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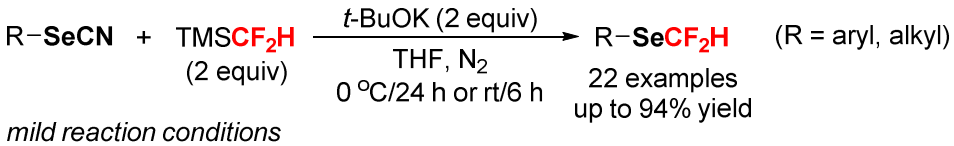
## Graphic Abstract




*mild reaction conditions*
*good functional group tolerance*
*a wide range of substrates*
*applicable to both aryl- and alkylselenocyanates*
*easy access to the starting materials*
*able to synthesize drug-like molecules*

# A Convenient, Transition Metal-Free Synthesis of Difluoromethyl Selenoethers from Organic Selenocyanates and $TMSCF_2H$

Tao Dong, Jing Nie, Cheng-Pan Zhang*

School of Chemistry, Chemical Engineering and Life Science, Wuhan University of Technology, 205 Luoshi Road, Wuhan, 430070, China

E-mail: cpzhang@whut.edu.cn, zhangchengpan1982@hotmail.com

## Abstract

An efficient and transition metal-free method for the synthesis of aryl or alkyl difluoromethyl selenides ($RSeCF_2H$) from the corresponding selenocyanates (RSeCN) and $TMSCF_2H$/*t*-BuOK is described. The reaction performed in THF at 0 $^oC$ for 24 h or at room temperature for 6 h supplied a series of $RSeCF_2H$ in good to high yields. The successful preparation of difluoromethylselenolated sulfadimethoxine derivative and the scaled-up synthesis of 1-benzyl-5-((difluoromethyl)selanyl)indoline, as examples, suggested good practicability of this method. Advantages of the reaction include mild reaction conditions, good functional group tolerance, a wide range of substrates, and high efficiency. This protocol offered a number of novel difluoromethyl selenoethers, which would accelerate use of such compounds in the areas of life science.

**Keywords**: Difluoromethyl Selenoether; Transition Metal-Free; Selenocyanate; Difluoromethylselenol; Difluoromethylation.

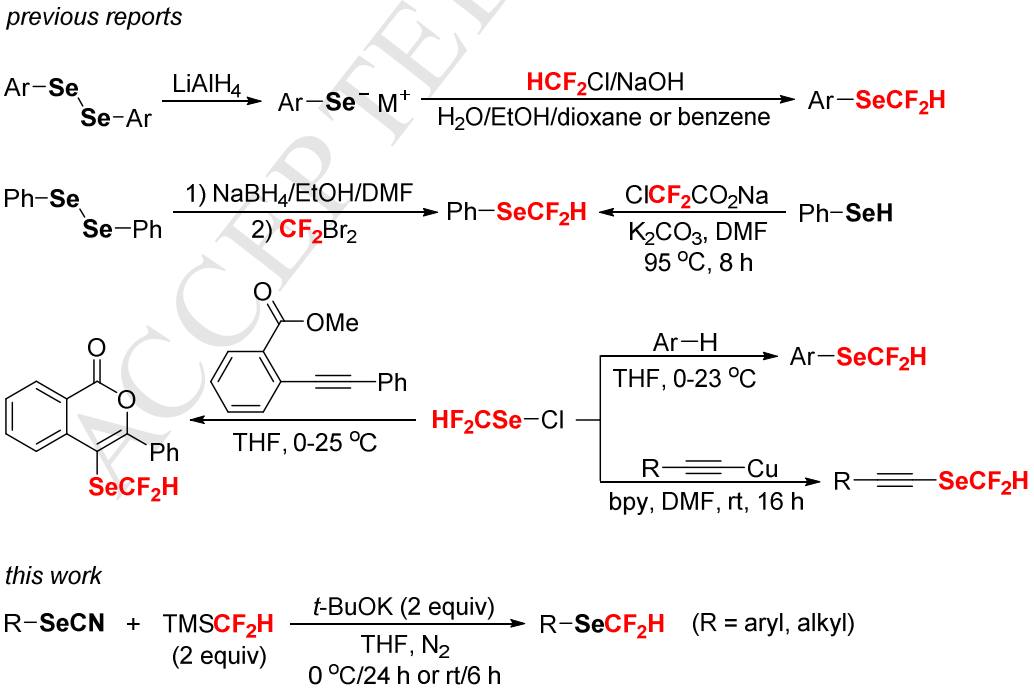
## 1. Introduction

Fluorinated compounds have found wide applications in many fields ranging from medicinal chemistry to materials science.[1] The incorporation of fluoroalkyl groups

into organic frameworks can dramatically change their physicochemical and biological properties.[2] In particular, the difluoromethyl group ($HCF_2$) has been one of the most privileged segments because of its unique stereoelectronic nature and great potentials in the synthesis of bioactive molecules.[3] The $HCF_2$ group is a good isopolar-isosteric substituent for hydroxy (OH) and thiol (SH) units, and it acts as a more lipophilic hydrogen donor than the OH and SH groups in various hydrogen bonding interactions.[3] The combination of $HCF_2$ group with chalcogens (X) gives $HCF_2X$ functionalities with more specific and interesting properties. Among all $HCF_2X$ moieties, the difluoromethylselenol group ($HCF_2Se$) is the least studied, despite the most relevant $HCF_2S$ functionality having been extensively explored.[4] This may be attributed to the cognition that selenium-containing compounds are usually highly toxic, easily oxidized, and with unpleasant odor.[5] Nonetheless, organoselenium compounds have possessed advantageous biological properties such as antifungal, anticancer, and antiviral activities,[5,6] some of which have been investigated for the treatment of Alzheimer's disease.[6a] The lack of difluoromethylselenolation reagents and appropriate starting materials is considered to be another bottleneck in the construction of $HCF_2Se$ molecules.

To date, there have been only several synthetic approaches reported for $HCF_2Se$ compounds.[7-11] In 1985, Suzuki et al. disclosed the first synthesis of aryl difluoromethyl selenides from the reactions of $HCF_2Cl$ with arylselenolates in alkaline aqueous media (5 examples).[7] Later, Uneyama et al found that reaction of $CF_2Br_2$ with benzeneselenolate, prepared *in situ* from diphenyl diselenide and sodium borohydride in EtOH/DMF, gave difluoromethyl phenyl selenide as a major product in 55% yield (1 example).[8] Greaney et al described the difluoromethylation of phenylselenol by using chlorodifluoroacetate as a difluorocarbene source, affording

difluoromethyl phenyl selenide in 65% yield (1 example).[9] Recently, Billard et al reported a reaction of electron-rich indol or resorcinol with $HCF_2SeCl$, which was *in situ* generated from benzyl(difluoromethyl)selane and $SO_2Cl_2$, furnishing the corresponding difluoromethylselenolated product in good yield (2 examples).[10] With $HCF_2SeCl$ reagent, the same research group again developed a transition metal-free difluoromethylselenolation/cyclization of alkyne to form a isocoumarin derivative and an oxidant-free difluoromethylselenolation of alkynyl copper(I) complex to yield a difluoromethyl alkynyl selenide (single example for each).[11] All these methods suffered from a very limited substrate scope, relative inaccessibility of starting materials, high cost, and/or low efficiency, supplying a small quantity of $HCF_2Se$-containing entities, which seriously restricted the application of this type of molecules. Thus, the development of efficient and convenient methodologies for the synthesis of various difluoromethylselenolated compounds is of great importance.



