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Graphical Abstract

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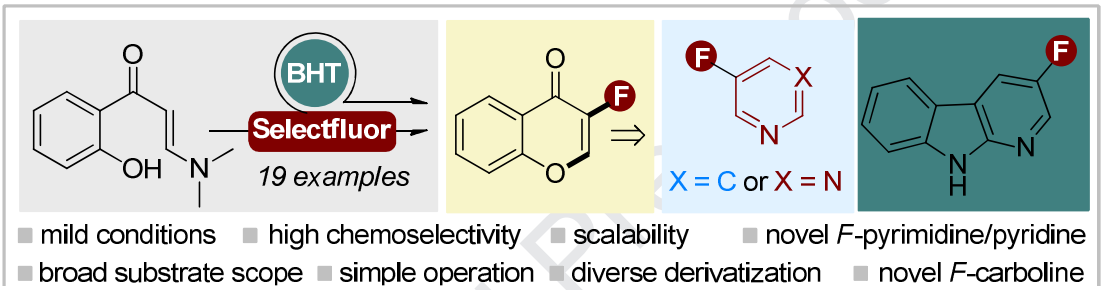

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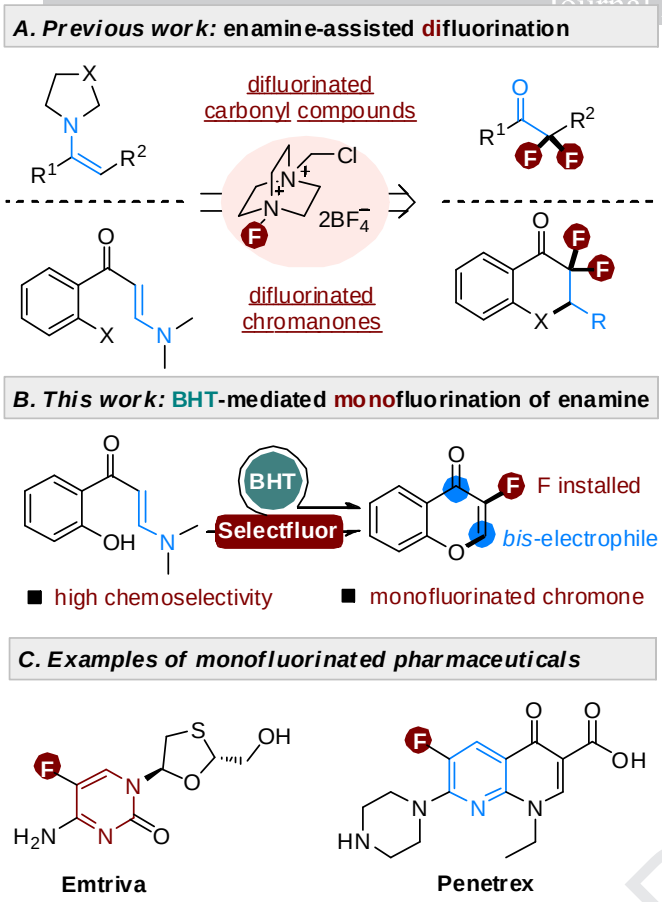
ABSTRACT

A BHT-regulated chemoselective monofluorination of enaminones with Selectfluor under mild reaction conditions was unveiled for the first time. As a result, an array of monofluorinated chromones were efficiently assembled in a simple operational manner. Moreover, the scalability of this protocol and the versatility for the downstream transformations of the obtained fluorinated chromones to installing diverse nitrogen-containing heterocycles greatly broaden the practical applications of this developed protocol.

1. Introduction

Fluorine-containing organic compounds are of significant interest in the fields of pharmaceuticals, agrochemicals and materials. It is unquestionable that the incorporation of fluorine can significantly affect the physical-chemical properties of the parent molecules, such as hydrophobicity, metabolic stability, membrane permeability and conformational preference.[1] Even ^{18}F-containing compounds have been designed and synthesized as imaging probes for positron emission tomography (PET), both in diagnosis and medicinal chemistry.[2] As a consequence, tremendous efforts have been devoted to exploring facile fluorination methods to address the current issues in the fluorination including high cost, operational difficulty, high toxicity, poor selectivity and involvement of transition metals.[3] Concurrently, a variety of new fluorinating reagents with *N-F* core structure, especially Selectfluor, have emerged as generally safer and easily manipulated alternative sources of fluorine, offering a number of synthetic potentials.[4] Essentially, these *N-F* based reagents are typically regarded as electrophilic fluorinating agents and thus can react with many kinds of nucleophilic partners. Following this concept, exploiting the *C-F* bond formation by employing these *N-F* based reagents in newly designed transformations would enrich the arsenal of fluorination and extend the boundary of fluorinated scaffolds, which is always pivotal in the synthetic and medicinal chemistry.

Enaminone, easily prepared from ketones or aldehydes, have been long recognized as valuable synthetic intermediates and synthons.[5] Given their structural and electronic features, enaminone could serve as effective nucleophiles in a wide range of transformations.[6] Not surprisingly, sufficient attention has been paid to the fluorination of enaminone with *N-F* based reagents. Back to 2005, enaminone were firstly employed to react with Selectfluor by Shreeve and co-workers, giving diverse difluorinated carbonyl compounds.[7] Noticeably, the monofluorinated product was only obtained as the minor product for limited examples while the difluorinated product dominated (Scheme 1A). Additionally, some limited examples for monofluorination of enaminones with Selectfluor were also reported with low to moderate yields.[8] However, our group[9] and Song's group[10] independently disclosed that another types of enamine derivatives, o-hydroxyarylenaminones or o-aminoarylenaminones, could react with Selectfluor, but giving the difluorinated products exclusively. Despite these advances, we were curious about the possibility of the monofluorination of the enaminone in this process, which would provide a facile installation of monofluorinated chromone.[11] (Scheme 1B). As well known, chromones are versatile building blocks for constructing diversely featured heterocycles with a variety of physiological and biological activities, such as pyrimidine and pyridine scaffolds.[12] Additionally, the introduction of one fluorine atom into these nitrogen-containing heterocycles is often adopted as a strategy to improve their biological and physicochemical properties (Scheme 1C).[1] Given the importance of the fluorinated heterocycles and our continued research interest,[13] we were attracted by the underdeveloped monofluorination of enamine. We serendipitously found that the cyclization of *o*-hydroxyarylenaminones promoted by Selectfluor could be manipulated by simply adding radical scavenger – TEMPO or



Scheme 1. Synthetic profiles of enamine and selectfluor, and representative monofluorinated pharmaceuticals.

