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Fluoroalkylation of Various Nucleophiles with Fluoroalkyl Sulfones Through a Single Electron Transfer Process

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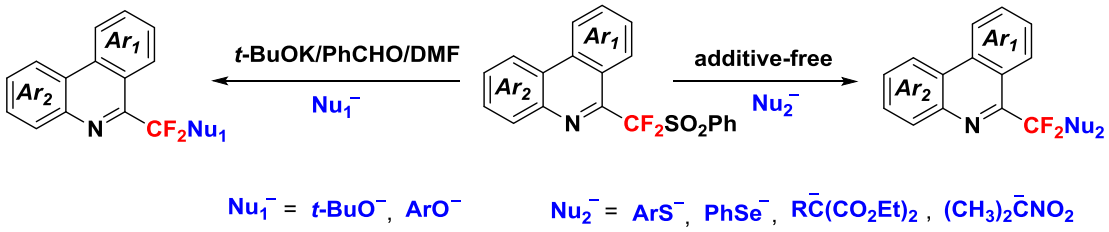
Table of Contents



Abstract: The fluoroalkylation of various nucleophilic reagents with (phenylsulfonyl)difluoromethyl ($PhSO_2CF_2$)-substituted phenanthridines was achieved to give fluorinated phenanthridine derivatives, which enables the construction of both carbon–heteroatom and carbon–carbon bonds via nucleophilic substitution of the phenylsulfonyl group. Mechanistic studies indicated that these reactions proceed through unimolecular radical nucleophilic substitution ($S_{RN}1$) mechanism. It is worthwhile noting that in the cases of *O*-nucleophiles (*t*-BuO^- and PhO^-), the addition of *t*-BuOK/PhCHO could significantly promote the reactions, due to the in-situ formation of a highly reactive electron donor species through the interaction of *t*-BuOK, PhCHO and the solvent DMF, which can effectively initiate the single electron transfer (SET) process.

Introduction

Recently, organofluorine chemistry has been a research field of great interest as fluorine plays conspicuous and increasing important roles in pharmaceuticals, agrochemicals, as well as in materials science.[1,2] Therefore, the quest for new reagents and methodologies to efficiently introduce various fluorine-containing moieties into structurally diverse non-fluorinated organic compounds makes this research area very attractive to scientists.[3] Meanwhile, nitrogen-containing heterocycles are a class of important chemical structures,[4] among which the phenanthridine core is commonly present in many biologically active and medicinally useful natural products.[5] In addition, some phenanthridine derivatives have been used as luminescent materials.[6] In this context, selectively incorporating organofluorine functionalities into phenanthridine rings may significantly improve their biological activity and optoelectronic property due to the unique role of fluorine substitution.[1c,2a,7,8]

Fluoroalkyl phenyl sulfones (R_fSO_2Ph) have been developed as versatile fluoroalkylation reagents and used for introducing diverse fluoroalkyl groups into organic molecules by us and others.[9-11] It has been reported that R_fSO_2Ph can be converted to R_fTMS (TMS = trimethylsilyl)[9a] or R_fH[9b-f] under the reduction of magnesium. In the presence of alkoxide or hydroxide, R_fSO_2Ph can be attacked by nucleophiles to remove the $PhSO_2$ group and to give rise to fluoroalkyl carbanions, which further react with electrophiles such as PhSSPh and PhCHO or are cuparated by Cu(I) salt to generate R_fCu.[10] Furthermore, R_fSO_2Ph can be transformed to fluorinated olefins under certain condtions.[11] However, the use of R_fSO_2Ph for radical fluoroalkylation by R_f–SO_2Ph bond cleavage to form R_f• radicals is still underdeveloped due to the weak electron-transfer ability of many conventional radical initiators towards R_fSO_2Ph.[12] Indeed, it is only in early 2016 that synthetically useful radical fluoroalkylations with fluorinated sulfones were reported by the virtue of heteroaryl sulfone reagents.[13] Recently, we have disclosed a method to prepare phenylsulfonyldifluoromethyl ($PhSO_2CF_2$)-substituted phenanthridines such as **1a** (Scheme 1) by the process of radical fluoroalkylation with difluoromethyl phenyl

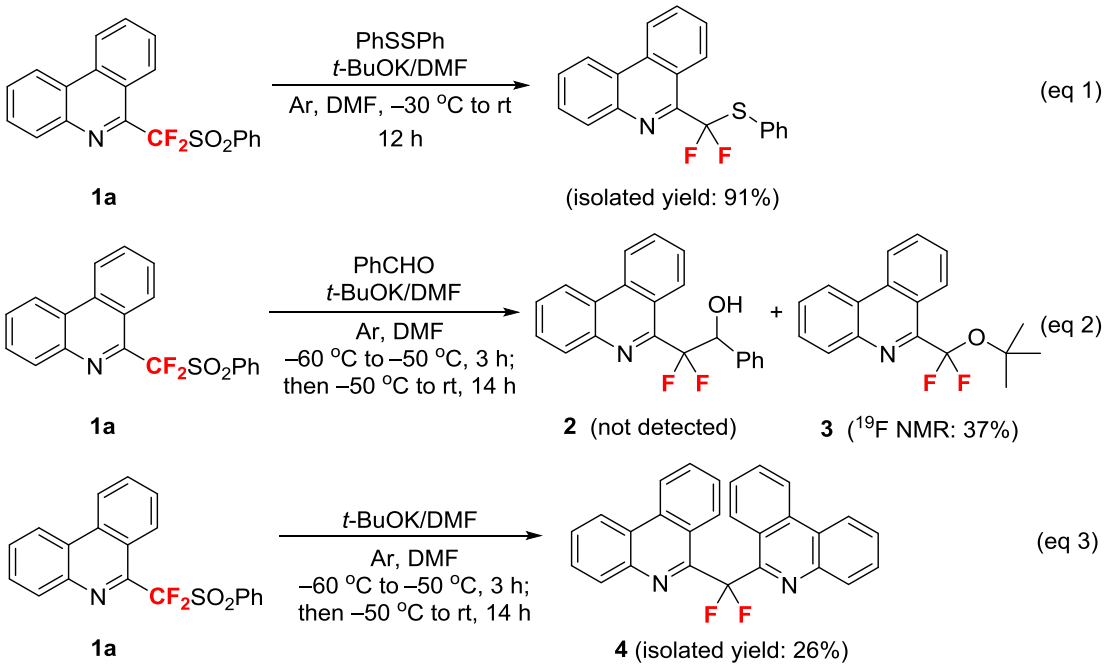
sulfone ($PhSO_2CF_2H$).[14] To expand the application of **1a** and its derivatives, it is of great interest to further modify these compounds by developing new desulfonative transformations. Herein, we report the radical difluoroalkylation reactions of 6-[difluoro(phenylsulfonyl)methyl]phenanthridines with various nucleophiles through unimolecular radical nucleophilic substitution ($S_{RN}1$) mechanism, which represent a new reaction mode of R_fSO_2Ph.

Results and Discussion

1. Initial results. Recently, we accomplished the substitution of $PhSO_2$ group in **1a** with PhS group using PhSSPh as the electrophilic reagent under the attack of *t*-BuOK (Scheme 1, eq 1),[14] which was shown to proceed through a fluoroalkyl carbanion intermediate.[10a-b] However, when PhCHO was used instead of PhSSPh as an electrophile, it was surprising to observe that the *O*-fluoroalkylation product **3** rather than the expected alcohol **2** was formed (Scheme 1, eq 2). This unusual result indicates that the reaction of **1a** with *t*-BuOK and PhCHO did not involve a fluoroalkyl carbanion intermediate. On the contrary, in the absence of PhCHO or any other electrophiles, **1a** underwent attack by *t*-BuOK and further reacted with another molecule of itself to generate **4** (instead of **3**) as the main product (Scheme 1, eq 3),[14] thus revealing that the addition of PhCHO plays an important role in the formation of the *O*-fluoroalkylation product **3**. Inspired by previous reports that a single electron transfer (SET) pathway may be involved in the Cannizzaro reaction,[15] we envisioned that the reaction of **1a** with *t*-BuOK in the presence of PhCHO may proceed through an unimolecular radical nucleophilic substitution ($S_{RN}1$) process, where the combination of *t*-BuOK/PhCHO serves as the initiator. The unprecedented reactivity of **1a** towards potassium *tert*-butoxide demonstrated a proof of concept for the further development of radical transformation of R_fSO_2Ph with a series of nucleophiles. To our knowledge, there has been no report describing the $S_{RN}1$ reaction between a fluoroalkyl sulfone and a nucleophilic reagent. Previously, fluoroalkyl halides rather

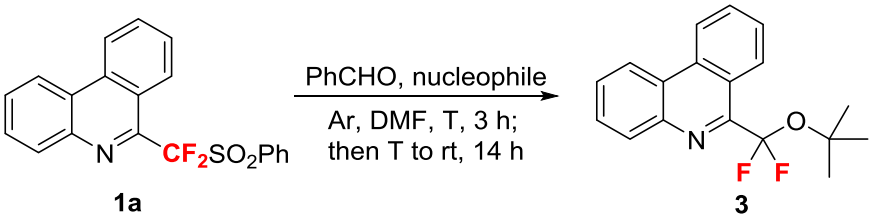
than fluoroalkyl sulfones were normally used for the fluoroalkylation of nucleophilic reagents.[16]

Scheme 1. Desulfonative transformations of 1a.



2. Alcoholates as nucleophiles. Our investigation for the desulfonative fluoroalkylations started from the optimization of the reaction conditions for the generation of compound **3** by using **1a** as substrate, *t*-BuOK as nucleophile, PhCHO as additive, and DMF as solvent, respectively (Table 1). When the molar ration of **1a**: *t*-BuOK: PhCHO was 1.0: 2.0: 1.0, we examined the effect of temperature on the reaction. As is shown in Table 1, it is clear that the starting temperature significantly affected the reaction. The yield of **3** decreased significantly as the starting temperature was elevated to room temperature, and temperatures between –60 °C and –50 °C were the optimal starting temperatures for the reaction (Table 1, entries 1-4). When *t*-BuONa was used instead of *t*-BuOK as the nucleophile, the reaction became very sluggish, which revealed the importance of the countercation effect in the reaction (Table 1, entry 5). Subsequently, we screened the equivalents of *t*-BuOK and found

Table 1. Optimization of reaction conditions for the formation of 3.[a]



1a **3**

entry	nucleophile	**1a**: nucleophile: PhCHO	T (°C)	**3** (%)[b]
1	*t*-BuOK[c]	1.0: 2.0: 1.0	–60~–50	52
2	*t*-BuOK[c]	1.0: 2.0: 1.0	–30	42
3	*t*-BuOK[c]	1.0: 2.0: 1.0	rt	11
4	*t*-BuOK[c]	1.0: 2.0: 1.0	50	17
5	*t*-BuONa[d]	1.0: 2.0: 1.0	–60~–50	6
6	*t*-BuOK[c]	1.0: 1.5: 1.0	–60~–50	22
7	***t*-BuOK**[c]	**1.0: 2.5: 1.0**	–60~–50	**67**
8	*t*-BuOK[c]	1.0: 3.0: 1.0	–60~–50	54
9	*t*-BuOK[c]	1.0: 2.5: 0	–60~–50	3
10	*t*-BuOK[c]	1.0: 2.5: 0.5	–60~–50	59
11	*t*-BuOK[c]	1.0: 2.5: 1.5	–60~–50	57
12	*t*-BuOK[c]	1.0: 2.5: 2.0	–60~–50	39

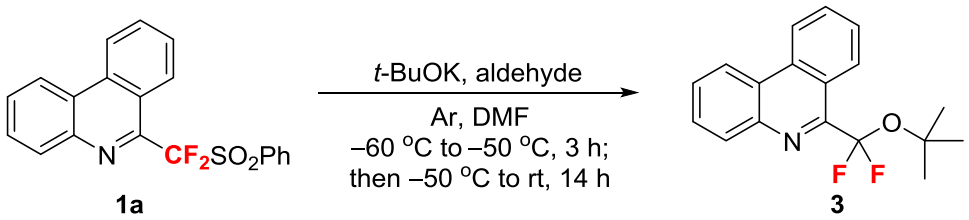
[a]Reaction conditions: **1a** (0.1 mmol), DMF (0.8 mL), under argon atmosphere. [b]Yields were determined by ^{19}F NMR spectroscopy using $PhOCF_3$ as an internal standard. [c]*t*-BuOK/DMF (1.0 M) was prepared by dissolving *t*-BuOK in DMF, and was then added dropwise into the reaction system. [d]*t*-BuONa/DMF (1.0 M) was used.

that 2.5 equiv of *t*-BuOK was optimal for the formation of **3** (Table 1, entries 1, 6-8). In addition, the amounts of PhCHO could also affect the reaction significantly, with 1.0 equiv being the optimal amount (Table 1, entries7, 9-12). It is noteworthy that the desired *O*-fluoroalkylation reaction was very sluggish in the absence of PhCHO (Table 1, entry 9), thus demonstrating that PhCHO plays a crucial role in the generation of **3**.

We also investigated the influence of other carbonyl compounds by replacing PhCHO with additives including aromatic aldehydes, aliphatic aldehydes and aromatic ketones (Table 2). Compared with PhCHO (Table 2, entry 1), electron-rich aromatic aldehydes (Table 2, entries 2-6), benzaldehydes bearing weak

electron-withdrawing groups (Table 2, entries 7-8), and 2-naphthaldehyde (Table 2, entry 13) had relatively small effect on the reaction. However, 1,4-phthalaldehyde (Table 2, entry 9) and benzaldehydes with strong electron-withdrawing groups such as -NO_2 and -CN (Table 2, entries 10-12) remarkably decreased the yields of **3**. In

Table 2. Optimization of reaction conditions for the formation of 3.[a]



entry	aldehyde	**3**, yield (%)[b]
1	**PhCHO**	**67**
2	2-Me-C_6H_4CHO	44
3	3-Me-C_6H_4CHO	56
4	4-Me-C_6H_4CHO	53
5	2-MeO-C_6H_4CHO	59
6	4-MeO-C_6H_4CHO	46
7	2-CHO-C_6H_4CHO	58
8	3-CHO-C_6H_4CHO	50
9	4-CHO-C_6H_4CHO	35
10	3-O_2N-C_6H_4CHO	17
11	4-O_2N-C_6H_4CHO	0
12	4-NC-C_6H_4CHO	20
13	2-naphthaldehyde	57
14	cinnamaldehyde	46
15	isobutyraldehyde	16
16	benzophenone	18

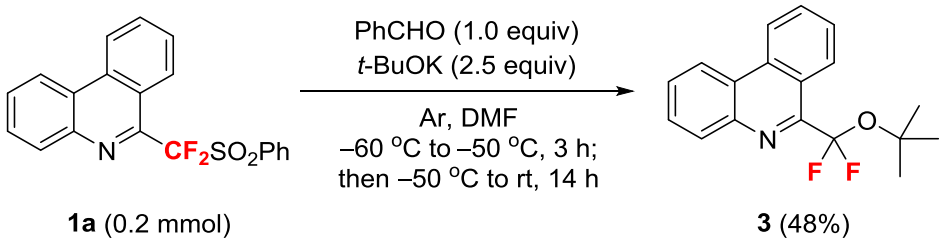
[a]Reaction conditions: **1a** (0.1 mmol), aldehyde (1.0 equiv), *t*-BuOK (2.5 equiv), DMF (0.8 mL), under argon atmosphere. [b]Yields were determined by ^{19}F NMR spectroscopy using $PhOCF_3$ as an internal standard.

addition to aromatic aldehydes, cinnamaldehyde could also give rise to moderate yield (Table 2, entry 14), but isobutyraldehyde could only afford a low yield of product (Table 2, entry 15). When benzophenone was used instead of PhCHO, the reaction

proceeded in quite low efficiency (Table 2, entry 16). In general, among all the carbonyl compounds examined, PhCHO was identified to be the most effective additive (Table 2, entry 1).

However, the "hard" nature of alkoxides (such as *tert*-butoxide) could lead to the competitive consumption of the starting material **1a** by the nucleophilic attack of an alkoxide towards $PhSO_2$, which restricted the improvement of the yield of the *O*-fluoroalkylation product. In our case, a full consumption of sulfone **1a** led to the desired product **3** only in moderate yield even under the optimized conditions, where the remainder of the mass balance was attributed to the unidentified decomposition of **1a** as well as the formation of trace amounts of 6-(difluoromethyl)phenanthridine and compound **4**. Moreover, the yield of **3** decreased significantly (Scheme 2) when the reaction was scaled up from 0.1 mmol scale to 0.2 mmol scale probably due to the increasingly competitive nucleophilic attack of *tert*-butoxide towards $PhSO_2$ to release $ArCF_2^-$.

