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Palladium-Catalyzed Oxalyl Amide-Directed γ-Arylation of Aliphatic Amines

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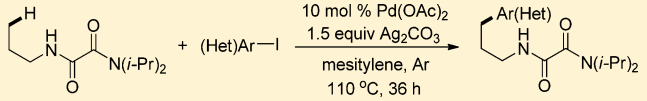
Supporting Information

ABSTRACT: A method for palladium-catalyzed oxalyl amide-directed arylation of α-unsubstituted aliphatic amines with aryl iodides has been developed. A wide variety of aryl iodides are tolerated in this transformation, affording various γ-arylpropylamine derivatives. Heterocyclic iodides can also be competent reagents in this γ-C(sp^3)−H bonds transformation.

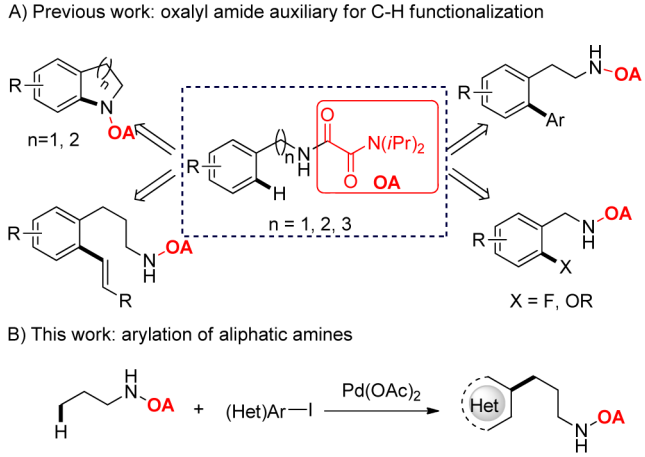


Transition-metal-catalyzed direct functionalization of C−H bonds is becoming an attractive and fundamental synthetic method.[1,2] Recent years, functionalization of unactivated C(sp^3)−H bonds has achieved fruitful results, which is becoming an important tool in synthesis of natural products and pharmaceuticals.[3−5] During these reports, high site selective γ-arylation of aliphatic amines and amino acids have been well achieved via directing-group-assisted strategy, which is developed by Daugulis,[6] Yu,[7] Chen,[8] Carretero[9] and Ma[10] groups, respectively. Despite these detailed studies on γ-arylation of unactivated C(sp^3)−H bonds in amine substrates, the substrates without α substituent still have few reports. In a seminal report in 2005, Daugulis disclosed the picolinamide-directed γ-arylation of amine derivatives,[6a] and one example of γ-arylpropylpicolinamide was prepared in good yield in neat conditions. In 2013, Chen and co-workers also prepared one analogous γ-arylpropylpicolinamide product in moderate yield via Pd-catalyzed C(sp^3)−H arylation.[11] As 3-arylpropylamine derivatives are fundamental building blocks in synthetic organic chemistry,[12] direct functionalization of γ-C(sp^3)−H bond of *n*-propylamine to realize 3-arylpropylamine is attractive and important. Herein, we report a method that Pd(II)-catalyzed γ-arylation of C(sp^3)−H bonds in α-unsubstituted aliphatic amines by employing oxalyl amide as directing group. Heterocyclice iodides are also tolerated in this transformation, highlighting the potential utility of this synthetic method in construction synthon and pharmacochemistry.[13,14]

Oxalyl amide presents an efficient directing ability for amines reported by our group, and has been employed in C−N, C−C, C−F, C−O bond formation via a five, six, or seven-membered palladacycle intermediate (Scheme 1A).[15] Inspired by the assistance ability of oxalyl amide, we embarked on the development of a practical protocol in synthesis of 3-arylpropylamine derivatives through direct arylation of *n*-propylamines with various iodides (Scheme 1B).

At the outset of our study, we treated oxalyl amide protected *n*-propylamine **1a** with 4-iodoanisole **2a** by employing

Scheme 1. Oxalyl Amide Directed C−H Functionalization



$Pd(OAc)_2$ (10 mol %) as catalyst, Ag_2CO_3 (1.5 equiv) as oxidant, and pivalic acid (0.3 equiv) as additive in 1,2-dichloroethane at 110 °C under an atmosphere of argon in a sealed vial. Unfortunately, only 33% γ-arylated *n*-propyloxalamide **3a** was detected by GC at the first run of the experiment, along with starting material **1a** recovered (Table 1, entry 1). Scanning other solvents, including 1,4-dioxane, *t*-Amyl-OH, and toluene, led to mesitylene being identified as the most effective one, affording **3a** in 65% yield (Table 1, entries 2−5). Several other additives which had been demonstrated to have the ability in enhancing many C−H transformations,[16] such as 1-AdOH, $(BnO)_2PO_2H$, Ac-Gly-OH, were tested in this arylation reaction, but none of them gave better results (Table 1, entries 6−8). Interestingly, the highest yield of 78% was obtained when Ag_2CO_3 was only used as oxidant without any additive. Further screening of the other oxidants showed

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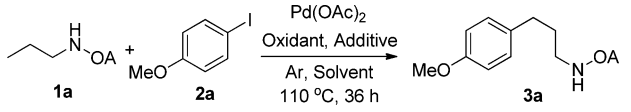
Table 1. Optimization of the Reaction Conditions[a]



entry	oxidant	additive	solvent	yield (%)[b]
1	Ag_2CO_3	PivOH	DCE	33
2	Ag_2CO_3	PivOH	1,4-dioxane	11
3	Ag_2CO_3	PivOH	*t*-Amyl-OH	29
4	Ag_2CO_3	PivOH	toluene	48
5	Ag_2CO_3	PivOH	mesitylene	65
6	Ag_2CO_3	1-AdOH	mesitylene	57
7	Ag_2CO_3	$(BnO)_2PO_2H$	mesitylene	45
8	Ag_2CO_3	Ac -Gly-OH	mesitylene	48
9[c]	Ag_2CO_3	none	mesitylene	78 (72)[c]
10	AgOAc	none	mesitylene	52
11	Ag_2O	none	mesitylene	34
12	BQ	none	mesitylene	<5
13	$Cu(OAc)_2$	none	mesitylene	<5
14	$K_2S_2O_8$	none	mesitylene	<5
15[d]	Ag_2CO_3	none	mesitylene	0
16[e]	Ag_2CO_3	none	mesitylene	0
17[f]	Ag_2CO_3	none	mesitylene	0
18[g]	Ag_2CO_3	none	mesitylene	0

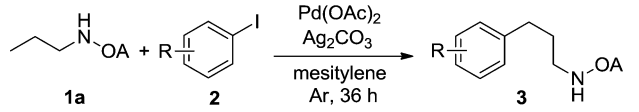
[a]Reaction conditions: **1a** (0.1 mmol), 4-iodoanisole (0.15 mmol), $Pd(OAc)_2$ (10 mol %), oxidant (0.15 mmol), additive (0.03 mmol), solvent (0.4 mL), Ar, 110 °C, 36 h. [b]GC yield of **3a** determined using tridecane as internal standard. [c]Isolated yield. [d]No catalyst. [e]4-Bromoanisole instead of 4-iodoanisole. [f]4-Chloroanisole instead of 4-iodoanisole. [g]4-Methoxyphenyl triflate instead of 4-iodoanisole.

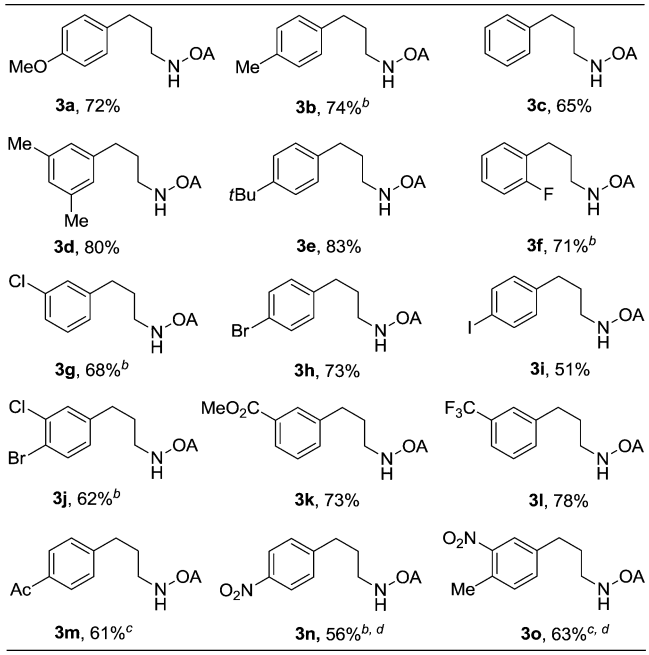
that Ag_2CO_3 was superior to AgOAc, Ag_2O, BQ, $Cu(OAc)_2$, and $K_2S_2O_8$. When the reaction was carried out in the absence of palladium catalyst, the reaction failed to proceed, indicating the palladium could not be replaced in this transformation (Table 1, entry 15). Several other arylation reagents, such as 4-bromoanisole, 4-chloroanisole and 4-methoxyphenyl triflate, were sceened to extend the scope of electrophilic reagent. However, all these arylation reagents were all unable to afford corresponding products, respectively (Table 1, entries 16−18).

