JOC The Journal of Organic Chemistry

Article

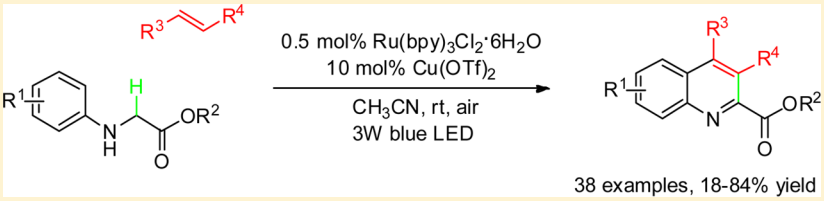
pubs.acs.org/joc

Visible-Light-Induced Photocatalytic Aerobic Oxidative C_{sp3}–H Functionalization of Glycine Derivatives: Synthesis of Substituted Quinolines

Xiaorong Yang, Liqi Li, Ying Li,* and Yuan Zhang*

State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, 222 Tianshui South Road, Lanzhou 730000, PR China

Supporting Information



ABSTRACT: A visible-light induced photocatalytic aerobic oxidative dehydrogenative coupling/aromatization tandem reaction of glycine esters with unactivated alkenes has been accomplished. This visible light-driven protocol has been successfully applied to a broad scope of glycine esters and simple alkenes, giving rise to diverse substituted quinoline derivatives in 18–84% yield under mild (at room temperature under air atmosphere) and operationally simple reaction conditions.

INTRODUCTION

The direct oxidative cross-dehydrogenative coupling (CDC) of two C–H bonds has long been considered an efficient and straightforward synthetic protocol for the construction of C–C bonds.[1] This type of reaction is more atom economical and environmentally friendly than traditional cross-coupling reactions, as it avoids the tedious prefunctionalization and defunctionalization procedures, and thus largely reduces the number of reaction steps. In this context, since the pioneering study of Li,[2] the direct oxidative C_{sp3}–H functionalization of glycine derivatives has gained widespread attention from the chemists.[3] In general, the active iminium ions are recognized to be the key intermediates for these types of reactions (Scheme 1), which are subsequently trapped with appropriate nucleophiles to furnish a large array of α-substituted α-amino acid derivatives (path a).[3] Recently, an alternative strategy has been disclosed whereby the iminium intermediates were captured by olefins (path b). This strategy offers rapid access to the convenient synthesis of quinoline derivatives,[4−7] which are common subunits in a wide range of bioactive natural products and pharmaceuticals.[8] The first example of this oxidative dehydrogenative coupling/aromatization tandem reaction was reported by Mancheño and co-workers in 2011,[4] who synthesized a variety of substituted quinolines from glycine derivatives using $FeCl_3$ as the Lewis acid catalyst and a stoichiometric amount of TEMPO oxoammonium salt as the oxidant. However, from economical and environmental prospectives, the use of molecular oxygen as a "green" oxidant is undoubtedly more attractive. In this regard, In 2012, Jia et al. reported the same tandem process via an aerobic C–H functionalization of glycine derivatives in the presence of radical cation salts and $InCl_3$ using pure O_2 as the sole oxidant.[5a] In 2014, Huo et al. developed an auto-oxidation coupling system for this reaction using air as the sole oxidant.[6a] However, under these conditions, the substrate scope was limited to high electron-rich alkenes, and only moderate yield could be obtained. Later, the same group disclosed that 1 equiv of CBr_4 can also promote this transformation under air atmosphere.[6b] Very recently, Liu et al. reported the Cu(II)-catalyzed aerobic oxidative C–H functionalization of glycine derivatives with olefins, employing NHPI as the cocatalyst and O_2 as the oxidant.[7] Though significant progress have been made in this oxidative dehydrogenative coupling/aromatization tandem process, however, most of the reactions employed stoichiometric amount of oxidants or pure O_2 as the oxidant, and some of them were undertaken at relative high temperature. Therefore, from environmental and practical standpoints, the development of new sustainable and green catalytic versions and milder conditions (e.g., under air atmosphere and at ambient temperature) for this type of reaction, is still highly desired.

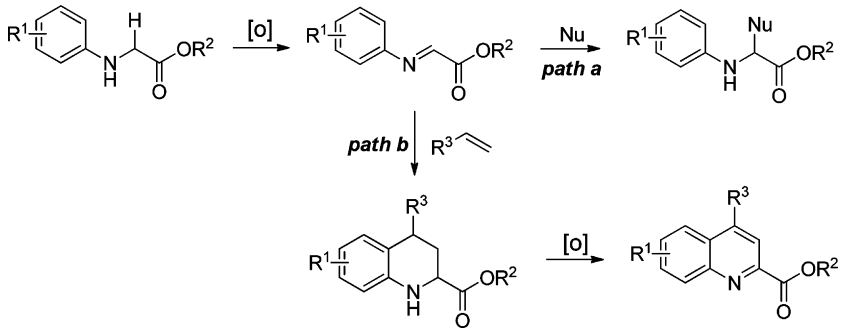
On the other hand, the application of visible light-induced photoredox catalysis in organic synthesis has attracted great interest in recent years, because visible light is natural abundance, environmentally benign, renewability, and ease of handle.[9] In particular, photoredox catalysis recently has emerged as powerful tools to initiate CDC reactions.[9d,10] The majority of such photocatalytic CDC reactions are focused on the oxidative coupling of C–H bonds in tertiary amines, such as

Received: November 7, 2016
Published: November 18, 2016

ACS Publications © 2016 American Chemical Society

DOI: 10.1021/acs.joc.6b02683
J. Org. Chem. 2016, 81, 12433–12442

Scheme 1. Oxidative Functionalization of Glycine Derivatives



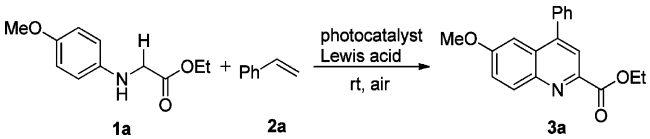
tetrahydroisoquinolines,[10] whereas only very few examples have been reported involving the C−H functionalization of secondary amines,[11] probably due to the relative higher oxidation potential of the latter. Recently, efforts from the groups of Li,[11a] Rueping,[11b] and Wu[11c] have demonstrated that aerobic visible-light catalysis is capable for the formation of iminium intermediate from glycine ester. Inspired by these results, we envisaged that this in situ generated iminium intermediate might be captured by alkenes to give quinoline derivatives. Herein, we present a new direct photocatalytic aerobic oxidative dehydrogenative coupling/aromatization tandem reaction of glycine esters and unactivated alkenes under mild conditions.

RESULTS AND DISCUSSION

We initiated our studies using glycine ester **1a** and styrene **2a** as model substrates to explore the reaction conditions (Table 1, for details see Supporting Information). To our delight, the desired product **3a** was obtained in 70% yield within 4 h using 1 mol % $Ru(bpy)_3(PF_6)_2$ as photocatalyst in combination with 10 mol % $Cu(OTf)_2$ as the Lewis acid cocatalyst in CH_3CN under the irradiation of a 3W blue LED bulb (entry 1). A brief screen of several photocatalysts revealed that $Ru(bpy)_3Cl_2{\cdot}6H_2O$ was most effective in this protocol (entries 2−4), affording **3a** in 75% yield after 4 h. We also examined other Lewis acids, and found that $Cu(OTf)_2$ led to optimal yields (entries 5−8). An evaluation of a variety of solvents identified CH_3CN as the optimal medium (entries 9−11). Importantly, the photocatalyst loading could be decreased to 0.5 mol % with no effect on the catalytic efficiency (entry 12), and this level of efficiency was only slightly decreased with the photocatalyst loading further reduced to 0.1 mol % (entry 13). Tuning the light source to a 26 W fluorescent lamp, the reaction proceeded to completion, albeit at a slower rate than reactions irradiated with blue LED (entry 14). Gratifyingly, this reaction also proceeded smoothly under the irradiation of sun light, affording **3a** in 74% yield after 6 h (entry 15). This result demonstrates the potential utility of this protocol. Moreover, molecular oxygen was found to play an important role in this system, and none of the desired product **3a** was observed when the reaction was carried out under Ar atmosphere (entry 16). Finally, control studies indicated the essential roles of light, photocatalyst, and Cu catalyst in this transformation (entries 17−19).

