JOC The Journal of Organic Chemistry

university of groningen

Subscriber access provided by University of Groningen

FeCl2-Catalyzed Decarboxylative Radical Alkylation/Cyclization of Cinnamamides: Access to Dihydroquinolinone and Pyrrolo[1,2-a]indole Analogues

Zhihao Cui, and Da-Ming Du

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b00511 • Publication Date (Web): 12 Apr 2018

Just Accepted

ACS Publications

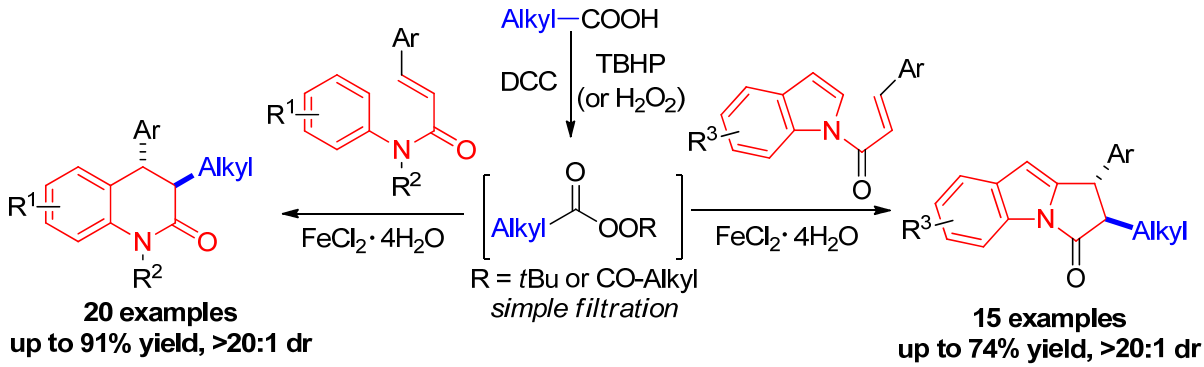
is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

$FeCl_2$-Catalyzed Decarboxylative Radical Alkylation/Cyclization of Cinnamamides: Access to Dihydroquinolinone and Pyrrolo[1,2-*a*]indole Analogues

Zhihao Cui and Da-Ming Du*

School of Chemistry and Chemical Engineering, Beijing Institute of Technology, Beijing 100081, People's Republic of China

e-mail: dudm@bit.edu.cn



ABSTRACT

A simple and unified method for the synthesis of alkylated dihydroquinolinone and pyrrolo[1,2-*a*]indole derivatives in moderate to high yields (up to 91%) with excellent diastereoselectivity (>20:1 dr) was developed. The inexpensive $FeCl_2 \cdot 4H_2O$ works as catalyst, and easily-prepared peresters (or peroxides) from aliphatic acids act as alkylating reagents and single electron oxidants. This environmental-friendly reaction proceeds via $FeCl_2$-catalyzed alkyl radical cascade addition/cyclization fashion.

INTRODUCTION

As an indispensable part, *N*-heterocyclic compounds invariably hold a huge proportion in the chemical compound library, and novel methodologies for prepared efficiently *N*-heterocycles are always highly sought-after.[1] In the recent years, there is a growing concern over two distinctive *N*-heterocycles, 3,4-dihydroquinolinones[2] and pyrrolo[1,2-*a*]indoles,[3] which often serve as bioactive alkaloids scaffolds[4] such as the pyrrolo[1,2-*a*]indole-containing anti-HIV Isatisine A[5] and the psychoactive Yuremamine[6] or as the core pharmacophores in drugs (Figure 1).[7] As always, high demand advances the rapid development of technologies and many protocols have been exploited to forge such useful frameworks. For instances, in terms of construction of dihydroquinolinone derivatives, Shi group developed a Pd-catalyzed intramolecular arylation of inert C(sp^3)-H bond in 2014[2b] and Mai reported a Ag-catalyzed radical addition/cyclization pattern.[2c] As for pyrrolo[1,2-*a*]indole, Shen and his coworkers achieved success via a one-pot protocol catalyzed successively by $Rh_2(OAc)_4$ and $Cu(OTf)_2$ in 2015[3b] and Lautens group developed a Pd-catalyzed dearomative indole bisfunctionalization.[3c] Notwithstanding these elegant breakthroughs, drawbacks still exist such as high temperature,[2b,2c] complicated starting materials[3a] and noble metals.[2a,3b] In addition, strategies of straightforward incorporation of alkyl group into these core skeletons have been relatively little studied, particularly into 2-position of pyrrolo[1,2-*a*] indoles.

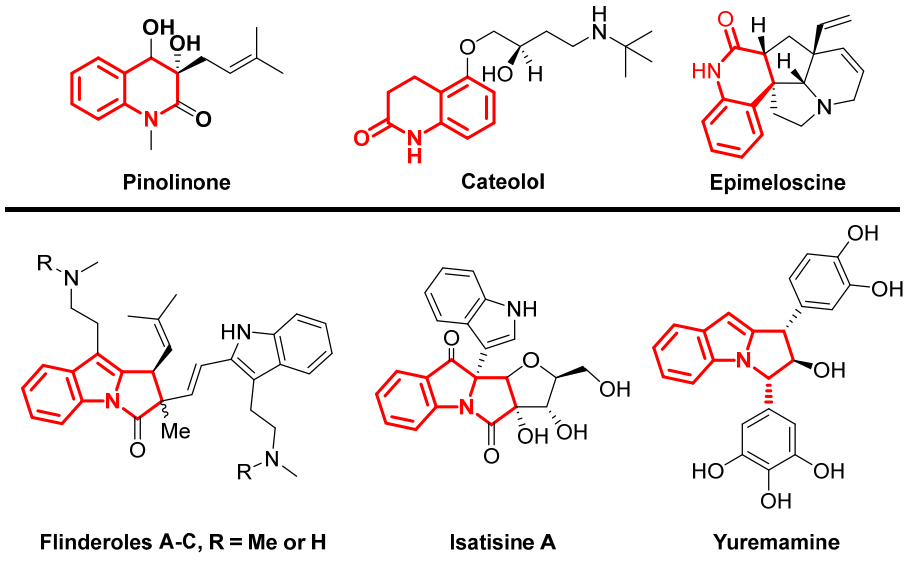
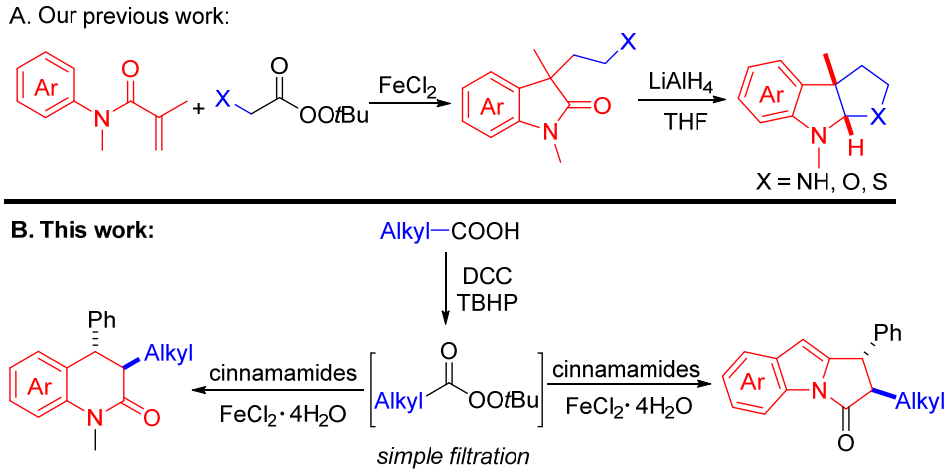


Figure 1. Representative alkaloids containing dihydroquinolinone and pyrrolo[1,2-*a*]indole moieties

Construction of complicated molecule scaffolds by alkyl radical addition strategy has emerged as a powerful tool in the past decades.[8] The frequently-used precursors of alkyl radicals are alkyl halides[9] and aliphatic acids.[2c,10] Recently, redox-active esters as the alkyl source attract more and more attention, because such strategies hold many outstanding advantages.[11] Peresters, employed more often as initiators and oxidants,[12] represent another type of redox-active esters.[13] Recently, the elaborate studies have been performed of alkyl radical addition reactions employing peresters as alkylating reagents and oxidants.[14] Also, based on the bifunctional features of perester, we have successfully developed a practical two-step sequence for synthesis of fused-indoline-heterocycles (Scheme1A).[15] Similarly, we envision that combination of peresters and different cinnamamides might allow convenient access to the alkylated 3,4-dihydroquinolinone and pyrrolo[1,2-*a*]indole derivatives via alkyl radical addition/annulation fashion (Scheme 1B).

