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Oxidative umpolung selenocyanation of ketones and arenes: An efficient protocol to the synthesis of selenocyanates

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ABSTRACT

A practical method for the umpolung selenocyanation of aryl ketones, alkyl ketones, β-ketoesters and electron-rich arenes has been developed, affording various selenocyanates in moderate to excellent yields. This transformation proceeds by an oxidative umpolung selenocyanation through nitrogen oxides-mediated electrophilic selenocyanation process. This method is simpler, more efficient, and less costly than precedent methods. Further transformations of the arylselenocyanate was performed to prove the synthetic utility of this methodology.

1. Introduction

Selenium is a necessary trace element for the human body and some animals to sustain life [1]. Compared with an inorganoselenium compound, organoselenium compounds have some excellent characteristics, such as higher bioavailability, stronger bioactivity, lower toxicity, smaller environmental pollution, anti-oxidation, anti-inflammatory and anti-cancer, etc. [2] At present, some organoselenium compounds have been used in clinical trials and possesses numerous biological activities such as anti-oxidation, anti-inflammatory or anti-tumor activities, such as ebselen [3], ethaselen [4] and selenazofurin [5], etc. Intrigued by the interested properties of organoselenium in pharmaceuticals and bioactive molecules, tremendous elegant methods have been developed to synthesize organoselenium compounds in recently [6].

Selenocyanates are a class of selenocompounds that generally show interesting properties as chemopreventive, anti-inflammatory agent or anticancer agents. They are also a valuable synthetic intermediate to access seleno-containing compounds [7]. After introducing the selenocyano group into organic molecules, it often endows the organic molecules with different biological activities, such as antitumor activity [8] and antioxidant activity [9].

Traditionally, the introduction of selenocyano groups involves KSeCN-mediated nucleophilic selenocyanation reaction. First, a halogen atom was introduced into an organic substrate by the halogenation. Then the selenocyanates were obtained by nucleophilic substitution of selenium cyanide anion to the halogen atom [10]. On the other hand, electron-rich arylselenocyanates were produced by electrophilic species such as diazonium salts [11], diaryliodonium salts [12] with selenocyanate salts (KSeCN).

Some new direct selenocyanation methods have been proposed [13]. For instance, natural deep eutectic solvent-catalyzed selenocyanation of activated alkynes [14], iodine catalyzed selenocayanation [15], bromine catalyzed selenocayanation [16], one-pot synthesis of selenocyanates by triselenium dicyanide [17], selenocyanation from olefin via hydroboration [18], selenocyanation via organocopper reagents [19] and certain oxidant-mediated selenocyanation [20]. In addition, some selenocyanations applied in electron-rich aromatic substrates have also been developed [21]. Recently, we reported a new selenocyanation using selenocyanobenziodoxolone as reagent by grinding under mild conditions [22].

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However, the existing direct selenocyanation methods have the disadvantages of expensive reagents or harsh reaction conditions, and it is difficult to realize large-scale industrial application. In this paper, a direct selenocyanation method which is simpler and more effective and can be applied on an industrial scale has been proposed for the synthesis of α-carbonyl selenocyanates and electron-rich arylselenocyanates (Scheme 1).

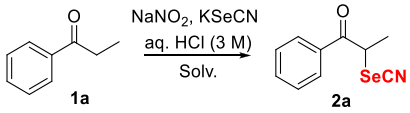
2. Results and discussion

The study began by examining electrophilic selenocyanation of propiophenone **1a** with KSeCN-$NaNO_2$-acid system. First, a variety of protic acids were evaluated. Delightedly, TFA, aq. HNO_3(1 M) and aq. HCl (3 M) delivered selenocyanate **2a** with 57%, 49% and 93% yields, respectively, by using sodium nitrite as an oxidant (Table 1, entries 1–4). Subsequently, the yield of desired product **2a** was slightly decreased when decreasing the amount of KSeCN and $NaNO_2$ (Table 1 entries 5–6). Additionally, the yield of selenocyanate **2a** was slightly improved when the title reaction was performed at 60 °C by using 1.0 equivalent of potassium selenocyanate (Table 1, entry 7). Further increase of the concentration of aqueous hydrochloric acid led to a relatively low yield of selenocyanate **2a** (28%, Table 1, entry 8). The amount of aq. HCl was also investigated and 3 equiv. HCl showed the best result with a yield above 93% (Table 1, entries 9–10 VS entry 4). Besides, other solvents, such as ethanol, methanol, dichloromethane, tetrahydrofuran (THF), dioxane and dimethyl sulfoxide (DMSO) were also examined and MeCN was found to be the best (Table 1, entries 11–16 VS entry 4). Notably, no desired product was detected when the title reaction was performed in CH_2Cl_2. Presumably, the results could mainly attribute to the poor solubility of potassium selenocyanate in dichloromethane. Furthermore, various oxidants such as ^{t}BuONO (*tert*-Butyl nitrite) and TBHP (*tert*-Butyl hydroperoxide) were also considered. Not surprisingly, the reaction performed smoothly by using ^{t}BuONO as the oxidant and led to desired product **2a** in 84% yield (Table 1, entry 17), while the TBHP failed to give the desired product (Table 1, entry 18). Thus, the optimized conditions were confirmed by using KSeCN (1.5 mmol, 3 equiv.), $NaNO_2$ (1.5 mmol, 3 equiv.), aq. HCl (3 M, 3 equiv.) in MeCN at room temperature.

With the optimized conditions established, we next investigated the scope of this reaction by employing a variety of ketones. As shown in Table 2, both electron-withdrawing and electron-donating groups were well tolerated and gave α-carbonyl selenocyanates in 32–99% yields for the aromatic ketones (Table 2, **2a**-**2p**). It is worth noting that low yields (37% and 32%, respectively) were observed for **2h** and **2k**. When 2-bromo substituted aryl ketones was employed, due to steric reasons (Table 2, **2h**). However, when the methoxyl group was at the para-position of the benzene ring, the benzene ring easily formed a quinone structure, which affected the progress of the reaction (Table 2, **2k**). The substrate scope of this transformation was also successfully expanded to other aromatic ketones and heterocyclic rings such as 2-acetylthiophene, affording corresponding selenocyanates with poor to excellent yields (Table 2, **2l**-**2n**). Besides, acyclic aromatic ketones bearing alkyl such as n-butyrophenone and valerophenone was also tolerated and gave the desired products in 93% and 76% yield, respectively (Table 2, **2o-2p**).

