JOC The Journal of Organic Chemistry

Note

Decarboxylative Alkylation of Heteroarenes using N-Hydroxybenzimidoyl Chloride Esters

Li xiaojuan, Qiang Zhang, Weigang Zhang, Yi Wang, and Yi Pan

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b02318 • Publication Date (Web): 09 Oct 2019

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

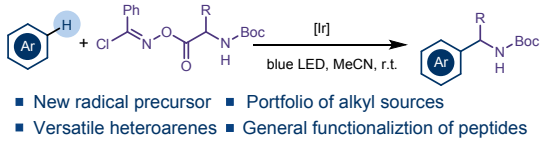
Decarboxylative Alkylation of Heteroarenes using *N*-Hydroxybenzimidoyl Chloride Esters

Xiaojuan Li, [a] Qiang Zhang, [a] Weigang Zhang,[a] Yi Wang,*[a] and Yi Pan [a]

[a] State Key Laboratory of Coordination Chemistry, Jiangsu Key Laboratory of Advanced Organic Materials, School of Chemistry and Chemical Engineering, Nanjing University, 163 Xianlin Ave., 210023 Nanjing, China

Supporting Information Placeholder

Imine *versus* amine: A general acid-free strategy to generate a portfolio of alkyl radicals, and it can be applied in Minisci reaction of heteroarenes under mild photocatalytic conditions.



- New radical precursor
- Portfolio of alkyl sources
- Versatile heteroarenes
- General functionaliztion of peptides

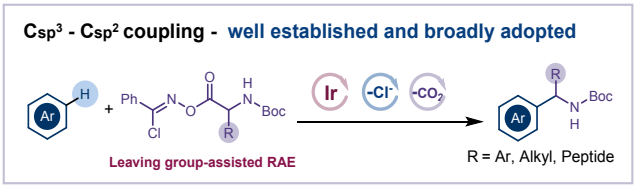
ABSTRACT: Functionalized *N*-heteroarenes are highly desired motifs in medicinal chemistry and pharmaceutical industry. Minisci-type reaction usually requires a protonated *N*-heteroarene for alkyl radical to attack. This work describes a leaving group assisted redox-active ester to enable direct coupling of amino acid with *N*-heteroarenes. The efficient and sustainable photoredox strategy provides a rapid access to alkylated heterocyclic manifold.

Introduction

Minisci-type additions of radical nucleophiles represent an attractive and versatile method for the rapid functionalization of heteroarenes.[1] Recent advances describe a variety of convenient radical precursors spawned under mild conditions.[1c,1d,2] Particularly, photoredox catalysis[3] has provided great opportunities for radical generation in Minisci-type additions with precursors that include alcohols,[4] ethers,[5] boronic acids,[6] carboxylic acids,[7] and redox-active esters (RAEs).[8] A significant progress has been made with *α*-aminoalkylation of *N*-heteroarenes using α-amino acids and peptides. *α*-Aminoalkyl radcials could be readily generated *via* the activation of *N*-(acyloxy)-phthalimide[9] in combination with photodredox and homolytically attacks protonated heteroarenes. Phipps developed enantioselective Minisci addition using chiral Brønsted acid catalyst.[10]

We recently developed a leaving group-assisted redox-active ester for photoinduced fluoroalkylations using *N*-hydroxybenzimidoyl chloride ester.[11] We envisioned that by simply installing a chlorine to oxime, this stabilized imine rivals with the electron-rich nitrogen of amino-acid, in favor of generating iminyl anion and *α*-amino carbon radical *via* decarboxylative fragmentation (Figure 1). Thus, *α*-amino alkylation of basic heteroarenes could furnish under similar photoredox strategy of fluoroalkylation. We herein reported a highly efficient Minisci addition using the newly developed *N*-hydroxybenzimidoyl chloride ester (NHBC) to activate amino acid.

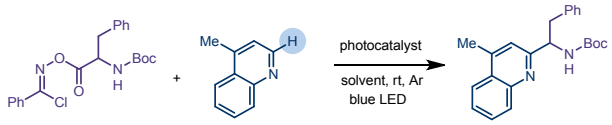
Figure 1 Functionalization of *N*-heteroarenes using Redox-active esters



Results and Discussion

Our experiments began with a brief survey of photocatalysts with NHBC ester and quninoline (Table 1). This study revealed that $[Ir(dF(CF_3)ppy)_2(dtbby)]PF_6$ was able to promote the desired radical alkylation sequence (entry 1). Other iridium and ruthenium catalysts delivered poor conversions (entries 3-6). Phosphoric acid could not promote the radical addition (entry 7). The reaction efficiency was reduced in air (entry 8).

Table 1 Optimization of the reaction conditions[a,b]

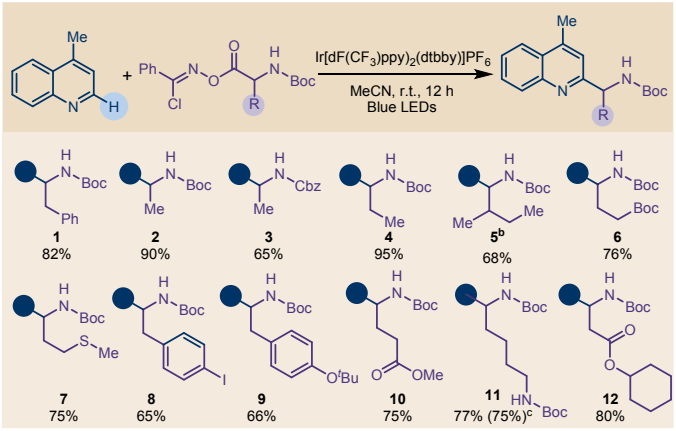


Entry	Variations from conditions [a]	Yield
1	none	70%
2	4CzIPN	20%
3	$[Ru(bpy)_3](PF_6)_2$	0%
4	$Ir(ppy)_3$	45%
5	$[Ir(dF(CF_3)ppy)_2(bpy)]PF_6$	50%
6[b]	$[Ir(dF(CF_3)ppy)_2(dtbby)]PF_6$	82%
7[b]	PA added	80%
8	In air	67%

[a] Heteroarene (0.40 mmol), NHBC esters (0.20 mmol), photocatalyst (2 mol%), in MeCN (2.0 mL), irradiated by 10 W blue LEDs for 12 h under Ar; [b] 60W blue LEDs used, PA: 1,1'-binaphthyl-2,2'-diyl hydrogenphosphate.

With the optimized reaction in hand, we studied the scope of the reaction with respect to the amino acid coupling partners. The reaction proceeds at room temperature without additional acid or oxidant, the reaction exhibits excellent functional group compatibility (Scheme 1). Various natural amino acid-derived redox-active esters are suitable substrates, including phenylalanine **1**, alanine **2** & **3**, isoleucine **5**, methionine **7**, tyrosine **9**, glutamic acid **10**, lysine **11**, aspartic acid **12**. Unnatural amino acids **4**, **6** and **8** are also tolerated under these conditions. Typical *N*-protecting groups in peptide chemistry, such as the tert-butyloxycarbonyl (-BOC) and benzyloxycarbonyl (-Cbz) groups, were suitable for their *N*-protection. The sulfide moiety in methionine, which is incompatible in the typical Minisci conditions, was well tolerated under this framework. This demonstrated the advantage of photoredox catalysis for selectively generating radicals while avoiding the use of stoichiometric oxidant.

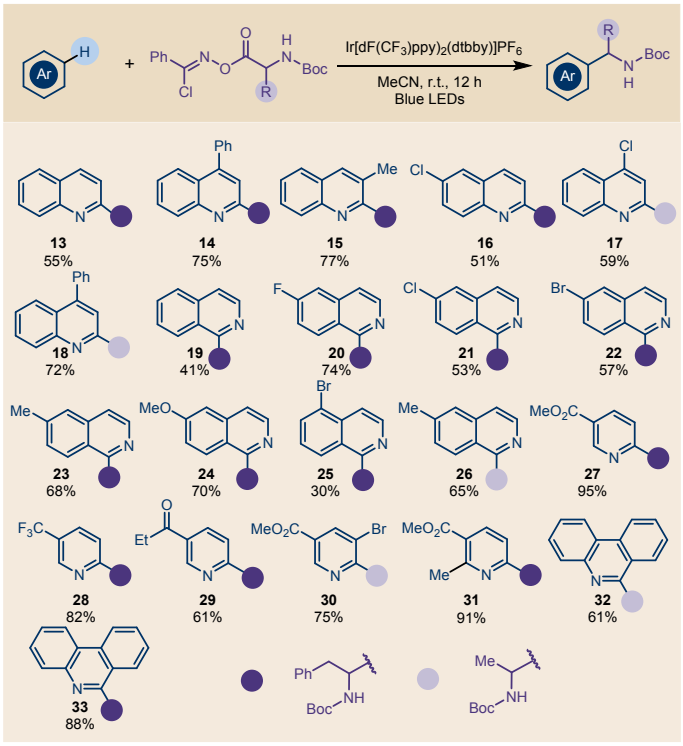
Scheme 1. Amino acid scope for the photocatalytic amination[a,b,c]



[a] Heteroarene (0.40 mmol), NHBC esters (0.20 mmol), photocatalyst (2 mol%), in MeCN (2.0 mL), irradiated by 60 W blue LEDs for 12 h under Ar. [b] 1:1 diastereomeric ratio. [c] Gram-scale; 2.5 mmol NHBC esters was added.

