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Palladium-Catalyzed *ortho*-Selective C-H Fluorination of Oxalyl Amide Protected Benzylamines

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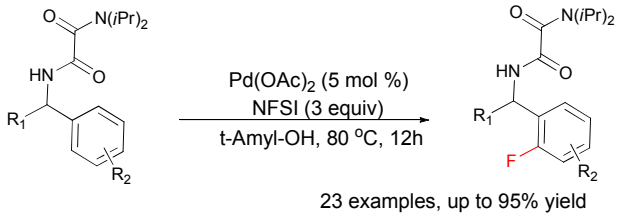


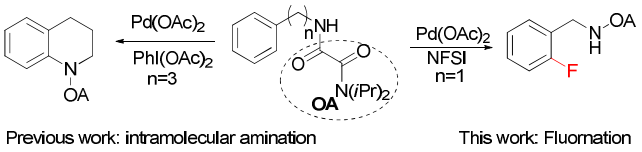
ABSTRACT: A novel and efficient synthetic method for *ortho*-fluorobenzylamines via palladium catalyst using an easily accessible oxalyl amide as directing group has been developed. The cheap *N*-Fluorobenzenesulfonimide could be used as the effective [F^+] source and *t*-Amyl-OH as the solvent with $Pd(OAc)_2$ as catalyst. Selective mono- or difluorination of oxalyl amide protected benzyl amie derivatives were achieved by modifying the reaction condition which presented an efficient way for the preparation of *ortho*-fluorinated benzyl amines.

INTRODUCTION

The fluorinated organic compounds mostly have a dramatic change in physical, chemical and biological properties, especially for the aryl fluorides,[1] which are very valuable components in pharmaceutical and agrochemical industries.[2] Thus, to develop a synthetic method for forming C-F bonds under mild condition is attractive and significant. In the past few years, important progress in this field has been achieved,[3] and transition-metal-catalyzed fluorination emerged as powerful method to access partially fluorinated aromatics.[4-12] However, compared to this successful development in fluorination with the prefunctionalized aromatic

rings that can lead to the C-F bonds under transition catalyst, the direct fluorination of unactived aryl C-H bonds still has few reports.[13] In 2006, the pioneering work of C-F bond formation was firstly reported by Sanford and co-workers with pyridine as the directing group via palladium catalyst,[14] and the electrophilic fluorinating agents were first applied in C-H functionalization as fluorine sources. Further mechanism studies revealed that the high-valent Pd(IV) complexs might be involved in the catalytic cycle.[15] Later, Yu and co-workers reported the Pd-catalyzed benzylamine triflamide[16] and benzoic acid perfluoroaniline amide[17] *ortho*-fluorination by electrophilic fluorinating agents. Very recently, a nitrate-promoted selective monofluorination of aromatic and olefinic C(sp^2)-H bonds with electrophilic fluorine reagents were discovered by Xu and co-workers.[18] Alternatively, the combination of nucleophilic fluoride (F^-) and external oxidant as fluorine sources could also be applied in C-H fluorination which was first reported by Sanford and co-workers.[19] Later, Daugulis and co-workeres also developed a copper-catalyzed *ortho*-fluorination of 8-aminoquinoline-coupled benzoic acid derivatives with nucleophilic fluoride (F^-) and oxidant of NMO (4-Methylmorpholine *N*-oxide).[20] Benzyl amines are broadly synthetic utility which are easily accessible through preparative methods. However, only one example of *ortho*-C-H fluorination for benzylamine derivatives with triflamide as directing groups via high loading of $Pd(OTf)_2 \cdot 2H_2O$ as catalyst was reported.[16] Herein we reported a convenient synthetic method for *ortho*-fluorination of oxalyl amide protected benzylamine derivatives via palladium(II) acetate as catalyst and the cheap NFSI (*N*-Fluorobis(phenylsulfony)amine) as fluorine source.

Scheme 1. Oxalyl Amide Assisted Fluorination

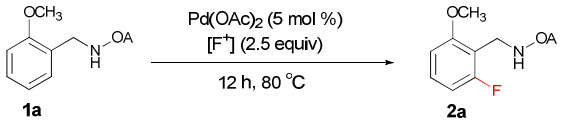


RESULTS AND DISCUSSION

Very recently, oxalyl amide was discovered as an easily accessible and efficient directing group for intramolecular amination by our group.[21] We hypothesized that the new developed *N,O*-bidentated directing group could promote Pd-catalyzed *ortho*-fluoroation of benzyl amine derivatives by applying the electrophilic fluorinating agents. At the outset of this study, we first treated oxalyl amide protected 2- methoxybenzyl amine **1a** with electrophilic fluorinating reagent (**F1**) with loading of (5 mol %) of $Pd(OAc)_2$ as catalyst in 1,4-dioxane at 80 ^oC under an atmosphere of air in a sealed tube (entry 1). To our delight, the desired fluorinated product **2a** was obtained in 79% yield, along with 5% yield of **1a** recovered. We further screened other [F^+] sources (entry 2-4, 14), in which the fluorinating reagents of **F3** gave slightly higher yield than that of F1. In assessing project cost, we decided to use the inexpensive **F1** as the fluorinating reagent for the further condition optimization. The solvent effect with **F1** (entry 5-8) were subsequently examined. The *t*-Amyl-OH turned out to be the best solvent, and excellent yield of **2a** (87%, entry 7) was achieved in 12 h. DCE and m-xylene gave

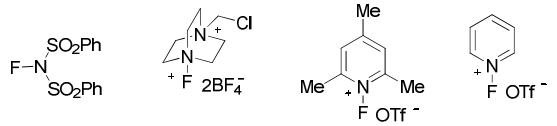
slightly poorer yield. Interestingly, no reaction happened with DMF as solvent. Attempts to further improve the conversion of starting material, several additives such as NMP, PivOH and PPh_3 were added in the reaction respectively. All these additives displayed suppressive effect in this transformation. Under an air or argon atmosphere, the product of **2a** was observed in higher than 80% yield, implying the oxygen has no promoting effect in this transformation. Combination of AgF and NMO with palladium acetate (entry 14) or copper salts were also tested, no reaction occurred in general reaction condition, and just starting material was recovered which was analyzed by GC-MS. Controlling experiments confirmed that no reaction happened without using palladium catalyst, implicating the crucial role of $Pd(OAc)_2$ for the transformation (Table 1, entry 15).

Table 1. Optimization of the Reaction Conditions.[a]



1a **2a**

entry	catalyst	[F+]	additive	solvent	yield (%)
1	$Pd(OAc)_2$	F1		1,4-Dioxane	79
2	$Pd(OAc)_2$	F2		1,4-Dioxane	0
3	$Pd(OAc)_2$	F3		1,4-Dioxane	81
4	$Pd(OAc)_2$	F4		1,4-Dioxane	31
5	$Pd(OAc)_2$	F1		DCE	73
6	$Pd(OAc)_2$	F1		m-Xylene	59
7	$Pd(OAc)_2$	F1		*t*-Amyl-OH	87
8	$Pd(OAc)_2$	F1		DMF	0
9	$Pd(OAc)_2$	F1	NMP	*t*-Amyl-OH	77
10	$Pd(OAc)_2$	F1	PivOH	*t*-Amyl-OH	81
11	$Pd(OAc)_2$	F1	PPh_3	*t*-Amyl-OH	80
12	$Pd(OAc)_2$	F1	O_2	*t*-Amyl-OH	83
13	$Pd(OAc)_2$	F1	Ar	*t*-Amyl-OH	80
14	$Pd(OAc)_2$	AgF	NMO	*t*-Amyl-OH	0
15	–	F1		*t*-Amyl-OH	0