With the optimized conditions in hand, a wide variety of aryl iodides were investigated in the arylation of oxalyl amide protected *n*-propylamine. Gratifyingly, a series of γ-arylpropyl-oxalamides were synthesized from the corresponding aryl iodides via palladium catalyzed γ-C(sp^3)−H arylation (Table 2). Various functional groups, such as Me, *t*Bu, MeO, F, Cl, Br, I, CF_3, and CO_2Me were all tolerated under the general reaction conditions (Table 2, **3a−l**). It's worth mentioning that the 1,4-diiodobenzene could be well coupled with **1a**, giving the desired product in acceptable yield (**3i**). With slightly modifying the reaction conditions, the aryl iodide with electron deficient groups of Ac and NO_2 were also successfully transformed into corresponding product in moderate yields (**3m−o**).

Heterocyclic compounds are important versatile synthetic precursors and usually key structures in drugs and natural products.[17] From this point of view, it is appealing to introduce heterocyclic compounds to aliphatic amines via palladium catalyzed γ-C(sp^3)−H functionalization. Delightedly, the optimized conditions were also applicable to challenging substrates of heterocyclic iodides, as shown in Table 3. For example, the substrate **2p** coupled well with **1a**, affording **3p** in

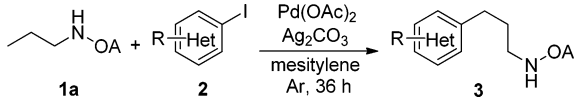
Table 2. Substrate Scope of Aryl Iodides[a]

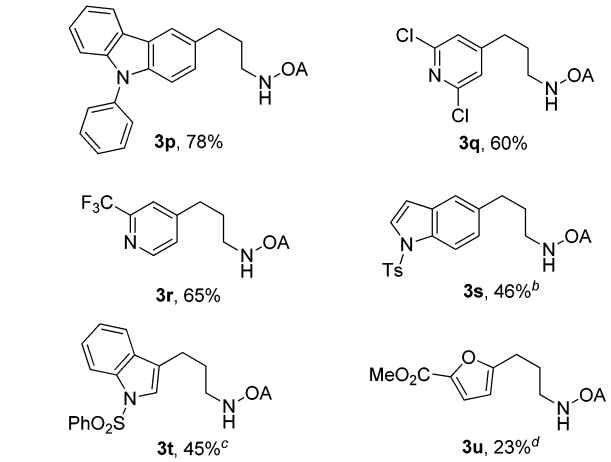




[a]Reaction conditions: **1a** (0.2 mmol), ArI (0.3 mmol), $Pd(OAc)_2$ (10 mol %), Ag_2CO_3 (0.3 mmol), mesitylene (0.8 mL), Ar, 110 °C, 36 h. Isolated yields. [b]130 °C. [c]150 °C, 48 h. [d]*m*-Xylene as solvent.

Table 3. Substrate Scope of Heterocylic Iodides[a]





[a]Reaction conditions: **1a** (0.2 mmol), heterocyclic iodides (0.3 mmol), $Pd(OAc)_2$ (10 mol %), Ag_2CO_3 (0.3 mmol), mesitylene (0.8 mL), Ar, 130 °C, 36 h. Isolated yields. [b]Ag_2CO_3 (0.8 mmol), 150 °C, DCE as solvent. [c]100 °C. [d]Bromide (0.3 mmol), Ag_2CO_3 (0.8 mmol), 150 °C.

78% yield. Notably, the strong electron-withdrawing group substituted iodopyridine proceeded cleanly, resulting in corresponding products in good yields (**3q−r**). However, when we used 4-iodopyridine, it failed to give any arylated product. We speculated that the electron rich pyridine might

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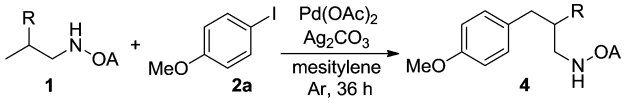
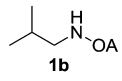
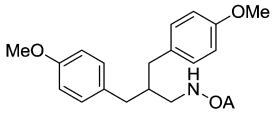
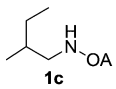
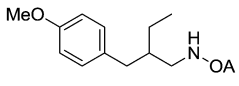
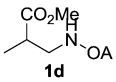
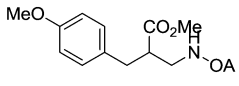
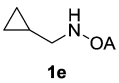
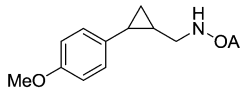
coordinate to palladium center, which could shut down the catalytic cycle. To our surprise, the coupling reaction of substrate **1a** with methyl 5-bromo-2-furoate could only give 23% yield of the product (**3u**), along with more than 50% starting material **1a** recovered. Several side products related to methyl 5-bromo-2-furoate were observed in the reaction.

We next moved our attention to explore the substrate scope of aliphtic amines. A series of oxalyl amide protected propylamine derivatives were tested under the modified reaction conditions. As illustrated in Table 4, the substrates

Table 4. Substrate Scope of the α-Unsubstituted Aliphatic Amines[a]

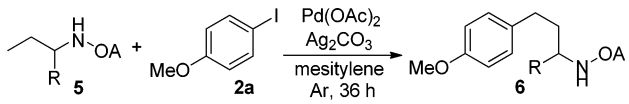


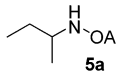
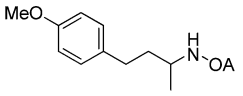
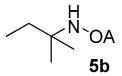
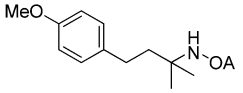
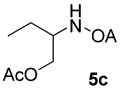
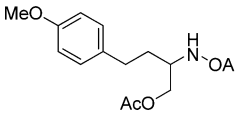
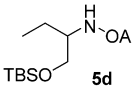
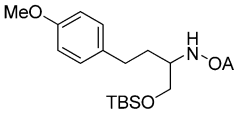
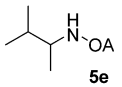
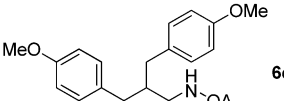
Entry	Substrate	Temp	Product	Yield
1	 **1b**	130 °C		**4a**, 53%[b]
2	 **1c**	130 °C		**4b**, 52%[c]
3	 **1d**	150 °C		**4c**, 47%[d]
4	 **1e**	90 °C		**4d**, 73%[e]

[a]Reaction conditions: **1** (0.2 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (10 mol %), Ag_2CO_3 (0.8 mmol), mesitylene (0.8 mL), Ar, 36 h. Isolated yields. [b]**2a** (0.6 mmol). [c]PivONa (0.06 mmol) as additive. [d]$Pd(TFA)_2$ (10 mol %), PhCl as solvent. [e]$Pd(OAc)_2$ (5 mol %), Ag_2CO_3 (0.3 mmol), 24 h.

without α substituents proceeded in higher reaction temperature (**4a**–**c**). Only the diarylated product could be isolated in 53% yield by increasing the amount of 4-iodoanisole. Unfortunately, the monoarylated product could not be isolated due to the nonselectivity in the reaction using the standard conditions (detailed information see Supporting Information). Substrate **1c** afforded the corresponding product in synthetic acceptable yield, accompanied by starting material recovered. The substrate of **1d** only gave 47% monoarylated product by increasing the temperature to 150 °C, we speculated that the functional group of ester might reduce the reactivity of **1d**. In contrast, the methylene C–H bond in cyclopropane ring was monoarylated just in mild conditions, affording 73% yield with 5 mol % $Pd(OAc)_2$ at 90 °C. Not surprisingly, substrates bearing substituents at α position exhibited high activity in this Pd-catalyzed γ-arylation of $C(sp^3)$–H bonds, also successfully arylated with 4-iodoanisole (Table 5). The substrate **5a** and **5b** only proceeded well under lower reaction temperature to avoid the side porducts of diarylated product respectively (See Supporting Information). The functional group of Ac and TBS were well sustained, giving the desired products in good yields (**6c**,**d**). As expected, when we increased the amount of Ag_2CO_3,

Table 5. Substrate Scope of the α-Substituted Aliphatic Amines[a]



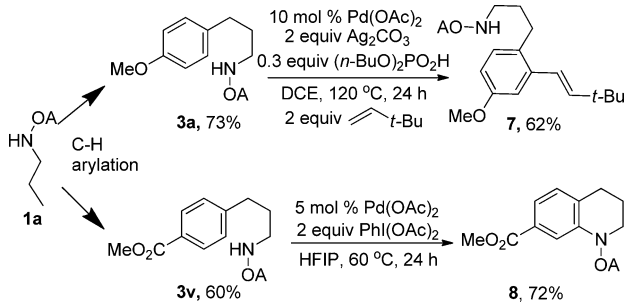
Entry	Substrate	Temp	Product	Yield
1	 **5a**	90 °C		**6a**, 83%[b]
2	 **5b**	60 °C		**6b**, 57%[c]
3	 **5c**	110 °C		**6c**, 71%[d]
4	 **5d**	150 °C		**6d**, 62%[d]
5	 **5e**	130 °C		**6e**, 60%[e]

[a]Reaction conditions: **5** (0.2 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (10 mol %), Ag_2CO_3 (0.3 mmol), mesitylene (0.8 mL), Ar, 36 h. Isolated yields. [b]$Pd(OAc)_2$ (5 mol %). [c]$Pd(TFA)_2$ (10 mol %), Ag_2CO_3 (0.6 mmol). [d]DCE as solvent. [e]**2a** (0.6 mmol), Ag_2CO_3 (0.8 mmol).

the arylation of substrate **5e** gave the diarylated product in 60% yield, and the monoarylated product in 17% yield.