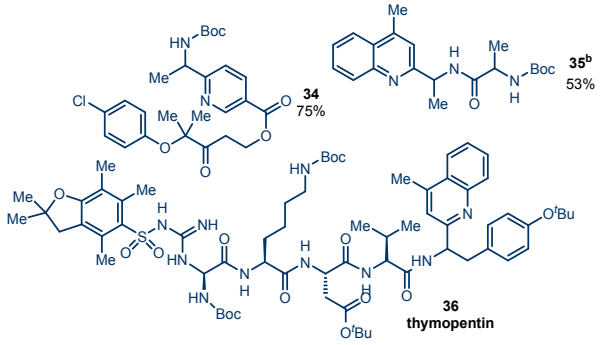
We then sought to demonstrate the generality of this approach with respect to *N*-heteroarenes (Scheme 2). A broad scope of *N*-heteroarenes was amenable despite their inherent differences in electrophilicity. Quinoline **13**-**18**, isoquinoline **19**-**26**, pyridine **27**-**31** and phenanthridine **32** and **33** can all be smoothly alkylated with good to excellent yields (50−90%). Reactions selectively took place on the most electrophilic position, which can be predicted by a radical nucleophilic attack mechanism.[7,13] Electron-withdrawing (-F, -Cl, -Br) and electron-donating (-Me and -OMe) substituents at 4-, 5- and 6-positions can afford the corresponding alkylation products in good yields.

Scheme 2 Aromatic scope for the photocatalytic amination[a]



[a] Heteroarene (0.40 mmol), NHBC esters (0.20 mmol), Photocatalyst (2 mol%), in MeCN (2.0 mL), irradiated by 60 W blue LEDs for 12 h under Ar.

Scheme 3 Peptides and drugs for Minisci reaction [a,b]

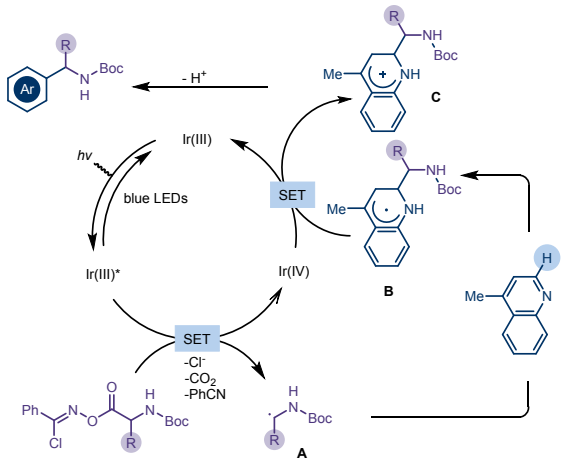


[a] Heteroarene (0.40 mmol), NHBC esters (0.20 mmol), Photocatalyst (2 mol%), in MeCN (2.0 mL), irradiated by 60 W blue LEDs for 12 h under Ar. [b] 3:1 diastereomeric ratio.

The mild reaction conditions and the broad substrate scope prompt us to explore further elarbolation of this reaction (Scheme 3). Bioactive etofibrate can be modified using this photocatalytic alkylation to form the pyridine derivative **34** in 75% yield. Direct installation of a *N*-heteroarene to peptides furnished various functionalized peptides at the C-terminal Dipeptide-derived redox-active esters can be successfully used in the decarboxylative α-aminoalkylation reaction, generating desired peptide **35** in 53% yield. This protocol has been further applied to the functionalization of thymopentin, a pentapeptide, which could have potential biomedical applications (**36**, See Supporting Inforamtion).

Based on the previous reports[8] and the quenching studies of photocatalysts (see Supporting Information), a possible mechanism for the Minisci reaction is illustrated in Scheme 4. The photoredox catalyst Ir(III) with suitable redox potential can interact with *N*-hydroxybenzimidoyl chloride ester to afford α-aminoalkyl radical **A** after decarboxylation. This radical **A** may not be further oxidize to form an iminium cation by photoredox catalyst, but able to attack a *N*-heteroarene to form a radical cation **B**, which is further oxidized by Ir(IV) and then deprotonation by a counteranion (Cl^-) to afford the α-aminoalkylation product and regenerate the photoredox catalyst.

Scheme 4 Proposed mechanism for Minisci reaction



Conclusion

In summary, we have developed photoredox catalyzed α-aminoalkylation of *N*-heteroarenes using RAE esters of amino acids. This radical sequence exhibited wide substrate scope of natural and unnatural amino acids and heteroarenes. It could be further elaborated to access functionalized peptides at the *C*-terminal. Future investigation in chemical biology is underway.

EXPERIMENTAL SECTION

General Information. All reactions were performed in flame-dried glassware with magnetic stirring bar and sealed with a rubber septum. The solvents were distilled by standard methods. Reagents were obtained from commercial suppliers and used without further purification unlessotherwise noted. Silica gel column chromatography was carried out using silica Gel 60 (230–400 mesh). Analytical thin layer chromatography (TLC) was done using silica Gel (silica gel 60 F254). TLC plates were analyzed by an exposure to ultraviolet (UV) light. NMR experiments were measured on a Bruker AVANCE III-400 or 500 spectrometer and carried out in deuterated chloroform ($CDCl_3$) ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz or 500 MHz and 100MHz or 125 MHz spectrometers, respectively. Chemical shifts are reported as δ values relative to internal TMS (δ 0.00 for ^{1}H NMR), chloroform (δ 7.26 for ^{1}H NMR), chloroform (δ77.00 for ^{13}C NMR). The following abbreviations are used for the multiplicities: s: singlet, d: doublet, dd:doublet of doublet, t: triplet, q: quadruplet, m: multiplet, br: broad signal for proton spectra; Coupling constants (J) are reported in Hertz (Hz). Melting points were uncorrected. HRMS were recorded on a Bruker microTOF-Q111. A borosilicate glass tube was used as a reaction tube. The reaction mixture was irradiated with two Kessil LEDs (Saltwater Aquarium Light A360WE Series Tuna Blue; Rating: 19VDC 90W Max from 5 cm away with no filters. Unless otherwise noted, all reagents were weighed and handled in air, and all reactions were under argon.

General Procedure for the synthesis of NHBC esters (a) – (l)

1) Hydroxylamine (50% aq. soln.) (72 mmol, 1.2 equiv.) was added to corresponding aldehydes (60 mmol, 1 eq.) in ethanol (40 mL). The mixture was stirred at room temperature for 1 hour. After the reaction was completed by TLC

monitoring, the reaction mixture was evaporated in *vacuo*. Then, the reaction mixture was quenched with water and extracted with ethyl acetate (60 mL x 3). The organic layer was dried over Na_2SO_4, and evaporated in *vacuo*. The corresponding oximes were directly used in the next step without further purification.

2) To a colorless, homogeneous solution of the corresponding oximes (60 mmol) in *N,N*-dimethylformamide (40 mL) at room temperature was added *N*- chlorosuccinimide (72 mmol, 1.2 eq.) portion-wise over 1 h. During each addition, the reaction mixture would turn yellow and then gradually return to near colorlessness. Additionally, an exotherm was noted with each portion added to ensure that the reaction initiated after the addition of *N*-chlorosuccinimide. An ice bath was available, if required, to cool the exotherm. After the addition was complete, the mixture was stirred at room temperature and monitored by thin layer chromatography (TLC) until the starting material was not detected. The reaction mixture was diluted with 250 mL of water and extracted with ether (3 x 100 mL). The organic layers were combined, washed with water (2 x 100 mL), washed with a 10percent aqueous solution of lithium chloride (2 x 100 mL), and washed with brine (100 mL). The aqueous layers were back extracted with ether (100 mL), and the combined organic layers (400 mL) were dried over Na_2SO_4. Concentration under reduced pressure afforded hydroximoyl chlorides as a light yellow oil. The hydroximoyl chloride was directly used in the next step without further purification.

3) The corresponding alkyl acid (72 mmol, 1.2 equiv.), corresponding hydroximoyl chlorides (60 mmol, 1 equiv.), and 4-dimethylaminopyridine (3 mmol, 5 mol%) was mixed in a flask with a stirring bar. DCM (50 mL) was added. Then a solution of *N,N'* -dicyclohexylcatbodiimide (72 mmol, 1.2 equiv.) in DCM (20 mL) was added slowly at 0 °C. The reaction mixture was stirred at room temperature for 4h. Then the white precipitate was filtered off and the solution was concentrated under vacuum, then purified by column chromatography on silica gel.

***tert*-butyl (Z)-(1-(((chloro(phenyl)methylene)amino)oxy)-1-oxo-3-phenylpropan-2-yl)carbamate (a)**

white solid (723.8mg, 90%); mp : 115-118 °C; Eluent: PE/EA (5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.5 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 2H), 7.29 – 7.24 (m, 1H), 7.21 (d, *J* = 7.0 Hz, 2H), 5.03 (d, *J* = 8.6 Hz, 1H), 4.88 (q, *J* = 6.9 Hz, 1H), 3.22 (dd, *J* = 9.1, 6.2 Hz, 2H), 1.43 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.5 , 155.0 , 148.7 , 135.3 , 132.3 , 131.0 , 129.4 , 128.7 , 128.6 , 128.3, 127.2 , 80.3 , 53.5 , 38.5 , 28.3 . HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{24}ClN_2O_4$ 403.1419; found 403.1426.