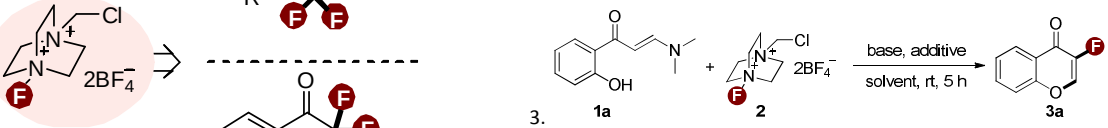
BHT, realizing the monofluorination to generate monofluorochromone (Scheme 1B). Furthermore, the resulting monofluorochromone could serve as a versatile platform to access diverse fluorinated hetereocycles.

2. Results and Discussion

2.1. Optimization of the reaction conditions

Our initial investigation started with the addition 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as the additive to the reaction of *o*-hydroxyarylenaminone **1a** and Selectfluor (Table 1). Encouragingly, the desired monofluorinated chromone **3a** was isolated in a moderate yield while only a trace amount of the corresponding difluorinated product was obtained (Table 1, entry 1). Next, solvent screening demonstrated that THF was the best choice, while DMSO or DMF was found to be ineffective for this transformation (Table 1, entries 1-8). Subsequently, several bases were evaluateded, of which NaOAc provided the highest yield (Table 1, entries 9-11). Either increasing or reducing the amount of NaOAc gave a similar chemical yield of **3a**, but the reaction was completely suppressed without base (Table 1, entries 12-14). *N*-fluorobenzenesulfonimide (NSFI) was also tested in this process, but with a relatively lower yield (Table 1, entry 15). The yield of monofluorinated chromone was obviously reduced with an increased amount of Selectfluor (Table 1, entry 16). Finally, instead of TEMPO, butylated hydroxytoluene (BHT) was employed in this reaction and a slightly improved chemical yield of **3a** was observed. This monofluorinated process can occur as well in the presence of a reduced, or even catalytic amount of BHT (Table 1, entries 18-20) albeit with moderate

Table 1. Optimizations of reaction conditions[a]



3.

Entry	Solvent	Base	Additive	Yield (%)[b]
1	acetone	NaOAc	TEMPO	58
2	CH_2Cl_2	NaOAc	TEMPO	51
3	CH_3OH	NaOAc	TEMPO	47
4	DMSO	NaOAc	TEMPO	trace
5	toluene	NaOAc	TEMPO	54
6	DMF	NaOAc	TEMPO	trace
7	CH_3CN	NaOAc	TEMPO	29
8	THF	NaOAc	TEMPO	70
9	THF	Na_2CO_3	TEMPO	65
10	THF	Et_3N	TEMPO	28
11	THF	DMAP	TEMPO	50
12	THF	-	TEMPO	NR
13	THF	NaOAc[c]	TEMPO	71
14	THF	NaOAc[d]	TEMPO	68
15[e]	THF	NaOAc[c]	TEMPO	15
16[f]	THF	NaOAc[c]	TEMPO	26
17	**THF**	**NaOAc[c]**	**BHT**(3 equiv)	**76**
18	THF	NaOAc[c]	BHT (2 equiv.)	61
19	THF	NaOAc[c]	BHT (1 equiv.)	56
20	THF	NaOAc[c]	BHT (0.2 equiv.)	54

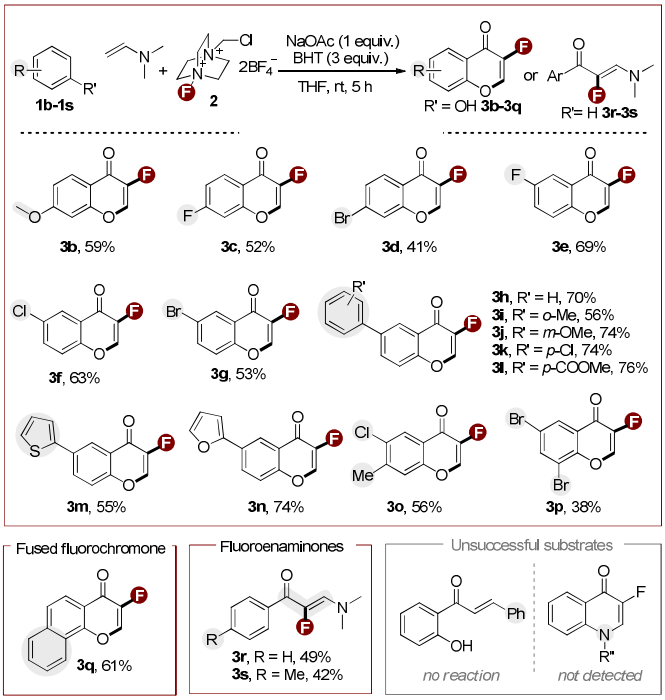
[a]Reaction conditions: **1a** (0.5 mmol), **2** (0.5 mmol), base (1.0 mmol), TEMPO (1.5 mmol) in solvent (2 mL), rt, 5 h. [b]Isolated yields. [c]NaOAc (1 equiv.). [d]NaOAc (3 equiv.). [e]NSFI was used instead of Selectfluor. [f]Selectfluor (2 equiv). NR: no reaction.

yields. After a series of screening, the optimal conditions were determined to be Selectfluor (1 equiv.) as the fluorine source, NaOAc (1 equiv.) as the base, BHT (3 equiv) as the additive, and THF as the solvent (Table 1, entry 17).