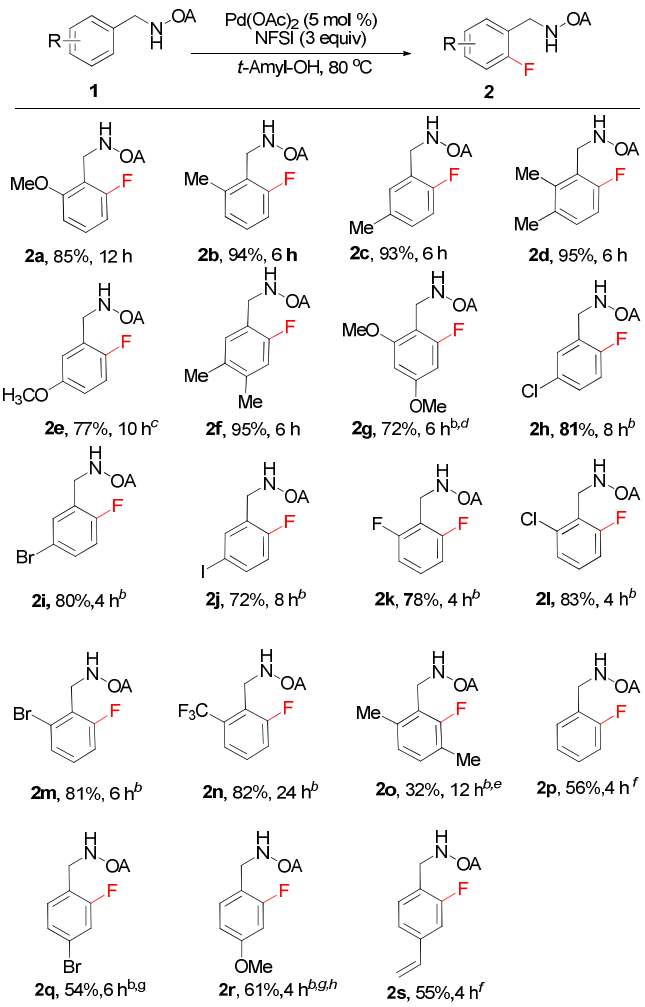
F1 **F2** **F3** **F4**

[a]Reaction conditions: 1a (0.1 mmol), $Pd(OAc)_2$ (5 mol %), NFSI (0.25 mmol), additive (0.02 mmol), solvent (1 mL), 80 °C, 12 h. Yield was based on GC using tridecane as the internal standard.

With the optimized conditions in hand, the scope and limitation of this reaction were next explored and repesentative data were shown in Table 2. To our great surprise, a remarkable broad substrates scope of benzylamines were tolerated. Substrates bearing electron-donating groups such as methyl or methoxyl substituents were transformed into corresponding fluorinated products in good to excellent yields (**2a-2g**). The substrates with electron-withdrawing substituents (**2h-2n**) were slightly lower activity which needed 10 mol% loading of Pd catalyst. The useful products containing F, Cl, Br and I were also obtained which were very important in synthetic elaborations. The high regioselective monofluorination also took place at the less hindered site giving

excellent yields(**2c, 2e, 2f, 2h-2j**). Notably, the challenging 2,5-disubstituted **1o** was also fluorinated with slight increase loading of the catalyst and temperature.

Table 2. Palladium-Catalyzed *ortho*-Fluorination of Benzylamines[a]

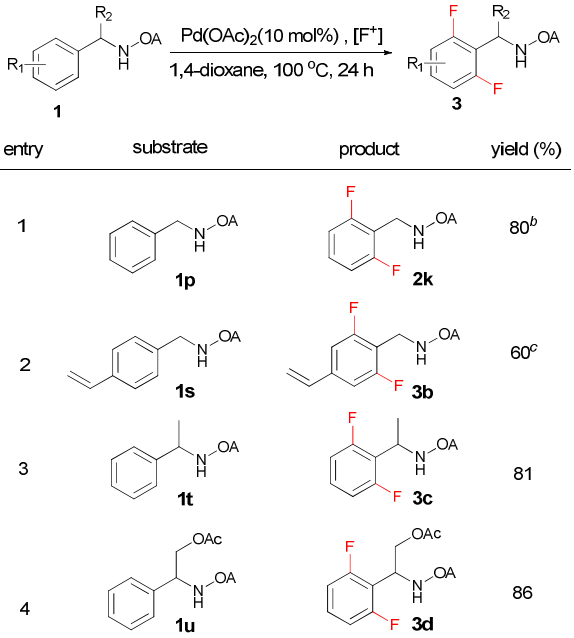


[a]Reaction conditions: **1** (0.2 mmol), $Pd(OAc)_2$ (5 mol %), NFSI (0.6 mmol), *t*-Amyl-OH (2 mL), 80 °C. Isolated yields. [b]$Pd(OAc)_2$ (10 mol%). [c]1,4-dioxane (2 mL). [d]*N*-fluoro-2,4,6-trimethyl-pyridinium triflate (0.4 mmol), DCE (2 mL). [e]100 °C. [f]1,4-dioxane:*t*-Amyl-OH = 3:1. [g]NFSI (1.0 mmol). [h]DCE:*t*-Amyl-OH = 1:1.

Monofluorination of oxalyl amide protected benzylamies were also achieved with modified reaction condition which listed in Table 2. The selective monofluorination of electron-rich (**1r)** and electron-poor (**1q**, **1s)** substituted oxalyl amide protected benzylamines were observed in moderate yield with shorter reaction time to avoid the difluorinated products, while the difluorinated products were observed less than 10% yield. To realize the difluorinated products, five equivalent of **F1** and 10 mol% $Pd(OAc)_2$ were applied in the reaction. However, the difluorinated products were obtained less than 60% yield except (**1t**, **1u)**. To reduce the amount of monofluorinated products, several other fluorine sources were

scanned. It is not surprising that **F3** yielded the difuorinated products in better yields at 100 °C in 24 h (Table 3, **2k, 3b-3d**).

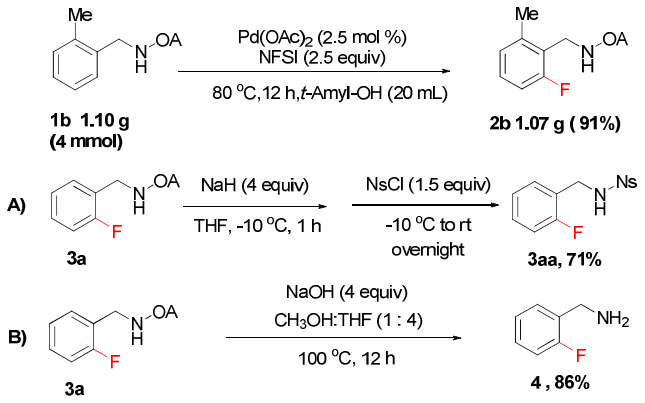
Table 3. Difluorination of Benzylamie Derivatives[a]



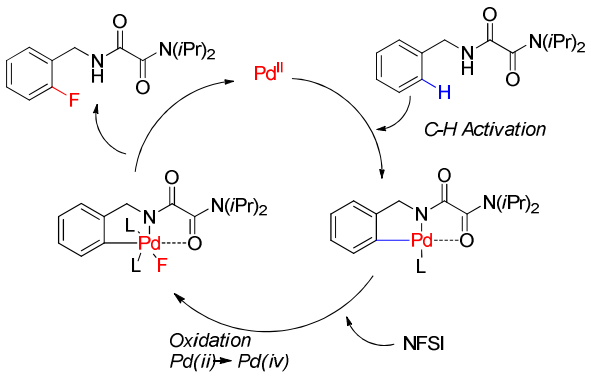
[a]Reaction conditions: **1** (0.2 mmol), $Pd(OAc)_2$ (10 mol %),**F3**（*N*-fluoro-2,4,6-trimethylpyridinium triflate）(0.6 mmol), 1,4-dioxane (2 mL), 80 °C, 24 h. Isolated yields. [b]$Pd(OAc)_2$ (15 mol %), [c]*t*-Amyl-OH (2 mL), NFSI (5 equiv).

Ortho-monofluorination of substrates **1b** was also carried out on gram scale. And excellent yield of **2b** was obtained, implicating the potential excellent versatility for synthetic application (Scheme 2). Due to the low cost of diisopropylamine and oxalyl chloride, oxalyl amide could be employed as a protecting group for benzyl amine substrates. And the oxalyl amide protected benzylamine derivative **3a** could be activated with NsCl (4-Nitrobenze ne-1-Sulfonyl Chloride) and cleaved by NaH in one pot to give the Ns-protected amine product **3aa** in high yield (Scheme 2, **A**).[22] The oxalyl amide could also be removed through 4 equiv of NaOH in CH_3OH:THF=1:4, giving compound **4** in 86% isolated yield (Scheme 2, **B**). On the basis of the observed experimental results and pioneering reports,[23] the palladium catalyst would lead to formation of a Pd^{iv} intermediate following C-H activation and oxidation with [F^+]. C-F reductive elimination afforded to the corresponding product finally (Scheme 3).

Scheme 2. Large Scale Synthesis and Removal of the Directing Group



Scheme 3. Proposed catalytic cycle



CONCLUSION

In conclusion, we have developed a highly selecive Pd^{II}-catalyzed *ortho*-monofluorination method for benzylamine derivatives using an easily accessible oxalyl amide as directing group. The cheap *N*-Fluorobenzenesulfonimide could be used as the efficient [F^+] source and *t*-Amyl-OH as the best solvent. Mono- and difluorination of oxalyl amide protected benzylamie derivatives were also achieved by modify the fluorine source in moderate to excellent yield with wide functional group tolerance. Oxalyl amide could be removed under mild condition afording the Ns protected amines. Detailed mechanistic studies are in progress, and the new application of oxalyl amide as directing group in construction of C–C, C–O or C–Heteroatom bonds are under study in our lab.