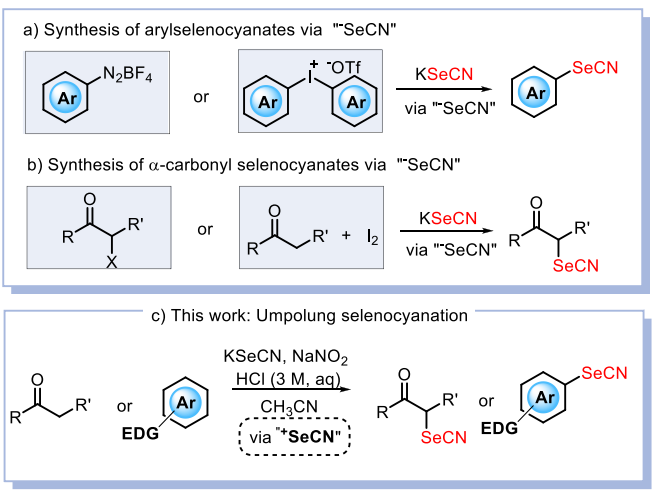
Subsequently, cyclic aryl ketones and alkyl ketones were examined. Satisfyingly, both the cyclic aryl ketones and alkyl ketones were well-tolerated, delivering corresponding selenocyanates in moderate yield (Table 2, **2q**-**2v**). Furthermore, substitutions with dual reactive site such as 1-cyclohexylethan-1-one, benzylacetone and isobutylacetone were performed under the optimized reaction conditions and afforded the corresponding selenocyanates in good to excellent yields with excellent regioselectivities (Table 2, **2s**-**2u**). It could be seen from **2t**-**2u** that the selenocyanate substitution mainly occurs in the α-carbon position which can form a stable enol-form structure (thermodynamic regioisomer). However, for the compound **2s**, since the steric hindrance of the cyclohexyl group is much larger than that of the methyl group, the selenocyanation occurs on the methyl group having a small steric hindrance, and a kinetic regioisomer is obtained. The commonly used solvent-acetone was also tested and led to the α-selenocyanate

Table 1
Optimization of reaction conditions.[a]



Entry	Acid (C)[b]	Acid (equiv.)	Solvent	Yield (%)[c]
1	*p*-TSA	3	MeCN	nr
2	TFA	3	MeCN	57
3	HNO_3 (1 M)	3	MeCN	49
4	HCl (3 M)	3	MeCN	93
5[d]	HCl (3 M)	3	MeCN	50
6[e]	HCl (3 M)	3	MeCN	80
7[d,f]	HCl (3 M)	3	MeCN	71
8	HCl (6 M)	3	MeCN	28
9	HCl (3 M)	1.5	MeCN	89
10	HCl (3 M)	4.5	MeCN	60
11	HCl (3 M)	3	ethanol	66
12	HCl (3 M)	3	methanol	45
13	HCl (3 M)	3	CH_2Cl_2	nr
14	HCl (3 M)	3	THF	84
15	HCl (3 M)	3	Dioxane	89
16	HCl (3 M)	3	DMSO	88
17[g]	HCl (3 M)	3	MeCN	84
18[h]	HCl (3 M)	3	MeCN	nr

[a] Unless otherwise noted, reactions were performed with propiophenone (**1a**) (0.5 mmol, 1.0 equiv.), KSeCN (1.5 mmol), $NaNO_2$ (1.5 mmol), HCl (aq., 5 mL, 3 M) at room temperature for 48 h.
[b] Concentration of acid.
[c] Isolated yield.
[d] KSeCN (0.5 mmol), $NaNO_2$ (0.5 mmol).
[e] KSeCN (1.0 mmol), $NaNO_2$ (1.0 mmol).
[f] The reaction was carried out at 60 °C.
[g] *tert*-Butyl nitrite was used as an oxidant.
[h] *tert*-Butyl hydroperoxide was used as an oxidant.



Scheme 1. Strategies of selenocyanation.

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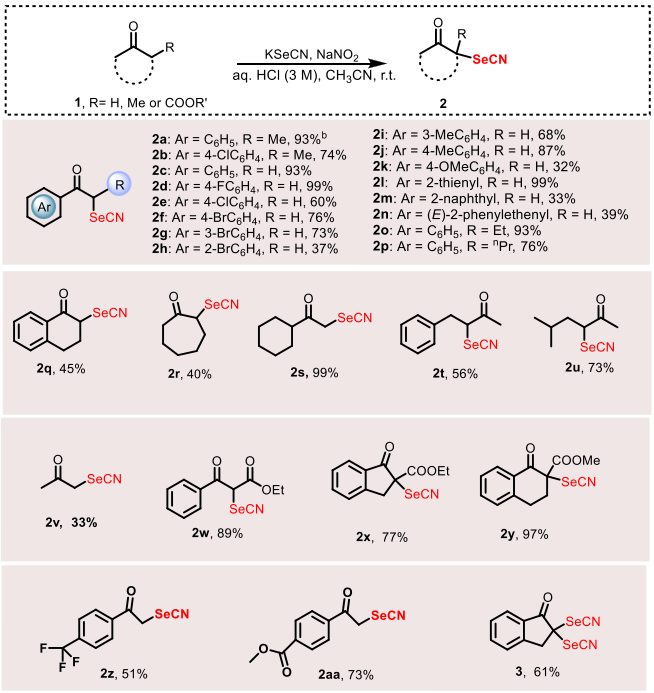
Table 2
Substrate scope of ketones and β-ketoesters.[a]

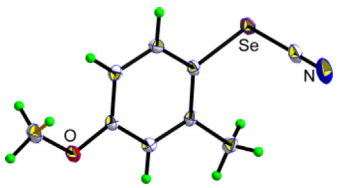


[a] Reactions conditions: **1** (0.5 mmol), KSeCN (1.5 mmol), $NaNO_2$ (1.5 mmol), HCl (aq., 5 mL, 3 M), in 15 mL of CH_3CN at room temperature for 48 h; [b] Isolated yield.

acetone in relatively low yield (33%, Table 2, **2v**). Notably, indanone resulted in β,β-diselenocyanate derivative **3** in 61% yield. We reason that five-membered cyclic selenocyanate derived from indanone is more active than six-membered cyclic selenocyanate **2q**, leading to the second electrophilic selenocyanation reaction. Besides, β-ketoesters were also screened and yielded the desired products in good to excellent yields (Table 2, **2w**-**2y**).

When *p*-trifluoromethylacetophenone and *p*-methylformate-acetophenone were used as the reaction substrates, the product **2z** and **2aa** were obtained in moderated yields (51% and 73%). However, when the *p*-nitroacetophenone was used as the reaction substrate, the reaction yield is only 22%, and when the *o*-nitroacetophenone was used as the reaction substrate, the corresponding selenocyanate was not obtained. The reason for this may be similar to that in the case of **2k**.

