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Transition-Metal-Free Oxyfluorination of Olefinic Amides for the Synthesis of Fluorinated Heterocycles

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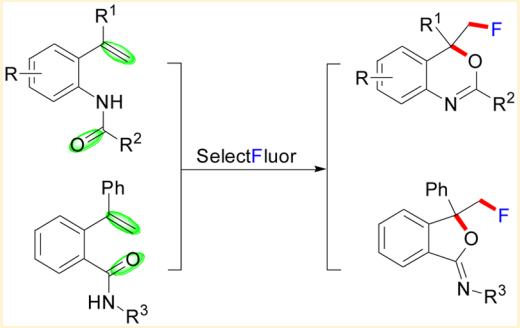
Supporting Information

ABSTRACT: A series of fluorinated 4*H*-3,1-benzoxazines and iminoisobenzofurans have been synthesized through the electrophilic fluorocyclization of olefinic amides. This methodology is highlighted by its mild conditions, wide substrate scope, and good functional group tolerance.



Organofluorine compounds have attracted special research interests in organic synthesis due to their remarkable applications in agrochemistry, medicinal chemistry, and materials science.[1] Over the past few years, significant progress has been made to introduce a fluorine atom into molecules by using the commercially available SelectFluor as a fluorinating reagent.[2] Among them, difunctionalization of alkenes in combination with SelectFluor provided an efficient access to various fluorine-containing compounds.[3−5] Particularly, the electrophilic fluorocyclization of functionalized alkenes represented an elegant strategy for the synthesis of fluorine-containing heterocycles.[5] In this aspect, Toste and co-workers described the asymmetric fluorocyclization of dihydropyran derivates to afford a series of fluorine-containing spiro-fused oxazolines.[5d] Meanwhile, Gouverneur and co-workers have also developed the asymmetric fluorocyclization of indoles bearing a heteronucleophile center, leading to fluorinated fused heterocyclic compounds.[5e,f] Very recently, Rueping and co-workers reported the electrophilic fluorocyclization of olefinic carboxylic acids, benzylic alcohols, and amines, providing an efficient approach to the corresponding fluorinated isobenzofurans and isoindolines.[5h,i] Despite these achievements, it is still highly desirable to develop efficient methods to construct structurally diverse fluorine-containing heterocyclic compounds under mild conditions.

4*H*-3,1-Benzoxazine is one of the important structural units because compounds containing a 4*H*-3,1-benzoxazine core usually exhibit broad biological activities and have been used as an anxiolytic and anticonvulsant drug, fungicide, and progesterone receptor agonist (Figure 1).[6] Thus, a series of efficient synthetic strategies have been developed to construct this N,O-heterocyclic compound. One of the most classical methods involves the condensation of 2-aminobenzyl alcohols with aldehydes or ketones under various conditions.[7] The transition-metal-catalyzed or metal-free cyclization of *o*-alkynylanilides provides an alternative route to substituted 4*H*-3,1-benzoxazines.[8] Recently, we and others developed an efficient radical difunctionalization of olefinic amides to access this 3,1-benzoxazine skeleton.[9] In addition, the halocyclization of olefinic amides represents another simple and convenient strategy to the halogenated 4*H*-3,1-benzoxazines.[10] However, there is no report on the synthesis of fluorinated 4*H*-3,1-benzoxazine derivatives. Herein, we report an efficient oxyfluorination of olefinic amides with SelectFluor, providing a mild and practical approach to fluorinated 4*H*-3,1-benzoxazines and iminoisobenzofurans in good yields.

Initially, we selected *N*-(2-isopropenylphenyl)benzamide (**1a**) as the test substrate and SelectFluor as the fluorine source for the optimization of the fluorocyclization reaction (Table 1). To our delight, treatment of **1a** with 1.1 equiv of SelectFluor in MeCN at room temperature afforded the desired product **2a** in 93% yield. A screen of solvents revealed that $MeNO_2$ was also a suitable solvent, while other solvents such as DCE, $PhCF_3$, and THF were not effective (entries 2−5). The results indicated that the polar solvents favor this fluorocyclization reaction. Subsequently, some weak base, such as Na_2CO_3, was added to the reaction system, leading to only 25% yield of **2a** (entry 6). In addition, increasing or reducing the amount of SelectFluor both resulted in lower yields (entries 7 and 8). Finally, when another inexpensive fluorinating agent, *N*-fluorobenzenesulfonimide (NFSI), was used instead of SelectFluor, only a trace amount of the desired product was detected (entry 9).[11] Satisfactorily, the reaction could also be

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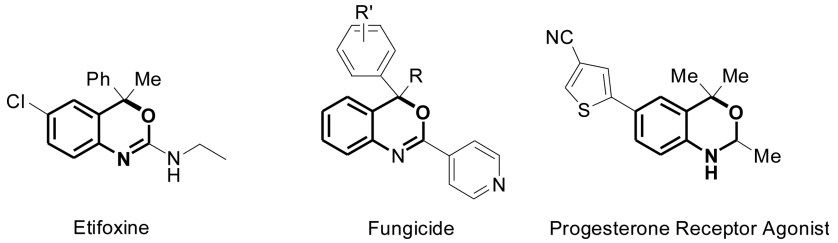
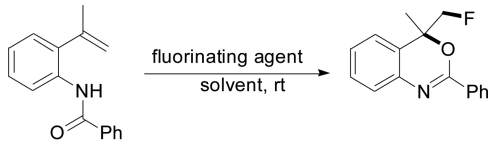


Figure 1. Bioactive compounds containing a 4*H*-3,1-benzoxazine core.

Table 1. Optimization of the Reaction Conditions[a]



1a **2a**

entry	F^+ source (equiv)	solvent	yield (%)[b]
1	SelectFluor (1.1)	MeCN	93 (74)[c]
2	SelectFluor (1.1)	$MeNO_2$	90
3	SelectFluor (1.1)	DCE	<5
4	SelectFluor (1.1)	$PhCF_3$	<5
5	SelectFluor (1.1)	THF	<5
6	SelectFluor (1.1)	MeCN	25[d]
7	SelectFluor (1.0)	MeCN	76
8	SelectFluor (1.5)	MeCN	85
9	NFSI (1.1)	MeCN	trace
10	SelectFluor (1.1)	MeCN	94[e]

[a]Reaction conditions: **1a** (0.20 mmol, 1.0 equiv), SelectFluor (0.22 mmol, 1.1 equiv), solvent (2 mL), under N_2, room temperature, 24 h. [b]Yield of isolated product. [c]Under air. [d]Na_2CO_3 (0.22 mmol, 1.1 equiv) was added. [e]Yield on a 1.5 mmol scale.

scaled up to 1.5 mmol, and the desired product **2a** was obtained in 94% yield (entry 10).