Scheme 2. The synthesis of 3 from 1a and *t*-BuOK.



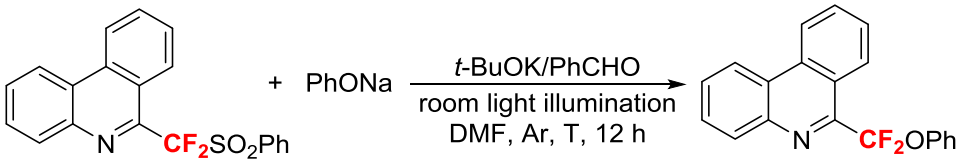
1a (0.2 mmol) **3** (48%)

To overcome the above-mentioned limitations of the substitution reaction of **1a** with alkoxides (such as *t*-BuOK), we turned our attention to the use of "soft" nucleophiles with the hope that we can develop more effective $S_{RN}1$ transformations of **1a**. Indeed, in 1974, Kornblum and co-workers reported the substitution reactions of α-nitro sulfone with several soft carbon nucleophiles via SET process, which encouraged us to pursuit the nucleophilic reactions with fluoroalkyl sulfones.[17]

3. Phenolates as nucleophiles. Phenolates has been used for the smooth displacement of the halogen atom (X) of fluoroalkyl halides (R_f-X; X = I, Br, Cl) under additive-free conditions;[16d-f] however, PhONa failed to react with **1a** under

similar conditions, even at elevated temperatures (Table 3, entries 1-3), indicating that the direct electron transfer from phenoxide ion to **1a** is inefficient. Considering that the addition of PhCHO could promote the reaction between **1a** and *t*-BuOK, we tried the reaction between **1a** and PhONa in the presence of *t*-BuOK and PhCHO. To our delight, when *t*-BuOK (1.0 equiv) and PhCHO (1.0 equiv) were added, the reaction proceeded smoothly at room temperature and the desired product **6a** was observed in 68% ^{19}F NMR yield (Table 3, entry 4). A screening of the amount of PhONa showed that 3.0 equiv are optimal for the reaction (Table 3, entries 5-6). In the above-mentioned conditions, *t*-BuOK was added in solid form. An optimization of the experimental procedures showed that the dropwise addition of the DMF solution of *t*-BuOK could result in a much higher yield of **6a** (> 99% yield based on ^{19}F NMR, 93% yield after isolation) than the addition of the *t*-BuOK solid in one portion (88% yield

Table 3. Optimization of reaction conditions for the formation of 6a.[a]



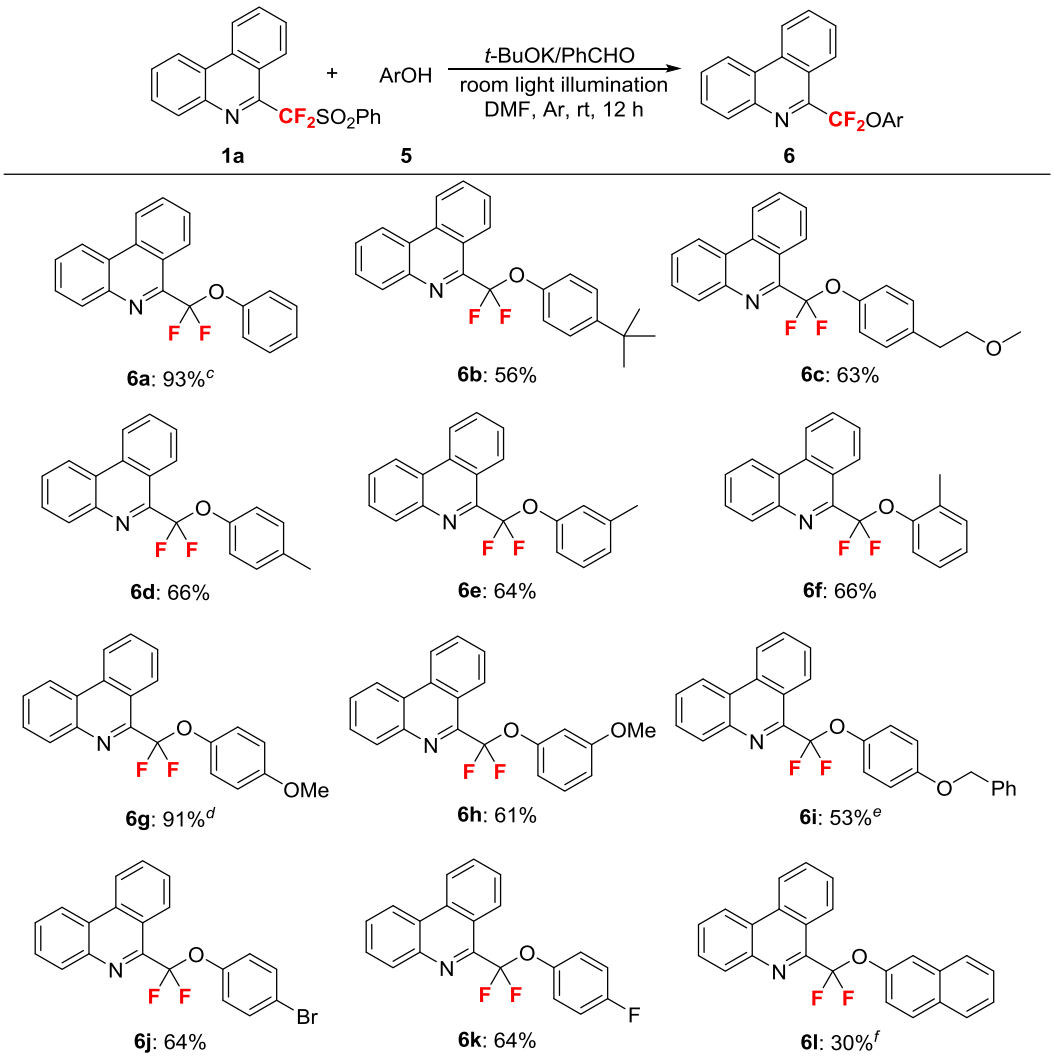
1a **5a** **6a**

entry	**1a**: PhONa	*t*-BuOK: PhCHO	T (°C)	**6a**, yield (%)[b]
1	1: 2	——	–50~rt	trace
2	1: 2	——	80	trace
3	1: 2	——	100	trace
4	1: 2	1.0: 1.0	rt	68
5	1: 3	1.0: 1.0	rt	88
6	1: 4	1.0: 1.0	rt	88
7[c,d]	**1: 3**	**1.0: 1.0**	**rt**	**> 99 (93**[e]**)**
8[c]	1: 3	0: 1.0	rt	trace
9[c]	1: 3	1.0: 0	rt	17

[a]Reaction conditions: **1a** (0.1 mmol), DMF (1.0 mL), under argon atmosphere. [b]Yields were determined by ^{19}F NMR spectroscopy using $PhOCF_3$ as an internal standard. [c]A DMF solution of *t*-BuOK was added dropwise into the reaction system. [d]Reaction conditions: **1a** (0.2 mmol), DMF (2.0 mL), under argon atmosphere. [e]Isolated yield.

based on ^{19}F NMR) (Table 3, entries 5 and 7). Control experiments in the presence of either *t*-BuOK or PhCHO afforded the product **6a** in only trace to low yields, demonstrating that the interaction between *t*-BuOK and PhCHO plays a crucial role (Table 3, entries 8 and 9).

Table 4. The substitution reactions of 1a with phenol derivatives 5.[a,b]

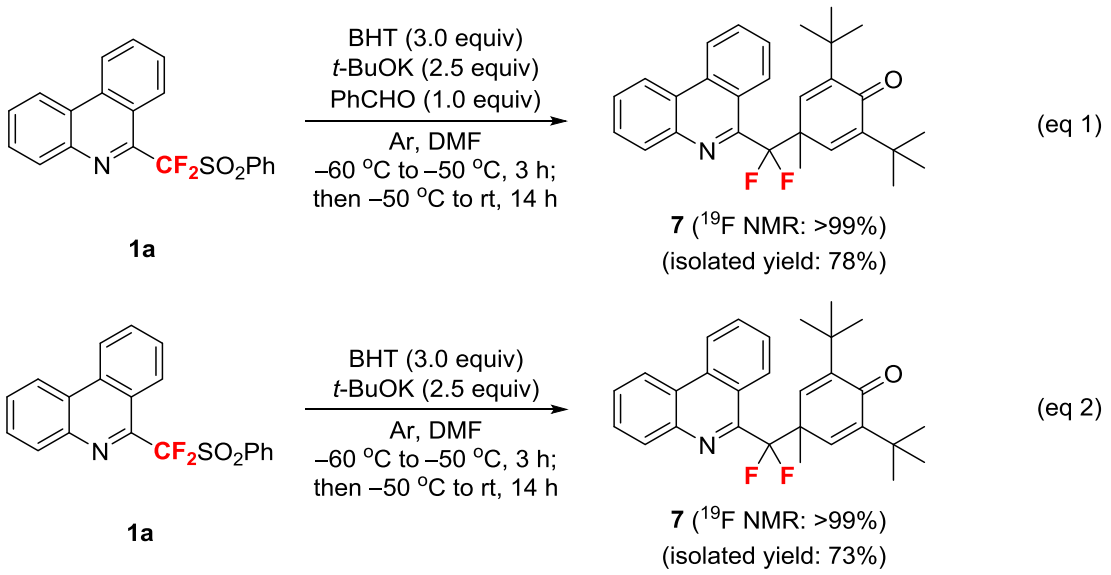


[a]Reaction conditions: **1a** (0.2 mmol), **5** (2.7 equiv), *t*-BuOK (3.6 equiv), PhCHO (1.0 equiv), DMF (2.0 mL), under argon atmosphere, 12 h (unoptimized reaction time). [b]Isolated yields. [c]Reaction conditions: **1a** (0.2 mmol), PhONa (3.0 equiv), *t*-BuOK (1.0 equiv), PhCHO (1.0 equiv), under argon atmosphere. [d]Contaning 4% of side product **2**. [e]Isolated yield was given by recrystallization. [f]Yield was determined by ^{19}F NMR spectroscopy using $PhOCF_3$ as an internal standard.

Encouraged by the above results, we investigated the scope of the phenolate nucleophiles by slightly modifying the optimized reaction conditions shown in entry 7 of Table 3. Although phenolates can be used as isolated reagents, we chose phenols **5** as the pronucleophiles due to their ready availability; meanwhile, *t*-BuOK was used as both the base for deprotonation and one of the components of the initiator (Table 4).

The reaction proved to be general and amenable to a range of structurally diverse phenols **5**, and the desired products **6** were obtained in moderate to excellent yields. We found that the electronic nature of the phenols can significantly affect the reaction, with the electron-rich phenols (**6b**-**6i**) being more reactive than the electron-deficient one (**6l**). In the cases of methyl-substituted phenols, the substitution site of methyl had little influence on the outcome (**6d**-**6f**); whereas in the cases of methoxy-substituted phenols, the *para*-substituted one (**6g**) was found to be more reactive than the *meta*-substituted one (**6h**). It is of note that some phenols with a halogen substituent are also viable pronucleophiles in the current reaction (**6j** and **6k**), probably due to the π-electron-donating (resonance) effect of the halogen atom. In most cases, the decrease of the yields probably arose from the side reaction of **1a** induced by *t*-BuOK. Interestingly, when the salt of an antioxidant, butylated hydroxytoluene (BHT) was used as the nucleophilic reagent, the *C*-alkylation product **7** was isolated in 78% yield. Moreover, the same reaction proceeded smoothly even in the absence of PhCHO (Scheme 3, eqs 1 and 2). Here, the extremely electron-rich phenolate anion derived from BHT serves as the reducing agent, which transfers a single electron to **1a** to afford a difluoroalkyl radical ($ArCF_2$•) and an aryloxy radical (ArO•). The following step may proceed either through the combination of two radicals or through an $S_{RN}1$ mechanism, where the *C*-alkylation selectivity can be explained by the steric hindrance of the aryloxy radical or anion.

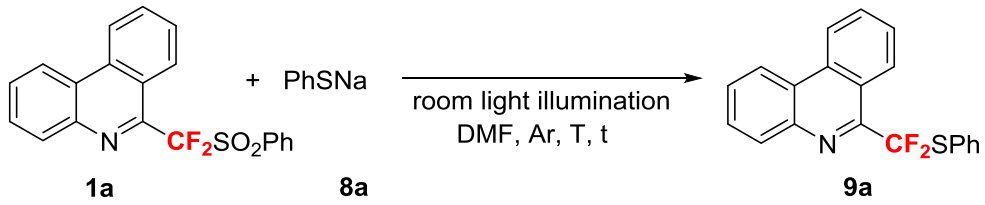
Scheme 3. The substitution reaction of 1a with BHT.



4. Thiolates and selenolates as nucleophiles. Thiolate and selenolate anions are softer nucleophiles than alcoholate and phenolate anions. On the basis of the successful reaction of **1a** with a wide variety of phenolates, we further explored the reactivity of **1a** towards thiolates and selenolates.

The reaction of PhSNa and **1a** in a molar ratio of 1:2 in DMF was chosen as the model reaction (Table 5). It was found that the displacement of $PhSO_2$ group with PhS group could readily occur at room temperature in the absence of any additive (Table 5, entry 1), which can be attributed to the strong single electron-donating ability of PhS^- endowed by the high electronic polarizability of sulfur atom. A quick optimization of the reaction conditions showed that there are two viable methods for improving the yields of **9a**: raising the reaction temperature from room temperature to 110 ^oC (Table 5, entry 3) or increasing the amount of PhSNa from 2 equiv to 4 equiv (Table 5, entry 4); the latter method can lead to slightly higher yield of **9a**.

Table 5. Optimization of reaction conditions for the formation of 9a.[a]



1a **8a** **9a**

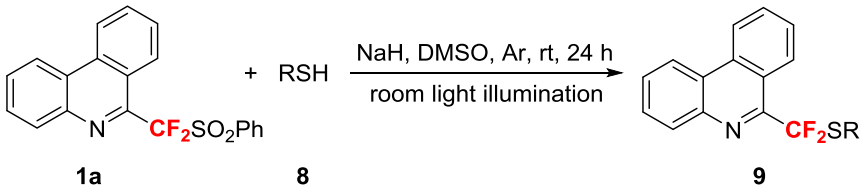
entry	**1a**: PhSNa	T (°C)	t (h)	**9a**, yield (%)[b]
1	1: 2	rt	24	83
2	1: 2	80	24	86
3	1: 2	110	8	98
4	**1: 4**	**rt**	**12**	**>99**

[a]Reaction conditions: **1a** (0.1 mmol), DMF (1.0 mL), under argon atmosphere. [b]Yields were determined by ^{19}F NMR spectroscopy using $PhOCF_3$ as an internal standard.

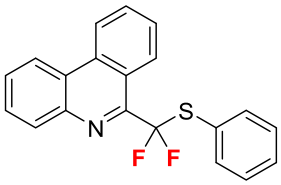
After achieving the fluoroalkylation of PhSNa with **1a**, we investigated the scope of the thiolate nucleophiles (Table 6). For convenience, the thiolates were *in situ* prepared by deprotonation of the corresponding thiols with NaH (95%) or *t*-BuOK. When 2-mercaptopyridine was used as the pronucleophile, we found that DMSO was superior to DMF in respect to promoting the reaction (**9b**). Therefore, in the subsequent investigation, DMSO was used as the solvent to conduct the reactions of **1a** with thiolates. For most of the thilolates tested, their reactions proceeded smoothly to afford **9** in moderate to excellent yields (**9a**-**9h**). Electron-neutral aryl substituted thiolates such as PhSNa and 2-naphthalenethiol exhibited the highest reactivity (**9a** and **9c**); whereas the substitution of thiophenolate with a weak electron-withdrawing group (EWG) such as F, Cl and Br, slightly decreased the efficiency of the reaction (**9d-9f**). However, further enhancing the electron-withdrawing ability of the substituent on the thiophenolates by incorporating CF_3 or five fluorine atoms dramatically or even completely inhibited the reaction (**9k** and **9l**) due to the decreased single electron donating ability of the thiloates, as is indicated by the low conversion of **1a**. Similarly, *para* electron-donating groups (EDG) such as MeS, MeO, and *t*-Bu also showed inhibition effect on the desired reaction (**9g**, **9i** and **9j**). However, MeS group showed less significant influence than MeO and *t*-Bu groups. In

the cases of MeO- and *t*-Bu-substituted thiolates, the low yields of **9** mainly arose from the decomposition of **1a**. In addition, a benzylmercaptan could also take part in the reaction, albeit affording product **9h** in only moderate yield.