2.2. Scope and limitations of substrates

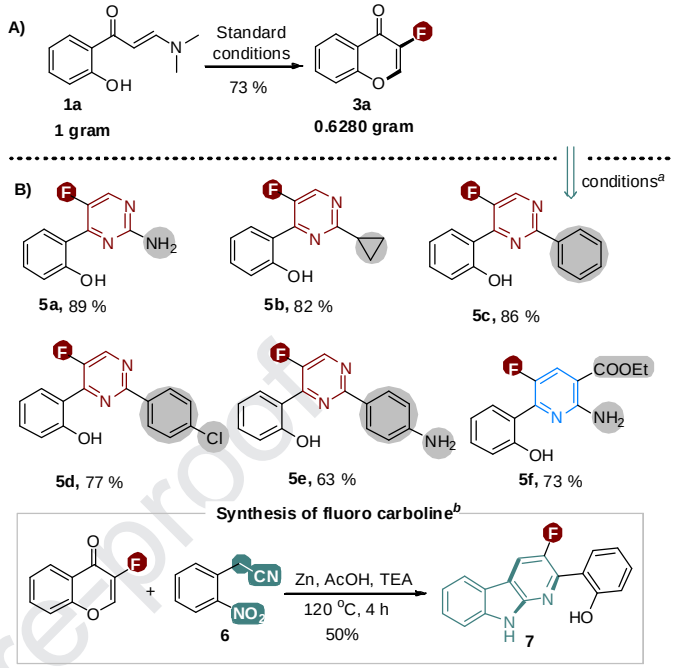
Having established the optimal conditions, we next explored the generality and the functional group tolerance of this protocol (Scheme 2). It was found that the electronic features of substituents at phenyl moiety slightly affected the efficacy of this transformation and thus satisfactory yields were thoroughly secured. Specifically, it was found that the substrate with a fluorine substituent at the meta-position of phenol moiety gave lower yield than the analogues substituted at the *para*-position (Scheme 2, **3c** *vs* **3e**), and the presence of a bromine substituent undermined the yield in all of the tested cases (Scheme 2, **3d**, **3g**, and **3p**). Aryl substituents were also suitable substrates, furnishing the corresponding products with higher yields (Scheme 2, **3h**-**3l**). Other substrates bearing heteroaromatic rings, such as thiophene or furan, also produced **3m** and **3n** in 55% and 74% yield respectively. Moreover, the disubstituted substrates and naphthalene analogue delivered the corresponding monofluorinated chromone in modest yields as well (Scheme 2, **3o**-**3q**). Meanwhile, direct C-H monofluorination of the conventional tertiary enaminones **1r** and **1s** was verified to proceed smoothly, further demonstrating the good tolerance of this synthetic protocol. In contrast to enamine substrate, the counterpart chalocone was unable to proceed the cyclization

Scheme 2. Substrate scope for the synthesis of monofluorinated chromones[a,b]



[a]Reaction conditions: **1** (0.5 mmol, 1 equiv.), **2** (0.5 mmol, 1 equiv.), NaOAc (0.5 mmol, 1 equiv.), BHT (1.5 mmol, 3 equiv.), in THF (2.0 mL) at room temperature for 5 h. [b]Isolated yields.

Scheme 3. Scale-up, synthetic utility of the protocol and control experiments

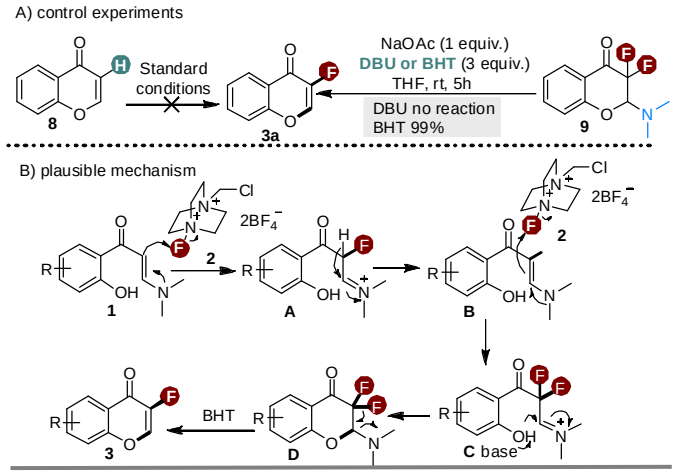


[a]Reaction conditions: **3a** (0.5 mmol, 1 equiv.), amidines (1 mmol, 2 equiv.), K_2CO_3 (1.5 mmol, 3 equiv.), in EtOH (2.0 mL), 80 °C for 3 h; isolated yields. [b]Reaction conditions: **3a** (0.5 mmol), **6** (1 mmol), Zn (4 mmol), TEA (1.5 mmol) in AcOH(15 mmol), heated at 120 °C for 4 h; isolated yield.

under the standard conditions, confirming the key role of the enamine in this tandem process. However, *o*-aminoarylenaminones only gave a fairly complex reaction and the corresponding monofluorinated quinolone was unobtainable. Given the mildness of the reaction conditions, the practicality and scalability of this protocol were subsequently exploited. The reaction of enaminone **1a** was performed on gram scale under the standard reaction conditions, giving the desired product **3a** in 73% yield without any loss of efficiency (Scheme 3A). Giving the versatile synthetic potentials of chromone, the monofluorinated chromone **3a** was utilized to proceed varied ring-reorganizations to access other interesting fluorinated nitrogen-containing heterocycles (Scheme 3B). Initially, various amidines were employed to react with monofluorinated chromone **3a**, furnishing a range of monofluorinated pyrimidines in good yields (Scheme 3B, **5a**-**5e**). To our delight, both aliphatic amidines including guanidine and cyclopropanecarbanidine, and aromatic amidines with electron-withdrawing or electron-donating substituents of the benzene ring were all tolerated well. Notably, cyclopropyl and amino fragment are both versatile players that frequently appear in drug molecules.[14] As expected, ethyl 2-amidinoacetate hydrochloride with multiple nucleophilic sites reacted smoothly with monofluorinated chromone **3a**, giving a monofluorinated pyridine **5f**.[12c] Furthermore, fused tricyclic analogue *α*-carboline **7** was efficiently assembled by treating 3a with *o*-nitrophenylacetonitrile in the presence of zinc dust, acetic acid and triethylamine.[15] Obviously, the diversified ring-reorganizations of the as-prepared monofluorinated chromone through simple and straightforward operations would endow this developed BHT-regulated protocol with greater impact and significance in drug discovery.

2.3. Control experiments and possible reaction mechanism

Scheme 4. Control experiments and possible reaction mechanism



To further mechanistically probe the reaction, the corresponding control experiments were carried out (Scheme 4). When 4*H*-chromen-4-one **8** was subjected to the standard conditions, the desired product was not observed. On the contrary, in the presence of BHT, the preformed difluorinated 2‑ amino-substituted chromanone **9** could be quantitatively converted to the corresponding monofluorinated chromone **3a.** Additionally, it was found that the difluorinated 2-amino-substituted chromanone **9** was unable to be converted to the corresponding monofluorinated chromone **3a** in the absence of BHT, even with a strong base DBU. On the basis of these results, it was found that BHT played a crucial role in the ultimate formation of the monofluorinated product. We thus reasoned that a BHT-

promoted defluorination of difluorinated intermediates was likely to be involved in this process. Surely, this strategy would provide a facile pathway to modulate the degree of fluorination.