Having identified the optimal conditions for this tandem protocol, we next focused on examining the scope of the alkene component (Table 2). To our delight, an extensive range of electronically modified styrenes with substituted groups at the ortho, meta, and para positions of benzene rings readily coupled with glycine esters **1a** or **1b**, affording the corresponding substituted quinoline derivatives **3b**−**3k** in 64−82% yield. Notably, potentially reactive chloro substituents at the benzene rings are well tolerated with this mild oxidation

Table 1. Optimization of the Reaction Conditions[a]



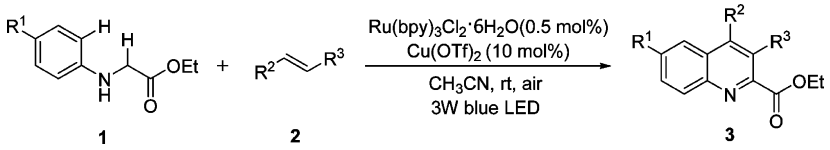
1a **2a** **3a**

entry	photocatalyst	additive	solvent	time (h)	yield (%)[b]
1	$Ru(bpy)_3(PF_6)_2$	$Cu(OTf)_2$	CH_3CN	4	70
2	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Cu(OTf)_2$	CH_3CN	4	75
3	Eosin B	$Cu(OTf)_2$	CH_3CN	4	61
4	Rhodamine 6G	$Cu(OTf)_2$	CH_3CN	4	57
5	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Cu(OAc)_2{\cdot}H_2O$	CH_3CN	4	nd
6	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$CuSO_4$	CH_3CN	4	10
7	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$In(OTf)_3$	CH_3CN	4	26
8	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Fe(OTf)_3$	CH_3CN	4	55
9	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Cu(OTf)_2$	DCE	4	60
10	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Cu(OTf)_2$	DCM	4	47
11	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Cu(OTf)_2$	DMF	4	nd
12[c]	**$Ru(bpy)_3Cl_2{\cdot}6H_2O$**	**$Cu(OTf)_2$**	**CH_3CN**	**5**	**78**
13[d]	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Cu(OTf)_2$	CH_3CN	6	68
14[c,e]	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Cu(OTf)_2$	CH_3CN	15	76
15[c,f]	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Cu(OTf)_2$	CH_3CN	6	74
16[g]	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Cu(OTf)_2$	CH_3CN	4	nd
17[h]	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	$Cu(OTf)_2$	CH_3CN	4	32
18	–	$Cu(OTf)_2$	CH_3CN	4	33
19	$Ru(bpy)_3Cl_2{\cdot}6H_2O$	–	CH_3CN	4	nd

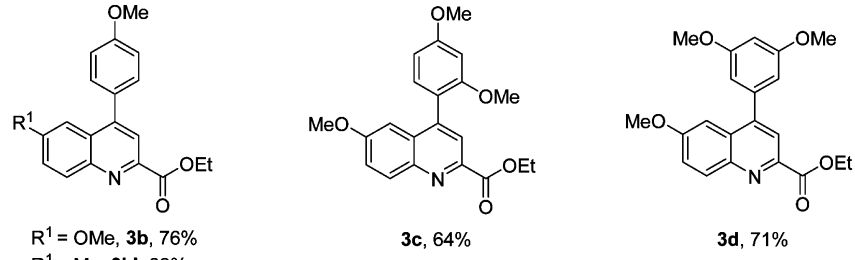
[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), photocatalyst (0.1−1 mol %), additive (10 mol %), solvent (1.0 mL), 3 W blue LED light irradiation under air at room temperature. [b]Yield of the isolated product. [c]0.5 mol % of $Ru(bpy)_3Cl_2{\cdot}6H_2O$ was used. [d]0.1 mol % of $Ru(bpy)_3Cl_2{\cdot}6H_2O$ was used. [e]Under the irradiation of a 26 W fluorescent lamp. [f]Under the irradiation of sun light. [g]Reaction was carried out under Ar. [h]Reaction was carried out in the dark.

DOI: 10.1021/acs.joc.6b02683
J. Org. Chem. 2016, 81, 12433−12442

Table 2. Oxidative Dehydrogenative Coupling/Aromatization Tandem Reaction: Alkenes Scope[a,b]

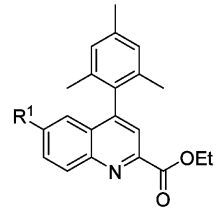


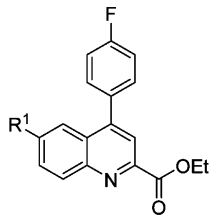
1 2 3

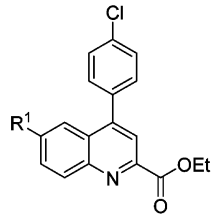

R1 = OMe, **3b**, 76%
R1 = Me, **3b'**, 82%

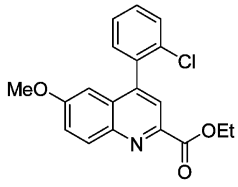
3c, 64%

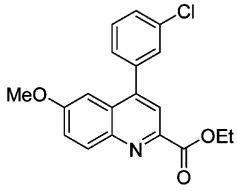
3d, 71%

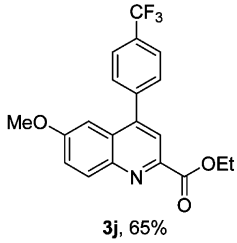

R1 = OMe, **3e**, 71%
R1 = Me, **3e'**, 80%

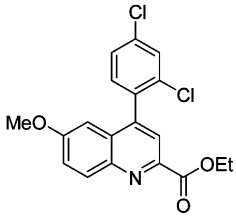

R1 = OMe, **3f**, 65%
R1 = Me, **3f'**, 65%

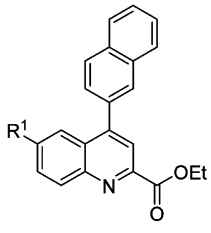

R1 = OMe, **3g**, 72%
R1 = Me, **3g'**, 76%

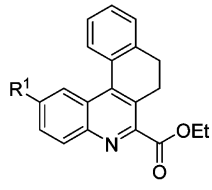

3h, 69%

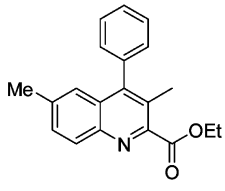

3i, 71%

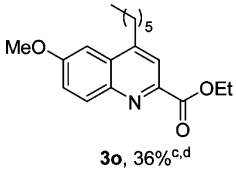

3j, 65%

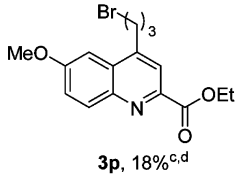

3k, 65%

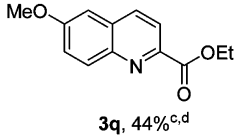

R1 = OMe, **3l**, 83%
R1 = Me, **3l'**, 78%

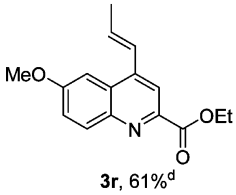

R1 = OMe, **3m**, 63%[c]
R1 = Me, **3m'**, 61%[c]

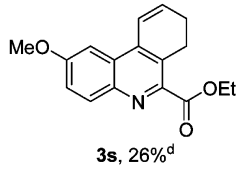

3n, 53%[c]


3o, 36%[c,d]


3p, 18%[c,d]


3q, 44%[c,d]

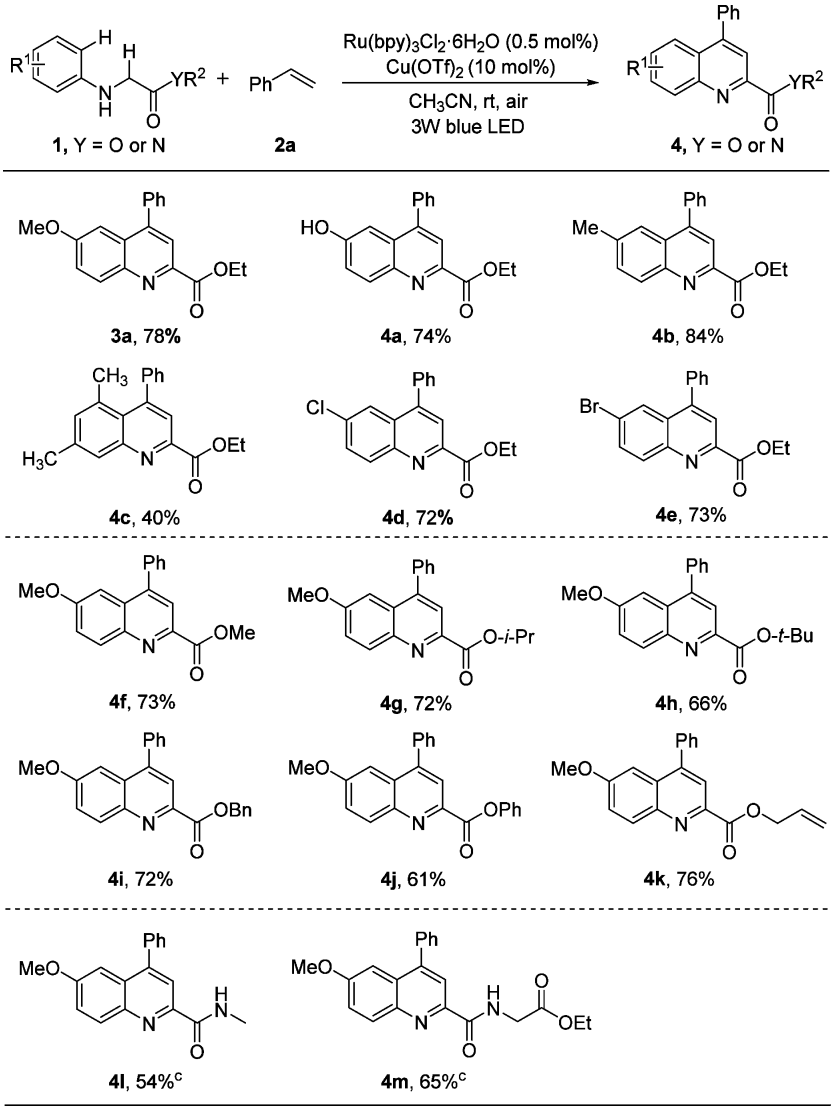

3r, 61%[d]


3s, 26%[d]

[a]Reaction conditions: **1** (0.1 mmol), **2** (0.2 mmol), $Ru(bpy)_3Cl_2·6H_2O$ (0.5 mol %), $Cu(OTf)_2$ (10 mol %), CH_3CN (1.0 mL), 3 W blue LED light irradiation under air for 5−15 h, rt. [b]Yield of the isolated product. [c]20 mol % of $Cu(OTf)_2$ was used. [d]0.5 mmol of alkenes were used.

