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

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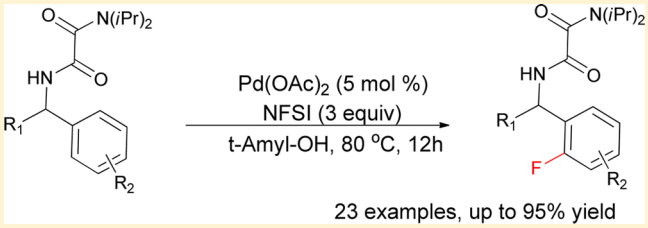
Supporting Information

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



INTRODUCTION

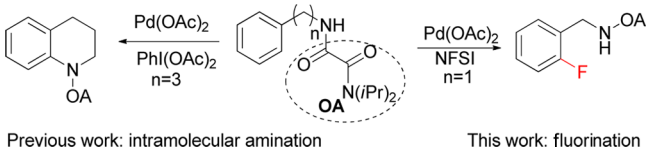
Fluorinated organic compounds have dramatic changes in physical, chemical, and biological properties, especially for the aryl fluorides,[1] which makes them very valuable components in pharmaceutical and agrochemical industries.[2] Thus, to develop a synthetic method for forming C−F bonds under mild condition would be attractive and significant. In the past few years, important progress in this field has been achieved,[3] and transition-metal-catalyzed fluorination has emerged as powerful method to access partially fluorinated aromatics.[4−12] However, compared to this successful development in fluorination with prefunctionalized aromatic rings that can lead to C−F bonds under transition catalyst, the direct fluorination of unactivated aryl C−H bonds still has few reports.[13] In 2006, pioneering work on C−F bond formation was first reported by Sanford and co-workers[14] with pyridine as the directing group via palladium catalyst, and electrophilic fluorinating agents were first applied in C−H functionalization as fluorine sources. Further mechanism studies revealed that high-valent Pd(IV) complexes might be involved in the catalytic cycle.[15] Later, Yu and co-workers reported Pd-catalyzed *ortho*-fluorination of benzylamine triflamide[16] and benzoic acid perfluoroaniline amide[17] by electrophilic fluorinating agents. Very recently, 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-workers[20] 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). Benzylamines have broad synthetic utility and 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 has been reported.[16] Herein we reported a convenient synthetic method for *ortho*-fluorination of oxalyl amide-protected benzylamine derivatives with palladium(II) acetate as catalyst and inexpensive *N*-fluorobis(phenylsulfonyl)amine (NFSI) as fluorine source.

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 newly developed N,O-bidentate directing group could promote Pd-catalyzed *ortho*-fluorination of benzylamine derivatives by applying electrophilic fluorinating agents (Scheme 1).

At the outset of this study, we first treated oxalyl amide-protected 2- methoxybenzylamine **1a** with electrophilic fluorinating reagent (**F1**) with loading of 5 mol % $Pd(OAc)_2$

Scheme 1. Oxalyl Amide-Assisted Fluorination



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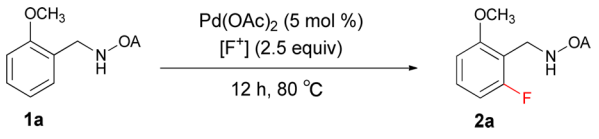
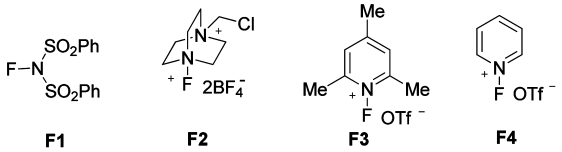
as catalyst in 1,4-dioxane at 80 °C under an atmosphere of air in a sealed tube (Table 1, entry 1). To our delight, the desired