Scheme 1. Alkyl Radical Addition/Cyclization of α,β-Unsaturated Amides

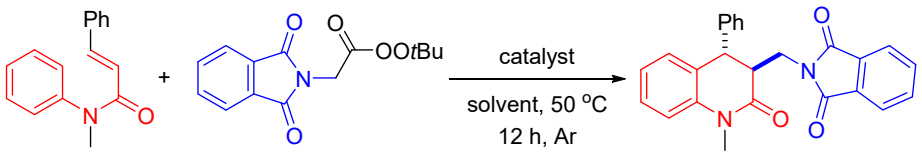


RESULTS AND DISCUSSION

Our investigation was initiated by employing cinnamamide **1a** and perester **3a** as the model substrates (Table 1). Results of screening catalysts showed that only iron salts took effect and the inexpensive $FeCl_2{\cdot}4H_2O$ gave the best outcome (Table 1, entries 1-6). The structure of **4aa** (CCDC 1818937) was confirmed by single-crystal X-ray diffraction analysis[16] and only *trans* isomer was detected and

achieved (Figure 2). In the presence of copper or nickel salts, the reaction process was completely suppressed and only starting materials were recovered (Table 1, entries 7-9). In the absence of catalyst, only trace amount of product **4aa** was obtained and when the reaction was conducted at elevated temperature (100 °C), the yield was improved (Table 1, entries 10 and 11). However, decomposition temperatures measured by DSC showed that upon heating over 100 °C, peresters were potentially explosive and it would cause unsafe operation.[15] The optimization of solvents displayed that DMF was superior to other solvents such as DMSO, MeCN, toluene and dioxane (Table 1, entries 5, 12-15).

Table 1. Optimization of Reaction Conditions.[a]



1a **3a** **4aa**

entry	catalyst	solvent	yield (%)[b]
1	$Fe(OTf)_2$	DMF	30
2	$Fe(OTf)_3$	DMF	33
3	$Fe(acac)_2$	DMF	51
4	$Fe(acac)_3$	DMF	56
5	$FeCl_2{\cdot}4H_2O$	DMF	64
6	Cp_2Fe	DMF	38
7	$NiCl_2{\cdot}6H_2O$	DMF	n.r.
8	CuBr	DMF	n.r.
9	$Cu(OAc)_2$	DMF	n.r.
10	–	DMF	trace
11[c]	–	DMF	34
12	$FeCl_2{\cdot}4H_2O$	DMSO	n.r.
13	$FeCl_2{\cdot}4H_2O$	MeCN	20
14	$FeCl_2{\cdot}4H_2O$	toluene	61
15	$FeCl_2{\cdot}4H_2O$	1,4-dioxane	56

[a]Reaction conditions: **1a** (0.1 mmol), **3a** (0.25 mmol), catalyst (0.01 mmol), solvent (2.0 mL), 50 °C, 12 h, Ar.
[b]Isolated yield. [c]100 °C. n.r. = no reaction

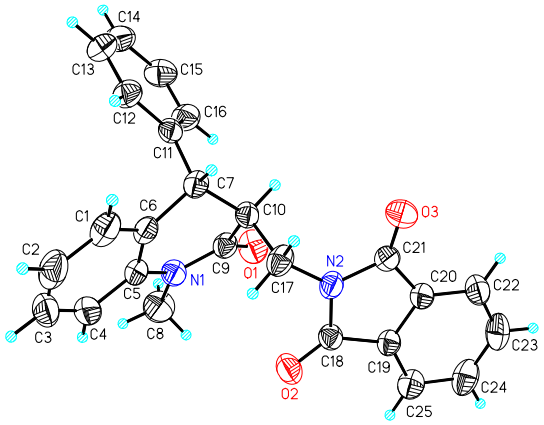
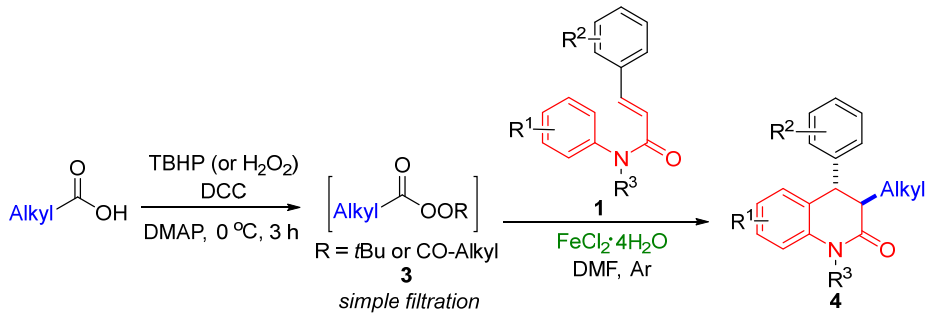
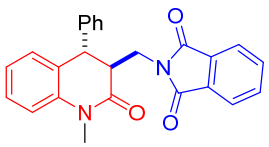


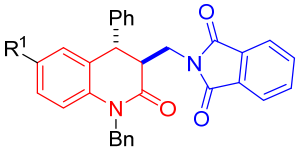
Figure 2. X-ray crystal structure of **4aa** (displacement ellipsoids are drawn at the 50% probability level)

Table 2. Substrate Scope for Construction of Dihydroquinolinone Derivatives[a-c]

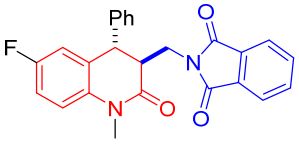




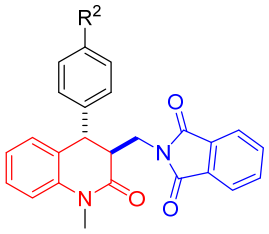
4aa, 64%, >20:1 dr



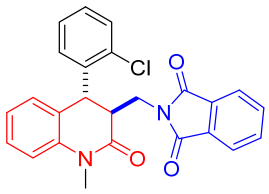
4ba, R^1 = Cl, 50%, >20:1 dr
4ca, R^1 = OMe, 59%, >20:1 dr
4ea, R^1 = CO_2Et, 52%, >20:1 dr



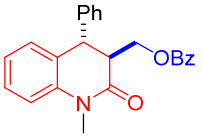
4da, 69%, >20:1 dr



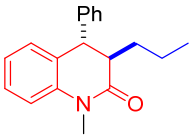
4fa, R^2 = CF_3, 75%, >20:1 dr
4ha, R^2 = Br, 69%, >20:1 dr