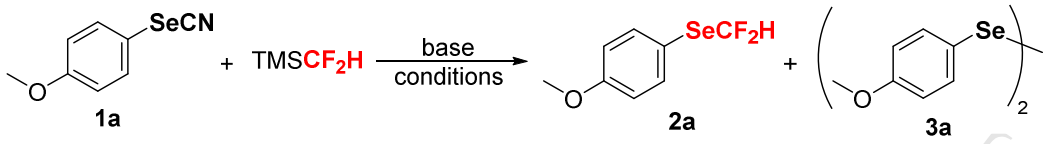
Although trifluoromethylation of selenocyanates with $TMSCF_3$ has been well documented,[12a,12d] the interaction between RSeCN and $TMSCF_2H$ (a less reactive reagent than $TMSCF_3$)[4f] is rarely known.[10] In this work, we successfully developed a transition metal-free direct difluoromethylation of selenocyanates with $TMSCF_2H$ in the presence of an appropriate initiator, building diverse difluoromethyl selenoethers under mild conditions.

## 2. Results and discussions

The reaction of 1-methoxy-4-selenocyanatobenzene (**1a**) and $TMSCF_2H$ was chosen as a model reaction to screen the optimal conditions. A mixture of **1a** and CsF (2 equiv.) reacted with $TMSCF_2H$ (2 equiv.) in DMF at room temperature under a $N_2$ atmosphere for 12 h to give (difluoromethyl)(4-methoxyphenyl)selane (**2a**) in 62% yield (entry 1, Table 1). 1,2-Bis(4-methoxyphenyl)diselane (**3a**) was also formed in this reaction (30% yield) (entry 1, Table 1). When the reaction of **1a**, $TMSCF_2H$, and CsF was conducted in DMSO or $CH_3CN$, the desired product (**2a**) was obtained in a very low yield and the formation of byproduct **3a** was enhanced (entries 2-3, Table 1). If the same reaction was performed in THF, only trace amount of **2a** and none of **3a** were observed (entry 4, Table 1), which might be accounted for by the much poor solubility of CsF in the reaction solvent. While if *t*-BuOK was employed as a base in THF, 65% of **2a** and 36% of **3a** were obtained (entry 5, Table 1). Reaction of **1a**, $TMSCF_2H$, and *t*-BuOK in DMF gave **2a** in 33% yield, accompanied by 32% of **3a** (entry 6, Table 1). To suppress the formation of **3a**, the adding order of the reaction materials was varied. Interestingly, when a solution of *t*-BuOK (2 equiv.) in THF was added to a mixture of **1a** and $TMSCF_2H$ (2 equiv.), the formation of byproduct (**3a**) was almost completely prohibited and the desired product was obtained in 66% yield

(entry 7, Table 1). These results suggested that the homocoupling of **1a** competed with the difluoromethylation of **1a** under the reaction conditions. Furthermore, shortening the reaction time of **1a**, $TMSCF_2H$ and *t*-BuOK from 12 h to 6 h or 2 h at room temperature resulted in 81% or 72% of **2a**, respectively (Entries 8-9, Table 1). The reaction temperature also had a considerable influence on the difluoromethylation. Lowering the reaction temperature from room temperature to 0 °C or -20 °C furnished the expected product in 71% or 65% yield (entries 10-11, Table 1). The production of **3a** was completely inhibited. When the reaction of **1a**, $TMSCF_2H$ and *t*-BuOK was run at 0 $^{o}$C for 24 h, **2a** was formed in 95% yield (91% isolated yield) (entry 12, Table 1). Nevertheless, further extension of the reaction time to 36 h did not continuously improve the yield of **2a** (entry 13, Table 1). In addition, the molar ratios of the reactants had a big effect on the reaction. By varying the molar ratio of **1a**/$TMSCF_2H$/*t*-BuOK from 1:2:2 to 1:1.5:1.5 or 1:1:1, the yield of **2a** was dramatically decreased (e.g., entry 14, Table 1). The use of 2 equivalents of *t*-BuOK to work with **1a** and $TMSCF_2H$ (1 equiv.) led to a lower yield of **2a** as well (entry 15, Table 1). Except formation of **2a** in these cases, appreciable amounts of **3a** were detected along with an unknown byproduct which couldn't be isolated by column chromatography (entries 14-15, Table 1). It should be mentioned that, if the reaction of **1a** and $TMSCF_2H$ was conducted in the absence of CsF or *t*-BuOK, there was no desired product or byproduct formed, suggesting the indispensability of a base (entry 16, Table 1). Interestingly, if **3a** (instead of **1a**) reacted with $TMSCF_2H$ and *t*-BuOK at room temperature for 6 h, **2a** was formed in 48% yield with recovery of 48% of **3a**, implying a much lower reactivity of 1,2-diaryldiselane in the present system (entry 17, Table 1).[4f]

**Table 1 Screening the optimal reaction conditions for difluoromethylation of 1a with $TMSCF_2H$ in the presence of CsF or *t*-BuOK**




| Entry | Base | Conditions | Yield (**2a**, %) [a] | Yield (**3a**, %) [a] |
|---|---|---|---|---|
| 1 [b] | CsF | DMF, $N_2$, rt, 12 h | 62 | 30 |
| 2 [b] | CsF | DMSO, $N_2$, rt, 12 h | 33 | 42 |
| 3 [b] | CsF | $CH_3CN$, $N_2$, rt, 12 h | 3 | 56 |
| 4 [b] | CsF | THF, $N_2$, rt, 12 h | <1 | 0 |
| 5 [b] | *t*-BuOK | THF, $N_2$, rt, 12 h | 65 | 36 |
| 6 [b] | *t*-BuOK | DMF, $N_2$, rt, 12 h | 33 | 32 |
| 7 [c] | *t*-BuOK | THF, $N_2$, rt, 12 h | 66 | <1 |
| **8** [c] | ***t*-BuOK** | **THF, $N_2$, rt, 6 h** | **81** | **4** |
| 9 [c] | *t*-BuOK | THF, $N_2$, rt, 2 h | 72 | 3 |
| 10 [c] | *t*-BuOK | THF, $N_2$, 0 °C, 12 h | 71 | 0 |
| 11 [c] | *t*-BuOK | THF, $N_2$, -20 °C, 12 h | 65 | 0 |
| **12** [c] | ***t*-BuOK** | **THF, $N_2$, 0 °C, 24 h** | **95 (91)** | **0** |
| 13 [c] | *t*-BuOK | THF, $N_2$, 0 °C., 36 h | 91 | 0 |
| 14 [c,d] | *t*-BuOK | THF, $N_2$, 0 °C, 24 h | 20 | 38 |
| 15 [c,e] | *t*-BuOK | THF, $N_2$, 0 °C, 24 h | 40 | 18 |
| 16 [c,f] | - | THF, $N_2$, 0 °C, 24 h | 0 | 0 |
| 17 [c,g] | *t*-BuOK | THF, $N_2$, rt, 6 h | 48 | 48 |

[a] Yields were determined by HPLC (λ = 232 nm, methanol/water = 90:10 (v/v)) using **2a** and **3a** as external standards, respectively (**2a**: $t_R$ = 4.47 min, **3a**: $t_R$ = 9.97 min ($t_R$ means the retention time)). [b] Reaction conditions: $TMSCF_2H$ (0.4 mmol) was