With the optimized reaction conditions in hand, we next evaluated the scope and limitations of our reaction with a variety of olefinic amides (Scheme 1). As expected, a series of olefinic amides derived from various 2-vinyl arylamine and carboxylic acids were effective substrates for this transformation. Both electron-donating and -withdrawing groups such as Me, MeO, NO_2, and X (Cl, Br) on the aromatic moiety of benzamides were tolerated well to produce the corresponding products in good to excellent yields (**2b–i**). It should be noted that the position of these substituents has little influence on the reaction efficiency. For the *ortho*-Cl benzamides, the addition of a stoichiometric amount of $NaHCO_3$ was required to obtain good yields (**2h**). Additionally, heteroarylamides such as **1j** and **1k** also reacted smoothly to give the corresponding products **2j** and **2k** in 53 and 86% yields, respectively. Gratifyingly, the aliphatic amides were also compatible with the present conditions and led to the desired products in good yields (**2l–n**). However, 2-phenoxyacetamide did not work in the present conditions (not shown). With the aim of incorporating other functional groups into the benzoxazine core, cinnamamide **1o** and 2-oxo-2-phenylacetamide **1p** were prepared. Satisfactorily, both of them underwent the fluorocyclization process smoothly to give the expected fluorinated 2-styryl benzoxazine **2o** and 2-benzoyl benzoxazine **2p** in 84 and 53% yields, respectively. In some cases, the base was necessary for this transformation because perhaps these substrates were particularly sensitive to trace acid from the SelectFluor byproduct (**2h**, **2m**, and **2p**).[5i] Furthermore, olefinic amides bearing ethyl or aryl groups at the α position of the styrene unit also worked well under the optimal conditions to furnish the corresponding cyclized products in good yields (**2q–u**).

To synthesize structurally diverse fluorine-containing heterocycles, 2-vinylbenzamides **3** were also examined (Scheme 2). After several trials, we found that when a stoichiometric amount of $NaHCO_3$ was used as an additive (for details, see the Supporting Information), the 2-vinylbenzamides reacted smoothly to give the desired iminoisobenzofurans **4a–f** in moderate to good yields at 50 °C. The substituents at the *ortho*, *meta*, or *para* positions of the aniline moiety showed no significant influence on this reaction. Moreover, the *Z*-configuration of product **4e** was assigned by the NOESY experiment.[12] In addition, the imino group of the product could be easily transformed to other functional groups. For instance, product **4a** could be easily hydrolyzed to give the corresponding lactone **5a** in 88% yield in the presence of hydrochloric acid (Scheme 3).

In conclusion, we have demonstrated an efficient electrophilic fluorocyclization of olefinic amides for the synthesis of fluorinated 4*H*-3,1-benzoxazines under mild conditions. This protocol features simple manipulation, a broad substrate scope, and excellent functional group tolerance. Moreover, this procedure could also be extended to access the fluorinated iminoisobenzofurans in good yields.

EXPERIMENTAL SECTION

General Methods. All reactions were carried out in Schlenk tubes filled with nitrogen. Column chromatography was carried out on silica gel. ^1H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer in solvents as indicated. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: ^1H NMR δ = 7.26; ^{13}C NMR δ = 77.0). IR spectra were recorded on a spectrometer, and only major peaks are reported in cm^{-1}. HRMS were obtained on a Q-TOF microspectrometer. Melting points were determined on a microscopic apparatus and were uncorrected. All olefinic amides **1** and 2-vinylbenzamides **3** were synthesized according to the literature, and the NMR spectra were in full accordance with the data in the literature.[9,10b,13]

Data of New Compound 3f: White solid, mp = 144–146 °C; R_f 0.2 (EtOAc/petroleum ether = 1:10); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.75 (d, J = 7.6 Hz, 1H), 7.57–7.45 (m, 3H), 7.40 (d, J = 7.2 Hz, 1H), 7.27–7.14 (m, 8H), 7.08 (t, J = 7.2 Hz, 1H), 5.78 (s, 1H), 5.46 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.5, 148.3, 139.1, 138.3, 137.5, 135.7, 134.1, 130.8, 128.9, 128.8, 128.5, 128.1, 124.5, 119.7, 116.2 ppm; IR (KBr) ν_{max} 3244, 1647, 1536, 1438, 1323, 752 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{17}ClNO$ $[M + H]^+$ 334.0993, found 334.0978.

General Procedure for the Fluorocyclization of 1 with SelectFluor. A 10 mL oven-dried Schlenk tube was charged with olefinic amides (**1**, 0.2 mmol, 1.0 equiv) and SelectFluor (0.22 mmol, 77.9 mg, 1.1 equiv). The tube was evacuated and backfilled with nitrogen (three times). Two milliliters of MeCN was injected into the