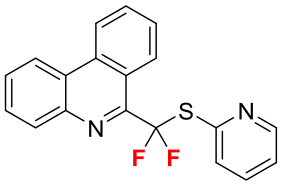
Table 6. The substitution reactions of 1a with thiolates.[a]



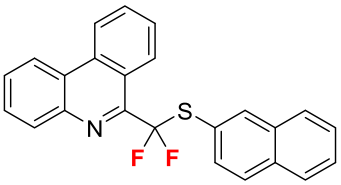
1a **8** **9**



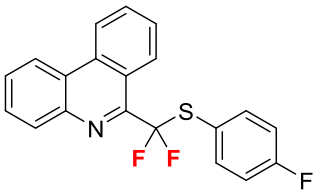
9a: 97%[b, c]



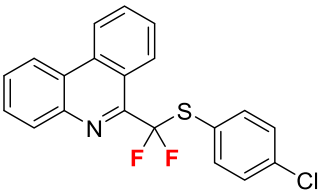
9b: 65%[b, d]



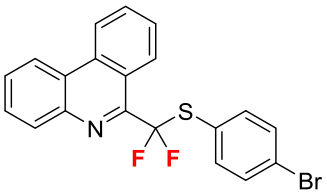
9c: 93%[b]



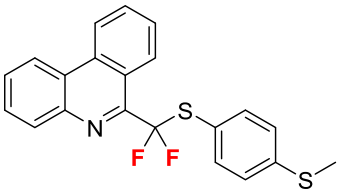
9d: 91%[b]



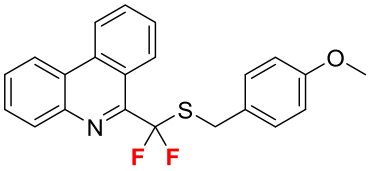
9e: 81%[b]



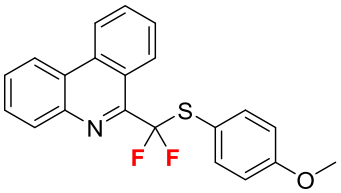
9f: 79%[b]



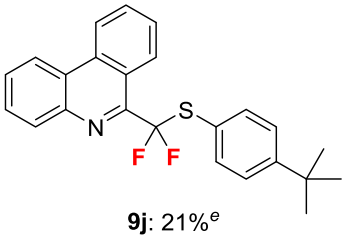
9g: 77%[b]



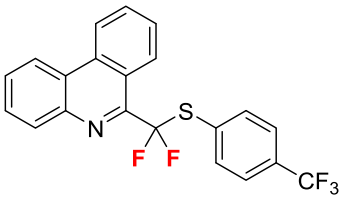
9h: 40%[b]



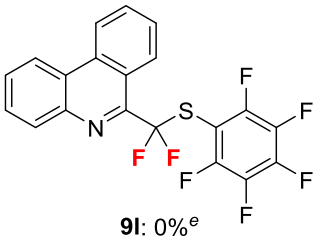
9i: 30%[e]



9j: 21%[e]



9k: < 20%[e]

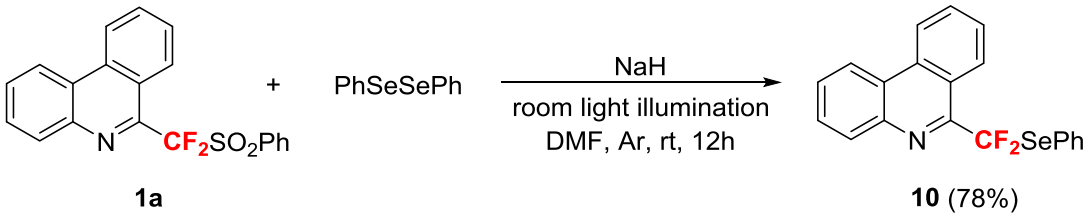


9l: 0%[e]

[a]Reaction conditions: **1a** (0.2 mmol), **8** (4.0 equiv), NaH (4.0 equiv), DMSO (2.0 mL), under argon atmosphere. [b]Isolated yields. [c]Reaction conditions: **1a** (0.2 mmol), PhSNa (4.0 equiv), DMF (2.0 mL), under argon atmosphere. [d]Reaction conditions: **1a** (0.2 mmol), 2-PySH (3.5 equiv), *t*-BuOK (4.4 equiv), PhCHO (1.0 equiv), DMSO (2.0 mL), under argon atmosphere, 72 h. [e]Yields were determined by ^{19}F NMR spectroscopy using $PhOCF_3$ as an internal standard.

Selenolates are also viable nucleophilic reagents. The fluoroalkylation of PhSeNa that was *in-situ* generated from the reduction of PhSeSePh with NaH[18] afforded the desired product **10** in 78% isolated yield by conducting the reaction of **1a**, PhSeSePh and NaH in a molar ratio of 1:4:8 in DMF (Scheme 4).

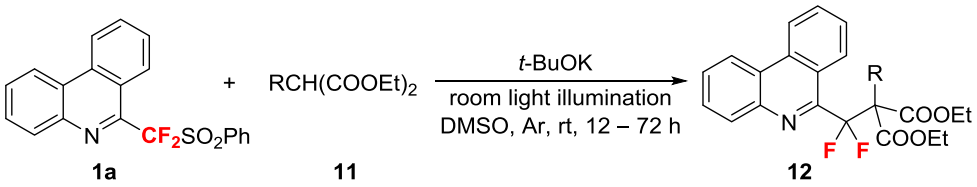
Scheme 4. The substitution reaction of 1a with *in situ* generated PhSeNa.



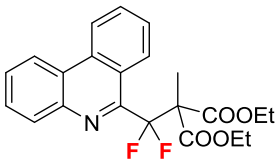
1a **10** (78%)

5. The salts of diethyl malonate derivatives as nucleophiles. A screening of carbon nucleophiles showed that the salts of monosubstituted diethyl malonates could react with **1a** efficiently, thus consisting a new protocol for the construction of FC–C bonds with the displacement of the sulfonyl group. We compared the reactivity of several *α*-monosubstituted diethyl malonates **11** towards **1a** with *t*-BuOK as the base and DMSO as the solvent, and found that the steric hindrance of **11** had a remarkable effect on this reaction (Table 7). The reaction of **1a** with the potassium salt of $CH_3CH(COOEt)_2$ (**11a**) proceeded smoothly in 12 h and the desired product **12aa** was obtained in 94% yield. However, the reaction rate declined gradually as the steric hindrance of pronucleophiles **11** increased and a reaction time of 24 h was needed to achieve a full conversion of the potassium salts of **11b** and **11c** (**12ab**, **12ac**). In the case of pronucleophile **11d** with an *α*-benzyl substituent, much longer reaction time (72 h) was required to complete the reaction (**12ad**). The diethyl malonate derivatives bearing more sterically hindered *α*-substituents such as *i*-Pr, COOEt and $COCH_3$ could not undergo this reaction. Moreover, the salt of nonsubstituted diethyl malonate also failed to react with **1a**, probably arising from its poor single electron-donating ability.

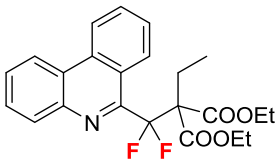
Table 7. The substitution reactions of 1a with the salts of diethyl malonate derivatives 11.[a,b]



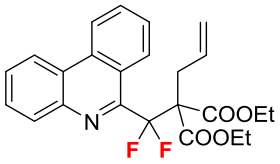
1a **11** **12**



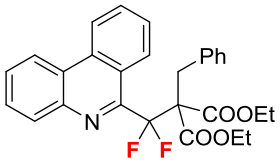
12aa: 12 h, 94%



12ab: 24 h, 95%



12ac: 24 h, 93%

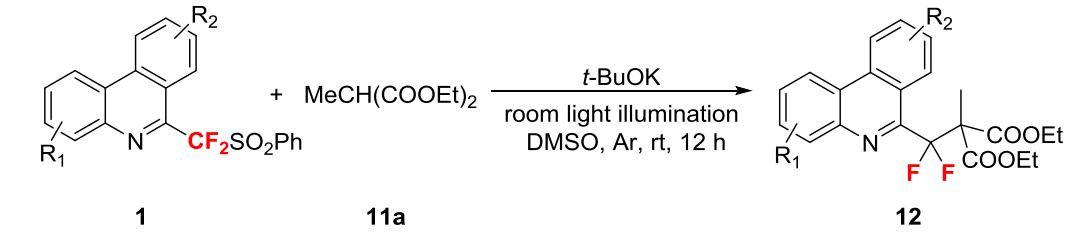


12ad: 72 h, 95%

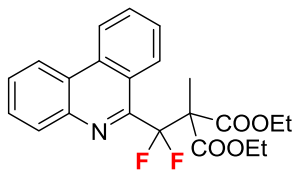
[a]Reaction conditions: **1a** (0.2 mmol), **11** (4.0 equiv), *t*-BuOK (4.0 equiv), DMSO (2.0 mL), under argon atmosphere. [b]Isolated yields.

We also investigated the scope of $PhSO_2CF_2$-substituted phenanthridines by using $CH_3CH(COOEt)_2$ (**11a**) as a representative pronucleophile, and found that a variety of previously prepared[14] 6-[difluoro(phenylsulfonyl)methyl]phenanthridine derivatives (**1a-1j)** bearing either electron-withdrawing or electron-donating groups could be transformed into the corresponding products **12** in excellent yields (Table 8). This desulfonative difluoroalkylation reaction tolerates various functional groups on **1**, such as sulfonyl, trifluoromethyl, methyl, phenyl, fluoride, and chloride. In the cases of sulfonyl-, fluoro- and chloro-substituted phenanthridines that were susceptible to undergo nucleophilic aromatic substitution (S_NAr), the reaction only took place at the $PhSO_2CF_2$ group.

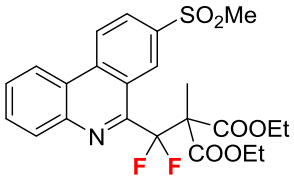
Table 8. The Substitution Reactions of 1 with the Salt of 11a.[a,b]



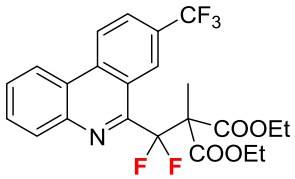
1 **11a** **12**



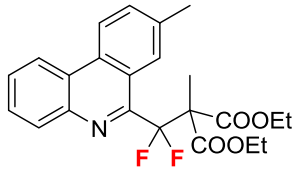
12aa: 94%



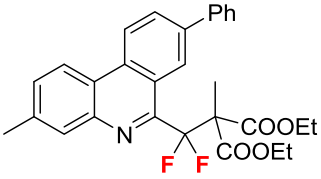
12ba: 98%



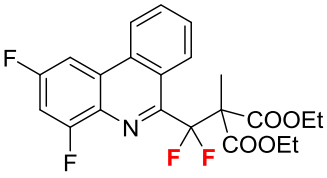
12ca: 96%



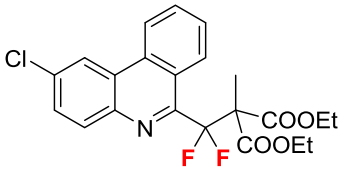
12da: 90%



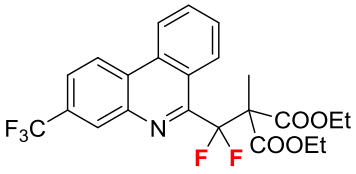
12ea: 93%



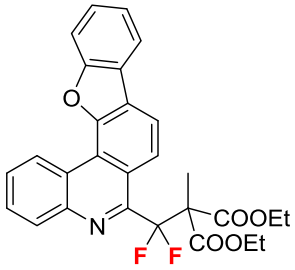
12fa: 90%



12ga: 99%



12ha: 88%



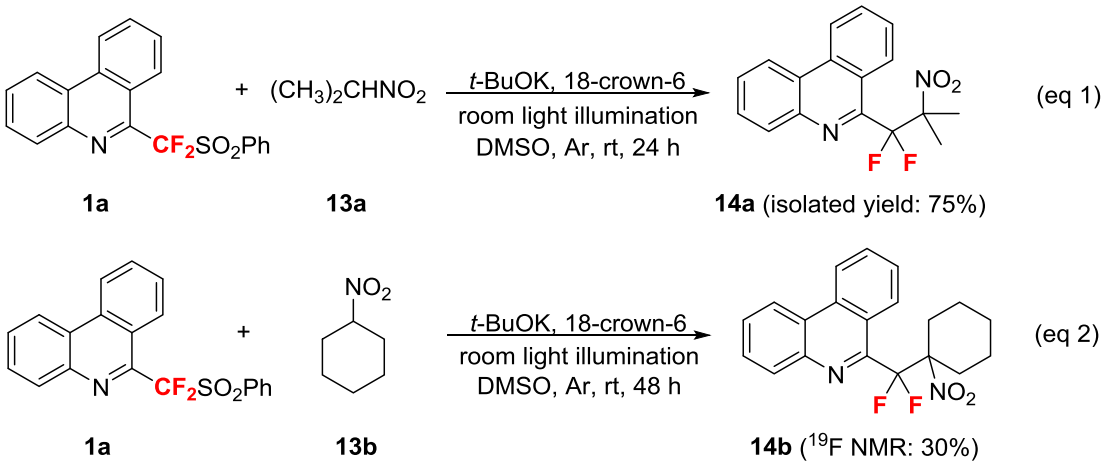
12ia: 91%

[a]Reaction conditions: **1** (1.0 equiv), **11a** (4.0 equiv), *t*-BuOK (4.0 equiv), DMSO, under argon atmosphere. [b]Isolated yields.

6. The salt of 2-nitropropane as nucleophile. 2-Nitropropane (**13a**) could be deprotonated by *t*-BuOK and then reacted with **1a** to give the corresponding product **14a**. However, the relatively low solubility of the *in situ* generated potassium salt of **13a** in DMSO led to a slow reaction rate at room temperature, thus the desired product **14a** was observed in a quite low yield (29% based on ^{19}F NMR spectroscopy) after 24 h. We found that the addition of 18-crown-6 could effectively improve the yield of **14a**, and we obtained **14a** in 75% isolated yield when 2.4 equiv of 18-crown-6 were used (Scheme 5, eq 1). On this basis, we further explored the

reaction of **1a** with nitrocyclohexane (**13b**) at room temperature. The result turned out to be unsatisfactory, with only 30% yield of the desired product **14b** being observed by ^{19}F NMR spectroscopy even when the reaction time was prolonged to 48 h (Scheme 4, eq 2). The significant drop of the yield reveals that increased steric hindrance was detrimental to the substitution reaction.

Scheme 5. The substitution reactions of 1a with the salt of niroalkanes 13.



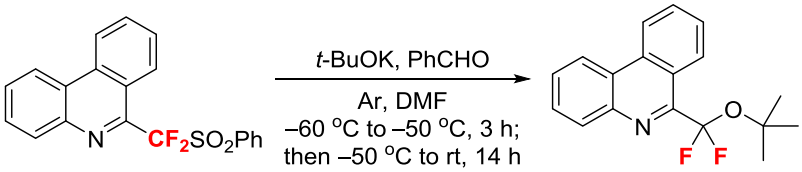
7. Mechanistic investigations. To gain more insights into the present desulfonative fluoroalkylation reaction, we carried out mechanistic investigations.

Firstly, to probe the possibility of a radical mechanism, we tested the retarding effect of several radical inhibitors on the standard reactions of **1a** with various nucleophiles. The results are summarized in Table 9 and Tables S1-S5 (See the Supporting Information).

As is shown in Table 9, the reaction of **1a** with *t*-BuOK was largely or completely inhibited by single electron transfer inhibitors such as *m*-dinitrobenzene and *p*-dinitrobenzene, and free radical scavengers such as 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and O_2. The reaction of **1a** with PhONa in the presence of *t*-BuOK/PhCHO was retarded similarly (See Supporting Information, Table S1). Taken together with our initial understanding on the role of *t*-BuOK/PhCHO, we believed that the reaction proceeded through a SET chain

process that was initiated by an electron donor species related to PhCHO (Scheme 6). Initially, "electron donor **A**" that is formed by the interaction of *t*-BuOK/PhCHO acts the initiator and donates a single electron to **1a** to generate the radical anion **B**. Then the resulting radical anion **B** undergoes a fragmentation to release difluoroalkyl radical **C** and $PhSO_2^-$. Subsequently, the combination of **C** with a nucleophile (Nu^- = *t*-BuO^-, PhO^-) leads to the formation of a new radical anion **D**. Finally, intermediate **D** transfers a single electron to another molecule of **1a** to produce the product **15** and regenerate intermediate **B**.

