dd, J = 8.4, 4.0 Hz, 4H), 3.00 (t, J = 6.8 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 182.3, 138.5, 128.78, 128.75, 126.8, 66.0, 49.4, 49.0, 35.1. IR (neat) 3328, 1553, 1455, 1334, 1236, 1118, 996, 877, 753 cm^{-1}. MS (ESI) 321 [M + Na^+]. HRMS (ESI) calcd for $C_{13}H_{18}N_2NaOSe$ [M + Na^+] 321.0477; found 321.0472.

Compound ***3n***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as brownish solid (130.1 mg, 71%). mp 223.5 °C (decomposed). ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.17 (br, 1H), 7.40−7.28 (m, 7H), 6.94 (d, J = 7.5 Hz, 2H), 3.82 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 178.7, 157.0, 139.7, 132.4, 128.43, 128.38, 126.7, 125.0, 124.7, 124.6, 123.8, 115.0, 113.7. IR (neat) 3171, 3009, 1557, 1506, 1451, 1338, 1249, 1182, 1103, 1036, 932, 842, 753 cm^{-1}. MS (ESI) 329 [M + Na^+]. HRMS (ESI) calcd for $C_{14}H_{14}N_2NaOSe$ [M + Na^+] 329.0164; found 329.0171.

Compound ***3o***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as orange solid (154.0 mg, 75%). mp 221.9 °C (decomposed). ^1H NMR (500 MHz, DMSO-d_6) δ 10.85 (s, 1H), 9.94 (s, 1H), 8.09 (s, 1H), 7.70 (d, J = 7.0 Hz, 1H), 7.36−7.31 (m, 3H), 7.23−7.17 (m, 4H), 7.07 (t, J = 7.0 Hz, 1H), 6.99 (t, J = 7.0 Hz, 1H), 3.84 (s, 2H), 3.00 (s, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 178.2, 138.4, 136.2, 129.0, 127.2, 125.0, 123.9, 122.7, 120.9, 118.6, 118.2, 111.4, 111.3, 47.5, 24.6. IR (neat) 3393, 3337, 3145, 1711, 1539, 1455, 1293, 1233, 1158, 1074, 946, 831 cm^{-1}. MS (ESI) 366 [M + Na^+]. HRMS (ESI) calcd for $C_{17}H_{17}N_3NaSe$ [M + Na^+] 366.0480; found 366.0483.

Compound ***3p***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (149.7 mg, 67%). mp 231.3−233.1 °C. ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.18 (s, 1H), 7.97 (s, 1H), 7.26−7.20 (m, 4H), 7.07 (d, J = 2.0 Hz, 1H), 6.89−6.87 (m, 4H), 6.35 (s, 1H), 4.02 (dd, J = 12.0, 6.4 Hz, 2H), 3.84 (s, 3H), 3.06 (t, J = 6.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 178.6, 154.3, 135.4, 131.4, 130.1, 127.6, 127.5, 125.0, 122.8, 112.8, 112.0, 111.9, 100.5, 55.9, 48.3, 24.4. IR (neat) 3442, 1539, 1486, 1448, 1353, 1263, 1170, 1095, 1026, 926, 841, 795 cm^{-1}. MS (ESI) 396 [M + Na^+]. HRMS (ESI) calcd for $C_{18}H_{19}N_3NaOSe$ [M + Na^+] 396.0586; found 396.0582.

Compound ***3q***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (97.9 mg, 58%). mp 146.5 °C (decomposed). ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.30 (s, 1H), 7.45 (t, J = 7.0 Hz, 2H), 7.33 (t, J = 7.0 Hz, 1H), 7.20 (d, J = 7.0 Hz, 2H), 6.14 (br, 1H), 4.35 (br, 1H), 2.10−2.08 (m, 2H), 1.67−1.60 (m, 3H), 1.44−1.37 (m, 2H), 1.15−1.13 (m, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 176.9, 135.7, 130.4, 127.6, 125.1, 56.8, 32.5, 25.3, 24.6. IR (neat) 3082, 2827, 2646, 2131, 1937, 1867, 1788, 1652, 1516, 1402, 1264, 1097, 982, 906, 823 cm^{-1}. MS (ESI) 305 [M + Na^+]. HRMS (ESI) calcd for $C_{13}H_{18}N_2NaSe$ [M + Na^+] 305.0528; found 305.0537.