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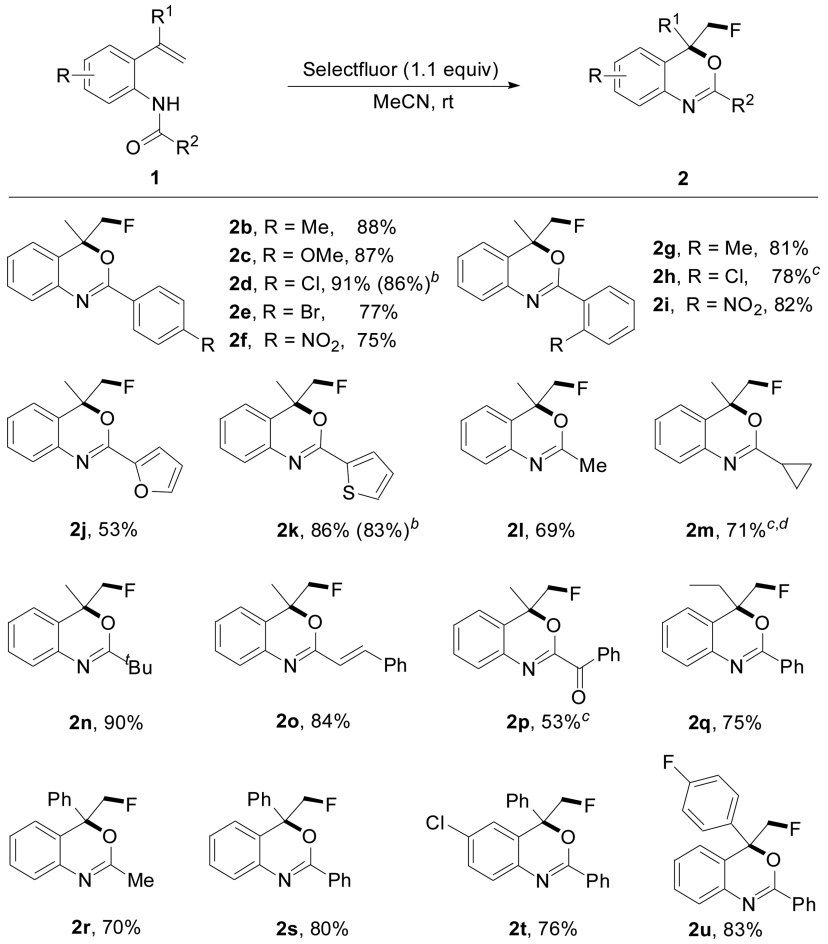
Scheme 1. Scope of Amide Derivatives 1[a]



[a]Reaction conditions: see Table 1, entry 1. [b]Yield on a 1 mmol scale is given in parentheses. [c]$NaHCO_3$ (1.5 equiv) was used as a base, at 50 °C for 24 h. [d]For 48 h.

tube by syringe. The tube was then sealed, and the mixture was stirred for 24 h at room temperature. Upon completion of the reaction, the mixture was diluted with EtOAc. The solvent was then removed in vacuo. The residue was purified by column chromatography on silica gel (gradient eluent of EtOAc/petroleum ether: 1/20 to 1/10) to give the corresponding products **2** in yields listed in Scheme 1.

4-Fluoromethyl-4-methyl-2-phenyl-4*H*-benzo[*d*][3,1]-oxazine (2a): Colorless liquid (93%, 47.4 mg); R_f 0.3 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.17 (d, J = 7.2 Hz, 2H), 7.53−7.44 (m, 3H), 7.39−7.33 (m, 2H), 7.23 (td, J = 6.4, 2.0 Hz, 1H), 7.17 (d, J = 7.2 Hz, 1H), 4.62 (dd, J_{H-F} = 48.0, 10.0 Hz, 1H), 4.43 (dd, J_{H-F} = 47.2, 10.0 Hz, 1H), 1.82 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.3, 139.4, 132.4, 131.5, 129.5, 128.3, 128.0, 126.8, 125.4, 125.4 (d, J_{C-F} = 3.4 Hz), 123.3, 86.0 (d, J_{C-F} = 182.9 Hz), 78.9 (d, J_{C-F} = 18.7 Hz), 22.4 (d, J_{C-F} = 3.5 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −225.1 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 3066, 2984, 1626, 1573, 1486, 1451, 1320, 1258, 1081, 1030, 762, 695 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{15}FNO$ [M + H]$^+$ 256.1132, found 256.1136.

4-Fluoromethyl-4-methyl-2-*p*-tolyl-4*H*-benzo[*d*][3,1]oxazine (2b): Colorless liquid (88%, 47.3 mg); R_f 0.3 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 (d, J = 8.4 Hz, 2H), 7.38−7.32 (m, 2H), 7.27−7.15 (m, 4H), 4.61 (dd, J_{H-F} = 48.0, 10.0 Hz, 1H), 4.42 (dd, J_{H-F} = 47.2, 10.0 Hz, 1H), 2.42 (s, 3H), 1.81 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.4, 142.0, 139.6, 129.6, 129.5, 129.0, 128.0, 126.6, 125.4 (d, J_{C-F} = 3.5 Hz), 125.3, 123.3, 85.9 (d, J_{C-F} = 182.6 Hz), 78.8 (d, J_{C-F} = 18.8 Hz), 22.3 (d, J_{C-F} = 3.3 Hz), 21.6 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −225.1 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2930, 1622, 1483, 1320, 1258, 1178, 1083, 1030, 828, 763 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}FNO$ [M + H]$^+$ 270.1289, found 270.1283.

4-Fluoromethyl-2-(4-methoxyphenyl)-4-methyl-4*H*-benzo-[*d*][3,1]oxazine (2c): Colorless liquid (87%, 49.6 mg); R_f 0.2 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.12 (dd, J = 8.8, 2.4 Hz, 2H), 7.37−7.31 (m, 2H), 7.22−7.14 (m, 2H), 6.93 (dd, J = 8.8, 2.8 Hz, 2H), 4.62 (dd, J_{H-F} = 48.0, 10.0 Hz, 1H), 4.43 (dd, J_{H-F} = 46.8, 10.0 Hz, 1H), 3.86 (s, 3H), 1.81 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.4, 156.2, 139.7, 130.0, 129.8, 129.5, 126.3, 125.3 (d, J_{C-F} = 3.6 Hz), 125.1, 124.8, 123.3, 113.6, 85.9 (d, J_{C-F} = 182.6 Hz), 78.7 (d, J_{C-F} = 18.6 Hz), 55.4, 22.2 (d, J_{C-F} = 3.5 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −225.2 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2930, 1612, 1510, 1320, 1254, 1172, 1084, 1030, 840, 762 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}FNO_2$ [M + H]$^+$ 286.1238, found 286.1238.