Encouragingly, the reaction was also applicable to the selenocyanation of electron-rich arenes. Satisfyingly, both the *N*,*N*-dimethylamino substituted arenes and methoxy substituted arenes were well tolerated, affording corresponding selenocyanates in moderate to excellent yields (Table 3, **5a**-**5j**). It is worth mentioning that *N*,*N*-dimethylamino-containing arenes afforded the selenocyanated products **5a**-**5c** in moderated yields (53%, 49% and 52%, respectively). In particular, the yields of corresponding selenocyanates were dramatically dropped when bromo-containing methoxy substituted arenes were employed (Table 3, **5k**). It could be seen that after a deactivating group halogen atom was introduced into the benzene ring, the yield of the reaction was significantly reduced. To further broaden the scope of the substrates, we also investigated variety aromatic heterocyclic compounds such as methoxynaphthalene and indole derivatives, and they were tolerated and afforded the corresponding selenocyanates in excellent yields (Table 3, **5l**, **5n** and **5o**), except for 1-methoxynaphthalene (Table 3, **5m**). Finally, the structure of selenocyanate **5j** was unambiguously confirmed by single-crystal X-ray diffraction (CCDC 1918411).



X-ray structure of **5j**

To demonstrate the practical utility of the above methodology, a gram scale experiment was performed on a 7 mmol scale of **1a** and 8 mmol scale of **4i** under the standard conditions. Satisfyingly, the desired product **2a** and the electron-rich arylselenocyanate **5i** were obtained in 95% and 99% yields, respectively, proving the scalability of the newly developed protocol. Moreover, the arylselenocyanate **5i** could be converted to diselenide **6** in a good yield (99%) (see Scheme 2).

The mechanism of the reaction was studied under different reaction conditions in preparation of **2a**. In the reaction, when only KSeCN and HCl were used, without $NaNO_2$, the product **2a** was not obtained. In addition, when HCl was not added, but only KSeCN and $NaNO_2$ were used, the reaction was unable to happen also. In the study of the selenocyanation of the arenes, we found that when the electron-withdrawing substituent is attached to the aromatic ring alone, the reaction cannot occur, and when the weaker electron-donating substituent such as alkyl is attached to the benzene

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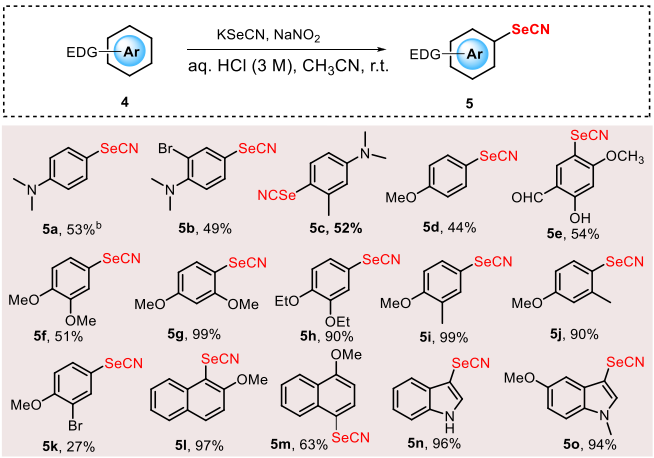
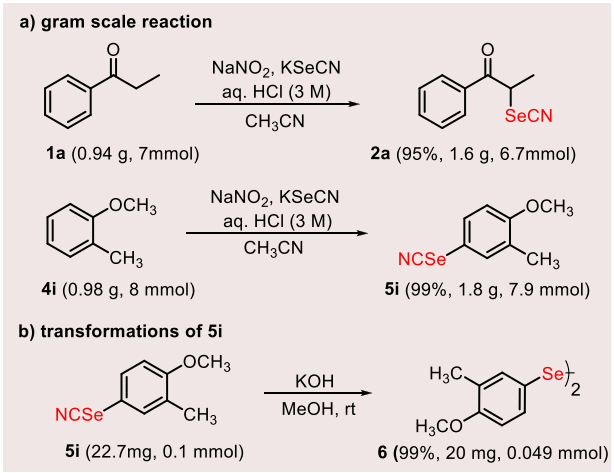
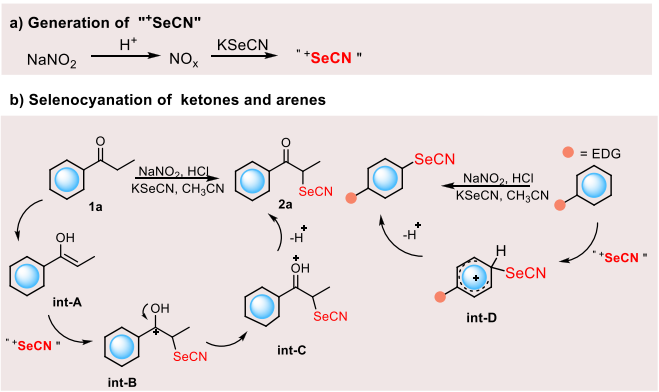
Table 3
Substrate scope of arenes containing elelctro-donating group.[a]



[a] Reactions conditions: 4 (0.5 mmol), KSeCN (1.5 mmol), $NaNO_2$ (1.5 mmol), HCl (aq., 5 mL, 3 M), in 15 mL of CH_3CN at room temperature for 48 h; [b] Isolated yield.



Scheme 2. Gram-scale reaction and transformations of **2a** and **5i**.



Scheme 3. Putative mechanism.

ring, such as toluene and xylene, the reaction does not occur also. This indicates that the reaction is not carried out by a free radical mechanism, but follows a general electrophilic substitution mechanism. Based on the experimental results, a plausible mechanism was proposed as shown in Scheme 3. Firstly, treating the sodium nitrite with aqueous hydrochloric acid affords nitrogen oxide active species. Subsequently, $^{+}$SeCN ion was generated *in situ* by the reaction of nitrogen oxide and potassium selenocyanate (Scheme 3a). Finally, the α-carbonyl selenocyanates and arylselenocyanates were delivered, respectively, through the direct electrophilic selenocyanation of ketones and electron-rich arenes with "$^{+}$SeCN" intermediate (Scheme 3b).

3. Conclusions

In conclusion, we have developed a new method for the umpolung selenocyanation of ketones and electron-rich arenes by using KSeCN-$NaNO_2$-HCl system. A variety of α-carbonyl selenocyanates, as well as arylselenocyanates were afforded in moderate to excellent yields. Experimental evidence reveals that the reaction may be performed through an umpolung "+SeCN" mechanism. Importantly, the synthetic utility of the newly developed protocol was further demonstrated by gram-scale reaction and the transformations of the selenocyanates. Moreover, this protocol might be suitable for industrial production since it possesses the advantages of low cost and easy operation. Further studies including in asymmetric selenocyanation and bioactivity evaluation of selenocyanates are currently ongoing in our laboratory.

4. Experimental

4.1. Reagents and instruments

All chemicals and solvents were analytical grade. Melting points were measured on an X_6 apparatus (Beijing Tech Instrument Co. Ltd., Beijing, China), uncorrected. Infrared spectra were determined with a Thermo Scientific Nicolet IS-10 Spectrophotometer (Thermo Scientific, America); The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer at working frequencies 400 and 100 MHz and a Bruker AV-300 spectrometer at working frequencies 300 and 75 MHz. Chemical shifts are expressed in parts per million

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(δ) values and coupling constants (J) in Hertz. HREIMS was measured on an Agilent 6210 TOFMS instrument (Agilent Technologies, America).