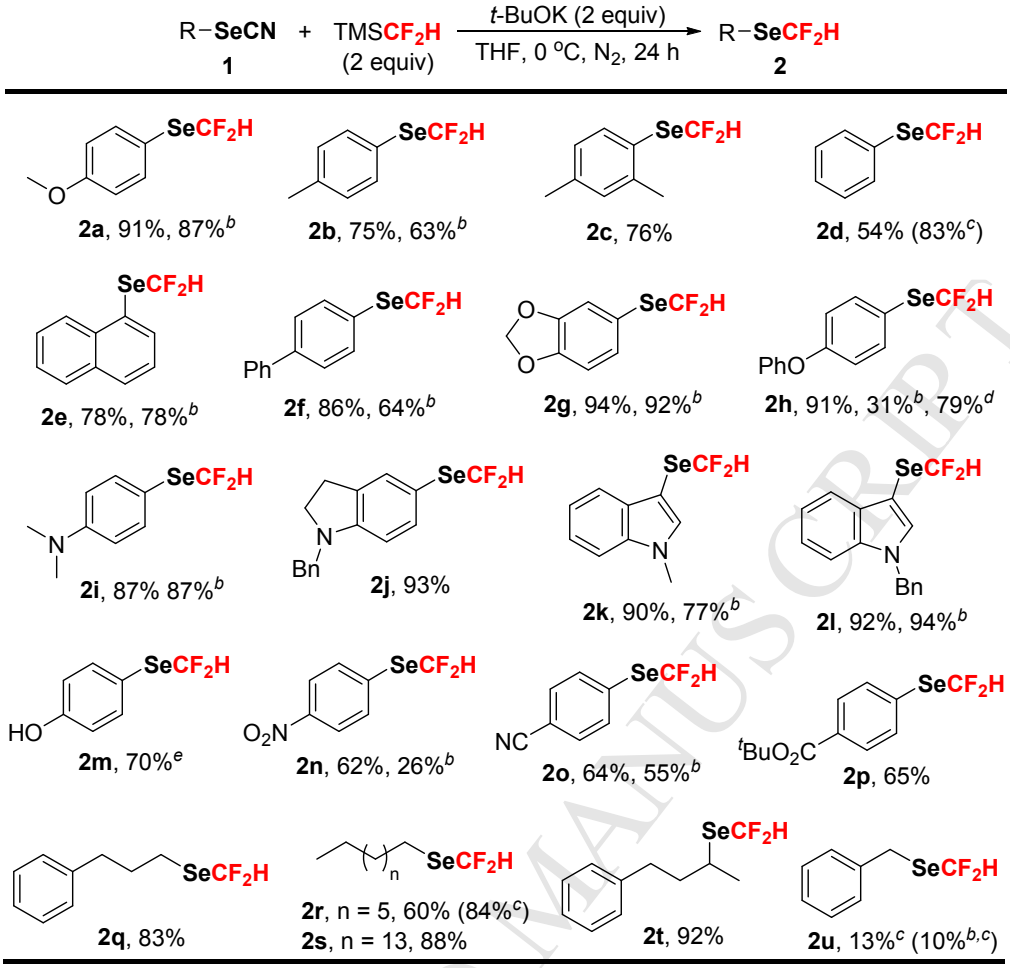
added to a mixture of **1a** (0.2 mmol) and base (0.4 mmol) in solvent (2 mL). [c] Reaction conditions: To a solution of **1a** (0.2 mmol) and $TMSCF_2H$ (0.4 mmol) in THF (1 mL) was added a solution of *t*-BuOK (0.4 mmol) in THF (1 mL). [d] **1a** (0.2 mmol), $TMSCF_2H$ (0.3 mmol), and *t*-BuOK (0.3 mmol). [e] **1a** (0.2 mmol), $TMSCF_2H$ (0.2 mmol), and *t*-BuOK (0.4 mmol). [f] No CsF or *t*-BuOK was used. [g] **3a** (0.2 mmol) was used instead of **1a** as starting material.

With the optimized (or standard) reaction conditions in hand (entry 12, Table 1), the substrate scope of the transformation was tested. As summarized in Table 2, numerous electron-rich arylselenocyanates (**1b-i**) reacted with $TMSCF_2H$/*t*-BuOK under the standard conditions to give the corresponding difluoromethylselenolated products (**2a-i**) in 54-94% yields. The indol derivatives such as 1-benzyl-5-selenocyanatoindoline (**1j**), 1-methyl-3-selenocyanato-1H-indole (**1k**), and 1-benzyl-3-selenocyanato-1H-indole (**1l**) treated similarly in the reaction provided **2j-l** in 90-93% yield. It is noteworthy that reaction of 4-selenocyanatophenol (**1m**) with 2 equivalents of $TMSCF_2H$ and 3.5 equivalents of *t*-BuOK furnished 70% of 4-((difluoromethyl)selanyl)phenol (**2m**). Since the acidic hydroxy group in **1m** would expend equal equivalent of *t*-BuOK, the use of a large excess of *t*-BuOK was helpful for the high conversion of the starting material. The results also implied that the hydroxy substituent on the aryl ring without protection hardly affected the difluoromethylation reaction. Furthermore, arylselenocyanates (**1n-p**) bearing electron-withdrawing groups such as nitro, cyano, and ester functionalities on the aryl rings reacted under the standard conditions to give the expected products (**2n-p**) in 62-65% yields. It seemed that the electron-rich arylselenocyanates were more efficiently transformed than the electron-deficient ones in these reactions.

Additionally, if the above reactions were performed at room temperature for 6 h (entry 8, Table 1), comparable yields of the desired products were achieved in some cases (e.g. **2a**, **2e**, **2g**, **2i**, **2l**), while for others much lower yields of products were observed (e.g. **2h**, **2n**). The nature of the substituents on the aryl moieties of arylselenocyanates might be responsible for these changes.

Encouragingly, the reaction was also applicable to alkylselenocyanates. The primary alkylselenocyanate, such as (3-selenocyanatopropyl)benzene (**1q**), 1-selenocyanatooctane (**1r**) and 1-selenocyanatohexadecane (**1s**), and the secondary alkylselenocyanate like (3-selenocyanatobutyl)benzene (**1t**) reacted readily under the standard conditions to furnish the difluoromethylselenolated products (**2q-t**) in excellent yields, demonstrating good availability of this method. To our surprise, treatment of (selenocyanatomethyl)benzene (**1u**) with $TMSCF_2H$ and *t*-BuOK at 0 $^oC$ for 24 h or at room temperature for 6 h afforded benzyl(difluoromethyl)selane (**2u**) only in 13% or 10% $^{19}F$ NMR yield, respectively (33% $^{19}F$ NMR yield was obtained in the literature using $TMSCF_2H$/CsF mixture).[10,11] The reason for these low yields remains unclear. Because compounds **2d** and **2r** were volatile and easily evaporated during the workup and the drying processes, the NMR yields were reasonably higher than the isolated ones. Moreover, it should be mentioned that all selenocyanates used in this reaction could be simply synthesized from the relevant aromatic amines, arenes and alkyl halides according to the literatures,[12] which guaranteed easy accessibility of diverse starting materials for the difluoromethylation.