EXPERIMENTAL SECTION

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, br = broad singlet, m = multiplet. General procedures for the synthesis of products are represented as follows:

Preparation of S1: A solution of Diisopropylamine (7.01 mL, 50 mmol, 1.0 equiv) in CH_2Cl_2 (50 mL) was added dropwise to a solution of oxalyl chloride (6.44 ml, 75 mmol, 1.5 equiv) in CH_2Cl_2 (100 mL) at 0 °C, after stirring for 5 min, triethylamine (7.30 mL, 52.5 mmol, 1.05 equiv) was added dropwise. The solution was warmed to room temperature and stirred for 6 hours. The excess of oxalyl chloride and the solvent were removed under reduce pressure and CH_2Cl_2 (30 mL) was added and evaporated. This

operation was performed twice to give S1 as a pale yellow solid. The crude product was used in the next step without any purification.

***N, N*–Diisopropyloxamoyl chloride S1:** Yield 95% (8.4 g), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (m, 1H), 3.51 (m, 1H), 1.41 (d, J = 6.9 Hz, 6H), 1.24 (d, J = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 158.8, 51.0, 46.5, 20.3, 19.8; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_8H_{14}ClNO_2Na$ 214.0611; Found: 214.0609.

General procedures for preparation of oxalyl amide protected benzyl amines (1a–1t)[21]: A solution of amine (20 mmol, 1.0 eq) in CH_2Cl_2 (40 mL) was added dropwise to a solution of *N,N*–Diisopropyloxamoyl chloride S1 (25 mmol, 1.25 equiv) in CH_2Cl_2 (50 mL) at 0 °C. After stirring for 5 min, triethylamine (2.92 ml, 21 mmol, 1.05 equiv) was added dropwise, and then the mixture was stirred for 6 hours at room temperature before quenched by water (50 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (20 mL × 3). The combined organic phase was washed with brine (30 mL), dried over anhydrous Na_2SO_4. Evaporation and column chromatography on silica gel afforded corresponding amide substrates as white solid or colourless liquid with >80% yield.

***N*^{1},*N*^{1}-diisopropyl-*N*^{2}-(2-methoxybenzyl)oxalamide (1a)**: Yield 86% (5.03 g); off-white solid; mp = 113-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (br, 1H), 7.26 (m, 2H), 6.89 (m, 2H), 4.79 – 4.69 (m, 1H), 4.46 (d, J = 5.8 Hz, 2H), 3.85 (s, 3H), 3.53 – 3.45 (m, 1H), 1.41 (d, J = 6.6 Hz, 6H), 1.21 (d, J = 6.5 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.9, 157.6, 129.7, 129.1, 125.5, 120.6, 110.3, 55.4, 49.6, 46.5, 39.1, 20.9, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{24}N_2O_3Na$ 315.1685; Found: 315.1678.

***N*^{1},*N*^{1}-diisopropyl-*N*^{2}-(2-methylbenzyl)oxalamide (1b)**: Yield 88% (4.86 g); off-white solid; mp = 124-125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 1H), 7.23 – 7.17 (m, 3H), 7.13 (br, 1H), 4.83– 4.76 (m, 1H), 4.47 (d, J = 5.7 Hz, 2H), 3.57– 3.50 (m, 1H), 2.36 (s, 3H), 1.43 (d, J = 6.8 Hz, 6H), 1.26 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 162.9, 136.5, 135.2, 130.6, 128.6, 128.0, 126.4, 49.8, 46.7, 41.6, 21.0, 20.2, 19.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{24}N_2O_2Na$ 299.1735; Found: 299.1729.

***N*^{1},*N*^{1}-diisopropyl-*N*^{2}-(3-methylbenzyl)oxalamide (1c)**: Yield 92% (5.07 g); off-white solid; mp = 89-91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (br, 1H), 7.22 (m, 1H), 7.09 (m, 3H), 4.81 – 4.73 (m, 1H), 4.41 (d, J = 5.9 Hz, 2H), 3.55 – 3.47 (m, 1H), 2.34 (s, 3H), 1.41 (d, J = 6.8 Hz, 6H), 1.24 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 163.0, 138.5, 137.4, 128.7, 128.65, 128.4, 124.9, 49.7, 46.7, 43.4, 21.5, 20.9, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{24}N_2O_2Na$ 299.1735; Found: 299.1731.

***N*^{1}-(2,3-dimethylbenzyl)-*N*^{2},*N*^{2}-diisopropyloxalamide (1d)**: Yield 91% (5.28 g); off-white solid; mp = 93-95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 – 7.02 (m, 3H), 6.97 (br, 1H), 4.82 – 4.76 (m, 1H), 4.47 (d, J = 5.6 Hz, 2H), 3.55 - 3.48 (m, 1H), 2.29 (s, 3H), 2.22 (s, 3H), 1.41 (d, J = 6.8 Hz, 6H), 1.24 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 162.9, 137.5, 135.2, 135.0,

129.8, 126.8, 125.8, 49.8, 46.6, 42.3, 21.0, 20.5, 20.1, 14.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{26}N_2O_2Na$ 313.1892; Found: 313.1887.

***N^1,N^1-diisopropyl-N^2-(3-methoxybenzyl)oxalamide (1e)*:** Yield 82% (4.79 g); off-white solid; mp = 54-56 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (br, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.79 (m, 2H), 4.74 – 4.64 (m, 1H), 4.39 (d, *J* = 6.0 Hz, 2H), 3.76 (s, 3H), 3.52 - 3.45 (m, 1H), 1.38 (d, *J* = 6.8 Hz, 6H), 1.21 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 163.0, 159.9, 139.1, 129.8, 120.0, 113.3, 113.2, 55.2, 49.7, 46.5, 43.3, 20.9, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{24}N_2O_3Na$ 315.1685; Found: 315.1673.

***N^1-(3,4-dimethylbenzyl)-N^2,N^2-diisopropyloxalamide (1f)*:** Yield 92% (5.33 g); off-white solid; mp = 113-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (br, 1H), 7.08 – 6.95 (m, 3H), 4.79 – 4.68 (m, 1H), 4.33 (d, *J* = 5.7 Hz, 2H), 3.50 - 3.43 (m, 1H), 2.20 (s, 6H), 1.36 (d, *J* = 6.8 Hz, 6H), 1.19 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.0, 137.0, 136.0, 134.8, 130.0, 129.26, 125.3, 49.7, 46.6, 43.2, 20.9, 20.1, 19.8, 19.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{26}N_2O_2Na$ 313.1892; Found: 313.1877.

***N^1-(2,4-dimethoxybenzyl)-N^2,N^2-diisopropyloxalamide (1g)*:** Yield 76% (4.89 g); off-white solid; mp = 137-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (m, 2H), 6.43 (m, 2H), 4.80 - 4.73 (m, 1H), 4.38 (d, *J* = 6.0 Hz, 2H), 3.82 (s, 3H), 3.79 (s, 3H), 3.52 - 3.45 (m, 1H), 1.40 (d, *J* = 6.8 Hz, 6H), 1.21 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 162.8, 160.7, 158.7, 130.5, 118.1, 103.9, 98.6, 55.4, 55.4, 49.6, 46.5, 38.7, 20.9, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{26}N_2O_4Na$ 345.1790; Found: 345.1783.

***N^1-(3-chlorobenzyl)-N^2,N^2-diisopropyloxalamide (1h)*:** Yield 81% (4.80 g); off-white solid; mp = 96-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 - 7.27 (m, 2H), 7.27 - 7.24 (m, 2H), 7.20 – 7.16 (m, 1H), 4.87 - 4.80 (m, 1H), 4.44 (d, *J* = 6.1 Hz, 2H), 3.57 - 3.50 (m, 1H), 1.43 (d, *J* = 6.8 Hz, 6H), 1.25 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 162.9, 139.7, 134.6, 130.1, 127.9, 127.8, 125.9, 49.8, 46.7, 42.8, 20.9, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}ClN_2O_2Na$ 319.1189; Found: 319.1173.

***N^1-(3-bromobenzyl)-N^2,N^2-diisopropyloxalamide (1i)*:** Yield 84% (5.71 g); off-white solid; mp = 103-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (br, 1H), 7.42 - 7.39 (m, 2H), 7.25 – 7.16 (m, 2H), 4.82 - 4.75 (m, 1H), 4.42 (d, *J* = 6.1 Hz, 2H), 3.56 - 3.49 (m, 1H), 1.41 (d, *J* = 6.8 Hz, 6H), 1.24 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 163.0, 140.0, 130.8, 130.7, 130.3, 126.4, 122.8, 49.8, 46.7, 42.7, 20.9, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}BrN_2O_2Na$ 363.0684; Found: 363.0677.