4.2. General procedure for the synthesis of selenocyanates

To a solution of acetonitrile (15 mL), aqueous hydrochloric acid (3 M, 5 mL) was added at 0 °C, following by the addition of aqueous sodium nitrite (0.104 g, 1.5 mmol, dissolved in 1.5 mL of distilled water). After stirred at the same temperature for 10 min, KSeCN (72.5 mg, 0.5 mmol) was added in one portion. The resulting solution was stirred at the ice bath for 20 min. Afterwards, carbonyl compound or electron-rich arene (0.5 mmol) was added and the reaction mixture was continuously stirred in room temperature until no starting material was observed (the progress was monitored by TLC). The solvent was removed, the residue was extracted with ethyl acetate and washed with brine. The combined organic phases were dried, concentrated and purified by flash column chromatography on silica gel to give pure target products.

1-Phenyl-2-selenocyanatopropan-1-one (**2a**): White solid, yield: 93%, m.p. 84–85 °C; IR(KBr) ν: 2929, 2155, 1679, 1446, 1238, 999, 707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)δ: 7.94 (d, J = 7.2 Hz, 2H), 7.68 (t, J = 7.2 Hz, 1H), 7.55 (t, J = 7.5 Hz, 2H), 5.42 (q, J = 7.2 Hz, 1H), 2.06 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 197.1, 134.7, 132.8, 129.2, 129.0, 102.7, 49.0, 21.4; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{10}H_9NOSeNa$ [M+Na]$^+$ 261.9742, found 261.9747.

1-(4-Chlorophenyl)-2-selenocyanatopropan-1-one (**2b**): White solid, yield: 74%, m.p. 72–73 °C (lit. 70–71 °C); IR (KBr) ν: 2921, 2514, 2160, 1791, 1440, 1230, 844 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.88 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 5.33 (q, J = 7.2 Hz, 1H), 2.03 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 195.8, 141.3, 131.2, 130.4, 129.6, 102.3, 48.1, 21.0; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{10}H_8NOSeClNa$ [M+Na]$^+$ 295.9352, found 295.9332.

1-Phenyl-2-selenocyanatoethanone (**2c**): Yellowish solid, yield: 93%, m.p. 81–82 °C (lit. 48–49 °C); IR (KBr) ν: 2955, 2514, 2155, 1796, 1462, 1268, 884 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.97 (d, J = 7.5 Hz, 2H), 7.70 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.5 Hz, 2H), 4.95 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 193.2, 134.9, 133.8, 129.2, 128.7, 101.8, 38.4; HRMS (TOF-ESI$^+$) m/z: calcd for $C_9H_7NOSeNa$ [M+Na]$^+$ 247.9585, found 247.9571.

1-(4-Fluorophenyl)-2-selenocyanatoethanone (**2d**): Yellowish solid, yield: 99%, m.p. 121–122 °C (lit. 112–113 °C); IR (KBr) ν: 2990, 2158, 1657, 1412, 1290, 1000, 824 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.98–8.03 (m, 2H), 7.21 (t, J = 8.4 Hz, 2H), 4.91 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 191.6, 166.7 (d [1]$J_{C\text{-}F}$ = 257.3 Hz), 131.6 (d [2]$J_{C\text{-}F}$ = 9.8 Hz), 130.3 (d [3]$J_{C\text{-}F}$ = 3.0 Hz), 116.5 (d [2]$J_{C\text{-}F}$ = 22.5 Hz), 101.7, 38.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ: 101.2; HRMS (TOF-ESI$^+$) m/z: calcd for $C_9H_6NOSeFNa$ [M+Na]$^+$ 265.9491, found 265.9499.

1-(4-Chlorophenyl)-2-selenocyanatoethanone (**2e**): Yellowish solid, yield: 60%, m.p. 83–84 °C; IR (KBr) ν: 2985, 2155, 1796, 1657, 1399, 1178, 816 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.91 (s, 2H), 7.54 (s, 2H), 4.90 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 192.0, 141.6, 132.1, 130.1, 129.6, 101.6, 37.9; HRMS (TOF-ESI$^+$) m/z: calcd for $C_9H_6NOSeClNa$ [M+Na]$^+$ 281.9195, found 281.9204.

4.2.1. 1-(4-Bromophenyl)-2-selenocyanatoethanone (**2f**)

Yellowish solid, yield: 76%, m.p. 142–143 °C (lit. 144–145 °C); IR (KBr) ν: 2509, 1794, 1652, 1465, 1397, 1008, 871 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.84 (d, J = 8.7 Hz, 2H), 7.70 (d, J = 8.7 Hz, 2H), 4.90 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 192.2, 132.6, 132.5, 130.5, 130.1, 101.5, 37.9; HRMS (TOF-ESI$^+$) m/z: calcd for $C_9H_6NOSeBrNa$ [M+Na]$^+$ 325.8690, found 325.8679.

1-(3-Bromophenyl)-2-selenocyanatoethanone (**2g**): Yellowish solid, yield: 73%, m.p. 77–78 °C; IR (KBr) ν: 3063, 2931, 2154, 1664, 1421, 1176, 1012, 789 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.07 (s, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 4.88 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 192.2, 137.6, 135.4, 131.6, 130.8, 127.4, 123.4, 101.8, 37.8; HRMS (TOF-ESI$^+$) m/z: calcd for $C_9H_7BrNOSe$ [M+H]$^+$ 303.8876, found 303.8865.

1-(2-Bromophenyl)-2-selenocyanatoethanone (**2h**): Yellowish solid, yield: 37%, m.p. 56–57 °C; IR (KBr) ν: 3315, 2935, 2151, 1796, 1469, 989 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.72–7.64 (m, 2H), 7.49–7.41 (m, 2H), 4.85 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 195.5, 137.0, 134.5, 133.8, 130.7, 127.9, 120.2, 101.3, 39.2; HRMS (TOF-ESI$^+$) m/z: calcd for $C_9H_7BrNOSe$ [M+H]$^+$ 303.8876, found 303.8863.

1-(3-Methylphenyl)-2-selenocyanatoethanone (**2i**): White solid, yield: 68%, m.p. 84–85 °C (lit. 43–44 °C); IR (KBr) ν: 3055, 2936, 2150, 1427, 1155, 785 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.75 (s, 1H), 7.74 (d, J = 6.0 Hz, 1H), 7.50–7.38 (m, 2H), 4.91 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 193.5, 139.1, 135.7, 133.8, 129.2, 129.0, 126.0, 102.1, 38.7, 21.3; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{10}H_9NOSeNa$ [M+Na]$^+$ 261.9742, found 261.9742.