2-(4-Chlorophenyl)-4-fluoromethyl-4-methyl-4*H*-benzo[*d*]-[3,1]oxazine (2d): Colorless liquid (91%, 52.6 mg); R_f 0.3 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.10 (dt, J = 9.2, 2.4 Hz, 2H), 7.42 (dt, J = 9.2, 2.4 Hz, 2H), 7.39−7.31 (m, 2H), 7.24 (td, J = 7.2, 1.6 Hz, 1H), 7.16 (td, J = 7.6, 0.8 Hz, 1H), 4.60 (dd, J_{H-F} = 48.0, 10.0 Hz, 1H), 4.42 (dd, J_{H-F} = 47.2, 10.0 Hz, 1H), 1.81 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.3, 139.2, 137.7, 130.9, 129.6, 129.3, 128.5, 127.0, 125.5, 125.3 (d, J_{C-F} = 3.6 Hz), 123.3, 86.0 (d, J_{C-F} = 183.0 Hz), 79.2 (d, J_{C-F} = 18.6 Hz), 22.4 (d, J_{C-F} = 3.3 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −225.1 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2960, 1624, 1485, 1319, 1261, 1090, 1027, 836, 766 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{14}ClFNO$ [M + H]$^+$ 290.0742, found 290.0741.

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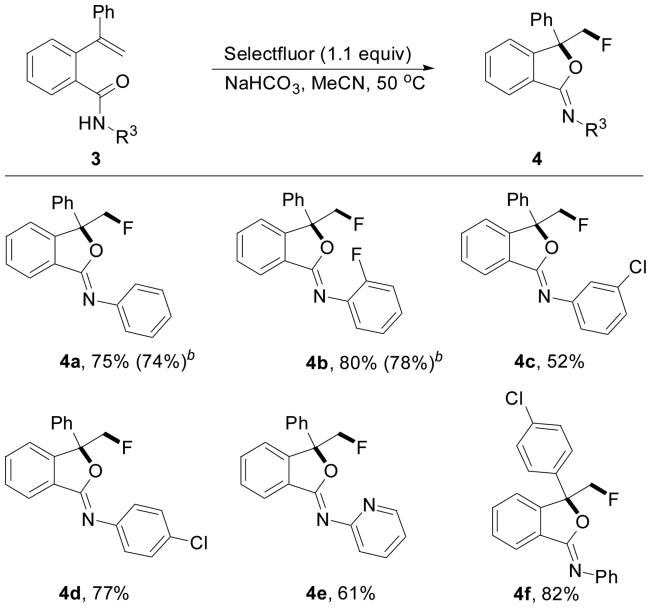
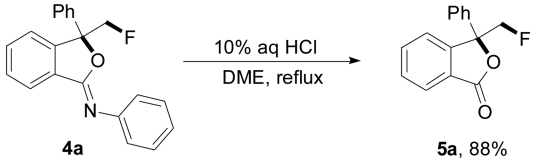
Scheme 2. Scope of Amide Derivatives 3[a]



[a]Reaction Conditions: **3** (0.20 mmol, 1.0 equiv), Selectfluor (0.22 mmol, 1.1 equiv), $NaHCO_3$ (0.3 mmol, 1.5 equiv), MeCN (2 mL), under N_2, 50 °C, 24 h. [b]Yield on a 1 mmol scale is given in parentheses.

Scheme 3. Hydrolysis of Product 4a



2-(4-Bromophenyl)-4-fluoromethyl-4-methyl-4*H*-benzo[*d*]-[3,1]oxazine (2e): Colorless liquid (77%, 51.3 mg); R_f 0.3 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.03 (dt, J = 9.2, 2.4 Hz, 2H), 7.58 (dt, J = 9.2, 2.4 Hz, 2H), 7.38−7.31 (m, 2H), 7.24 (td, J = 7.2, 1.6 Hz, 1H), 7.16 (td, J = 7.6, 0.8 Hz, 1H), 4.59 (dd, J_{H-F} = 48.0, 10.0 Hz, 1H), 4.41 (dd, J_{H-F} = 46.8, 10.0 Hz, 1H), 1.81 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.3, 139.1, 131.5, 131.3, 129.6, 129.5, 127.0, 126.2, 125.4, 125.2 (d, J_{C-F} = 3.5 Hz), 123.3, 86.0 (d, J_{C-F} = 182.9 Hz), 79.1 (d, J_{C-F} = 18.5 Hz), 22.3 (d, J_{C-F} = 3.5 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −225.0 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2984, 1626, 1593, 1484, 1318, 1260, 1080, 1022, 834, 762 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{14}BrFNO$ [M + H]$^+$ 334.0237, found 334.0226.

4-Fluoromethyl-4-methyl-2-(4-nitrophenyl)-4*H*-benzo[*d*]-[3,1]oxazine (2f): Yellow solid, mp = 130−132 °C (75%, 45.0 mg); R_f 0.5 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.36−8.27 (m, 4H), 7.41−7.35 (m, 2H), 7.29 (td, J = 7.6, 1.6 Hz, 1H), 7.18 (d, J = 7.2 Hz, 1H), 4.61 (dd, J_{H-F} = 48.0, 10.4 Hz, 1H), 4.45 (dd, J_{H-F} = 47.2, 10.4 Hz, 1H), 1.83 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.0, 149.5, 138.7, 138.3, 129.8, 128.8, 127.8, 125.9, 125.2 (d, J_{C-F} = 3.5 Hz), 123.4, 86.2 (d, J_{C-F} = 183.2 Hz), 79.7 (d, J_{C-F} = 18.6 Hz), 22.5 (d, J_{C-F} = 3.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ = −224.9 (t, J_{H-F} = 48.9 Hz) ppm; IR (KBr) ν_{max} 1591, 1522, 1346, 1262, 1093, 1029, 859, 763, 702 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{14}FN_2O_3$ [M + H]$^+$ 301.0983, found 301.0979.

4-Fluoromethyl-4-methyl-2-*o*-tolyl-4*H*-benzo[*d*][3,1]oxazine (2g): Colorless liquid (81%, 43.6 mg); R_f 0.3 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 (dd, J = 7.6, 1.2 Hz, 1H), 7.39−7.34 (m, 3H), 7.32−7.23 (m, 3H), 7.17 (dd, J = 7.6, 1.2 Hz, 1H), 4.67 (dd, J_{H-F} = 48.0, 10.0 Hz, 1H), 4.46 (dd, J_{H-F} = 47.2, 10.0 Hz, 1H), 2.66 (s, 3H), 1.82 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.0, 139.3, 138.3, 132.4, 131.3, 130.5, 129.9, 129.5, 126.9, 125.7, 125.4, 124.9 (d, J_{C-F} = 3.6 Hz), 123.2, 86.2 (d, J_{C-F} = 182.9 Hz), 79.3 (d, J_{C-F} = 18.7 Hz), 22.5 (d, J_{C-F} = 3.6 Hz), 21.4 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −223.9 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2929, 1629, 1452, 1315, 1251, 1034, 763 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}FNO$ [M + H]$^+$ 270.1289, found 270.1281.