***N^1-(3-iodobenzyl)-N^2,N^2-diisopropyloxalamide (1j)*:** Yield 80% (6.21 g); off-white solid; mp = 78-80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (m, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.28 (d, *J* = 6.6 Hz, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 4.74 - 4.67 (m, 1H), 4.39 (d, *J* = 6.1 Hz, 2H), 3.56 - 3.49 (m, 1H), 1.41 (d, *J* = 6.8 Hz, 6H), 1.25 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 163.0, 140.0, 136.7, 130.5, 127.1, 94.6, 49.8, 46.6, 42.5, 20.9, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}IN_2O_2$ Na 411.0545; Found: 411.0551.

N^1-(2-fluorobenzyl)-N^2,N^2-diisopropyloxalamide (1k)**:** Yield 79% (4.42 g); off-white solid; mp = 111-113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 - 7.32 (m, 1H), 7.31 – 7.26 (m, 2H), 7.13 - 7.09 (m, 1H), 7.07 – 7.02 (m, 1H), 4.83 - 4.76 (m, 1H), 4.52 (d, *J* = 6.2 Hz, 2H), 3.55-3.49 (m, *J* = 1H), 1.42 (d, *J* = 6.8 Hz, 6H), 1.23 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 162.7, 135.9, 131.42 (d, J_{C-F} = 222.0 Hz), 128.36 (d, J_{C-F} = 30.0 Hz), 127.9, 126.18 (d, J_{C-F} = 6.0 Hz), 125.98(d, J_{C-F} = 29 Hz), 49.8, 46.8, 39.9, 21.0, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.63. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}FN_2O_2Na$ 303.1485; Found: 303.1485.

N^1-(2-chlorobenzyl)-N^2,N^2-diisopropyloxalamide (1l)**:** Yield 83% (4.91 g); off-white solid; mp = 147-149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (br, 1H), 7.40 – 7.31 (m, 2H), 7.25 – 7.18 (m, 2H), 4.73 – 4.63 (m, 1H), 4.54 (d, *J* = 6.2 Hz, 2H), 3.53 – 3.44 (m, 1H), 1.38 (d, *J* = 6.8 Hz, 6H), 1.20 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2,162.9. 134.9, 133.7, 129.9, 129.6, 129.0, 127.1, 49.7, 46.6, 41.2, 20.9, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}ClN_2O_2Na$ 319.1189; Found: 319.1188.

N^1-(2-bromobenzyl)-N^2,N^2-diisopropyloxalamide (1m)**:** Yield 82% (5.58 g); off-white solid; mp = 155-157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.54 (m, 1H), 7.40 – 7.37 (m, 1H), 7.35 (br, 1H), 7.31 – 7.24 (m, 1H), 7.17 - 7.13 (m, 1H), 4.79 - 4.73 (m, 1H), 4.54 (d, *J* = 6.3 Hz, 2H), 3.55 - 3.48 (m, 1H), 1.41 (d, *J* = 6.8 Hz, 6H), 1.22 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.8, 136.6, 133.0, 130.1, 129.4, 127.9, 123.8, 49.7, 46.7, 43.7, 21.0, 20.2. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}BrN_2O_2Na$ 363.0684; Found: 363.0677.

N^1,N^1-diisopropyl-N^2-(2-(trifluoromethyl)benzyl)oxala-mide (1n)**:** Yield 73% (4.82 g); off-white solid; mp = 121-123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.9 Hz, 1H), 7.57 – 7.52 (m, 2H), 7.40 (m, 1H), 7.20 (br, 1H), 4.82 - 4.75 (m, 1H), 4.66 (d, *J* = 6.3 Hz, 2H), 3.56 - 3.49 (m, 1H), 1.42 (d, *J* = 6.8 Hz, 6H), 1.24 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1 , 162.8, 161.10 (d, J_{C-F} = 245.0 Hz) , 130.19 (d, J_{C-F} = 5.0 Hz), 129.57 (d, J_{C-F} = 8.1 Hz), 124.56 (d, J_{C-F} = 15.0, Hz), 124.44 (d, J_{C-F} = 4.0 Hz). 115.55 (d, J_{C-F} = 21.0 Hz), 49.7, 46.7, 37.38 (d, J_{C-F} = 4.0 Hz), 21.0, 20.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.68. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{21}F_3N_2O_2Na$ 353.1453; Found: 353.1459.

N^1-(2,5-dimethylbenzyl)-N^2,N^2-diisopropyloxalamide (1o)**:** Yield 88% (5.10 g); off-white solid; mp = 95-97 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (br, 1H), 7.06 – 7.04 (m, 2H), 7.01 – 6.99 (m, 1H), 4.82 – 4.64 (m, 1H), 4.40 (d, *J* = 5.7 Hz, 2H), 3.53 - 3.46 (m, 1H), 2.29 – 2.28 (m, 6H), 1.39 (d, *J* = 6.8 Hz, 6H), 1.23 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2. 163.0, 135.7, 134.9, 133.2, 130.4, 129.3, 128.5, 49.7, 46.5, 41.4, 21.0, 20.9, 20.1, 18.6. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{26}N_2O_2Na$ 313.1892; Found: 313.1894.

N^1-benzyl-N^2,N^2-diisopropyloxalamide (1p)**:** Yield 91% (4.77 g); off-white solid; mp = 102-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 7.20 (br, 1H), 4.87 - 4.80 (m, 1H), 4.46 (d, *J* = 6.0 Hz, 2H), 3.56 - 3.49 (m, 1H), 1.42 (d, *J* = 6.8 Hz, 6H), 1.24 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 163.0, 137.5, 128.8, 127.9, 127.7, 49.7, 46.7, 43.4, 21.0, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{22}N_2O_2Na$ 285.1579; Found: 285.1579.

***N^1-(4-bromobenzyl)-N^2,N^2-diisopropyloxalamide (1q)*:** Yield 83% (5.64 g); off-white solid; mp = 159-161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 - 7.43 (m, 3H), 7.17 (d, *J* = 8.3 Hz, 2H), 4.78 - 4.71 (m, 1H), 4.38 (d, *J* = 6.1 Hz, 2H), 3.55 - 3.48 (m, 1H), 1.40 (d, *J* = 6.8 Hz, 6H), 1.23 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 163.0, 136.7, 131.9, 129.6, 121.6, 49.8, 46.7, 42.7, 21.0, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}BrN_2O_2Na$ 363.0684; Found: 363.0685.

***N^1,N^1-diisopropyl-N^2-(4-methoxybenzyl)oxalamide (1r)*:** Yield 87% (5.08 g); off-white solid; mp = 87-89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (br, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.89 – 6.80 (m, 2H), 4.76 - 4.69 (m, 1H), 4.36 (d, *J* = 5.9 Hz, 2H), 3.77 (s, 3H), 3.52 - 3.45 (m, 1H), 1.38 (d, *J* = 6.8 Hz, 6H), 1.22 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 163.0, 159.1, 129.6, 129.2, 114.1, 55.3, 49.7, 46.6, 42.8, 20.9, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{24}N_2O_3Na$ 315.1685; Found: 315.1686.

***N^1,N^1-diisopropyl-N^2-(4-vinylbenzyl)oxalamide (1s)*:** Yield 78% (4.49 g); off-white solid; mp = 91-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.33 (m, 3H), 7.28 – 7.22 (m, 2H), 6.69 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.73 (d, *J* = 17.6, 1H), 5.24 (d, *J* = 10.9, 1H), 4.80 - 4.73 (m,1H), 4.43 (d, *J* = 6.0 Hz, 2H), 3.55 - 3.48 (m, 1H), 1.41 (d, *J* = 6.8 Hz, 6H), 1.23 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 137.1, 136.9, 136.4, 128.0, 126.5, 113.9, 49.7, 46.5, 43.0, 20.9, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{24}N_2O_2Na$ 311.1735; Found:311.1731.

***N^1,N^1-diisopropyl-N^2-(1-phenylethyl)oxalamide (1t)*:** Yield 86% (4.75 g); off-white solid; mp = 142-144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (br, 1H), 7.37 - 7.30 (m, 4H), 7.28 – 7.21 (m, 1H), 5.09 – 5.02 (m, 1H), 4.65 (s, 1H), 3.55 – 3.43 (m, 1H), 1.50 (d, *J* = 7.0 Hz, 3H), 1.41 (dd, *J* = 9.7, 6.8 Hz, 6H), 1.20 (dd, *J* = 9.9, 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 162.4, 143.0, 128.7, 127.3, 126.1, 49.7, 49.1, 46.5, 22.0, 20.8, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{24}N_2O_2Na$ 299.1735; Found: 299.1734.