Table 1. Optimization of 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



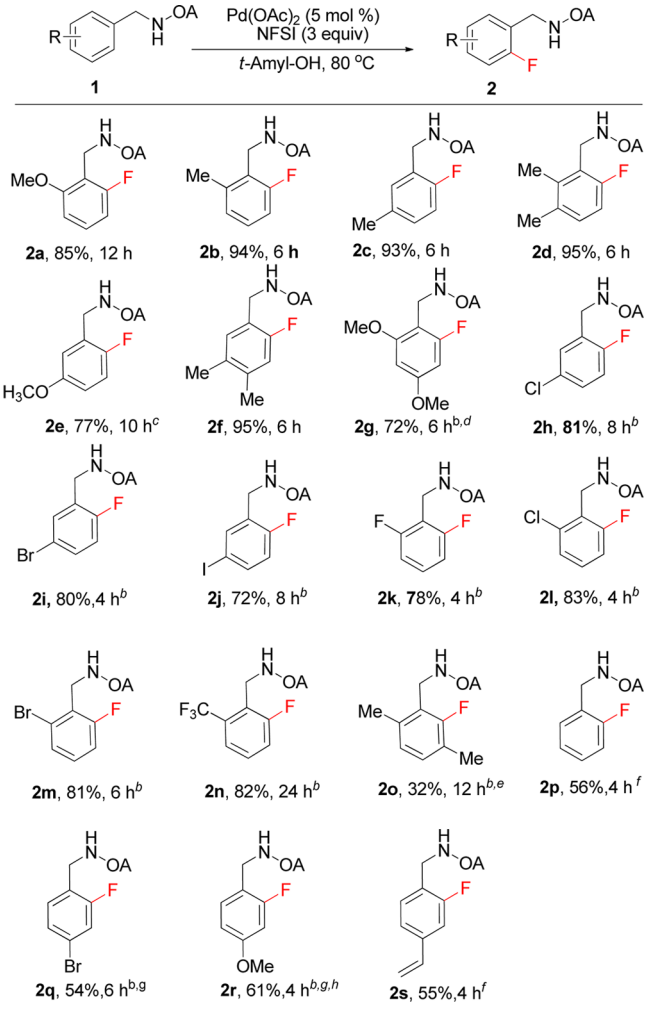
F1 F2 F3 F4

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

fluorinated product **2a** was obtained in 79% yield, along with 5% **1a** recovered. We further screened other [F+] sources (Table 1, entries 2–4 and 14), in which the fluorinating reagent **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 further optimization of conditions. The solvent effect with **F1** (Table 1, entries 5–8) were subsequently examined. *t*-Mmyl-OH turned out to be the best solvent, and excellent yield of **2a** (87%; Table 1, entry 7) was achieved in 12 h. Dichloroethylene (DCE) and *m*-xylene gave slightly poorer yields. Interestingly, no reaction happened with *N*,*N*-dimethylformamide (DMF) as solvent. In attempts to further improve the conversion of starting material, several additives such as *N*-methylpyrrolidone (NMP), PivOH, and PPh_3 were added in the reaction, respectively. All these additives displayed suppressive effects in this transformation. Under an air or argon atmosphere, the product of **2a** was observed in higher than 80% yield, implying that oxygen has no promoting effect in this transformation. Combinations of AgF and NMO with palladium acetate (entry 14) or copper salts were also tested: no reaction occurred under general reaction conditions and just starting material was recovered, which was analyzed by GC/MS. Control experiments confirmed that no reaction happened without use of palladium catalyst, implicating the crucial role of $Pd(OAc)_2$ for the transformation (Table 1, entry 15).

With the optimized conditions in hand, the scope and limitation of this reaction were next explored, and repesentative data are shown in Table 2. To our great surprise, a remarkably

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), and *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-trimethylpyridinium 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.

broad range of benzylamine substrates 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**). Substrates with electron-withdrawing substituents (**2h**–**2n**) showed slightly lower activity and needed 10 mol % loading of Pd catalyst. Useful products containing F, Cl, Br, and I were also obtained, which were very important in synthetic elaborations. Highly regioselective monofluorination also took place at the less hindered site, giving excellent yields (**2c**, **2e**, **2f**, and **2h**–**2j**). Notably, the challenging 2,5-disubstituted **1o** was also fluorinated with slightly increased loading of catalyst and temperature.

Monofluorination of oxalyl amide-protected benzylamines was also achieved with modified reaction conditions as listed in Table 2. Selective monofluorination of electron-rich (**1r**) and electron-poor (**1q** and **1s**) substituted oxalyl amide-protected benzylamines was observed in moderate yield with shorter reaction times to avoid difluorinated products, while difluorinated products were observed in less than 10% yield. To realize