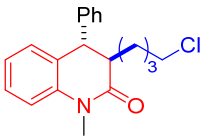
4ga, 72%, >20:1 dr



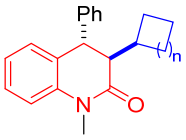
4ab, 70%, >20:1 dr



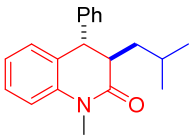
4ac, 57%[d], >20:1 dr



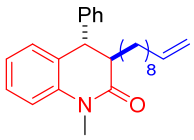
4ad, 51%[d], >20:1 dr



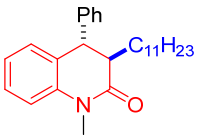
4ae, n =1, 58%[e], >20:1 dr
4af, n = 2, 56%[d], >20:1 dr
4ag, n = 3, 49%[d], >20:1 dr



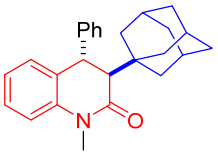
4ai, 72%[f,g], 94:6 dr



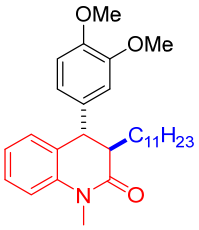
4aj, 91%[f,g], 86:14 dr



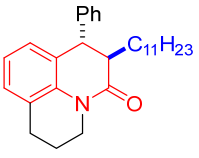
4ak, 90%[f], 89:11 dr



4al, trace[d]



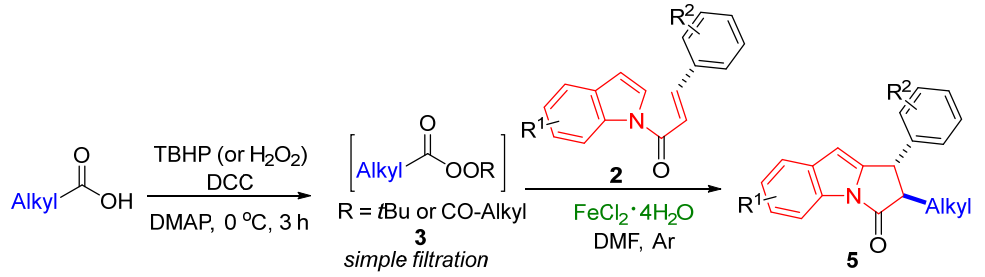
4ik, 63%[f], >20:1 dr

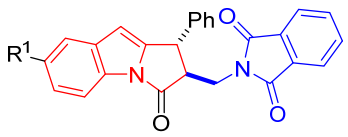


4jk, 83%[f], >20:1 dr

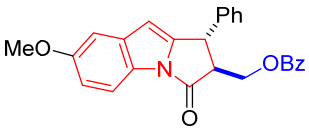
[a]Unless note otherwise, the reaction conditions are as following: cinnamamide **1** (0.2 mmol), perester **3** (0.5 mmol), $FeCl_2·4H_2O$ (0.02 mmol), DMF (2.0 mL), Ar, 50 °C, 12 h. [b]Isolated yield after silica gel column chromatography. [c]The dr value was determined by ^1H NMR. [d]Perester **3** (0.6 mmol), 60 °C, 12 h. [e]Perester **3** (0.6 mmol), 60 °C, 36 h. [f]Cinnamamide **1** (0.2 mmol), diacyl peroxide **3** (0.5 mmol), $FeCl_2·4H_2O$ (0.02 mmol), DMF (2.0 mL), Ar, 50 °C, 12 h. [g]Diacyl peroxide **3** (0.6 mmol), 60 °C, 12 h.

Table 3. Substrate Scope for Construction of Pyrrolo[1,2-*a*]indole Derivatives[a-c]

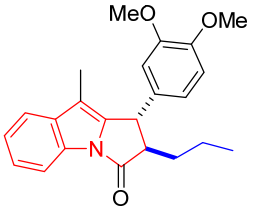




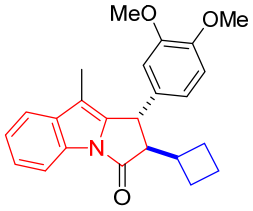
5aa, R^1 = H, 43%, >20:1 dr
5ba, R^1 = CH_3, 45%, >20:1 dr
5ca, R^1 = OMe, 53%, >20:1 dr



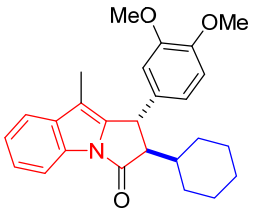
5cb, 32%, >20:1 dr



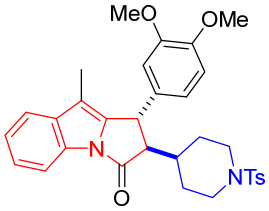
5dc, 50%[d], 89:11 dr



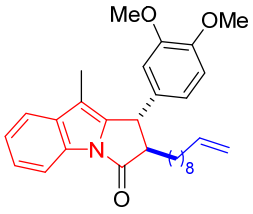
5de, 40%[e], >20:1 dr



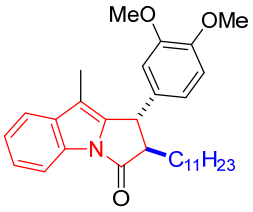
5dg, 52%[d], >20:1 dr



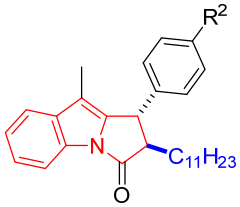
5dh, 40%[d], >20:1 dr



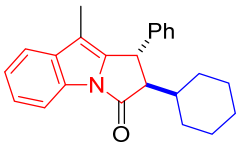
5dj, 47%[f,g], >20:1 dr



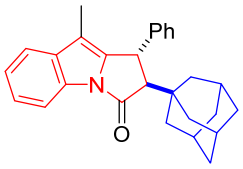
5dk, 62%[f], >20:1 dr



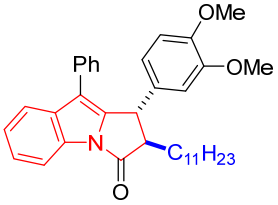
5ek, R^2 = Br, 74%[f], >20:1 dr
5fk, R^2 = CF_3, 63%[f], >20:1 dr



5gg, 60%[d], >20:1 dr



5gl, trace[d]



5hk, 65%[f,g], >20:1 dr

[a]Unless note otherwise, the reaction conditions are as following: cinnamamide **2** (0.2 mmol), perester **3** (0.5 mmol), $FeCl_2 \cdot 4H_2O$ (0.02 mmol), DMF (2.0 mL), Ar, 50 °C, 12 h. [b]Isolated yield after silica gel column chromatography. [c]The dr value was determined by ^1H NMR. [d]Perester **3** (0.6 mmol), 60 °C, 12 h. [e]Perester **3** (0.6 mmol), 60 °C, 36 h. [f]Cinnamamide **2** (0.2 mmol), diacyl peroxide **3** (0.5 mmol), $FeCl_2 \cdot 4H_2O$ (0.02 mmol), DMF (2.0 mL), Ar, 50 °C, 12 h. [g]Diacyl peroxide **3** (0.6 mmol), 60 °C, 12 h.