1-(4-Methylphenyl)-2-selenocyanatoethanone (**2j**): White solid, yield: 87%, m.p. 135–136 °C; IR (KBr) ν: 2987, 2933, 2153, 1655, 1178, 806 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.83 (d, J = 7.5 Hz, 2H), 7.31 (d, J = 7.5 Hz, 2H), 4.89 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 192.9, 146.2, 131.3, 129.8, 128.9, 102.2, 38.6, 21.9; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{10}H_9NOSeNa$ [M+Na]$^+$ 261.9742, found 261.9744.

4.2.2. 1-(4-Methoxyphenyl)-2-selenocyanatoethanone (**2k**)

White solid, yield: 32%, m.p. 117–119 °C; IR (KBr) ν: 2934, 2848, 2151, 1686, 1298, 997, 822 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.94 (d, J = 8.7 Hz, 2H), 6.99 (d, J = 8.7 Hz, 2H), 4.91 (s, 2H), 3.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 191.5, 164.9, 131.2, 126.8, 114.4, 102.2, 55.7, 38.6; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{10}H_{10}NO_2Se$ [M+H]$^+$ 255.9877, found 255.9880.

4.2.3. 2-Selenocyanato-1-(thiophen-3-yl)ethanone (**2l**)

White solid, yield: 99%, m.p. 107–109 °C; IR (KBr) ν: 3096, 2928, 2154, 1650, 1170, 798 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.20 (s, 1H), 7.55 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 4.8 Hz, 1H), 4.79 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 187.1, 138.6, 134.6, 127.6, 126.8, 101.9, 38.1; HRMS (TOF-ESI$^+$) m/z: calcd for $C_7H_5NOSSeNa$ [M+Na]$^+$ 253.9149, found 253.9143.

4.2.4. 1-(β-Naphthyl)-2-selenocyanatoethanone (**2m**)

White solid, yield: 33%, m.p. 147–148 °C; IR (KBr) ν: 2997, 2151, 1657, 1383, 1238, 996, 745 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.43 (s, 1H), 7.99–7.90 (m, 4H), 7.71–7.59 (m, 2H), 5.01 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 193.1, 136.2, 132.3, 131.5, 130.9, 129.8, 129.6, 129.1, 128.0, 127.5, 123.4, 102.1, 38.6; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{13}H_{10}NOSe$ [M+H]$^+$ 275.9928, found 275.9928.

4.2.5. 1-Selenocyanato-4-phenyl-2-butanone (**2n**)

White solid, yield: 39.0%, m.p. 126–128 °C; IR (KBr) ν: 2923, 2504, 2153, 1794, 1654, 1389, 1150 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.68 (d, J = 16.2 Hz, 1H), 7.61–7.58 (m, 2H), 7.47–7.45 (m, 3H), 6.84 (d, J = 16.2 Hz, 1H), 4.57 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 192.6, 147.0, 133.5, 131.7, 129.2, 128.8, 122.8, 101.8, 38.3; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{11}H_9NOSeNa$ [M+Na]$^+$ 273.9742, found 273.9745.

1-Phenyl-2-selenocyanatobutanone (**2o**): White solid, yield: 93%, m.p. 89–90 °C; IR (KBr) ν 2966, 2927, 2154, 1674, 1449, 1358, 1267, 1142 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.92 (d, J = 7.8 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 5.38 (t, J = 5.6 Hz, 1H), 2.26–2.35 (m, 2H), 1.01 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.8, 134.6, 133.5, 129.2, 128.9, 102.7, 56.0 (d, J = 11.7 Hz), 27.0, 10.7 (d, J = 6.7 Hz); HRMS (TOF-ESI+) m/z: calcd for $C_{11}H_{11}NNaOSe$ [M+Na]$^+$ 275.9904, found 275.9897.

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1-Phenyl-2-selenocyanatopentanone (**2p**): White solid, yield: 76%, m.p. 66–67 °C; IR (KBr) ν 2960, 2927, 2155,1374, 1447, 1270, 707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ:7.93 (d, J = 7.2 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H),7.51 (t, J = 7.7 Hz, 2H), 5.33 (t, J = 6.2 Hz, 1H), 2.19–2.29 (m, 2H), 1.52–1.64 (m, 1H, 1.32–1.45 (m, 1H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:196.7, 134.6, 133.6, 129.2, 128.8, 102.6, 53.7(J = 12.4 Hz), 35.8, 20.0, 13.9 (d, J = 7.0 Hz); HRMS (TOF-ESI+) m/z: calcd for $C_{12}H_{13}NNaOSe$ $[M+Na]^+$ 290.0060, found 290.0055.

2-Selenocyanato-3,4-dihydronaphthalen-1(2*H*)-one (**2q**): White solid, yield: 45%, m.p. 79–80 °C (lit. 82–83 °C); IR (KBr) ν 2906, 2512, 2148, 1797, 1594, 1457, 896 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)δ: 8.00 (d, J = 8.1 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.40–7.32 (m, 2H), 5.01 (dd, J = 5.1, 13.5 Hz, 1H), 3.23–3.18 (m, 2H), 2.96–2.87 (m, 1H), 2.62–2.47 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 30.3, 32.5, 53.2, 102.5 (SeCN), 127.4, 127.8, 129.1, 130.5, 135.0, 144.1, 194.2; HREIMS (m/z): 251.9920 $[M+H]^+$ (calcd.for $C_{11}H_{10}NOSe$ 251.9928).

2-Selenocyanatocycloheptanone (**2r**): Colorless oil, yield: 40%; IR (KBr) ν 2923, 2861, 2150, 1794, 1670, 1447, 1123, 1026, 879 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ: 5.22 (dd, J = 3.6, 10.5 Hz, 1H), 2.63–2.72 (m, 1H), 2.36–2.47 (m, 2H), 2.02 (dd, J = 12.0, 25.5 Hz, 1H), 1.80–1.84 (m, 2H), 1.68–1.72 (m, 2H), 1.53–1.61 (m, 1H), 1.34–1.45 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 211.5, 104.9, 59.6, 41.5, 32.8, 29.2, 28.9, 23.9; HRMS (TOF-ESI$^+$) m/z: calcd for $C_8H_{11}NOSeK$ $[M+K]^+$ 255.9637, found 255.9657.

1-Cyclohexyl-2-selenocyanatoethanone (**2s**): White solid, yield: 99%, m.p. 61–62 °C; IR (KBr) ν: 2940, 2855, 2513, 2151, 1796, 1682, 1388, 1229, 999 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 4.37 (s, 2H), 2.57–2.50 (m, 1H), 1.93–1.67 (m, 5H), 1.45–1.19 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 207.0, 101.7, 49.6, 38.8, 28.5, 25.5, 25.3; HRMS (TOF-ESI$^+$) m/z: calcd for $C_9H_{14}NOSe$ $[M+H]^+$ 232.0241, found 232.0240.