2-(2-Chlorophenyl)-4-fluoromethyl-4-methyl-4*H*-benzo[*d*]-[3,1]oxazine (2h): Colorless liquid (78%, 45.2 mg); R_f 0.3 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.77 (dd, J = 7.2, 1.6 Hz, 1H), 7.75 (dd, J = 8.0, 1.6 Hz, 1H), 7.44−7.25 (m, 5H), 7.16 (dd, J = 7.6, 1.2 Hz, 1H), 4.75 (d, 10.0 Hz, 1H), 4.61 (dd, J = 14.4, 10.4 Hz, 1H), 1.82 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.5, 138.8, 133.2, 132.5, 131.4, 131.3, 130.6, 129.5, 127.4, 126.7, 125.6, 125.1 (d, J_{C-F} = 2.9 Hz), 123.4, 86.3 (d, J_{C-F} = 182.4 Hz), 80.1 (d, J_{C-F} = 18.8 Hz), 22.9 (d, J_{C-F} = 3.5 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −223.8 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2928, 1636, 1478, 1319, 1260, 1096, 1037, 762 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{14}ClFNO$ [M + H]$^+$ 290.0742, found 290.0733.

4-Fluoromethyl-4-methyl-2-(2-nitrophenyl)-4*H*-benzo[*d*]-[3,1]oxazine (2i): Yellow liquid (82%, 49.2 mg); R_f 0.5 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95 (dd, J = 7.6, 1.6 Hz, 1H), 7.82 (dd, J = 8.0, 1.2 Hz, 1H), 7.67−7.57 (m, 2H), 7.35 (td, J = 7.6, 1.2 Hz, 1H), 7.29−7.24 (m, 2H), 7.14 (dd, J = 7.6, 1.2 Hz, 1H), 4.62 (dd, J_{H-F} = 47.2, 10.0 Hz, 1H), 4.46 (dd, J_{H-F} = 47.2, 10.0 Hz, 1H), 1.74 (d, J = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.2, 149.2, 138.3, 132.2, 131.2, 131.1, 129.5, 127.7, 125.7, 124.8, 123.8, 123.5, 86.3 (d, J_{C-F} = 182.0 Hz), 80.5 (d, J_{C-F} = 18.7 Hz), 23.0 (d, J_{C-F} = 3.4 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −224.2 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2925, 1638, 1532, 1457, 1362, 1260, 1027, 760 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{14}FN_2O_3$ [M + H]$^+$ 301.0983, found 301.0976.

4-Fluoromethyl-2-furan-2-yl-4-methyl-4*H*-benzo[*d*][3,1]-oxazine (2j): Colorless liquid (53%, 26.0 mg); R_f 0.2 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60 (d, J = 0.8 Hz, 1H), 7.39−7.32 (m, 2H), 7.21 (td, J = 7.6, 1.6 Hz, 1H), 7.13 (dd, J = 8.0, 1.2 Hz, 1H), 7.10 (d, J = 3.6 Hz, 1H), 6.52 (dd, J = 3.2, 1.6 Hz, 1H), 4.59 (dd, J_{H-F} = 48.0, 10.0 Hz, 1H), 4.42 (dd, J_{H-F} = 47.2, 10.0 Hz, 1H), 1.78 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.1, 146.4, 145.7, 138.8, 129.6, 126.9, 125.6, 125.4 (d, J_{C-F} = 3.1 Hz), 123.3, 115.0, 111.8, 85.9 (d, J_{C-F} = 182.7 Hz), 79.2 (d, J_{C-F} = 18.5 Hz), 22.3 (d, J_{C-F} = 3.3 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −225.2 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2928, 1637, 1482, 1320, 1268, 1101, 1023, 759 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{13}FNO_2$ [M + H]$^+$ 246.0925, found 246.0923.

4-Fluoromethyl-4-methyl-2-thiophen-2-yl-4*H*-benzo[*d*][3,1]-oxazine (2k): Colorless liquid (86%, 44.9 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.76 (dd, J = 8.0, 0.8 Hz, 1H), 7.49 (dd, J = 8.8, 0.8 Hz, 1H), 7.36−7.28 (m, 2H), 7.21 (td, J = 7.2, 1.2 Hz, 1H), 7.14 (dd, J = 7.6, 1.2 Hz, 1H), 7.11 (dd, J = 4.8, 3.6 Hz, 1H), 4.61 (dd, J_{H-F} = 48.0, 10.0 Hz, 1H), 4.42 (dd, J_{H-F} = 46.8, 10.0 Hz, 1H), 1.79 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.8, 139.3, 136.7, 130.5, 130.1, 129.5, 127.7, 126.6, 125.3 (d, J_{C-F} = 3.4 Hz), 125.2, 123.3, 85.9 (d, J_{C-F} = 183.0 Hz), 79.4 (d, J_{C-F} = 18.8 Hz), 22.3 (d, J_{C-F} = 3.3 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −225.2 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2937, 1587, 1481, 1425, 1263, 1029, 762, 715 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{12}FNNaOS$ [M + Na]$^+$ 284.0516, found 284.0516.

4-Fluoromethyl-2,4-dimethyl-4*H*-benzo[*d*][3,1]oxazine (2l): Colorless liquid (69%, 26.6 mg); R_f 0.4 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30−7.26 (m, 1H), 7.18−7.12 (m, 2H), 7.06 (d, J = 7.6 Hz, 1H), 4.49 (dd, J_{H-F} = 47.6, 10.0 Hz, 1H), 4.35 (dd, J_{H-F} = 47.6, 10.0 Hz, 1H), 2.13 (s, 3H), 1.66 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.6, 138.6, 129.4, 126.5, 124.6 (d, J_{C-F} = 3.4 Hz), 124.4, 123.2, 86.5 (d, J_{C-F} = 182.0 Hz), 78.7 (d, J_{C-F} = 18.4 Hz), 22.8 (d, J_{C-F} = 3.6 Hz), 21.6 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −224.8 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2935, 1646, 1595, 1446, 1377, 1263, 1032, 763 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{13}FNO$ [M + H]$^+$ 194.0976, found 194.0973.