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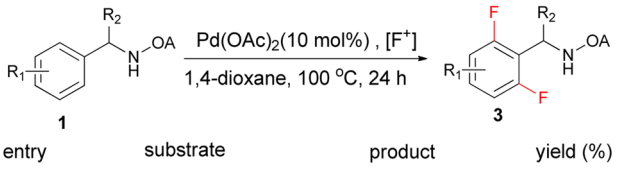
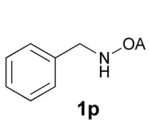
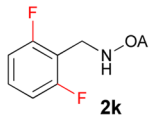
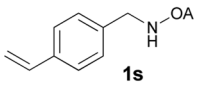
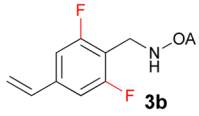
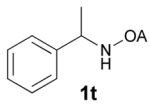
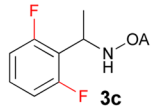
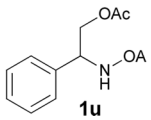
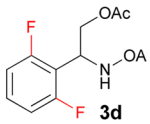
the difluorinated products, 5 equiv of **F1** and 10 mol % $Pd(OAc)_2$ were applied in the reaction. However, the difluorinated products were obtained in less than 60% yield except for **1t** and **1u**. To reduce the amount of monofluorinated products, several other fluorine sources were scanned. It is not surprising that **F3** yielded the difluorinated products in better yields at 100 °C in 24 h (Table 3, **2k** and **3b**–**3d**).

Table 3. Difluorination of Benzylamine Derivatives[a]

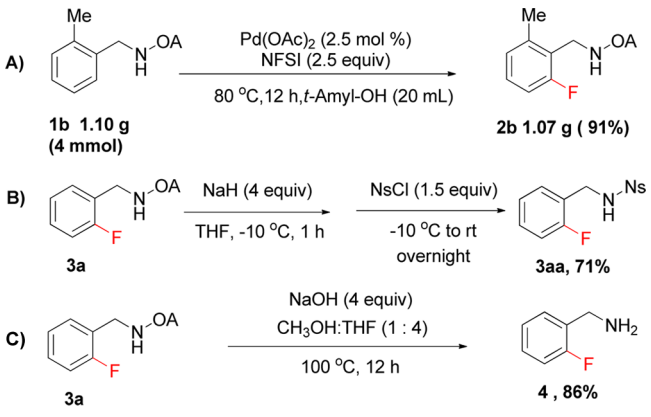


entry	substrate	product	yield (%)
1	 **1p**	 **2k**	80[b]
2	 **1s**	 **3b**	60[c]
3	 **1t**	 **3c**	81
4	 **1u**	 **3d**	86

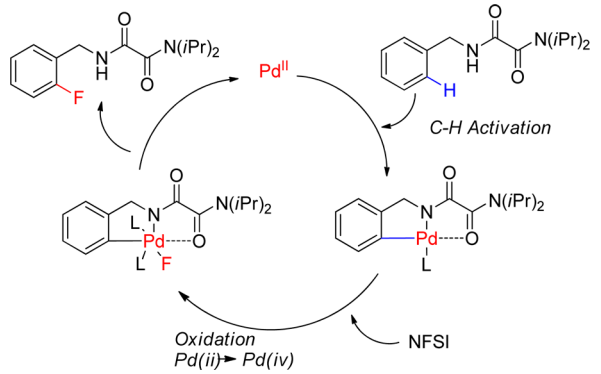
[a]Reaction conditions: **1** (0.2 mmol), $Pd(OAc)_2$ (10 mol %), *N*-fluoro-2,4,6-trimethylpyridinium triflate (**F3**, 0.6 mmol), amd 1,4-dioxane (2 mL), 80 °C, 24 h. Isolated yields. [b]$Pd(OAc)_2$ (15 mol %). [c]*t*-Amyl-OH (2 mL), NFSI (5 equiv).

ortho-Monofluorination of substrate **1b** was also carried out on the gram scale. An excellent yield of **2b** was obtained, implicating the potential excellent versatility for synthetic application (Scheme 2A). Due to the low cost of diisopropylamine and oxalyl chloride, oxalyl amide could be employed as a protecting group for benzylamine substrates. The oxalyl amide-protected benzylamine derivative **3a** could be activated with NsCl (4-nitrobenzene-1-sulfonyl chloride) and cleaved by NaH in one pot to give the Ns-protected amine product **3aa** in high yield (Scheme 2B).[22] The oxalyl amide could also be removed through 4 equiv of NaOH in CH_3OH/THF = 1:4, giving **4** in 86% isolated yield (Scheme 2C). 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 the corresponding product finally (Scheme 3).