**Table 2 Synthesis of difluoromethyl selenoethers from different types of aryl- and alkylselenocyanates.**[a]

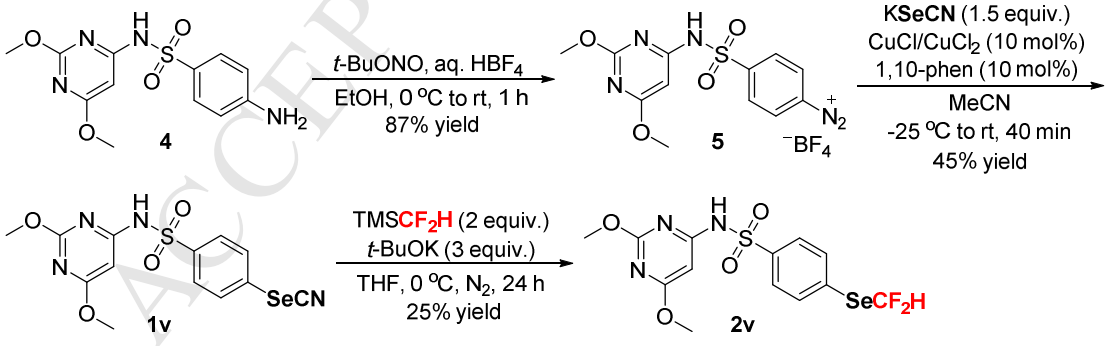



[a] Reaction conditions: To a solution of selenocyanate **1** (0.2 mmol) and $TMSCF_2H$ (0.4 mmol) in THF (1 mL) was added a solution of *t*-BuOK (0.4 mmol) in THF (1 mL), and the mixture was reacted at 0 °C under a $N_2$ atmosphere for 24 h. Isolated yields. [b] Room temperature for 6 h. [c] The yields were determined by $^{19}F$ NMR using $PhOCF_3$ as an internal standard. [d] 0 °C for 6 h. [e] *t*-BuOK (0.7 mmol) was used.

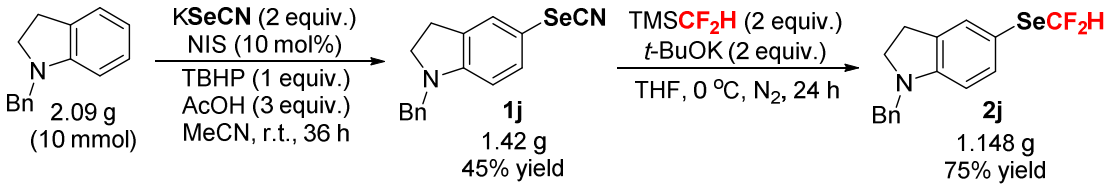
To further illustrate the practicability of this method, a difluoromethylselenolated analogue of sulfadimethoxine (a long-lasting sulfonamide antimicrobial) was synthesized in a similar manner (**Scheme 1**). In the first step of the synthesis, 4-(*N*-(2,6-dimethoxypyrimidin-4-yl)sulfamoyl)benzenediazonium tetrafluoroborate (**5**) was derived from the reaction of

4-amino-*N*-(2,6-dimethoxypyrimidin-4-yl)benzenesulfonamide (**4**) with $HBF_4$ and *tert*-butyl nitrite. Then, a solution of **5** in $CH_3CN$ was treated with KSeCN in the presence of CuCl, $CuCl_2$, and 1,10-phenanthroline to give *N*-(2,6-dimethoxypyrimidin-4-yl)-4-selenocyanatobenzenesulfonamide (**1v**) in 45% yield.[12a] Finally, reaction of **1v** with $TMSCF_2H$ (2 equiv) and *t*-BuOK (3 equiv) in THF (1 mL) at 0 °C for 24 h provided the difluoromethylselenolated product (**2v**) in 25% yield. In addition, the scaled-up synthesis of **2j** from 1-benzylindoline was investigated (**Scheme 2**). Treatment of 1-benzylindoline (10 mmol) with KSeCN (2 equiv.) in the presence of NIS, TBHP (70% aqueous solution), and acetic acid in acetonitrile at room temperature for 36 h afforded 1-benzyl-5-selenocyanatoindoline (**1j**) in 45% yield.[12b] Subsequently, **1j** reacted with $TMSCF_2H$ (2 equiv.) and *t*-BuOK (2 equiv.) in THF (10 mL) under the standard conditions to form **2j** in 75% yield (1.148 g). These selected examples hinted at usefulness of the present reactions for the synthesis of various difluoromethyl selenoethers.

**Scheme 1** Synthesis of **2v** from sulfadimethoxine (**4**)

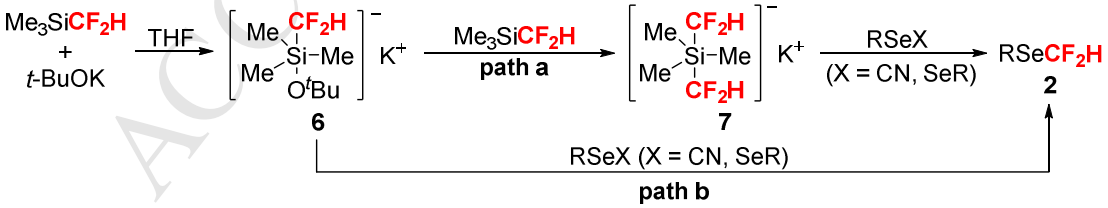



**Scheme 2** Scaled-up synthesis of **2j** from 1-benzylindoline




Based on the above results and the previous reports,[13] a plausible reaction mechanism was suggested for this difluoromethylation (**Scheme 3**). First, *t*-BuOK coordinates with the silicon center of $Me_3SiCF_2H$ to form a pentacoordinate silicate (**6**). Reaction of **6** with another equivalent of $Me_3SiCF_2H$ generates a $K[Me_3Si(CF_2H)_2]$ intermediate (**7**), which then undergoes a nucleophilic attack at the selenium atom of RSeX (X = CN, SeR) to afford the desired product $RSeCF_2H$ (**2**). However, construction of $RSeCF_2H$ by the direct difluoromethylation of RSeX with **6** cannot be excluded in the reactions at this stage. Additionally, minor RSeSeR species observed in some reactions might be generated *in situ* from RSeCN, which could be further converted to $RSeCF_2H$ under the reaction conditions. This hypothesis was partially supported by the experimental data described in Table 1.

**Scheme 3 A plausible reaction mechanism for the construction of $RSeCF_2H$ from RSeX and $Me_3SiCF_2H$/*t*-BuOK**




## 3. Conclusions

In summary, we have developed a convenient and transition metal-free method for the construction of aryl and alkyl difluoromethyl selenides from the corresponding

selenocyanates (RSeCN) and $TMSCF_2H$ in the presence of *t*-BuOK. The reaction performed in THF at 0 $^oC$ for 24 h or at room temperature for 6 h supplied a series of $RSeCF_2H$ in good to high yields. Various functionalities such as methoxy, hydroxyl, ester, nitro, cyano, and amide groups, as well as heterocyclic moieties, were well tolerated in the reaction. It was remarkable that the secondary alkyl selenocyanate reacted under the standard conditions to give the desired product without formation of *β*-H elimination byproduct even in the presence of strongly alkaline *t*-BuOK. Furthermore, the successful synthesis of difluoromethylselenolated sulfadimethoxine derivative and the scaled-up preparation of **2j** suggested good versatility of the method. This protocol offered an efficient way to a family of novel difluoromethyl selenoethers, which would encourage application of these molecules in life sciences.