***tert*-butyl (Z)-(1-(((chloro(phenyl)methylene)amino)oxy)-1-oxopropan-2-yl)carbamate (b)**

white solid (599.8mg, 92%); mp : 115-117 °C; Eluent: PE/EA (5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (dt, J = 7.4Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 5.11 (d, J = 8.0 Hz, 1H), 4.60 (q, J = 7.5 Hz, 1H), 1.53 (d, J = 7.3 Hz, 3H), 1.46 (s, 9H). ^{13}C{^{1}H} (126 MHz, $CDCl_3$) δ 169.9 , 155.0 , 148.7 , 132.2 , 131.1 , 128.6 , 128.2 , 80.22 , 48.33 , 28.3 , 18.6 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{15}H_{20}ClN_2O_4$ 327.1106; found 327.1117.

benzyl (Z)-(1-(((chloro(phenyl)methylene)amino)oxy)-1-oxopropan-2-yl)carbamate (c)

white solid (641.0mg, 89%); mp : 92-95 °C; Eluent: PE/EA (7:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.4 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.40 – 7.29 (m, 5H), 5.39 (d, *J* = 8.0 Hz, 1H), 5.15 (s, 2H), 4.77-4.64 (m, *J* = 7.2 Hz, 1H), 1.58 (d, *J* = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 169.5 , 155.5 , 149.03, 136.1 , 132.3 , 131.0 , 128.7 , 128.5 , 128.3 , 128.2 , 128.18, 67.17, 48.8 , 18.8 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{18}H_{18}ClN_2O_4$ 361.0950; found 361.0956.

***tert*-butyl (Z)-(1-(((chloro(phenyl)methylene)amino)oxy)-1-oxobutan-2-yl)carbamate (d)**

white solid (578.2mg, 85%); mp : 92-95 °C; Eluent: PE/EA (7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.6 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 5.11 (d, *J* = 8.6 Hz, 1H), 4.54 (q, *J* = 7.3 Hz, 1H), 1.98 (dt, *J* = 14.1, 6.9 Hz, 1H), 1.83 (dt, *J* = 14.2, 7.3 Hz, 1H), 1.47 (s, 9H), 1.05 (t, *J* = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 169.3, 155.3 , 148.6 , 132.2 , 131.0, 128.6 , 128.2 , 80.18, 53.7 , 28.3 , 26.0, 9.7 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{16}H_{22}ClN_2O_4$ 341.1263; found 341.1267.

***tert*-butyl (Z)-(1-(((chloro(phenyl)methylene)amino)oxy)-3-methyl-1-oxopentan-2-yl)carbamate (e)**

white solid (618.2mg, 84%); mp : 50-53 °C; Eluent: PE/EA (7:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 5.13 (d, *J* = 9.1 Hz, 1H), 4.54 (dd, *J* = 9.1, 5.0 Hz, 1H), 2.05 – 1.85 (m, 1H), 1.56 (m, 1H), 1.45 (s, 9H), 1.37 – 1.18 (m, 1H), 1.02 (d, J = 6.9 Hz, 3H), 0.97 (t, J = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.8 , 155.4 , 148.5 , 132.2 , 131.0 , 128.6 , 128.2 , 80.1 , 56.9 , 49.0 , 38.1 , 33.9 , 28.3 , 25.6 , 25.1 , 24.9 , 15.5 , 11.6 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{18}H_{26}ClN_2O_4$ 369.1576; found 369.1584.

***di-tert*-butyl (6-(((chloro(phenyl)methylene)amino)oxy)-6-oxohexane-1,5-diyl)(Z)- dicarbamate (f)**

white solid (840.4mg, 87%); mp : 97-100 °C; Eluent: PE/EA (4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.4 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.6 Hz, 2H), 5.21 (d, J = 8.4 Hz, 1H), 4.74 – 4.36 (m, 2H), 3.13 (q, J = 6.4 Hz, 2H), 1.98 – 1.90 (m, 1H), 1.85 – 1.75 (m, 1H), 1.58 – 1.47 (m, 4H), 1.45 (s, 9H), 1.43 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 169.3 , 156.0 , 155.4 , 148.7 , 132.2 , 131.0 , 128.6 , 128.2 , 80.2 , 79.1 , 52.4 , 39.9 , 32.2 , 29.6 , 28.4 , 28.3 , 22.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{23}H_{35}ClN_3O_6$ 484.2209; found 484.2216.

tert-butyl (Z)-(3-(4-(tert-butoxy)phenyl)-1-(((chloro(phenyl)methylene)amino)oxy)-1-oxopropan-2-yl)carbamate (g) white solid (872.2mg, 92%); mp : 117- 120 °C; Eluent: PE/EA (4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.5 Hz, 2H), 7.53 (t, J = 7.0 Hz, 1H), 7.44 (t, J = 7.4 Hz, 2H), 7.10 (s, 2H), 6.93 (d, J = 8.0 Hz, 2H), 5.05 (d, J = 8.6 Hz, 1H), 4.84 (q, J = 7.6, 7.2 Hz, 1H), 3.16 (d, J = 6.3 Hz, 2H), 1.43 (s, 9H), 1.31 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.6 , 155.0 , 154.6 , 148.7 , 132.3 , 131.0 , 130.1 , 129.8 , 128.6 , 128.3 , 124.3 , 80.2 , 78.4 , 53.6 , 37.9 , 28.8 , 28.3 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{25}H_{32}ClN_2O_5$ 475.1994; found 475.2001.

(Z)-4-(2-((tert-butoxycarbonyl)amino)-3-(((chloro(phenyl)methylene)amino)oxy)-3-oxopropyl)phenylhypoiodite (h) white solid (971.5mg, 92%); mp : 125-128 °C; Eluent: PE/EA (5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.4 Hz, 2H), 7.63 (d, J = 8.2 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 6.96 (d, J = 8.2 Hz, 2H), 5.04 (d, J = 8.5 Hz, 1H), 4.86 (dd, J = 13.5, 6.3 Hz, 1H), 3.16 (dd, J = 8.8, 6.0 Hz, 2H), 1.43 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.3 , 154.9 , 149.0 , 137.8 , 135.1 , 132.4 , 131.4 , 130.9 , 128.7 , 128.3 , 92.8 , 53.3 , 38.1 , 28.3 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{21}H_{23}ClIN_2O_4$ 529.0386; found 529.0382.

cyclohexyl (Z)-3-((tert-butoxycarbonyl)amino)-4-(((chloro(phenyl)methylene) amino)oxy)-4-oxobutanoate (i) white solid (822.6mg, 92%); mp: 104-107 °C; Eluent: PE/EA (5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.5 Hz, 2H), 7.53 (t, J = 7.3 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 5.61 (d, J = 9.2 Hz, 1H), 4.90 – 4.78 (m, 2H), 3.13 (dd, J = 17.1, 4.9 Hz, 1H), 2.91 (dd, J = 17.1, 4.6 Hz, 1H), 1.86 – 1.84 (m, 2H), 1.76 – 1.64 (m, 2H), 1.48 (s, 9H), 1.44 – 1.18 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.1 , 167.5 , 155.3 , 148.8 , 132.2 , 131.0 , 128.6 , 128.3 , 80.4 , 73.9 , 49.3 , 37.1 , 31.4 , 28.3 , 25.2 , 23.6 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{22}H_{30}ClN_2O_6$ 453.1787; found 453.1794.

tert-butyl (Z)-(6-(tert-butoxy)-1-(((chloro(phenyl)methylene)amino)oxy)-1,5- dioxohexan-2-yl)carbamate (j)

white solid (783.2mg, 89%); mp : 115-118 °C; Eluent: PE/EA (5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 7.4 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 5.19 (d, J = 8.7 Hz, 1H), 4.59 (q, J = 7.4, 6.7 Hz, 1H), 2.54 – 2.34 (m, 2H), 2.31 – 2.18 (m, 1H), 2.14 – 2.01 (m, 1H), 1.46 (s, 18H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 171.8 , 168.9 , 155.3 , 148.9 , 132.3 , 131.1 , 128.6 , 128.3 , 80.9 , 80.3 , 52.2 , 31.6 , 28.3 , 28.1 , 27.6 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{21}H_{30}ClN_2O_6$ 441.1787; found 441.1793.

tert-butyl (Z)-(1-(((chloro(phenyl)methylene)amino)oxy)-6-methoxy-1,5-dioxo hexan-2-yl)carbamate (k)

white solid (678.3mg, 85%); mp : 94-97 °C; Eluent: PE/EA (5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.4 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2), 5.21 (d, J = 8.6 Hz, 1H), 4.62 (q, J = 7.7 Hz, 1H), 3.69 (s, 3H), 2.62 – 2.42 (m, 2H), 2.35 – 2.27 (m, 1H), 2.17 – 1.96 (m, 1H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.9 , 168.7 , 155.2 , 148.9 , 132.3 , 131.0 , 128.6 , 128.3 , 80.4 , 52.0 , 51.9 , 30.0 , 28.2 , 27.7 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{18}H_{24}ClN_2O_6$ 399.1317; found 399.1327.

tert-butyl (Z)-(1-(((chloro(phenyl)methylene)amino)oxy)-4-(methylthio)-1-oxobutan-2-yl)carbamate (l)

white solid (669.1mg, 82%); mp : 90-93 °C; Eluent: PE/EA (8:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.4 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 5.19 (d, *J* = 8.7 Hz, 1H), 4.93 – 4.61 (m, 1H), 2.64 (m, 2H), 2.32 – 2.18 (m, 1H), 2.13 (s, 3H), 2.08 (m, 1H), 1.47 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 169.0 , 155.2 , 148.9 , 132.3 , 131.0 , 128.7 , 128.3 , 80.4 , 51.8 , 32.1 , 29.9 , 28.3 , 15.4 . HRMS(ESI) m/z: $[M + Na]^+$ Caled for $C_{17}H_{23}ClN_2O_4SNa$ 409.0959; found 409.0964.