DOI: 10.1021/acs.joc.6b02683
J. Org. Chem. 2016, 81, 12433−12442

Table 3. Oxidative Dehydrogenative Coupling/Aromatization Tandem Reaction: Glycine Esters Scope[a,b]



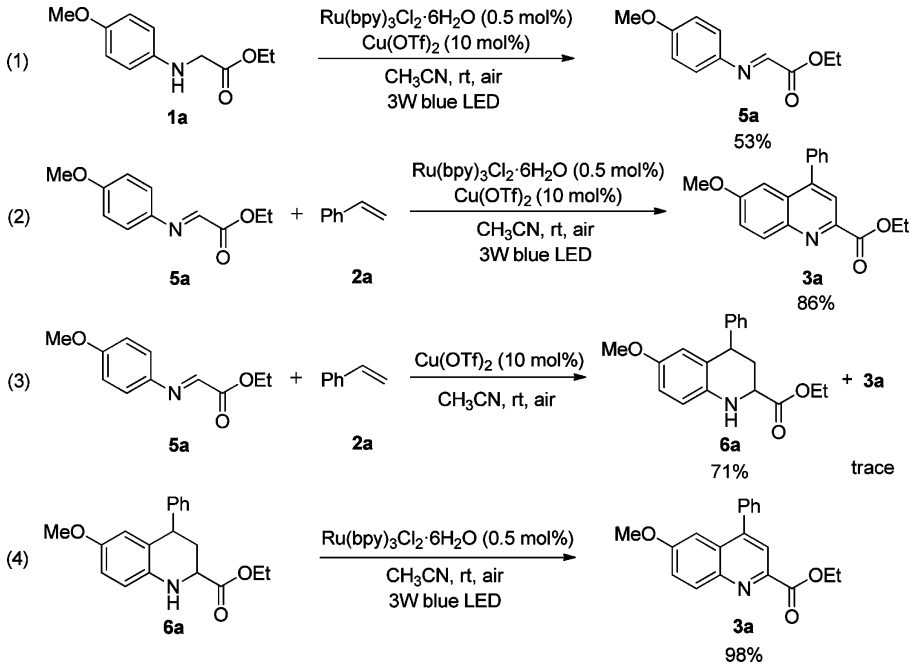
[a]Reaction conditions: **1** (0.1 mmol), **2** (0.2 mmol), $Ru(bpy)_3Cl_2·6H_2O$ (0.5 mol %), $Cu(OTf)_2$ (10 mol %), CH_3CN (1.0 mL), 3 W blue LED light irradiation under air for 5−15 h, rt. [b]Yield of the isolated product. [c]20 mol % of $Cu(OTf)_2$ was used.

system, which afford a handle for further modification. The use of naphthyl ethylenes as the substrates gave similar results (**3l**, **3l′**). Remarkably, 1,2-disubstituted alkenes were also suitable for this reaction, for example, 1,2-dihydronaphthalene and propenylbenzene reacted smoothly with glycine esters, leading to trisubstituted quinolines **3m**, **3m′** and **3n** in moderate yields, although a higher Lewis acid loading was required for optimal rate. To further demonstrate the generality of this tandem protocol, we also examined other alkenes beyond the realm of styrene derivatives. Gratifyingly, aliphatic alkenes can be readily utilized in this procedure to build quinolines directly, albeit the yields were decreased compared to those of the styrene derivatives (**3o**−**3q**). Interestingly, when vinyl acetate was used as the substrate, a 4-unsubstituted quinoline was obtained (**3q**).[12e] However, alkenes with strong electron-withdrawing substituents, such as methyl acrylate and acrylonitrile, were not suitable substrates for this tandem reaction. We considered that the strong electron-withdrawing groups (−COOMe and −CN) would largely decrease the electron density of the double bonds, accordingly, the iminium intermediate would be difficult to react with these electron-deficient alkenes. Furthermore, conjugated dienes, such as 1,3-cyclohexadiene and 1,3-pentadiene, were also successfully utilized in this transformation to generate quinolines (**3r**, **3s**).

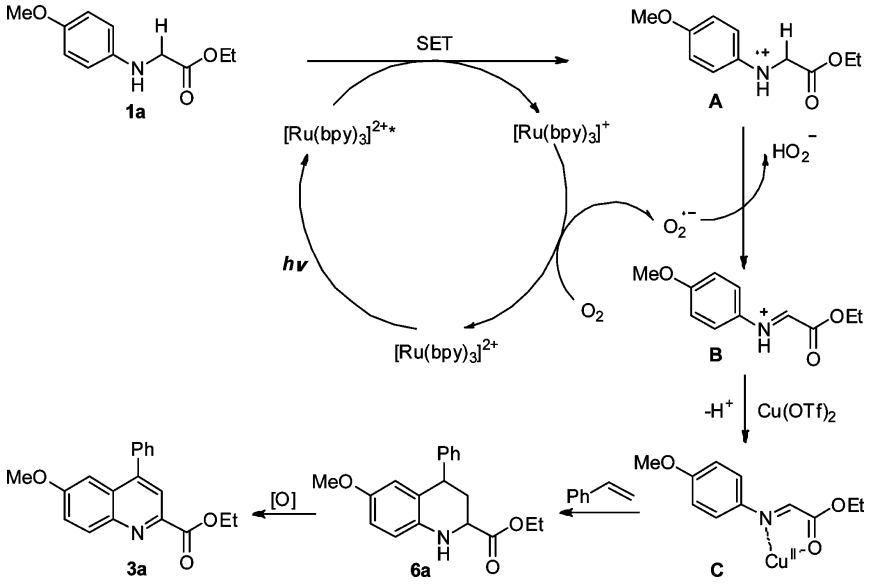
We next explored the structural diversity of the glycine ester component in this tandem protocol (Table 3). We first examined the electronic substituent effect on the aniline fragment. A variety of glycine esters bearing either electron-donating or electron-withdrawing substituents at the para-position of the benzene rings were suitable partners for this tandem reaction, affording the corresponding substituted quinolines in good yields (**4a**-**4e**). Notably, a 3,5-dimethyl substituted substrate was also amenable to reaction with styrene, although a relatively lower yield was obtained (**4c**). We then explored the scope of the ester fragment. The reaction proceeded readily with a range of esters, such as methyl ester, isopropyl ester, *tert*-butyl ester, benzyl ester, phenyl ester, and allyl ester, to afford the products **4f**−**4k** with 61−76% yield. Furthermore, in addition to glycine esters, glycine amide as well as glycine derived dipeptide were found to be viable substrates

DOI: 10.1021/acs.joc.6b02683
J. Org. Chem. 2016, 81, 12433−12442

Scheme 2. Control Experiments



Scheme 3. Proposed Mechanism for the Photocatalytic Oxidative Dehydrogenative Coupling/Aromatization Tandem Reaction



for this reaction, providing the corresponding substituted quinolines in moderate yield (**4l**, **4m**). Other α-amino carbonyls, such as ketones and nitriles were also tried in this transformation, however, only trace products could be detected for α-amino ketones, while no reaction occurred for α-amino nitriles.

The active species of oxygen in this photocatalytic reaction was detected by electron paramagnetic resonance (EPR) studies (Figure S1). When the solution of **1a**, $Ru(bpy)_3Cl_2 \cdot 6H_2O$ and 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO) in air-saturated CH_3CN was irradiated with blue LED, a signal of the trapping radical was captured (Figure S1a), the spectrum and hyperfine coupling constants of which are in good consistent with the literature values for the adduct of $O_2^{-\bullet}$ with DMPO.[13] By contrast, only very weak EPR signal could be detected when 2,2,6,6-tetramethylpiperidine (TEMP), an $^1O_2$ scavenger, was used as a probe in the same air-saturated CH_3CN solution (Figure S1b). These results illustrate that $O_2^{-\bullet}$ generated from molecular oxygen is the active species in this photocatalytic oxidative reaction.

Several control experiments were further conducted to probe the mechanism of this reaction (Scheme 2). Upon irradiation of **1a** with visible light in the presence of $Ru(bpy)_3Cl_2 \cdot 6H_2O$ and $Cu(OTf)_2$, the iminium intermediate **5a** could be isolated in 53% yield, along with some unknown byproducts. It should be noted that in the tandem reaction, these byproducts could not be observed. While in the absence of $Cu(OTf)_2$, the products of this reaction were very complicated, and only trace of iminium **5a** could be observed. The obtained iminium

DOI: 10.1021/acs.joc.6b02683
J. Org. Chem. 2016, 81, 12433−12442

intermediate **5a** could readily react with styrene in the same reaction conditions, affording **3a** in 86% yield.

Interestingly, in the absence of photocatalyst, $Cu(OTf)_2$ alone could also promote the coupling reaction of **5a** with styrene, however, in this case, the Povarov cyclization product tetrahydroquinoline **6a** was obtained in 71% yield, and only trace amount of **3a** was observed. Strikingly, tetrahydroquinoline **6a** could be almost quantitatively transformed to **3a** within 1 h in the presence of $Ru(bpy)_3Cl_2{\cdot}6H_2O$ under the irradiation of visible light. These results suggest that photocatalyst plays a key role in both the iminium formation and the oxidative dehydrogenation processes, while the Cu salt is responsible for the stabilization and the activation of the iminium intermediate during the Povarov cyclization step.