On the basis of the observed results, a plausible mechanism involving iminium intermediate was proposed in Scheme 4. It could be assumed that the first round of fluorination of enaminone **1** by Selectfluor formed the intermediate iminium ion **A**, which facilely tautomerized to form enamine **B**. Afterthat, the difluorinated iminium intermediate **C** could be generated in a similar manner. The resulting reactive iminium ion would significantly drive the intramolecular cyclization to accomplish the difluorinated chromanones **D** rapidly. The subsequent defluorination and deamination ultimately delivered the desired products **3** in the presence of BHT.

3. Conclusion

In conclusion, we successfully developed a facile protocol accessing a range of monofluorinated chromones under mild conditions. The key to the monofluorination process is the addition of BHT or TEMPO. The notable features of this process include excellent chemoselectivity, mild reaction conditions, synthetic simplicity, and broad substrate scope. Significantly, the diversified transformations for the obtained monofluorinated chromone scaffold will enrich the library of fluorinated heterocycles and provide more options for drug screening in the future. Further synthetic applications and studies to unveil the biological activities of these privileged scaffolds are ongoing in our laboratory.

4. Experimental section

Unless otherwise noted, all the reagents were purchased from commercial suppliers and used without further purification. ^{1}H NMR spectra were recorded at 400 MHz. The chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = quint, m = multiplet), coupling constants (Hz), integration. ^{13}C NMR data were collected at 100 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. ^{19}F NMR data were collected at 376 MHz with complete proton decoupling. UV–Vis spectra were recorded using a shimadzu UV-2600. Infrared spectra (IR) were measured by FT-IR apparatus. High resolution mass spectroscopy (HRMS) was recorded on TOF MS ES+ mass spectrometer and acetonitrile was used to dissolve the sample. Column chromatography was carried out on silica gel (200-300 mesh). The starting materials enaminones **1** were prepared according to the previously described method.[5]

*5.1 General procedures for synthesis of **3a-3s**.*

o-Hydroxyarylenaminone **1** (0.5 mmol, 1 equiv.), Selectfluor (0.5 mmol, 1.0 equiv), NaOAc (0.5 mmol, 1.0 equiv) and BHT (1.5 mmol, 3 equiv.) were added to THF (2.0 mL) in a 10 mL reaction tube equipped with a stirring bar. The reaction mixture was stirred at room temperature for 5 h. After completion of the reaction (confirmed by TLC analysis, petroleum ether/ethyl acetate = 10/1), the solvent was removed *in vacuo*, and the resulting residue was purified via silica gel chromatography (petroleum ether/ethyl acetate = 50/1) to yield the corresponding monofluorinated chromone **3**.

3-Fluorochromone **3a.** White solid (62 mg, 76%): m.p. 160-161 ℃; IR (neat) *ν* 2921, 1640, 1466, 1184, 899, 529 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.29 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.18 (d, *J* = 3.4 Hz, 1H), 7.72 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H); ^{19}F NMR (376 MHz, Chloroform-d) δ -165.76; ^{13}C{^{1}H} NMR (100 MHz, Chloroform-*d*) δ 170.5 (d, $^{2}J_{C\text{-}F}$ = 15.5 Hz), 155.8, 149.4 (d, $^{1}J_{C\text{-}F}$ = 249.0 Hz), 143.0 (d, $^{2}J_{C\text{-}F}$ = 40.0 Hz), 134.1, 126.0 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 125.3, 124.8 (d, $^{3}J_{C\text{-}F}$ = 7.7 Hz), 118.4; HRMS (ESI): m/z [M+H]$^{+}$ called for $C_9H_6FO_2^+$: 165.0346, found 165.0350.

3-Fluorochromone **3b**. White solid (57 mg, 59%): m.p. 147-148 ℃; IR (neat) *ν* 3094, 1645, 1612, 1440, 1203, 1018, 893, 613 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 8.9 Hz, 1H), 8.08 (d, *J* = 2.8 Hz, 1H), 7.00 (d, *J* = 8.7 Hz, 1H), 6.86 (s, 1H), 3.91 (s, 3H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -166.84; ^{13}C{^{1}H} NMR (100 MHz, Chloroform-*d*) δ169.9 (d, $^{2}J_{C\text{-}F}$ =15.9 Hz), 164.4, 157.7, 149.4 (d, $^{1}J_{C\text{-}F}$ = 248.7 Hz), 142.4 (d, $^{2}J_{C\text{-}F}$ = 40.5 Hz), 127.2 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 118.6 (d, $^{3}J_{C\text{-}F}$ = 7.4 Hz), 115.0, 100.3, 55.9; HRMS (ESI) m/z [M+H]$^{+}$ calcd for $C_{10}H_8FO_3^+$: 195.0452, found 195.0476.

3-Fluorochromone **3c.** White solid (47 mg, 52%): m.p. 123-124 ℃; IR (neat) *ν* 3086, 2922, 1661, 1617, 1443, 1240, 1201, 1086, 955, 530 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.35–8.28 (m, 1H), 8.16 (s, 1H), 7.19 (t, *J* = 7.6 Hz, 2H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -101.76, -165.72; ^{13}C{^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.7 (d, $^{2}J_{C\text{-}F}$ = 16.0 Hz), 165.8 (d, $^{1}J_{C\text{-}F}$ = 256.5 Hz), 156.8 (d, $^{3}J_{C\text{-}F}$ = 14 Hz), 149.4 (d, $^{1}J_{C\text{-}F}$ = 250.4 Hz), 143.1 (d, $^{2}J_{C\text{-}F}$ = 40.6 Hz), 128.6 (dd, $^{3,4}J_{C\text{-}F}$ = 10.8, 3.4 Hz), 121.7 (dd, $^{3,4}J_{C\text{-}F}$ = 7.8, 1.9 Hz), 114.4 (d, $^{2}J_{C\text{-}F}$ = 23.1 Hz), 105.0 (d, $^{2}J_{C\text{-}F}$ = 25.6 Hz); HRMS (ESI) m/z [M+H]$^{+}$ calcd for $C_9H_5F_2O_2^+$: 183.0252, found 183.0270.