3-Selenocyanato-4-phenyl-2-butanone (**2t**): White solid, yield: 56%, m.p. 95–96 °C (Lit. 57–58 °C); IR (KBr) ν: 2924, 2855, 2150, 1704, 1361, 1152, 954, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.31–7.38 (m, 3H), 7.18–7.25 (m, 2H), 4.36 (t, J = 7.4 Hz, 1H), 3.48 (dd, J = 7.8, 14.4 Hz,1H), 3.36 (dd, J = 6.9, 14.4 Hz,1H), 2.29 (s, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.6, 136.4, 129.1, 129.0, 127.7, 100.6, 55.4(d, J = 7.7 Hz), 38.0, 28.5 (d, J = 7.1 Hz); HRMS (TOF-ESI+) m/z: calcd for $C_{11}H_{11}NNaOSe$ $[M+Na]^+$ 275.9898, found 275.9903.

3-Selenocyanato-5-methyl-2-hexanone (**2u**): Brown oil, yield: 73%; IR (KBr) ν: 2960, 2153, 1708, 1362, 1179, 877 cm^{-1}; ^1H NMR (300 MHz, CDCl3) δ: (300 MHz, $CDCl_3$) 4.14 (t, J = 7.2 Hz,1H), 2.40 (s, 3H), 1.99–2.08 (m, 1H), 1.78–1.93 (m, 2H), 1.01 (d, J = 1.8 Hz, 3H), 0.98 (d, J = 1.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.9, 100.5, 52.5, 40.1, 27.4, 26.7, 22.3, 22.1; HRMS (TOF-ESI+) m/z: calcd for $C_8H_{13}NNaOSe$ $[M+Na]^+$242.0055, found 242.0057.

1-Selenocyanatoacetone (**2v**): Brown oil, yield: 33%; IR (KBr) ν: 2921, 2509, 2150, 1699, 1356, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 4.25 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 201.2, 101.2, 39.7, 28.4; HRMS (TOF-ESI$^+$) m/z: calcd for C_4H_6NOSe $[M+H]^+$ 163.9609, found 163.9615.

Ethyl 3-oxo-3-phenyl-2-selenocyanatopropanoate (**2w**): Colorless oil, yield: 89%; IR (KBr) ν: 2978, 2155, 1796, 1734, 1450, 1235, 876 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ: 8.01 (d, J = 7.5 Hz, 2H), 7.75 (t, J = 7.2 Hz, 1H), 7.60 (t, J = 7.5 Hz, 2H), 6.37 (s, 1H), 4.17–4.23 (m, 2H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ: 191.5, 167.2, 135.3, 133.9, 129.6, 129.4, 103.3, 63.0, 51.8, 14.2; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{12}H_{11}NO_3SeNa$ $[M+Na]^+$ 319.9796, found 319.9800.

Ethyl 1-Oxo-2-selenocyanato-2,3-dihydro-1*H*-indene-2-carboxylate (**2x**): White solid, yield: 77%, m.p. 83–85 °C; IR (KBr) ν: 3062, 2986, 2151, 1726, 1603, 1269, 1025, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.91 (d, J = 7.8 Hz, 1H), 7.76 (t, J = 7.5 Hz, 1H), 7.49–7.56 (m, 2H), 4.19–4.34 (m, 3H), 3.84 (d, J = 18.6 Hz, 1H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 196.1, 167.5, 151.2, 137.0, 132.9, 128.9, 126.3, 125.7, 100.8, 64.3, 61.8, 41.0, 13.9; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{13}H_{11}NO_3SeNa$ $[M+Na]^+$ 331.9796, found 331.9813.

Methyl 1-Oxo-2-selenocyanato-1,2,3,4-tetrahydronaphthalene-2-carboxylate (**2y**): White solid, yield: 97%, m.p.133–135 °C; IR (KBr) ν: 2959, 2158, 1799, 1671, 1477, 1323, 1071, 641 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)δ: 8.00 (d, J = 7.9, 1H), 7.58 (t, J = 7.8 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.29 (d, J = 7.8 Hz, 1H), 3.79 (s, 3H), 3.23–3.29 (m, 1H), 3.05–3.16 (m, 2H), 2.69–2.79 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 191.5, 167.8, 143.5, 135.4, 130.0, 129.2, 128.3, 127.5, 101.8 (SeCN), 64.3, 54.0, 35.0, 27.92; HRMS (TOF-ESI$^+$) m/z: $C_{13}H_{11}NO_3$-SeNa $[M+Na]^+$ 331.9796, found 331.9803.

1-(4-trifluoromethylphenyl)-2-selenocyanatoethanone (**2z**): White solid, yield: 51%, m.p. 106–107 °C; IR (KBr) ν: 2929, 2364, 2152, 1797, 1664, 1581, 1514, 1414, 1329, 1284, 1330, 1182, 1128, 1069, 999, 827 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)δ: 8.10 (d, J = 8.1 Hz, 2H), 7.82 (d, J = 8.1 Hz, 2H), 4.93 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 37.8, 100.3 (SeCN), 123.2 (d [1],$J_{C\text{-}F}$ = 204 Hz), 126.3 (d [3],$J_{C\text{-}F}$ = 2.8 Hz), 129.1, 135.8, 136.3 (d [2],$J_{C\text{-}F}$ = 14 Hz), 192.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ: 101.2; HREIMS (m/z): calcd. For $C_{10}H_6F_3NOSeNa$ $[M+Na]^+$ 315.9459, found 315.9465.

1-(4-methylbenzoate)-2-selenocyanatoethanone (**2aa**)White solid, yield: 73%, m.p. 97–99 °C; IR (KBr) ν: 2931, 2153, 1719, 1660, 1505, 1436, 1408, 1383, 1289, 1183, 1111, 999, 840, 762, 691 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.20 (d, J = 8.4 Hz, 2H), 8.04 (d, J = 8.4 Hz, 2H), 4.95 (s, 2H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.8, 165.7, 136.8, 135.4, 130.3, 128.7, 101.5, 52.7, 38.2; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{11}H_9NO_3SeNa$ $[M+Na]^+$ 305.9640, found 305.9633.

2-Diselenocyano-2,3-dihydro-1H-indanone **(3)**: White solid, yield: 61%, m.p. 69–71 °C; IR (KBr) ν: 3135, 2153, 1712, 1654, 1603, 1588, 1560, 1465, 1431, 1401, 1327, 1299, 1274, 1210, 1153, 1184, 1023, 1007, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)δ: 7.90 (d, J = 7.5 Hz, 1H), 7.80 (t, J = 7.5 Hz, 1H), 7.52–7.58 (m, 2H), 4.08 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): 44.5, 55.9, 100.12 (SeCN), 126.3, 126.5, 129.7, 130.3, 137.9, 148.4, 195.4; HREIMS (m/z): calcd. For $C_{11}H_6N_2OSe_2Na$ $[M+Na]^+$ 364.8708, found 364.8706.