General procedures for preparation of 1u[21]: The first step using 2-amino-2-phenylethanol (2.74 g, 20 mmol, 1.0 eq) as starting material followed the general procedure , affords a white solid which was analyzed by LC-MS. The solid (5.25 g) was dissolved in DCM (30 mL), treated with AcCl (1.56 mL, 22 mmol, 1.1 eq) and Et_3N (5.56 mL, 40 mmol, 2.0 eq) at room temperature overnight. The reaction was quenched with water and extracted with DCM (30 mL× 3). The combined organic layers was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the product **1u** 5.55 g, 83%.

***2-(2-(diisopropylamino)-2-oxoacetamido)-2-phenylethyl acetate (1u)*:** Yield 82% (5.48 g); off-white solid; mp = 114-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (br, 1H), 7.40 – 7.24 (m, 5H), 5.26 - 5.21 (m, 1H), 4.74 - 4.67 (m, 1H), 4.35 (d, *J* = 5.8 Hz, 2H), 3.55 - 3.48 (m, 1H), 2.03 (s, 3H), 1.42 (dd, *J* = 9.7, 6.8 Hz, 6H), 1.21 (dd, *J* = 6.6, 4.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 162.8, 137.8, 128.9, 128.1, 126.8, 66.2, 52.4, 49.7, 46.7, 20.9, 20.8, 20.2, 20.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{26}N_2O_4Na$ 357.1790; Found: 357.1791.

General Procedure for Palladium-catalyzed mono-Fluorinationof Benzylamines (Table 2) (2a-2d, 2f): A mixture of oxalamide (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (22 mg, 0.05 eq), NFSI (0.6 mmol, 3.0 eq) and *t*-Amyl-OH (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 ^oC. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding product.

***N^1-(2-fluoro-6-methoxybenzyl)-N^2,N^2-diisopropyloxala-mide (2a)*:** Yield 85% (52.7 mg); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 - 7.19 (m, 2H), 6.74 – 6.63 (m, 2H), 4.86 - 4.80 (m, 1H), 4.54 (d, J = 5.9 Hz, 2H), 3.87 (s, 3H), 3.53 - 3.46 (m, 1H), 1.39 (d, J = 6.8 Hz, 6H), 1.21 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 162.6, 161.51 (d, J_{C-F} = 245.0 Hz), 159.27 (d, J_{C-F} = 7.6 Hz), 129.62 (d, J_{C-F} = 10.7 Hz), 113.03 (d, J_{C-F} = 18.1 Hz), 108.24(d, J_{C-F} =23.0 Hz), 106.35 (d, J_{C-F} = 2.9 Hz), 56.18, 49.6, 46.6, 31.74 (d, J_{C-F} = 5.3 Hz), 21.0, 20.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.28. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{23}FN_2O_3Na$ 333.1590; Found: 333.1582.

***N^1-(2-fluoro-6-methylbenzyl)-N^2,N^2-diisopropyloxala-mide (2b)*:** Yield 94% (55.3 mg); pale yellow solid; mp = 77-79 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.18 - 7.13 (m, 1H), 7.03 (br, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.89 (t, J = 9.0 Hz, 1H), 4.79 - 4.72 (m, 1H), 4.53 – 4.51 (m, 2H), 3.52 - 3.46 (m, 1H), 2.40 (s, 3H), 1.38 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ, 162.8, 162.8, 161.95 (d, J_{C-F} = 244.0 Hz), 139.72 (d, J_{C-F} = 3.0 Hz), 129.25 (d, J_{C-F} = 9.4 Hz), 126.21 (d, J_{C-F} = 3.0 Hz), 122.69 (d, J_{C-F} = 14.0 Hz), 113.08(d, J_{C-F} = 23.0 Hz) , 49.7, 46.7, 34.21 (d, J_{C-F} = 5.3 Hz), 20.9, 20.1, 19.25 (d, J_{C-F} = 3.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.05. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{23}FN_2O_2Na$ 317.1641; Found:317.1641.

***N^1-(2-fluoro-5-methylbenzyl)-N^2,N^2-diisopropyloxala-mide (2c)*:** Yield 93% (54.7 mg); pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (br, 1H), 7.11 (d, J = 7.1 Hz, 1H), 7.05 - 7.01 (m, 1H), 6.96 – 6.86 (m, 1H), 4.79 - 4.72 (m, 1H), 4.46 (d, J = 6.1 Hz, 2H), 3.52-3.47 (m, 1H), 2.28 (s, 3H), 1.40 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.8, 159.29 (d, J_{C-F} = 242.0 Hz), 133.89 (d, J_{C-F} = 3.7 Hz), 130.59 (d, J_{C-F} = 3.9 Hz), 129.92 (d, J_{C-F} = 7.9 Hz), 123.99 (d, J_{C-F} = 15.1 Hz), 115.21(d, J_{C-F} = 21.0 Hz), 49.7, 46.7, 37.42 (d, J_{C-F} = 3.8 Hz), 20.9, 20.7, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.05. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{23}FN_2O_2H$ 295.1822; Found: 295.1817.

***N^1-(6-fluoro-2,3-dimethylbenzyl)-N^2,N^2-diisopropyloxal-amide (2d)*:** Yield 95% (58.5 mg); pale yellow solid; mp = 114-116 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.06 - 7.03 (m, 1H), 6.95 (br, 1H), 6.80 (t, J = 9.0 Hz, 1H), 4.81 - 4.74 (m, 1H), 4.54 (dd, J = 5.6, 1.9 Hz, 2H), 3.52-3.45 (m, 1H), 2.27 (s, 3H), 2.23 (s, 3H), 1.38 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 162.7, 160.24 (d, J_{C-F} = 242.0 Hz), 137.85 (d, J_{C-F} = 2.9 Hz), 132.86 (d, J_{C-F} = 3.4 Hz), 130.54 (d, J_{C-F} = 8.8 Hz), 122.33 (d, J_{C-F} = 13.9 Hz), 112.29 (d, J_{C-F} = 22.0 Hz), 49.7, 46.6, 34.39 (d, J_{C-F} = 5.8 Hz), 20.9, 20.2, 20.1, 15.63 (d, J_{C-F} = 2.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.91. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{25}FN_2O_2H$ 309.1978; Found: 309.1978

***N^1-(2-fluoro-5-methoxybenzyl)-N^2,N^2-diisopropyloxala-mide (2e)*:** A mixture of oxalamide **1e** (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (22 mg, 0.05 eq), NFSI (0.6 mmol, 3.0 eq) and 1,4-dioxane (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 ^oC for 10 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by

column chromatography on silica gel to give the product of **2e**. Yield 77% (47.8 mg); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (br, 1H), 6.96 (t, J = 9.1 Hz, 1H), 6.86 – 6.84 (m, 1H), 6.78 - 6.74 (m,1H), 4.79 - 4.73 (m, 1H), 4.47 (d, J = 6.1 Hz, 2H), 3.76 (s, 3H), 3.54 - 3.48 (m, 1H), 1.41 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.7, 155.90 (d, J_{C-F} = 2.0 Hz), 155.44 (d, J_{C-F} =237.0 Hz), 125.16 (d, J_{C-F} = 16.7 Hz), 116.11(d, J_{C-F} = 23.0 Hz), 114.96 (d, J_{C-F} = 4.0 Hz), 114.42 (d, J_{C-F} = 8.0 Hz), 55.9, 49.7, 46.7, 37.59 (d, J_{C-F} = 3.6 Hz), 20.9, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -129.61. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{23}FN_2O_3H$ 311.1771; Found: 311.1777.

***N^1-(2-fluoro-4,5-dimethylbenzyl)-N^2,N^2-diisopropyloxa-lamide (2f)*:** Yield 95% (58.5 mg); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (br, 1H), 7.05 (d, J = 7.7 Hz, 1H), 6.82 (d, J = 10.7 Hz, 1H), 4.80 - 4.74 (m, 1H), 4.43 (d, J = 6.1 Hz, 2H), 3.53 - 3.47 (m, 1H), 2.21 (s, 3H), 2.18 (s, 3H), 1.40 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 162.8, 159.26 (d, J_{C-F} = 243 Hz), 138.33 (d, J_{C-F} = 7.7 Hz), 132.44 (d, J_{C-F} = 3.4 Hz), 131.08 (d, J_{C-F} = 4.3 Hz), 121.14 (d, J_{C-F} = 14.0 Hz), 116.47 (d, J_{C-F} = 21.0 Hz) , 49.7, 46.7, 37.23 (d, J_{C-F} = 3.5 Hz), 20.9, 20.1, 19.72 (d, J_{C-F} = 1.4 Hz), 19.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.24. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{25}FN_2O_2H$ 309.1978; Found: 309.1981.