The new developed synthetic method provided a convenient protocol for synthesis of 3-arylpropylamine derivatives. All these substrates could be further transformed into other useful synthetic building blocks. For example, the product **3a** could be selectively mono-olenfinated at δ position using our previous reported synthetic protocol.[15b] In addition, compound **3v** could also undergo intramolecular amination with $PhI(OAc)_2$ to give tetrahydroquinoline **8** in good yield[15a] (Scheme 2).

Scheme 2. Synthesis of 3-Arylpropylamine Derivatives



On the basis of our previous studies and recent reports,[15c,18] a plausible mechanism is proposed in Scheme 3. The oxalyl amide **1a** reaction with $Pd(OAc)_2$ generated the palladium amide **9**, followed by a C–H insertion to give the intermediate **10**. Oxidative addition of aryl iodide to **10** produced a high-valent Pd intermediate **11**. Subsequent rapid reductive

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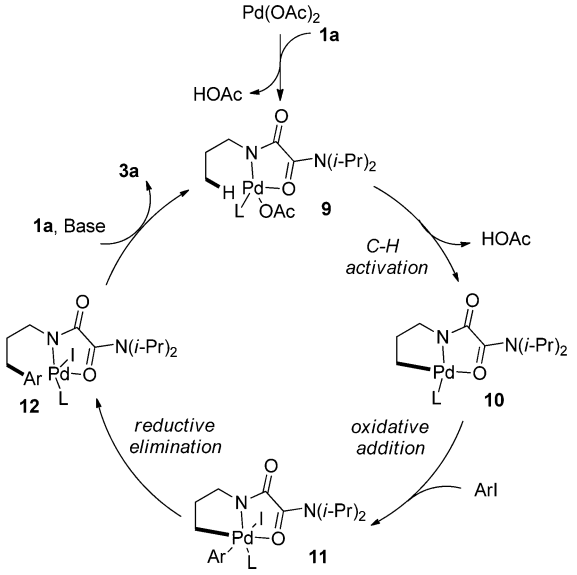
Scheme 3. Proposed Catalytic Cycle



elimination followed by ligand exchange afforded the product, accompanied by active specie of palladium intermediate **9**.

In conclusion, we have developed a practical synthetic method for the palladium-catalzyed oxalyl amide-directed arylation of unactivated γ-(sp^3)−H bonds of α-unsubstituted aliphatic amines substrates with aryl iodides. Broad ranges of aryl iodides and heterocyclic iodide are well tolerated in this transformation, affording various γ-arylpropylamine derivatives. Oxalyl amide-directed γ-arylation of α-substituted aliphatic amines can also proceed smoothly, giving the corresponding products in moderate to good yields. Further functionalization of the 3-arylpropylamine derivatives with previous reported protocol gives the useful synthetic building block under mild conditions.

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, 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-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 Amines (1a−1c, 1e, 5a−5b, 5e).[19] 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 solid >80% yield.

N^1,N^1-Diisopropyl-N^2-propyloxalamide ***(1a)***. Yield 86% (3.69 g); off-white solid; mp = 77−79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (br s, 1H), 4.62−4.58 (m, 1H), 3.49−3.42 (m, 1H), 3.19 (dd, J = 13.6, 6.7 Hz, 2H), 1.57−1.47 (m, 2H), 1.36 (d, J = 6.8 Hz, 6H), 1.17 (d, J = 6.7 Hz, 6H), 0.89 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 163.5, 49.7, 46.4, 41.0, 22.5, 20.9, 20.1, 11.4; HRMS (ESI-TOF) m/z [M − H]$^+$ Calcd for $C_{11}H_{21}N_2O_2$ 213.1603, found 213.1608.

N^1-Isobutyl-N^2,N^2-diisopropyloxalamide ***(1b)***. Yield 84% (3.84 g); off-white solid; mp = 75−76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (br s, 1H), 4.73−4.69 (m, 1H), 3.53−3.48 (m, 1H), 3.09 (t, J = 6.5 Hz, 2H), 1.84−1.76 (m, 1H), 1.40 (d, J = 6.8 Hz, 6H), 1.21 (d, J = 6.7 Hz, 6H), 0.92 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 49.8, 46.7, 46.6, 28.5, 21.0, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{12}H_{24}N_2NaO_2$, 251.1735, found 251.1734.

N^1,N^1-Diisopropyl-N^2-(2-methylbutyl)oxalamide ***(1c)***. Yield 81% (3.93 g); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (br s, 1H), 4.79−4.43 (m, 1H), 3.54−3.47 (m, 1H), 3.25−3.19 (m, 1H), 3.12−3.05 (m, 1H), 1.64−1.56 (m, 1H), 1.48−1.36 (m, 7H), 1.23−1.12 (m, 7H), 0.92−0.88 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 163.3, 49.7, 46.7, 45.0, 34.9, 27.1, 20.10, 20.2, 17.3, 11.4; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{13}H_{26}N_2NaO_2$ 265.1892, found 265.1892.

N^1-(Cyclopropylmethyl)-N^2,N^2-diisopropyloxalamide ***(1e)***. Yield 88% (3.98 g); off-white solid; mp = 108−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (br s, 1H), 4.67−4.60 (m, 1H), 3.50−3.44 (m, 1H), 3.11−3.08 (m, 2H), 1.38 (d, J = 6.8 Hz, 6H), 1.19 (d, J = 6.7 Hz, 6H), 0.98−0.91 (m, 1H), 0.50−0.45 (m, 2H), 0.20−0.17 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 163.3, 49.7, 46.5, 44.2, 20.9, 20.1, 10.4, 3.6; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{12}H_{22}N_2NaO_2$ 249.1579, found 249.1573.

N^1-(sec-Butyl)-N^2,N^2-diisopropyloxalamide ***(5a)***. Yield 87% (3.97 g); off-white solid; mp = 91−92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (br s, 1H), 4.75−4.68 (m, 1H), 3.89−3.81 (m, 1H), 3.52−3.45 (m, 1H), 1.53−1.46 (m, 2H), 1.40 (d, J = 6.8 Hz, 6H), 1.21 (d, J = 6.7 Hz, 6H), 1.15 (d, J = 6.6 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 162.8, 49.7, 46.9, 46.6, 29.5, 20.97, 20.9, 20.2, 20.2, 20.1, 10.45; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{12}H_{24}N_2NaO_2$ 251.1735, found 251.1735.

N^1,N^1-Diisopropyl-N^2-(tert-pentyl)oxalamide ***(5b)***. Yield 84% (4.07 g); off-white solid; mp = 106−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.60 (br s, 1H), 4.72−4.66 (m, 1H), 3.51−3.44 (m, 1H), 1.76−1.40 (m, 2H), 1.40 (d, J = 6.8 Hz, 6H), 1.31 (s, 6H), 1.21 (d, J = 6.7 Hz, 6H), 0.85 (t, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 162.8, 54.3, 49.7, 46.4, 32.6, 26.1, 20.9, 20.2, 8.4; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{13}H_{26}N_2NaO_2$ 265.1892, found 265.1902.

N^1,N^1-Diisopropyl-N^2-(3-methylbutan-2-yl)oxalamide ***(5e)***. Yield 81% (3.93 g); off-white solid; mp = 105−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, J = 7.4 Hz, 1H), 4.77−4.67 (m, 1H), 3.85−3.77 (m, 1H), 3.53−3.46 (m, 1H), 1.77−1.69 (m, 1H), 1.41 (dd, J = 6.8, 1.6 Hz, 6H), 1.21 (dd, J = 6.7, 0.7 Hz, 6H), 1.11 (d, J = 6.8 Hz, 3H), 0.91 (dd, J = 6.8, 3.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 162.8, 50.2, 49.8, 46.4, 33.0, 20.9, 20.8, 20.2, 20.1, 18.62, 18.57, 17.3; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{13}H_{26}N_2NaO_2$ 265.1892, found 265.1889.