Upon the basis of these observations, a possible mechanism for this oxidative dehydrogenative coupling/aromatization tandem reaction was proposed, as shown in Scheme 3. It is well established that upon irradiation with visible-light, $[Ru(bpy)_3]^{2+}$ is excited to the oxidizing excited state $[Ru(bpy)_3]^{2+*}$,[9f] which would readily accept a single electron from **1a** to produce $[Ru(bpy)_3]^{+}$ and the radical cation **A**. The photocatalyst may be regenerated by the molecular oxygen, and at the same time, an active species $O_2^{-\bullet}$ may be formed during this process.[11c] This active radical anion may abstract a hydrogen atom from **A**, to produce the iminium ion **B**. Then, the in situ generated HOO^- may abstract another hydrogen atom from **B**, to form the iminium intermediate, which subsequently forms the active electrophile **C** under the influence of $Cu(OTf)_2$. This active intermediate can be captured by styrene to form the tetrahydroquinoline **6a**, which is further dehydrogenated via photocatalysis to afford **3a**. Additionally, an α-amino radical is also likely to be generated from radical cation **A**, which may directly react with alkenes. More details for the mechanism of this transform are currently under investigation.

In conclusion, we have developed a photocatalytic oxidative dehydrogenative coupling/aromatization tandem reaction of glycine esters with unactivated alkenes. This visible-light-promoted method was shown to tolerate a broad scope with regard to both the glycine ester and alkene substrates, affording a range of substituted quinolines with moderate to good yields. Remarkably, this tandem protocol was conducted under very mild (at room temperature under air atmosphere) and operationally simple reaction conditions, without the use of any other oxidant. Given the diverse range of organic substrates, and the mild and operationally simple reaction conditions, this visible-light-induced C−H functionalization/aromatization protocol should find broad application in organic synthesis.

EXPERIMENTAL SECTION

General Experimental Methods. All reagents were used as received from commercial suppliers unless otherwise indicated. All solvents were dried by standard techniques and freshly distilled before use. *N*-arylglycine esters,[3a] 2-((4-methoxyphenyl)amino)-*N*-methylacetamide[2b] and ethyl 2-(2-((4-methoxyphenyl)amino)acetamido) acetate[2b] were prepared according to literature procedures. All experiments were carried out under air atmosphere, unless otherwise indicated. The silica gel (200−300 meshes) was used for column chromatography and TLC inspections were taken on silica gel GF254 plates. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were measured on a 400 MHz spectrometer. The chemical shifts δ are given in ppm relative to tetramethylsilane and the coupling constants J are given in Hz. The spectra were recorded with $CDCl_3$ or DMSO-d_6 as solvent at room temperature. EPR spectra were recorded at room temperature using an EPR spectrometer at 9.447 GHz. Typical spectrometer parameters are shown as follows, sweep width: 100.0 G; center field set: 3365.2 G; time constant: 81.920 ms; sweep time: 75.0 s; modulation amplitude: 1.0 G; modulation frequency: 100.0 kHz; receiver gain: 2.00×10^4; microwave power: 24.590 mW. IR spectra were recorded on an FT-IR spectrometer. High resolution mass spectra (HRMS) were obtained on a mass spectrometer by using electrospray ionization (ESI) analyzed by quadrupole time-of-flight (QTof). Irradiation of photochemical reactions was carried out using a 3 W blue LED bulb.

General Procedure for the Visible-Light-Induced Photocatalytic Aerobic Oxidative Dehydrogenative Coupling/Aromatization Tandem Reaction. To a solution of *N*-arylglycine esters **1** (0.1 mmol, 1 equiv), $Ru(bpy)_3Cl_2{\cdot}6H_2O$ (0.5 mol %) and olefin **2** (0.2 mmol, 2 equiv) in dry CH_3CN (1.0 mL) was added $Cu(OTf)_2$ (10 mol %). The mixed solution was irradiated with a 3 W blue LED under air atmosphere at room temperature. After completion of the reaction as monitored by TLC, the solvent was concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (petroleum ether/EtOAc) to afford the products.

*Ethyl 6-methoxy-4-phenylquinoline-2-carboxylate (**3a**).*[5a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). White solid, 24.0 mg, 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 9.3 Hz, 1H), 8.09 (s, 1H), 7.58−7.48 (m, 5H), 7.43 (dd, J = 9.3, 2.8 Hz, 1H), 7.21 (d, J = 2.8 Hz, 1H), 4.55 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 1.48 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 159.5, 148.0, 145.4, 144.3, 137.9, 132.7, 129.3, 129.1, 128.7, 128.6, 122.7, 121.8, 103.3, 62.0, 55.5, 14.4.

*Ethyl 6-methoxy-4-(4-methoxyphenyl)quinoline-2-carboxylate (**3b**).*[12a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). White solid, 25.7 mg, 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 9.3 Hz, 1H), 8.07 (s, 1H), 7.49 (d, J = 8.7 Hz, 2H), 7.42 (dd, J = 9.3, 2.8 Hz, 1H), 7.26 (d, J = 2.8 Hz, 1H), 7.08 (d, J = 8.7 Hz, 2H), 4.55 (q, J = 7.1 Hz, 2H), 3.91 (s, 3H), 3.82 (s, 3H), 1.48 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 159.9, 159.4, 147.7, 145.4, 144.3, 132.7, 130.6, 130.1, 129.3, 122.6, 121.7, 114.2, 103.3, 62.0, 55.5, 55.3, 14.4.

*Ethyl 4-(4-methoxyphenyl)-6-methylquinoline-2-carboxylate (**3b′**).*[5a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). Pale yellow solid, 26.3 mg, 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.7 Hz, 1H), 8.07 (s, 1H), 7.75 (s, 1H), 7.61 (dd, J = 8.7, 1.5 Hz, 1H), 7.48 (d, J = 8.6 Hz, 2H), 7.09 (d, J = 8.6 Hz, 2H), 4.56 (q, J = 7.1 Hz, 2H), 3.92 (s, 3H), 2.50 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 160.0, 148.6, 146.9, 146.86, 138.7, 132.2, 130.9, 130.8, 130.0, 128.0, 124.4, 121.3, 114.1, 62.1, 55.4, 22.0, 14.4.

*Ethyl 4-(2,4-dimethoxyphenyl)-6-methoxyquinoline-2-carboxylate (**3c**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). Pale yellow solid, 23.5 mg, 64% yield, mp 112−114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 9.3 Hz, 1H), 8.06 (s, 1H), 7.39 (dd, J = 9.3, 2.7 Hz, 1H), 7.22 (d, J = 8.3 Hz, 1H), 6.92 (d, J = 2.7 Hz, 1H), 6.68−6.62 (m, 2H), 4.54 (q, J = 7.1 Hz, 2H), 3.91 (s, 3H), 3.78 (s, 3H), 3.71 (s, 3H), 1.47 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 161.5, 159.1, 157.8, 145.34, 145.32, 144.1, 132.4, 131.7, 130.3, 122.9, 122.5, 119.3, 104.8, 103.8, 98.9, 61.9, 55.5, 55.4, 14.4. IR (KBr, cm^{-1}) ν 3441, 3077, 2956, 2836, 1732, 1681, 1583, 1471, 1364, 1265, 1104, 1025, 924, 830, 790. HRMS-ESI calcd for $C_{21}H_{22}NO_5$ $(M + H)^+$ 368.1492, found 368.1486.

*Ethyl 4-(3,5-dimethoxyphenyl)-6-methoxyquinoline-2-carboxylate (**3d**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). White solid, 26.1 mg, 71% yield, mp 150−151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 9.3 Hz, 1H), 8.10 (s, 1H), 7.43 (dd, J = 9.3, 2.8 Hz, 1H), 7.28 (d, J = 3.5 Hz, 1H), 6.67 (d, J = 2.3 Hz, 2H), 6.61−6,59(m, 1H), 4.55 (q, J = 7.1 Hz, 2H), 3.85 (s, 6H), 3.83 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 161.0, 159.5, 147.9, 145.3, 144.3, 139.8, 132.7, 129.1, 122.8, 121.5, 107.4, 103.3, 100.6, 62.1, 55.6, 55.5, 14.4. IR (KBr, cm^{-1}) ν 3400, 3063, 2956, 2845, 1731, 1598, 1479,

DOI: 10.1021/acs.joc.6b02683
J. Org. Chem. 2016, 81, 12433−12442

1369, 1228, 1152, 1026, 826, 787. HRMS-ESI calcd for $C_{21}H_{22}NO_5$ $(M + H)^+$ 368.1492, found 368.1497.

*Ethyl 4-mesityl-6-methoxyquinoline-2-carboxylate (**3e**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). White solid, 24.7 mg, 71% yield, mp 137−139 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 9.3 Hz, 1H), 7.96 (s, 1H), 7.42 (dd, J = 9.3, 2.8 Hz, 1H), 7.02 (s, 2H), 6.65 (d, J = 2.8 Hz, 1H), 4.54 (q, J = 7.1 Hz, 2H), 3.73 (s, 3H), 2.39 (s, 3H), 1.88 (s, 6H), 1.48 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 159.6, 147.7, 145.7, 144.2, 137.8, 135.7, 133.7, 132.7, 130.0, 128.4, 122.9, 122.2, 102.6, 62.0, 55.5, 21.1, 20.1, 14.4. IR (KBr, cm^{-1}) ν 3406, 2997, 2831, 1712, 1617, 1475, 1365, 1228, 1110, 1024, 849. HRMS-ESI calcd for $C_{22}H_{24}NO_3$ $(M + H)^+$ 350.1751, found 350.1756.

*Ethyl 4-mesityl-6-methylquinoline-2-carboxylate (**3e′**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). Pale yellow solid, 26.8 mg, 80% yield, mp 113−115 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.7 Hz, 1H), 7.96 (s, 1H), 7.60 (dd, J = 8.7, 1.7 Hz, 1H), 7.18 (s, 1H), 7.03 (s, 2H), 4.55 (q, J = 7.1 Hz, 2H), 2.44 (s, 3H), 2.40 (s, 3H), 1.86 (s, 6H), 1.48 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 148.7, 147.3, 146.7, 139.1, 137.8, 135.9, 133.8, 132.5, 130.9, 128.5, 128.3, 123.8, 121.9, 62.1, 21.9, 21.1, 20.2, 14.4. IR (KBr, cm^{-1}) ν 3395, 2921, 2859, 1718, 1613, 1556, 1444, 1373, 1250, 1109, 1023, 829, 755. HRMS-ESI calcd for $C_{22}H_{24}NO_2$ $(M + H)^+$ 334.1802, found 334.1804.