N,*N*-dimethyl-4-selenocyanatoaniline **(5a)**: White solid, yield: 53%, m.p.129–131 °C; IR (KBr) ν: 2917, 2141, 1510, 1374, 1076.18, 805 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)δ: 3.01 (s, 6H), 6.66 (d, J = 6.9 Hz, 2H), 7.53 (d, J = 6.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 151.65, 136.38, 113.32, 104.40, 102.85, 40.13; HRMS (TOF-ESI$^+$) m/z: calcd for $C_9H_{11}N_2Se$ $[M+H]^+$ 227.0087, found 227.0090.

3-Bromo-4-selenocyano-*N*,*N*-dimethylaniline **(5b)**: White solid, yield: 49%, m.p.78–80 °C; IR (KBr) ν: 3091, 2154, 1656, 1454, 1092, 959 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)δ: 7.52 (d, J = 8.7 Hz, 1H), 6.87 (d, J = 2.7 Hz, 1H), 6.58 (dd, J = 2.7, 8.7 Hz, 1H), 2.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.1, 134.9, 127.2, 116.2 (d, J = 5), 112.7, 107.9, 102.3, 40.2 (d, J = 4); HRMS (TOF-ESI$^+$) m/z: calcd for $C_9H_{10}BrN_2Se$ $[M+H]^+$ 304.9187, found 304.9179.

3-Methyl-4-selenocyano-*N*,*N*-dimethylaniline **(5c)**: yellowish solid, yield: 52%, m.p. 94–96 °C; IR(KBr) ν: 2922, 2806, 2140, 1591, 1501, 1368, 1074, 804 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$)δ: 7.54 (d, J = 8.7 Hz, 1H), 6.63 (s, 1H), 6.51 (d, J = 8.7 Hz, 1H), 3.00 (s, 6H), 2.55 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 152.3, 142.9, 137.6, 114.2, 111.0, 106.3, 102.4, 40.1, 23.7; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{10}H_{13}N_2Se$ $[M+H]^+$ 241.0328, found 241.0242.

4-selenocyanoanisole **(5d)**: White solid, yield: 44%, m.p.67–68 °C; IR (KBr) ν: 3071, 2846, 2150, 1586, 1490, 1181, 826 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.61 (d, J = 8.7 Hz, 2H), 6.93 (d, J = 8.7 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.4, 136.0, 116.0, 111.1, 102.1, 55.5; HRMS (TOF-ESI$^+$) m/z: calcd for $C_8H_7NNaOSe$ $[M+Na]^+$ 235.9591, found 235.9593.

2-hydroxyl-4-methoxy-5-selenocyanobenzaldehyde **(5e)**: White solid, yield: 54%, m.p.136–137 °C; IR(KBr) ν: 3232, 2951,

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2838, 2154, 1662, 1483, 1041, 878 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 11.66 (s, 1H), 9.79 (s, 1H), 7.81 (s, 1H), 6.53 (s, 1H), 3.99 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 194.0, 165.6, 163.0, 137.0, 116.5, 102.7, 100.9, 100.2, 57.0; HRMS (TOF-ESI$^+$) *m/z*: calcd for $C_9H_8NO_3Se$ $[M+H]^+$ 257.9664, found 257.9671.

2-methoxy-4-selenocyanoanisole **(5f)**: White solid, yield: 51%, m.p. 65–66 °C; IR (KBr) *v:* 3109, 2841, 2146, 1578, 1330, 1018, 803 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.22 (d, J = 8.4 Hz, 1H), 7.13 (s, 1H), 6.86 (d, J = 8.4 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 151.0, 150.0, 127.5, 116.9, 112.4, 111.0, 102.1, 56.2, 56.0; HRMS (TOF-ESI$^+$) *m/z*: calcd for $C_9H_9NNaO_2Se$ $[M+Na]^+$ 265.9696, found 265.9694.

3-methoxy-4-selenocyanoanisole **(5g)**: Colorless oil, yield: 99%; IR (KBr) *v:* 2942,2153,1588,1309,1163,834 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.45 (d, J = 8.4 Hz, 1H), 6.50 (dd, J = 2.1, 8.4 Hz, 1H), 6.45 (d, J = 2.1 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.5, 157.9, 132.9, 107.0, 101.9, 101.5, 99.3, 56.2, 55.7; HRMS (TOF-ESI$^+$) *m/z*: calcd for $C_9H_9NNaO_2Se$ $[M+Na]^+$ 265.9696, found 265.9698.

1, 2-ethoxy-4-selenocyanobenzene **(5h)**: White solid, yield: 90%, m.p. 146–148 °C; IR (KBr) *v:* 3103, 2978, 2147, 1578, 1228, 1041, 800 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.20 (d, J = 8.4 Hz, 1H), 7.15 (s, 1H), 6.85 (d, J = 8.4 Hz, 1H), 4.10 (q, J = 6.6 Hz, 4H), 1.47 (t, J = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 150.7, 149.7, 127.4, 118.7, 114.0, 110.8, 102.2, 64.9, 64.6, 14.6; HRMS (TOF-ESI$^+$) *m/z*: calcd for $C_{11}H_{13}NNaO_2Se$ $[M+Na]^+$ 294.0009, found 294.0005.

2-methyl-4-selenocyanoanisole **(5i)**: White solid, yield: 99%, m.p. 52–53 °C; IR (KBr) *v:* 3016, 2841, 2146, 1571, 1021, 814 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.46 (d, J = 8.7 Hz, 1H), 7.44 (s, 1H), 6.81 (d, J = 8.7 Hz, 1H), 3.84 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.5, 136.4, 133.5, 129.4, 111.5, 110.5, 102.4, 55.5, 16.2; HRMS (TOF-ESI$^+$) *m/z*: calcd for $C_9H_9NNaOSe$ $[M+Na]^+$ 249.9742, found 249.9750.

3-methyl-4-selenocyanoanisole **(5j)**: White solid, yield: 90%, m.p. 53–55 °C; IR (KBr) *v:* 3081, 3007, 2938, 2155, 1567, 1242, 1053, 878 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.60 (d, J = 8.7 Hz, 1H), 6.86 (d, J = 2.1 Hz, 1H), 6.72 (dd, J = 2.1, 8.7 Hz, 1H), 3.79 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.8, 143.2, 137.3, 117.0, 113.2, 112.6, 101.8, 55.4, 23.2; HRMS (TOF-ESI$^+$) *m/z*: calcd for $C_9H_9NNaOSe$ $[M+Na]^+$ 249.9747, found 249.9750.