Scheme 2. Large-Scale Synthesis and Removal of 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. Inexpensive *N*-fluorobenzenesulfonimide could be used as an efficient [F^+] source and *t*-amyl-OH as the best solvent. Mono- and difluorination of oxalyl amide-protected benzylamine derivatives were also achieved by modifying the fluorine source, in moderate to excellent yield with wide functional group tolerance. Oxalyl amide could be removed under mild conditions, affording the Ns-protected amines. Detailed mechanistic studies are in progress, and the new application of oxalyl amide as a directing group in construction of C–C, C–O, or C–heteroatom bonds is 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 s = broad singlet, and 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 5 min of stirring, triethylamine (7.30 mL, 52.5 mmol, 1.05 equiv) was added dropwise. The solution was warmed to room temperature and stirred for 6 h. Excess oxalyl chloride and solvent were removed under reduced 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-

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TOF) m/z [M + Na]$^+$ calcd for $C_8H_{14}ClNO_2Na$ 214.0611, found 214.0609.

General Procedure for Preparation of Oxalyl Amide-Protected Benzylamines (1a−1t).[21] A solution of amine (20 mmol, 1.0 equiv) 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 5 min of stirring, triethylamine (2.92 mL, 21 mmol, 1.05 equiv) was added dropwise, and then the mixture was stirred for 6 h at room temperature before being 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) and dried over anhydrous Na_2SO_4. Evaporation and column chromatography on silica gel afforded corresponding amide substrates as white solids or colorless liquids 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 s, 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 s, 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 s, 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 s, 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 s, 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 s, 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 s, 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, 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 s, 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 s, 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]oxalamide (**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 s, 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 s, 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,

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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 s, 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 s, 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 s, 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 Procedure for Preparation of 1u.[21] The first step, with 2-amino-2-phenylethanol (2.74 g, 20 mmol, 1.0 equiv) as starting material, followed the general procedure and afforded a white solid, which was analyzed by LC/MS. The solid (5.25 g) was dissolved in dichloromethane (DCM, 30 mL) and treated with AcCl (1.56 mL, 22 mmol, 1.1 equiv) and Et_3N (5.56 mL, 40 mmol, 2.0 equiv) at room temperature overnight. The reaction was quenched with water and extracted with DCM (30 mL × 3). The combined organic layers were 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 s, 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 Monofluorination of Benzylamines (Table 2) (2a−2d and 2f). A mixture of oxalamide (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (22 mg, 0.05 equiv), NFSI (0.6 mmol, 3.0 equiv), and *t*-amyl-OH (2 mL) in a 25 mL glass vial [sealed with poly(tetrafluoroethylene) (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-(2-Fluoro-6-methoxybenzyl)-N^2,N^2-diisopropyloxalamide (**2a**).* Yield 85% (52.7 mg); pale yellow oil; ^{1}H 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-diisopropyloxalamide (**2b**).* Yield 94% (55.3 mg); pale yellow solid; mp = 77−79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18−7.13 (m, 1H), 7.03 (br s, 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, found317.1641.

*N^1-(2-Fluoro-5-methylbenzyl)-N^2,N^2-diisopropyloxalamide (**2c**).* Yield 93% (54.7 mg); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (br s, 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-diisopropyloxalamide (**2d**).* Yield 95% (58.5 mg); pale yellow solid; mp = 114−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06−7.03 (m, 1H), 6.95 (br s, 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-4,5-dimethylbenzyl)-N^2,N^2-diisopropyloxalamide (**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-5-methoxybenzyl)-*N^2*,*N^2*-diisopropyloxalamide (2e).** A mixture of oxalamide **1e** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (22 mg, 0.05 equiv), NFSI (0.6 mmol, 3.0 equiv), and 1,4-dioxane (2 mL) in a 25 mL glass vial (sealed with PTFE cap) was heated at 80 °C 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 **2e**. Yield 77% (47.8 mg); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (br s, 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