General procedures for decarboxylative Minisci reaction. Condition A: Under argon, $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (2 mol%) and NHBC esters (0.2 mmol, 1 equiv.), corresponding N-heteroarene (0.4 mmol, 2 equiv.) were placed in a tube with a stirring bar, then dry MeCN (2 mL) was added at room temperature. After that, the tube was exposed to two 60 W blue LEDs at room temperature about 12 h until the reaction was completed as monitored by TLC analysis. The reaction mixture was evaporated in *vacuo*. The crude products were directly purified by flash chromatography on silica gel to give the desired product.

Condition B: The corresponding aminoacid (1.2 mmol, 1.2 equiv.), hydroximoyl chlorides (1 mmol, 1 equiv.), and 4-dimethylaminopyridine (0.05 mmol, 5 mol%) was mixed in a flask with a stirring bar before dichloromethane (8 mL) was added. Then a solution of N,N'-dicyclohexylcarbodiimide (1.2 mmol, 1.2 equiv.) in DCM (2 mL) was added

slowly at 0 °C. The reaction mixture was stirred at room temoerature for 4 h. Then Ir[{dF(CF_3)ppy}$_2$(dtbbpy)]PF_6 (2 mol%), and corresponding N-heteroarene (2 mmol, 2.0 equiv.) were dissolved in DCM (1 ml), then added to the flask. After that, the flask was exposed to two 60 W blue LEDs at room temperature about 12 h until the reaction was completed as monitored by TLC analysis. The reaction mixture was evaporated in vacuo. The crude products were directly purified by flash chromatography on silica gel to give the desired product.

Large-Scale Synthesis. The reaction took place in flask (100 mL) equipped with a stir bar then NHBC ester **f** (1.21 g, 2.5 mmol, 1.0 eq), 4-methylquinoline (0.75 g, 5 mmol， 2.0 eq) and Ir[{dF(CF_3)ppy}$_2$(dtbbpy)]PF_6 (56mg, 2 mol%) was added into bottle. Then 50 mL of MeCN were added into bottle by syringe. The flask was sealed and irradiated with blue LED lamps for 12 h. When the reaction was finished, the solution was removed with a rotary evaporator. The pure product was obtained in 75% yield (0.83 g) by column chromatography on silica gel (PE/EA=10:1).

tert-butyl (1-(4-methylquionlin-2-yl)-2phenylethy)carbamate (1) Following the general procedure condition A, **1** was purified by silica gel chromatography (PE/EA=10:1); 61.8 mg (82%); white solid; mp :124-126 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 8.3 Hz, 1H), 7.95 (d, J = 8.2 Hz, 1H), 7.69 (t, J = 7.5 Hz, 2H), 7.53 (t, J = 7.5 Hz, 1H), 7.22 – 7.17 (m, 3H), 7.08 – 6.97 (m, 2H), 6.81 (s, 1H), 6.14 (d, J = 7.8 Hz, 1H), 5.14 – 5.10 (m, 1H), 3.30 (dd, J = 13.4, 5.8 Hz, 1H), 3.16 (dd, J = 13.3, 7.7 Hz, 1H), 2.58 (s, 3H), 1.46 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.3 , 155.3, 147.3 , 144.2 , 137.5 , 129.7 , 129.1 , 128.1 , 127.3 , 126.4 ,126.3 , 125.9 , 123.7 , 121.2 , 79.2 , 56.9 , 42.7 , 28.4 , 18.6 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{23}H_{27}N_2O_2$ 363.2067; found 363.2074.

tert-butyl (1-(4-methylquionlin-2-yl)ethyl)carbamate (2) Following the general procedure condition A, **2** was purified by silica gel chromatography (PE:EA=10:1) ; 61.8 mg (90%); white solid; mp : 117-120 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.3 Hz, 1H), 7.67 (t, J = 8.3 Hz, 1H), 7.51 (t, J = 8.1 Hz, 1H), 7.15 (s, 1H), 6.30 (d, J = 7.0 Hz, 1H), 4.98 – 4.92 (m, 1H), 2.66 (s, 3H), 1.53 (d, J = 6.8 Hz, 3H), 1.47 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 161.1 , 155.3 , 147.0, 144.8 , 129.5 , 129.1 , 127.2 , 125.9 , 123.6 , 120.0 , 79.0 , 51.2 , 28.4 , 22.7 , 18.7 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{17}H_{23}N_2O_2$ 287.1754; found 287.1765.

benzyl (2-phenyl-1-(4- methylquionlin-2-yl)ethyl) carbamate (3) Following the general procedure condition A, **3** was purified by silica gel chromatography (PE:EA=10:1) ; 41.6 mg (65%); white solid; mp ; 88-91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 9.2 Hz, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 8.1 Hz, 1H), 7.45 – 7.27 (m, 5H), 7.17 (s, 1H), 6.67 (d, J = 6.9 Hz, 1H), 5.18 – 5.10 (m, 2H), 5.05 – 4.96 (m, 1H), 2.70 (s, 3H), 1.57 (d, J = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.4, 155.8, 147.0 , 145.1 , 136.7 , 129.6 , 129.3 , 128.5 , 128.2 , 128.0 , 127.3 , 126.1 , 123.7 , 119.9 , 66.6 , 51.6 , 22.8 , 18.8 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{20}H_{21}N_2O_2$ 321.1598; found 321.1607.

tert-butyl (1-(4-methylquinolin-2-yl)propyl)carbamate (4) Following the general procedure condition A, **4** was purified by silica gel chromatography (PE:EA=10:1) ; 57.0 mg (95%); white solid; mp : 91-94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.3 Hz, 1H), 7.95 (d, J = 8.3 Hz, 1H), 7.68 (t, J = 7.0 Hz, 1H), 7.52 (t, J = 8.3 Hz, 1H), 7.16 (s, 1H), 6.13 (d, J = 7.8 Hz, 1H), 4.83 (q, J = 6.7 Hz, 1H), 2.68 (s, 3H), 2.08 – 1.95 (m, 1H), 1.91 – 1.76 (m, 1H), 1.46 (s, 9H), 0.87 (t, J = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.2 , 155.6 , 147.2 , 144.5 , 129.6 , 129.1 , 127.3 , 125.9 , 123.6 , 120.8 , 79.0 , 56.5 , 29.4 , 28.4 , 18.7 , 9.7. HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{18}H_{24}N_2O_2$ 301.1911; found 301.1917.

tert-butyl (2-methyl-1-(4-methylquinolin-2-yl)-2l3-butyl)carbamate (5) Following the general procedure condition A, **5** was purified by silica gel chromatography (PE:EA=10:1) ; 44.6 mg (61%) (dr = 1:1); white solid; mp : 78-81 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.69 (t, J = 7.7 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.16 (d, J = 4.2 Hz, 1H), 6.09 (t, J = 7.3 Hz, 1H), 4.84 (ddd, J = 56.1, 8.7, 5.6 Hz, 1H), 2.70 (s, 3H), 2.12 – 1.91 (m, 1H), 1.67 – 1.52 (m, 1H), 1.48 (d, J = 4.6 Hz, 9H), 1.23 – 1.12 (m, 1H), 0.95 (dt, J = 25.9, 7.4 Hz, 3H), 0.87 (dd, J = 6.9, 3.4 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.2& 159.9 , 156.0&155.8 , 147.3& 147.1 , 144.1&144.0 , 129.6 , 129.0 , 127.2, 125.8, 123.6, 121.7& 121.3 , 79.0 , 59.8&58.9 , 41.0& 40.7 , 28.4 , 26.6& 25.0, 18.7, 15.6 &14.1 , 11.9 &11.6 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{20}H_{29}N_2O_2$ 329.2224; found 329.2228.

tert-butyl 4-((tert-butoxycarbonyl)amino)-4-(4-methylquinolin-2-yl)butanoate (6) Following the general procedure condition A, **6** was purified by silica gel chromatography (PE:EA=5:1) ; 60.8 mg (76%); white solid; mp : 147-149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.68 (t, J = 8.2 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.19 (s, 1H), 6.16 (d, J = 7.8 Hz, 1H), δ 4.94 (q, J = 6.7 Hz, 1H), 2.69 (s, 3H), 2.40 – 2.15 (m, 3H), 2.12 – 1.95 (m, 1H), 1.46 (s, 9H), 1.40 (s, 9H), ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 172.6 , 159.7 , 155.6 , 147.2 , 144.9 , 129.6 , 129.2 , 127.4 , 126.0 , 123.6 , 120.5 , 80.2 , 79.2 , 54.7 , 31.5 , 31.5 , 28.4 , 28.0 , 18.8 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{23}H_{33}N_2O_4$ 401.2435; found 401.2448.

tert-butyl (1-(4-methylquinolin-2-yl)-3-(methylthio)propyl)carbamate (7) Following the general procedure condition A, **7** was purified by silica gel chromatography (PE:EA=5:1) ; 51.9 mg (75%); white solid; mp : 87-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.3 Hz, 1H), 7.68 (t, J = 8.2 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.18 (s, 1H), 6.18 (d, J = 7.8 Hz, 1H), 5.01 (d, J = 6.9 Hz, 1H), 2.68 (s, 3H), 2.60 – 2.50 (m, 1H), 2.46 – 2.34 (m, 1H), 2.31 – 2.21 (m, 1H), 2.15 – 2.08 (m, 1H), 2.07 (s, 3H), 1.46 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.4 , 155.5 , 147.2 , 144.9 , 129.6 , 129.2 , 127.3 , 126.0 , 123.6 , 120.6 , 79.2 , 54.6 , 36.1 , 30.0 , 28.4 , 18.7 , 15.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{19}H_{27}N_2O_2S$ 347.1788; found 347.1794.