Compound ***3r***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (146.4 mg, 75%). mp 212.4 °C (decomposed). ^1H NMR (500 MHz, DMSO-d_6) δ 9.81 (s, 1H), 8.05 (s, 1H), 7.35 (t, J = 7.5 Hz, 2H), 7.29 (d, J = 7.5 Hz, 2H), 7.17 (t, J = 7.5 Hz, 1H), 3.54−3.53 (m, 2H), 1.56−1.54 (m, 2H), 1.27 (s, 12H), 0.86 (t, J = 6.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 178.5, 138.6, 129.4, 128.8, 128.5, 124.9, 123.8, 46.7, 31.2, 28.8, 28.5, 26.2, 22.0, 13.8. IR (neat) 3209, 3048, 2923, 2855, 2139, 1630, 1583, 1493, 1312, 1235, 1069, 861 cm^{-1}. MS (ESI) 349 [M + Na^+]. HRMS (ESI) calcd for $C_{16}H_{26}N_2NaSe$ [M + Na^+] 349.1154; found 349.1153.

Compound ***3s***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (125.6 mg, 75%). mp 108.5−109.4 °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.59 (br, 1H), 7.44 (t, J = 7.5 Hz, 2H), 7.34−7.31 (m, 2H), 7.22 (d, J

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= 7.5 Hz, 2H), 6.54 (br, 1H), 6.32 (s, 2H), 4.93 (d, J = 3.5 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 179.2, 149.7, 142.5, 135.6, 130.4, 127.8, 125.1, 110.5, 108.4, 100.0, 45.2. IR (neat) 3425, 3347, 3280, 3022, 2811, 1960, 1707, 1581, 1413, 1282, 1136, 1058, 938, 756 cm^{-1}. MS (ESI) 303 [M + Na^+]. HRMS (ESI) calcd for $C_{12}H_{12}N_2NaOSe$ [M + Na^+] 303.0007; found 303.0012.

Compound ***3t***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as pink solid (118.7 mg, 64%). mp 126.1−128.1 °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.34 (s, 1H), 7.33 (s, 1H), 7.15 (d, J = 8.5 Hz, 2H), 6.93 (d, J = 8.5 Hz, 2H), 6.31−6.30 (m, 3H), 4.92 (d, J = 4.0 Hz, 2H), 3.82 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 179.6, 159.3, 149.9, 142.4, 127.9, 127.4, 115.5, 110.5, 108.3, 55.5, 45.1. IR (neat) 3321, 3159, 2364, 1607, 1547, 1511, 1354, 1308, 1244, 1147, 1069, 1019, 945, 828, 757 cm^{-1}. MS (ESI) 333 [M + Na^+]. HRMS (ESI) calcd for $C_{13}H_{14}N_2O_2Se$ [M + Na^+] 333.0113; found 333.0108.

Compound ***3u***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as pink solid (116.2 mg, 63%). mp 128.3−128.5 °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.07 (br, 1H), 7.32 (s, 1H), 7.11 (s, 1H), 7.06 (s, 2H), 6.29 (d, J = 5.5 Hz, 2H), 6.10 (br, 1H), 4.91 (d, J = 4.0 Hz, 2H), 2.32 (s, 3H), 2.20 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 179.6, 150.0, 142.4, 139.1, 135.4, 132.5, 131.2, 128.3, 127.1, 110.4, 108.2, 45.1, 21.0, 17.5. IR (neat) 3129, 2960, 1541, 1505, 1416, 1284, 1227, 1185, 1103, 1010, 949, 839, 794, 738 cm^{-1}. MS (ESI) 331 [M + Na^+]. HRMS (ESI) calcd for $C_{14}H_{16}N_2NaOSe$ [M + Na^+] 331.0320; found 331.0323.

Compound ***3v***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as red solid (169.8 mg, 76%). mp 248.9 °C (decomposed). ^1H NMR (400 MHz, DMSO-d_6) δ 10.84 (s, 1H), 9.77 (s, 1H), 7.81 (s, 1H), 7.69 (d, J = 7.6 Hz, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.15 (s, 1H), 7.09−7.05 (m, 3H), 6.98 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 8.4 Hz, 2H), 3.81−3.72 (m, 5H), 2.97 (t, J = 7.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 178.2, 157.1, 136.2, 130.8, 127.2, 126.4, 122.7, 120.9, 118.6, 118.1, 114.3, 111.4, 111.3, 55.2, 47.5, 24.7. IR (neat) 3310, 3249, 1824, 1553, 1509, 1455, 1297, 1246, 1180, 1098, 1031, 905, 835, 741 cm^{-1}. MS (ESI) 396 [M + Na^+]. HRMS (ESI) calcd for $C_{18}H_{19}N_3NaOSe$ [M + Na^+] 396.0586; found 396.0597.