3-Fluorochromone **3d**. White solid (50 mg, 41%): m.p. 135-136 ℃; IR (neat) *ν* 3081, 2363, 1655, 1599, 1430, 1196, 1145, 958, 524 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (s, 1H), 8.14 (d, *J* = 4.6 Hz, 1H), 7.71 (d, *J* = 1.8 Hz, 1H), 7.56 (dd, *J* = 8.6, 1.7 Hz, 1H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -164.86; ^{13}C{^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.8 (d, $^{2}J_{C\text{-}F}$ = 16.0 Hz), 155.7, 149.4 (d, $^{1}J_{C\text{-}F}$ = 250.8 Hz), 143.0 (d, $^{1}J_{C\text{-}F}$ = 40.3 Hz), 129.0, 128.6, 127.3 (d, $^{4}J_{C\text{-}F}$ = 3.5 Hz), 123.7 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 121.5; HRMS (ESI) m/z [M+H]$^{+}$ calcd for $C_9H_5BrFO_2^+$: 242.9451, found 242.9476.

3-Fluorochromone **3e**. White solid (63 mg, 69%): m.p. 270-271 ℃; IR (neat) *ν* 3078, 2920, 1645, 1472, 1260, 1176, 885, 563 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 3.3 Hz, 1H), 7.93 (dd, *J* = 8.1, 3.3 Hz, 1H), 7.54 (dd, *J* = 9.2, 4.2 Hz, 1H), 7.45 (ddd, *J* = 9.3, 7.4, 3.0 Hz, 1H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -114.61, -166.33; ^{13}C{^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.7 (dd, $^{2,4}J_{C\text{-}F}$ = 15.9, 2.3 Hz), 159.5 (d, $^{1}J_{C\text{-}F}$ = 248.3 Hz), 152.1, 149.0 (dd, $^{1,5}J_{C\text{-}F}$ = 249.3, 1.4 Hz), 143.2 (d, $^{2}J_{C\text{-}F}$ = 40.0 Hz), 126.1 (t, $^{3}J_{C\text{-}F}$ = 8.2 Hz), 122.6 (d, $^{2}J_{C\text{-}F}$ = 25.7 Hz), 120.6 (d, $^{3}J_{C\text{-}F}$ = 8.3 Hz), 110.8 (dd, $^{2,4}J_{C\text{-}F}$ = 24.2, 3.8 Hz); HRMS (ESI) m/z [M+H]$^{+}$ calcd for $C_9H_5F_2O_2^+$: 183.0252, found 183.0271.

3-Fluorochromone **3f**. White solid (63 mg, 63%): m.p. 157-158 ℃; IR (neat) *ν* 2923, 1647, 1463, 1373, 1257, 1185, 1117, 893, 633 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.23 (d, *J* = 2.6 Hz, 1H), 8.18 (d, *J* = 3.1 Hz, 1H), 7.65 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.49 (d, *J* = 9.0 Hz, 1H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -165.23; ^{13}C{^{1}H} NMR (100 MHz, Chloroform-*d*) δ 169.3 (d, $^{2}J_{C\text{-}F}$ = 16.0 Hz), 154.1, 149.3 (d, $^{1}J_{C\text{-}F}$ = 250.2 Hz), 143.2 (d, $^{1}J_{C\text{-}F}$ = 40.1 Hz), 134.4, 131.5, 125.8 (d, $^{3}J_{C\text{-}F}$ = 8.2 Hz), 125.2 (d, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 120.2; HRMS (ESI) m/z [M+H]$^{+}$ calcd for $C_9H_5ClFO_2^+$: 198.9957, found 199.9971.

3-Fluorochromone **3g**. White solid (64 mg, 53%): m.p. 200-201 ℃; IR (neat) *v* 3745, 2209, 2141, 2026, 1939, 1450, 1268, 648, 574 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 2.4 Hz, 1H), 8.18 (d, *J* = 3.3 Hz, 1H), 7.79 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.42 (d, *J* = 9.0 Hz, 1H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -164.93; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 169.2 (d, $^{2}J_{C\text{-}F}$ =15.9 Hz), 154.6, 149.3 (d, $^{1}J_{C\text{-}F}$ = 250.5 Hz), 143.2 (d, $^{2}J_{C\text{-}F}$ = 40.1 Hz), 137.1, 128.5 (d, $^{4}J_{C\text{-}F}$ = 3.5 Hz), 126.2 (d, $^{3}J_{C\text{-}F}$ = 8.1 Hz), 120.3, 119.0; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_9H_5BrFO_2^+$: 242.9451, found 242.9474.

3-Fluorochromone **3h**. White solid (84 mg, 70%): m.p. 95-96 ℃; IR (neat) *v* 3062, 2920, 1642, 1466, 1260, 1209, 1172, 832, 525 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.46 (s, 1H), 8.15 (d, *J* = 3.1 Hz, 1H), 7.92 (d, *J* = 8.7 Hz, 1H), 7.62 (d, *J* = 7.5 Hz, 2H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.46 (t, *J* = 7.4 Hz, 2H), 7.41–7.36 (m, 1H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -165.70; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 170.6 (d, $^{2}J_{C\text{-}F}$ = 15.5 Hz), 155.2, 149.4 (d, $^{1}J_{C\text{-}F}$ = 248.9 Hz), 143.0 (d, $^{2}J_{C\text{-}F}$ = 40 Hz), 138.8, 138.5, 133.1, 129.1, 128.1, 127.2, 125.0 (d, $^{3}J_{C\text{-}F}$ = 7.7 Hz), 123.6 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 118.9; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{15}H_9FNaO_2^+$: 263.0479, found 263.0500.

3-Fluorochromone **3i**. White solid (71 mg, 56%): m.p. 125-126 ℃; IR (neat) *v* 2925, 1646, 1470, 1263, 1206, 1173, 1110, 890, 767, 579 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 (s, 1H), 8.19 (d, *J* = 3.1 Hz, 1H), 7.69 (d, *J* = 8.6 Hz, 1H), 7.56 (d, *J* = 8.7 Hz, 1H), 7.30–7.22 (m, 4H), 2.26 (s, 3H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -165.74; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 170.6 (d, $^{2}J_{C\text{-}F}$ = 15.5 Hz), 154.8, 149.5 (d, $^{1}J_{C\text{-}F}$ = 249.0 Hz), 143.0 (d, $^{2}J_{C\text{-}F}$ = 40.0 Hz), 139.6, 139.4, 135.4, 135.3, 130.6, 129.9, 128.1, 126.1, 125.9 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 124.6 (d, $^{3}J_{C\text{-}F}$ = 7.7 Hz), 118.2, 20.5; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{16}H_{11}FNaO_2^+$: 277.0634, found 277.0659.