Table 9. Control Experiments of 1a with *t*-BuOK.[a]

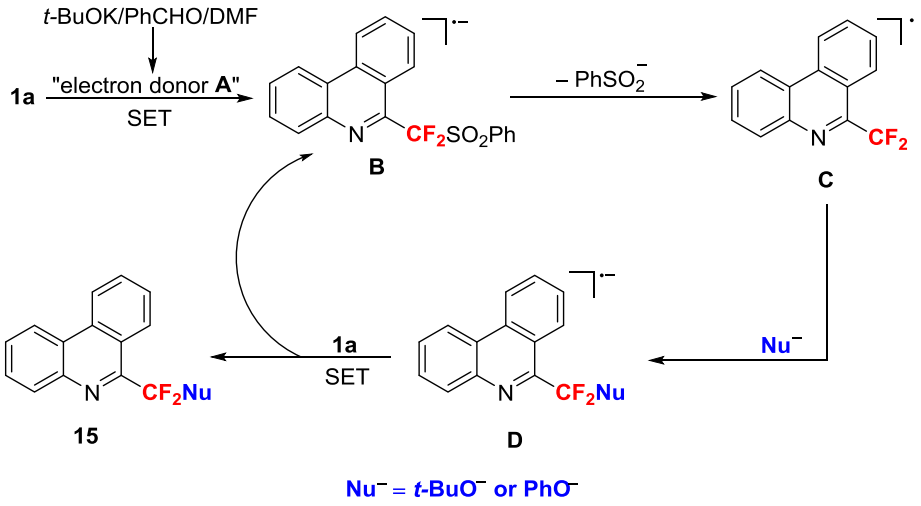


1a **3**

entry	change of standard conditions	**3**, yield (%)[b]
1	——	67
2	In the presence of *m*-dinitrobenzene (1.0 equiv)	4
3	In the presence of *p*-dinitrobenzene (1.0 equiv)	6
4	In the presence of TEMPO (3.0 equiv)	0
5	Replacing Ar with O_2	0

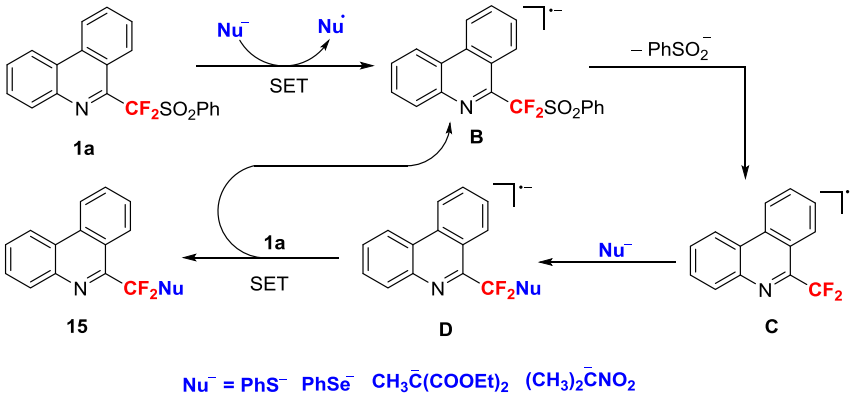
[a]Reaction conditions: **1a** (0.1 mmol), PhCHO (1.0 equiv), *t*-BuOK/DMF (1.0 M) (0.25 mL), DMF (0.8 mL), under argon atmosphere. [b]Yields were determined by ^{19}F NMR spectroscopy using $PhOCF_3$ as an internal standard.

Scheme 6. Plausible mechanism of the reaction of 1a with *t*-BuOK (or PhONa).



Radical inhibition experiments (See the Supporting Information, Tables S2-S5) also support a $S_{RN}1$ mechanism in the reactions of **1a** with other nucleophilic species (PhS^-, $PhSe^-$, $^-CCH_3(COOEt)_2$ and $^-C(CH_3)_2NO_2$) (Scheme 7). In these cases, the nucleophiles itself can act as the initiators to trigger the propagation step. The radicals derived from these nucleophiles should end up with homocoupling reaction.

Scheme 7. Plausible mechanism of the reaction of 1a with other nucleophiles.



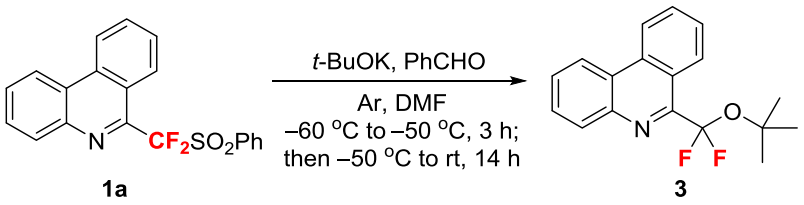
Secondly, to understand the exact role of light, we conducted the control experiments both under room light illumination and in the dark (See the Supporting Information, Tables S1-S5). It was found that room light illumination is necessary in the reactions of PhSNa, PhSeNa, and a malonate salt $KC(Me)(CO_2Et)_2$ with the

sulfone **1a** (Tables S2-S4). The same reactions in the absence of room light were found to be very sluggish. The promoting role of room light can be explained by the formation of a charge-transfer complex (CTC) of **1a** and the nucleophile (Nu^-) and its subsequent activation by the visible light to afford $\mathbf{1a}^{\bullet-}$ and Nu :[19]

However, when PhONa was used as the nucleophile (with *t*BuOK/PhCHO/DMF as the initiator) (Table S1), the reaction in DMF completed in 1 hour, giving the desired product in high yield both in the presence and the absence of the light. This indicates that room light has little influence on the reaction of phenolates.

Thirdly, to figure out the possible initiator in the reaction of **1a** with *t*-BuOK or PhONa, we investigated the roles of both the intermediates and the possible final products that are related to the Cannizzaro reaction between *t*-BuOK and PhCHO (Table 10). To evaluate the role of the Cannizzaro reaction intermediates, the mixture of *t*-BuOK and PhCHO in DMF was pre-stirred for 1 h or 2 h before adding **1a**. However, the thus formed reaction mixture could also promote the reaction of *t*-BuOK with **1a** smoothly, albeit with slightly lower yields (Table 10, entries 2-3), indicating that the initiator might be the final products rather than the intermediates. Accordingly, we replaced PhCHO with $PhCH_2OH$ and $PhCO_2t$-Bu (the main products of the Cannizzaro reaction of PhCHO), respectively, and found that the reaction yield was remarkably decreased (Table 10, entries 4-5). Also, $PhCO_2H$ resulting from either the autoxidation of PhCHO or hydroxide promoted Cannizzaro reaction of PhCHO could not promote the reaction (Table 10, entries 5-6). Thus, we ruled out the participation of either the intermediates or the final products of the Cannizzaro reaction in triggering the SET process. The participation of benzoin condensation is also unlikely, as the formation of **3** was not observed when benzoin was used instead of PhCHO (Table 10, entry 7).

Table 10. The study of intermediates in the reaction system of 1a with *t*-BuOK.[a]



1a **3**

entry	change of standard conditions	**3**, yield (%)[b]
1	——	67
2	The mixture of *t*-BuOK and PhCHO was pre-stirred for 1 h before adding **1a**	56
3	The mixture of *t*-BuOK and PhCHO was pre-stirred for 2 h before adding **1a**	59
4	Replacing PhCHO with $PhCH_2OH$ (1.0 equiv)	10
5	Replacing PhCHO with $PhCO_2t$-Bu (1.0 equiv)	2
6	Replacing PhCHO with $PhCO_2H$ (1.0 equiv)	0
7	Replacing PhCHO with benzoin (1.0 equiv)	0

[a]Reaction conditions: **1a** (0.1 mmol), PhCHO (1.0 equiv), *t*-BuOK/DMF (1.0 M) (0.25 mL), DMF (0.8 mL), under argon atmosphere. [b]Yields were determined by ^{19}F NMR spectroscopy using $PhOCF_3$ as an internal standard.

Recently, Murphy and coworkers made an elegant investigation on *t*-BuOK promoted SET processes and disclosed that the dimerization of formamides can afford strong organic electron donors such as **G** and **H** (Scheme 8, eq 1)[20], which inspired us to take into account the combinational effect of *t*-BuOK, PhCHO and DMF in our reaction system. We envisioned that the addition of the acyl anion derived from DMF to PhCHO followed by proton transfer should lead to the generation of electron donor $\mathbf{A_1}$, and further deprotonation of $\mathbf{A_1}$ should afford $\mathbf{A_2}$ with stronger electron-donating ability (Scheme 8, eq 2). To confirm this assumption, we separately prepared the precursor of intermediate **I**, *α*-hydroxyl amide **16** by reacting PhCHO and DMF with LDA as the base (Scheme 8, eq 3)[21] and examined its influence on the reaction of **1a** with *t*-BuOK and PhONa, respectively (Tables 11 and 12). Gratifyingly, by using **16** instead of PhCHO, the reaction of **1a** with *t*-BuOK afforded **3** in 47% yield when 0.4 equiv of **16** was loaded (Table 11, entry 4). For the reaction system of PhONa, only 0.2 equiv of **16** was needed to achieve an excellent conversion of **1a** (Table 12, entries 1-3). In addition, *t*-BuOK also played an important role in the reaction, as is

Scheme 8. Possible structure of "electron donor A".

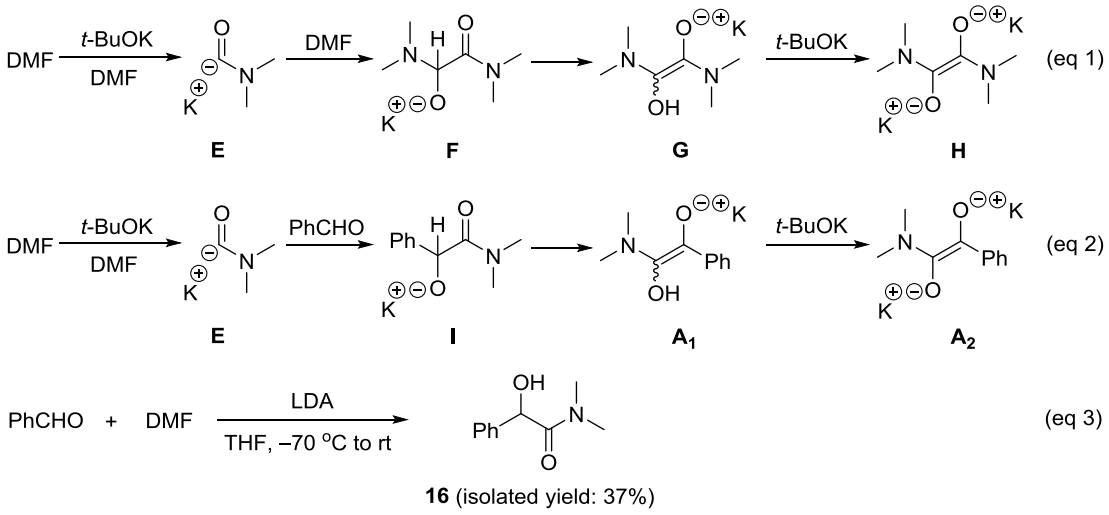
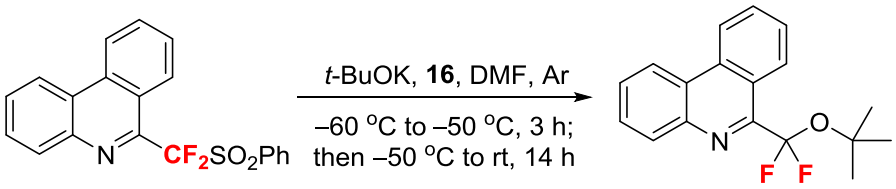


Table 11. The effect of compound 16 on the reaction of 1a with *t*-BuOK.[a]

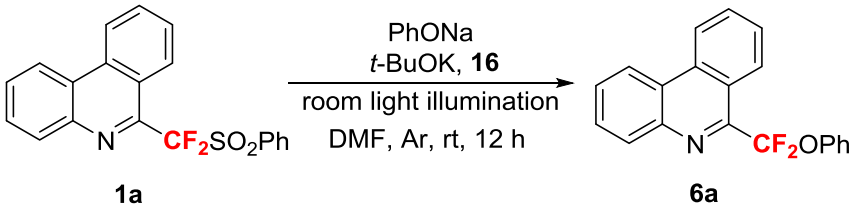


entry	**1a**: *t*-BuOK: **16**[b]	**3** (%)[c]
1	1.0: 2.5: 0	trace
2	1.0: 2.5: 0.2	11
3	1.0: 2.5: 0.3	26
4	1.0: 2.5: 0.4	47
5	1.0: 2.5: 0.5	46
6	1.0: 2.5: 0.6	40
7	1.0: 2.5: 1.0	28

[a]Reaction conditions: **1a** (0.1 mmol), DMF (0.8 mL), under argon atmosphere. [b]*t*-BuOK (1.0 M in DMF) was prepared by dissolving *t*-BuOK in DMF just before the reaction and was then dropped slowly into the reaction system. [c]Yields were determined by ^{19}F NMR spectroscopy using $PhOCF_3$ as an internal standard.

demonstrated by the dramatic decrease of the yield of **6a** when less than 1 equiv of *t*-BuOK was used (Table 12, entries 3-5). It is clear that *t*-BuOK not only promoted the deprotonation of **16** to generate intermediate **I** (Scheme 8), but also facilitated the formation of enolate $\mathbf{A_1}$ and dianion $\mathbf{A_2}$, which should serve as key electron donors in the reaction system.[20]

Table 12. The effect of compound 16 on the reaction of 1a with PhONa.[a]



1a **6a**

entry	**1a**: *t*-BuOK: **16**	**6a** (%)[b]
1	1.0: 0: 0	trace
2	1.0: 1.0: 0	17
3	1.0: 1.0: 0.2	96
4	1.0: 0.5: 0.2	38
5	1.0: 0.2: 0.2	6

[a]Reaction conditions: **1a** (0.1 mmol), PhONa (3.0 equiv), DMF (1.0 mL), under argon atmosphere. [b]Yields were determined by ^{19}F NMR spectroscopy using $PhOCF_3$ as an internal standard.

Finally, to investigate the influence of the π-system connecting to the difluoromethylene group on the single electron transfer process, we conducted the reaction of 2-$PyCF_2SO_2Ph$ and $PhCF_2SO_2Ph$ with the most challenging nucleophile *t*-BuOK. Interestingly, none of them could undergo the desired nucleophilic substitution reaction, indicating that a large conjugated structure is beneficial for the reaction. We also measured the first reduction potentials of the phenanthridine derivative **1a** (–1.20 V vs. SCE), 2-$PyCF_2SO_2Ph$ (–1.44 V vs. SCE), and $PhCF_2SO_2Ph$ (–1.55 V vs. SCE) by cyclic voltammetry (CV) and found that the single electron transfer reactivity of **1a** towards *t*-BuOK is consistent with its highest first reduction potential.[22]

Conclusions

In summary, we have developed the desulfonative fluoroalkylation of various nucleophiles with 6-[difluoro(phenylsulfonyl)methyl]phenanthridine and its derivatives, leading to the formation of new carbon–heteroatom bonds and carbon–carbon bonds with the removal of the sulfonyl group. A process of single electron transfer is likely to be involved in our reaction system. In particular, the interaction of *t*-BuOK, PhCHO and DMF might facilitate the formation of "electron donors", which then initiate the reaction between the substrate and the nucleophiles such as *t*-BuOK and PhONa which are difficult to donate a single electron.

Experimental Section

General Methods. Unless otherwise mentioned, all manipulations were conducted with a standard Schlenk tube under argon atmosphere, and reagents were purchased from commercial sources and used without further purification. Dry DMF and DMSO were distilled over CaH_2, and stored over activated molecular sieves. NMR spectra were obtained on a Bruker AV400 or Agilent MR400 (400 MHz for ^1H; 376 MHz for ^{19}F; 100 MHz for ^{13}C). ^1H NMR chemical shifts were determined relative to internal $(CH_3)_4Si$ (TMS) at : δ 0.00 ppm or to the signal of a residual protonated solvent: $CDCl_3$: δ 7.26 ppm. ^{13}C NMR chemical shifts were determined relative to internal $CDCl_3$ at : δ 77.0 ppm. ^1H, ^{13}C and ^{19}F multiplicities are reported as follows: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), triplet of quartets (tq), multiplet (m), and broad resonance (br). All the melting points were uncorrected. Mass spectra were obtained on a mass spectrometer. High-resolution mass data were recorded on a high-resolution mass spectrometer in the ESI mode.