*Ethyl 4-(4-fluorophenyl)-6-methoxyquinoline-2-carboxylate (**3f**).*[12a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). White solid, 21.2 mg, 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 9.3 Hz, 1H), 8.06 (s, 1H), 7.55−7.50 (m, 2H), 7.44 (dd, J = 9.3, 2.8 Hz, 1H), 7.29−7.22 (m, 2H), 7.15 (d, J = 2.7 Hz, 1H), 4.56 (q, J = 7.1 Hz, 2H), 3.82 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 162.9 (d, J_{C-F} = 247.0 Hz), 159.6, 146.9, 145.4, 144.3, 133.9 (d, J_{C-F} = 3.4 Hz), 132.8, 131.0 (d, J_{C-F} = 8.1 Hz), 129.1, 122.8, 121.8, 115.9 (d, J_{C-F} = 21.5 Hz), 103.1, 62.1, 55.5, 14.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.8 (s, F).

*Ethyl 4-(4-fluorophenyl)-6-methylquinoline-2-carboxylate (**3f′**).*[5a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). White solid, 20.2 mg, 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.6 Hz, 1H), 8.07 (s, 1H), 7.65−7.61 (m, 2H), 7.53−7.48 (m, 2H), 7.27−7.21 (m, 2H), 4.56 (q, J = 7.1 Hz, 2H), 2.50 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 163.0 (d, J_{C-F} = 247.0 Hz), 147.8, 146.8 (d, J_{C-F} = 10.6 Hz), 139.1, 133.7 (d, J_{C-F} = 3.4 Hz), 132.4, 131.3, 131.2, 131.0, 127.8, 124.1, 121.4, 115.7 (d, J_{C-F} = 21.5 Hz), 62.2, 22.0, 14.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.9 (s, F).

*Ethyl 4-(4-chlorophenyl)-6-methoxyquinoline-2-carboxylate (**3g**).*[12a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). White solid, 24.6 mg, 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 9.3 Hz, 1H), 8.06 (s, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.49 (d, J = 8.6 Hz, 2H), 7.44 (dd, J = 9.3, 2.8 Hz, 1H), 7.13 (d, J = 2.7 Hz, 1H), 4.55 (q, J = 7.1 Hz, 2H), 3.82 (s, 3H), 1.48 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$) δ 165.5, 159.7, 146.6, 145.3, 144.3, 136.3, 134.8, 132.8, 130.6, 129.0, 128.9, 122.9, 121.7, 102.9, 62.1, 55.5, 14.4.

*Ethyl 4-(4-chlorophenyl)-6-methylquinoline-2-carboxylate (**3g′**).*[5a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). White solid, 24.8 mg, 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 9.2 Hz, 1H), 8.06 (s, 1H), 7.65−7.60 (m, 2H), 7.56−7.51 (m, 2H), 7.48−7.44 (m, 2H), 4.56 (q, J = 7.1 Hz, 2H), 2.50 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 147.6, 146.9, 146.8, 139.2, 136.1, 134.8, 132.4, 131.0, 130.8, 128.9, 127.5, 124.0, 121.3, 62.2, 22.0, 14.4.

*Ethyl 4-(2-chlorophenyl)-6-methoxyquinoline-2-carboxylate (**3h**).*[12b] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). White solid, 23.4 mg, 69% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 9.3 Hz, 1H), 8.07 (s, 1H), 7.58 (dd, J = 7.6, 1.6 Hz, 1H), 7.49−7.41 (m, 3H), 7.37 (dd, J = 7.2, 2.0 Hz, 1H), 6.76 (d, J = 2.7 Hz, 1H), 4.55 (m, 2H), 3.77 (s, 3H), 1.48 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 159.6, 145.4, 145.3, 144.0, 136.5, 133.2, 132.7, 131.2, 130.0, 129.9, 129.3, 127.0, 123.0, 122.3, 103.2, 62.1, 55.5, 14.4.

*Ethyl 4-(3-chlorophenyl)-6-methoxyquinoline-2-carboxylate (**3i**).*[12b] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). Pale yellow solid, 24.3 mg, 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 9.3 Hz, 1H), 8.07 (s, 1H), 7.55−7.54 (m, 1H), 7.51−7.41 (m, 4H), 7.14 (d, J = 2.7 Hz, 1H), 4.56 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 159.7, 146.3, 145.3, 144.3, 139.6, 134.8, 132.8, 130.0, 129.3, 128.8, 128.7, 127.5, 122.9, 121.7, 102.9, 62.1, 55.5, 14.4.

*Ethyl 6-methoxy-4-(4-(trifluoromethyl)phenyl)quinoline-2-carboxylate (**3j**).*[12c] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). Pale yellow solid, 24.2 mg, 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 9.3 Hz, 1H), 8.08 (s, 1H), 7.83 (d, J = 8.1 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.46 (dd, J = 9.3, 2.8 Hz, 1H), 7.09 (d, J = 2.7 Hz, 1H), 4.56 (q, J = 7.1 Hz, 2H), 3.82 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 159.8, 146.3, 145.3, 144.3, 141.6, 132.9, 130.8 (q, J = 32.5 Hz), 129.7, 128.7, 126.2 (q, J = 2.5 Hz), 125.8 (q, J = 3.8 Hz), 124.1 (q, J = 270.6 Hz), 123.0, 121.7, 102.8, 62.1, 55.6, 14.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.6 (s, 3F).

*Ethyl 4-(2,4-dichlorophenyl)-6-methoxyquinoline-2-carboxylate (**3k**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). Pale yellow solid, 24.3 mg, 65% yield, mp 128−130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 9.3 Hz, 1H), 8.04 (s, 1H), 7.62 (d, J = 2.0 Hz, 1H), 7.46−7.42 (m, 2H), 7.32 (d, J = 8.2 Hz, 1H), 6.72 (d, J = 2.7 Hz, 1H), 4.58−4.53 (m, 2H), 3.80 (s, 3H), 1.48 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 159.8, 145.2, 144.2, 144.0, 135.4, 135.1, 134.1, 132.8, 132.0, 129.9, 129.1, 127.5, 123.2, 122.3, 102.9, 62.1, 55.6, 14.4. IR (KBr, cm^{-1}) ν 3352, 2928, 1699, 1619, 1479, 1378, 1276, 1224, 1143, 1106, 1033, 866, 840, 791. HRMS-ESI calcd for $C_{19}H_{16}Cl_2NO_3$ $(M + H)^+$ 376.0502, found 376.0507.

*Ethyl 4-(2-Naphthyl)-6-methoxyquinoline-2-carboxylate (**3l**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). White solid, 29.5 mg, 83% yield, mp 94−95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 9.3 Hz, 1H), 8.20 (s, 1H), 8.04−7.99 (m, 2H), 7.97−7.91 (m, 2H), 7.65 (dd, J = 8.4, 1.7 Hz, 1H), 7.60−7.55 (m, 2H), 7.45 (dd, J = 9.3, 2.8 Hz, 1H), 7.25 (d, J = 2.8 Hz, 1H), 4.56 (q, J = 7.1 Hz, 2H), 3.75 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 159.6, 147.9, 145.4, 144.3, 135.4, 133.3, 133.1, 132.7, 129.3, 128.6, 128.3, 128.2, 127.8, 126.9, 126.8, 126.7, 122.8, 122.0, 103.3, 62.1, 55.5, 14.4. IR (KBr, cm^{-1}) ν 3406, 2980, 2849, 1715, 1620, 1478, 1368, 1227, 1111, 1024, 833, 750. HRMS-ESI calcd for $C_{23}H_{20}NO_3$ $(M + H)^+$ 358.1438, found 358.1442.

*Ethyl 4-(2-Naphthyl)-6-methylquinoline-2-carboxylate (**3l′**).*[4b] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). White solid, 26.7 mg, 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.7 Hz, 1H), 8.19 (s, 1H), 8.04−8.00 (m, 2H), 7.99−7.91 (m, 2H), 7.74 (s, 1H), 7.66−7.56 (m, 4H), 4.57 (q, J = 7.1 Hz, 2H), 2.47 (s, 3H), 1.50 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 148.9, 146.9, 146.8, 139.0, 135.3, 133.2, 133.1, 132.4, 130.9, 128.8, 128.3, 128.2, 128.0, 127.8, 127.2, 126.8, 126.7, 124.5, 121.6, 62.2, 22.0, 14.4.

*Ethyl 2-methoxy-7,8-dihydrobenzo[k]phenanthridine-6-carboxylate (**3m**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). Pale yellow solid, 20.9 mg, 63% yield, mp 134−135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 9.2 Hz, 1H), 8.00−7.94 (m, 1H), 7.78 (d, J = 2.7 Hz, 1H), 7.44−7.36 (m, 4H), 4.53 (q, J = 7.1 Hz, 2H), 3.91 (s, 3H), 3.14−3.06 (m, 2H), 2.86−2.79 (m, 2H), 1.47 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 159.2, 146.6, 143.4, 140.3, 140.2, 132.3, 131.9, 130.4, 128.9, 128.4, 128.0, 126.3, 126.27, 121.5, 103.4, 61.9, 55.5, 28.7, 25.6, 14.3. IR (KBr, cm^{-1}) ν 3395, 2929, 2844, 1709, 1619, 1500, 1350, 1211, 1170, 1035, 821, 752. HRMS-ESI calcd for $C_{21}H_{20}NO_3$ $(M + H)^+$ 334.1438, found 334.1429.