## 4. Experimental Section

All reactions were carried out under a nitrogen atmosphere. Unless otherwise specified, the NMR spectra were recorded in $CDCl_3$ on a 500 MHz (for $^1H$), 471 MHz (for $^{19}F$), and 126 MHz (for $^{13}C$) spectrometer. All chemical shifts were reported in ppm relative to TMS for $^1H$ NMR (0 ppm) and $PhCF_3$ for $^{19}F$ NMR (-63.0 ppm) as an internal or external standard. The coupling constants were reported in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Melting points were measured and uncorrected. MS experiments were performed on a TOF-Q ESI or EI instrument. Solvents (such as THF, $CH_3CN$, DMF, DMSO) were dried before use according to the literature.[14] $TMSCF_2H$ was prepared according to the literature.[15] Substrates such as **1a-i**,[12a] **1j-m**,[12b] **1n**-p,[12a] **1q-u**,[12c] and **1v**[12a] were synthesized according to the literatures. Other reagents used in the reactions were all purchased

from the commercial sources and used without further purification.

### 4.1. Procedures for the synthesis of organic selenocyanates.

**Procedure**:[12a] Under a $N_2$ atmosphere, an oven-dried round-bottom flask (100 mL) was charged with CuCl (50 mg, 0.5 mmol), $CuCl_2$ (68 mg, 0.5 mmol), 1,10-phenanthroline (90 mg, 0.5 mmol), KSeCN (1.08 g, 7.5 mmol), and $CH_3CN$ (10 mL) with stirring. The mixture was cooled to -25 $^oC$ and a solution of aryldiazonium tetrafluoroborate (5 mmol) in $CH_3CN$ (10 mL) was dropwise added (within 10 min). The reaction mixture was maintained at -25 °C for 10 min, and then warmed to room temperature for about 30 min. The resulting slurry was filtered through a short pad of silica and washed with $CH_3CN$ (3 × 10 mL). The collected solutions were concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate as eluents to give the desired product.

*Note*: all aryldiazonium tetrafluoroborates were prepared from the reactions of the relevant aryl amines with an aqueous $HBF_4$ solution and $NaNO_2$ or *tert*-butyl nitrite according to the literature.[16]

5-Selenocyanatobenzo[d][1,3]dioxole (**1g**). White solid (780 mg, 69% yield), petroleum ether/ethyl acetate = 10:1 (v/v) as eluents for column chromatography. M.p.: 55-57 $^oC$. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.16 (dd, $J$ = 8.0, 1.7 Hz, 1H), 7.15 (d, $J$ = 1.7 Hz, 1H), 6.83 (d, $J$ = 8.0 Hz, 1H), 6.04 (s, 2H). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 149.9, 149.0, 128.8, 114.5, 111.9, 109.9, 102.0, 101.8. IR (KBr): 3098, 3044, 3008, 2913, 2148, 1593, 1498, 1475, 1438, 1416, 1400, 1347, 1250, 1236, 1164, 1106, 1032, 928, 875, 850, 816, 722, 669 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_8H_5NO_2{}^{74}Se$:

220.9545, found: 220.9548.

1-Phenoxy-4-selenocyanatobenzene (**1h**). White solid (718 mg, 52% yield), petroleum ether/ethyl acetate = 20:1 (v/v) as eluents for column chromatography. M.p.: 60-62 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.8 Hz, 2H), 7.40 (t, *J* = 7.9 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.05 (d, *J* = 8.6 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 159.8, 155.7, 135.8, 130.1, 124.6, 119.9, 119.8, 113.7, 101.8. IR (KBr): 3080, 3052, 2150, 1593, 1572, 1484, 1454, 1404, 1300, 1283, 1240, 1196, 1169, 1154, 1102, 1069, 1019, 1005, 918, 867, 836, 816, 800, 757, 700 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_{13}H_9NO^{74}Se$: 268.9909, found: 268.9915.

*N*-(2,6-Dimethoxypyrimidin-4-yl)-4-selenocyanatobenzenesulfonamide (**1v**). White solid (898 mg, 45% yield), petroleum ether/ethyl acetate = 2:1 (v/v) as eluents for column chromatography. M.p.: 173-175 $^{o}$C. $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 11.80 (brs, 1H), 7.98 (d, *J* = 7.9 Hz, 2H), 7.94 (d, *J* = 8.2 Hz, 2H), 5.97 (s, 1H), 3.81 (s, 3H), 3.75 (s, 3H). $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 172.2, 164.5, 160.2, 141.1, 133.6, 131.5, 128.8, 105.3, 85.3, 55.1, 54.4. IR (KBr): 3242, 3096, 2987, 2952, 2156, 1583, 1493, 1473, 1446, 1376, 1352, 1328, 1279, 1261, 1209, 1198, 1159, 1102, 1070, 1008, 985, 884, 825, 816, 740, 716, 659, 631 $cm^{-1}$. HRMS-ESI (m/z) calcd. for $[C_{13}H_{13}N_4O_4SSe]^+$ ($[M + H]^+$): 400.9783, found: 400.9782.

**Procedure**:[12c] An oven-dried round-bottom flask (50 mL) was charged with (3-iodobutyl)benzene (0.52 g, 2.0 mmol), KSeCN (346 mg, 2.4 mmol), and ethanol (10 mL) with vigorous stirring. The mixture was reacted at 80 $^{o}$C for 3 h, quenched by aqueous saturated NaCl solution (20 mL), and extracted with ethyl acetate (3 × 20

mL). The combined organic layers were dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate = 20:1 (v/v) as eluents to give (3-selenocyanatobutyl)benzene (**1t**) as a light yellow liquid (404 mg, 85%). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 7.3 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 2H), 3.45 (m, 1H), 2.79 (m, 2H), 2.15 (m, 2H), 1.73 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 140.1, 128.7, 128.5, 126.5, 101.1, 43.4, 39.6, 34.0, 23.5. IR (KBr): 3085, 3062, 3027, 2960, 2925, 2861, 2148, 1603, 1584, 1496, 1454, 1381, 1357, 1285, 1255, 1231, 1211, 1163, 1113, 1091, 1060, 1031, 1003, 915, 816, 749, 700, 621 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_{11}H_{13}N^{74}Se$: 233.0273, found: 233.0278.

**4.2. General procedures for difluoromethylation of selenocyanates by $TMSCF_2H$.**

**Procedure A**: Under a $N_2$ atmosphere, an oven-dried tube was charged with alkyl or aryl selenocyanate **1** (0.2 mmol), $TMSCF_2H$ (0.4 mmol), and THF (1 mL) with stirring. Then, a solution of *t*-BuOK (0.4 mmol) in THF (1 mL) was added dropwise at 0 $^o$C. The mixture was reacted at 0 $^o$C for 24 hours, quenched by $H_2O$ (2 drops), and concentrated to dryness. The residue was purified by column chromatography on silica gel using petroleum ether or a mixture of petroleum ether and ethyl acetate as eluents to give the difluoromethylated product.

**Procedure B**: Under a $N_2$ atmosphere, an oven-dried tube was charged with aryl selenocyanate **1** (0.2 mmol), $TMSCF_2H$ (0.4 mmol), and THF (1 mL) with stirring. Then, a solution of *t*-BuOK (0.4 mmol) in THF (1 mL) was added at room temperature. The mixture was reacted at room temperature for 6 hours, quenched by $H_2O$ (2 drops), and concentrated to dryness. The residue was purified by column

chromatography on silica gel using petroleum ether or a mixture of petroleum ether and ethyl acetate as eluents to give the difluoromethylated product.