Compound ***3w***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as brown solid (176.3 mg, 73%). mp 241.5 °C (decomposed). ^1H NMR (400 MHz, DMSO-d_6) δ 10.65 (s, 1H), 9.75 (s, 1H), 7.77 (br, 1H), 7.28 (br, 1H), 7.23 (d, J = 8.4 Hz, 1H), 7.09 (s, 2H), 7.06 (s, 1H), 6.89 (d, J = 8.8 Hz, 2H), 6.72 (dd, J = 8.8, 2.4 Hz, 1H), 3.81−3.77 (m, 2H), 3.76 (s, 3H), 3.75 (s, 3H), 2.94 (t, J = 7.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 178.2, 157.1, 152.9, 131.4, 130.8, 127.6, 126.4, 124.0, 123.3, 114.3, 111.9, 111.2, 100.7, 55.3, 55.2, 47.4, 24.8. IR (neat) 3159, 1546, 1511, 1442, 1385, 1303, 1249, 1171, 1026, 924, 846, 805 cm^{-1}. MS (ESI) 426 [M + Na^+]. HRMS (ESI) calcd for $C_{19}H_{21}N_3NaO_2Se$ [M + Na^+] 426.0692; found 426.0697.

Compound ***3x***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (158.0 mg, 79%). mp 257.6 °C (decomposed). ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.19 (s, 1H), 7.27−7.21 (m, 3H), 7.12 (d, J = 6.4 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 9.2 Hz, 2H), 6.03 (br, 1H), 3.93 (q, J = 6.8 Hz, 2H), 3.80 (s, 3H), 2.91 (t, J = 6.8 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 179.0, 159.1, 138.2, 128.7, 128.7, 127.8, 127.5, 126.6, 115.3, 55.5, 48.8, 34.8. IR (neat) 3317, 3135, 1553, 1509, 1447, 1361, 1300, 1242, 1161, 1104, 1029, 941, 825, 781 cm^{-1}. MS (ESI) 357 [M + Na^+]. HRMS (ESI) calcd for $C_{16}H_{18}N_2NaOSe$ [M + Na^+] 357.0477; found 357.0479.

Compound ***3y***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (137.8 mg, 62%). mp 221.2 °C (decomposed). ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.05 (s, 1H), 7.77 (s, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 7.5 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 6.96 (s, 1H), 6.88 (s, 1H), 6.84 (d, J = 7.5 Hz, 1H), 6.77 (d, J = 7.5 Hz, 1H), 5.91 (s, 1H), 3.99 (q, J = 6.0 Hz, 2H), 3.04 (t, J = 6.0, 2H), 2.28 (s, 3H), 2.04 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 178.8, 138.7, 136.3, 135.3, 132.2, 131.1, 128.0, 127.1, 127.0, 122.2, 122.0, 119.6, 118.6, 112.3, 111.1, 48.2, 24.5, 21.0, 17.4. IR (neat) 3344, 3167, 1543, 1505, 1337, 1223, 1176, 1087, 933, 743 cm^{-1}. MS (ESI) 394 [M + Na^+]. HRMS (ESI) calcd for $C_{19}H_{21}N_3NaSe$ [M + Na^+] 394.0794; found 394.0781.

Compound ***3z***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (165.8 mg, 69%). mp 247.5 °C (decomposed). ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.94 (s, 1H), 7.74 (s, 1H), 7.23 (d, J = 8.5 Hz, 1H), 7.03 (s, 1H), 6.95 (s, 1H), 6.86−6.84 (m, 3H), 6.76 (d, J = 7.5 Hz, 1H), 5.92 (s, 1H), 3.97 (q, J = 6.5 Hz, 2H), 3.83 (s, 3H), 3.01 (t, J = 6.5 Hz, 2H), 2.28 (s, 3H), 2.03 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 178.8, 154.1, 138.7, 135.2, 132.2, 131.3, 131.1, 128.0, 127.6, 126.9, 122.6, 112.7, 112.0, 11.8, 100.2, 55.8, 48.2, 24.5, 21.0, 17.4. IR (neat) 3362, 3221, 3134, 1732, 1560, 1479, 1405, 1256, 1201, 1160, 1012, 868, 809 cm^{-1}. MS (ESI) 402 [M + H^+]. HRMS (ESI) calcd for $C_{20}H_{24}N_3OSe$ [M + H^+] 402.1080; found 402.1086.