General Procedures for Preparation of 1d.[20] To a solution of 3-aminoisbutyric acid (2.06 g, 20 mmol, 1.0 equiv) in MeOH (30 mL) was added dropwise $SOCl_2$ (4.35 mL, 60 mmol, 3.0 equiv) at 0 °C. The resulting mixture was allowed to stir from 0 °C to room temperature overnight. The solvent was removed under reduced pressure afford a white solid, which was used directly for next step. The second step followed the general oxalamide coupling procedure to give compound **1d**.

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*3-(2-(Diisopropylamino)-2-oxoacetamido)-2-methylpropanoate (**1d**).* Yield 78% (4.25 g); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (br s, 1H), 4.56−4.51 (m, 1H), 3.66 (d, J = 2.1 Hz, 3H), 3.50−3.36 (m, 3H), 2.73−2.68 (m, 1H), 1.38−1.36 (m, 6H), 1.19−1.16 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.4, 163.7, 163.2, 52.0, 49.8, 46.5, 41.5, 39.4, 20.9, 20.1, 14.9; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{13}H_{24}N_2NaO_4$ 295.1634, found 295.1634.

General Procedures for Preparation of 5c. The first step, with 2-amino-1-butanol (1.78 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 was dissolved in CH_2Cl_2 (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 CH_2Cl_2 (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 **5c**.

*2-(2-(Diisopropylamino)-2-oxoacetamido)butyl acetate (**5c**).* Yield 75% (4.30 g); off-white solid; mp = 79−81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, J = 7.8 Hz, 1H), 4.71−4.65 (m, 1H), 4.13−4.07 (m, 2H), 4.05−4.02 (m, 1H), 3.54−3.47 (m, 1H), 2.05 (s, 3H), 1.66−1.49 (m, 2H), 1.41 (d, J = 6.8 Hz, 6H), 1.21 (dd, J = 6.6, 3.8 Hz, 6H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 163.2, 65.4, 49.8, 49.8, 46.7, 24.5, 21.0, 20.94, 20.91, 20.2, 20.1, 10.4; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{14}H_{26}N_2NaO_4$ 309.1790, found 309.1783.

General Procedures for Preparation of 5d.[7b] The first step, with 2-amino-1-butanol (1.78 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 and Et_3N (5.56 mL, 40 mmol, 2.0 equiv) were dissolved in CH_2Cl_2 (30 mL) and dropped by TBSCl (3.32g, 22 mmol, 1.1 equiv) at room temperature overnight. The reaction was quenched with saturated NH_4Cl (aq) and extracted with CH_2Cl_2 (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 **5d**.

*N^1-(1-((tert-Butyldimethylsilyl)oxy)butan-2-yl)-N^2,N^2-diisopropyloxalamide (**5d**).* Yield 71% (5.09 g); off-white solid; mp = 74−75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (d, J = 8.8 Hz, 1H), 4.74−4.67 (m, 1H), 3.90−3.82 (m, 1H), 3.69−3.61 (m, 2H), 3.55−3.49 (m, 1H), 1.71−1.64 (m, 1H), 1.58−1.50 (m, 1H), 1.44 (dd, J = 6.8, 1.5 Hz, 6H), 1.24 (t, J = 6.2 Hz, 6H), 0.95 (t, J = 7.5 Hz, 3H), 0.90 (s, 9H), 0.06 (d, J = 3.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 163.2, 64.1, 52.3, 49.7, 46.6, 26.0, 25.8, 24.3, 21.02, 21.00, 20.2, 18.4, 10.6, −5.32, −5.35; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{18}H_{38}N_2NaO_2Si$ 381.2549, found 381.2558.

General Procedure for Palladium-Catalyzed Arylation of *n*-Propylamine with Aryl Iodides (Table 2) (3a, 3c−3e, 3h−3i, 3k−3l, 3v). A mixture of *n*-propylamine **1a** (42.9 mg, 0.2 mmol, 1.0 equiv), ArI (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 110 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel to give the corresponding product.

*N^1,N^1-Diisopropyl-N^2-(3-(4-methoxyphenyl)propyl)oxalamide (**3a**).* 4-Iodoanisole was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (10/1) as an eluent; Yield 72% (46.1 mg); brown solid; mp = 66−67 °C; R_f = 0.48 (petroleum ester/ethyl acetate, 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, J = 8.6 Hz, 2H), 6.95 (br s, 1H), 6.82 (d, J = 8.6 Hz, 2H), 4.81−4.74 (m, 1H), 3.78 (s, 3H), 3.54−3.48 (m, 1H), 3.29 (dd, J = 13.3, 7.0 Hz, 2H), 2.63−2.59 (m, 2H), 1.88−1.81 (m, 2H), 1.42 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 163.1, 158.0, 133.3, 129.4, 114.0, 55.4, 49.7, 46.7, 39.0, 32.4, 31.2, 21.0, 20.2; HRMS (ESI-TOF) m/z [M − H]$^+$ Calcd for $C_{18}H_{27}N_2O_3$ 319.2022, found 319.2045.

*N^1,N^1-Diisopropyl-N^2-(3-phenylpropyl)oxalamide (**3c**).* Iodobenzene was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (12/1) as an eluent; Yield 65% (37.8 mg); off-white solid; mp = 72−73 °C; R_f = 0.44 (petroleum ester/ethyl acetate, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.26 (m, 2H), 7.20−7.17 (m, 3H), 7.10 (br s, 1H), 4.77−4.71 (m, 1H), 3.55−3.48 (m, 1H), 3.31 (dd, J = 13.3, 7.1 Hz, 2H), 2.69−2.65 (m, 2H), 1.92−1.85 (m, 2H), 1.42 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 163.3, 141.3, 128.6, 128.5, 126.1, 49.8, 46.7, 39.0, 33.3, 30.9, 21.0, 20.2; HRMS (ESI-TOF) m/z [M − H]$^+$ Calcd for $C_{17}H_{25}N_2O_2$ 289.1916, found 289.1913.

*N^1-(3-(3,5-Dimethylphenyl)propyl)-N^2,N^2-diisopropyloxalamide (**3d**).* 1-Iodo-3,5-dimethylbenzene was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (12/1) as an eluent; Yield 80% (50.9 mg); yellow solid; mp = 79−82 °C; R_f = 0.41 (petroleum ester/ethyl acetate, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (br s, 1H), 6.81 (d, J = 11.1 Hz, 3H), 4.73−4.66 (m, 1H), 3.54−3.48 (m, 1H), 3.30 (dd, J = 13.2, 6.7 Hz, 2H), 2.59 (t, J = 7.6 Hz, 2H), 2.28 (s, 6H), 1.90−1.82 (m, 2H), 1.42 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 141.2, 138.0, 127.7, 126.3, 49.8, 46.6, 39.1, 33.1, 31.0, 21.3, 20.9, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{19}H_{30}N_2NaO_2$ 341.2205, found 341.2208.

*N^1-(3-(4-(tert-Butyl)phenyl)propyl)-N^2,N^2-diisopropyloxalamide (**3e**).* 4-Iodo-1-*tert*-butylbenzene was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (12/1) as an eluent; Yield 83% (57.5 mg); yellow oil; R_f = 0.51 (petroleum ester/ethyl acetate, 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.29 (m, 2H), 7.26 (br s, 1H), 7.11 (d, J = 8.2 Hz, 2H), 4.73−4.66 (m, 1H), 3.54−3.47 (m, 1H), 3.31 (dd, J = 13.3, 7.0 Hz, 2H), 2.66−2.62 (m, 2H), 1.91−1.84 (m, 2H), 1.42 (d, J = 6.8 Hz, 6H), 1.30 (s, 9H), 1.23 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.52, 163.46, 148.8, 138.2, 128.1, 125.4, 49.8, 46.5, 39.0, 34.4, 32.7, 31.5, 30.8, 20.9, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{21}H_{34}N_2NaO_2$ 369.2518, found 369.2524.

*N^1-(3-(4-Bromophenyl)propyl)-N^2,N^2-diisopropyloxalamide (**3h**).* 1-Bromo-4-iodobenzene was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (9/1) as an eluent; Yield 73% (53.9 mg); yellow solid; mp = 96−98 °C; R_f = 0.44 (petroleum ester/ethyl acetate, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.36 (m, 2H), 7.22 (br s, 1H), 7.04 (d, J = 8.3 Hz, 2H), 4.73−4.67 (m, 1H), 3.54−3.47 (m, 1H), 3.28 (dd, J = 13.3, 7.0 Hz, 2H), 2.63−2.59 (m, 2H), 1.88−1.80 (m, 2H), 1.41 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 163.3, 140.3, 131.6, 130.2, 119.9, 49.8, 46.6, 38.9, 32.6, 30.8, 21.0, 20.2; HRMS (ESI-TOF) m/z [M − H]$^+$ Calcd for $C_{17}H_{24}BrN_2O_2$ 367.1021, found 367.1028.