With the optimal conditions in hand, the effect of substituent variation on cinnamamide **1** and peresters **3** was investigated (Table 2). Whether halogens anchoring on aniline motifs (R^1) or cinnamamide moieties (R^2), remained intact in the reaction (**4ba**, **4da**, **4ga**, **4ha**). Substrates containing the electron-donating or electron-withdrawing group proceeded well, affording the cyclized products with excellent diastereoselectivity (**4ca**, **4ea**, **4fa**). Subsequently, the scope of peresters was examined. Peresters stemmed from primary acids were amenable to the addition/annulation process (**4ac**, **4ad**). Alternatively, the analogues of peresters, the alkyl diacyl peroxides, also worked well under the conditions and delivered the desired alkylated products **4ai, 4aj, 4ak**, **4ik** and **4jk** with good diastereoselectivity. It is worth noting that the existence of terminal alkene of peroxide **3j** did not alter the radical addition pathway (**4aj**). Peresters of secondary acids displayed moderate reactivity in this transformation (**4ae**, **4af**, **4ag**). Possibly due to the steric hindrance, employing tertiary perester would lead to only trace amount of isolated product **4al**.

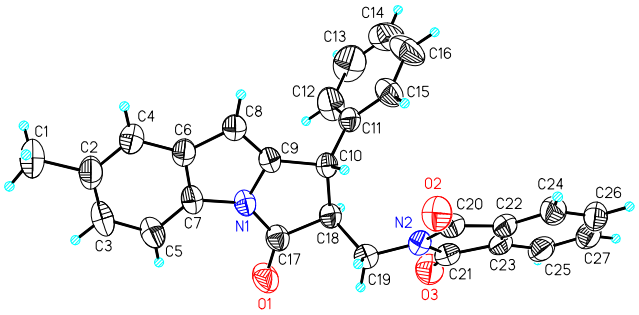


Figure 3. X-ray crystal structure of **5ba** (Displacement ellipsoids are drawn at the 50% probability level)

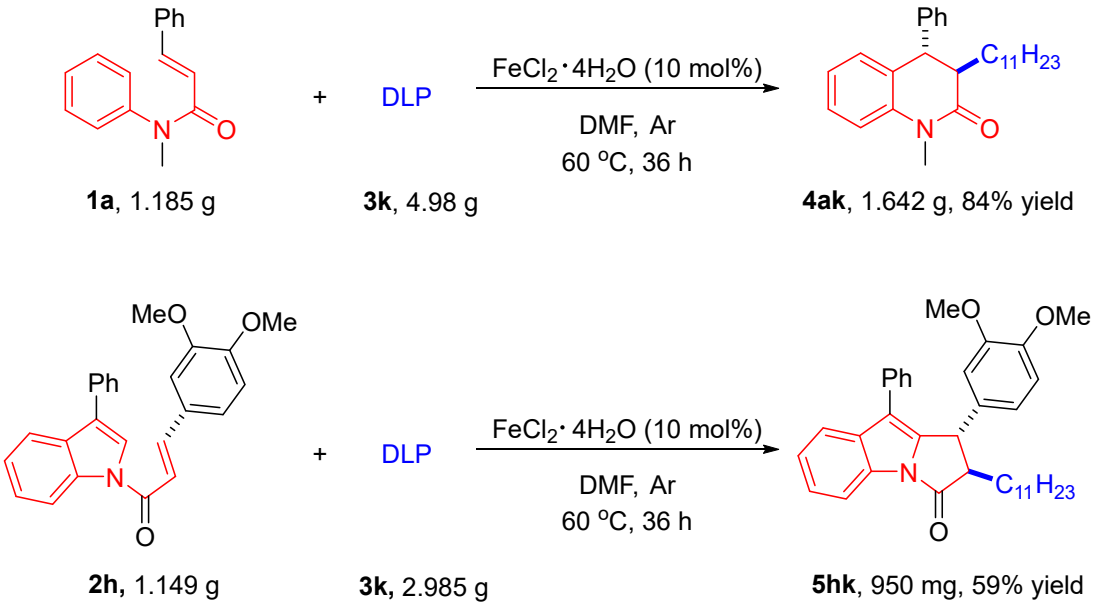
Then, the optimal conditions was successfully applied to construction of pyrrolo[1,2-*a*]indole derivatives without any change (Table 3). Substituents such as methyl and methoxy on indoles moiety (R^1) had no big effect on the reaction results (**5aa**, **5ba**, **5cb**). The *trans* isomer of **5ba** (CCDC 1819940) was confirmed by single-crystal X-ray diffraction analysis (Figure 3).[16] Substrates bearing CF_3, MeO and Br on R^2 moiety reacted well with commercially available dilauroyl peroxide (DLP), providing the expected product with excellent diastereoselectivity (**5dk**, **5ek**, **5fk**). Besides, peresters (or peroxides) of primary alkyl acids could be applied to this reaction and give the tricycle products in moderate yields

(**5dc**, **5dj** and **5hk**). Also, peresters of secondary acids proved to be suitable substrates for this reaction (**5de**, **5dg**, **5dh** and **5gg**). Unfortunately, perester of tertiary aliphatic acid was ill-suited to this protocol (**5gl**).

To showcase the scalability of this transformation, two scale-up experiments were carried out. DLP as the alkylating reagents separately afforded the bicycle product **4ak** in 84% yield and the tricycle product **5hk** in 59% yield (Scheme 2).

To probe into the mechanism, radical trapping experiments were performed. With respect to the construction of product **4aa**, neither did the addition of TEMPO, a common radical scavenger, make this transformation run, nor did BHT. Analysis by TLC and LC-MS exhibited that only adduct **6a** or **6b** was detected and no the expected product **4aa** was generated (Scheme 3). Similarly, the addition of TEMPO or BHT into the reaction for synthesis of product **5ca** had the same results as well (Scheme 3) (see Supporting Information).

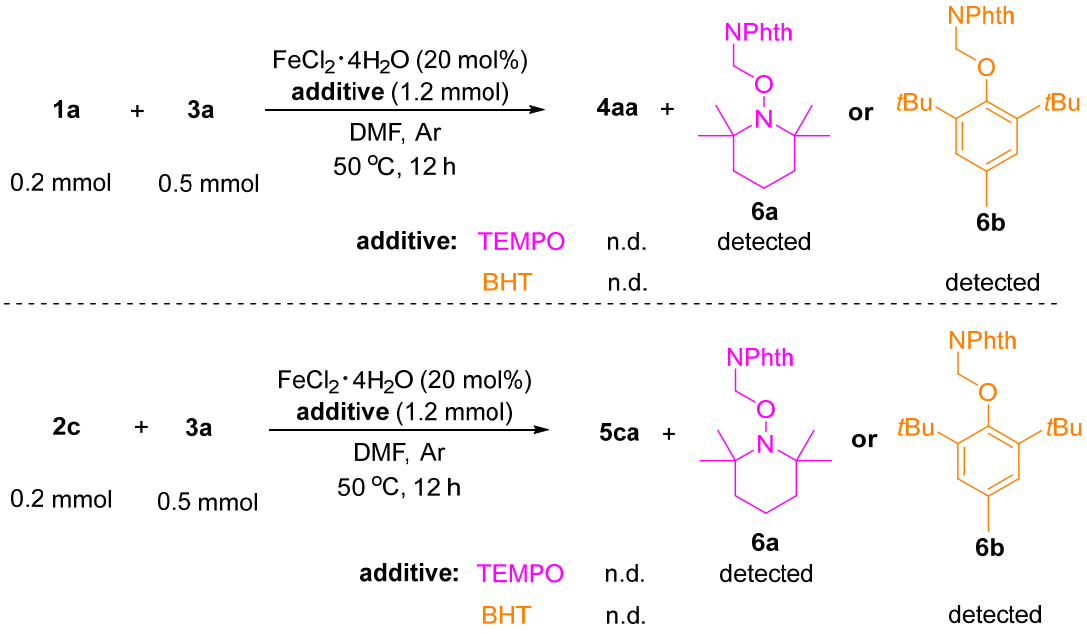
Scheme 2. Scale-up experiments.