Preparation of Starting Material 6-(Difluoro(phenylsulfonyl)methyl)phenanthridine Derivatives 1. All the compounds **1a-1i** (for a list, see the Supporting Information) are known and prepared according to our reported procedures.[14] Compounds **1b-1i** were prepared on 0.2 mmol

scale in similar yields as previously reported.[14] Compound **1a** was prepared on gram scale by a modification of the purification procedure as follows:

To an oven-dried 300 mL Schlenk Tube were added (diacetoxyiodo)benzene (17.8766 g, 55.5 mmol, 6.0 equiv) and cesium carbonate (3.0138 g, 9.25 mmol, 1.0 equiv) in glove box. Under argon atmosphere, iodine (I_2, 469.5 mg, 1.85 mmol, 0.2 equiv) was added quickly and DMF (40 mL) was injected into the flask. The reaction mixture was stirred, and then the tube was cooled to –50 ^{o}C ~ –60 ^{o}C with dry ice/acetone cold bath. After the addition of difluoromethyl phenyl sulfone (3.5550 g, 18.5 mmol, 2.0 equiv), a DMF (15 mL) solution of sodium *tert*-butoxide (2.6665 g, 27.75 mmol, 3.0 equiv) was added dropwise into the reaction system. Then a DMF (10 mL) solution of 2-isocyano-1,1'-biphenyl (1.6579 g, 9.25 mmol, 1.0 equiv) was injected with a syringe, followed by the slowly addition of another portion of sodium *tert*-butoxide (2.6665 g, 27.75 mmol, 3.0 equiv) in DMF (15 mL). The resulting reaction mixture was stirred at –50 ^{o}C ~ –60 ^{o}C under Ar atmosphere for 2 h. Then the mixture was warmed to room temperature and water (150 mL) was added. The aqueous layer was extracted with ethyl acetate (EtOAc) (150 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was evaporated under reduced pressure and the residue was mixed with silica gel and preliminarily purified by column chromatography on silica gel by using PE/EtOAc as eluent (20:1~5:1, v/v) to provide crude product of **1a**, which was further recrystallized with EtOAc/petroleum ether (PE) to provide **1a** as white crystals (1.4692g, 43%). M.p. 144 – 146 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) *:* δ 8.69 (t, J = 8.8 Hz, 2H), 8.61 – 8.59 (m, 1H), 8.29 – 8.13 (m, 1H), 8.09 (d, J = 7.8 Hz, 2H), 7.91 (t, J = 7.6 Hz, 1H), 7.80 – 7.74 (m, 4H), 7.61 (t, J = 7.8 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) *:* δ –95.7 (s, 2F). All the characterization data are consistent with previous report.[14]

Procedures for the Preparation of 6-(*tert*-Butoxydifluoromethyl)phenanthridine (3) (Scheme 2). To an oven-dried 10 mL Schlenk Tube was added 6-(difluoro(phenylsulfonyl)methyl)phenanthridine (**1a)** (73.9 mg, 0.2 mmol, 1.0 equiv) and then the flask was evacuated and backfilled with

argon for 3 times. PhCHO (21.2 mg, 0.2 mmol, 1.0 equiv) mixed with DMF (1.6 mL) was added via syringe in one portion. The reaction mixture was stirred, and then the tube was cooled to –50 ^{o}C ~ –60 ^{o}C with dry ice/acetone cold bath. A DMF solution of *t*-BuOK (1.0 mol/L, 0.5 mL, 0.5 mmol), which was prepared just before the experiment, was added dropwise into the reaction system. The resulting reaction mixture was stirred at –50 ^{o}C ~ –60 ^{o}C under Ar atmosphere for 3 h and was stirred further at room temperature for 14 h. After the reaction was complete, the mixture was quenched with H_2O (5 mL). The aqueous layer was extracted with EtOAc (8 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was evaporated under reduced pressure and the residue was mixed with silica gel and purified by column chromatography on silica gel by using PE/EtOAc (40:1 ~20:1, v/v) as eluent to provide **3** as pale yellow solid (28.9 mg, 48%). M.p. 59 – 61 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) *:* δ 8.65 (d, *J* = 8.0 Hz, 1H), 8.58 (t, *J* = 7.0 Hz, 2H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.86 (t, *J* = 7.8 Hz, 1H), 7.78 – 7.70 (m, 3H), 1.66 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) *:* δ –63.8 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) *:* δ 151.3 (t, *J* = 33.1 Hz), 142.0, 134.1, 131.0, 130.7, 129.0, 128.3, 127.6, 127.3, 125.0, 122.5, 122.2, 122.0, 121.9 (t, *J* = 264.2 Hz), 83.3, 30.4 (t, *J* = 1.9 Hz). IR (KBr): 3084, 2994, 2929, 1579, 1469, 1372, 1247, 1183, 1165, 1152, 1120, 1046, 1028, 968, 884, 758, 729, 717 cm^{-1}. MS (ESI, m/z): 302.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{18}H_{18}F_2NO^+$ ($M+H^+$): 302.1351, found: 302.1349.

Procedures for the Preparation of 6-(Difluoro(phenoxy)methyl)phenanthridine (6a) (**Table 4**)**.** To an oven-dried 10 mL Schlenk Tube was added 6-(difluoro(phenylsulfonyl)methyl)phenanthridine (**1a)** (73.9 mg, 0.2 mmol, 1.0 equiv) and PhONa (69.7 mg, 0.6 mmol, 3.0 equiv) in glove box. Then the flask was moved out of the glove box and was evacuated and backfilled with pure argon for 3 times. PhCHO (21.2 mg, 0.2 mmol, 1.0 equiv) in DMF (1.0 mL) was added via syringe in one portion. The reaction mixture was stirred, and then a DMF (1.0 mL) solution of *t*-BuOK (22.4 mg, 0.2 mmol, 1.0 equiv), which was prepared just before the experiment, was added dropwise into the reaction system. The resulting reaction mixture was stirred at room temperature and room light

illumination under argon atmosphere for 12 h. After the reaction was complete, the mixture was quenched with H_2O (5 mL). The aqueous layer was extracted with EtOAc (8 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was evaporated under reduced pressure and the residue was mixed with silica gel and purified by column chromatography on silica gel by using PE/EtOAc (100:1 ~ 80:1, v/v) as eluent to provide **6a** as white solid (59.5 mg, 93%). M.p. 77 – 79 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.68 (t, *J* = 6.8 Hz, 2H), 8.61 – 8.59 (m, 1H), 8.33 – 8.31 (m, 1H), 7.92 – 7.88 (m, 1H), 7.82 – 7.74 (m, 3H), 7.43 – 7.36 (m, 4H), 7.25 – 7.21 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –67.8 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) : δ 150.6, 149.4 (t, *J* = 31.6 Hz), 142.0, 134.2, 131.23, 131.16, 129.7, 129.2, 128.9, 127.8, 127.1 (t, *J* = 2.9 Hz), 125.8, 125.2, 122.52, 122.50, 122.1, 121.8, 120.5 (t, *J* = 264.7 Hz). IR (film): 3067, 2929, 1590, 1491, 1465, 1374, 1250, 1201, 1156, 1134, 1066, 968, 753, 726, 689 cm^{-1}. MS (ESI, m/z): 322.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{20}H_{14}F_2NO^+$ ($M+H^+$): 322.1038, found: 322.1040.

General Procedures for the Preparation of Compounds 6b-6k (**Table 4**)**.** To an oven-dried 10 mL Schlenk Tube A was added *t*-BuOK (107.7 mg, 0.96 mmol) in glove box and then the flask was moved out of the glove box. Under argon atmosphere, DMF (0.3 mL) was injected and the reaction mixture was stirred. ArOH (**5b-k**) (0.72 mmol) was dissolved in DMF (0.9 mL) and was added dropwise into the reaction system. The resulting reaction mixture was stirred at room temperature for 30 min and was left to be used.

To another oven-dried 10 mL Schlenk Tube B was added 6-(difluoro(phenylsulfonyl)methyl)phenanthridine (**1a)** (73.9 mg, 0.2 mmol, 1.0 equiv) and then the flask was evacuated and backfilled with pure argon for 3 times. PhCHO (21.2 mg, 0.2 mmol, 1.0 equiv) mixed with DMF (1.0 mL) was added via syringe in one portion and the reaction mixture was stirred. Next, 1.0 mL of the reaction mixture [containing ArOK (0.53 mmol, 2.7 equiv) and *t*-BuOK (0.18 mmol, 0.9 equiv)] was taken out from the Schlenk Tube A and was added dropwise into the reaction system of Schlenk Tube B. Then, the resulting reaction mixture was stirred at room

temperature and room light illumination under argon atmosphere for 12 h. After the reaction was complete, the mixture was quenched with H_2O (5 mL). The aqueous layer was extracted with EtOAc (8 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was evaporated under reduced pressure and the residue was mixed with silica gel and purified by column chromatography on silica gel by using PE/EtOAc (80:1, v/v) as eluent to provide compounds **6b-6k.**

6-((4-(*tert*-Butyl)phenoxy)difluoromethyl)phenanthridine (**6b**) (**Table 4**) Pale yellow solid (37.9 mg, 56%). M.p. 103 – 105 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.68 (t, *J* = 9.8 Hz, 2H), 8.58 (d, *J* = 8.0 Hz, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 7.90 – 7.86 (m, 1H), 7.81 – 7.73 (m, 3H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.37 (d, *J* = 8.8 Hz, 2H), 1.34 (s,9H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –68.0 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) : δ 149.5 (t, *J* = 31.4 Hz), 148.7, 148.2 (t, *J* = 1.8 Hz), 142.0, 134.2, 131.2, 131.1, 129.2, 128.8, 127.7, 127.2 (t, *J* = 2.9 Hz), 126.5, 125.1, 122.49, 122.45, 122.1, 121.2, 120.4 (t, *J* = 265.0 Hz), 34.6, 31.5. IR (film): 3080, 2963, 2906, 1619, 1510, 1465, 1446, 1373, 1332, 1250, 1209, 1173, 1137, 1103, 1067, 1017, 968, 856, 788, 762, 727, 559 cm^{-1}. MS (ESI, m/z): 378.1 (M+H^{+}). HRMS (ESI): Calcd. for $C_{24}H_{22}F_2NO^{+}$ (M+H^{+}): 378.1664, found: 378.1662.

6-(Difluoro(4-(2-methoxyethyl)phenoxy)methyl)phenanthridine (**6c**) (**Table 4**) Yellow oil (48.0 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.70 – 8.67 (m, 2H), 8.61 – 8.59 (m, 1H), 8.34 – 8.31 (m, 1H), 7.92 – 7.88 (m, 1H), 7.82 – 7.74 (m, 3H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 3.60 (t, *J* = 7.0 Hz, 2H), 3.36 (s, 3H), 2.88 (t, *J* = 7.0 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –67.9 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) : δ 149.4 (t, *J* = 31.6 Hz), 148.9, 142.0, 136.7, 134.1, 131.12, 131.09, 130.0, 129.2, 128.8, 127.7, 127.1 (t, *J* = 2.8 Hz), 125.1, 122.4, 122.1, 121.7, 120.4 (t, *J* = 264.8 Hz), 73.5, 58.8, 35.6. IR (film): 3067, 3028, 2925, 2870, 1612, 1573, 1532, 1508, 1465, 1446, 1374, 1333, 1307, 1250, 1204, 1156, 1067, 1019, 967, 852, 762, 727 cm^{-1}. MS (ESI, m/z): 380.1 (M+H^{+}). HRMS (ESI): Calcd. for $C_{23}H_{20}F_2NO_2^{+}$ (M+H^{+}): 380.1457, found: 380.1455.

6-(Difluoro(p-tolyloxy)methyl)phenanthridine (**6d**) (**Table 4**) White solid (44.2 mg, 66%). M.p. 88 – 90 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.69 (dd, *J* = 8.4 Hz, 0.8Hz, 1H), 8.65 (d, *J* = 8.4 Hz, 1H), 8.56 (d, *J* = 8.0 Hz, 1H), 8.33 (dd, *J* = 8.0 Hz, 1.2 Hz, 1H), 7.89 – 7.85 (m, 1H), 7.81 – 7.71 (m, 3H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 2.34 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –67.8 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) : δ 149.5 (t, *J* = 31.5 Hz), 148.3, 142.0, 135.5, 134.1, 131.14, 131.07, 130.1, 129.2, 128.8, 127.7, 127.1 (t, *J* = 2.9 Hz), 125.1, 122.46, 122.44, 122.1, 121.7, 120.4 (t, *J* = 264.3 Hz), 20.9. IR (film): 3076, 3050, 2924, 1617, 1573, 1507, 1465, 1446, 1374, 1333, 1307, 1250, 1203, 1169, 1134, 1066, 967, 819, 758, 724, 555 cm^{-1}. MS (ESI, m/z): 336.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{21}H_{16}F_2NO^+$ ($M+H^+$): 336.1194, found: 336.1192.

6-(Difluoro(m-tolyloxy)methyl)phenanthridine (**6e**) (**Table 4**) Yellow oil (42.9 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.67 – 8.62 (m, 2H), 8.54 (d, *J* = 8.0 Hz, 1H), 8.31 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.78 – 7.69 (m, 3H), 7.29 – 7.21 (m, 3H), 7.04 – 7.02 (m, 1H), 2.36 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –67.8 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) : δ 150.5 (t, *J* = 1.7 Hz), 149.4 (t, *J* = 31.4 Hz), 142.0, 139.8, 134.1, 131.10, 131.06, 129.3, 129.1, 128.8, 127.7, 127.1 (t, *J* = 2.9 Hz), 126.6, 125.1, 122.44, 122.42, 122.07 , 120.4 (t, *J* = 265.1 Hz), 118.7, 21.5. IR (film): 3080, 2915, 1612, 1587, 1529, 1488, 1464, 1446, 1373, 1333, 1252, 1187, 1157, 1066, 970, 762, 730, 687 cm^{-1}. MS (ESI, m/z): 336.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{21}H_{16}F_2NO^+$ ($M+H^+$): 336.1194, found: 336.1195.

6-(Difluoro(o-tolyloxy)methyl)phenanthridine (**6f**) (**Table 4**) White solid (44.1 mg, 66%). M.p. 103 – 105 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.69 (d, *J* = 8.4 Hz, 1H), 8.65 (d, *J* = 8.4 Hz, 1H), 8.56 (d, *J* = 8.0 Hz, 1H), 8.32 (d, *J* = 8.8 Hz, 1H), 7.86 (t, *J* = 7.8 Hz, 1H), 7.79 – 7.70 (m, 3H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 2.32 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –67.2 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) : δ 149.6 (t, *J* = 31.9 Hz), 149.2, 142.1, 134.2, 131.5, 131.2, 131.1, 131.0, 129.2, 128.8, 127.7, 127.2 (t, *J* = 3.3 Hz), 126.9, 125.6, 125.1, 122.49, 122.47, 122.1, 121.5, 120.7 (t, *J* = 265.2 Hz), 16.9. IR (film): 3080, 2963, 2933, 1614, 1588, 1528, 1493, 1465, 1446, 1374, 1333, 1307, 1250, 1221,

1189, 1155, 1136, 1111, 1066, 1044, 968, 762, 746, 725 cm^{-1}. MS (ESI, m/z): 336.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{21}H_{16}F_2NO^+$ ($M+H^+$): 336.1194, found: 336.1192.

6-(Difluoro(4-methoxyphenoxy)methyl)phenanthridine (**6g**) (**Table 4**) White solid (66.3 mg, contaminated by 4% of side product **2** according to ^{19}F NMR spectroscopic analysis, Calcd. 91% yield). An analytically pure sample of compound **6g** was obtained after recrystallization from EtOAc/PE. M.p. 87 – 88 ^oC. ^1H NMR (400 MHz, $CDCl_3$) : δ 8.69 (d, *J* = 8.8 Hz, 2H), 8.61 – 8.59 (m, 1H), 8.34 – 8.31 (m, 1H), 7.92 – 7.88 (m, 1H), 7.82 – 7.74 (m, 3H), 7.34 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –67.9 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) : δ 157.5, 149.5 (t, *J* = 31.6 Hz), 143.9 (t, *J* = 1.9 Hz), 142.1, 134.2, 131.2, 131.1, 129.2, 128.8, 127.8, 127.2 (t, *J* = 3.0 Hz), 125.1, 123.2, 122.54, 122.51, 122.1, 120.5 (t, *J* = 263.9 Hz), 114.6, 55.7. IR (film): 3076, 2963, 2933, 2837, 1612, 1575, 1506, 1465, 1445, 1374, 1333, 1307, 1247, 1200, 1154, 1134, 1103, 1065, 1035, 967, 844, 790, 761, 732, 724 cm^{-1}. MS (ESI, m/z): 352.0 ($M+H^+$). HRMS (ESI): Calcd. for $C_{21}H_{16}F_2NO_2^+$ ($M+H^+$): 352.1144, found: 352.1144.