*N^1-(3-(4-Iodophenyl)propyl)-N^2,N^2-diisopropyloxalamide (**3i**).* 1,4-Diiodobenzene was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (9/1) as an eluent; Yield 51% (42.5 mg); brown solid; mp = 95−97 °C; R_f = 0.45 (petroleum ester/ethyl acetate, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.3 Hz, 2H), 7.01 (br s, 1H), 6.93 (d, J = 8.3 Hz, 2H), 4.82−4.76 (m, 1H), 3.55−3.48 (m, 1H), 3.29 (dd, J = 13.4, 7.0 Hz, 2H), 2.63−2.59 (m, 2H), 1.89−1.81 (m, 2H), 1.42 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 163.0, 141.0, 137.6, 130.6, 91.2, 49.7, 46.8, 38.9, 32.8, 30.8, 21.0, 20.2; HRMS (ESI-TOF) m/z [M − H]$^+$ Calcd for $C_{17}H_{24}IN_2O_2$ 415.0882, found 415.0880.

*Methyl 3-(3-(2-(diisopropylamino)-2-oxoacetamido)propyl)-benzoate (**3k**).* Methyl 3-iodobenzoate was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (6/1) as an eluent; Yield 73% (50.9 mg); brown solid; mp = 77−79 °C; R_f = 0.52 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, J = 6.0, 1.8 Hz, 2H), 7.39−7.32 (m, 2H), 7.10 (br s, 1H), 4.79−4.73 (m, 1H), 3.90 (s, 3H), 3.54−3.47 (m, 1H), 3.31 (dd, J = 13.4, 6.9 Hz, 2H), 2.73−2.69 (m, 2H), 1.93−

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1.86 (m, 2H), 1.41 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.27, 163.35, 163.08, 141.65, 133.16, 130.45, 129.54, 128.65, 127.51, 52.21, 49.74, 46.71, 38.96, 33.07, 30.88, 20.99, 20.19; HRMS (ESI-TOF) m/z [M − H]$^+$ Calcd for $C_{19}H_{27}N_2O_4$ 347.1971, found 347.1951.

*N^1,N^1-Diisopropyl-N^2-(3-(3-(trifluoromethyl)phenyl)propyl)-oxalamide (**3l**).* 3-Iodobenzotrifluoride was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (10/1) as an eluent; Yield 78% (55.9 mg); brown oil; R_f = 0.44 (petroleum ester/ethyl acetate, 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.36 (m, 4H), 7.25 (br s, 1H), 4.75−4.69 (m, 1H), 3.54−3.48 (m, 1H), 3.32 (dd, J = 13.3, 7.0 Hz, 2H), 2.74−2.70 (m, 2H), 1.93−1.86 (m, 2H), 1.41 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 163.3, 142.4, 132.01 (d, J_{C-F} = 1.0 Hz), 130.97 (q, J_{C-F} = 32.0 Hz), 129.1, 124.41 (q, J_{C-F} = 271.0 Hz), 125.25 (q, J_{C-F} = 3.0 Hz), 123.17 (d, J_{C-F} = 4.0 Hz), 123.06, 49.9, 46.8, 39.0, 33.2, 30.9, 21.1, 20.3; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{18}H_{25}F_3N_2NaO_2$ 381.1766, found 381.1775.

*Methyl 4-(3-(2-(diisopropylamino)-2-oxoacetamido)propyl)-benzoate (**3v**).* Methyl 4-iodobenzoate was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (6/1) as an eluent; Yield 60% (41.8 mg); yellow solid; mp = 118−120 °C; R_f = 0.54 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 7.13 (br s, 1H), 4.76−4.69 (m, 1H), 3.89 (s, 3H), 3.54−3.47 (m, 1H), 3.30 (dd, J = 13.5, 6.8 Hz, 2H), 2.73−2.69 (m, 2H), 1.93−1.85 (m, 2H), 1.41 (d, J = 6.8 Hz, 6H), 1.23 (t, J = 5.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 163.4, 163.1, 146.9, 130.0, 128.5, 128.2, 52.1, 49.8, 46.7, 38.9, 33.3, 30.6, 21.0, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{19}H_{28}N_2NaO_4$ 371.1947, found 371.1956.

General Procedure for Palladium-Catalyzed Arylation of *n*-Propylamine with Aryl Iodides (Table 2) (3b, 3f−3g, 3j). A mixture of *n*-propylamine **1a** (42.9 mg, 0.2 mmol, 1.0 equiv), ArI (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 130 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel to give the corresponding product.

*N^1,N^1-Diisopropyl-N^2-(3-(p-tolyl)propyl)oxalamide (**3b**).* 4-Iodotoluene was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (15/1) as an eluent; Yield 74% (45.1 mg); pale yellow solid; mp = 77−80 °C; R_f = 0.56 (petroleum ester/ethyl acetate, 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10−7.05 (m, 4H), 6.96 (br s, 1H), 4.79−4.72 (m, 1H), 3.54−3.48 (m, 1H), 3.30 (dd, J = 13.5, 6.8 Hz, 2H), 2.65−2.61 (m, 2H), 2.31 (s, 3H), 1.89−1.82 (m, 2H), 1.42 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 163.1, 138.2, 135.6, 129.3, 128.4, 49.7, 46.7, 39.1, 32.8, 31.0, 21.1, 21.0, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{18}H_{28}N_2NaO_2$ 327.2048, found 327.2055.

*N^1-(3-(2-Fluorophenyl)propyl)-N^2,N^2-diisopropyloxalamide (**3f**).* 2-Fluoroiodobenzene was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (12/1) as an eluent; Yield 71% (43.8 mg); off-white solid; mp = 63−64 °C; R_f = 0.47 (petroleum ester/ethyl acetate, 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20−7.13 (m, 2H), 7.12 (br s, 1H), 7.06−7.02 (m, 1H), 7.01−6.97 (m, 1H), 4.74−4.68 (m, 1H), 3.54−3.47 (m, 1H), 3.31 (dd, J = 13.3, 6.9 Hz, 2H), 2.69 (t, J = 7.6 Hz, 2H), 1.90−1.78 (m, 2H), 1.41 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 163.3, 161.21 (d, J_{C-F} = 243.0 Hz), 130.72 (d, J_{C-F} = 5.0 Hz), 128.10 (d, J_{C-F} = 16 Hz), 127.91 (d, J_{C-F} = 8.0 Hz), 124.19 (d, J_{C-F} = 4.0 Hz), 115.37 (d, J_{C-F} = 22.0 Hz), 49.8, 46.6, 38.9, 29.6, 26.49, 26.46, 21.0, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{25}FN_2NaO_2$ 331.1798, found 331.1799.

*N^1-(3-(3-Chlorophenyl)propyl)-N^2,N^2-diisopropyloxalamide (**3g**).* 3-Chloroiodobenzene was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (15/1) as an eluent; R_f = 0.53 (petroleum ester/ethyl acetate, 4/1); Yield 68% (44.2 mg); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.15 (m, 3H), 7.10 (br s, 1H), 7.05 (d, J = 7.2 Hz, 1H), 4.79−4.72 (m, 1H), 3.55−3.48 (m, 1H), 3.30 (dd, J = 13.4, 6.8 Hz, 2H), 2.66−2.62 (m, 2H), 1.90−1.83 (m, 2H), 1.42 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 162.1, 142.4, 133.3, 128.8, 127.6, 125.7, 125.4, 48.8, 45.7, 37.9, 31.9, 29.7, 20.0, 19.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{25}ClN_2NaO_2$ 347.1502, found 347.1510.

*N^1-(3-(4-Bromo-3-chlorophenyl)propyl)-N^2,N^2-diisopropyloxalamide (**3j**).* 4-Bromo-3-chloroiodobenzene was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (9/1) as an eluent; Yield 62% (50.1 mg); brown oil; R_f = 0.44 (petroleum ester/ethyl acetate, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 8.2 Hz, 1H), 7.41 (br s, 1H), 7.25 (d, J = 1.9 Hz, 1H), 6.92 (dd, J = 8.2, 1.9 Hz, 1H), 4.67−4.60 (m, 1H), 3.53−3.46 (m, 1H), 3.28 (dd, J = 13.3, 6.8 Hz, 2H), 2.60−2.57 (m, 2H), 1.88−1.80 (m, 2H), 1.39 (d, J = 6.8 Hz, 6H), 1.21 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 163.4, 142.4, 134.3, 133.7, 130.3, 128.2, 119.7, 49.9, 46.6, 38.7, 32.4, 30.5, 20.9, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{24}BrClN_2NaO_2$ 425.0607, found 425.0603.