(Difluoromethyl)(4-methoxyphenyl)selane (**2a**). Light yellow oil (43.2 mg, 91% yield from **procedure A**; 41.2 mg, 87% yield from **procedure B**), petroleum ether/ethyl acetate = 40:1 (v/v) as eluents for column chromatography. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.2 Hz, 2H), 7.10 (t, *J* = 55.6 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 2H), 3.83 (s, 3H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -91.1 (d, *J* = 55.6 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 160.9, 138.4, 117.1 (t, *J* = 289.7 Hz), 115.2, 113.5 (t, *J* = 2.8 Hz), 55.3. IR (KBr): 3069, 3007, 2964, 2942, 2908, 2840, 1592, 1572, 1493, 1462, 1441, 1404, 1290, 1271, 1251, 1176, 1104, 1079, 1062, 1039, 1005, 827, 811, 793, 712, 691, 670, 631, 602 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_8H_8OF_2{}^{74}Se$: 231.9768, found: 231.9769.

(Difluoromethyl)(4-tolyl)selane (**2b**). Light yellow oil (33.2 mg, 75% yield from **procedure A**; 27.9 mg, 63% yield from **procedure B**), petroleum ether as eluent for column chromatography. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.13 (t, *J* = 55.5 Hz, 1H), 2.38 (s, 3H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -90.5 (d, *J* = 55.5 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 139.8, 136.5, 130.3, 119.8 (t, *J* = 2.7 Hz), 117.2 (t, *J* = 289.0 Hz), 21.3. IR (KBr): 3025, 2965, 2924, 2868, 1491, 1448, 1397, 1292, 1271, 1211, 1183, 1078, 1063, 1016, 805, 706, 690, 669 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_8H_8F_2{}^{74}Se$: 215.9819, found: 215.9817.

(Difluoromethyl)(2,4-dimethylphenyl)selane (**2c**). Yellow oil (35.7 mg, 76% yield from **procedure A**), petroleum ether as eluent for column chromatography. $^{1}$H NMR

(500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.8 Hz, 1H), 7.15 (s, 1H), 7.09 (t, *J* = 55.4 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 2.49 (s, 3H), 2.34 (s, 3H). $^{19}F$ NMR (471 MHz, $CDCl_3$) δ -90.0 (d, *J* = 55.4 Hz, 2F). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 142.7, 140.3, 138.0, 131.5, 127.7, 121.1 (t, *J* = 2.7 Hz), 117.4 (t, *J* = 289.1 Hz), 23.4, 21.1. IR (KBr): 3010, 2965, 2924, 2862, 1600, 1475, 1446, 1379, 1291, 1270, 1234, 1067, 1031, 877, 812, 722, 709, 689, 669 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_9H_{10}F_2{}^{74}Se$: 229.9975, found: 229.9969.

(Difluoromethyl)(phenyl)selane (**2d**).[9] Yellow oil (22.5 mg, 54% yield from **procedure A**), petroleum ether as eluent for column chromatography. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.17 (t, *J* = 55.0 Hz, 1H). $^{19}F$ NMR (471 MHz, $CDCl_3$) δ -90.3 (d, *J* = 55.0 Hz, 2F). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 136.4, 129.5, 129.5, 123.5 (t, *J* = 2.6 Hz), 117.1 (t, *J* = 289.4 Hz).

(Difluoromethyl)(naphthalen-1-yl)selane (**2e**). Light yellow oil (40.1 mg, 78% yield from **procedure A**; 40.3 mg, 78% yield from **procedure B**), petroleum ether/ethyl acetate = 40:1 (v/v) as eluents for column chromatography. $^1H$ NMR (500 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.4 Hz, 1H), 8.01 (dd, *J* = 7.1, 0.7 Hz, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.63 (tm, *J* = 7.5 Hz, 1H), 7.57 (tm, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 55.3 Hz, 1H). $^{19}F$ NMR (471 MHz, $CDCl_3$) δ -89.5 (d, *J* = 55.3 Hz, 2F). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 137.2, 135.4, 134.2, 131.0, 128.7, 128.1, 127.4, 126.6, 125.9, 123.2 (t, *J* = 2.7 Hz), 117.4 (t, *J* = 289.7 Hz). IR (KBr): 3055, 2968, 2917, 2848, 1589, 1561, 1502, 1379, 1337, 1290, 1271, 1253, 1201, 1135, 1060, 958, 862, 797, 770, 736, 694, 676, 652, 620 $cm^{-1}$. HRMS-EI (m/z)

calcd. for $C_{11}H_8F_2{}^{74}Se$: 251.9819, found: 251.9825.

[1,1'-Biphenyl]-4-yl(difluoromethyl)selane (**2f**). Light yellow oil (48.9 mg, 86% yield from **procedure A**; 36.1 mg, 64% yield from **procedure B**), petroleum ether as eluent for column chromatography. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.62-7.59 (m, 4H), 7.48 (t, *J* = 7.4 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 1H), 7.22 (t, *J* = 55.3 Hz, 1H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -90.2 (d, *J* = 55.3 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 142.5, 140.0, 136.8, 129.0, 128.2, 128.0, 127.2, 122.3 (t, *J* = 2.8 Hz), 117.1 (t, *J* = 289.3 Hz). IR (KBr): 3061, 3024, 3009, 2967, 2922, 2852, 1589, 1553, 1476, 1446, 1392, 1318, 1289, 1107, 1080, 1060, 1045, 1031, 1007, 968, 950, 920, 831, 765, 718, 700, 670, 645 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_{13}H_{10}F_2{}^{74}Se$: 277.9975, found: 277.9984.

5-((Difluoromethyl)selanyl)benzo[d][1,3]dioxole (**2g**). Colorless oil (47.2 mg, 94% yield from **procedure A**; 46.2 mg, 92% yield from **procedure B**), petroleum ether/ethyl acetate = 40:1 (v/v) as eluents for column chromatography. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.14 (d, *J* = 1.6 Hz, 1H), 7.11 (t, *J* = 55.5 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.01 (s, 2H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -91.1 (d, *J* = 55.3 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 149.2, 148.3, 131.2, 117.0 (t, *J* = 289.6 Hz), 116.8, 114.3 (t, *J* = 2.9 Hz), 109.4, 101.6. IR (KBr): 3074, 3012, 2976, 2901, 2781, 1598, 1502, 1476, 1453, 1416, 1400, 1336, 1291, 1271, 1255, 1236, 1161, 1109, 1065, 1038, 935, 878, 861, 808, 721, 696, 673 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_8H_6O_2F_2{}^{74}Se$: 245.9561, found: 245.9568.

(Difluoromethyl)(4-phenoxyphenyl)selane (**2h**). Colorless oil (54.6 mg, 91% yield

from **procedure A**; 18.5 mg, 31% yield from **procedure B**; 47.2 mg, 79% yield from reaction at 0 °C for 6 h), petroleum ether as eluent for column chromatography. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.7 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 55.4 Hz, 1H), 7.06 (dd, *J* = 8.5, 1.0 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -90.8 (d, *J* = 55.4 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 159.2, 156.1, 138.5, 130.0, 124.2, 119.8, 119.1, 116.9 (t, *J* = 289.8 Hz), 116.1 (t, *J* = 2.9 Hz). IR (KBr): 3065, 3040, 2966, 1591, 1579, 1485, 1456, 1401, 1331, 1275, 1241, 1198, 1168, 1077, 1063, 1011, 962, 908, 869, 832, 795, 754, 711, 693, 669 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_{13}H_{10}OF_2{}^{74}Se$: 293.9924, found: 293.9919.