6-(Difluoro(3-methoxyphenoxy)methyl)phenanthridine (**6h**) (**Table 4**) Yellow oil (42.6 mg, 61%). ^1H NMR (400 MHz, $CDCl_3$) : δ 8.65 – 8.63 (m, 2H), 8.56 – 8.54 (m, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 7.88 – 7.83 (m, 1H), 7.79 – 7.70 (m, 3H), 7.28 – 7.23 (m, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 6.96 (s, 1H), 6.78 – 6.75 (m, 1H), 3.77 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –67.8 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) : δ 160.6, 151.5 (t, *J* = 1.7 Hz), 149.3 (t, *J* = 31.3 Hz), 142.0, 134.1, 131.1, 130.0, 129.2, 128.8, 127.8, 127.0 (t, *J* = 2.9 Hz), 125.1, 122.5, 122.4, 122.1, 120.4 (t, *J* = 265.3 Hz), 113.8, 111.6, 107.8, 55.5. IR (film): 3084, 2946, 2850, 1608, 1590, 1490, 1465, 1446, 1373, 1333, 1311, 1286, 1248, 1193, 1155, 1131, 1067, 1044, 1001, 972, 858, 800, 763, 730, 684 cm^{-1}.MS (ESI, m/z): 352.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{21}H_{16}F_2NO_2^+$ ($M+H^+$): 352.1144, found: 352.1142.

6-((4-(Benzyloxy)phenoxy)difluoromethyl)phenanthridine (**6i**) (**Table 4**) White solid (45.5 mg, 53%. Isolated yield was given by recrystallization). M.p. 108 – 110 ^oC. ^1H NMR (400 MHz, $CDCl_3$) : δ 8.71 – 8.68 (m, 2H), 8.60 (d, *J* = 8.0 Hz, 1H), 8.34 (d, *J* = 7.6 Hz, 1H), 7.92 – 7.88 (m, 1H), 7.82 – 7.74 (m, 3H), 7.45 – 7.35

(m, 7H), 6.98 (d, *J* = 8.8 Hz, 2H), 5.05 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –67.9 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) : δ 156.7, 149.5 (t, *J* = 31.6 Hz), 144.09, 144.07, 142.0, 136.9, 134.2, 131.2, 131.1, 129.2, 128.8, 128.7, 128.2, 127.8, 127.6, 127.1 (t, *J* = 2.9 Hz), 125.1, 123.2, 122.5, 122.1, 120.4 (t, *J* = 264.3 Hz), 115.6, 70.5. IR (film): 3067, 3028, 2868, 1612, 1588, 1504, 1465, 1446, 1375, 1335, 1307, 1247, 1196, 1154, 1134, 1065, 1010, 967, 843, 761, 726, 697 cm^{-1}. MS (ESI, m/z): 428.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{27}H_{20}F_2NO_2^+$ ($M+H^+$): 428.1457, found: 428.1456.

6-((4-Bromophenoxy)difluoromethyl)phenanthridine (**6j**) (**Table 4**) Yellow solid (51.3 mg, 64%). M.p. 63 – 66 ^oC. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.68 (d, *J* = 8.4 Hz, 1H), 8.62 – 8.58 (m, 2H), 8.32 – 8.30 (m, 1H), 7.89 (t, *J* = 7.8 Hz, 1H), 7.82 – 7.74 (m, 3H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 8.8 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –67.8 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) : δ 149.7, 148.9 (t, *J* = 31.2 Hz), 142.0, 134.2, 132.7, 131.21, 131.18, 129.3, 129.0, 127.9, 126.9 (t, *J* = 3.0 Hz), 125.1, 123.5, 122.6, 122.4, 122.1, 120.4 (t, *J* = 265.5 Hz), 119.0. IR (film): 3076, 1614, 1580, 1528, 1485, 1465, 1446, 1374, 1333, 1251, 1204, 1154, 1102, 1068, 1012, 967, 848, 827, 761, 726, 492 cm^{-1}. MS (ESI, m/z): 401.9 ($M+H^+$). HRMS (ESI): Calcd. for $C_{20}H_{13}BrF_2NO^+$ ($M+H^+$): 400.0143, found: 400.0140.

6-(Difluoro(4-fluorophenoxy)methyl)phenanthridine (**6k**) (**Table 4**) White solid (43.5 mg, 64%). M.p. 148 – 150 ^oC. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.65 (t, *J* = 8.2 Hz, 2H), 8.57 (d, *J* = 7.6 Hz, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 7.88 (t, *J* = 7.6 Hz, 1H), 7.81 – 7.73 (m, 3H), 7.40 – 7.37 (m, 2H), 7.07 (t, *J* = 8.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –67.9 (s, 2F), –117.3 (s, 1F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) : δ 160.4 (d, *J* = 243.3 Hz), 149.07 (t, *J* = 31.5 Hz), 146.3 (q, *J* = 2.2 Hz), 141.9, 134.1, 131.15, 131.12, 129.2, 128.9, 127.8, 126.9 (t, *J* = 3.1 Hz), 125.1, 123.6 (d, *J* = 8.4 Hz), 122.5, 122.4, 122.1, 120.4 (t, *J* = 265.0 Hz), 116.3 (d, *J* = 23.3 Hz). IR (film): 3067, 1619, 1532, 1502, 1463, 1446, 1376, 1333, 1251, 1195, 1130, 1044, 974, 795, 755, 719, 542 cm^{-1}. MS (ESI, m/z): 340.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{20}H_{13}F_3NO^+$ ($M+H^+$): 340.0944, found: 340.0942.

Procedures for the Preparation of 2,6-Di-*tert*-butyl-4-(difluoro(phenanthridin-6-yl)methyl)-4-methylcyclohexa-2,5-

dienone (7) (Scheme 3). To an oven-dried 10 mL Schlenk Tube were added 6-(difluoro(phenylsulfonyl)methyl)phenanthridine (**1a)** (36.9 mg, 0.1 mmol, 1.0 equiv) and butylated hydroxytoluene (BHT, 66.1 mg, 0.3 mmol, 3.0 equiv). The flask was evacuated and backfilled with pure argon for 3 times and then DMF (0.8 mL) was added via syringe. The reaction mixture was stirred, and then the tube was cooled to –50 ^{o}C ~ –60 ^{o}C with dry ice/acetone cold bath. A DMF solution of *t*-BuOK (1.0 mol/L, 0.25 mL, 0.25 mmol), which was prepared just before the experiment, was added dropwise into the reaction system. The resulting reaction mixture was stirred at –50 ^{o}C ~ –60 ^{o}C under argon atmosphere for 3 h and was stirred further at room temperature for 14 h. After the reaction was complete, the mixture was quenched with H_2O (2 mL). The aqueous layer was extracted with EtOAc (4 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was evaporated under reduced pressure. The residue was purified by PTLC (preparative thin layer chromatography) to provide **7** as off-white solid (32.5 mg, 73%). M.p. 157 – 158 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.65 (d, *J* = 8.0 Hz, 1H), 8.58 (d, *J* = 8.4 Hz, 1H), 8.55 – 8.53 (m, 1H), 8.00 – 7.98 (m, 1H), 7.84 (t, *J* = 7.4 Hz, 1H), 7.72 – 7.68 (m, 3H), 6.87 (s, 2H), 1.63 (s, 3H), 1.09 (s, 18H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –99.3 (s, 2F). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) : δ 186.1, 151.0 (t, *J* = 28.7 Hz), 147.1, 141.4, 140.8 (t, *J* = 2.9 Hz), 133.8, 130.7, 130.6, 129.0, 128.6, 127.6, 127.5 (t, *J* = 8.2 Hz), 124.5, 123.2 (t, *J* = 1.7 Hz), 122.8 (t, *J* = 253.2 Hz), 122.6, 122.0, 47.6 (t, *J* = 23.3 Hz), 34.9, 29.3, 21.4 (t, *J* = 4.8 Hz). IR (film): 3080, 2957, 2867, 1662, 1642, 1485, 1460, 1446, 1372, 1364, 1249, 1170, 1141, 1095, 1068, 1047, 930, 914, 903, 881, 761, 742, 727 cm^{-1}. MS (ESI, m/z): 448.2 (M+H^{+}). HRMS (ESI): Calcd. for $C_{29}H_{32}F_2NO^{+}$ (M+H^{+}): 448.2446, found: 448.2446.

Procedures for the Preparation of 6-(Difluoro(phenylthio)methyl)phenanthridine (9a)[14] (**Table 6**)**.** To an oven-dried 10 mL Schlenk Tube was added 6-(difluoro(phenylsulfonyl)methyl)phenanthridine (**1a)** (73.9 mg, 0.2 mmol, 1.0 equiv) and then the flask was evacuated and backfilled with pure argon for 3 times. Under argon atmosphere, PhSNa (105.7 mg, 0.8 mmol, 4.0 equiv) was added quickly and DMF (2.0 mL) was injected into the flask. The

resulting reaction mixture was stirred at room temperature and room light illumination under argon atmosphere for 24 h. After the reaction was complete, the mixture was diluted with H_2O (5 mL). The aqueous layer was extracted with EtOAc (8 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was evaporated under reduced pressure and the residue was mixed with silica gel and purified by column chromatography on silica gel by using PE/EtOAc (100:1, v/v) as eluent to provide **9a** as white solid (65.2 mg, 97%). M.p. 136 – 138 ^oC. ^1H NMR (400 MHz, $CDCl_3$) : δ 8.66 (d, *J* = 8.4 Hz, 1H), 8.61 – 8.55 (m, 2H), 8.31 – 8.28 (m, 1H), 7.89 – 7.68 (m, 6H), 7.52 – 7.43 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ -66.0 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) : δ 151.2 (t, *J* = 27.9 Hz), 141.8, 137.3, 134.1, 131.1, 131.0, 130.0, 129.7 (t, *J* = 277.1 Hz), 129.2, 129.1, 128.9, 127.7, 127.5, 127. (t, *J* = 5.4 Hz), 125.1, 122.5, 122.1, 122.0. IR (KBr): 3084, 2920, 1585, 1478, 1365, 1311, 1133, 1052, 1011, 879, 759, 508 cm^{-1}. MS (ESI, m/z): 338.0 ($M+H^+$). HRMS (ESI): Calcd. for $C_{20}H_{14}F_2NS^+$ ($M+H^+$): 338.0810, found: 338.0802. All the characterization data are consistent with previous report.[14]

Procedures for the Preparation of 6-(Difluoro(pyridin-2-ylthio)methyl)phenanthridine (9b) (**Table 6**)**.** To an oven-dried 5 mL Schlenk Tube A was added *t*-BuOK (134.7 mg, 1.2 mmol) in glove box and then the flask was moved out of the glove box. Under argon atmosphere, 2-mercaptopyridine (**8b**, 106.7 mg, 0.96 mmol) was added quickly and then DMF (1.2 mL) was injected. The resulting reaction mixture was stirred at room temperature for 30 min and was left to be used.

To another oven-dried 10 mL Schlenk Tube B was added 6-(difluoro(phenylsulfonyl)methyl)phenanthridine (**1a)** (73.9 mg, 0.2 mmol, 1.0 equiv) and then the flask was evacuated and backfilled with argon for 3 times. PhCHO (21.2 mg, 0.2 mmol, 1.0 equiv) mixed with DMF (1.0 mL) was added via syringe in one portion and the reaction mixture was stirred. Next, 1.0 mL of the reaction mixture [containing 2-PySK (0.71 mmol, 3.5 equiv) and *t*-BuOK (0.18 mmol, 0.9 equiv)] was taken out from the Schlenk Tube A and was added dropwise into the reaction system of Schlenk Tube B. Then, the resulting reaction mixture was stirred at room

temperature and room light illumination under argon atmosphere for 72 h. After the reaction was complete, the mixture was quenched with H_2O (5 mL). The aqueous layer was extracted with EtOAc (8 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was evaporated under reduced pressure and the residue was mixed with silica gel and purified by column chromatography on silica gel by using PE/EtOAc (20:1, v/v) as eluent to provide **9b** as pale yellow solid (43.7 mg, 65%). M.p. 123 – 125 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.66 (d, *J* = 4.0 Hz, 1H), 8.61 (d, *J* = 8.4 Hz, 2H), 8.53 – 8.51 (m, 1H), 8.25 – 8.23 (m, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.84 (t, *J* = 7.8 Hz, 1H), 7.77 – 7.67 (m, 4H), 7.28 (dd, *J* = 7.4, 5.4 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –66.1 (s, 2F). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) : δ 152.8, 150.7 (t, *J* = 27.4 Hz), 150.4, 141.7, 137.1, 134.1, 131.2, 130.9, 130. 5 (t, *J* = 279.0 Hz), 129.6, 129.2, 128.9, 127.8, 126.9 (t, *J* = 5.3 Hz), 125.1, 123.2, 122.5, 122.1, 121.8 (d, *J* = 1.9 Hz). IR (film): 3063, 1614, 1572, 1561, 1128, 1491, 1450, 1420, 1365, 1309, 1283, 1242, 1225, 1134, 1095, 1050, 1039, 1011, 989, 976, 877, 845, 780, 758, 722, 675, 650, 508, 423 cm^{-1}. MS (ESI, m/z): 339.0 ($M+H^+$). HRMS (ESI): Calcd. for $C_{19}H_{13}F_2N_2S^+$ ($M+H^+$): 339.0762, found: 339.0761.

General Procedures for the Preparation of Compounds 9c-9h (**Table 6**)**.** To an oven-dried 10 mL Schlenk Tube was added NaH (95% purity, 20.2 mg, 0.8 mmol, 4.0 equiv) in glove box and then the flask was moved out of the glove box. Under argon atmosphere, DMSO (0.4 mL) was injected and the reaction mixture was stirred. thiol (**8c-8h**) (0.8 mmol, 4.0 equiv) was dissolved in DMSO (1.6 mL) and was added dropwise into the reaction system. The resulting reaction mixture was stirred at room temperature for 30 min. Under argon atmosphere, 6-(difluoro(phenylsulfonyl)methyl)phenanthridine (**1a)** (73.9 mg, 0.2 mmol, 1.0 equiv) was added quickly into the reaction system. The resulting reaction mixture was stirred at room temperature and room light illumination under argon atmosphere for 24 h. After the reaction was complete, the mixture was quenched with H_2O (5 mL). The aqueous layer was extracted with EtOAc (8 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was

evaporated under reduced pressure and the residue was mixed with silica gel and purified by column chromatography on silica gel by using PE/EtOAc (200:1 ~100:1, v/v) as eluent to provide compounds **9c-9h.**

6-(Difluoro(naphthalen-2-ylthio)methyl)phenanthridine (**9c**) (**Table 6**). White solid (72.3 mg, 93%). M.p. 135 – 138 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (d, *J* = 8.4 Hz, 1H), 8.62 – 8.59 (m, 2H), 8.36 (s, 1H), 8.33 – 8.31 (m, 1H), 7.92 – 7.85 (m, 5H), 7.83 – 7.75 (m, 2H), 7.74 – 7.70 (m, 1H), 7.60 – 7.53 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –66.2 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 151.1 (t, *J* = 27.8 Hz), 141.7, 137.5, 134.1, 133.7, 133.5, 133.2, 131.1, 130.9, 129.9 (t, *J* = 277.3 Hz), 129.1, 128.8, 128.6, 128.2, 127.8, 127.7, 127.3, 126.9 (t, *J* = 5.2 Hz), 126.6, 125.0, 124.8, 122.4, 122.1, 121.9. IR (KBr): 3054, 2963, 1584, 1362, 1262, 1130, 1093, 1049, 1036, 875, 842, 818, 752, 722, 672, 656, 478 cm^{-1}. MS (ESI, m/z): 388.0 ($M+H^+$). HRMS (ESI): Calcd. for $C_{24}H_{16}F_2NS^+$ ($M+H^+$): 388.0966, found: 388.0965.