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(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-4,6-dimethoxybenzyl)-*N*^{2},*N*^{2}-diisopropyloxalamide (2g).** A mixture of oxalamide **1g** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (44 mg, 0.10 equiv), **F3** (0.4 mmol, 2.0 equiv), and DCE (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 72% (49.0 mg); pale yellow solid; mp = 125−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (br s, 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 Monofluorination of Benzylamines (Table 2) (2h−2n). A mixture of oxalamide (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (44 mg, 0.10 equiv), NFSI (0.6 mmol, 3.0 equiv), 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}*-diisopropyloxalamide (2h).* Yield 81% (50.9 mg); pale yellow solid; mp = 78−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (br s, 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); ^{13}C 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} = 3.0 Hz), 129.34 (d, J_{C-F} = 8.0 Hz), 126.52 (d, J_{C-F} = 16.6 Hz), 116.90 (d, J_{C-F} = 23.0 Hz), 49.8, 46.7, 36.98 (d, J_{C-F} = 3.9 Hz), 20.9, 20.1; ^{19}F NMR (376 MHz, $CDCl_3$) 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}*-diisopropyloxalamide (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-F} = 246.0 Hz), 132.82 (d, J_{C-F} = 4.2 Hz), 132.44 (d, J_{C-F} = 8.2 Hz), 126.92 (d, J_{C-F} = 16.3 Hz), 117.40 (d, J_{C-F} =22.0 Hz), 116.92 (d, J_{C-F} = 3.5 Hz), 49.7, 46.8, 37.00 (d, J_{C-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 s, 1H), 6.81 (t, J = 9.5 Hz, 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-F} = 247.0 Hz), 138.76 (d, J_{C-F} = 4.1 Hz), 138.50 (d, J_{C-F} = 8.0 Hz), 127.31 (d, J_{C-F} = 15.8 Hz), 117.84 (d, J_{C-F} = 22.0 Hz), 87.36 (d, J_{C-F} = 3.7 Hz), 49.7, 46.8, 36.84 (d, J_{C-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-F} = 7.8 Hz), 162.6, 162.4, 160.43 (d, J_{C-F} = 8 Hz), 129.91 (t, J_{C-F} = 10.3 Hz), 113.26 (t, J_{C-F} = 19.3 Hz), 111.60 (d, J_{C-F} =25.0 Hz). 111.60 (d, J_{C-F} = 13.0 Hz), 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}*-diisopropyloxalamide (2l).* Yield 83% (49.0 mg); pale yellow solid; mp = 78−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (br s, 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-F} = 249.0 Hz), 135.75 (d, J_{C-F} = 5.2 Hz), 130.00 (d, J_{C-F} = 9.7 Hz), 125.56 (d, J_{C-F} = 3.5 Hz), 123.17 (d, J_{C-F} = 17.9 Hz), 114.47 (d, J_{C-F} = 22.0 Hz), 49.6, 46.7, 34.61 (d, J_{C-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}*-diisopropyloxalamide (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-F} = 250.0 Hz), 130.56 (d, J_{C-F} = 9.4 Hz), 128.87 (d, J_{C-F} = 3.6 Hz), 125.59 (d, J_{C-F} = 4.2 Hz), 124.84 (d, J_{C-F} = 17.5 Hz), 115.17 (d, J_{C-F} = 23.0 Hz), 49.6, 46.7, 37.07 (d, J_{C-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}*-diisopropyloxalamide (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 s, 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}-diisopropyloxalamide (2o).** A mixture of oxalamide **1o** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (44 mg, 0.10 equiv), NFSI (0.6 mmol, 3.0 equiv) 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-F} = 243.0 Hz), 136.64 (d, J_{C-F} = 3.3 Hz), 130.73 (d, J_{C-F} = 6.3 Hz), 125.63 (d, J_{C-F} = 3.6 Hz), 122.33 (d, J_{C-F} = 24 Hz), 122.31 (d, J_{C-F} = 9 Hz) 49.7, 46.7, 34.46 (d, J_{C-F} = 5.7 Hz), 21.0, 20.1, 19.00 (d, J_{C-F} = 2.5 Hz), 14.44 (d, J_{C-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.

***N*^{1}-(2-Fluorobenzyl)-*N*^{2},*N*^{2}-diisopropyloxalamide (2p).** A mixture of oxalamide **1p** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (22 mg, 0.05 equiv), NFSI (0.6 mmol, 3.0 equiv), 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-F} = 222.0 Hz), 128.36 (d, J_{C-F} = 30.0 Hz), 127.8,