*N^1-(3-(4-Acetylphenyl)propyl)-N^2,N^2-diisopropyloxalamide (**3m**).* A mixture of *n*-propylamine **1a** (42.9 mg, 0.2 mmol, 1.0 equiv), 4-iodoacetophenone **2m** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 150 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (6/1) as an eluent to give the corresponding product **3m**. Yield 61% (40.6 mg); brown solid; mp = 94−96 °C; R_f = 0.43 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.2 Hz, 2H), 7.40 (br s, 1H), 7.24 (d, J = 8.1 Hz, 2H), 4.66−4.59 (m, 1H), 3.52−3.45 (m, 1H), 3.29 (dd, J = 13.3, 6.8 Hz, 2H), 2.72−2.68 (m, 2H), 2.54 (s, 3H), 1.91−1.84 (m, 2H), 1.38 (d, J = 6.8 Hz, 6H), 1.20 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 163.6, 163.5, 147.2, 135.3, 128.7, 128.6, 49.8, 46.5, 38.8, 33.2, 30.5, 26.6, 20.9, 20.1; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{19}H_{29}N_2O_3$ 333.2178, found 333.2178.

*N^1,N^1-Diisopropyl-N^2-(3-(4-nitrophenyl)propyl)oxalamide (**3n**).* A mixture of *n*-propylamine **1a** (42.9 mg, 0.2 mmol, 1.0 equiv), 4-iodo-1-nitrobenzene **2n** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and m-xylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 130 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (6/1) as an eluent to give the corresponding product **3n**. Yield 56% (37.6 mg); brown solid; mp = 121−122 °C; R_f = 0.47 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.6 Hz, 2H), 7.39 (br s, 1H), 7.32 (d, J = 8.5 Hz, 2H), 4.68−4.62 (m, 1H), 3.53−3.47 (m, 1H), 3.33−3.28 (m, 2H), 2.78−2.73 (m, 2H), 1.94−1.86 (m, 2H), 1.39 (d, J = 6.8 Hz, 6H), 1.21 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 149.3, 146.6, 129.3, 123.8, 49.9, 46.6, 38.7, 33.1, 30.5, 20.9, 20.1; HRMS (ESI-TOF) m/z [M + H]$^+$ Calcd for $C_{17}H_{26}N_3O_4$ 336.1923, found 336.1917.

*N^1,N^1-Diisopropyl-N^2-(3-(4-methyl-3-nitrophenyl)propyl)-oxalamide (**3o**).* A mixture of *n*-propylamine **1a** (42.9 mg, 0.2 mmol, 1.0 equiv), 4-iodo-1-methyl-2-nitrobenzene **2o** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and m-xylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 150 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column

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chromatography on silica gel with petroleum ester/ethyl acetate (7/1) as an eluent to give the corresponding product **3o**. Yield 63% (44.0 mg); yellow solid; mp = 121−123 °C; R_f = 0.49 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 1.3 Hz, 1H), 7.35 (br s, 1H), 7.31 (dd, J = 7.8, 1.7 Hz, 1H), 7.22 (d, J = 7.8 Hz, 1H), 4.69−4.63 (m, 1H), 3.53−3.46 (m, 1H), 3.30 (dd, J = 13.3, 6.9 Hz, 2H), 2.71−2.69 (m, 2H), 2.53 (s, 3H), 1.92−1.84 (m, 2H), 1.40 (d, J = 6.8 Hz, 6H), 1.21 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 163.4, 149.2, 140.7, 133.2, 132.9, 131.3, 124.4, 49.9, 46.6, 38.7, 32.3, 30.6, 20.9, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{18}H_{27}N_3NaO_4$ 372.1899, found 372.1901.

General Procedure for Palladium-Catalyzed Arylation of *n*-Propylamine with Heterocyclic Iodides (Table 3) (3p−3r). A mixture of *n*-propylamine **1a** (42.9 mg, 0.2 mmol, 1.0 equiv), heterocyclic iodides (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 130 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel to give the corresponding product.

*N^1,N^1-Diisopropyl-N^2-(3-(9-phenyl-9H-carbazol-3-yl)propyl)-oxalamide (**3p**).* 3-Iodo-9-phenylcarbazole was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (9/1) as an eluent; Yield 78% (71.1 mg); brown oil; R_f = 0.44 (petroleum ester/ethyl acetate, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 7.7 Hz, 1H), 7.95 (s, 1H), 7.62−7.55 (m, 4H), 7.45 (t, J = 7.1 Hz, 1H), 7.41−7.33 (m, 3H), 7.29−7.22 (m, 2H), 7.08 (br s, 1H), 4.81−4.74 (m, 1H), 3.55−3.48 (m, 1H), 3.38 (dd, J = 13.4, 6.7 Hz, 2H), 2.88 (t, J = 7.6 Hz, 2H), 2.05−1.97 (m, 2H), 1.43 (d, J = 6.8 Hz, 6H), 1.24 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 141.2, 139.6, 137.9, 132.9, 129.9, 127.4, 127.1, 126.6, 126.0, 123.6, 123.3, 120.4, 119.9, 119.8, 109.8, 49.7, 46.7, 39.1, 33.4, 31.7, 21.0, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{29}H_{33}N_3NaO_2$ 478.2470, found 478.2462.

*N^1-(3-(2,6-Dichloropyridin-4-yl)propyl)-N^2,N^2-diisopropyloxalamide (**3q**).* 2,6-Dichloro-4-iodopyridine was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (6/1) as an eluent; Yield 60% (43.2 mg); brown oil; R_f = 0.41 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (br s, 1H), 7.09 (s, 2H), 4.71−4.65 (m, 1H), 3.55−3.48 (m, 1H), 3.34−3.29 (m, 2H), 2.66−2.62 (m, 2H), 1.91−1.84 (m, 2H), 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. 7, 163.2, 156.5, 150.8, 123.1, 50.0, 46.8, 38.7, 32.2, 29.7, 21.1, 20.3; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{16}H_{23}Cl_2N_3NaO_2$ 382.1065, found 382.1065.

*N^1,N^1-Diisopropyl-N^2-(3-(2-(trifluoromethyl)pyridin-4-yl)propyl)-oxalamide (**3r**).* 4-Iodo-2-(trifluoromethyl)pyridine was used as arylation reagent. Purified by column chromatography on silica gel with petroleum ester/ethyl acetate (3/1) as an eluent; Yield 65% (46.8 mg); yellow oil; R_f = 0.58 (petroleum ester/ethyl acetate, 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 5.0 Hz, 1H), 7.49 (d, J = 5.5 Hz, 2H), 7.31 (d, J = 4.4 Hz, 1H), 4.67−4.60 (m, 1H), 3.53−3.46 (m, 1H), 3.32 (dd, J = 13.2, 6.8 Hz, 2H), 2.76−2.72 (m, 2H), 1.95−1.87 (m, 2H), 1.39 (d, J = 6.8 Hz, 6H), 1.21 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 163.3, 152.5, 150.1, 148.46 (q, J_{C-F} = 34.0 Hz), 126.5, 121.19 (q, J_{C-F} = 273.0 Hz), 120.61 (d, J_{C-F} = 3.0 Hz), 49.9, 46.6, 38.7, 32.6, 29.8, 20.9, 20.1; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{24}F_3N_3NaO_2$ 382.1718, found 382.1719.

*N^1,N^1-Diisopropyl-N^2-(3-(1-tosyl-1H-indol-5-yl)propyl)oxalamide (**3s**).* A mixture of *n*-propylamine **1a** (42.9 mg, 0.2 mmol, 1.0 equiv), 5-iodo-1-(4-methylphenylsulfonyl)indole **2s** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (220.8 mg, 4 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 150 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (5/1) as an eluent to give the corresponding product **3s**. Yield 46% (44.5 mg); brown oil; R_f = 0.33 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.5 Hz, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 3.6 Hz, 1H), 7.31 (d, J = 0.8 Hz, 1H), 7.21 (d, J = 8.1 Hz, 2H), 7.12 (dd, J = 8.5, 1.5 Hz, 1H), 6.97 (br s, 1H), 6.58 (d, J = 3.6 Hz, 1H), 4.79−4.73 (m, 1H), 3.54−3.47 (m, 1H), 3.33 (dd, J = 13.4, 6.8 Hz, 2H), 2.73−2.69 (m, 2H), 2.33 (s, 3H), 1.91−1.84 (m, 2H), 1.41 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 163.1, 145.0, 136.4, 135.5, 133.5, 131.2, 130.0, 126.9, 126.7, 125.4, 120.8, 113.6, 109.0, 49.7, 46.7, 39.0, 33.1, 31.3, 21.7, 21.0, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{26}H_{33}N_3NaO_4S$ 506.2089, found 506.2080.