6-(Difluoro((4-fluorophenyl)thio)methyl)phenanthridine (**9d**) (**Table 6**). White solid (65.0 mg, 91%). M.p. 130 – 132 ^{o}C. ^{1}H NMR (400 MHz, CDCl3): δ8.67 – 8.63 (m, 1H), 8.55 (d, *J* = 7.6 Hz, 2H), 8.29 – 8.27 (m, 1H), 7.89 – 7.84 (m, 1H), 7.80 – 7.68 (m, 5H), 7.17 – 7.11 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –66.7 (s, 2F), –111.3 (s, 1F). ^{13}C{^{1}H} NMR (100MHz, $CDCl_3$): δ 164.3 (d, *J* = 249.0 Hz), 151.0 (t, *J* = 28.0 Hz), 141.7, 139.4 (d, *J* = 8.5 Hz), 134.1, 131.2, 130.9, 129.6 (t, *J* = 277.0 Hz), 129.2, 128.9, 127.8, 126.9 (t, *J* = 5.3 Hz), 125.1, 122.8, 122.5, 122.1, 121.9, 116.28 (d, *J* = 21.7 Hz). IR (film): 3084, 1589, 1529, 1490, 1463, 1445, 1397, 1362, 1228, 1158, 1134, 1097, 1052, 1014, 913, 876, 833, 760, 725, 677, 650, 614, 521 cm^{-1}. MS (ESI, m/z): 356.0 ($M+H^+$). HRMS (ESI): Calcd. for $C_{20}H_{13}F_3NS^+$ ($M+H^+$): 356.0715, found: 356.0716.

6-(((4-Chlorophenyl)thio)difluoromethyl)phenanthridine (**9e**) (**Table 6**). White solid (60.6 mg, 81%). M.p. 137 – 139 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (d, *J* = 8.4 Hz, 1H), 8.56 – 8.53 (m, 2H), 8.28 – 8.26 (m, 1H), 7.87 – 7.83 (m, 1H), 7.80 – 7.67 (m, 5H), 7.44 – 7.41 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –66.2 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 150.9 (t, *J* = 28.1 Hz), 141.7, 138.4, 136.6,

134.1, 131.2, 130.9, 129.8 (t, *J* = 277.5 Hz), 129.3, 129.2, 129.0, 127.8, 126.8 (t, *J* = 5.4 Hz), 126.1, 125.1, 122.5, 122.1, 121.9 (t, *J* = 2.0 Hz). IR (film): 3079, 1902, 1611, 1586, 1572, 1527, 1487, 1475, 1462, 1445, 1389, 1363, 1305, 1261, 1226, 1164, 1133, 1097, 1050, 1038, 1015, 875, 845, 822, 760, 746, 725, 677, 649, 614, 581, 505 cm^{-1}. MS (ESI, m/z): 371.9 ($M+H^+$). HRMS (ESI): Calcd. for $C_{20}H_{13}ClF_2NS^+$ ($M+H^+$): 372.0420, found: 372.0421.

6-(((4-Bromophenyl)thio)difluoromethyl)phenanthridine (**9f**) (**Table 6**). White solid (65.5 mg, 79%). M.p. 156 – 157 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.63 (t, *J* = 7.8 Hz, 1H), 8.54 (t, *J* = 7.4 Hz, 2H), 8.27 (d, *J* = 8.0 Hz, 1H), 7.88 – 7.66 (m, 6H), 7.58 (d, *J* = 8.4 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –66.1 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 150.8 (t, *J* = 28.1 Hz), 141.7, 138.7, 134.1, 132.3, 131.2, 130.9, 129.7 (t, *J* = 277.6 Hz), 129.2, 129.0, 127.8, 126.81 (t, *J* = 5.3 Hz), 126.75, 125.1, 125.0, 122.5, 122.1, 121.8 (t, *J* = 1.9 Hz). IR (film): 3080, 1611, 1585, 1574, 1565, 1528, 14898, 1473, 14638, 1444, 1386, 1363, 1307, 1261, 1166, 1133, 1095, 1066, 1050, 1037, 1009, 876, 843, 819, 758, 724, 675, 647, 511 cm^{-1}. MS (ESI, m/z): 415.9 ($M+H^+$). HRMS (ESI): Calcd. for $C_{20}H_{13}BrF_2NS^+$ ($M+H^+$): 415.9915, found: 415.9914.

6-(Difluoro((4-(methylthio)phenyl)thio)methyl)phenanthridine (**9g**) (**Table 6**). White solid (58.9 mg, 77%). M.p. 137 – 140 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.63 (d, *J* = 8.0 Hz, 1H), 8.58 – 8.53(m, 2H), 8.28 (d, *J* = 7.6 Hz, 1H), 7.85 (t, *J* = 7.8 Hz, 1H), 7.79 – 7.67 (m, 5H), 7.29 (d, *J* = 8.4 Hz, 2H), 2.50 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –66.8 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 151.1 (t, *J* = 27.9 Hz), 141.8, 141.7, 137.5, 134.1, 131.1, 130.9, 129.5 (t, *J* = 277.1 Hz), 129.1, 128.9, 127.7, 127.0 (t, *J* = 5.4 Hz), 126.3, 125.0, 123.0, 122.5, 122.1, 121.9, 15.3. IR (film): 3080, 2928, 1575, 1477, 1444, 1387, 1365, 1242, 1186, 1132, 1105, 1095, 1052, 1012, 875, 844, 818, 759, 724, 679, 646, 511 cm^{-1}. MS (ESI, m/z): 384.0 ($M+H^+$). HRMS (ESI): Calcd. for $C_{21}H_{16}F_2NS_2^+$ ($M+H^+$): 384.0687, found: 384.0685.

6-(Difluoro((4-methoxybenzyl)thio)methyl)phenanthridine (**9h**) (**Table 6**). Off-white solid (30.5 mg, 40%). M.p. 123 – 126 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.65 (t, *J* = 8.4 Hz, 2H), 8.58 – 8.55 (m, 1H), 8.24 – 8.22 (m, 1H), 7.88 (t, *J* = 7.8 Hz,

1H), 7.78 – 7.72 (m, 3H), 7.36 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 4.29 (s, 2H), 3.79 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –68.8 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 159.0, 151.2 (t, *J* = 27.4 Hz), 141.9, 134.1, 131.1, 131.0, 130.6 (t, *J* = 275.8 Hz), 130.5, 129.1, 128.8, 128.4, 127.7, 127.2 (t, *J* = 5.1 Hz), 125.1, 122.5, 122.1, 122.0, 114.2, 55.4, 32.4 (t, *J* = 3.8 Hz). IR (film): 3080, 3002, 2937, 2837, 1611, 1512, 1463, 1444, 1363, 1302, 1248, 1176, 1131, 1095, 1052, 1040, 1000, 918, 880, 840, 762, 726, 677 cm^{-1}. MS (ESI, m/z): 382.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{22}H_{18}F_2NOS^+$ ($M+H^+$): 382.1072, found: 382.1072.

Procedures for the Preparation of 6-(Difluoro(phenylselanyl)methyl)phenanthridine (10)[14] (Scheme 4). To an oven-dried 10 mL Schlenk Tube was added NaH (95% purity, 40.4 mg, 1.6 mmol, 8.0 equiv) in glove box and then the flask was moved out of the glove box. Under argon atmosphere, the solid of PhSeSePh (249.7 mg, 0.8 mmol, 4.0 equiv) was added quickly and then DMF (2.0 mL) was injected. After being stirred at room temperature for 30 min, to the reaction system was added 6-(difluoro(phenylsulfonyl)methyl)phenanthridine (**1a)** (73.9 mg, 0.2 mmol, 1.0 equiv). The resulting reaction mixture was stirred at room temperature and room light illumination under argon atmosphere for 12 h. After the reaction was complete, the mixture was quenched with H_2O (5 mL). The aqueous layer was extracted with EtOAc (8 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was evaporated under reduced pressure and the residue was mixed with silica gel and purified by column chromatography on silica gel by using PE/EtOAc (ether ~50:1, v/v) as eluent to provide **10** as white solid (60.2 mg, 78%). M.p. 141 – 144 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67 (d, *J* = 8.4 Hz, 1H), 8.58 (d, *J* = 8.4 Hz, 1H), 8.52 (d, *J* = 8.0 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 7.91 – 7.88 (m, 3H), 7.81 – 7.74 (m, 2H), 7.71 – 7.68 (m, 1H), 7.50 – 7.41 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –63.3 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 151.8 (t, *J* = 26.9 Hz), 141.8, 138.0 (t, *J* = 4.6 Hz), 134.3, 131.3, 130.8, 129.43, 129.39 (t, *J* = 291.5Hz), 129.2, 129.1, 128.9, 127.9, 126.8 (t, *J* = 5.3 Hz), 125.9, 125.3, 122.5, 122.2, 121.5 (t, *J* = 2.0 Hz). IR (KBr): 3076, 1585, 1478, 1443, 1365, 1305,

1132, 1100, 1048, 1035, 1024, 870, 835, 759, 742, 725, 693 cm^{-1}. MS (ESI, m/z): 386.0 ($M+H^+$). HRMS (ESI): Calcd. for $C_{20}H_{14}F_2N^{74}Se^+$ ($M+H^+$): 380.0314, found: 380.0315. All the characterization data are consistent with previous report.[14]

General Procedures for the Preparation of Compounds 12 (Table 7, Table 8). To an oven-dried 10 mL Schlenk Tube was added *t*-BuOK (0.8 mmol, 89.8 mg, 4.0 equiv) in glove box and then the flask was moved out of the glove box. Under argon atmosphere, DMSO (0.4 mL) was injected and the reaction mixture was stirred. $RCH(COOEt)_2$ (**11**) (0.8 mmol, 4.0 equiv) was dissolved in DMSO (1.6 mL) and was added dropwise into the reaction system. The resulting reaction mixture was stirred at room temperature for 30 min. Under argon atmosphere, 6-(difluoro(phenylsulfonyl)methyl)phenanthridine (**1a**) (73.9 mg, 0.2 mmol, 1.0 equiv) was added quickly into the reaction system. The resulting reaction mixture was stirred at room temperature and room light illumination under argon atmosphere for 12 h (24 h or 72 h). After the reaction was complete, the mixture was quenched with H_2O (5 mL). The aqueous layer was extracted with EtOAc (8 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was evaporated under reduced pressure and the residue was mixed with silica gel and purified by column chromatography on silica gel by using PE/EtOAc (20:1, v/v) as eluent to provide compound **12.**

Diethyl 2-(difluoro(phenanthridin-6-yl)methyl)-2-methylmalonate (12aa) (Table 7). Yellow solid (75.8 mg, 94%). M.p. 79 – 80 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.67 (d, *J* = 8.4 Hz, 2H), 8.58 – 8.56 (m, 1H), 8.06 – 8.03 (m, 1H), 7.88 (t, *J* = 7.6 Hz, 1H), 7.75 – 7.72 (m, 3H), 4.31 – 4.19 (m, 4H), 2.06 (s, 3H), 1.18 (t, *J* = 7.0 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –90.3 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.7 (t, *J* = 2.3 Hz), 150.3 (t, *J* = 31.1 Hz), 141.0, 134.2, 131.0, 130.3, 129.0, 128.6, 127.8, 127.3 (t, *J* = 6.2 Hz), 124.7, 122.8 (t, *J* = 2.2 Hz), 122.5, 122.14, 122.10 (t, *J* = 251.2 Hz), 61.9, 61.1 (t, *J* = 21.1 Hz), 18.8 (t, *J* = 4.4 Hz), 14.0. IR (film): 3080, 2982, 2903, 1749, 1616, 1489, 1465, 1447, 1465, 1269, 1113, 1095, 1074, 1049, 1021, 945, 763, 728, 683, 565 cm^{-1}. MS (ESI, m/z): 402.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{22}H_{22}F_2NO_4^+$ ($M+H^+$): 402.1511, found: 402.1514.

Diethyl 2-(difluoro(phenanthridin-6-yl)methyl)-2-ethylmalonate (12ab) (Table 7). Off-white solid (79.0 mg, 95%). M.p. 74 – 77 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, J = 8.0 Hz, 1H), 8.63 (d, J = 8.0 Hz, 1H), 8.55 – 8.52 (m, 1H), 8.07 – 8.05 (m, 1H), 7.84 (t, J = 7.6 Hz, 1H), 7.73 – 7.68 (m, 3H), 4.31 – 4.19 (m, 4H), 2.61 (q, J = 7.3 Hz, 2H), 1.28 (t, J = 7.4 Hz, 3H), 1.17 (t, J = 7.0 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –88.4 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.1 (t, J = 2.4 Hz), 150.6 (t, J = 31.3 Hz), 141.0, 134.1, 130.9, 130.1, 129.0, 128.7, 127.7, 127.2 (t, J = 6.4 Hz), 124.7, 122.7, 122.5 (t, J = 252.1 Hz), 122.4, 122.1, 65.1 (t, J = 20.2 Hz), 61.5, 25.7 (t, J = 4.2 Hz), 14.0, 10.6. IR (film): 3084, 2981, 2941, 2904, 1736, 1612, 1532, 1465, 1446, 1367, 1317, 1241, 1125, 1055, 1028, 960, 885, 826, 263, 728, 566 cm^{-1}. MS (ESI, m/z): 416.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{23}H_{24}F_2NO_4^+$ ($M+H^+$): 416.1668, found: 416.1666.

Diethyl 2-allyl-2-(difluoro(phenanthridin-6-yl)methyl)malonate (12ac) (Table 7). White solid (79.5 mg, 93%). M.p. 96 – 97 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (t, *J* = 9.6 Hz, 2H), 8.57 – 8.54 (m, 1H), 8.08 – 8.06 (m, 1H), 7.86 (t, *J* = 7.6 Hz, 1H), 7.73 – 7.70 (m, 3H), 6.36 – 6.26 (m, 1H), 5.21 (d, *J* = 16.8 Hz, 1H), 5.12 (d, *J* = 10.0 Hz, 1H), 4.29 – 4.17 (m, 4H), 3.31 (d, *J* = 7.2 Hz, 2H), 1.17 (t, *J* = 7.2 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –88.4 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.7, 150.5 (t, J = 31.4 Hz), 141.0, 134.2, 134.1, 131.0, 130.1, 129.0, 128.8, 127.7, 127.2 (t, J = 6.3 Hz), 124.7, 122.7 (t, J = 2.2 Hz), 122.5, 122.1, 122.0 (t, J = 252.4 Hz), 118.6, 65.1 (t, J = 20.3 Hz), 61.7, 37.0, 14.0. IR (film): 3084, 2983, 1738, 1638, 1610, 1530, 1465, 1446, 1367, 1310, 1293, 1248, 1221, 1167, 1145, 1127, 1044, 931, 891, 763, 728, 684, 644, 566 cm^{-1}. MS (ESI, m/z): 428.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{24}H_{24}F_2NO_4^+$ ($M+H^+$): 428.1668, found: 428.1668.

Diethyl 2-benzyl-2-(difluoro(phenanthridin-6-yl)methyl)malonate (12ad) (Table 7). Off-white solid (91.1 mg, 95%). M.p. 102 – 105 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (d, *J* = 8.0 Hz, 1H), 8.64 (d, *J* = 8.4 Hz, 1H), 8.55 – 8.53 (m, 1H), 8.09 – 8.07 (m, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.74 – 7.69 (m, 3H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 2H), 7.16 (t, *J* = 7.0 Hz, 1H), 4.12 – 4.00 (m, 4H), 3.92 (s, 2H), 1.01 (t, *J* = 7.0 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –88.2 (s, 2F). ^{13}C{^{1}H} NMR

(100 MHz, $CDCl_3$): δ 167.6, 150.5 (t, *J* = 31.1 Hz), 141.0, 137.0, 134.2, 131.5, 131.0, 130.2, 129.0, 128.8, 127.8, 127.3 (t, *J* = 6.1 Hz), 126.7, 124.7, 122.7 (t, *J* = 253.1 Hz), 122.5, 122.1, 66.4 (t, *J* = 20.2 Hz), 61.6, 37.9 (t, *J* = 3.9 Hz), 13.8. IR (film): 3067, 2982, 1739, 1608, 1578, 1532, 1495, 1465, 1446, 1367, 1326, 1242, 1200, 1152, 1098, 1079, 1040, 892, 861, 763, 728, 700, 683, 657, 584, 561, 536 cm^{-1}. MS (ESI, m/z): 478.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{28}H_{26}F_2NO_4^+$ ($M+H^+$): 478.1824, found: 478.1823.