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126.18 (d, J_{C-F} = 6.0 Hz), 125.98(d, J_{C-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-diisopropyloxalamide (2q). A mixture of oxalamide **1q** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (44 mg, 0.10 equiv), NFSI (1.0 mmol, 5.0 equiv), 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 s, 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-F} = 250.0 Hz), 131.09 (d, J_{C-F} = 4.7 Hz), 127.52 (d, J_{C-F} = 3.5 Hz), 124.02 (d, J_{C-F} = 14.9 Hz), 121.51 (d, J_{C-F} = 9.3 Hz), 118.99 (d, J_{C-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-diisopropyloxalamide (2r). A mixture of oxalamide **1r** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (44 mg, 0.10 equiv), NFSI (1.0 mmol, 5.0 equiv), 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 s, 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-F} = 245.0 Hz), 160.78 (d, J_{C-F} = 11.0 Hz), 130.96 (d, J_{C-F} = 6.1 Hz), 116.45 (d, J_{C-F} =16.0 Hz), 110.05 (d, J_{C-F} = 3.1 Hz), 101.93 (d, J_{C-F} =25 Hz), 55.7, 49.7, 46.7, 37.12 (d, J_{C-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 equiv), $Pd(OAc)_2$ (22 mg, 0.05 equiv), NFSI (0.6 mmol, 3.0 equiv), 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 s, 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-F} =245.0 Hz), 139.67 (d, J_{C-F} = 7.8 Hz), 135.57 (d, J_{C-F} = 2.3 Hz), 130.28 (d, J_{C-F} = 4.7 Hz), 123.85 (d, J_{C-F} = 15.4 Hz), 122.53 (d, J_{C-F} = 3.1 Hz), 115.5, 112.83 (d, J_{C-F} = 22.0 Hz), 49.7, 46.8, 37.33 (d, J_{C-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 equiv), $Pd(OAc)_2$ (66 mg, 0.15 equiv), *N*-fluoro-2,4,6-trimethylpyridinium triflate (**F3**; 0.6 mmol, 3.0 equiv), 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 product. Yield 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-F} = 7.8 Hz), 162.6, 162.4, 160.43 (d, J_{C-F} = 8 Hz), 129.91 (t, J_{C-F} = 10.3 Hz), 113.26 (t, J_{C-F} = 19.3 Hz), 111.60 (d, J_{C-F} = 25.0 Hz). 111.60 (d, J_{C-F} = 13.0 Hz), 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-diisopropyloxalamide (3b). A mixture of oxalamide **1s** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (44 mg, 0.10 equiv), NFSI (1.0 mmol, 5.0 equiv), 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 s, 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 Preparation of Difluorination Substrates (Table 3) (3c and 3d). A mixture of oxalamide (**1t** or **1u**) (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (44 mg, 0.10 equiv), *N*-fluoro-2,4,6-trimethylpyridinium triflate **F3**, (0.6 mmol, 3.0 equiv), 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 product.

*N^1-[1-(2,6-difluorophenyl)ethyl]-N^2,N^2-diisopropyloxalamide (**3c**).* Yield 81% (50.5 mg); pale yellow solid; mp = 105−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (br s, 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-oxoacetamido]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.

Gram-Scale Preparation of 2b (Scheme 2A). A mixture of **1b** (1.10 g, 4 mmol, 1.0 equiv), $Pd(OAc)_2$ (22 mg, 0.025 equiv), 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 °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 **2b** as a pale yellow solid (1.07 g) in 91% yield.

Gram-Scale Preparation of 3aa (Scheme 2B). A mixture of **3a** (0.14 g, 0.5 mmol, 1.0 equiv) in tetrahydrofuran (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 the mixture was stirred for another 1 h. NsCl (0.1662 g, 7.5 mmol, 1.5 equiv) was added slowly for 30 min. The mixture was stirred overnight at room temperature, quenched with water (20 mL), and extracted with CH_2Cl_2 (10 mL × 2). The combined organic phase was washed with brine (20 mL) and dried over anhydrous Na_2SO_4. Evaporation and column chromatography on silica gel afforded **3aa** (110 mg) as a pale yellow solid in 71% yield.

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*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 s, 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.

Gram-Scale Preparation of 4a (Scheme 2C). Compound **3a** (0.14 g, 0.5 mmol, 1.0 equiv) was dissolved in a mixture of THF/MeOH (0.4/0.1 mL). NaOH (80 mg, 2.0 mmol, 4.0 equiv) was added later. The mixture was heated at 100 °C for 12 h and then diluted with water (10 mL) and extracted with DCM (10 mL × 3). The combined organic layers were 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 colorless oil in 86% yield.

*(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 s, 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

Additional text with detailed procedures for preparation of **S1**; one table listing conditions for screening of fluorination reaction; and NMR spectra for characterization of 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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