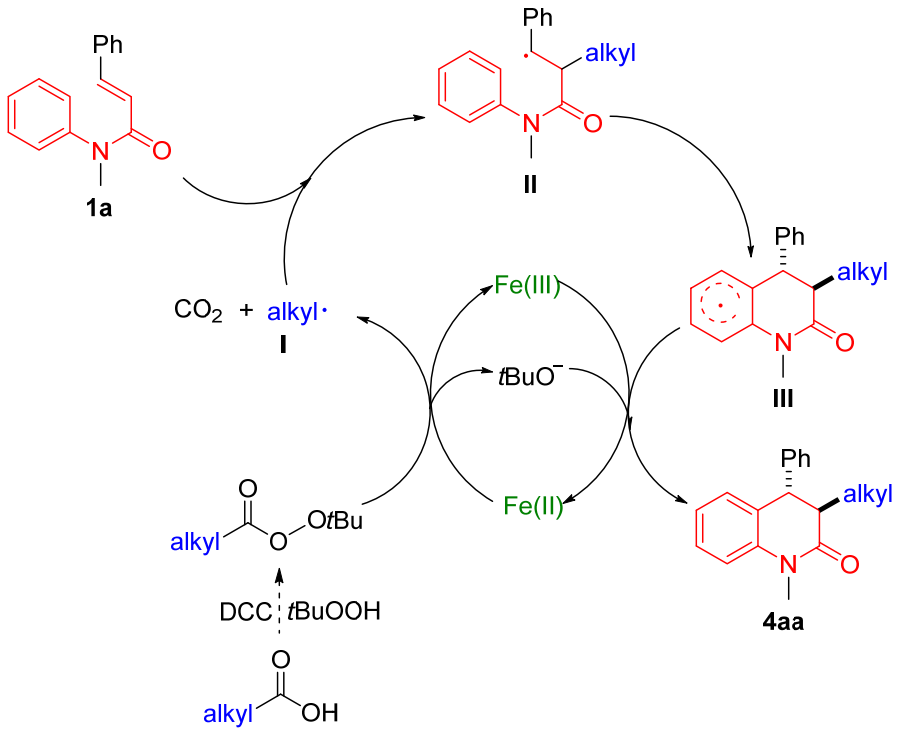
Based on these experiments, a $FeCl_2$-catalyzed alkyl radical addition/cyclization mechanism was proposed (Scheme 4). Outer-sphere single-electron transfer from Fe(II) to perester leads to the O-O

bond cleavage, generating the reactive alkyl radical **I**, Fe(III), CO_2 and tBuO$^-$. The addition of radical **I** to α,β-unsaturated amide **1a** delivers the relatively stable benzyl radical **II**. Subsequently, intramolecular cyclization of **II** generates radical intermediate **III**, which then successively undergoes single electron oxidation by Fe(III) and deprotonation by tBuO$^-$ to give the annulated product **4aa** and Fe(II).

Scheme 3. Preliminary Investigation of Mechanism



Scheme 4. Plausible Mechanism



CONCLUSIONS

In conclusion, we have developed an inexpensive and environmental-friendly $FeCl_2{\cdot}4H_2O$-catalyzed unified approach for highly diastereoselective synthesis of alkylated dihydroquinolinone and pyrrolo[1,2-*a*]indole derivatives. This reaction is enabled by the alkyl radical addition/annulation of different cinnamamides. Peresters (or peroxides) not only serve as alkyl source, but also as single electron oxidizing agents. This approach demonstrates strong regio-selectivity and special cinnamamides produce cycles with specific size.

EXPERIMENTAL SECTION

General Information: All commercial reagents were used without further purification. Solvents were distilled according to the purification procedures. ^{1}H NMR spectra were measured with 400 MHz spectrometer, chemical shifts were reported in δ (ppm) units relative to tetramethylsilane (TMS) as internal standard. ^{13}C NMR spectra were measured at 176 MHz with 700 MHz spectrometer, chemical shifts are reported in ppm relative to tetramethylsilane and referenced to solvent peak ($CDCl_3$, δ C =

77.00). Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). The ESI-HRMS spectra were obtained with Accurate-Mass-Q-TOF MS spectrometer.

Peresters **3a-3h, 3l** and peroxides **3i, 3j** were synthesized according to the following procedure **A** and B. **3k** (DLP) was commercially available.

General procedures A: A solution of alkyl carboxylic acid (6 mmol), DMAP (73.2 mg, 0.6 mmol), *t*BuOOH (900 mg, 7 mmol, 70% w/w solution in water) in CH_2Cl_2 (5 mL) was cooled to 0 ºC, followed by dropwise addition of DCC (1.44 g, 7 mmol) in CH_2Cl_2. After the resulting solution was stirred for 3h at 0 °C, petroleum ether (30 mL) was added. Then the resulting mixture was quickly filtered by silica gel flash chromatography (3–5 cm height) with pressure pump and the chromatography was quickly washed by 80 mL eluent (petroleum ether/AcOEt = 20:1). The filtration was concentrated under reduced pressure to give the crude peresters **3a-3h, 3l**, which would keep intact and undegraded for months at –20 ºC and would be directly used in the next step without any further purification.

The simply-filtered crude perester (0.5 mmmol or 0.6 mmol), $FeCl_2{\cdot}4H_2O$ (3.98 mg, 0.02 mmol, 10 mol%), cinnamamide (0.2 mmol) were added into a Schlenk tube under Ar atmosphere, followed by the addition of degassed DMF (2.0 mL) via syringe. The tube was immediately placed in a preheated 50 or 60 °C oil bath for 12 h under stirring**.** After completion, the mixture was added into 0.1 M aqueous HCl (not for acid-sensitive substrates) and extracted with EtOAc for 3 times. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum to furnish the title product **4**, which was then purified by silica gel flash column chromatography (EtOAc/petroleum ether as eluant) to furnish the title product.

General procedures B: a solution of alkyl carboxylic acid (6 mmol), DMAP (73.2 mg, 0.6 mmol), H_2O_2 (245 mg, 3.5 mmol, 50% w/w solution in water) in CH_2Cl_2 (5 mL) was cooled to 0 ºC, followed by dropwise addition of DCC (1.44 g, 7 mmol) in CH_2Cl_2. After the resulting solution was stirred for 3h at 0 °C, petroleum ether (30 mL) was added. Then the resulting mixture was quickly filtered by silica

gel chromatography (3–5 cm height) with pressure pump and the chromatography was quickly washed by 80 mL eluent (petroleum ether/AcOEt = 20:1). The filtration was concentrated under reduced pressure to give the crude peroxides **3i** and **3j**, which would keep intact and undegraded for months at –20 ºC and would be directly used in the next step without any further purification.

The simply-filtered crude peroxide (0.5 mmol or 0.6 mmol), $FeCl_2{\cdot}4H_2O$ (3.98 mg, 0.02 mmol, 10 mol%), cinnamamide (0.2 mmol) were added into a Schlenk tube under Ar atmosphere, followed by the addition of degassed DMF (2.0 mL) via syringe. The tube was immediately placed in a preheated 50 or 60 °C oil bath for 12 h under stirring**.** After completion, the mixture was added into 0.1 M aqueous HCl (not for acid-sensitive substrates) and extracted with EtOAc for 3 times. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum to furnish the title product, which was then purified by silica gel flash column chromatography (EtOAc/petroleum ether as eluant) to furnish the title product **5**.