tert-butyl (2-(4-iodophenyl)-1-(4-methylquinolin-2-yl)ethyl)carbamate (8) Following the general procedure condition A, **8** was purified by silica gel chromatography (PE:EA=5:1) ; 63.5 mg (65%); white solid; mp : 127-130 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.48 (d, J = 7.9 Hz, 2H), 6.86 (s, 1H), 6.74 (d, J = 7.8 Hz, 2H), 6.11 (d, J = 7.7 Hz, 1H), 5.06 (q, J = 7.0 Hz, 1H), 3.25 – 3.16 (m, 2H), 2.62 (s, 3H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 158.8 , 155.3 , 147.3 , 144.5 , 137.1 , 131.8 , 129.6 , 129.2 , 127.3 , 126.1 , 123.7 , 121.1 , 91.7 , 79.4 , 56.6 , 42.0 , 28.4 , 18.7 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{23}H_{26}IN_2O_2$ 489.1033; found 489.1040.

tert-butyl (2-(4-(tert-butoxy)phenyl)-1-(4-methylquinolin-2-yl)ethyl)carbamate (9) Following the general procedure condition A, **9** was purified by silica gel chromatography (PE:EA=5:1) ; 57.3 mg (66%); white solid; mp :120-123 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 1H), 7.92 (d, J = 7.1 Hz, 1H), 7.67 (t, J = 8.1 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 6.88 (d, J = 8.0 Hz, 2H), 6.79 (d, J = 8.1 Hz, 2H), 6.73 (s, 1H), 6.21 (d, J = 7.7 Hz, 1H), 5.05 (q, J = 7.3 Hz, 1H), 3.28 (dd, J = 13.3, 5.7 Hz, 1H), 3.05 (dd, J = 13.3, 8.1 Hz, 1H), 2.54 (s, 3H), 1.45 (s, 9H), 1.29 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.3 , 155.3 , 153.6 , 147.2 , 144.0 , 132.5 , 129.9 , 129.5 , 129.0 , 127.2 , 125.9 , 123.9 , 123.6 , 121.3 , 79.1 , 78.1 , 57.1 , 42.2 , 28.7 , 28.4 , 18.6. HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{27}H_{35}N_2O_3$ 435.2648; found 435.2648.

methyl 4-((tert-butoxycarbonyl)amino)-4-(4-methylquinolin-2-yl)butanoate (10) Following the general procedure condition A, **10** was purified by silica gel chromatography (PE:EA=5:1) ; 53.7 mg (75%); white solid; mp : 99-102 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 1H), 7.95 (dd, J = 8.4, 1.3 Hz, 1H), 7.68 (t, J = 8.2 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.18 (s, 1H), 6.20 (d, J = 7.7 Hz, 1H), 5.07 – 4.89 (m, 1H), 3.60 (s, 3H), 2.68 (s, 3H), 2.49 – 2.39 (m, 1H), 2.37 – 2.25 (m, 2H), 2.13 – 2.02 (m, 1H), 1.46 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 173.7 , 159.3 , 155.6 , 147.1 , 145.0 , 129.6 , 129.2 , 127.3 , 126.1 , 123.6 , 120.5 , 79.3 , 54.5 , 51.5 , 31.6 , 30.0 , 28.4 , 18.8. HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{20}H_{27}N_2O_4$ 359.1965; found 359.1970.

Di-tert-butyl (1-(4-methylquinolin-2-yl)pentane-1,5-diyl)dicarbamate (11) Following the general procedure condition A, **11** was purified by silica gel chromatography (PE:EA=5:1) ; 68.2 mg (77%); white solid; mp :133-136 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.68 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.15 (s, 1H), 6.11 (d, J = 7.5 Hz, 1H), 4.87 (q, J = 7.0 Hz, 1H), 4.60 (s, 1H), 3.07 (t, J = 7.4 Hz, 2H), 2.69 (s, 3H), 2.01 – 1.88 (m, 1H), 1.81 (d, J = 11.9 Hz, 1H), 1.49–1.30 (m, 22H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.3 , 156.0 , 155.7 , 147.3 , 144.8 , 129.6 , 129.2 , 127.3 , 126.0 , 123.7 , 120.6 , 79.2 , 78.9, 55.2, 40.3, 36.4, 29.6, 28.4, 28.4 , 22.6 , 18.8 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{25}H_{38}N_3O_4$ 444.2857; found 444.2861.

Cyclohexyl 3-((tert-butoxycarbonyl)amino)-3-(4-methylquinolin-2-yl)propanoate (12) Following the general procedure condition A, **12** was purified by silica gel chromatography (PE:EA=5:1) ; 66.1 mg (80%); white solid; mp :

107-110 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.32 (s, 1H), 6.08 (d, J = 8.6 Hz, 1H), 5.41 – 5.14 (m, 1H), 4.70 (dq, J = 9.0, 4.8, 4.3 Hz, 1H), 3.12 (dd, J = 15.5, 5.3 Hz, 1H), 2.95 (dd, J = 15.5, 6.6 Hz, 1H), 2.68 (s, 3H), 1.80 – 1.68 (m, 2H), 1.63 (d, J = 7.6 Hz, 2H), 1.47 (s, 9H), 1.38 – 1.09 (m, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 170.9 , 159.3 , 155.4 , 147.2 , 144.8 , 129.7 , 129.1 , 127.4 , 126.1 , 123.6 , 120.7 , 79.5 , 72.8 , 52.3 , 40.0 , 31.5 , 28.4 , 25.3 , 23.6 , 18.8 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{24}H_{33}N_2O_4$ 413.2435; found 413.2442.

tert-butyl (2-phenyl-1-(quinolin-2-yl)ethyl)carbamate (13) Following the general procedure condition A, **13** was purified by silica gel chromatography (PE:EA=5:1) ; 38.3 mg (55%); white solid; mp : 129-132 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J = 8.5 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.71 (t, J = 7.7 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), δ 7.2 – 7.1 (m, 3H), 7.0 – 7.0 (m, 2H), 7.0 (d, J = 8.4 Hz, 1H).5.16 (q, J = 7.1 Hz, 1H), 3.34 (dd, J = 13.5, 5.6 Hz, 1H), 3.15 (dd, J = 13.1, 8.0 Hz, 1H), 1.46 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.7 , 155.3 , 147.5 , 137.4 , 135.9 , 129.6 , 129.4 , 129.1 , 128.1 , 127.5 , 127.3 , 126.3 , 126.2 , 120.6 , 79.3 , 57.1 , 42.8 , 28.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{22}H_{25}N_2O_2$ 349.1911; found 349.1917.

tert-butyl (2-phenyl-1-(4-phenylquinolin-2-yl)ethyl)carbamate (14) Following the general procedure condition A, **14** was purified by silica gel chromatography (PE:EA=5:1) ; 63.6 mg (75%); white solid; mp : 147-150 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.3 Hz, 1H), 7.72 (t, J = 7.7 Hz, 1H), 7.47 (dt, J = 7.6, 4.8 Hz, 4H), 7.32 (d, J = 6.7 Hz, 2H), 7.20 (d, J = 5.8 Hz, 3H), 7.04 (d, J = 6.6 Hz, 2H), 6.83 (s, 1H), 6.25 (d, J = 7.7 Hz, 1H), 5.19 (q, J = 7.3 Hz, 1H), 3.40 (dd, J = 13.3, 5.7 Hz, 1H), 3.14 (dd, J = 13.2, 7.9 Hz, 1H), 1.48 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.1 , 155.3 , 148.1 , 148.0 , 137.9 , 137.5 , 129.7 , 129.5 , 129.4 , 129.2 , 128.4 , 128.3 , 128.2 , 126.3 , 126.2 , 125.8 , 125.7 , 120.8 , 79.3 , 57.2 , 43.1 , 28.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{28}H_{29}N_2O_2$ 425.2224; found 425.2230.

tert-butyl (1-(3-methylquinolin-2-yl)-2-phenylethyl)carbamate (15) Following the general procedure condition A, **15** was purified by silica gel chromatography (PE:EA=5:1) ; 55.8 mg (77%); white solid; mp : 129-132 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J = 8.4 Hz, 1H), 7.78 (s, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.20 – 7.15 (m, 3H), 7.00 (dt, J = 7.3, 3.6 Hz, 2H), 6.22 (d, J = 8.5 Hz, 1H), 5.40 (q, J = 7.7 Hz, 1H), 3.30 – 3.16 (m, 2H), 2.19 (s, 3H), 1.48 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.7 , 155.2 , 146.2 , 137.4 , 136.0 , 129.6 , 128.9 , 128.7 , 128.4 , 128.0 , 127.4 , 126.7 , 126.2 , 126.2 , 79.1 , 53.1 , 43.0 , 28.4 , 18.3 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{23}H_{27}N_2O_2$ 363.2067; found 363.2074.