*Ethyl 2-methyl-7,8-dihydrobenzo[k]phenanthridine-6-carboxylate (**3m′**).* Purified by flash column chromatography (silica gel,

DOI: 10.1021/acs.joc.6b02683
J. Org. Chem. 2016, 81, 12433−12442

petroleum ether/EtOAc = 8/1 as eluent). White solid, 19.4 mg, 61% yield, mp 100−102 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.13 (d, J = 8.6 Hz, 1H), 7.94−7.89 (m, 1H), 7.55 (dd, J = 8.6, 1.7 Hz, 1H), 7.45−7.37 (m, 3H), 4.54 (q, J = 7.1 Hz, 2H), 3.12−3.04 (m, 2H), 2.87−2.78 (m, 2H), 2.55 (s, 3H), 1.48 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 148.3, 145.9, 140.9, 140.3, 138.1, 131.8, 131.1, 130.4, 129.7, 129.3, 128.9, 127.9, 126.3, 125.1, 124.1, 62.0, 28.8, 25.6, 22.2, 14.3. IR (KBr, cm^{-1}) ν 3387, 2925, 2367, 1721, 1601, 1561, 1458, 1372, 1305, 1242, 1177, 1073, 754. HRMS-ESI calcd for $C_{21}H_{20}NO_2$ (M + H)$^+$ 318.1489, found 318.1487.

*Ethyl 3,6-dimethyl-4-phenylquinoline-2-carboxylate (**3n**).*[4b] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). White solid, 16.3 mg, 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.6 Hz, 1H), 7.57−7.48 (m, 4H), 7.26−7.21 (m, 2H), 7.11 (s, 1H), 4.54 (q, J = 7.1 Hz, 2H), 2.39 (s, 3H), 2.29 (s, 3H), 1.47 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 150.5, 147.9, 144.3, 137.8, 136.9, 131.3, 129.6, 129.2, 128.6, 128.2, 128.0, 126.3, 124.7, 61.9, 21.9, 16.8, 14.3.

*Ethyl 4-hexyl-6-methoxyquinoline-2-carboxylate (**3o**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). Pale yellow solid, 11.2 mg, 36% yield, mp 51−52 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 9.3 Hz, 1H), 8.00 (s, 1H), 7.41 (dd, J = 9.3, 2.7 Hz, 1H), 7.25 (d, J = 2.7 Hz, 1H), 4.54 (q, J = 7.1 Hz, 2H), 3.97 (s, 3H), 3.05 (t, J = 7.8 Hz, 2H), 1.84−1.76 (m, 2H), 1.49 (t, J = 7.1 Hz, 3H), 1.45−1.23 (m, 6H), 0.90 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 159.1, 148.2, 145.4, 143.7, 133.0, 129.9, 122.1, 120.8, 101.3, 61.9, 55.5, 32.3, 31.6, 29.32, 29.27, 22.5, 14.4, 14.0. IR (KBr, cm^{-1}) ν 2930, 2857, 1715, 1621, 1510, 1477, 1372, 1280, 1253, 1228, 1175, 1144, 1109, 1025, 951, 863, 834, 790, 732. HRMS-ESI calcd for $C_{19}H_{26}NO_3$ (M + H)$^+$ 316.1907, found 316.1903.

*Ethyl 4-(3-bromopropyl)-6-methoxyquinoline-2-carboxylate (**3p**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). Pale yellow solid, 6.4 mg, 18% yield, mp 79−81 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 9.3 Hz, 1H), 8.03 (s, 1H), 7.43 (dd, J = 9.3, 2.7 Hz, 1H), 7.33 (d, J = 2.7 Hz, 1H), 4.54 (q, J = 7.1 Hz, 2H), 3.99 (s, 3H), 3.53 (t, J = 6.1 Hz, 2H), 3.30−3.24 (m, 2H), 2.39−2.30 (m, 2H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 159.5, 146.2, 145.4, 143.8, 133.1, 129.7, 122.7, 121.2, 101.1, 62.0, 55.7, 33.3, 32.4, 30.6, 14.4. IR (KBr, cm^{-1}) ν 3076, 2987, 1710, 1619, 1510, 1480, 1438, 1369, 1345, 1261, 1232, 1109, 1022, 954, 837, 788. HRMS-ESI calcd for $C_{16}H_{19}BrNO_3$ (M + H)$^+$ 352.0543, found 352.0545.

*Ethyl 6-methoxyquinoline-2-carboxylate (**3q**).*[12e] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). White solid, 10.1 mg, 44% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 9.3 Hz, 1H), 8.16 (s, 2H), 7.43 (dd, J = 9.3, 2.8 Hz, 1H), 7.10 (d, J = 2.8 Hz, 1H), 4.55 (q, J = 7.1 Hz, 2H), 3.96 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 159.3, 145.7, 143.7, 135.5, 132.2, 130.7, 123.3, 121.5, 104.6, 62.0, 55.6, 14.3.

*Ethyl (E)-6-methoxy-4-(prop-1-en-1-yl)quinoline-2-carboxylate (**3r**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). White solid, 16.5 mg, 61% yield, mp 113−114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (t, J = 4.6 Hz, 2H), 7.40 (dd, J = 9.3, 2.7 Hz, 1H), 7.32−7.28 (m, 1H), 7.01 (d, J = 15.6 Hz, 1H), 6.66−6.54 (m, 1H), 4.55 (q, J = 7.1 Hz, 2H), 3.97 (s, 3H), 2.06 (dd, J = 6.7, 1.5 Hz, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 159.1, 145.5, 144.1, 143.1, 133.6, 132.7, 128.4, 125.6, 122.5, 117.7, 101.2, 62.0, 55.5, 19.1, 14.4. IR (KBr, cm^{-1}) ν 3352, 2976, 2933, 1717, 1620, 1584, 1474, 1416, 1367, 1254, 1224, 1144, 1112, 1022, 960, 916, 896, 856, 832, 785. HRMS-ESI calcd for $C_{16}H_{18}NO_3$ (M + H)$^+$ 272.1281, found 272.1278.

*Ethyl 2-methoxy-7,8-dihydrophenanthridine-6-carboxylate (**3s**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). Pale yellow oil, 7.4 mg, 26% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 9.2 Hz, 1H), 7.34 (dd, J = 9.2, 2.7 Hz, 1H), 7.24 (d, J = 2.6 Hz, 1H), 7.17 (dt, J = 9.8, 1.6 Hz, 1H), 6.57−6.50 (m, 1H), 4.52 (q, J = 7.1 Hz, 2H), 3.95 (s, 3H), 3.15 (t, J = 8.0 Hz, 2H), 2.45−2.39 (m, 2H), 1.47 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 158.8, 146.5, 142.6, 136.9, 134.9, 132.1, 126.1, 125.7, 121.81, 121.78, 100.0, 61.8, 55.5, 23.3, 22.5, 14.3. IR (KBr, cm^{-1}) ν 3405, 2936, 2833, 1720, 1621, 1500, 1467, 1428, 1301, 1227, 1179, 1105, 1031, 863, 831, 754. HRMS-ESI calcd for $C_{17}H_{18}NO_3$ (M + H)$^+$ 284.1281, found 284.1277.

*Ethyl 6-hydroxy-4-phenylquinoline-2-carboxylate (**4a**).*[5a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 4/1−2/1 as eluent). White solid, 21.7 mg, 74% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.38 (brs, 1H), 8.11 (d, J = 9.1 Hz, 1H), 7.87 (s, 1H), 7.62−7.53 (m, 5H), 7.43 (dd, J = 9.1, 2.6 Hz, 1H), 7.16 (d, J = 2.6 Hz, 1H), 4.41 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.9, 157.9, 146.5, 144.1, 142.8, 137.4, 132.3, 129.1, 128.8, 128.7, 128.6, 123.2, 120.8, 105.9, 61.2, 14.2.

*Ethyl 6-methyl-4-phenylquinoline-2-carboxylate (**4b**).*[5a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). White solid, 24.5 mg, 84% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 8.7 Hz, 1H), 8.09 (s, 1H), 7.70 (s, 1H), 7.62 (dd, J = 8.7, 1.7 Hz, 1H), 7.57−7.50 (m, 5H), 4.56 (q, J = 7.1 Hz, 2H), 2.49 (s, 3H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 148.9, 146.9, 146.8, 138.9, 137.7, 132.3, 130.8, 129.5, 128.6, 128.5, 127.8, 124.3, 121.4, 62.1, 22.0, 14.4.

*Ethyl 5,7-dimethyl-4-phenylquinoline-2-carboxylate (**4c**).*[4b] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). Pale yellow solid, 12.3 mg, 40% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.92 (s, 1H), 7.49−7.42 (m, 3H), 7.35−7.31 (m, 2H), 7.22 (s, 1H), 4.54 (q, J = 7.1 Hz, 2H), 2.52 (s, 3H), 2.00 (s, 3H), 1.47 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 150.0, 149.7, 146.4, 142.0, 139.7, 135.0, 134.1, 128.9, 128.7, 127.9, 125.4, 122.6, 62.1, 24.2, 21.3, 14.4.

*Ethyl 6-chloro-4-phenylquinoline-2-carboxylate (**4d**).*[5a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). White solid, 22.5 mg, 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 9.0 Hz, 1H), 8.15 (s, 1H), 7.93 (d, J = 2.3 Hz, 1H), 7.72 (dd, J = 9.0, 2.3 Hz, 1H), 7.59−7.50 (m, 5H), 4.57 (q, J = 7.1 Hz, 2H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 149.1, 148.0, 146.6, 136.9, 134.8, 132.7, 131.1, 129.4, 129.0, 128.9, 128.5, 124.5, 122.0, 62.4, 14.4.