3-Fluorochromone **3j**. White solid (100 mg, 74%): m.p. 155-156 ℃; IR (neat) *v* 3091, 1647, 1612, 1472, 1265, 1209, 1181, 1029, 892, 560 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.44 (s, 1H), 8.15 (d, *J* = 3.4 Hz, 1H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 8.7 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 7.4 Hz, 1H), 7.13 (s, 1H), 6.92 (d, *J* = 7.4 Hz, 1H), 3.86 (s, 3H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -165.72; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 170.5 (d, $^{2}J_{C\text{-}F}$ = 15.6 Hz), 160.1, 155.2, 149.4 (d, $^{1}J_{C\text{-}F}$ = 248.9 Hz), 143.0 (d, $^{2}J_{C\text{-}F}$ = 40.1 Hz), 140.2, 138.3, 133.1, 130.1, 124.9 (d, $^{3}J_{C\text{-}F}$ = 7.7 Hz), 123.6 (d, $^{4}J_{C\text{-}F}$ = 3.5 Hz), 119.6, 118.9, 113.6, 112.8, 55.4; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{16}H_{11}FNaO_3^+$: 293.0584, found 293.0614.

3-Fluorochromone **3k**. White solid (101 mg, 74%): m.p. 149-150 ℃; IR (neat) *v* 2921, 1644, 1467, 1192, 1117, 1086, 575 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.44 (s, 1H), 8.17 (d, *J* = 3.4 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.59–7.56 (m, 3H), 7.44 (d, *J* = 8.0 Hz, 2H); ^{19}F NMR (376 MHz, Chloroform-d) δ -165.50; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 170.4 (d, $^{2}J_{C\text{-}F}$ = 15.7 Hz), 155.3, 149.5 (d, $^{1}J_{C\text{-}F}$ = 249.7 Hz), 143.0 (d, $^{2}J_{C\text{-}F}$ = 40.1 Hz), 137.31, 137.29, 134.4, 132.7, 129.2, 128.5, 125.1 (d, $^{3}J_{C\text{-}F}$ = 7.9 Hz), 123.6 (d, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 119.1; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{15}H_8ClFNaO_2^+$: 297.0089, found 297.0112.

3-Fluorochromone **3l**. White solid (113 mg, 76%): m.p. 202-203 ℃; IR (neat) *v* 3078, 2157, 1712, 1657, 1289, 1178, 1113, 828, 708 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.52 (s, 1H), 8.19 (s, 1H), 8.13 (d, *J* = 7.7 Hz, 2H), 7.97 (d, *J* = 8.6 Hz, 1H), 7.71 (d, *J* = 7.7 Hz, 2H), 7.61 (d, *J* = 8.6 Hz, 1H), 3.95 (s, 3H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -165.37; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 170.3 (d, $^{2}J_{C\text{-}F}$ = 15.7 Hz), 166.7, 155.6, 149.5 (d, $^{1}J_{C\text{-}F}$ = 250.0 Hz), 143.0 (d, $^{2}J_{C\text{-}F}$ = 40 Hz), 143.1, 137.3, 133.0, 130.3, 129.8, 127.1, 125.1 (d, $^{3}J_{C\text{-}F}$ = 7.9 Hz), 124.2 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 119.2, 52.2; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{17}H_{11}FNaO_4^+$: 321.0534, found 321.0565.

3-Fluorochromone **3m**. White solid (68 mg, 55%): m.p. 143-144℃; IR (neat) *v* 3093, 2921, 1648, 1480, 1269, 1204, 1168, 819, 570 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.43 (d, *J* = 2.4 Hz, 1H), 8.14 (d, *J* = 3.4 Hz, 1H), 7.91 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.40 (d, *J* = 3.7 Hz, 1H), 7.34 (d, *J* = 5.1 Hz, 1H), 7.10 (t, *J* = 4.4 Hz, 1H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -165.52; ^{13}C NMR$\{^{1}H\}$ (100 MHz, Chloroform-*d*) δ 170.3 (d, $^{2}J_{C\text{-}F}$ = 15.6 Hz), 154.9, 149.4 (d, $^{1}J_{C\text{-}F}$ = 249.1 Hz), 143.0 (d, $^{1}J_{C\text{-}F}$ = 40.1 Hz), 141.8, 132.0, 131.8, 128.4, 126.2, 125.2 (d, $^{3}J_{C\text{-}F}$ = 7.9 Hz), 124.5, 121.9 (d, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 119.1; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{13}H_7FNaO_2S^+$: 269.0043, found 269.0067.

3-Fluorochromone **3n**. White solid (85 mg, 74%): m.p. 150-151 ℃; IR (neat) *v* 3093, 2922, 1462, 1466, 1256, 1175, 985, 823, 594 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.44 (s, 1H), 8.13 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.50–7.48 (m, 2H), 6.76 (s, 1H), 6.50 (s, 1H); ^{19}F NMR (376 MHz, Chloroform-d) δ -165.73; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 170.3 (d, $^{2}J_{C\text{-}F}$ = 15.6 Hz), 154.8, 151.8, 149.3 (d, $^{1}J_{C\text{-}F}$ = 249.0 Hz), 143.0, 142.9 (d, $^{2}J_{C\text{-}F}$ = 40.1 Hz), 129.6, 128.3, 125.0 (d, $^{3}J_{C\text{-}F}$ = 7.8 Hz), 120.0 (d, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 118.9, 112.1, 106.7; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{13}H_7FNaO_3^+$: 253.0271, found 253.0289.

3-Fluorochromone **3o**. White solid (59 mg, 56%): m.p. 172-173℃; IR (neat) *v* 3392, 2918, 1641, 1464, 1186, 895, 753, 683 616 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 (s, 1H), 8.13 (d, *J* = 3.4 Hz, 1H), 7.39 (s, 1H), 2.50 (s, 3H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -165.72; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 169.3 (d, $^{2}J_{C\text{-}F}$ = 16.1 Hz), 154.1, 149.2 (d, $^{1}J_{C\text{-}F}$ = 249.6 Hz), 143.6, 142.9 (d, $^{2}J_{C\text{-}F}$ = 40.2 Hz), 132.3, 125.4 (d, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 123.8 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 120.1, 20.8; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{10}H_7ClFO_2^+$: 213.0113, found 213.0130.