***N^1-(2-fluoro-4,6-dimethoxybenzyl)-N^2,N^2-diisopropylo-xalamide (2g)*:** A mixture of oxalamide **1g** (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (44 mg, 0.10 eq), **F3** (0.4 mmol, 2.0 eq) and DCE (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 ^{o}C for 6 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding product. Yield 72% (49.0 mg); pale yellow solid; mp = 125-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (br, 1H), 7.03 (d, J = 11.3 Hz, 1H), 6.51 (d, J = 7.0 Hz, 1H), 4.80 - 4.74 (m, 1H), 4.36 (d, J = 6.1 Hz, 2H), 3.90 (s, 3H), 3.84 (s, 3H), 3.53 - 3.47(m, 1H), 1.41 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 162.9, 153.9, 147.50 (d, J_{C-F} = 11.7 Hz), 146.58(d, J_{C-F} = 237.0 Hz), 117.72 (d, J_{C-F} = 5.5 Hz), 117.29(d, J_{C-F} = 20.0 Hz), 98.2, 56.9, 56.1, 49.6, 46.7, 38.3, 20.9, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -145.23. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{25}FN_2O_4Na$ 363.1696; Found: 363.1705.

General Procedure for Palladium-catalyzed mono-Fluorinationof Benzylamines (Table 2) (2h-2n): A mixture of oxalamide (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (44 mg, 0.10 eq), NFSI (0.6 mmol, 3.0 eq) and *t*-Amyl-OH (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 °C. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding product.

***N^1-(5-chloro-2-fluorobenzyl)-N^2,N^2-diisopropyloxala-mide (2h)*:** Yield 81% (50.9 mg); pale yellow solid; mp = 78-80 °C; 1H NMR (400 MHz, CDCl3) δ 7.50 (br, 1H), 7.32 (dd, J = 6.4, 2.6 Hz, 1H), 7.24 – 7.17 (m, 1H), 6.98 (t, J = 9.0 Hz, 1H), 4.77 - 4.71 (m, 1H), 4.47 (d, J = 6.3 Hz, 2H), 3.55 - 3.48 (m, 1H), 1.40 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.7 Hz, 6H); 13C NMR (101 MHz, CDCl3) δ 163.2, 162.6, 159.50(d, J_{C-F} = 245.0 Hz), 129.81 (d, J_{C-F} = 4.4 Hz), 129.49 (d, J_{C-F} = 3.0Hz), 129.34 (d, J_{C-F} =8.0Hz), 126.52 (d, J_{C-F} = 16.6 Hz), 116.90 (d, J_{C-F} =23.0Hz), 49.8, 46.7, 36.98 (d, J_{C-F} = 3.9 Hz), 20.9, 20.1; 19F NMR (376 MHz, CDCl3) δ -121.22. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}ClFN_2O_2Na$ 337.1095; Found: 337.1103.

***N^1-(5-bromo-2-fluorobenzyl)-N^2,N^2-diisopropyloxala-mide (2i)*:** Yield 80% (57.3 mg); pale yellow solid; mp = 86-88 °C;; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, J = 6.5, 2.5 Hz, 1H), 7.39 - 7.35 (m,2H), 6.94 (t, J = 9.1 Hz, 1H), 4.81 - 4.75 (m, 1H), 4.47 (d, J = 6.3 Hz, 2H), 3.56 - 3.49 (m, 1H), 1.41 (d, J = 6.8 Hz, 6H), 1.24 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.5, 160.11 (d, $J_{C\text{-}F}$ = 246.0Hz), 132.82 (d, $J_{C\text{-}F}$ = 4.2 Hz), 132.44 (d, $J_{C\text{-}F}$ = 8.2 Hz), 126.92 (d, $J_{C\text{-}F}$ = 16.3 Hz), 117.40 (d, $J_{C\text{-}F}$ =22.0 Hz), 116.92 (d, $J_{C\text{-}F}$ = 3.5 Hz), 49.7, 46.8, 37.00 (d, $J_{C\text{-}F}$ = 3.9 Hz), 21.0, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.61. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}BrFN_2O_2Na$ 381.0590; Found: 381.0602.

***N^1-(2-fluoro-5-iodobenzyl)-N^2,N^2-diisopropyloxalamide (2j)*:** Yield 72% (58.5 mg); pale yellow solid; mp = 90-92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 6.9, 2.2 Hz, 1H), 7.58 - 7.54 (m, 1H), 7.41 (br, 1H), 6.81 (t, J = 9.5, 1H), 4.79 - 4.72 (m, 1H), 4.45 (d, J = 6.2 Hz, 2H), 3.55 - 3.48 (m, 1H), 1.41 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.6, 161.03(d, $J_{C\text{-}F}$ = 247.0 Hz) , 138.76 (d, $J_{C\text{-}F}$ = 4.1 Hz), 138.50 (d, $J_{C\text{-}F}$ = 8.0 Hz), 127.31 (d, $J_{C\text{-}F}$ = 15.8 Hz), 117.84(d, $J_{C\text{-}F}$ = 22.0 Hz), 87.36 (d, $J_{C\text{-}F}$ = 3.7 Hz), 49.7, 46.8, 36.84 (d, $J_{C\text{-}F}$ = 4.0 Hz), 21.0, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.70. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}IFN_2O_2Na$ 429.0451; Found: 429.0456.

***N^1-(2,6-difluorobenzyl)-N^2,N^2-diisopropyloxalamide (2k)*:** Yield 78% (46.5 mg); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.22 (m, 2H), 6.91 – 6.87 (m, 2H), 4.87 - 4.80 (m, 1H), 4.57 (d, J = 6.0 Hz, 2H), 3.54 - 3.47 (m, 1H), 1.40 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.76 (d, $J_{C\text{-}F}$ = 7.8 Hz), 162.6, 162.4, 160.43 (d, $J_{C\text{-}F}$ = 8 Hz), 129.91 (t, $J_{C\text{-}F}$ = 10.3 Hz), 113.26 (t, $J_{C\text{-}F}$ = 19.3 Hz), 111.60 (d, $J_{C\text{-}F}$ =25.0 Hz). 111.60 (d, $J_{C\text{-}F}$ = 13.0Hz), 49.6, 46.8, 31.2, 20.9, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.72. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}F_2N_2O_2Na$ 321.1391; Found:321.1396.

***N^1-(2-chloro-6-fluorobenzyl)-N^2,N^2-diisopropyloxala-mide (2l)*:** Yield 83% (49.0 mg); pale yellow solid; mp = 78-80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (br,1H), 7.25 – 7.18 (m, 2H), 7.05 – 6.97 (m, 1H), 4.85 - 4.79 (m, 1H), 4.66 (dd, J = 5.9, 1.5 Hz, 2H), 3.54 - 3.47 (m, 1H), 1.39 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 161.74 (d, $J_{C\text{-}F}$ = 249.0 Hz), 135.75 (d, $J_{C\text{-}F}$ = 5.2 Hz), 130.00 (d, $J_{C\text{-}F}$ = 9.7 Hz), 125.56 (d, $J_{C\text{-}F}$ = 3.5 Hz), 123.17 (d, $J_{C\text{-}F}$ = 17.9 Hz), 114.47 (d, $J_{C\text{-}F}$ = 22.0Hz), 49.6, 46.7, 34.61 (d, $J_{C\text{-}F}$ = 4.1 Hz), 20.9, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.86. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}ClFN_2O_2Na$ 337.1095; Found: 337.1102.

***N^1-(2-bromo-6-fluorobenzyl)-N^2,N^2-diisopropyloxala-mide (2m)*:** Yield 81% (58.0 mg); pale yellow solid; mp = 98-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.0 Hz, 1H), 7.17 (m, 2H), 7.09 – 7.00 (m, 1H), 4.88 - 4.81 (m, 1H), 4.66 (dd, J = 5.9, 1.8 Hz, 2H), 3.54 - 3.47 (m, 1H), 1.40 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 162.5, 161.62 (d, $J_{C\text{-}F}$ = 250.0 Hz), 130.56 (d, $J_{C\text{-}F}$ = 9.4 Hz), 128.87 (d, $J_{C\text{-}F}$ = 3.6 Hz), 125.59 (d, $J_{C\text{-}F}$ = 4.2 Hz), 124.84 (d, $J_{C\text{-}F}$ = 17.5 Hz), 115.17 (d, $J_{C\text{-}F}$ = 23.0 Hz), 49.6, 46.7, 37.07 (d, $J_{C\text{-}F}$ = 4.0 Hz), 21.0, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.59. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}BrFN_2O_2Na$ 381.0590; Found: 381.0591.