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2-Cyclopropyl-4-fluoromethyl-4-methyl-4*H*-benzo[*d*][3,1]-oxazine (2m): Colorless liquid (71%, 15.6 mg); R_f 0.2 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.28 (td, J = 7.6, 1.2 Hz, 1H), 7.15−7.11 (m, 2H), 7.05 (dd, J = 7.6, 1.2 Hz, 1H), 4.46 (dd, J_{H-F} = 48.0, 10.0 Hz, 1H), 4.26 (dd, J_{H-F} = 47.2, 10.0 Hz, 1H), 1.74−1.70 (m, 1H), 1.64 (d, J = 2.0 Hz, 3H), 1.21−1.04 (m, 2H), 0.89−0.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.8, 139.3, 129.4, 125.9, 124.9 (d, J_{C-F} = 3.6 Hz), 124.1, 123.2, 85.7 (d, J_{C-F} = 182.9 Hz), 78.4 (d, J_{C-F} = 18.6 Hz), 22.0 (d, J_{C-F} = 3.3 Hz), 14.6, 7.5, 6.3 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −225.1 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2932, 1637, 1484, 1271, 1193, 1030, 763 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{15}FNO$ $[M + H]^+$ 220.1132, found 220.1127.

2-*tert*-Butyl-4-fluoromethyl-4-methyl-4*H*-benzo[*d*][3,1]-oxazine (2n): White solid, mp = 73−74 °C (90%, 42.3 mg); R_f 0.4 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.29 (t, J = 8.0 Hz, 1H), 7.20−7.15 (m, 2H), 7.09 (dd, J = 7.6, 0.4 Hz, 1H), 4.48 (dd, J_{H-F} = 48.0, 10.0 Hz, 1H), 4.32 (dd, J_{H-F} = 47.2, 10.0 Hz, 1H), 1.68 (d, J = 2.0 Hz, 3H), 1.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.5, 139.3, 129.3, 126.4, 125.1, 123.1, 86.0 (d, J_{C-F} = 182.4 Hz), 77.9 (d, J_{C-F} = 18.7 Hz), 37.3, 27.4, 22.1 (d, J_{C-F} = 3.4 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −225.0 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2963, 1636, 1262, 1098, 1027, 802 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{19}FNO$ $[M + H]^+$ 236.1445, found 236.1438.

4-Fluoromethyl-4-methyl-2-styryl-4*H*-benzo[*d*][3,1]oxazine (2o): Colorless liquid (84%, 47.2 mg); R_f 0.4 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57−7.53 (m, 3H), 7.41−7.32 (m, 4H), 7.27−7.19 (m, 2H), 7.14 (dd, J = 7.6, 1.2 Hz, 1H), 6.69 (d, J = 16.0 Hz, 1H), 4.65−4.35 (m, 2H), 1.78 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.6, 139.5, 139.2, 135.3, 129.5, 128.8, 127.7, 126.9, 125.6 (d, J_{C-F} = 3.5 Hz), 125.2, 123.3, 121.7, 86.1 (d, J_{C-F} = 182.7 Hz), 78.6 (d, J_{C-F} = 18.5 Hz), 22.4 (d, J_{C-F} = 3.4 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −225.2 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 3062, 2938, 1635, 1580, 1483, 1449, 1326, 1273, 1034, 982, 761, 693 cm^{-1}; HRMS (ESI) calcd for C18H17FNO $[M + H]^+$ 282.1289, found 282.1279.

(4-Fluoromethyl-4-methyl-4*H*-benzo[*d*][3,1]oxazin-2-yl)-phenylmethanone (2p): Colorless liquid (53%, 30.0 mg); R_f 0.1 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.20 (dd, J = 8.8, 1.6 Hz, 2H), 7.63 (td, J = 8.4, 1.2 Hz, 1H), 7.49 (t, J = 8.0 Hz, 2H), 7.38−7.32 (m, 3H), 7.19 (d, J = 6.8 Hz, 1H), 4.67−4.48 (m, 2H), 1.79 (d, J = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 186.4, 152.3, 137.5, 134.6, 133.9, 130.8, 129.6, 128.9, 128.4, 126.6, 126.0, 123.5, 87.2 (d, J_{C-F} = 181.7 Hz), 80.3 (d, J_{C-F} = 18.6 Hz), 23.2 (d, J_{C-F} = 3.8 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −223.8 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2926, 1677, 1633, 1452, 1325, 1270, 1236, 1177, 1035, 998, 764 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}FNNaO_2$ $[M + Na]^+$ 306.0901, found 306.0886.

4-Ethyl-4-fluoromethyl-2-phenyl-4*H*-benzo[*d*][3,1]oxazine (2q): Colorless liquid (75%, 40.4 mg); R_f 0.3 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.17−8.15 (m, 2H), 7.51−7.43 (m, 3H), 7.35−7.34 (m, 2H), 7.24−7.20 (m, 1H), 7.11 (d, J = 7.6 Hz, 1H), 4.64 (dd, J_{H-F} = 47.6, 10.0 Hz, 1H), 4.51 (dd, J_{H-F} = 47.6, 10.0 Hz, 1H), 2.22−2.06 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.2, 140.0, 132.5, 131.4, 129.3, 128.2, 127.9, 126.7, 125.6, 123.6, 123.4 (d, J_{C-F} = 3.3 Hz), 86.2 (d, J_{C-F} = 181.9 Hz), 82.0 (d, J_{C-F} = 17.8 Hz), 28.5 (d, J_{C-F} = 2.9 Hz), 7.4 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −226.6 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2971, 1627, 1486, 1321, 1259, 1084, 765, 696 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}FNO$ $[M + H]^+$ 270.1289, found 270.1288.

4-Fluoromethyl-2-methyl-4-phenyl-4*H*-benzo[*d*][3,1]-oxazine (2r): Colorless liquid (70%, 35.7 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38−7.32 (m, 6H), 7.24−7.21 (m, 2H), 7.16 (d, J = 7.6 Hz, 1H), 4.95 (dd, J = 12.0, 10.4 Hz, 1H), 4.83 (dd, J = 12.4, 10.4 Hz, 1H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.5, 139.3, 139.1 (d, J_{C-F} = 2.6 Hz), 129.5, 128.8, 128.5, 126.4, 126.3, 124.9, 124.7, 123.4, 84.3 (d, J_{C-F} = 185.3 Hz), 82.1 (d, J_{C-F} = 18.7 Hz), 21.8 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −219.5 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 3064, 2959, 1646, 1483, 1258, 1031, 765, 699 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{15}FNO$ $[M + H]^+$ 256.1132, found 256.1129.