Compound ***3aa***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as white solid (148.0 mg, 74%). mp 121.3 °C (decomposed). ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.32 (s, 1H), 7.43−7.40 (m, 1H), 7.33 (t, J = 7.5 Hz, 2H), 7.28 (d, J = 8.0 Hz, 1H), 7.17 (t, J = 8.0 Hz, 1H), 7.00 (d, J = 7.5 Hz, 2H), 6.76 (d, J = 8.0 Hz, 1H), 6.71 (d, J = 7.5 Hz, 1H), 6.24 (s, 1H), 3.96 (q, J = 6.5 Hz, 2H), 3.77 (s, 3H), 2.91 (t, J = 6.5 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 178.6, 159.9, 139.7, 135.4, 130.2, 129.8, 127.6, 125.7, 125.1, 120.9, 114.4, 112.1, 100.0, 55.1, 48.9, 34.8. IR (neat) 3350, 3167, 2939, 1583, 1529, 1480, 1289, 1238, 1152, 1012, 896, 790 cm^{-1}. MS (ESI) 357 [M + Na^+]. HRMS (ESI) calcd for $C_{16}H_{18}N_2NaOSe$ [M + Na^+] 357.0477; found 357.0480.

Compound ***3ab***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (194.4 mg, 86%). mp 134.5 °C (decomposed). ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.43 (s, 1H), 8.13 (s, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.22 (td, J = 8.0, 0.8 Hz, 1H), 7.12−7.08 (m, 3H), 6.93 (br, 1H), 6.76 (d, J = 8.4 Hz, 2H), 6.22 (br, 1H), 4.02 (q, J = 6.8 Hz, 2H), 3.08 (t, J = 6.8 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 178.5, 136.3, 133.8, 133.0, 130.1, 127.0, 126.3, 122.5, 122.2, 199.9, 118.6, 112.1, 111.3, 48.3, 24.1. IR (neat) 3390, 3032, 1922, 1616, 1556, 1490, 1323, 1231, 1091, 1005, 818 cm^{-1}. MS (ESI) 378 [M + H^+]. HRMS (ESI) calcd for $C_{17}H_{17}ClN_3Se$ [M + H^+] 378.0271; found 378.0272.

Compound ***3ac***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as brown solid (127.9 mg, 60%). mp 251.4 °C (decomposed). ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 8.16 (s, 1H), 7.15 (d, J = 8.4 Hz, 2H), 6.95 (d, J = 8.4 Hz, 2H), 6.04 (br, 1H), 3.83 (s, 3H), 3.67 (q, J = 6.4 Hz, 2H), 1.55 (t, J = 6.4 Hz, 2H), 1.26−1.24 (m, 12H), 0.88 (t, J = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 179.1, 159.2, 128.0, 127.6, 115.4, 55.5, 48.2, 31.8, 29.4, 29.14, 29.09, 28.9, 26.7, 22.6, 14.0. IR (neat) 3198, 2925, 2851, 1575, 1508, 1464, 1343, 1296, 1244, 1098, 1032, 835 cm^{-1}. MS (ESI) 357 [M + H^+]. HRMS (ESI) calcd for $C_{17}H_{29}N_2OSe$ [M + H^+] 357.1440; found 357.1464.

Compound ***3ad***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as brown solid (173.0 mg, 76%). mp 127.4 °C (decomposed). ^1H NMR (400 MHz, DMSO-d_6) δ 9.94 (s, 1H), 8.62 (br, 1H), 7.65 (t, J = 8.8 Hz, 4H), 7.47−7.33 (m, 9H), 7.26 (t, J = 7.2 Hz, 1H), 5.80 (br, 1H), 1.51 (d, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 178.1, 141.6, 140.6, 139.6, 128.9, 128.8, 127.8, 126.9, 126.2, 125.3, 57.1, 21.1. IR (neat) 3360, 3022, 2122, 1884, 1519, 1483, 1312, 1235, 1110, 1007, 912, 832, 761 cm^{-1}. MS (ESI) 403 [M + Na^+]. HRMS (ESI) calcd for $C_{21}H_{20}N_2NaSe$ [M + Na^+] 403.0685; found 403.0686.