***N^1-(2-fluoro-6-(trifluoromethyl)benzyl)-N^2,N^2-diisoprop-yloxalamide (2n)*:** Yield 82% (57.1 mg); pale yellow solid; mp = 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.48 (m, 1H), 7.46 - 7.40 (m, 1H), 7.31 (t, *J* = 8.8 Hz, 1H), 7.05 (br, 1H), 4.86 - 4.80 (m, 1H), 4.70 (d, *J* = 5.6 Hz, 2H), 3.54 - 3.47 (m, 1H), 1.39 (d, *J* = 6.8 Hz, 6H), 1.23 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 163.2, 162.8, 162.5, 162.3, 160.9, 132.5, 131.3, 131.3, 131.0, 131.0, 130.2, 130.1, 130.0, 127.8, 126.1, 126.1, 124.9, 124.9, 123.0, 122.9, 122.2, 122.1, 122.1, 122.0, 122.0, 122.0, 121.9, 121.9, 119.9, 119.6, 49.7, 46.7, 33.6, 33.60 33.5, 33.5, 20.9, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.87, -112.75. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}F_4N_2O_2Na$ 371.1359; Found: 371.1363.

***N^1-(2-fluoro-3,6-dimethylbenzyl)-N^2,N^2-diisopropyloxa-lamide (2o)*:** A mixture of oxalamide **1o** (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (44 mg, 0.10 eq), NFSI (0.6 mmol, 3.0 eq) and *t*-Amyl-OH (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 100 °C for 12 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding product. Yield 32% (19.7 mg); pale yellow solid; mp = 74-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 – 6.99 (m, 2H), 6.85 (d, *J* = 7.7 Hz, 1H), 4.82 - 4.76 (m, 1H), 4.51 (d, *J* = 5.7 Hz, 2H), 3.53 - 3.46 (m, 1H), 2.36 (s, 3H), 2.22 (s, 3H), 1.39 (d, *J* = 6.8 Hz, 6H), 1.22 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 160.41(d, $J_{C\text{-}F}$ = 243.0 Hz), 136.64 (d, $J_{C\text{-}F}$ = 3.3 Hz), 130.73 (d, $J_{C\text{-}F}$ = 6.3 Hz), 125.63 (d, $J_{C\text{-}F}$ = 3.6 Hz), 122.33 (d, $J_{C\text{-}F}$ = 24 Hz), 122.31 (d, $J_{C\text{-}F}$ = 9 Hz) 49.7, 46.7, 34.46 (d, $J_{C\text{-}F}$ = 5.7 Hz), 21.0, 20.1, 19.00 (d, $J_{C\text{-}F}$ = 2.5 Hz), 14.44 (d, $J_{C\text{-}F}$ = 4.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -122.14. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{25}FN_2O_2Na$ 331.1798; Found: 331.1801.

N1-(2-fluorobenzyl)-N2,N2-diisopropyloxalamide (2p): A mixture of oxalamide **1p** (0.2 mmol, 1.0 eq), Pd(OAc)2 (22 mg, 0.05 eq), NFSI (0.6 mmol, 3.0 eq) and 1,4-dioxane : t-Amyl-OH=3:1 (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 °C for 4 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding product. Yield 56% (31.4 mg); pale yellow solid; mp = 111-113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 - 7.32 (m, 1H), 7.31 – 7.26 (m, 2H), 7.13 - 7.09 (m, 1H), 7.07 - 7.02 (m, 1H), 4.83-4.76 (m, 1H), 4.52 (d, *J* = 6.2 Hz, 2H), 3.55-3.49 (m, *J* = 13.6, 6.8 Hz, 1H), 1.42 (d, *J* = 6.8 Hz, 6H), 1.23 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.7, 135.9, 131.42 (d, $J_{C\text{-}F}$ = 222.0 Hz), 128.36 (d, $J_{C\text{-}F}$ = 30.0 Hz), 127.8,126.18 (d, $J_{C\text{-}F}$ = 6.0 Hz),125.98(d, $J_{C\text{-}F}$ = 29 Hz), 49.7, 46.7, 39.9, 20.9, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.63. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}FN_2O_2$ [M+Na]: 303.1485; Found: 303.1485.

***N^1-(4-bromo-2-fluorobenzyl)-N^2,N^2-diisopropyloxala-mide (2q)*:** A mixture of oxalamide **1q** (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (44 mg, 0.10 eq), NFSI (1.0 mmol, 5.0 eq) and *t*-Amyl-OH (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 °C for 6 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding product. Yield 54% (38.7 mg); pale yellow solid; mp = 120-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (br, 1H), 7.22 - 7.19 (m, 3H), 4.79 – 4.55 (m, 1H), 4.42 (d, *J* = 6.2 Hz, 2H), 3.52-3.45 (m, 1H), 1.36 (d, *J* = 6.8 Hz, 6H), 1.20 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 163.2, 160.56 (d, $J_{C\text{-}F}$ = 250.0 Hz), 131.09 (d, $J_{C\text{-}F}$ = 4.7 Hz), 127.52 (d, $J_{C\text{-}F}$ = 3.5 Hz), 124.02 (d, $J_{C\text{-}F}$ = 14.9 Hz), 121.51 (d, $J_{C\text{-}F}$ = 9.3 Hz), 118.99 (d, $J_{C\text{-}F}$ = 24.0 Hz), 49.8,

46.4, 36.5, 20.7, 19.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.80. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}BrFN_2O_2Na$ 381.0590; Found: 381.0593.

***N^1-(2-fluoro-4-methoxybenzyl)-N^2,N^2-diisopropyloxala-mide (2r)*:** A mixture of oxalamide **1r** (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (44 mg, 0.10 eq), NFSI (1.0 mmol, 5.0 eq) and DCE:*t*-Amyl-OH=1:1 (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 °C for 4 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding product. Yield 61% (37.8 mg); pale yellow solid; mp = 70-72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 8.6 Hz, 1H), 7.15 (br, 1H), 6.66 - 6.59 (m, 2H), 4.81 - 4.74 (m, 1H), 4.43 (d, J = 6.0 Hz, 2H), 3.78 (s, 3H), 3.54 - 3.47 (m, 1H), 1.41 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 162.8, 161.77 (d, $J_{C\text{-}F}$ = 245.0 Hz), 160.78 (d, $J_{C\text{-}F}$ = 11.0 Hz), 130.96 (d, $J_{C\text{-}F}$ = 6.1 Hz), 116.45 (d, $J_{C\text{-}F}$ =16.0 Hz), 110.05 (d, $J_{C\text{-}F}$ = 3.1 Hz), 101.93 (d, $J_{C\text{-}F}$ =25 Hz), 55.7, 49.7, 46.7, 37.12 (d, $J_{C\text{-}F}$ = 3.3 Hz), 21.0, 20.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.51. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{23}FN_2O_3Na$ 333.1590; Found:333.1594.

***N^1-(2-fluoro-4-vinylbenzyl)-N^2,N^2-diisopropyloxalamide (2s)*:** A mixture of oxalamide **1s** (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (22 mg, 0.05 eq), NFSI (0.6 mmol, 3.0 eq) and 1,4-dioxane:*t*-Amyl-OH=3:1 (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 °C for 4 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding product. Yield 55% (33.7 mg); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, J = 7.8 Hz, 1H), 7.22 (br, 1H), 7.15 – 7.07 (m, 2H), 6.65 (dd, J = 17.5, 10.8 Hz, 1H), 5.73 (d, J = 17.5 Hz, 1H), 5.29 (d, J = 10.9 Hz, 1H), 4.82 - 4.75 (m, 1H), 4.49 (d, J = 6.2 Hz, 2H), 3.55 - 3.48 (m, 1H), 1.41 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.7, 161.31 (d, $J_{C\text{-}F}$ =245.0 Hz), 139.67 (d, $J_{C\text{-}F}$ = 7.8 Hz), 135.57 (d, $J_{C\text{-}F}$ = 2.3 Hz), 130.28 (d, $J_{C\text{-}F}$ = 4.7 Hz), 123.85 (d, $J_{C\text{-}F}$ = 15.4 Hz), 122.53 (d, $J_{C\text{-}F}$ = 3.1 Hz), 115.5, 112.83(d, $J_{C\text{-}F}$ = 22.0 Hz), 49.7, 46.8, 37.33 (d, $J_{C\text{-}F}$ = 3.7 Hz), 21.0, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.04. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{23}FN_2O_2Na$ 329.1641; Found: 329.1630.