4-Fluoromethyl-2,4-diphenyl-4*H*-benzo[*d*][3,1]oxazine (2s): Colorless liquid (80%, 50.7 mg); R_f 0.3 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.27−8.25 (m, 2H), 7.54−7.41 (m, 7H), 7.37−7.27 (m, 4H), 7.22 (d, J = 7.6 Hz, 1H), 5.09 (dd, J = 12.8, 10.4 Hz, 1H), 4.98 (dd, J = 12.8, 10.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.1, 139.9, 138.8 (d, J_{C-F} = 2.5 Hz), 132.2, 131.6, 129.6, 128.8, 128.5, 128.3, 128.0, 126.5, 125.6, 125.0, 124.2 (d, J_{C-F} = 2.0 Hz), 84.0 (d, J_{C-F} = 185.8 Hz), 82.5 (d, J_{C-F} = 18.5 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −219.5 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 3064, 2958, 1624, 1582, 1486, 1317, 1255, 1081, 1031, 762, 695 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{17}FNO$ $[M + H]^+$ 318.1289, found 318.1283.

6-Chloro-4-fluoromethyl-2,4-diphenyl-4*H*-benzo[*d*][3,1]-oxazine (2t): Colorless liquid (76%, 53.4 mg); R_f 0.3 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.22 (dd, J = 7.2, 1.2 Hz, 2H), 7.55−7.45 (m, 3H), 7.42−7.33 (m, 7H), 7.20 (d, J = 2.4 Hz, 1H), 5.06 (dd, J = 19.6, 10.4 Hz, 1H), 4.95 (dd, J = 19.2, 10.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.3, 138.6, 138.1 (d, J_{C-F} = 2.6 Hz), 131.8, 131.6, 129.8, 129.1, 128.7, 128.4, 128.0, 126.9, 126.4, 125.7, 125.1, 83.9 (d, J_{C-F} = 186.1 Hz), 82.2 (d, J_{C-F} = 18.8 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −219.7 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2956, 1622, 1479, 1314, 1254, 1074, 1033, 831, 768, 696 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{16}ClFNO$ $[M + H]^+$ 352.0899, found 352.0894.

4-Fluoromethyl-4-(4-fluorophenyl)-2-phenyl-4*H*-benzo[*d*]-[3,1]oxazine (2u): Colorless liquid (83%, 55.6 mg); R_f 0.3 (EtOAc/petroleum ether = 1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.24−8.22 (m, 2H), 7.53−7.38 (m, 7H), 7.31−7.27 (m, 1H), 7.18 (d, J = 7.6 Hz, 1H), 7.05−7.00 (m, 2H), 5.06 (dd, J = 13.2, 10.8 Hz, 1H), 4.94 (dd, J = 13.2, 10.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.8 (d, J_{C-F} = 247.2 Hz), 155.9, 139.8, 134.7, 132.0, 131.7, 129.8, 128.6 (d, J_{C-F} = 8.8 Hz), 128.4, 128.0, 126.6, 125.7, 124.8, 124.0 (d, J_{C-F} = 1.9 Hz), 115.5 (d, J_{C-F} = 21.5 Hz), 83.9 (d, J_{C-F} = 185.9 Hz), 81.9 (d, J_{C-F} = 18.7 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −112.7 (m), −219.5 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 3067, 2955, 1621, 1500, 1316, 1237, 1166, 1078, 1029, 835, 764, 696 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{16}F_2NO$ $[M + H]^+$ 336.1194, found 336.1187.

General Procedure for the Fluorocyclization of 3 with SelectFluor. A 10 mL oven-dried Schlenk tube was charged with olefinic amides (**3**, 0.2 mmol, 1.0 equiv), $NaHCO_3$ (0.3 mmol, 25.2 mg, 1.5 equiv), and SelectFluor (0.22 mmol, 77.9 mg, 1.1 equiv). The tube was evacuated and backfilled with nitrogen (three times). Two milliliters of MeCN was injected into the tube by syringe. The tube was then sealed, and the mixture was stirred at 50 °C for 24 h. Upon completion of the reaction, the mixture was diluted with EtOAc. The solvent was then removed in vacuo. The residue was purified by column chromatography on silica gel (gradient eluent of EtOAc/petroleum ether: 1/20 to 1/10) to give the corresponding products **4** in yields listed in Scheme 2.

(3-Fluoromethyl-3-phenyl-3*H*-isobenzofuran-1-ylidene)-phenylamine (4a): Colorless liquid (75%, 47.6 mg); R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 (d, J = 7.6 Hz, 1H), 7.68−7.35 (m, 12H), 7.18 (t, J = 7.2 Hz, 1H), 5.01−4.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.6, 146.1, 144.9, 137.0, 132.1, 131.3, 129.6, 128.8, 128.6, 125.5, 124.3, 124.2, 123.7, 122.4, 90.3 (d, J_{C-F} = 19.2 Hz), 85.0 (d, J_{C-F} = 183.2 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −222.2 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 3063, 2951, 1690, 1592, 1491, 1336, 1294, 1209, 1099, 1027, 955, 913, 761, 691 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{17}FNO$ $[M + H]^+$ 318.1289, found 318.1273.

(3-Fluoromethyl-3-phenyl-3*H*-isobenzofuran-1-ylidene)-(2-fluorophenyl)amine (4b): Colorless liquid (80%, 53.7 mg); R_f 0.4 (EtOAc/petroleum ether = 1:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05 (d, J = 7.2 Hz, 1H), 7.64−7.50 (m, 5H), 7.41−7.33 (m, 4H), 7.17−7.09 (m, 3H), 5.00−4.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.4, 154.7 (d, J_{C-F} = 244.8 Hz), 145.6 (d, J_{C-F} = 2.0 Hz), 136.8 (d, J_{C-F} = 2.4 Hz), 134.6 (d, J_{C-F} = 12.8 Hz), 132.4, 130.5, 129.7, 129.0, 128.8, 125.5, 124.8 (d, J_{C-F} = 7.3 Hz), 124.6, 124.0 (d,

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J_{C-F} = 3.6 Hz), 122.5, 115.8 (d, J_{C-F} = 20.3 Hz), 90.5 (d, J_{C-F} = 19.6 Hz), 85.0 (d, J_{C-F} = 183.2 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −222.2 (t, J_{H-F} = 48.9 Hz), −123.2 (m); IR (KBr) ν_{max} 2926, 1694, 1492, 1233, 1104, 1029, 756, 692 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{16}F_2NO$ $[M + H]^+$ 336.1194, found 336.1198.