Compound ***3ae***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (143.8 mg, 79%). mp 84.6 °C (decomposed). ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.48 (br, 1H), 7.41−7.27 (m, 8H), 7.18 (d, J = 7.5 Hz, 2H), 6.45 (br, 1H), 5.84 (br, 1H), 1.57 (d, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 178.1, 141.6, 135.6, 132.7, 130.3, 128.8, 127.7, 126.2, 125.2, 57.1, 21.1. IR (neat) 3300, 1560, 1452, 1312, 1248, 1061, 936, 850, 752 cm^{-1}. MS (ESI) 327 [M + Na^+]. HRMS (ESI) calcd for $C_{15}H_{16}N_2NaSe$ [M + Na^+] 327.0371; found 327.0374.

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Compound ***3af***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as brown solid (134.0 mg, 67%). mp 106.5 °C (decomposed). ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 8.18 (br, 1H), 7.35−7.27 (m, 5H), 7.12 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 8.4 Hz, 2H), 6.23 (br, 1H), 5.82 (br, 1H), 3.81 (s, 3H), 1.54 (d, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 178.6, 159.2, 141.8, 128.7, 127.6, 127.5, 126.2, 115.4, 56.9, 55.5, 21.2. IR (neat) 3350, 3150, 2969, 1607, 1511, 1443, 1389, 1300, 1241, 1164, 1104, 1027, 950, 829, 787 cm^{-1}. MS (ESI) 335 [M + H$^+$]. HRMS (ESI) calcd for $C_{16}H_{19}N_2OSe$ [M + H$^+$] 335.0658; found 335.0658.

Compound ***3ag***. Purification on silica gel (petroleum ether/ethyl acetate = 3:1) afforded the compound as yellow solid (76.3 mg, 43%). mp 182.7 °C (decomposed). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.07 (br, 2H), 7.24−7.17 (m, 4H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 159.0, 132.9, 122.2, 109.4. IR (neat) 3147, 2988, 1508, 1461, 1262, 1169, 1050, 922, 739 cm^{-1}. MS (ESI) 221 [M + Na$^+$]. HRMS (ESI) calcd for $C_7H_6N_2NaSe$ [M + Na$^+$] 220.9588; found 220.9597.

Compound ***3ah***. Purification on silica gel (petroleum ether/ethyl acetate = 3:1) afforded the compound as yellow solid (89.3 mg, 47%). mp 187.1 °C (decomposed). ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.04 (br, 2H), 7.07−7.04 (m, 2H), 6.96 (d, J = 6.0 Hz, 1H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 158.7, 133.3, 133.0, 123.5, 122.8, 120.4, 107.5, 16.3. IR (neat) 3087, 2985, 2902, 1501, 1379, 1183, 1067, 859, 735 cm^{-1}. MS (ESI) 213 [M + H$^+$]. HRMS (ESI) calcd for $C_8H_9N_2Se$ [M + H$^+$] 212.9926; found 212.9932.

Compound ***3ai***. Purification on silica gel (petroleum ether/ethyl acetate = 3:1) afforded the compound as yellow solid (83.6 mg, 44%). mp 149.3 °C (decomposed). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.96 (br, 2H), 7.12 (d, J = 8.0 Hz, 1H), 7.05 (s, 1H), 6.98 (d, J = 8.0 Hz, 1H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 158.9, 133.7, 132.2, 131.5, 123.8, 110.0, 109.6, 20.9. IR (neat) 3120, 2972, 2860, 1621, 1490, 1430, 1339, 1260, 1065, 970, 804, 713 cm^{-1}. MS (ESI) 213 [M + H$^+$]. HRMS (ESI) calcd for $C_8H_9N_2Se$ [M + H$^+$] 212.9926; found 212.9929.

Compound ***3aj***. Purification on silica gel (petroleum ether/ethyl acetate = 3:1) afforded the compound as yellow solid (97.3 mg, 48%). mp 221.5 °C (decomposed). ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.85 (br, 2H), 7.03 (s, 2H), 2.23 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 157.4, 132.0, 131.1, 110.5, 19.6. IR (neat) 3093, 2364, 1663, 1470, 1330, 1245, 1161, 1001, 848 cm^{-1}. MS (ESI) 227 [M + H$^+$]. HRMS (ESI) calcd for $C_9H_{11}N_2Se$ [M + H$^+$] 227.0082; found 227.0083.