*N^1,N^1-Diisopropyl-N^2-(3-(1-(phenylsulfonyl)-1H-indol-3-yl)-propyl)oxalamide (**3t**).* A mixture of *n*-propylamine **1a** (42.9 mg, 0.2 mmol, 1.0 equiv), 3-iodo-1-(phenylsulfonyl)indole **2t** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 100 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (9/1) as an eluent to give the corresponding product **3t**. Yield 45% (42.3 mg); brown oil; R_f = 0.58 (petroleum ester/ethyl acetate, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.3 Hz, 1H), 7.87−7.85 (m, 2H), 7.53−7.40 (m, 4H), 7.35−7.29 (m, 2H), 7.25−7.21 (m, 1H), 7.05 (br s, 1H), 4.83−4.76 (m, 1H), 3.56−3.49 (m, 1H), 3.33 (dd, J = 13.4, 6.8 Hz, 2H), 2.71 (t, J = 7.5 Hz, 2H), 1.98−1.90 (m, 2H), 1.43 (d, J = 6.8 Hz, 6H), 1.24 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 162.0, 137.3, 134.5, 132.8, 129.9, 128.4, 125.9, 123.9, 122.3, 122.0, 121.4, 118.5, 112.9, 48.8, 45.8, 38.0, 27.6, 21.4, 20.0, 19.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{25}H_{31}N_3NaO_4S$ 492.1933, found 492.1920.

*Methyl 5-(3-(2-(diisopropylamino)-2-oxoacetamido)propyl)-furan-2-carboxylate (**3u**).* A mixture of *n*-propylamine **1a** (42.9 mg, 0.2 mmol, 1.0 equiv), methyl 2-bromo-5-furancarboxylate **2u** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (220.8 mg, 4 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 150 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (5/1) as an eluent to give the corresponding product **3u**. Yield 23% (15.6 mg); brown oil; R_f = 0.34 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09−7.07 (m, 2H), 6.18 (d, J = 3.4 Hz, 1H), 4.80−4.74 (m, 1H), 3.87 (s, 3H), 3.55−3.48 (m, 1H), 3.33 (dd, J = 13.4, 6.8 Hz, 2H), 2.76 (t, J = 7.6 Hz, 2H), 1.98−1.91 (m, 2H), 1.41 (d, J = 6.8 Hz, 6H), 1.23 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 162.9, 159.9, 159.3, 143.4, 119.4, 108.3, 51.9, 49.8, 46.8, 38.7, 27.5, 25.8, 21.0, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{17}H_{26}N_2NaO_5$ 361.1739, found 361.1740.

*N^1,N^1-Diisopropyl-N^2-(2-(4-methoxybenzyl)-3-(4-methoxyphenyl)propyl)oxalamide (**4a**).* A mixture of oxalamide **1b** (0.2 mmol, 1.0 equiv), 4-iodoanisole **2a** (0.6 mmol, 3.0 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (220.8 mg, 4 equiv), PivONa (7.4 mg, 0.3 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 130 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (8/1) as an eluent to give the corresponding product **4a**. Yield 53% (46.7 mg); pale yellow oil; R_f = 0.47 (petroleum ester/ethyl acetate, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, J = 8.6 Hz, 4H), 6.82 (d, J = 8.6 Hz, 5H), 4.78−4.72 (m, 1H), 3.78 (s, 6H), 3.53−3.47 (m, 1H), 3.21 (t, J = 6.1 Hz, 2H), 2.60−2.50 (m, 4H), 2.16−2.09 (m, 1H), 1.42 (d, J = 6.8 Hz, 6H), 1.21 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 163.0, 158.1, 132.0, 130.1, 114.0, 55.4,

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49.7, 46.7, 42.5, 42.2, 37.6, 21.0, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{26}H_{36}N_2NaO_4$ 463.2573, found 463.2563.

*N^1,N^1-Diisopropyl-N^2-(2-(4-methoxybenzyl)butyl)oxalamide (**4b**).* A mixture of oxalamide **1c** (0.2 mmol, 1.0 equiv), 4-iodoanisole **2a** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (220.8 mg, 4 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 130 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (10/1) as an eluent to give the corresponding product **4b**. Yield 50% (34.8 mg); pale yellow oil; R_f = 0.40 (petroleum ester/ethyl acetate, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, J = 8.5 Hz, 2H), 6.89 (br s, 1H), 6.82 (d, J = 8.6 Hz, 2H), 4.78−4.71 (m, 1H), 3.78 (s, 3H), 3.54−3.47 (m, 1H), 3.28−3.16 (m, 2H), 2.60−2.48 (m, 2H), 1.81−1.75 (m, 1H), 1.43−1.41 (m, 6H), 1.34 (dd, J = 14.2, 7.2 Hz, 2H), 1.22 (d, J = 6.6 Hz, 6H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 163.2, 158.0, 132.3, 130.1, 113.9, 55.3, 49.7, 46.7, 41.9, 41.7, 37.4, 24.1, 21.0, 20.2, 11.1; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{20}H_{32}N_2NaO_3$ 371.2311, found 371.2311.

*Methyl 3-(2-(diisopropylamino)-2-oxoacetamido)-2-(4-methoxybenzyl)propanoate (**4c**).* A mixture of oxalamide **1d** (0.2 mmol, 1.0 equiv), 4-iodoanisole **2a** (0.3 mmol, 1.5 equiv), $Pd(TFA)_2$ (6.6 mg, 10 mol %), Ag_2CO_3 (220.8 mg, 4 equiv) and PhCl (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 130 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (6/1) as an eluent to give the corresponding product **4c**. Yield 47% (35.6 mg); pale yellow oil; R_f = 0.46 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (br s, 1H), 7.06 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 4.63−4.56 (m, 1H), 3.76 (s, 3H), 3.64 (s, 3H), 3.55−3.45 (m, 2H), 3.42−3.35 (m, 1H), 2.96−2.89 (m, 2H), 2.81−2.74 (m, 1H), 1.40 (d, J = 6.8 Hz, 6H), 1.20 (d, J = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.4, 163.6, 163.1, 158.5, 130.0, 129.9, 114.1, 55.3, 52.0, 49.8, 46.9, 46.6, 40.0, 35.2, 20.9, 20.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{20}H_{30}N_2NaO_5$ 401.2052, found 401.2050.

*N^1,N^1-Diisopropyl-N^2-((2-(4-methoxyphenyl)cyclopropyl)methyl)-oxalamide (**4d**).* A mixture of oxalamide **1e** (0.2 mmol, 1.0 equiv), 4-iodoanisole **2a** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (2.2 mg, 5 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 90 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (9/1) as an eluent to give the corresponding product **4d**. Yield 73% (48.5 mg); yellow solid; mp = 92−94 °C; R_f = 0.50 (petroleum ester/ethyl acetate, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (t, J = 5.5 Hz, 2H), 6.83−6.79 (m, 3H), 4.65−4.58 (m, 1H), 3.77 (s, 3H), 3.51−3.44 (m, 1H), 3.06−2.99 (m, 1H), 2.94−2.88 (m, 1H), 2.22−2.16 (m, 1H), 1.40 (dd, J = 6.8, 1.8 Hz, 6H), 1.36−1.28 (m, 1H), 1.18 (dd, J = 9.9, 6.7 Hz, 6H), 1.03−0.98 (m, 1H), 0.80−0.76 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 163.1, 158.2, 130.1, 129.9, 113.8, 55.3, 49.7, 46.5, 39.6, 20.93, 20.90, 20.2, 20.1, 20.0, 17.4, 8.6; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{19}H_{28}N_2NaO_3$ 355.1998, found 355.1994.

*N^1,N^1-Diisopropyl-N^2-(4-(4-methoxyphenyl)butan-2-yl)-oxalamide (**6a**).* A mixture of oxalamide **5a** (0.2 mmol, 1.0 equiv), 4-iodoanisole **2a** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (2.2 mg, 5 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 90 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (9/1) as an eluent to give the corresponding product **6a**. Yield 83% (55.5 mg); yellow solid; mp = 113−114 °C; R_f = 0.51 (petroleum ester/ethyl acetate, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, J = 8.5 Hz, 3H), 6.80 (d, J = 8.6 Hz, 2H), 4.74−4.67 (m, 1H), 4.02−3.95 (m, 1H), 3.76 (s, 3H), 3.53−3.46 (m, 1H), 2.62−2.56 (m, 2H), 1.83−1.70 (m, 2H), 1.42 (dd, J = 6.8, 1.4 Hz, 6H), 1.21 (dd, J = 10.7, 6.7 Hz, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 162.8, 157.9, 133.7, 129.3, 113.9, 55.3, 49.7, 46.5, 45.2, 38.6, 31.6, 21.0, 20.9, 20.7, 20.21, 20.16; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{19}H_{30}N_2NaO_3$ 357.2154, found 357.2153.