(3-Chlorophenyl)-(3-fluoromethyl-3-phenyl-3*H*-isobenzofuran-1-ylidene)amine (4c): Colorless liquid (52%, 36.6 mg); R_f 0.2 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 (d, J = 7.6 Hz, 1H), 7.63−7.52 (m, 3H), 7.47 (d, J = 7.2 Hz, 2H), 7.41−7.30 (m, 4H), 7.31−7.24 (m, 2H), 7.11 (d, J = 7.6 Hz, 1H), 4.98−4.81 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.4, 147.5, 145.0, 136.7, 134.1, 132.4, 131.1, 129.8, 129.6, 129.0, 128.9, 125.5, 124.4, 124.2, 123.8, 122.5, 121.9, 90.7 (d, J_{C-F} = 19.6 Hz), 85.0 (d, J_{C-F} = 183.4 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −222.2 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2924, 2857, 1685, 1581, 1460, 1026, 877, 763 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{16}ClFNO$ $[M + H]^+$ 352.0899, found 352.0887.

(4-Chlorophenyl)-(3-fluoromethyl-3-phenyl-3*H*-isobenzofuran-1-ylidene)amine (4d): Colorless liquid (77%, 54.1 mg); R_f 0.4 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00−7.97 (m, 1H), 7.64−7.60 (m, 1H), 7.58−7.54 (m, 2H), 7.48 (dd, J = 8.0, 1.2 Hz, 2H), 7.42−7.31 (m, 7H), 5.00−4.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.1, 145.0, 144.7, 136.8, 132.3, 131.2, 129.7, 129.5, 129.0, 128.9, 1287, 1256, 125.2, 124.4, 122.5, 90.6 (d, J_{C-F} = 19.5 Hz), 85.1 (d, J_{C-F} = 183.5 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −222.2 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2924, 2859, 1776, 1688, 1458, 1289, 1025, 758, 693 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{16}ClFNO$ $[M + H]^+$ 352.0899, found 352.0883.

(3-Fluoromethyl-3-phenyl-3*H*-isobenzofuran-1-ylidene)-pyridin-2-ylamine (4e): White solid, mp = 126−128 °C (61%, 38.8 mg); R_f 0.2 (EtOAc/petroleum ether = 1:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.51 (d, J = 4.0 Hz, 1H), 8.07 (d, J = 7.6 Hz, 1H), 7.70−7.47 (m, 6H), 7.39−7.30 (m, 4H), 7.04 (dd, J = 6.8, 5.2 Hz, 1H), 4.99−4.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.1, 158.6, 148.9, 145.3, 137.4, 136.6, 132.6, 130.8, 129.8, 128.9, 125.5, 124.9, 122.3, 119.4, 117.4, 90.9 (d, J_{C-F} = 19.4 Hz), 84.9 (d, J_{C-F} = 183.6 Hz) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ = −222.2 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 2936, 1694, 1577, 1466, 1427, 1294, 1235, 1109, 1029, 768, 693 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{16}FN_2O$ $[M + H]^+$ 319.1241, found 319.1228.

[3-(4-Chlorophenyl)-3-fluoromethyl-3*H*-isobenzofuran-1-ylidene]phenylamine (4f): White solid, mp = 134−135 °C (82%, 57.7 mg); R_f 0.4 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02 (dd, J = 6.8, 0.8 Hz, 1H), 7.63−7.51 (m, 3H), 7.45−7.35 (m, 8H), 7.17−7.13 (m, 1H), 4.92 (dd, J = 15.6, 10.0 Hz, 1H), 4.80 (dd, J = 16.0, 10.0 Hz, H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.1, 146.0, 144.7, 135.8, 135.0, 132.2, 131.3, 129.9, 129.1, 128.7, 127.1, 124.5, 124.4, 123.6, 122.4, 89.6 (d, J_{C-F} = 20.0 Hz), 85.0 (d, J_{C-F} = 183.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ = −222.1 (t, J_{H-F} = 48.9 Hz); IR (KBr) ν_{max} 3064, 2950, 1691, 1592, 1492, 1292, 1211, 1089, 1023, 952, 827, 760 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{16}ClFNO$ $[M + H]^+$ 352.0899, found 352.0884.

Acid-Promoted Hydrolysis of 4a.[14] To a solution of **4a** (63.4 mg, 0.2 mmol) in 2.5 mL of 1,2-dimethoxyethane at 0 °C was added 10% aq HCl (0.6 mL). The mixture was then heated at reflux for 30 min. Upon completion of the reaction, the resulting mixture was diluted with EtOAc and washed with aq NH_4Cl and brine and dried over Na_2SO_4. The solvent was then removed in vacuo. The residue was purified by column chromatography on silica gel to give the corresponding product **5a** in 88% (42.6 mg) yield.

3-Fluoromethyl-3-phenyl-3*H*-isobenzofuran-1-one (5a):[5h] White solid, mp = 103−105 °C; R_f 0.3 (EtOAc/petroleum ether = 1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95 (d, J = 7.6 Hz, 1H), 7.74 (td, J = 7.6, 0.8 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.62−7.54 (m, 3H), 7.44−7.36 (m, 3H), 4.99 (dd, J = 14.4, 10.0 Hz, 1H), 4.87 (dd, J = 15.6, 10.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.1, 148.4, 135.7 (d, J_{C-F} = 2.8 Hz), 134.4, 129.9, 129.2, 129.0, 126.3, 126.2, 125.6, 123.0, 87.6 (d, J_{C-F} = 19.6 Hz), 84.8 (d, J_{C-F} = 183.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ = −222.1 (t, J_{H-F} = 48.9 Hz).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01909.

^{1}H and ^{13}C spectra of all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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