3-Fluorochromone **3p.** White solid (61mg, 38%): m.p. 130-131 ℃; IR (neat) *v* 3053, 2921, 1659, 1551, 1443, 1237, 1150, 874, 621 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 2.1 Hz, 1H), 8.25 (d, *J* = 2.9 Hz, 1H), 8.05 (d, *J* = 2.1 Hz, 1H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -163.77; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 168.5 (d, $^{2}J_{C\text{-}F}$ = 16.4 Hz), 151.4, 149.3 (d, $^{1}J_{C\text{-}F}$ = 252.5 Hz), 143.4 (d, $^{2}J_{C\text{-}F}$ = 40.4 Hz), 139.9, 128.0 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 126.9 (d, $^{3}J_{C\text{-}F}$ = 8.3 Hz), 118.9, 113.2; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_9H_3Br_2NaFO_2^+$: 342.8376 , found 342.8392.

Fluorochromone **3q.** White solid (65 mg, 61%): m.p. 174-175 ℃; IR (neat) *v* 3391, 2920, 1740, 1642, 1459, 1362, 1196, 1080, 965, 766 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.43 (d, *J* = 8.0 Hz, 1H), 8.30 (d, *J* = 2.9 Hz, 1H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.76–7.65 (m, 3H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -164.37; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 170.2 (d, $^{2}J_{C\text{-}F}$ =15.5 Hz), 153.4, 150.6 (d, $^{1}J_{C\text{-}F}$ = 250.6 Hz), 142.1 (d, $^{2}J_{C\text{-}F}$ = 40.2 Hz), 135.8, 129.8, 128.2, 127.6, 125.7, 123.8, 122.3, 121.4 (d, $^{3}J_{C\text{-}F}$ = 7.9 Hz), 120.4 (d, $^{4}J_{C\text{-}F}$ = 3.0 Hz); HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_8FO_2^+$: 215.0503, found 215.0521.

Fluoro enaminone **3r.** Ilky liquid (47 mg, 49%): IR (neat) *v* 2918, 1656, 1539, 1336, 1116, 946, 847, 699 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 7.1 Hz, 2H), 7.45–7.37 (m, 3H), 6.66 (d, *J* = 27.6 Hz, 1H), 3.08 (s, 6H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -166.45; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-

d) δ 185.5 (d, $^{2}J_{C\text{-}F}$ = 19.1 Hz), 140.0 (d, $^{1}J_{C\text{-}F}$ = 228.4 Hz), 138.7, 137.4 (*br*), 130.6, 128.4 (d, $^{3}J_{C\text{-}F}$ = 3.6 Hz), 128.1, 42.8 (*br*); HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{11}H_{13}FNO^+$: 194.0976, found:194.0986.

Fluoro enaminone **3s.** Ilky liquid (43 mg, 42%): IR (neat) *v* 2920, 1657, 1578, 1433, 1331, 1114, 942, 746 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 7.7 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 6.68 (d, *J* = 27.8 Hz, 1H), 3.08 (s, 6H), 2.38 (s, 3H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -166.14; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 185.4 (d, $^{2}J_{C\text{-}F}$ = 19.2 Hz), 141.1, 140.2 (d, $^{1}J_{C\text{-}F}$ = 229.0 Hz), 136.8 (*br*), 135.8, 128.7, 128.6 (d, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 42.8 (*br*), 21.5; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{12}H_{15}FNO^+$: 208.1132, found : 208.1137.

*5.2 General procedures for synthesis of **5a-5f**.*

A suspension of **3a** (0.5 mmol, 1 equiv.), amidines or guanidine (1.0 mmol, 2 equiv.), and K_2CO_3 (1.0 mmol, 2 equiv.) in EtOH (2.0 mL) was refluxed for 3h. After the solvent was removed *in vacuo*, the resulting residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 100/3 to 10/1) to yield fluoro-pyrimidines or fluoro-pyridine.

Fluoro pyrimidine **5a.** White solid (91 mg, 89%): m.p. 212-213 ℃; IR (neat) *v* 3374, 3180, 2920, 1645, 1574, 1453, 1193, 753, 542 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.41 (s, 1H), 8.43 (d, *J* = 3.8 Hz, 1H), 7.81 (d, *J* = 7.7 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.04 (s, 2H), 7.00–6.91 (m, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -151.34; $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 159.3 (d, $J_{C\text{-}F}$ = 2.4 Hz), 159.1, 151.4 (d, $J_{C\text{-}F}$ = 9.0 Hz), 148.5 (d, $^{1}J_{C\text{-}F}$ = 247.9 Hz), 148.5 (d, $J_{C\text{-}F}$ = 26.4 Hz), 132.8, 130.5 (d, $J_{C\text{-}F}$ = 14.5 Hz), 119.3, 118.1, 117.1 (d, $J_{C\text{-}F}$ = 5.5 Hz); HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{10}H_9FN_3O^+$: 206.0724 , found 206.0720.

Fluoro pyrimidine **5b.** White solid (94 mg, 82%): m.p. 118-119 ℃; IR (neat) *v* 2691, 1573, 1444, 1302, 1265, 1192, 1060, 923, 540 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.45 (s, 1H), 8.47 (d, *J* = 4.7 Hz, 1H), 8.06 (d, *J* = 8.1 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 8.2 Hz, 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 2.26 (p, *J* = 6.4 Hz, 1H), 1.13 (d, *J* = 6.5 Hz, 4H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ −137.14; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 165.7 (d, $J_{C\text{-}F}$ = 6.0 Hz), 160.8, 152.5 (d, $^{1}J_{C\text{-}F}$ = 264.6 Hz), 151.5 (d, $J_{C\text{-}F}$ = 6.1 Hz), 146.8 (d, $J_{C\text{-}F}$ = 25.8 Hz), 133.5 (d, $J_{C\text{-}F}$ = 2.2 Hz), 130.3 (d, $J_{C\text{-}F}$ = 19.8 Hz), 119.2 (d, $J_{C\text{-}F}$ = 2.2 Hz), 118.6, 114.7 (d, $J_{C\text{-}F}$ = 6.1 Hz), 17.6, 11.0; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{12}FN_2O^+$: 231.0928, found 231.0922.

Fluoro pyrimidine **5c.** White solid (114 mg, 86%): m.p. 121-122 ℃; IR (neat) *v* 2919, 1560, 1432, 1280, 1195, 830, 637 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.46 (*br* s, 1H), 8.58 (d, *J* = 3.9 Hz, 1H), 8.18–8.09 (m, 2H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.46–7.34 (m, 3H), 7.31 (t, *J* = 7.3 Hz, 1H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.84 (t, *J* = 7.3 Hz, 1H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -134.52; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 160.7, 158.7 (d, $J_{C\text{-}F}$ = 6.3 Hz), 153.1 (d, $^{1}J_{C\text{-}F}$ = 268.2 Hz), 152.0 (d, $J_{C\text{-}F}$ = 6.4 Hz), 147.2 (d, $J_{C\text{-}F}$ = 26.0 Hz), 135.5, 133.8 (d, $J_{C\text{-}F}$ = 2.1 Hz), 131.2, 130.4 (d, $^{2}J_{C\text{-}F}$ = 19.5 Hz), 129.0, 128.0, 119.4 (d, $J_{C\text{-}F}$ = 2.1 Hz), 118.7, 114.9 (d, $J_{C\text{-}F}$ = 6.0 Hz); HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{12}FN_2O^+$: 267.0928, found 267.0927.