2-Bromo-4-selenocyanoanisole **(5k)**: White solid, yield: 27%, m.p. 56–57 °C; IR (KBr) *v:* 3087, 2923, 2147, 1573, 1293, 1050, 814 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.88 (s, 1H), 7.62 (d, J = 8.7 Hz, 1H), 6.93 (d, J = 8.7 Hz, 1H), 3.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 157.8, 138.6, 134.9, 113.2, 111.8, 101.5, 56.5; HRMS (TOF-ESI$^+$) *m/z*: calcd for $C_8H_6BrNNaOSe$ $[M+Na]^+$ 313.8696, found 313.8693.

1-selenocyano-2-methoxynaphthalene **(5l)**: White solid, yield: 97%, m.p. 146–148 °C; IR (KBr) *v:* 2947, 2143, 1591, 1270, 1058, 810 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.25 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 9.0 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.63 (t, J = 7.8 Hz, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.26 (d, J = 9.0 Hz, 1H), 4.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 158.1, 134.8, 133.8, 129.7, 128.7, 128.6, 126.2, 124.5, 112.9, 104.8, 101.6, 57.0; HRMS (TOF-ESI$^+$) *m/z*: calcd for $C_{12}H_9NNaOSe$ $[M+Na]^+$ 285.9747, found 285.9745.

4-selenocyano-1-methoxynaphthalene **(5m)**: White solid, yield: 63%, m.p. 116–118 °C; IR (KBr) *v:* 3727, 2926, 2514, 2120, 1797, 1588, 1527, 1365, 1091 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.34 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.71 (t, J = 7.5 Hz, 1H), 7.59 (t, J = 7.8 Hz, 1H), 6.77 (d, J = 8.1 Hz, 1H), 4.02 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.6, 136.9, 134.4, 128.7, 127.0, 126.8, 126.4, 123.0, 110.3, 104.3, 101.7, 55.9 (d, J = 8.0 Hz); HRMS (TOF-ESI$^+$) *m/z*: calcd for $C_{12}H_9NNaOSe$ $[M+Na]^+$ 285.9742, found 285.9745.

3-selenocyanato-1*H*-indole **(5n)**: Brown solid, yield: 96%, m.p. 84–85 °C; IR (KBr) *v:* 3350, 2934,2149, 1797, 1494, 1405, 1065, 745 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.86 (s, 1H), 7.45–7.78 (m, 1H), 7.41–7.46 (m, 2H), 7.28–7.34 (m, 2H);^{13}C NMR (100 MHz, $CDCl_3$) δ:136.1, 131.9, 128.8, 123.8, 121.9, 121.9, 119.6; HRMS (TOF-ESI+) *m/z*: calcd for $C_9H_6N_2SeNa$ $[M+Na]^+$ 244.9594, found 244.9590.

1-methyl-5-methoxy-3-selenocyanato-1*H*-indole **(5o)**: Brown solid, yield: 94%, m.p. 98–99 °C; IR (KBr) *v:* 3108, 2926, 2362, 2148, 1619, 1219, 1029, 803 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.33 (s, 1H), 7.26 (d, J = 9.0 Hz,1H), 7.14–7.15 (m, 1H), 6.98–7.01 (m, 1H), 3.93 (s, 1H), 3.77 (s, 1H);^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.7, 136.2, 136.2, 132.3, 130.3, 114.0, 111.0, 101.9, 100.9, 86.5, 55.9(J = 7.9 Hz), 33.54 (J = 7.3 Hz); HRMS (TOF-ESI+) *m/z*: calcd for $C_{11}H_{10}N_2OSeNa$ $[M+Na]^+$ 288.9856, found 288.9856.

4.3. Gram scale experiments

4.3.1. Synthesis of 1-phenyl-2-selenocyanatopropan-1-one (*2a*) on 7 mmol scale

To a solution of acetonitrile (210 mL), aqueous hydrochloric acid (3 M, 70 mL) was added at 0 °C, following by the addition of aqueous sodium nitrite (1.45 g, 21 mmol, dissolved in 21 mL of distilled water). After stirred at the same temperature for 10 min, KSeCN (3.042 g, 21 mmol) was added in one portion. The resulting solution was stirred at the ice bath for 20 min. Afterwards, propiophenone **1a** (0.94 g, 7.8 mmol) was added and the reaction mixture was continuously stirred in room temperature until no starting material was observed (the progress was monitored by TLC). The solvent was removed, the residue was extracted with ethyl acetate (60 mL × 3) and washed with brine. The combined organic phases were dried, concentrated and purified by flash column chromatography on silica gel (hexane/EtOAc = 4:1) to give 1.58 g of **2a** in 95% yield.

4.3.2. Synthesis of 2-methyl-4-selenocyanoanisole *(5i)* on 8 mmol scale

To a solution of acetonitrile (240 mL), aqueous hydrochloric acid (3 M, 80 mL) was added at 0 °C, following by the addition of aqueous sodium nitrite (1.66 g, 24 mmol, dissolved in 24 mL of distilled water). After stirred at the same temperature for 10 min, KSeCN (3.48 mg, 24 mmol) was added in one portion. The resulting solution was stirred at the ice bath for 20 min. Afterwards, 2-methylanisole (0.98 g, 8 mmol) was added and the reaction mixture was continuously stirred in room temperature until no starting material was observed (the progress was monitored by TLC). The solvent was removed, the residue was extracted with ethyl acetate (80 mL × 3) and washed with brine. The combined organic phases were dried, concentrated and purified by flash column chromatography on silica gel (hexane/EtOAc = 4:1) to give 1.83 g of **5i** in 99% yield.

4.4. Experimental procedure for the synthesis of 3-methyl-4-methoxyphenyldiselenide 6

To a solution of 2-methyl-4-selenocyanoanisole **5i** (0.1 mmol, 22.7 mg) in methanol (1 mL), KOH (0.2 mmol, 11.2 mg, 2 equiv.) was added. The reaction mixture was stirred at room temperature for 12 h. Then, solvent was removed *in vacuo* and the residue was extracted with EtOAc (3 mL × 2) and washed with brine. The combined organic phases were dried, concentrated and purified by flash column chromatography on silica gel (hexane/EtOAc = 19:1) to give 20.0 mg of diselenide **6** as orange solid.

2 Bis(3-methyl-4-methoxyphenyl)diselenide **(6)**: Orange solid, yield: 99%, m.p. 62–64 °C; IR (KBr) *v* 2922, 1796, 1586, 1486, 1246, 1140, 1026, 815; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.52 (d, J = 8.1 Hz, 2H),

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7.49 (s, 2H), 6.79 (d, $J = 8.1$ Hz, 2H), 3.87 (s, 6H), 2.30 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 158.4, 136.4, 133.0, 127.7, 121.7, 110.6, 55.4, 16.3; HRMS (TOF-ESI$^+$) m/z: calcd for $C_{16}H_{18}O_2Se_2Na$ $[M+Na]^+$ 424.9529, found 424.9521.

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office.

Declaration of competing interest

There are no conflicts to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2020.130978.

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