2-((1-Methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)methyl)isoindoline-1,3-dione (4aa). Following procedure **A:** the reaction of **1a** (47.4 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (10:1 to 4:1) to afford **4aa** (51.0 mg, 64% yield) as white solid. R_f = 0.30 (PE/EtOAc 2:1). M. p. 205-207 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75-7.63 (m, 4H), 7.26-7.19 (m, 3H), 7.13-6.95 (m, 6H), 4.13 (d, J = 4.0 Hz, 1H), 4.04 (dd, J_1 = 14.0 Hz, J_2 = 8.8 Hz, 1H), 3.84 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1H), 3.50 (dt, J_1 = 8.8 Hz, J_2 = 4.8 Hz, 1H), 3.34 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 168.7, 167.9, 140.5, 139.2, 133.7, 131.8, 129.4, 128.7, 128.2, 127.4, 127.0, 126.0, 123.2, 123.1, 114.8, 46.4, 45.3, 38.7, 29.6. HRMS (ESI): m/z calcd. for $C_{25}H_{21}N_2O_3$ $[M + H]^+$ 397.1547, found 397.1545.

2-((1-Benzyl-6-chloro-2-oxo-4-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)methyl)isoindoline-1,3-dione (4ba). Following procedure **A:** the reaction of **1b** (69.4 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using

PE/EtOAc (10:1 to 4:1) to afford **4ba** (51.0 mg, 50% yield) as white solid. R_f = 0.30 (PE/EtOAc 2:1). M. p. 233-235 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 2H), 7.67 (d, J = 2.8 Hz, 2H), 7.24-7.18 (m, 5H), 7.16-7.11 (m, 3H), 7.07-6.99 (m, 4H), 6.92 (d, J = 8.8 Hz, 1H), 5.48 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.4 Hz, 1H), 4.16-4.11 (m, 2H), 3.91 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1H), 3.70-3.68 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 168.7, 167.9, 139.5, 136.8, 136.1, 133.9, 131.8, 129.5, 128.8, 128.6, 128.1, 128.0, 127.6, 127.32, 127.26, 127.1, 123.2, 117.0, 46.2, 45.6, 45.2, 38.8. HRMS (ESI): *m*/*z* calcd. for $C_{31}H_{24}ClN_2O_3$ $[M + H]^+$ 507.1470, found 507.1477.

2-((1-Benzyl-6-methoxy-2-oxo-4-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)methyl)isoindoline-1,3-dione (4ca). Following procedure **A:** the reaction of **1c** (68.6 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (10:1 to 4:1) to afford **4ca** (59.0 mg, 59% yield) as white solid. R_f = 0.20 (PE/EtOAc 2:1). M. p. 91-92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78-7.76 (m, 2H), 7.67-7.65 (m, 2H), 7.25-7.13 (m, 8H), 7.03 (d, J = 7.6 Hz, 2H), 6.94 (d, J = 8.8 Hz, 1H), 6.64 (d, J = 8.8 Hz, 1H), 6.58 (s, 1H), 5.45 (d, J = 16.0 Hz, 1H), 4.81 (d, J = 16.0 Hz, 1H), 4.18-4.13 (m, 2H), 3.91 (dd, J_1 = 14.0 Hz, J_2 = 6.0 Hz, 1H), 3.68-3.63 (m, 4H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 168.6, 168.0, 155.5, 140.1, 136.7, 133.8, 131.9, 131.7, 128.7, 128.5, 127.7, 127.6, 127.2, 127.1, 123.2, 116.8, 115.7, 112.7, 55.3, 46.6, 45.7, 45.6, 38.9. HRMS (ESI): *m*/*z* calcd. for $C_{32}H_{27}N_2O_4$ $[M + H]^+$ 503.1965, found 503.1975.

2-((6-Fluoro-1-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)methyl)isoindoline-1,3-dione (4da). Following procedure **A:** the reaction of **1d** (51 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (10:1 to 4:1) to afford **4da** (57.0 mg, 69% yield) as white solid. R_f = 0.20 (PE/EtOAc 2:1). M. p. 244-246 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 3.2 Hz, 2H), 7.67 (J = 3.2 Hz, 2H), 7.26-7.21 (m, 2H), 7.14 (t, J = 7.2 Hz, 1H), 7.07 (d, J = 7.6 Hz, 2H), 6.99 (dd, J_1 = 8.4 Hz, J_2 = 4.8 Hz, 1H), 6.92 (t, J = 8.0 Hz, 1H), 6.72 (d, J = 8.4 Hz, 1H), 4.09-4.03 (m, 2H), 3.84 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1H), 3.53-3.48 (m, 1H), 3.33 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 168.4, 168.0, 158.7 (d,

$^{1}J_{C\text{-}F}$ = 243.8 Hz), 139.8, 135.6, 133.8, 131.8, 128.9, 128.4 (d, $^{3}J_{C\text{-}F}$ = 7.0 Hz), 127.5, 127.3, 123.2, 116.4 (d, $^{2}J_{C\text{-}F}$ = 23.4 Hz), 116.0 (d, $^{3}J_{C\text{-}F}$ = 7.9 Hz), 114.6 (d, $^{2}J_{C\text{-}F}$ = 22.2 Hz), 45.9, 45.5, 38.7, 29.9. HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{20}FN_2O_3$ $[M + H]^+$ 415.1452, found 415.1457.

Ethyl 1-benzyl-3-((1,3-dioxoisoindolin-2-yl)methyl)-2-oxo-4-phenyl-1,2,3,4-tetrahydro-quinolone-6-carboxylate (4ea). Following procedure **A:** the reaction of **1e** (77 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (10:1 to 4:1) to afford **4ea** (56.0 mg, 52% yield) as colorless liquid. R_f = 0.40 (PE/EtOAc 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 6.0 Hz, 3H), 7.67 (d, J = 4.0 Hz, 2H), 7.23-7.16 (m, 6H), 7.14-7.08 (m, 3H), 7.00 (d, J = 7.6 Hz, 2H), 5.54 (d, J = 16.0 Hz, 1H), 4.82 (d, J = 16.0 Hz, 1H), 4.32-4.27 (m, 3H), 4.09 (dd, J_1 = 13.6 Hz, J_2 = 9.2 Hz, 1H), 3.93 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1H), 3.70 (dt, J_1 = 8.8 Hz, J_2 = 4.0 Hz, 1H), 1.33 (t, J = 7.2 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 169.1, 167.9, 165.7, 141.8, 139.8, 136.0, 133.9, 131.8, 131.2, 130.0, 128.8, 128.5, 127.5, 127.3, 127.2, 125.7, 125.4, 123.3, 115.6, 60.8, 46.8, 45.5, 45.1, 38.8, 14.3. HRMS (ESI): *m*/*z* calcd. for $C_{34}H_{29}N_2O_5$ $[M + H]^+$ 545.2071, found 545.2075 .

2-((1-Methyl-2-oxo-4-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydroquinolin-3-yl)methyl)isoindoline-1,3-dione (4fa). Following procedure **A:** the reaction of **1f** (71 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (10:1 to 4:1) to afford **4fa** (70.0 mg, 75% yield) as white solid. R_f = 0.35 (PE/EtOAc 3:1). M. p. 207-208 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 2.4 Hz, 2H), 7.67 (d, J = 2.8 Hz, 2H), 7.46 (d, J = 7.6 Hz, 2H), 7.28 (t, J = 7.6 Hz, 1H), 7.19 (d, J = 7.6 Hz, 2H), 7.08 (d, J = 8.0 Hz, 1H), 7.01-6.97 (m, 2H), 4.19 (d, J = 4.0 Hz, 1H), 4.08 (dd, J_1 = 14.0 Hz, J_2 = 8.8 Hz, 1H), 3.88 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1H), 3.53-3.48 (m, 1H), 3.35 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 168.3, 167.9, 144.6, 139.3, 133.9, 131.7, 129.4 (q, $^{2}J_{CF}$ = 32.6 Hz), 129.3, 128.7, 128.0, 125.7 (q, $^{3}J_{CF}$ = 3.5 Hz), 125.1, 123.9 (q, $^{1}J_{CF}$ = 271.9 Hz), 123.5, 123.2, 115.0, 46.1, 45.3, 38.7, 29.7. HRMS (ESI): *m*/*z* calcd. for $C_{26}H_{20}F_3N_2O_3$ $[M + H]^+$ 465.1421, found 465.1404.