*Ethyl 6-bromo-4-phenylquinoline-2-carboxylate (**4e**).*[5a] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). White solid, 26.0 mg, 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 9.0 Hz, 1H), 8.14 (s, 1H), 8.11 (d, J = 2.1 Hz, 1H), 7.86 (dd, J = 9.0, 2.2 Hz, 1H), 7.60−7.50 (m, 5H), 4.57 (q, J = 7.1 Hz, 2H), 1.49 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 149.0, 148.1, 146.8, 136.9, 133.6, 132.8, 129.4, 129.0, 128.9, 128.87, 127.9, 123.3, 122.0, 62.4, 14.4.

*Methyl 6-methoxy-4-phenylquinoline-2-carboxylate (**4f**).*[12d] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). White solid, 21.4 mg, 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 9.3 Hz, 1H), 8.11 (s, 1H), 7.55−7.49 (m, 5H), 7.44 (dd, J = 9.3, 2.7 Hz, 1H), 7.23 (d, J = 2.7 Hz, 1H), 4.08 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 159.6, 148.1, 145.0, 144.2, 137.8, 132.6, 129.3, 129.2, 128.7, 128.6, 122.8, 121.8, 103.3, 55.5, 53.0.

*Isopropyl 6-methoxy-4-phenylquinoline-2-carboxylate (**4g**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). Pale yellow solid, 23.0 mg, 72% yield, mp 151−152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 9.3 Hz, 1H), 8.04 (s, 1H), 7.57−7.50 (m, 5H), 7.43 (dd, J = 9.3, 2.8 Hz, 1H), 7.20 (d, J = 2.8 Hz, 1H), 5.44−5.35 (m, 1H), 3.80 (s, 3H), 1.47 (s, 3H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 159.4, 147.9, 145.7, 144.4, 138.0, 132.8, 129.3, 129.0, 128.7, 128.6, 122.6, 121.7, 103.2, 69.6, 55.5, 21.9. IR (KBr, cm^{-1}) ν 3432, 2972, 1729, 1619, 1474, 1373, 1223, 1104, 1027, 841, 707. HRMS-ESI calcd for $C_{20}H_{20}NO_3$ (M + H)$^+$ 322.1438, found 322.1442.

*tert-Butyl 6-methoxy-4-phenylquinoline-2-carboxylate (**4h**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). Pale yellow solid, 22.2 mg, 66% yield, mp 156−158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 9.3 Hz, 1H), 7.98 (s, 1H), 7.56−7.50 (m, 5H), 7.42 (dd, J = 9.3, 2.8 Hz, 1H), 7.18 (d, J = 2.8 Hz, 1H), 3.80 (s, 3H), 1.68 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 159.3, 147.8, 146.5, 144.4, 138.1, 132.8, 129.3, 128.9,

DOI: 10.1021/acs.joc.6b02683
J. Org. Chem. 2016, 81, 12433−12442

128.7, 128.5, 122.5, 121.6, 103.2, 82.3, 55.5, 28.2. IR (KBr, cm^{-1}) ν 3444, 2972, 1734, 1622, 1490, 1367, 1266, 1239, 1144, 1032, 828, 710. HRMS-ESI calcd for $C_{21}H_{22}NO_3$ $(M + H)^+$ 336.1594, found 336.1597.

*Benzyl 6-methoxy-4-phenylquinoline-2-carboxylate (**4i**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). White solid, 26.6 mg, 72% yield, mp 140−142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 9.3 Hz, 1H), 8.07 (s, 1H), 7.55−7.49 (m, 7H), 7.42 (dd, J = 9.3, 2.8 Hz, 1H), 7.39−7.32 (m, 3H), 7.19 (d, J = 2.8 Hz, 1H), 5.52 (s, 2H), 3.79 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 159.5, 147.9, 145.0, 144.4, 137.8, 135.8, 132.7, 129.2, 129.16, 128.7, 128.6, 128.5, 128.3, 122.8, 121.8, 103.2, 67.5, 55.4. IR (KBr, cm^{-1}) ν 3391, 2966, 1708, 1619, 1476, 1355, 1224, 1126, 1025, 828, 734. HRMS-ESI calcd for $C_{24}H_{20}NO_3$ $(M + H)^+$ 370.1438, found 370.1443.

*Phenyl 6-methoxy-4-phenylquinoline-2-carboxylate (**4j**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1−4/1 as eluent). Pale yellow solid, 21.6 mg, 61% yield, mp 187−188 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 9.3 Hz, 1H), 8.22 (s, 1H), 7.57 (d, J = 3.9 Hz, 4H), 7.49−7.43 (m, 3H), 7.33−7.28 (m, 3H), 7.27−7.20 (m, 2H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 159.8, 151.1, 148.2, 144.5, 137.8, 132.8, 129.4, 129.3, 128.8, 128.7, 126.0, 123.0, 122.2, 121.8, 103.3, 55.5. IR (KBr, cm^{-1}) ν 3108, 2931, 2362, 1751, 1619, 1587, 1492, 1373, 1216, 1195, 1100, 1031, 936, 917, 832, 758, 731. HRMS-ESI calcd for $C_{23}H_{18}NO_3$ $(M + H)^+$ 356.1281, found 356.1285.

*Allyl 6-methoxy-4-phenylquinoline-2-carboxylate (**4k**).* Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 8/1 as eluent). Pale yellow solid, 24.4 mg, 76% yield, mp 139−141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 9.3 Hz, 1H), 8.10 (s, 1H), 7.59−7.50 (m, 5H), 7.43 (dd, J = 9.3, 2.2 Hz, 1H), 7.22 (d, J = 2.1 Hz, 1H), 6.17−6.07 (m, 1H), 5.47 (d, J = 17.2 Hz, 1H), 5.33 (d, J = 10.4 Hz, 1H), 4.99 (d, J = 5.8 Hz, 2H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 159.5, 148.0, 145.1, 144.3, 137.8, 132.7, 131.9, 129.3,129.2, 128.7, 128.6, 122.8, 121.8, 119.0, 103.3, 66.6, 55.5. IR (KBr, cm^{-1}) ν 3440, 2945, 1732, 1619, 1473, 1358, 1221, 1110, 1030, 945, 842, 708. HRMS-ESI calcd for $C_{20}H_{18}NO_3$ $(M + H)^+$ 320.1287, found 320.1285.

*6-Methoxy-N-methyl-4-phenylquinoline-2-carboxamide (**4l**).*[5b] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 4/1 as eluent). White solid, 15.9 mg, 54% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (brs, 1H), 8.21 (s, 1H), 8.03 (d, J = 9.2 Hz, 1H), 7.56−7.52 (m, 4H), 7.51−7.46 (m, 1H), 7.40 (dd, J = 9.2, 2.8 Hz, 1H), 7.24 (d, J = 2.8 Hz, 1H), 3.80 (s, 3H), 3.11 (d, J = 5.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 158.9, 148.3, 147.2, 143.1, 138.0, 131.4, 129.3, 128.9, 128.7, 128.5, 122.6, 119.4, 103.5, 55.5, 26.2.

*Ethyl N-[(6-Methoxy-4-phenylquinolin-2-yl)carbonyl]-aminoacetate (**4m**).*[5b] Purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 4/1 as eluent). Pale yellow solid, 23.7 mg, 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (t, J = 5.4 Hz, 1H), 8.19 (s, 1H), 8.08 (d, J = 9.2 Hz, 1H), 7.55−7.47 (m, 5H), 7.41 (dd, J = 9.2, 2.8 Hz, 1H), 7.23 (d, J = 2.7 Hz, 1H), 4.33 (d, J = 5.7 Hz, 2H), 4.28 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 165.0, 159.0, 148.2, 146.4, 143.2, 138.0, 131.7, 129.3, 129.0, 128.6, 128.5, 122.6, 119.4, 103.4, 61.5, 55.4, 41.5, 14.2.

Procedure for the Synthesis of Tetrahydroquinoline. To a solution of iminium **5a** (0.1 mmol, 1.0 equiv) and olefin **2a** (0.2 mmol, 2.0 equiv) in dry CH_3CN (1.0 mL) was added $Cu(OTf)_2$ (10 mol %). The mixed solution was stirred under air atmosphere at room temperature. After completion of the reaction as monitored by TLC, the reaction solvent was concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (petroleum ether/EtOAc = 8:1) to afford the product.

*Ethyl 6-methoxy-4-phenyl-1,2,3,4-tetrahydroquinoline-2-carboxylate (**6a**).* Pale yellow oil, 22.0 mg, 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.17 (m, 6H), 6.69−6.62 (m, 2 H), 6.22 (d, J = 2.4 Hz, 1H), 4.19−4.12 (m, 4H), 3.57 (s, 3H), 2.58−2.53 (m, 1H), 2.16−2.08 (m, 1H), 1.24 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 152.2, 144.5, 137.5, 128.7, 128.5, 126.7, 125.5, 115.9, 115.0, 113.5, 61.3, 55.6, 54.4, 44.0, 35.1, 14.1. HRMS-ESI calcd for $C_{19}H_{22}NO_3$ $(M + H)^+$ 312.1594, found 312.1594.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02683.

Details for the optimization of the reaction conditions, the EPR spectra, and copies of NMR spectra of the products (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: liying@lzu.edu.cn.

*E-mail: zhangyuan@lzu.edu.cn.