4-((Difluoromethyl)selanyl)-*N*,*N*-dimethylaniline (**2i**). Light yellow oil (43.6 mg, 87% yield from **procedure A**; 43.5 mg, 87% yield from **procedure B**), petroleum ether/ethyl acetate = 40:1 (v/v) as eluents for column chromatography. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 5.9 Hz, 2H), 7.06 (t, *J* = 55.9 Hz, 1H), 6.67 (d, *J* = 6.7 Hz, 2H), 3.00 (s, 6H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -91.4 (d, *J* = 55.9 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 151.2, 138.2, 117.4 (t, *J* = 289.6 Hz). 112.9, 107.8 (t, *J* = 2.8 Hz), 40.2. IR (KBr): 3087, 3030, 2891, 2858, 2813, 1594, 1551, 1506, 1482, 1444, 1361, 1316, 1289, 1268, 1226, 1195, 1170, 1126, 1084, 1062, 997, 946, 811, 711, 691, 667 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_9H_{11}NF_2{}^{74}Se$: 245.0084, found: 245.0088.

1-Benzyl-5-((difluoromethyl)selanyl)indoline (**2j**). Yellow oil (62.8 mg, 93% yield from **procedure A**; 1.148 g, 75% yield on a large scale (**1j**, 4.53 mmol)), petroleum ether/ethyl acetate = 40:1 (v/v) as eluents for column chromatography. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.39-7.35 (m, 6H), 7.31 (m, 1H), 7.08 (t, *J* = 55.8 Hz, 1H), 6.45 (d, *J*

= 8.6 Hz, 1H), 4.32 (s, 2H), 3.44 (t, *J* = 8.5 Hz, 2H), 3.03 (t, *J* = 8.5 Hz, 2H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -91.3 (d, *J* = 55.8 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 153.7, 137.8, 137.1, 133.2, 131.4, 128.7, 127.8, 127.4, 117.6 (t, *J* = 289.3 Hz), 108.8 (t, *J* = 2.8 Hz), 107.1, 53.1, 52.7, 28.1. IR (KBr): 3167, 3085, 3062, 3029, 2958, 2923, 2844, 2705, 2582, 1596, 1495, 1471, 1454, 1439, 1384, 1356, 1315, 1269, 1202, 1178, 1155, 1107, 1065, 980, 943, 888, 804, 763, 734, 697, 670 $cm^{-1}$. HRMS-ESI (m/z) calcd. for $[C_{16}H_{16}NF_2{}^{74}Se]^+$ ($[M + H]^+$), 334.0470; found, 334.0472.

3-((Difluoromethyl)selanyl)-1-methyl-1*H*-indole (**2k**). Light yellow solid (46.9 mg, 90% yield from **procedure A**; 40.1 mg, 77% yield from **procedure B**), petroleum ether/ethyl acetate = 40:1 (v/v) as eluents for column chromatography. M.p.: 53-55 $^{o}$C. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.34 (td, *J* = 6.9, 1.1 Hz, 1H), 7.32 (s, 1H), 7.28 (td, *J* = 7.8, 1.0 Hz, 1H), 6.98 (t, *J* = 55.8 Hz, 1H), 3.84 (s, 3H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -90.8 (d, *J* = 55.8 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 137.3, 136.4, 131.0, 122.7, 120.8, 120.2, 117.2 (t, *J* = 290.3 Hz), 109.7, 91.1 (t, *J* = 3.5 Hz), 33.1. IR (KBr): 3116, 3070, 3053, 2943, 2912, 2872, 2823, 1636, 1612, 1588, 1570, 1510, 1481, 1459, 1424, 1372, 1355, 1334, 1296, 1240, 1169, 1151, 1129, 1111, 1063, 1038, 1027, 1008, 952, 929, 821, 763, 739, 668 $cm^{-1}$. HRMS-ESI (m/z) calcd. for $[C_{10}H_{10}NF_2{}^{74}Se]^+$ ($[M + H]^+$), 256.0001; found, 256.0001.

1-Benzyl-3-((difluoromethyl)selanyl)-1*H*-indole (**2l**). White solid (61.8 mg, 92% yield from **procedure A**; 63.1 mg, 94% yield from **procedure B**), petroleum ether/ethyl acetate = 40:1 (v/v) as eluents for column chromatography. M.p.: 51-53 $^{o}$C. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.81 (m, 1H), 7.40 (s, 1H), 7.37-7.33 (m, 4H),

7.31-7.27 (m, 2H), 7.18 (d, *J* = 6.7 Hz, 2H), 7.01 (t, *J* = 55.7 Hz, 1H), 5.35 (s, 2H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -90.6 (d, *J* = 55.7 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 136.9, 136.5, 135.8, 131.3, 129.0, 128.1, 127.1, 122.9, 121.1, 120.4, 117.2 (t, *J* = 290.3 Hz), 110.2, 92.1 (t, *J* = 3.6 Hz), 50.5. IR (KBr): 3106, 3060, 3028, 2963, 1651, 1603, 1508, 1495, 1479, 1458, 1442 1387, 1357 1339, 1314, 1285, 1255, 1199, 1165, 1054, 1039, 759, 741, 731, 698, 667, 632 $cm^{-1}$. HRMS-ESI (m/z) calcd. for $[C_{16}H_{14}NF_2{}^{74}Se]^+$ ($[M + H]^+$), 332.0314; found, 332.0317.

4-((Difluoromethyl)selanyl)phenol (**2m**). Light yellow oil (31.1 mg, 70% yield from **procedure A** (*note*: *t*-BuOK (0.7 mmol) was used); petroleum ether/ethyl acetate = 5:1 (v/v) as eluents for column chromatography. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.6 Hz, 2H), 7.09 (t, *J* = 55.6 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 2H), 5.16 (s, 1H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -91.1 (d, *J* = 55.4 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.0, 138.7, 117.0 (t, *J* = 289.0 Hz), 116.6, 113.7 (t, *J* = 3.0 Hz). IR (KBr): 3398, 2931, 2855, 1622, 1596, 1584, 1510, 1493, 1450, 1433, 1336, 1268, 1190, 1172, 1150, 1077, 1062, 828, 758, 711, 686, 671, 606 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_7H_6OF_2{}^{74}Se$: 217.9611, found: 217.9607.

(Difluoromethyl)(4-nitrophenyl)selane (**2n**). Yellow oil (31.9 mg, 62% yield from **procedure A**; 13.2 mg, 26% yield from **procedure B**), petroleum ether/ethyl acetate = 20:1 (v/v) as eluents for column chromatography. $^1$H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.7 Hz, 2H), 7.82 (d, *J* = 8.7 Hz, 2H), 7.27 (t, *J* = 54.6 Hz, 1H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -89.8 (d, *J* = 54.6 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 148.4, 136.0, 132.3 (t, *J* = 2.7 Hz), 124.2, 116.1 (t, *J* = 290.7 Hz). IR (KBr): 3055, 2974, 1589, 1561, 1502, 1379, 1337, 1290, 1271, 1253, 1201, 1064, 958, 797, 770, 736, 694,

676, 652, 620 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_7H_5NO_2F_2{}^{74}Se$: 246.9513, found: 246.9506.