***N^1-(2,6-difluorobenzyl)-N^2,N^2-diisopropyloxalamide (2k)*:** A mixture of oxalamide**1p** (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (66 mg, 0.15 eq), **F3** (*N*-fluoro-2,4,6-trimethylpyridinium triflate） (0.6 mmol, 3.0 eq) and 1,4-dioxane (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 °C for 24 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding produYield 80% (47.7 mg); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.22 (m, 2H), 6.91 – 6.87 (m, 2H), 4.87 - 4.80 (m, 1H), 4.57 (d, J = 6.0 Hz, 2H), 3.54 - 3.47 (m, 1H), 1.40 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.76 (d, $J_{C\text{-}F}$ = 7.8 Hz), 162.6, 162.4, 160.43 (d, $J_{C\text{-}F}$ = 8 Hz), 129.91 (t, $J_{C\text{-}F}$ = 10.3 Hz), 113.26 (t, $J_{C\text{-}F}$ = 19.3 Hz), 111.60 (d, $J_{C\text{-}F}$ =25.0 Hz). 111.60 (d, $J_{C\text{-}F}$ = 13.0Hz), 49.6, 46.8, 31.2, 21.0, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.72. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}F_2N_2O_2Na$ 321.1391; Found:321.1396.

***N^1-(2,6-difluoro-4-vinylbenzyl)-N^2,N^2-diisopropyloxala-mide (3b)*:** A mixture of oxalamide **1s** (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (44 mg, 0.10 eq), NFSI (1.0 mmol, 5.0 eq) and *t*-Amyl-OH (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 °C

for 24 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding product. Yield 60% (38.9 mg); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (br, 1H), 6.97 – 6.89 (m, 2H), 6.60 (dd, J = 17.5, 10.8 Hz, 1H), 5.75 (d, J = 17.5 Hz, 1H), 5.36 (d, J = 10.8 Hz, 1H), 4.86 - 4.79 (m, 1H), 4.54 (d, J = 6.0 Hz, 2H), 3.54 - 3.47 (m, 1H), 1.40 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 162.56(d, J_{C-F} = 16 Hz), 160.47 (d, J_{C-F} = 8.7 Hz), 140.18(t), 134.81(t), 116.9, 112.25 (t), 109.16 (d, J_{C-F} = 26 Hz), 109.16 (d, J_{C-F} = 12.0 Hz), 49.6, 46.8, 31.21(t), 29.8, 21.0, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.10. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{22}F_2N_2O_2Na$ 347.1547; Found:347.1534.

General Procedure for the Preparation of the Difluorination Substrates (Table 3) (3c-3d): A mixture of oxalamide (**1t,1u)** (0.2 mmol, 1.0 eq), $Pd(OAc)_2$ (44 mg, 0.10 eq), **F3** (*N*-fluoro-2,4,6-trimethylpyridinium triflate） (0.6 mmol, 3.0 eq) and 1,4-dioxane (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 ℃ for 24 h. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the corresponding product.

***N^1-(1-(2,6-difluorophenyl)ethyl)-N^2,N^2-diisopropyloxala-mide (3c)*:** Yield 81% (50.5 mg); pale yellow solid; mp = 105-107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (br, 1H), 7.23 - 7.16 (m, 1H), 6.87 (t, J = 8.3 Hz, 2H), 5.61 – 5.43 (m, 1H), 4.81 - 4.75 (m, 1H), 3.53 - 3.46 (m, 1H), 1.55 (d, J = 7.1 Hz, 3H), 1.41 (dd, J = 12.9, 6.8 Hz, 6H), 1.19 (dd, J = 11.6, 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 162.18 (d, J_{C-F} = 7.8 Hz), 162.1, 159.71 (d, J_{C-F} = 8.4 Hz), 129.10 (t, J_{C-F} = 10.6 Hz), 118.41 (t, J_{C-F} = 17.3 Hz), 111.92 (d, J_{C-F} = 25.0 Hz), 111.92 (d, J_{C-F} = 13.0 Hz),49.5, 46.7, 40.12 (t, J_{C-F} = 2.8 Hz), 20.96 (d, J_{C-F} = 7.0 Hz),20.8, 20.17 (d, J_{C-F} = 2.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.12. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{22}F_2N_2O_2Na$ 335.1547; Found: 335.1549.

***2-(2,6-difluorophenyl)-2-(2-(diisopropylamino)-2-oxo-acetamido)ethyl acetate (3d)*:** Yield 86% (63.6 mg); pale yellow solid; mp = 70-72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.66 (m, 1H), 7.34 – 7.21 (m, 1H), 6.92 (t, J = 8.3 Hz, 2H), 5.78 - 5.73 (m, 1H), 4.80 - 4.73 (m, 1H), 4.43 (dd, J = 11.2, 7.3 Hz, 1H), 4.31 (dd, J = 11.2, 5.8 Hz, 1H), 3.56 - 3.49 (m, 1H), 2.04 (s, 3H), 1.42 (dd, J = 14.4, 6.8 Hz, 6H), 1.22 (dd, J = 8.6, 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 162.55 (t, J_{C-F} = 3.9 Hz), 162.1, 160.07 (d, J_{C-F} = 7.9 Hz), 130.00 (d, J_{C-F} = 208.0 Hz), 130.23 (t, J_{C-F} = 10.6 Hz), 113.65 (t, J_{C-F} = 17.5 Hz), 112.03 (d, J_{C-F} = 26.0 Hz), 112.03 (d, J_{C-F} = 13.0 Hz), 64.6, 49.6, 46.8, 43.70, 21.06 (d, J_{C-F} = 9.0 Hz), 20.7, 20.16 (d, J_{C-F} = 9.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.76. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{24}F_2N_2O_4Na$ 393.1602; Found: 393.1596.

General Procedure for the Preparation of the Gram scale reaction(Scheme 2) (2b). A mixture of **1b** (1.10 g, 4 mmol, 1.0 equiv), $Pd(OAc)_2$ (22 mg, 0.025 eq), NFSI (3.343 g, 2.5 equiv) and *t*-Amyl-OH (20 mL) in a 100 mL glass vial (sealed with PTFE cap) was heated at 80 ^{o}C for 12 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give **2b** as pale yellow solid (1.07 g) in 91% yield.

General Procedure for the Preparation of the Gram scale reaction(Scheme 2). (**A**): A mixture of **3a** (0.14 g, 0.5 mmol, 1.0 equiv) in THF (4 mL) was stirred for 5 min at -10 °C, NaH (60 %) (0.1 g, 2.5 mmol, 5.0 equiv) was slowly added, and then stirred

for another 1 hour. NsCl (0.1662 g, 7.5 mmol, 1.5 equiv) was added slowly for thirty minutes. The mixture was stirred over night at room temperature, quenched with water (20 mL), extracted with CH_2Cl_2 (10 mL × 2). The combined organic phase was washed with brine (20 mL), dried over anhydrous Na_2SO_4. Evaporation and column chromatography on silica gel afforded **3aa** (110 mg) as pale yellow solid in 71% yield.

(**B**): Compound **3a** (0.14 g, 0.5 mmol, 1.0 eq) was dissolved in a mixture of THF/MeOH (0.4/0.1 mL). NaOH (80 mg, 2.0 mmol, 4.0 eq) was added later. The mixture was heated at 100 ^oC for 12 hours, then diluted with water (10 mL), extracted with DCM(10 m × 3L). The combined organic layers was washed with brine (15 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give the desired product (2-fluorophenyl)methanamine **4** (47.7 mg) as a colourless oil in 86% yield.

***N-(2-fluorobenzyl)-4-nitrobenzenesulfonamide (3aa)*:** Yield 71% (110 mg); pale yellow solid; mp = 125-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.9 Hz, 2H), 7.93 (d, J = 8.8 Hz, 2H), 7.24 – 7.17 (m, 2H), 7.05 – 6.99 (m, 1H), 6.88 (m, 1H), 5.35 (br, 1H), 4.30 (d, J = 5.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.83 (d, J_{C-F} = 246 Hz), 149.9, 146.1, 130.4, 130.40 (d, J_{C-F} = 12 Hz), 128.3, 124.49 (d, J_{C-F} = 3.6 Hz), 124.2, 122.90 (d, J_{C-F} = 14.4 Hz), 115.57 (d, J_{C-F} = 21 Hz), 41.87 (d, J_{C-F} = 3.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.36. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{11}FN_2O_4SNa$ 333.0321; Found: 333.0325.

***(2-fluorophenyl)methanamine (4)*:** Yield 86% (53.8 mg); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 1H), 7.25 – 7.17 (m, 1H), 7.09 (m, 1H), 7.05 – 6.97 (m, 1H), 3.88 (s, 2H); 1.57 (br, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.99 (d, J_{C-F} = 244.0 Hz), 130.30 (d, J_{C-F} = 15.0 Hz), 129.19 (d, J_{C-F} = 4.9 Hz), 128.53 (d, J_{C-F} = 8.1 Hz), 124.22 (d, J_{C-F} = 3.6 Hz), 115.33(d, J_{C-F} = 21.0 Hz), 40.65 (d, J_{C-F} = 3.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.06.[24]

ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures and characterization data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org

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Notes

The authors declare no competing financial interest.

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