tert-butyl (1-(6-chloroquinolin-2-yl)-2-phenylethyl)carbamate (16) Following the general procedure condition A, **16** was purified by silica gel chromatography (PE:EA=10:1) ; 39.0 mg (51%); white solid; mp : 118-121 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.9 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 2.3 Hz, 1H), 7.63 (dd, J = 9.0, 2.4 Hz, 1H), 7.20 – 7.10 (m, 3H), 6.97 (q, J = 3.8 Hz, 3H), 6.07 (d, J = 7.7 Hz, 1H), 5.14 (q, J = 7.3 Hz, 1H), 3.31 (dd, J = 13.3, 5.6 Hz, 1H), 3.13 (dd, J = 13.2, 8.0 Hz, 1H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.2 , 155.3 , 145.9 , 137.2 , 135.0 , 131.9 , 130.7 , 130.4 , 129.6 , 128.2 , 127.8 , 126.4 , 126.2 , 121.4 , 79.4 , 57.1 , 42.7 , 28.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{22}H_{24}ClN_2O_2$ 383.1521; found 383.1527.

tert-butyl (1-(4-chloroquinolin-2-yl)ethyl)carbamate (17) Following the general procedure condition A, **17** was purified by silica gel chromatography (PE:EA=10:1) ; 36.1 mg (59%); white solid; mp : 130-135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.75 (t, J = 8.3 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.45 (s, 1H), 6.02 (d, J = 6.7 Hz, 1H), 5.03 – 4.91 (m, 1H), 1.54 (d, J = 6.8 Hz, 3H), 1.47 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.8 , 155.2 , 148.2 , 143.0 , 130.4 , 129.4 , 127.2 , 125.4 , 124.0 , 119.4 , 79.4 , 51.4 , 28.4 , 22.5 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{16}H_{20}ClN_2O_2$ 307.1208; found 307.1217.

tert-butyl (1-(4-phenylquinolin-2-yl)ethyl)carbamate (18) Following the general procedure condition A, **18** was purified by silica gel chromatography (PE:EA=10:1) ; 50.1 mg (72%); white solid; mp : 160-163 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 9.3 Hz, 1H), 7.71 (t, J = 8.3 Hz, 1H), 7.58 – 7.39 (m, 6H), 7.28 (s, 1H), 7.26 (s, 1H), 6.25 (d, J = 7.1 Hz, 1H), 5.19 – 4.86 (m, 1H), 1.58 (d, J = 6.8 Hz, 3H), 1.49 (s, 9H). ^{13}C{^{1}H} NMR

(126 MHz, $CDCl_3$) δ 161.12 , 155.41 , 149.25 , 147.86 , 138.04 , 129.53 , 129.44 , 128.59 , 128.47 , 126.30 , 125.75 , 119.57 , 79.29 , 51.53 , 28.50 , 22.95 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{22}H_{25}N_2O_2$ 349.1911; found 349.1914.

tert-butyl (1-(isoquinolin-1-yl)-2-phenylethyl)carbamate (19) Following the general procedure condition A, **19** was purified by silica gel chromatography (PE:EA=5:1) ; 28.5 mg (41%); white solid; mp : 166-168 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.42 (d, J = 5.6 Hz, 1H), 8.03 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 8.2 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.55 (d, J = 5.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.16 – 7.05 (m, 3H), 6.88 (dd, J = 6.6, 3.0 Hz, 2H), 6.18 (d, J = 8.3 Hz, 1H), 5.91 (q, J = 6.5 Hz, 1H), 3.30 (dd, J = 13.3, 6.6 Hz, 1H), 3.26 (ddd, J = 43.0, 13.3, 6.3 Hz, 2H), 1.43 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 159.0 , 155.2 , 141.2 , 137.2 , 136.1 , 129.9 , 129.6 , 127.9 , 127.3 , 127.2 , 126.2 , 125.7 , 124.3 , 120.2 , 79.1 , 52.0 , 42.9 , 28.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{22}H_{25}N_2O_2$ 349.1911; found 349.1918.

tert-butyl (1-(6-fluoroisoquinolin-1-yl)-2-phenylethyl)carbamate (20) Following the general procedure condition A, **20** was purified by silica gel chromatography (PE:EA=5:1) ; 54.2 mg (74%); liquid； ^1H NMR (500 MHz, $CDCl_3$) δ 8.42 (d, J = 5.7 Hz, 1H), 7.98 (dd, J = 9.4, 5.4 Hz, 1H), 7.50 (d, J = 5.7 Hz, 1H), 7.37 (dd, J = 9.1, 2.6 Hz, 1H), 7.21 (td, J = 8.9, 2.6 Hz, 1H), 7.11 – 7.06 (m, 3H), 6.87 (dd, J = 6.3, 3.0 Hz, 2H), 6.16 (d, J = 8.3 Hz, 1H), 5.92 – 5.69 (m, 1H), 3.30 – 3.20 (m, 2H), 1.43 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 163.7 , 161.7 , 159.2 , 155.2 , 142.3 , 137.8 , 137.7 , 137.1 , 129.5 , 128.0 , 127.6 , 127.6 , 126.3 , 123.1 , 119.8 , 119.8 , 117.7 , 117.5 , 110.4 , 110.2 , 79.3 , 52.2 , 43.0 , 28.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{22}H_{24}FN_2O_2$ 367.1816; found 367.1821.

tert-butyl (1-(6-chloroisoquinolin-1-yl)-2-phenylethyl)carbamate (21) Following the general procedure condition A, **21** was purified by silica gel chromatography (PE:EA=5:1) ; 40.5 mg (53%); liquid; ^1H NMR (500 MHz, $CDCl_3$) δ 8.46 (d, J = 5.7 Hz, 1H), 7.93 (d, J = 9.1 Hz, 1H), 7.77 (d, J = 2.1 Hz, 1H), 7.47 (d, J = 5.7 Hz, 1H), 7.42 (dd, J = 9.1, 2.2 Hz, 1H), 7.17 – 7.07 (m, 3H), 6.89 (dd, J = 6.5, 3.1 Hz, 2H), 6.17 (d, J = 8.4 Hz, 1H), 5.86 (q, J = 6.6 Hz, 1H), 3.27 (d, J = 6.5 Hz, 2H), 1.46 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 159.3 , 155.2 , 142.4 , 137.0 , 136.9 , 136.2 , 129.5 , 128.1 , 128.0 , 126.3 , 126.2 , 125.8 , 124.0 , 119.3 , 79.3 , 52.1 , 42.9 , 28.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{22}H_{24}ClN_2O_2$ 383.1521; found 383.1521.

tert-butyl (1-(6-bromoisoquinolin-1-yl)-2-phenylethyl)carbamate (22) Following the general procedure condition A, **22** was purified by silica gel chromatography (PE:EA=5:1) ; 48.6 mg (57%); white solid; mp : 158-161 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.44 (d, J = 5.6 Hz, 1H), 7.96 (d, J = 2.0 Hz, 1H), 7.83 (d, J = 9.0 Hz, 1H), 7.54 (dd, J = 9.0, 2.0 Hz, 1H), 7.46 (d, J = 5.7 Hz, 1H), 7.11 – 7.08 (m, 3H), 6.86 (dd, J = 6.6, 3.0 Hz, 2H), 6.09 (d, J = 8.4 Hz, 1H), 5.82 (q, J = 6.7 Hz, 1H), 3.23 (d, J = 6.4 Hz, 2H), 1.43 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 159.5 , 155.2 , 142.4 , 137.2 , 137.0 , 130.7 , 129.5 , 129.3 , 128.0 , 126.4 , 126.1 , 124.8 , 124.3 , 119.1 , 79.3 , 52.1 , 43.0 , 28.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{22}H_{24}BrN_2O_2$ 427.1016; found 427.1023.

tert-butyl (1-(6-methylisoquinolin-1-yl)-2-phenylethyl)carbamate (23) Following the general procedure condition A, **23** was purified by silica gel chromatography (PE:EA=5:1) ; 49.4 mg (68%); white solid; mp : 140-142 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.36 (d, J = 5.6 Hz, 1H), 7.94 (d, J = 8.7 Hz, 1H), 7.55 (s, 1H), 7.45 (d, J = 5.7 Hz, 1H), 7.34 (d, J = 8.6 Hz, 1H), 7.12 – 7.09 (m, 3H), 6.89 (dd, J = 6.6, 2.9 Hz, 2H), 6.21 (d, J = 8.3 Hz, 1H), 5.88 (dt, J = 8.4, 6.3 Hz, 1H), 3.31 (dd, J = 13.3, 6.5 Hz, 1H), 3.21 (dd, J = 13.3, 6.0 Hz, 1H), 2.51 (s, 3H), 1.44 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 158.6 , 155.2 , 141.3 , 140.2 , 137.3 , 136.5 , 129.6 , 129.5 , 127.8 , 126.1 , 126.1 , 124.1 , 124.1 , 119.7 , 79.0 , 52.0 , 42.7 , 28.4 , 21.8 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{23}H_{27}N_2O_2$ 363.2067; found 363.2071.

tert-butyl (1-(6-methoxyisoquinolin-1-yl)-2-phenylethyl)carbamate (24) Following the general procedure condition A, **24** was purified by silica gel chromatography (PE:EA=5:1) ; 52.9 mg (70%); white solid; mp : 134-136 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, J = 5.7 Hz, 1H), 7.88 (d, J = 9.3 Hz, 1H), 7.43 (d, J = 5.7 Hz, 1H), 7.11 – 7.02 (m, 5H), 6.89 (dd, J = 6.5, 2.9 Hz, 2H), 6.19 (d, J = 8.3 Hz, 1H), 5.81 (q, J = 6.7 Hz, 1H), 3.91 (s, 3H), 3.24 (qd, J = 13.2, 6.4 Hz, 2H), 1.43 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 160.3 , 158.3 , 155.2 , 141.8 , 138.2 , 137.3 , 129.5 , 127.9 , 126.2 , 126.1 , 121.4 , 120.0 , 119.5 , 104.6 , 79.0 , 55.3 , 52.0 , 42.9 , 28.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{23}H_{27}N_2O_3$ 379.2016; found 379.2020.