4-((Difluoromethyl)selanyl)benzonitrile (**2o**). Light yellow oil (29.6 mg, 64% yield from **procedure A**; 25.5 mg, 55% yield from **procedure B**), petroleum ether/ethyl acetate = 10:1 (v/v) as eluents for column chromatography. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.24 (t, *J* = 54.7 Hz, 1H). $^{19}F$ NMR (471 MHz, $CDCl_3$) δ -89.9 (d, *J* = 54.6 Hz, 2F). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 136.0, 132.7, 130.0 (t, *J* = 2.7 Hz), 118.1, 116.2 (t, *J* = 290.8 Hz), 113.2. IR (KBr): 3088, 3035, 2922, 2849, 2232, 1586, 1481, 1398, 1390, 1322, 1303, 1283, 1051, 1030, 1016, 961, 830, 717, 678, 664 $cm^{-1}$. HRMS-ESI (m/z) calcd. for $[C_8H_6NF_2{}^{74}Se]^+$ ($[M + H]^+$), 227.9688; found, 227.9688.

*Tert*-butyl 4-((difluoromethyl)selanyl)benzoate (**2p**). White solid (40.2 mg, 65% yield from **procedure A**), petroleum ether/ethyl acetate = 20:1 (v/v) as eluents for column chromatography. M.p.: 30-32 $^oC$. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 55.0 Hz, 1H), 1.60 (s, 9H). $^{19}F$ NMR (471 MHz, $CDCl_3$) δ -90.0 (d, *J* = 55.0 Hz, 2F). $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 165.0, 135.4, 132.8, 130.3, 128.8 (t, *J* = 2.7 Hz), 116.7 (t, *J* = 289.3 Hz). 81.6, 28.2. IR (KBr): 2978, 2933, 1714, 1591, 1565, 1478, 1456, 1394, 1369, 1296, 1274, 1258, 1165, 1121, 1077, 1062, 1015, 881, 849, 761, 694, 685, 667, 630 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_{12}H_{14}O_2F_2{}^{74}Se$: 302.0187, found: 302.0178.

(Difluoromethyl)(3-phenylpropyl)selane (**2q**). Yellow oil (41.2 mg, 83% yield from **procedure A**), petroleum ether as eluent for column chromatography. $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.4 Hz, 2H), 7.24-7.20 (m, 3H), 7.17 (t, *J* = 55.1 Hz, 1H),

2.88 (t, *J* = 7.3 Hz, 2H), 2.76 (t, *J* = 7.4 Hz, 2H), 2.12 (m, 2H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -91.2 (d, *J* = 55.1 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 140.9, 128.5, 128.5, 126.2, 115.5 (t, *J* = 285.8 Hz), 35.7, 32.4, 22.2 (t, *J* = 2.6 Hz). IR (KBr): 3085, 3063, 3027, 2937, 2855, 1603, 1496, 1454, 1422, 1299, 1279, 1239, 1195, 1179, 1060, 1033, 909, 795, 745, 699 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_{10}H_{12}F_2{}^{74}Se$: 244.0132, found: 244.0135.

(Difluoromethyl)(octyl)selane (**2r**). Colorless oil (29.1 mg, 60% yield from **procedure A**), petroleum ether as eluent for column chromatography. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.17 (t, *J* = 55.2 Hz, 1H), 2.86 (t, *J* = 7.5 Hz, 2H), 1.76 (m, 2H), 1.40 (m, 2H), 1.34-1.27 (m, 8H), 0.89 (t, *J* = 6.8 Hz, 3H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -91.5 (d, *J* = 55.2 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 115.5 (t, *J* = 286.2 Hz), 31.8, 30.8, 29.8, 29.1, 29.0, 22.9 (t, *J* = 2.5 Hz), 22.6, 14.1; IR (KBr): 2957, 2927, 2855, 1465, 1378, 1297, 1279, 1235, 1060, 1041, 721, 692 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_9H_{18}F_2{}^{74}Se$: 238.0601, found: 238.0593.

(Difluoromethyl)(hexadecyl)selane (**2s**). Colorless oil (62.8 mg, 88% yield from **procedure A**), petroleum ether as eluent for column chromatography. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.17 (t, *J* = 55.1 Hz, 1H), 2.86 (t, *J* = 7.5 Hz, 2H), 1.76 (m, 2H), 1.39 (m, 2H), 1.32-1.26 (m, 24H), 0.89 (t, *J* = 6.8 Hz, 3H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -91.5 (d, *J* = 55.0 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 115.5 (t, *J* = 286.3 Hz), 32.0, 30.8, 29.8, 29.7, 29.7 (overlap), 29.7, 29.7, 29.6, 29.5, 29.4, 29.0, 22.9 (t, *J* = 2.4 Hz), 22.7, 14.1. IR (KBr): 2924, 2853, 1465, 1376, 1297, 1278, 1058, 1042, 721, 691 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_{17}H_{34}F_2{}^{74}Se$: 350.1853, found: 350.1857.

(Difluoromethyl)(4-phenylbutan-2-yl)selane (**2t**). Yellow oil (48.3 mg, 92% yield

from **procedure A**), petroleum ether as eluent for column chromatography. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 8.2 Hz, 2H), 7.24-7.21 (m, 3H), 7.22 (t, *J* = 55.1 Hz, 1H), 3.43 (m, 1H), 2.79 (m, 2H), 2.04 (m, 2H), 1.62 (d, *J* = 7.0 Hz, 3H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -90.5 (dd, *J* = 55.1, 13.5 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 141.2, 128.5, 128.4, 126.1, 116.0 (t, *J* = 286.2 Hz), 39.8, 36.5 (t, *J* = 1.7 Hz), 33.8, 23.5. IR (KBr): 3085, 3063, 3027, 2958, 2925, 2859, 1603, 1496, 1454, 1380, 1296, 1280, 1230, 1211, 1166, 1059, 1034, 747, 698, 680 $cm^{-1}$. HRMS-EI (m/z) calcd. for $C_{11}H_{14}F_2{}^{74}Se$: 258.0288, found: 258.0293.

4-((Difluoromethyl)selanyl)-*N*-(2,6-dimethoxypyrimidin-4-yl)benzenesulfonamide (**2v**). White solid (21.2 mg, 25% yield from **procedure A** (*note*: *t*-BuOK (0.6 mmol) was used)), petroleum ether/ethyl acetate = 2:1 (v/v) as eluents for column chromatography. M.p.: 140-142 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.14 (brs, 1H), 7.92 (d, *J* = 7.6 Hz, 2H), 7.78 (d, *J* = 7.7 Hz, 2H), 7.23 (t, *J* = 54.7 Hz, 1H), 6.24 (s, 1H), 3.93 (s, 3H), 3.89 (s, 3H). $^{19}$F NMR (471 MHz, $CDCl_3$) δ -89.7 (d, *J* = 54.9 Hz, 2F). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 172.8, 164.5, 158.4, 140.2, 135.9, 130.9 (t, *J* = 3.0 Hz), 128.1, 116.3 (t, *J* = 290.3 Hz), 85.9, 54.9, 54.3. IR (KBr): 3216, 3082, 2996, 2954, 2897, 2864, 1600, 1585, 1476, 1458, 1440, 1384, 1361, 1326, 1287, 1208, 1181, 1153, 1108, 1088, 1075 1062, 1042, 1011, 998, 983, 884, 825, 786, 743, 667, 624 $cm^{-1}$. HRMS-ESI (m/z) calcd. for $[C_{13}H_{14}F_2N_3O_4S^{74}Se]^+$ ($[M + H]^+$): 419.9892, found: 419.9898.

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**Supplementary data**

The Supplementary data ($^{1}H$, $^{19}F$, and $^{13}C$ NMR spectra for all products) associated with this article can be found free of charge online.

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