2-((4-(2-Chlorophenyl)-1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)methyl)isoindoline-1,3-dione (4ga). Following procedure **A:** the reaction of **1g** (54.2 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (10:1 to 4:1) to afford **4ga** (62.0 mg, 72% yield) as white solid. R_f = 0.3 (PE/EtOAc 2:1). M. p. 215-216 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78-7.75 (m, 2H), 7.69-7.66 (m, 2H), 7.36 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.13-6.97 (m, 5H), 6.62 (d, J = 7.6 Hz, 1H), 4.62 (s, 1H), 4.04 (dd, J_1 = 13.6 Hz, J_2 = 8.8 Hz, 1H), 3.91 (dd, J_1 = 13.6 Hz, J_2 = 5.6 Hz, 1H), 3.45-3.41 (m, 1H), 3.37 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 168.2, 167.9, 140.0, 138.0, 133.8, 133.6, 131.8, 130.0, 129.9, 128.62, 128.57, 128.4, 127.2, 124.4, 123.6, 123.2, 114.8, 46.0, 42.0, 38.7, 29.7. HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{20}ClN_2O_3$ $[M + H]^+$ 431.1157, found 431.1146 .

2-((4-(4-Bromophenyl)-1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)methyl)isoindoline-1,3-dione (4ha). Following procedure **A:** the reaction of **1h** (63 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (10:1 to 4:1) to afford **4ha** (65.0 mg, 69% yield) as white solid. R_f = 0.3 (PE/EtOAc 2:1). M. p. 217-219 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76-7.74 (m, 2H), 7.67-7.65 (m, 2H), 7.32 (d, J = 7.2 Hz, 2H), 7.29-7.24 (m, 1H), 7.06 (d, J = 8.0 Hz, 1H), 6.98-6.93 (m, 4H), 4.09-4.02 (m, 2H), 3.84 (dd, J_1 = 14.0 Hz, J_2 = 6.0 Hz, 1H), 3.49-3.42 (m, 1H), 3.34 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 168.4, 167.9, 139.5, 139.2, 133.9, 131.9, 131.8, 129.3, 128.5, 125.5, 123.4, 123.2, 121.0, 114.9, 46.1, 44.9, 38.7, 29.7. HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{20}BrN_2O_3$ $[M + H]^+$ 475.0652, found 475.0644.

1-Methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)methyl benzoate (4ab). Following procedure **A:** the reaction of **1a** (47.4 mg, 0.2 mmol) and **3b** (124 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (10:1 to 4:1) to afford **4ab** (50.0 mg, 70% yield) as colorless liquid. R_f = 0.3 (PE/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.2 Hz, 2H), 7.33-7.25 (m, 4H), 7.14 (d, J = 7.6 Hz, 2H), 7.08 (d, J = 8.0 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H),

4.71 (dd, J_1 = 11.2 Hz, J_2 = 4.8 Hz, 1H), 4.37 (d, J = 8.4 Hz, 1H), 4.30 (dd, J_1 = 11.2 Hz, J_2 = 4.4 Hz, 1H), 3.45 (s, 3H), 3.28 (dt, J_1 = 8.0 Hz, J_2 = 4.8 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 168.3, 166.0, 140.2, 139.5, 132.9, 129.9, 129.6, 129.0, 128.9, 128.3, 128.13, 128.05, 127.6, 127.4, 123.3, 114.7, 62.8, 47.3, 44.2, 30.0. HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{22}NO_3$ $[M + H]^+$ 372.1594, found 372.1582.

1-Methyl-4-phenyl-3-propyl-3,4-dihydroquinolin-2(1*H*)-one (4ac). Following procedure **A:** the reaction of **1a** (47.4 mg, 0.2 mmol) and **3c** (96 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (20:1 to 12:1) to afford **4ac** (32 mg, 57% yield) as colorless liquid. R_f = 0.5 (PE/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (t, J = 7.6 Hz, 1H), 7.24 (d, J = 8.0 Hz, 2H), 7.18 (t, J = 7.2 Hz, 1H), 7.10-7.02 (m, 5H), 4.02 (d, J = 3.6 Hz, 1H), 3.37 (s, 3H), 2.93-2.91 (m, 1H), 1.52-1.44 (m, 4H), 0.89 (t, J = 6.4 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 171.5, 141.8, 139.7, 129.5, 128.7, 127.9, 127.4, 127.0, 126.8, 123.1, 114.6, 48.4, 46.5, 32.6, 29.5, 20.2, 13.9. HRMS (ESI): *m*/*z* calcd. for $C_{19}H_{22}NO$ $[M + H]^+$ 280.1696, found 280.1691.

3-(4-chlorobutyl)-1-methyl-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (4ad). Following procedure **A:** the reaction of **1a** (47.4 mg, 0.2 mmol) and **3d** (124.8 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (15:1 to 10:1) to afford **4ad** (33 mg, 51% yield) as colorless liquid. R_f = 0.3 (PE/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.19 (m, 4H), 7.06-7.02 (m, 5H). 4.03 (d, J = 5.2 Hz, 1H), 3.48 (t, J = 6.4 Hz, 2H), 3.38 (s, 3H), 2.93-2.88 (m, 1H), 1.76-1.69 (m, 2H), 1.61-1.55 (m, 4H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 171.1, 141.40, 139.6, 129.4, 128.8, 128.0, 127.5, 127.1, 127.0, 123.2, 114.7, 48.1, 46.5, 44.7, 32.3, 29.6, 29.5, 24.2. HRMS (ESI): *m*/*z* calcd. for $C_{20}H_{23}ClNO$ $[M + H]^+$ 328.1463, found 328.1462.

3-Cyclobutyl-1-methyl-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (4ae). Following procedure **A:** the reaction of **1a** (47.4 mg, 0.2 mmol) and **3e** (103.2 mg, 0.6 mmol) was performed at 60 °C for 36 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (15:1 to 7:1) to afford **4ae** (34 mg, 58% yield) as white solid. R_f = 0.5 (PE/EtOAc 5:1). M. p. 83-85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (t, J = 8.0 Hz, 1H), 7.24-7.13 (m, 4H), 7.06-7.04 (m, 2H), 6.98 (d, J = 7.2 Hz, 2H), 3.92

(s, 1H), 3.34 (s, 3H), 2.89 (d, J = 10.8 Hz, 1H), 2.35-2.25 (m, 1H), 2.11-2.02 (m, 2H), 1.90-1.74 (m, 4H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 169.8, 142.2, 139.7, 129.8, 128.7, 128.0, 127.0, 126.7, 126.2, 123.2, 114.7, 55.7, 44.7, 36.2, 29.3, 27.5, 26.4, 17.7. HRMS (ESI): m/z calcd. for $C_{20}H_{22}NO$ $[M + H]^+$ 292.1696, found 292.1689.