tert-butyl (1-(5-bromoisoquinolin-1-yl)ethyl)carbamate (25) Following the general procedure condition A, **25** was purified by silica gel chromatography (PE:EA=5:1) ; 21.0 mg (30%) ; white solid; mp : 157-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 5.9 Hz, 1H), 8.18 (d, J = 8.5 Hz, 1H), 8.03 – 7.85 (m, 2H), 7.52 – 7.43 (m, 1H), 6.32 (d, J = 7.8 Hz, 1H), 5.85 – 5.52 (m, 1H), 1.54 (d, J = 6.7 Hz, 3H), 1.46 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 161.1 , 155.3 , 142.7 , 135.5 , 133.9 , 127.7 , 126.2 , 124.0 , 122.5 , 119.1 , 79.3 , 47.2 , 28.4 , 23.2 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{16}H_{20}BrN_2O_2$ 351.0703; found 351.0703.

tert-butyl (1-(3-methylquinolin-2-yl)ethyl)carbamate (26) Following the general procedure condition A, **26** was purified by silica gel chromatography (PE:EA=5:1) ; 37.2 mg (65%); white solid; mp : 136-138 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, J = 5.7 Hz, 1H), 8.05 (d, J = 8.6 Hz, 1H), 7.57 (s, 1H), 7.48 – 7.37 (m, 2H), 6.42 (d, J = 7.7 Hz, 1H), 5.67 (p, J = 6.8 Hz, 1H), 2.51 (s, 3H), 1.53 (d, J = 6.7 Hz, 3H), 1.46 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.2 , 155.3 , 141.3 , 140.3 , 136.7 , 129.6 , 126.3 , 124.1 , 123.3 , 119.7 , 79.0 , 47.1 , 28.4 , 23.1 , 21.8 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{17}H_{23}N_2O_2$ 287.1754; found 287.1764.

methyl 6-(1-((tert-butoxycarbonyl)amino)-2-phenylethyl)nicotinate (27) Following the general procedure condition A, **27** was purified by silica gel chromatography (PE:EA=5:4) ; 67.6 mg (95%); white solid; mp : 83-85 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.08 (d, J = 7.5 Hz, 1H), 7.19 – 7.14 (m, 3H), 6.95 – 6.92 (m, 3H), 5.75 (d, J = 8.3 Hz, 1H), 5.03 (q, J = 6.8 Hz, 1H), 3.93 (s, 3H), 3.22 (dd, J = 13.4, 6.0 Hz, 1H), 3.05 (dd, J = 13.3, 7.9 Hz, 1H), 1.41 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.6 , 163.9 , 155.1 , 150.5 , 137.2 , 136.9 , 129.4 , 128.3 , 126.5 , 124.6 , 121.9 , 79.5 , 56.9 , 52.3 , 42.5 , 28.3 . HRMS(ESI) m/z: $[M + Na]^+$ Caled for $C_{20}H_{24}N_2O_4Na$ 379.1628; found 379.1627.

tert-butyl (2-phenyl-1-(5-(trifluoromethyl)pyridin-2-yl)ethyl)carbamate (28) Following the general procedure condition A, **28** was purified by silica gel chromatography (PE:EA=5:1); 60.1 mg (82%); white solid; mp : 80-83 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.73 (d, J = 7.7 Hz, 1H), 7.22 – 7.16 (m, 3H), 7.05 – 6.86 (m, 3H), 5.72 (d, J = 8.2 Hz, 1H), 5.06 (q, J = 7.1 Hz, 1H), 3.22 (dd, J = 13.5, 6.2 Hz, 1H), 3.06 (dd, J = 13.3, 7.8 Hz, 1H), 1.42 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 163.7 , 155.1 , 146.2 (q, J = 4.1 Hz), 136.8 , 133.2 (q, J = 3.5 Hz), 129.3 , 128.3, 126.6 , 125.2 (q, J = 33.0 Hz), 123.4 (q, J = 272.2 Hz), 121.9 , 79.7 , 56.8 , 42.5 , 28.3 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{19}H_{22}F_3N_2O_2$ 367.1628; found 367.1638.

tert-butyl (2-phenyl-1-(5-propionylpyridin-2-yl)ethyl)carbamate (29) Following the general procedure condition A, **29** was purified by silica gel chromatography (PE:EA=5:4) ; 43.2 mg (61%); white solid; mp : 84-86 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (d, J = 2.2 Hz, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.17 (d, J = 7.2 Hz, 3H), 6.96 (d, J = 7.2 Hz, 3H), 5.74 (d, J = 8.1 Hz, 1H), 5.03 (q, J = 7.1 Hz, 1H), 3.21 (dd, J = 13.4, 6.1 Hz, 1H), 3.05 (dd, J = 13.3, 7.9 Hz, 1H), 2.98 (q, J = 7.2 Hz, 2H), 1.41 (s, 9H), 1.22 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 199.1 , 163.8 , 155.1 , 149.1 , 136.9 , 135.5 , 130.8 , 129.3 , 128.3 , 126.5 , 122.1 , 79.6 , 56.8 , 42.4 , 32.1 , 28.3 , 7.8 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{21}H_{27}N_2O_3$ 355.2016; found 355.2026.

methyl 5-bromo-6-(1-((tert-butoxycarbonyl)amino)ethyl)nicotinate (30) Following the general procedure condition A, **30** was purified by silica gel chromatography (PE:EA=10:1) ; 53.7 mg (75%); white solid; mp : 108-111 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (d, J = 1.8 Hz, 1H), 8.42 (d, J = 1.8 Hz, 1H), 5.88 (d, J = 8.3 Hz, 1H), 5.33 (dd, J = 9.5, 5.2 Hz, 1H), 3.95 (s, 3H), 1.56 – 1.28 (m, 12H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 164.4 , 164.0 , 155.0 , 148.6 , 141.5 , 126.0 , 118.9 , 79.5 , 52.7 , 49.9 , 28.4 , 21.2 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{14}H_{20}BrN_2O_4$ 359.0601; found 359.0603.

methyl 6-(1-((tert-butoxycarbonyl)amino)-2-phenylethyl)-2-methylnicotinate (31) Following the general procedure condition A, **31** was purified by silica gel chromatography (PE:EA=5:4) ; 67.4 mg (91%); white solid; mp : 79-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.0 Hz, 1H), 7.26 – 7.10 (m, 3H), 6.97 (d, J = 6.9 Hz, 2H), 6.71 (d, J = 8.1 Hz, 1H), 5.81 (d, J = 8.0 Hz, 1H), 4.97 (q, J = 7.5 Hz, 1H), 3.89 (s, 3H), 3.22 (dd, J = 13.3, 5.8 Hz, 1H), 3.01 (dd, J = 13.2, 7.9 Hz, 1H), 2.83 (s, 3H), 1.43 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.7 , 161.7 , 159.7 , 155.1 , 138.5

, 137.1 , 129.4 , 128.1 , 126.3 , 123.6 , 119.2 , 79.3 , 56.7 , 52.0 , 42.6 , 28.3 , 24.8 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{20}H_{25}N_2O_4$ 371.1965; found 371.1970.

tert-butyl (1-(phenanthridin-6-yl)ethyl)carbamate (32) Following the general procedure condition A, **32** was purified by silica gel chromatography (PE:EA=5:1) ; 39.3 mg (61%)； white solid; mp : 180-183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 8.3 Hz, 1H), 8.54 (dd, J = 8.1, 1.4 Hz, 1H), 8.25 (d, J = 8.2 Hz, 1H), 8.15 (d, J = 7.8 Hz, 1H), 7.85 (t, J = 8.2 Hz, 1H), 7.72 (q, J = 7.0 Hz, 2H), 7.65 (t, J = 6.9 Hz, 1H), 6.73 (d, J = 7.3 Hz, 1H), 6.31 – 5.56 (m, 1H), 1.63 (d, J = 6.7 Hz, 3H), 1.52 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.3 , 155.4 , 142.9 , 133.2 , 130.6 , 129.7 , 128.7 , 127.5 , 126.8 , 125.3 , 123.8 , 123.3 , 122.6 , 122.0 , 79.2 , 47.6 , 28.5 , 23.1 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{20}H_{23}N_2O_2$ 323.1754; found 323.1768.

tert-butyl (1-(phenanthridin-6-yl)-2-phenylethyl)carbamate (33) Following the general procedure condition A, **33** was purified by silica gel chromatography (PE:EA=5:1) ; 70.1 mg (88%)； white solid; mp : 205-207 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 8.3 Hz, 1H), 8.55 (d, J = 8.1 Hz, 1H), 8.15 (d, J = 8.3 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.81 (t, J = 7.5 Hz, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.68 – 7.58 (m, 2H), 7.17 – 7.07 (m, 3H), 6.98 (dd, J = 6.6, 3.0 Hz, 2H), 6.35 (d, J = 8.3 Hz, 1H), 5.98 (dt, J = 8.4, 6.3 Hz, 1H), 3.42 (dd, J = 13.3, 6.5 Hz, 1H), 3.25 (dd, J = 13.4, 6.2 Hz, 1H), 1.46 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.1 , 155.3 , 142.9 , 137.3 , 132.9 , 130.5 , 129.8 , 129.7 , 128.5 , 127.9 , 127.3 , 126.8 , 126.2 , 125.4 , 123.9 , 123.7 , 122.4 , 121.9 , 79.2 , 52.3 , 42.7 , 28.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{26}H_{28}N_2O_2$ 399.2067; found 399.2072.