Diethyl 2-(difluoro(8-(methylsulfonyl)phenanthridin-6-yl)methyl)-2-methylmalonate (12ba) (Table 8). Prepared from compound **1b** (0.17 mmol, 1.0 equiv) and , following the procedures for the preparation of **12aa**. White solid (78.7 mg, 97%). M.p. 149 – 151 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ 9.19 (d, *J* = 2.0 Hz, 1H), 8.78 (d, *J* = 8.8 Hz, 1H), 8.55 – 8.53 (m, 1H), 8.30 (dd, *J* = 8.8, 1.6 Hz, 1H), 8.02 – 8.00 (m, 1H), 7.80 – 7.73 (m, 2H), 4.27 – 4.16 (m, 4H), 3.14 (s, 3H), 2.01 (s, 3H), 1.16 (t, *J* = 7.0 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –89.7 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.3 (t, *J* = 2.6 Hz), 150.3 (t, *J* = 31.2 Hz), 141.7, 139.4, 137.2, 130.8 , 130.4 (d, *J* = 2.2 Hz), 129.7, 128.0, 127.6 (td, *J* = 6.8, 3.1 Hz), 124.3, 123.4, 122.8, 122.1 (d, *J* = 1.9 Hz), 121.6 (t, *J* = 251.0 Hz), 62.0, 60.9 (t, *J* = 21.2 Hz), 44.6, 18.5 (t, *J* = 4.4 Hz), 14.0. IR (film): 3074, 2987, 2935, 1747, 1610, 1467, 1402, 1378, 1363, 1314, 1271, 1154, 1095, 1073, 1049, 961, 866, 831, 758, 736, 649, 584, 558, 537 cm^{-1}. MS (ESI, m/z): 480.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{23}H_{24}F_2NO_6S^+$ ($M+H^+$): 480.1287, found: 480.1280.

Diethyl 2-(difluoro(8-(trifluoromethyl)phenanthridin-6-yl)methyl)-2-methylmalonate (12ca) (Table 8). Prepared from compound **1c** (0.05 mmol, 1.0 equiv), following the procedures for the preparation of **12aa**. White solid (22.6 mg, 96%). M.p. 108 – 109 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ 8.94 (s, 1H), 8.77 (d, *J* = 8.8 Hz, 1H), 8.60 – 8.57 (m, 1H), 8.07– 8.05 (m, 2H), 7.83 – 7.76 (m, 2H), 4.32 – 4.20 (m, 4H), 2.06 (s, 3H), 1.19 (t, *J* = 7.0 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.9 (s, 3F), –90.0 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.5 (t, *J* = 2.5 Hz), 150.3 (t, *J* = 31.4 Hz), 141.6, 136.3, 130.5, 130.3, 129.6 (q, *J* = 32.6 Hz), 129.4, 126.9 (q, *J* = 3.1 Hz), 125.0 – 124.8 (m), 124.0 (q, *J* = 270.8 Hz), 123.8, 123.6, 122.5, 122.1

(t, *J* = 2.2 Hz), 121.8 (t, *J* = 251.1 Hz), 62.0, 61.0 (t, *J* = 21.1 Hz), 18.7 (t, *J* = 4.5 Hz), 14.0. IR (film): 3078 , 2985, 2913, 1733, 1630, 1538, 1465, 1378, 1316, 1178, 1049, 1022, 952, 866, 837, 766, 735, 648, 566 cm^{-1}. MS (ESI, m/z): 470.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{23}H_{21}F_5NO_4^+$ ($M+H^+$): 470.1385, found: 470.1382.

Diethyl 2-(difluoro(8-methylphenanthridin-6-yl)methyl)-2-methylmalonate (12da) (Table 8). Prepared from compound **1d** (0.16 mmol, 1.0 equiv), following the procedures for the preparation of **12aa**. White solid (60.0 mg, 90%). M.p. 125 – 126 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ 8.50 – 8.47 (m, 2H), 8.42 (s, 1H), 8.03 – 7.99 (m, 1H), 7.69 – 7.63 (m, 3H), 4.32 – 4.20 (m, 4H), 2.57 (s, 3H), 2.08 (s, 3H), 1.19 (t, *J* = 7.0 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –90.5 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.7 (t, *J* = 2.1 Hz), 149.8 (t, *J* = 31.0 Hz), 140.6, 137.7, 132.7, 132.0, 130.1, 128.6, 128.5, 126.5 (t, *J* = 5.9 Hz), 124.7, 122.8, 122.3, 122.2 (t, *J* = 251.2 Hz), 121.9, 61.8, 61.1 (t, *J* = 21.1 Hz), 21.9, 18.9 (t, *J* = 4.3 Hz), 14.0. IR (film): 3082, 2983, 2939, 1750, 1577, 1536, 1467, 1369, 1269, 1117, 1096, 1074, 1048, 957, 881, 829, 764, 738, 647, 573 cm^{-1}. MS (ESI, m/z): 416.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{23}H_{24}F_2NO_4^+$ ($M+H^+$): 416.1668, found: 416.1662.

Diethyl 2-(difluoro(3-methyl-8-phenylphenanthridin-6-yl)methyl)-2-methylmalonate (12ea) (Table 8). Prepared from compound **1e** (0.05 mmol, 1.0 equiv), following the procedures for the preparation of **12aa**. White solid (22.8 mg, 93%). M.p. 148 – 150 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ 8.84 (d, *J* = 1.2 Hz, 1H), 8.68 (d, *J* = 8.8 Hz, 1H), 8.46 (d, *J* = 8.4 Hz, 1H), 8.10 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.84 (s, 1H), 7.76 (d, *J* = 7.2 Hz, 2H), 7.58 – 7.50 (m, 3H), 7.43 (t, *J* = 7.4 Hz, 1H), 4.32 – 4.20 (m, 4H), 2.59 (s, 3H), 2.07 (s, 3H), 1.19 (t, *J* = 7.0 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) : δ –90.2 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.8 (t, *J* = 2.2 Hz), 150.3 (t, *J* = 31.0 Hz), 141.2, 140.4, 140.1, 139.4, 133.3, 130.7, 130.3, 129.7, 129.1, 128.0, 127.7, 125.2 (t, *J* = 6.1 Hz), 122.89, 122.86, 122.3, 122.2 (t, *J* = 251.1 Hz), 121.9, 61.9, 61.1 (t, *J* = 21.1 Hz), 21.6, 18.9 (t, *J* = 4.4 Hz), 14.1. IR (film): 3039, 2996, 2952, 2931, 1738, 1481, 1463, 1266, 1123, 1096, 1074, 1046, 953, 814, 762, 695 cm^{-1}. MS (ESI, m/z): 492.2 ($M+H^+$). HRMS (ESI): Calcd. for $C_{29}H_{28}F_2NO_4^+$ ($M+H^+$): 492.1981, found: 492.1975.

Diethyl 2-((2,4-difluorophenanthridin-6-yl)difluoromethyl)-2-methylmalonate (12fa) (Table 8). Prepared from compound **1f** (0.2 mmol, 1.0 equiv), following the procedures for the preparation of **12aa**. White solid (78.7 mg, 90%). M.p. 151 – 154 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, *J* = 8.4 Hz, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 9.6 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 7.15 (t, *J* = 9.0 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 4H), 2.07 (s, 3H), 1.26 (t, *J* = 7.0 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –90.1 (s, 2F), –106.6 (q, *J* = 8.6 Hz, 1F), -117.4 (t, *J* = 9.0 Hz, 1F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.4 (t, *J* = 2.5 Hz), 161.7 (dd, *J* = 249.2, 12.0 Hz), 159.5 (dd, *J* = 260.0, 13.4 Hz), 149.9 (t, *J* = 31.4 Hz), 132.8, 131.4, 128.9, 127.7 (d, *J* = 12.2 Hz), 127.4 (t, *J* = 6.2 Hz), 127.3 (d, *J* = 1.8 Hz), 123.2, 122.9, 122.1 (t, *J* = 250.8 Hz), 104.5 (dd, *J* = 28.0, 22.3 Hz), 103.0 (dd, *J* = 23.2, 4.5 Hz), 61.9, 61.0 (t, *J* = 20.9 Hz), 18.7 (t, *J* = 4.4 Hz), 13.9. IR (film): 3113, 2987, 2909, 1739, 1629, 1588, 1530, 1499, 1444, 1419, 1376, 1272, 1230, 1134, 1099, 1091, 1048, 1001, 866, 771, 682, 603 cm^{-1}. MS (ESI, m/z): 438.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{22}H_{20}F_4NO_4^+$ ($M+H^+$): 438.1323, found: 438.1323.

Diethyl 2-((2-chlorophenanthridin-6-yl)difluoromethyl)-2-methylmalonate (12ga) (Table 8). Prepared from compound **1g** (0.2 mmol, 1.0 equiv), following the procedures for the preparation of **12aa**. White solid (86.1 mg, 99%). M.p. 88 – 89 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, *J* = 8.4 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.44 (s, 1H), 7.94 (d, *J* = 8.8 Hz, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 4.31 – 4.19 (m, 4H), 2.05 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –90.5 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.5 (t, *J* = 2.3 Hz), 150.5 (t, *J* = 31.2 Hz), 139.3, 134.8, 133.0, 131.5, 131.2, 129.6, 128.3, 127.2 (t, *J* = 6.1 Hz), 125.7, 122.8, 122.4, 121.9 (t, *J* = 251.2 Hz), 121.8, 61.8, 61.0 (t, *J* = 21.2 Hz), 18.7 (t, *J* = 4.4 Hz), 14.0. IR (film): 3087, 2982, 2905, 1732, 1602, 1525, 1488, 1448, 1415, 1365, 1267, 1176, 1049, 1020, 945, 868, 828, 771, 683 cm^{-1}. MS (ESI, m/z): 436.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{22}H_{21}ClF_2NO_4^+$ ($M+H^+$): 436.1122, found: 436.1116.

Diethyl 2-(difluoro(3-(trifluoromethyl)phenanthridin-6-yl)methyl)-2-methylmalonate (12ha) (Table 8). Prepared from compound **1h** (0.08 mmol, 1.0

equiv), following the procedures for the preparation of **12aa**. White solid (33.0 mg, 88%). M.p. 102 – 105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 – 8.65 (m, 3H), 8.27 (s, 1H), 7.92 (t, *J* = 8.0 Hz, 2H), 7.79 (t, *J* = 7.6 Hz, 1H), 4.33 – 4.21 (m, 4H), 2.07 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –62.8 ((s, 3F), –90.7 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.5 (t, *J* = 2.5 Hz), 152.1 (t, *J* = 31.0 Hz), 140.3, 133.4, 131.7, 131.1 (q, *J* = 32.9 Hz), 129.0, 127.7 – 127.5 (m), 127.1, 124.6 (q, *J* = 3.1 Hz), 123.9 (q, *J* = 270.7 Hz), 123.4, 122.9, 121.8 (t, *J* = 251.5 Hz), 62.0, 61.1 (t, *J* = 21.1 Hz), 18.7 (t, *J* = 4.5 Hz), 14.0. IR (film): 3087, 2991, 2918, 1739, 1629, 1612, 1532, 1462, 1445, 1335, 1272, 1239, 1175, 1126, 1098, 1074, 1052, 951, 884, 840, 777, 734, 691 cm^{-1}. MS (ESI, m/z): 470.1 (M+H$^+$). HRMS (ESI): Calcd. for $C_{23}H_{21}F_5NO_4^+$ (M+H$^+$): 470.1385, found: 470.1383.

Diethyl 2-(benzofuro[3,2-k]phenanthridin-6-yldifluoromethyl)-2-methylmalonate (12ia) (Table 8). Prepared from compound **1i** (0.08 mmol, 1.0 equiv), following the procedures for the preparation of **12aa**. White solid (35.6 mg, 91%). M.p. 160 – 162 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.51 (t, *J* = 8.2 Hz, 1H), 8.63 – 8.61 (m, 1H), 8.17 – 8.13 (m, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.97 (t, *J* = 8.2 Hz, 1H), 7.84 – 7.75 (m, 2H), 7.70 (t, *J* = 8.4 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.39 – 7.34 (m, 1H), 4.35 – 4.23 (m, 4H), 2.13 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –90.0 (s, 2F). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 168.8 (t, *J* = 2.7 Hz), 156.6, 152.0, 149.9 (t, *J* = 31.1 Hz), 141.3, 129.8, 129.12, 129.06, 128.2, 127.2, 125.4, 123.6, 123.2, 122.8, 122.3 (t, *J* = 252.0 Hz), 122.2, 121.9 (t, *J* = 6.7 Hz), 121.8, 121.1, 120.0, 112.1, 61.9, 61.3 (t, *J* = 21.1 Hz), 19.0 (t, *J* = 4.2 Hz), 14.1. IR (film): 3074, 2987, 2900, 1747, 1625, 1457, 1419, 1370, 1269, 1204, 1189, 1106, 1084, 1050, 997, 860, 767, 749, 733, 628, 582 cm^{-1}. MS (ESI, m/z): 492.1 (M+H$^+$). HRMS (ESI): Calcd. for $C_{28}H_{24}F_2NO_5^+$ (M+H$^+$): 492.1617, found: 492.1612.

Procedures for the Preparation of 6-(1,1-Difluoro-2-methyl-2-nitropropyl)phenanthridine (14a) (Scheme 5). To an oven-dried 10 mL Schlenk Tube was added *t*-BuOK (89.8 mg, 0.8 mmol, 4.0 equiv) and 18-crown-6 (126.9 mg, 0.48 mmol, 2.4 equiv) in glove box and then the flask was moved out of the glove box. Under argon atmosphere, DMSO (0.4 mL) was injected and the reaction mixture was

stirred. Me_2CHNO_2 (**13a**) (71.3 mg, 0.8 mmol, 4.0 equiv) was dissolved in DMSO (1.6 mL) and was added dropwise into the reaction system. The resulting reaction mixture was stirred at room temperature for 30 min. Under argon atmosphere, the solid of 6-(difluoro(phenylsulfonyl)methyl)phenanthridine (**1a)** (73.9 mg, 0.2 mmol, 1.0 equiv) was added quickly into the reaction system. The resulting reaction mixture was stirred at room temperature and room light illumination under argon atmosphere for 24 h. After the reaction was complete, the mixture was quenched with H_2O (5 mL). The aqueous layer was extracted with EtOAc (8 mL × 3) and the combined organic layer was dried over anhydrous $MgSO_4$. After the solution was filtered, the solvent was evaporated under reduced pressure and the residue was mixed with silica gel and purified by column chromatography on silica gel by using PE/EtOAc (30:1, v/v) as eluent to provide **14a** as off-white solid (47.2 mg, 75%). M.p. 131 – 134 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ 8.58 (t, *J* = 9.0 Hz, 2H), 8.49 – 8.47 (m, 1H), 8.02 – 7.99 (m, 1H), 7.83 (t, *J* = 8.2 Hz, 1H), 7.71 – 7.67 (m, 3H), 2.11 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ –94.6 (s, 2F). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.1 (t, *J* = 30.5 Hz), 140.9, 134.2, 131.0, 130.7, 129.03, 128.99, 127.7, 126.8 (t, *J* = 6.3 Hz), 124.7, 122.9, 122.5, 122.0, 120.2 (t, *J* = 250.3 Hz), 89.2 (t, *J* = 25.3 Hz), 23.3 (t, *J* = 3.6 Hz). IR (KBr): 3080, 3002, 2955, 1616, 1552, 1445, 1397, 1369, 1350, 1236, 1132, 1102, 1090, 1053, 954, 886, 847, 761, 723, 678, 575 cm^{-1}. MS (ESI, m/z): 317.1 ($M+H^+$). HRMS (ESI): Calcd. for $C_{17}H_{15}F_2N_2O_2^+$ ($M+H^+$): 317.1096, found: 317.1094.

Procedures for the Preparation of 2-Hydroxy-*N*,*N*-dimethyl-2-phenylacetamide (**16**) **(Scheme 8).** The preparation of **16** was based on reported procedures.[21] White solid (200 mg, 37%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.30 (m, 5H), 5.19 (d, *J* = 6.4 Hz, 1H), 4.74 (d, *J* = 6.4 Hz, 1H), 3.02 (s, 3H), 2.76 (s, 3H). The characterization data are consistent with previous report.[21]

ASSOCIATED CONTENT

Supporting Information

List of compounds **1**; control experiments of the reactions between **1a** and nucleophiles; cyclic voltammetry study; and ^{1}H, ^{19}F and ^{13}C NMR spectra of isolated compounds (PDF). The Supporting Information is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.

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(22) Based on the reduction potential of **1a** (–1.20 V vs. SCE) and the nucleophile scope of its substitution reaction, we can predict that many soft nucleophiles (good electron-donors), including PhSNa, PhSeNa and $KC(Me)(CO_2Et)_2$, may be reactive not only towards fluorinated sulfones with higher first reduction potential than **1a**, but also towards fluorinated sulfones with somewhat lower first reduction potential than **1a**, such as 2-$PyCF_2SO_2Ph$ (–1.44 V vs. SCE) and $PhCF_2SO_2Ph$ (–1.55 V vs. SCE). For a list of other possible fluorinated sulfones that may undergo SET reaction with soft nucleophiles such as PhSNa, PhSeNa and $KC(Me)(CO_2Et)_2$, see Ref. 13a and the Supporting Information.