*N^1,N^1-Diisopropyl-N^2-(4-(4-methoxyphenyl)-2-methylbutan-2-yl)-oxalamide (**6b**).* A mixture of oxalamide **5b** (0.2 mmol, 1.0 equiv), 4-iodoanisole **2a** (0.3 mmol, 1.5 equiv), $Pd(TFA)_2$ (6.6 mg, 10 mol %), Ag_2CO_3 (165.6 mg, 3.0 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 60 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (12/1) as an eluent to give the corresponding product **6b**. Yield 57% (39.7 mg); yellow solid; mp = 119−120 °C; R_f = 0.57 (petroleum ester/ethyl acetate, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, J = 8.6 Hz, 2H), 6.82−6.74 (m, 2H), 6.74 (s, 1H), 4.75−4.68 (m, 1H), 3.76 (s, 3H), 3.52−3.46 (m, 1H), 2.56−2.52 (m, 2H), 2.05−2.01 (m, 2H), 1.42−1.40 (m, 12H), 1.23 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 161.8, 156.8, 133.2, 128.3, 112.9, 54.3, 53.1, 48.8, 45.6, 41.0, 28.8, 25.8, 20.0, 19.2; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{20}H_{32}N_2NaO_3$ 371.2311, found 371.2314.

*2-(2-(Diisopropylamino)-2-oxoacetamido)-4-(4-methoxyphenyl)-butyl acetate (**6c**).* A mixture of oxalamide **5c** (0.2 mmol, 1.0 equiv), 4-iodoanisole **2a** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and DCE (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 110 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (6/1) as an eluent to give the corresponding product **6c**. Yield 71% (55.7 mg); pale yellow oil; R_f = 0.42 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, J = 7.9 Hz, 1H), 7.07 (d, J = 8.6 Hz, 2H), 6.82−6.78 (m, 2H), 4.71−4.64 (m, 1H), 4.20−4.15 (m, 1H), 4.14−4.09 (m, 2H), 3.76 (s, 3H), 3.55−3.48 (m, 1H), 2.67−2.56 (m, 2H), 2.04 (s, 3H), 1.87−1.80 (m, 2H), 1.42 (d, J = 6.8 Hz, 6H), 1.23 (t, J = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 163.2, 158.0, 133.1, 129.3, 114.0, 65.7, 55.3, 49.8, 48.0, 46.6, 33.4, 31.3, 20.92, 20.91, 20.85, 20.2, 20.1; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{21}H_{32}N_2NaO_5$ 415.2209, found 415.2206.

*N^1-(1-((tert-Butyldimethylsilyl)oxy)-4-(4-methoxyphenyl)butan-2-yl)-N^2,N^2-diisopropyloxalamide (**6d**).* A mixture of oxalamide **5d** (0.2 mmol, 1.0 equiv), 4-iodoanisole **2a** (0.3 mmol, 1.5 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (82.8 mg, 1.5 equiv) and DCE (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 150 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (20/1) as an eluent to give the corresponding product **6d**. Yield 62% (57.6 mg); pale yellow oil; R_f = 0.63 (petroleum ester/ethyl acetate, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (dd, J = 9.0, 2.3 Hz, 2H), 6.91 (d, J = 9.1 Hz, 1H), 6.83−6.80 (m, 2H), 4.75−4.68 (m, 1H), 4.01−3.93 (m, 1H), 3.77 (s, 3H), 3.67−3.61 (m, 2H), 3.55−3.48 (m, 1H), 2.64−2.57 (m, 2H), 1.90−1.80 (m, 2H), 1.44−1.42 (m, 6H), 1.23 (t, J = 7.1 Hz, 6H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 163.1, 157.9, 133.8, 129.4, 113.9, 64.5, 55.3, 50.5, 49.7, 46.6, 33.4, 31.5, 26.0, 21.0, 20.2, 18.4, −5.3; HRMS (ESI-TOF) m/z [M + Na]$^+$ Calcd for $C_{25}H_{44}N_2NaO_4Si$ 487.2968, found 487.2966.

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*N^1,N^1-Diisopropyl-N^2-(3-(4-methoxybenzyl)-4-(4-methoxyphenyl)butan-2-yl)oxalamide (**6e**).* A mixture of oxalamide **5e** (0.2 mmol, 1.0 equiv), 4-iodoanisole **2a** (0.6 mmol, 3.0 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (220.8 mg, 4.0 equiv) and mesitylene (0.8 mL) under Ar atmosphere in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 130 °C with vigorous stirring for 36 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (9/1) as an eluent to give the corresponding product **6e**. Yield 60% (54.5 mg); yellow oil; R_f = 0.46 (petroleum ester/ethyl acetate, 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, J = 8.5 Hz, 2H), 7.02 (d, J = 8.5 Hz, 2H), 6.80 (dd, J = 13.8, 8.6 Hz, 5H), 4.73−4.66 (m, 1H), 4.11−4.03 (m, 1H), 3.77 (d, J = 8.2 Hz, 6H), 3.53−3.46 (m, 1H), 2.66−2.61 (m, 1H), 2.57−2.45 (m, 3H), 2.16−2.12 (m, 1H), 1.43−1.40 (m, 6H), 1.25−1.17 (t, J = 7.0 Hz, 6H), 1.17 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 162.6, 158.02, 157.96, 132.6, 132.2, 130.1, 130.0, 114.0, 113.9, 55.33, 55.29, 49.7, 47.0, 46.6, 46.4, 35.6, 35.1, 21.0, 20.21, 20.20, 17.1; HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{27}H_{38}N_2NaO_4$ 477.2729, found 477.2729.

*(E)-N^1-(3-(2-(3,3-Dimethylbut-1-en-1-yl)-4-methoxyphenyl)-propyl)-N^2,N^2-diisopropyloxalamide (**7**).* A mixture of **3a** (0.2 mmol, 1.0 equiv), 3,3-Dimethyl-1-Butene (2 equiv), $Pd(OAc)_2$ (4.5 mg, 10 mol %), Ag_2CO_3 (110.4 mg, 2 equiv), $(n\text{-BuO})_2PO_2H$ (12.6 mg, 0.3 equiv) and (1,2-dichloroethane)(1 mL) in a 15 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 120 °C with vigorous stirring for 24 h. The reaction mixture was cooled to room tempreture, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (12/1) as an eluent to give the alkenylated product **7**. Yield 62% (49.9 mg); yellow oil; R_f = 0.41 (petroleum ester/ethyl acetate, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, J = 8.4 Hz, 1H), 6.94 (d, J = 2.7 Hz, 2H), 6.71 (dd, J = 8.3, 2.7 Hz, 1H), 6.47 (d, J = 15.9 Hz, 1H), 6.10 (d, J = 15.9 Hz, 1H), 4.83−4.76 (m, 1H), 3.80 (s, 3H), 3.54−3.48 (m, 1H), 3.29 (dd, J = 13.3, 6.9 Hz, 2H), 2.68−2.64 (m, 2H), 1.80−1.77 (m, 2H), 1.42 (d, J = 6.8 Hz, 6H), 1.22 (d, J = 6.7 Hz, 6H), 1.12 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 162.1, 157.4, 143.3, 137.1, 129.9, 129.6, 121.2, 111.7, 110.6, 54.5, 48.8, 45.8, 38.2, 32.8, 29.6, 29.1, 28.9, 20.1, 19.3. HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{24}H_{38}N_2NaO_3$ 425.2780, found 425.2784.

*Methyl 1-(2-(diisopropylamino)-2-oxoacetyl)-1,2,3,4-tetrahydroquinoline-7-carboxylate (**8**).* A mixture of **3v** (0.25 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.8 mg, 5 mol %), $PhI(OAc)_2$ (161.1 mg, 2.0 equiv) and hexafluoroisopropanol (12.5 mL) under Ar atmosphere in a 50 mL glass vial [sealed with poly(tetrafluoroethylene) (PTFE) cap] was heated at 60 °C with vigorous stirring for 24 h. room tempreture, diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel with petroleum ester/ethyl acetate (6/1) as an eluent to give the cyclized product **8**. Yield 72% (49.9 mg); yellow solid; mp = 140−142 °C; R_f = 0.53 (petroleum ester/ethyl acetate, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 1.4 Hz, 0.28H), 7.85 (d, J = 1.3 Hz, 0.73H), 7.81−7.76 (m, 1H), 7.22 (t, J = 7.4 Hz, 1H), 3.88 (d, J = 6.8 Hz, 4.28H), 3.72−3.69 (m, 0.66H), 3.56−3.49 (m, 0.34H), 3.42−3.35 (m, 0.74H), 2.94 (t, J = 6.8 Hz, 0.61H), 2.84 (t, J = 5.8 Hz, 1.38H), 2.03 (s, 2H), 1.52 (d, J = 6.8 Hz, 1.82H), 1.33−1.20 (m, 11H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 165.6, 164.2, 163.33, 163.26, 162.9, 137.0, 136.3, 135.7, 133.5, 128.6, 128.3, 127.8, 127.5, 126.2, 125.2, 124.5, 122.6, 51.4, 51.3, 50.1, 45.2, 41.3, 26.4, 26.2, 22.3, 22.1, 20.0, 19.3; HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{19}H_{26}N_2NaO_4$ 369.1790, found 369.1798.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00968.

Arylation of **1b**, **1d**, and **5b**, and ^{1}H and ^{13}C NMR spectra of all new compounds. (PDF)

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Notes

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