2-((2-(4-chlorophenoxy)-2-methylpropanoyl)oxy)ethyl 6-(1-((tert-butoxycarbonyl)amino)ethyl)nicotinate (34) Following the general procedure condition A, **34** was purified by silica gel chromatography (PE:EA=10:1) ; 75.9 mg (75%); colourless oil； ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (dd, J = 2.0, 0.8 Hz, 1H), 8.05 (dd, J = 8.1, 2.2 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.12 – 7.01 (m, 2H), 6.80 – 6.68 (m, 2H), 5.68 (d, J = 7.7 Hz, 1H), 4.89 (p, J = 7.0 Hz, 1H), 4.68 – 4.35 (m, 4H), 1.57 (s, 6H), 1.53 – 1.20 (m, 12H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 173.8 , 166.5 , 164.7 , 155.1 , 153.8 , 150.4 , 137.7 , 129.1 , 127.1 , 123.9 , 120.6 , 120.0 , 79.4 , 79.2 , 62.9 , 62.6 , 51.2 , 28.3 , 25.2 , 25.2 , 22.4 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{25}H_{32}ClN_2O_7$ 507.1893; found 507.1894.

tert-butyl (1-((1-(4-methylquinolin-2-yl)ethyl)amino)-1-oxopropan-2-yl)carbamate (35) Following the general procedure condition B, **35** was purified by silica gel chromatography (PE:EA=5:4) ; 40.0 mg (56%)； colourless oil ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.88 (s, 1H), 7.69 (t, J = 9.1 Hz, 1H), 7.54 (t, J = 8.1 Hz, 1H), 7.15 (s, 1H), 5.36 – 5.05 (m, 2H), 4.32 (s, 1H), 2.68 (s, 3H), 1.53 (d, J = 6.8 Hz, 3H), 1.43 (s, 9H), 1.40 (d, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 171.8 , 160.1 , 155.3 , 146.9 , 145.3 , 129.5 , 129.4 , 129.3 , 129.3 , 127.3 , 126.1 , 123.7 , 120.0 , 79.7 , 50.3 , 50.2 , 50.0 , 49.9 , 22.4 , 22.2 , 19.0 , 18.8 . HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{20}H_{29}N_3O_3$ 358.2125; found 358.2133.

tert-butyl 12-((1-((2-(4-(tert-butoxy)phenyl)-1-(4-methylquinolin-2-yl)ethyl)amino)-3-methyl-1-oxobutan-2-yl)carbamoyl)-9-(4-((tert-butoxycarbonyl)amino)butyl)-2,2-dimethyl-4,7,10-trioxo-6-(3-(3-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)propyl)-3-oxa-5,8,11-triazatetradecan-14-oate (36) Following the general procedure condition B, HRMS(ESI) m/z: $[M + H]^+$ Caled for $C_{70}H_{10}5N_{10}O_{14}S$ 1341.7527; found 1341.7512.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Optimization, quenching experiment and NMR spectra.

AUTHOR INFORMATION

Corresponding Author

Email: yiwang@nju.edu.cn.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We gratefully acknowledge the financial support from the National Natural Science Foundation of China (Nos. 21772085 and 21971107).

REFERENCES

(1) (a) Minisci, F.; Vismara, E.; Fontana, F. Recent Developments of Free-Radical Substitutions of Heteroaromatic Bases. *Heterocycles* **1989**, *28* (1), 489–519. (b) Fujiwara, Y.; Domingo, V.; Seiple, I. B.; Gianatassio, R.; Del Bel, M.; Baran, P. S. Practical C−H Functionalization of Quinones with Boronic Acids. *J. Am. Chem. Soc.* **2011**, *133* (10), 3292–3295. (c) Molander, G. A.; Colombel, V.; Braz, V. A. Direct Alkylation of Heteroaryls Using Potassium Alkyl- and Alkoxymethyltrifluoroborates. *Org. Lett.* **2011**, *13* (7), 1852–1855. (d) Fujiwara, Y.; Dixon, J. A.; O'Hara, F.; Funder, E. D.; Dixon, D. D.; Rodriguez, R. A.; Baxter, R. D.; Herlé, B.; Sach, N.; Collins, M. R.; et al. Practical and Innate Carbon–Hydrogen Functionalization of Heterocycles. *Nature* **2012**, *492* (7427), 95–99. (e) Antonchick, A. P.; Burgmann, L. Direct Selective Oxidative Cross-Coupling of Simple Alkanes with Heteroarenes. *Angew. Chem. Int. Ed.* **2013**, *52* (11), 3267–3271.

(2) (a) Seiple, I. B.; Su, S.; Rodriguez, R. A.; Gianatassio, R.; Fujiwara, Y.; Sobel, A. L.; Baran, P. S. Direct C−H Arylation of Electron-Deficient Heterocycles with Arylboronic Acids. *J. Am. Chem. Soc.* **2010**, *132* (38), 13194–13196. (b) Ji, Y.; Brueckl, T.; Baxter, R. D.; Fujiwara, Y.; Seiple, I. B.; Su, S.; Blackmond, D. G.; Baran, P. S. Innate C-H Trifluoromethylation of Heterocycles. *Proc. Natl. Acad. Sci.* **2011**, *108* (35), 14411–14415. (c) Matsui, J. K.; Primer, D. N.; Molander, G. A. Metal-Free C–H Alkylation of Heteroarenes with Alkyltrifluoroborates: A General Protocol for 1°, 2° and 3° Alkylation. *Chem. Sci.* **2017**, *8* (5), 3512–3522.

(3) (a) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. *Chem. Rev.* **2013**, *113* (7), 5322–5363. (b) Schultz, D. M.; Yoon, T. P. Solar Synthesis: Prospects in Visible Light Photocatalysis. *Science* **2014**, *343* (6174), 1239176–1239176. (c) Ouyang, X.-H.; Li, Y.; Song, R.-J.; Li, J.-H. Alkylamination of Styrenes with Alkyl N-Hydroxyphthalimide Esters and Amines by B(C6H5)3-Facilitated Photoredox Catalysis. *Org. Lett.* **2018**, *20* (21), 6659–6662.

(4) (a) Jin, J.; MacMillan, D. W. C. Alcohols as Alkylating Agents in Heteroarene C–H Functionalization. *Nature* **2015**, *525* (7567), 87–90. (b) Correia, C. A.; Yang, L.; Li, C.-J. Palladium-Catalyzed Minisci Reaction with Simple Alcohols. *Org. Lett.* **2011**, *13* (17), 4581–4583.

(5) Huff, C. A.; Cohen, R. D.; Dykstra, K. D.; Streckfuss, E.; DiRocco, D. A.; Krska, S. W. Photoredox-Catalyzed Hydroxymethylation of Heteroaromatic Bases. *J. Org. Chem.* **2016**, *81* (16), 6980–6987.

(6) (a) Jin, J.; MacMillan, D. W. C. Direct α-Arylation of Ethers through the Combination of Photoredox-Mediated C–H Functionalization and the Minisci Reaction. *Angew. Chem. Int. Ed.* **2015**, *54* (5), 1565–1569. (b) J. Barker, T.; L. Biaco, J.; L. Jones, S. Lewis Acid-Catalyzed Borono-Minisci Reactions of Arylboronic Acids and Heterocycles. *Heterocycles* **2016**, *92* (9), 1687–1697.

(7) Li, G.-X.; Morales-Rivera, C. A.; Wang, Y.; Gao, F.; He, G.; Liu, P.; Chen, G. Photoredox-Mediated Minisci C–H Alkylation of *N*-Heteroarenes Using Boronic Acids and Hypervalent Iodine. *Chem. Sci.* **2016**, *7* (10), 6407–6412.

(8) Garza-Sanchez, R. A.; Tlahuext-Aca, A.; Tavakoli, G.; Glorius, F. Visible Light-Mediated Direct Decarboxylative C–H Functionalization of Heteroarenes. *ACS Catal.* **2017**, *7* (6), 4057–4061.

(9) (a) Cheng, W.-M.; Shang, R.; Fu, Y. Photoredox/Brønsted Acid Co-Catalysis Enabling Decarboxylative Coupling of Amino Acid and Peptide Redox-Active Esters with N-Heteroarenes. *ACS Catal.* **2017**, *7* (1), 907–911. (b) Cheng, W.-M.; Shang, R.; Fu, M.-C.; Fu, Y. Photoredox-Catalysed Decarboxylative Alkylation of N-Heteroarenes with *N* -(Acyloxy)Phthalimides. *Chem. - Eur. J.* **2017**, *23* (11), 2537–2541.

(10) Proctor, R. S. J.; Davis, H. J.; Phipps, R. J. Catalytic Enantioselective Minisci-Type Addition to Heteroarenes. *Science* **2018**, *360* (6387), 419–422.

(11) Zhang, W.; Zou, Z.; Wang, Y.; Wang, Y.; Liang, Y.; Wu, Z.; Zheng, Y.; Pan, Y. Leaving Group Assisted Strategy for Photoinduced Fluoroalkylations Using *N*-Hydroxybenzimidoyl Chloride Esters. *Angew. Chem. Int. Ed.* **2019**, *58* (2), 624–627.