Fluoro pyrimidine **5d.** White solid (97 mg, 77%): m.p. 157-158 ℃; IR (neat) *v* 2920, 1584, 1429, 1279, 1191, 1084, 800, 569 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.32 (*br* s, 1H), 8.66 (d, *J* = 4.5 Hz, 1H), 8.15 (d, *J* = 8.6 Hz, 2H), 8.09 (d, *J* = 8.2 Hz, 1H), 7.45–7.39 (m, 3H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -133.95; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 160.7, 157.7 (d, $^{5}J_{C\text{-}F}$ = 6.3 Hz), 153.1 (d, $^{1}J_{C\text{-}F}$ = 268.8 Hz), 152.1 (d, $J_{C\text{-}F}$ = 6.5 Hz), 147.2 (d, $J_{C\text{-}F}$ = 26.1 Hz), 137.6, 133.9, 130.4 (d, $J_{C\text{-}F}$ = 19.5 Hz), 129.2, 119.5 (d, $J_{C\text{-}F}$ = 2.2 Hz), 118.7, 114.7 (d, $J_{C\text{-}F}$ = 6.1 Hz); HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{11}ClFN_2O^+$: 301.0538, found 301.0541.

Fluoro pyrimidine **5e.** White solid (89 mg, 63%): m.p. 227-228 ℃; IR (neat) *v* 3093, 1643, 1500, 1256, 1206, 1175, 986, 823, 732, 593 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.24 (s, 1H), 8.80 (s, 1H), 8.02 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 7.0 Hz, 1H), 7.40 (t, *J* = 6.9 Hz, 1H), 7.07–6.92 (m, 2H), 6.67 (d, *J* = 8.0 Hz, 2H), 5.71 (s, 2H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -138.14; $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 160.2 (d, $J_{C\text{-}F}$ = 5.8 Hz), 157.4, 153.4 (d, $^{1}J_{C\text{-}F}$ = 262.1 Hz), 152.0, 151.96 (d, $J_{C\text{-}F}$ = 10.5 Hz), 146.2 (d, $J_{C\text{-}F}$ = 24.3 Hz), 132.6, 131.0 (d, $J_{C\text{-}F}$ = 7.0 Hz), 129.6, 123.8, 119.7, 119.6 (d, $J_{C\text{-}F}$ = 4.6 Hz), 117.1, 114.0; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{13}FN_3O^+$: 282.1037, found : 282.1049.

Fluoro pyridine **5f.** White solid (100 mg, 73%): m.p. 191-192 ℃; IR (neat) *v* 3425, 3291, 2921, 1691, 1575, 1456, 1188, 617 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.43 (*br* s, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 8.02 (d, *J* = 12.7 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.91 (t, *J* = 7.6 Hz, 1H), 6.41 (*br* s, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -133.26; $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 165.5, 159.7, 153.3, 148.9 (d, $^{1}J_{C\text{-}F}$ = 248.8 Hz), 148.5 (d, $J_{C\text{-}F}$ = 9.5 Hz), 132.5 (d, $J_{C\text{-}F}$ = 2.1 Hz), 130.0 (d, $J_{C\text{-}F}$ = 20.3 Hz), 128.9 (d, $J_{C\text{-}F}$ = 24.9 Hz), 119.0 (d, $J_{C\text{-}F}$ = 2.3 Hz), 118.3, 116.4 (d, $J_{C\text{-}F}$ = 6.7 Hz), 104.8 (d, $J_{C\text{-}F}$ = 3.9 Hz), 61.4, 14.3; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{14}H_{13}FN_2NaO_3^+$: 299.0802, found 299.0818.

5.3 Synthetic procedure for the preparation of 7.

Monofluorinated chromone **3a** (0.5 mmol, 1 equiv.), *o*-nitrophenylactonitrile (1 mmol, 2 equiv.), Zn dust (4.0 mmol, 8 equiv.), TEA (1.5 mmol, 3 equiv.) and AcOH (15 mmol) were added to a reaction flask. The reaction mixture was stirred and heated to reflux for 4 h. After completion of the reaction, the mixture was diluted with water and extracted by EtOAc. After drying by anhydrous Na_2SO_4, EtOAc was removed under reduced pressure. The residue was purified by was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to yield product **7** (70 mg, 50%).

fluoro carboline **7.** White solid, m.p: 240-241 ℃; IR (neat) *v* 3275, 2919, 1598, 1492, 1432, 1280, 1165, 825, 744, 629, 593 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.97 (s, 1H), 10.96 (s, 1H), 8.57 (d, *J* = 11.1 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.55–7.48 (m, 2H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.26 (t, *J* = 7.3 Hz, 1H), 7.01–6.92 (m, 2H); ^{19}F NMR (376 MHz, DMSO-d_6) δ -131.76; $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 156.7, 152.5 (d, $^{1}J_{C\text{-}F}$ = 244.1 Hz), 147.5, 141.6 (d, $J_{C\text{-}F}$ = 17.2 Hz), 140.7, 130.84, 130.78, 127.7, 122.1, 122.0 (d, $J_{C\text{-}F}$ = 4.8 Hz), 120.6, 120.1, 119.4, 117.0, 116.99 (d, $J_{C\text{-}F}$ = 24.3 Hz), 115.5 (d, $J_{C\text{-}F}$ = 6.8 Hz), 112.0; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{17}H_{11}FN_2NaO^+$: 301.0748, found : 301.0768.

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A BHT-regulated chemoselective monofluorination of enaminones with Selectfluor under mild reaction conditions was unveiled for the first time. As a result, an array of monofluorinated chromones were efficiently assembled in a simple operational manner. Moreover, the scalability of this protocol and the versatility for the downstream transformations of the obtained fluorinated chromones to installing diverse nitrogen-containing heterocycles greatly broaden the practical applications of this developed protocol.

The authors declared that they have no conflicts of interest to this work. We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.