Compound ***3ak***. Purification on silica gel (petroleum ether/ethyl acetate = 1:3) afforded the compound as brown solid (96.9 mg, 53%). mp 172.8−174.6 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.82 (br, 2H), 3.05−2.96 (m, 2H), 1.93 (d, J = 10.8 Hz, 2H), 1.68 (d, J = 8.4 Hz, 2H), 1.36−1.19 (m, 4H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 180.9, 64.1, 28.0, 23.0. IR (neat) 3213, 2943, 2867, 1504, 1450, 1353, 1212, 1096, 828, 658 cm^{-1}. MS (ESI) 227 [M + Na$^+$]. HRMS (ESI) calcd for $C_7H_{12}N_2NaSe$ [M + Na$^+$] 227.0058; found 227.0058.

Compound ***3al***. Purification on silica gel (petroleum ether/ethyl acetate = 1:3) afforded the compound as yellow solid (64.6 mg, 44%). mp 88.9−91.8 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.63 (s, 1H), 8.43 (s, 1H), 3.94−3.87 (m, 1H), 3.61 (t, J = 10.0 Hz, 1H), 3.04 (dd, J = 10.0, 7.6 Hz, 1H), 1.12 (d, J = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 175.4, 52.4, 51.4, 20.0. IR (neat) 3212, 2972, 2862, 1525, 1496, 1368, 1301, 1274, 1197, 1006, 699 cm^{-1}. MS (ESI) 187 [M + Na$^+$]. HRMS (ESI) calcd for $C_4H_8N_2NaSe$ [M + Na$^+$] 186.9745; found 186.9755.

Compound ***3am***. Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (127.3 mg, 67%). mp 200.5−201.5 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.70 (s, 1H), 9.06 (s, 1H), 7.17 (td, J = 8.0, 1.2 Hz, 1H), 7.07 (d, J = 7.2 Hz, 1H), 7.01−6.96 (m, 2H), 4.36 (s, 2H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 170.8, 134.4, 128.1, 126.1, 123.4, 117.2, 114.1, 42.9. IR (neat) 3128, 3075, 3005, 1933, 1559, 1503, 1378, 1243, 1166, 1093, 920, 789 cm^{-1}. MS (ESI) 213 [M + H$^+$]. HRMS (ESI) calcd for $C_8H_9N_2Se$ [M + H$^+$] 212.9925; found 212.9926.

Compound ***3an***. Purification on silica gel (petroleum ether/ethyl acetate = 1:3) afforded the compound as pink solid (67.5 mg, 46%). mp 96 °C (decomposed). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.23 (br, 2H), 3.09−3.06 (m, 4H), 1.74 (penta, J = 5.6 Hz, 2H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 168.6, 39.5, 18.2. IR (neat) 3197, 2968, 1559, 1422, 1314, 1199, 1067, 799, 746 cm^{-1}. MS (ESI) 187 [M + Na$^+$]. HRMS (ESI) calcd for $C_4H_8N_2NaSe$ [M + Na$^+$] 186.9745; found 186.9739.

Compound ***II***.[1d] Purification on silica gel (petroleum ether/ethyl acetate = 2:1) afforded the compound as yellow solid (1.87 g, 82%). ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.48 (br, 1H), 7.35 (t, J = 7.5 Hz, 2H), 7.23−7.20 (m, 3H), 3.34 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 182.4, 140.3, 128.9, 126.0, 125.2, 43.4.

Compound ***4***.[18] Purification on silica gel (petroleum ether) afforded the compound as yellow liquid (69.9 mg, 32%). ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.39−7.32 (m, 3H), 7.30−7.28 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 129.6, 129.5, 128.1, 126.1.

Crystal Structure Determinations. Single crystal of compound **3a** was obtained in ethanol. The intensity data was collected on a Bruker APEX II CCD area detector using graphite-monochromated Mo Kα radiation. Data were integrated using SAINT[19] and a semiempirical absorption correction applied using SADABS.[20] The structures were solved by direct methods (SHELXL-2018/3)[21] and refined by full-matrix least-squares techniques against F_o^2 (SAINT; Bruker, 2014). Molecular structures were prepared using SHELXTL (Sheldrick, 2018). All hydrogen atoms were included at calculated positions with fixed thermal parameters. Crystallographic data as well as structure solution and refinement details are summarized in Table S1 (see the Supporting Information).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02179.

Copy of ^{1}H and ^{13}C NMR spectra of compounds **3** and **4**, HPLC spectra of compound **3ad**, and X-ray data of compound **3a** (CCDC-2015425) (PDF)

Accession Codes

CCDC 2015425 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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