ORCID

Yuan Zhang: 0000-0002-4403-0995

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the National Natural Science Foundation of China (No. 21572092, 21472078), the Fundamental Research Funds for the Central Universities (No. lzujbky-2016-56) for financial support. We thank professor Qiang Liu (Lanzhou University) for helpful discussion.

■ REFERENCES

(1) For selected reviews, see: (a) Li, C.-J.; Li, Z. *Pure Appl. Chem.* **2006**, *78*, 935. (b) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (c) Scheuermann, C. J. *Chem. - Asian J.* **2010**, *5*, 436. (d) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (e) Liu, C.; Zhang, H.; Shi, W.; Lei, A. W. *Chem. Rev.* **2011**, *111*, 1780. (f) Zhang, C.; Tang, C. H.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3464. (g) Girard, S. A.; Knauber, T.; Li, C.-J. *Angew. Chem., Int. Ed.* **2014**, *53*, 74.

(2) (a) Zhao, L.; Li, C.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 7075. (b) Zhao, L.; Basle, O.; Li, C.-J. *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106*, 4106.

(3) For selected examples, see: (a) Xie, J.; Huang, Z. Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 10181. (b) Zhang, G.; Zhang, Y.; Wang, R. *Angew. Chem., Int. Ed.* **2011**, *50*, 10429. (c) Li, K.; Tan, G.; Huang, J.; Song, F.; You, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 12942. (d) Huo, C. D.; Wang, C.; Wu, M. X.; Jia, X. D.; Xie, H. S.; Yuan, Y. *Adv. Synth. Catal.* **2014**, *356*, 411. (e) Zhu, Z. Q.; Bai, P.; Huang, Z. Z. *Org. Lett.* **2014**, *16*, 4881. (f) Wei, X.-H.; Wang, G.-W.; Yang, S.-D. *Chem. Commun.* **2015**, *51*, 832. (g) Huo, C. D.; Chen, F. J.; Yuan, Y.; Xie, H. S.; Wang, Y. J. *Org. Lett.* **2015**, *17*, 5028. (h) Xie, Z.; Liu, X.; Liu, L. *Org. Lett.* **2016**, *18*, 2982. (i) Jia, X.; Zhu, Y.; Yuan, Y.; Zhang, X.; Lü, S.; Zhang, L.; Luo, L. *ACS Catal.* **2016**, *6*, 6033.

(4) (a) Richter, H.; Mancheño, O. G. *Org. Lett.* **2011**, *13*, 6066. (b) Rohlmann, R.; Stopka, T.; Richter, H.; Mancheño, O. G. *J. Org. Chem.* **2013**, *78*, 6050.

(5) (a) Jia, X. D.; Peng, F. F.; Qing, C.; Huo, C. D.; Wang, X. C. *Org. Lett.* **2012**, *14*, 4030. (b) Jia, X. D.; Wang, Y. X.; Peng, F. F.; Huo, C. D.; Yu, L. L.; Liu, J.; Wang, X. C. *J. Org. Chem.* **2013**, *78*, 9450. (c) Liu, J.; Wang, Y. X.; Yu, L. L.; Huo, C. D.; Wang, X. C.; Jia, X. D. *Adv. Synth. Catal.* **2014**, *356*, 3214. (d) Liu, J.; Liu, F.; Zhu, Y. Z.; Ma, X. G.; Jia, X. D. *Org. Lett.* **2015**, *17*, 1409. (e) Wang, Y. X.; Peng, F. F.; Liu, J.; Huo, C. D.; Wang, X. C.; Jia, X. D. *J. Org. Chem.* **2015**, *80*, 609.

(6) (a) Huo, C.; Yuan, Y.; Wu, M.; Jia, X.; Wang, X.; Chen, F.; Tang, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 13544. (b) Huo, C. D.; Xie, H. S.; Wu, M. X.; Jia, X. D.; Wang, X. C.; Chen, F. J.; Tang, J. *Chem. - Eur. J.* **2015**, *21*, 5723.

DOI: 10.1021/acs.joc.6b02683
J. Org. Chem. 2016, 81, 12433−12442

(7) Xie, Z. Y.; Jia, J.; Liu, X. G.; Liu, L. *Adv. Synth. Catal.* **2016**, *358*, 919.
(8) Musiol, R.; Serda, M.; Hensel-Bielowka, S.; Polanski, J. *Curr. Med. Chem.* **2010**, *17*, 1960.
(9) For selected reviews, see: (a) Zeitler, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9785. (b) Yoon, T. P.; Ischay, M. A.; Du, J. N. *Nat. Chem.* **2010**, *2*, 527. (c) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102. (d) Shi, L.; Xia, W. J. *Chem. Soc. Rev.* **2012**, *41*, 7687. (e) Xuan, J.; Xiao, W. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828. (f) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322. (g) Corrigan, N.; Shanmugam, S.; Xu, J.; Boyer, C. *Chem. Soc. Rev.* **2016**, *45*, 6165.
(10) For selected examples, see: (a) Condie, A. G.; Gonzalez-Gomez, J. C.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2010**, *132*, 1464. (b) Rueping, M.; Vila, C.; Koenigs, R. M.; Poscharny, K.; Fabry, D. C. *Chem. Commun.* **2011**, *47*, 2360. (c) Rueping, M.; Zhu, S. Q.; Koenigs, R. M. *Chem. Commun.* **2011**, *47*, 8679. (d) Liu, Q.; Li, Y.-N.; Zhang, H.-H.; Chen, B.; Tung, C.-H.; Wu, L.-Z. *Chem. - Eur. J.* **2012**, *18*, 620. (e) Meng, Q.-Y.; Zhong, J.-J.; Liu, Q.; Gao, X.-W.; Zhang, H.-H.; Lei, T.; Li, Z.-J.; Feng, K.; Chen, B.; Tung, C.-H.; Wu, L.-Z. *J. Am. Chem. Soc.* **2013**, *135*, 19052. (f) Zhong, J.-J.; Meng, Q.-Y.; Liu, B.; Li, X.-B.; Gao, X.-W.; Lei, T.; Wu, C.-J.; Li, Z.-J.; Tung, C.-H.; Wu, L.-Z. *Org. Lett.* **2014**, *16*, 1988. (g) Wu, C.-J.; Zhong, J.-J.; Meng, Q.-Y.; Lei, T.; Gao, X.-W.; Tung, C.-H.; Wu, L.-Z. *Org. Lett.* **2015**, *17*, 884. (h) Xu, G. Q.; Li, C. G.; Liu, M. Q.; Cao, J.; Luo, Y. C.; Xu, P. F. *Chem. Commun.* **2016**, *52*, 1190. (i) Liu, X.; Ye, X.; Bureš, F.; Liu, H.; Jiang, Z. *Angew. Chem., Int. Ed.* **2015**, *54*, 11443. (j) Wei, G.; Zhang, C.; Bureš, F.; Ye, X.; Tan, C.-H.; Jiang, Z. *ACS Catal.* **2016**, *6*, 3708.
(11) (a) Wang, Z. Q.; Hu, M.; Huang, X. C.; Gong, L. B.; Xie, Y. X.; Li, J. H. *J. Org. Chem.* **2012**, *77*, 8705. (b) Zhu, S. Q.; Rueping, M. *Chem. Commun.* **2012**, *48*, 11960. (c) Gao, X. W.; Meng, Q. Y.; Xiang, M.; Chen, B.; Feng, K.; Tung, C. H.; Wu, L. Z. *Adv. Synth. Catal.* **2013**, *355*, 2158. (d) Gao, X. W.; Meng, Q. Y.; Li, J. X.; Zhong, J. J.; Lei, T.; Li, X. B.; Tung, C. H.; Wu, L. Z. *ACS Catal.* **2015**, *5*, 2391. (e) Tan, Y.; Yuan, W.; Gong, L.; Meggers, E. *Angew. Chem., Int. Ed.* **2015**, *54*, 13045. (f) Upon the submission of this manuscript, we noticed that a visible-light-induced photocatalytic intramolecular Povarov cyclization reaction for the construction of quinoline-fused lactones had just been reported: Dong, W. H.; Hu, B.; Gao, X. S.; Li, Y. Y.; Xie, X. M.; Zhang, Z. G. *J. Org. Chem.* **2016**, *81*, 8770.
(12) (a) Huang, H.; Jiang, H.; Chen, K.; Liu, H. *J. Org. Chem.* **2009**, *74*, 5476. (b) McNulty, J.; Vemula, R.; Bordon, C.; Yolken, R.; Jones-Brando, L. *Org. Biomol. Chem.* **2014**, *12*, 255. (c) Bharate, J. B.; Wani, A.; Sharma, S.; Reja, S. I.; Kumar, M.; Vishwakarma, R. A.; Kumar, A.; Bharate, S. B. *Org. Biomol. Chem.* **2014**, *12*, 6267. (d) Wu, Y. C.; Liu, L.; Li, H. J.; Wang, D.; Chen, Y. J. *J. Org. Chem.* **2006**, *71*, 6592. (e) Isambert, N.; Cruz, M.; Arevalo, M. J.; Gomez, E.; Lavilla, R. *Org. Lett.* **2007**, *9*, 4199.
(13) (a) Villamena, F. A.; Liu, Y. P.; Zweier, J. L. *J. Phys. Chem. A* **2008**, *112*, 12607. (b) Ou, Z. Z.; Chen, J. R.; Wang, X. S.; Zhang, B. W.; Cao, Y. *New J. Chem.* **2002**, *26*, 1130. (c) Ma, J. H.; Zhao, J. Q.; Jiang, L. J. *Photochem. Photobiol.* **2001**, *74*, 143.

DOI: 10.1021/acs.joc.6b02683
J. Org. Chem. 2016, 81, 12433−12442