3-Cyclopentyl-1-methyl-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (4af). Following procedure **A:** the reaction of **1a** (47.4 mg, 0.2 mmol) and **3f** (111.6 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (20:1 to 12:1) to afford **4af** (34 mg, 56% yield) as colorless liquid. R_f = 0.5 (PE/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (t, J = 7.6 Hz, 1H), 7.22 (t, J = 7.2 Hz, 3H), 7.14 (t, J = 7.2 Hz, 1H), 7.08-7.05 (m, 2H), 6.97 (d, J = 7.6 Hz, 2H), 4.13 (s, 1H), 3.35 (s, 3H), 2.70 (d, J = 10.4 Hz, 1H), 1.93-1.87 (m, 1H), 1.67-1.62 (m, 2H), 1.58-1.43 (m, 4H), 1.38-1.32 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 170.8, 142.0, 140.0, 129.7, 128.7, 128.0, 127.0, 126.7, 126.4, 123.2, 114.8, 55.0, 46.5, 40.3, 31.4, 30.8, 29.4, 25.1, 24.5. HRMS (ESI): m/z calcd. for $C_{21}H_{24}NO$ $[M + H]^+$ 306.1852, found 306.1841.

3-Cyclohexyl-1-methyl-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (4ag). Following procedure **A:** the reaction of **1a** (47.4 mg, 0.2 mmol) and **3g** (120 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (20:1 to 12:1) to afford **4ag** (31 mg, 49% yield) as colorless liquid. R_f = 0.5 (PE/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (t, J = 8.0 Hz, 1H), 7.23-7.12 (m, 4H), 7.07-7.04 (m, 2H), 6.96 (d, J = 8.0 Hz, 2H), 4.21 (s, 1H), 3.36 (s, 3H), 2.67 (d, J = 8.4 Hz, 1H), 1.92 (d, J = 10.4 Hz, 1H), 1.71-1.67 (m, 2H), 1.59-1.56 (m, 2H), 1.29-1.23 (m, 2H), 1.17-1.05 (m, 4H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 170.4, 142.3, 140.1, 129.6, 128.7, 128.0, 127.1, 126.7, 126.6, 123.2, 114.8, 55.6, 44.5, 37.8, 31.4, 31.1, 29.4, 26.2, 26.1, 26.0. HRMS (ESI): m/z calcd. for $C_{22}H_{26}NO$ $[M + H]^+$ 320.2009, found 320.2000.

3-Isobutyl-1-methyl-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (4ai). Following procedure **B:** the reaction of **1a** (47.4 mg, 0.2 mmol) and **3i** (121.2 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (15:1 to 10:1) to afford

4ai (42 mg, 72% yield) as colorless liquid. R_f = 0.7 (PE/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (t, J = 7.6 Hz, 1H), 7.24 (t, J = 7.2 Hz, 2H), 7.18 (d, J = 6.8 Hz, 1H), 7.14 (d, J = 7.6 Hz, 1H), 7.06 (d, J = 8.8 Hz, 2H), 7.01 (d, J = 7.6 Hz, 2H), 3.98 (s, 1H), 3.36 (s, 3H), 3.01 (t, J = 7.6 Hz, 1H), 1.77 (dt, J_1 = 13.2 Hz, J_2 = 6.8 Hz, 1H), 1.46 (dt, J_1 = 13.6 Hz, J_2 = 7.2 Hz, 1H), 1.32-1.26 (m, 1H), 0.92 (d, J = 6.8 Hz, 6H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 171.7, 142.0, 139.8, 129.7, 128.7, 128.0, 127.2, 126.8, 126.6, 123.2, 114.7, 46.79, 46.77, 39.8, 29.5, 25.6, 22.7, 22.3. HRMS (ESI): m/z calcd. for $C_{20}H_{24}NO$ $[M + H]^+$ 294.1852, found 294.1850.

3-(Dec-9-en-1-yl)-1-methyl-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (4aj). Following procedure **B:** the reaction of **1a** (47.4 mg, 0.2 mmol) and **3j** (219.6 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (15:1 to 10:1) to afford **4aj** (68 mg, 91% yield) as colorless liquid. R_f = 0.7 (PE/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.16 (m, 4H), 7.09-7.02 (m, 5H), 5.85-5.75 (m, 1H), 4.98 (d, J = 17.2 Hz, 1H), 4.92 (d, J = 10.0 Hz, 1H), 4.02 (d, J = 3.6 Hz, 1H), 3.37 (s, 3H), 2.92-2.88 (m, 1H), 2.02 (dd, J_1 = 13.6 Hz, J_2 = 6.4 Hz,, 2H), 1.55-1.46 (m, 2H), 1.35-1.24 (m, 12H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 171.5, 141.8, 139.7, 139.2, 129.5, 128.7, 127.9, 127.4, 127.0, 126.8, 123.1, 114.6, 114.1, 48.6, 46.5, 33.8, 30.5, 29.5, 29.4, 29.33, 29.30, 29.0, 28.9, 26.9. HRMS (ESI): m/z calcd. for $C_{26}H_{34}NO$ $[M + H]^+$ 376.2635, found 376.2635.

1-Methyl-4-phenyl-3-undecyl-3,4-dihydroquinolin-2(1*H*)-one (4ak). Following procedure **B:** the reaction of **1a** (47.4 mg, 0.2 mmol) and **3k** (199 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (20:1 to 12:1) to afford **4ak** (70.0 mg, 90% yield) as colorless liquid. R_f = 0.65 (PE/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.18 (m, 4H), 7.09-7.02 (m, 5H), 4.03 (d, J = 4.0 Hz, 1H), 3.37 (s, 3H), 2.92-2.88 (m, 1H), 1.57-1.48 (m, 2H), 1.23 (s, 18H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 171.6, 141.8, 139.8, 129.5, 128.7, 127.9, 127.4, 127.0, 126.8, 123.1, 114.6, 48.6, 46.5, 31.9, 30.5, 29.60, 29.58, 29.55, 29.5, 29.43, 29.38, 29.3, 27.0, 22.7, 14.11. HRMS (ESI): m/z calcd. for $C_{27}H_{38}NO$ $[M + H]^+$ 392.2948, found 392.2946.

4-(3,4-Dimethoxyphenyl)-1-methyl-3-undecyl-3,4-dihydroquinolin-2(1*H*)-one (4ik). Following procedure **B:** the reaction of **1i** (59.4 mg, 0.2 mmol) and **3k** (199 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (13:1 to 7:1) to afford **4ik** (57 mg, 63% yield) as colorless liquid. R_f = 0.28 (PE/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (t, J = 7.6 Hz, 1H), 7.09-7.01 (m, 3H), 6.74 (d, J = 8.4 Hz, 1H), 6.60 (s, 1H), 6.53 (d, J = 8.4 Hz, 1H), 3.97 (d, J = 4.0 Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.37 (s, 3H), 2.91-2.87 (m, 1H), 1.65-1.60 (m, 1H), 1.54-1.49 (m, 1H), 1.23 (s, 18H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 178.6, 171.8, 149.0, 147.8, 139.6, 134.2, 129.4, 127.9, 123.1, 119.5, 114.6, 111.3, 110.6, 55.82, 55.75, 48.5, 46.1, 31.9, 30.3, 29.59, 29.57, 29.56, 29.53, 29.48, 29.4, 29.3, 27.0, 22.6, 14.1. HRMS (ESI): *m*/*z* calcd. for $C_{29}H_{41}NO_3$ $[M + H]^+$ 452.3159, found 452.3142.

1-Phenyl-2-undecyl-1,2,6,7-tetrahydropyrido[3,2,1-*ij*]quinolin-3(5*H*)-one (4jk). Following procedure **B:** the reaction of **1j** (52.6 mg, 0.2 mmol) and **3k** (199 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (13:1 to 7:1) to afford **4jk** (69 mg, 83% yield) as colorless liquid. R_f = 0.45 (PE/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.16 (m, 3H), 7.04 (d, J = 6.8 Hz, 3H), 6.91 (d, J = 3.6 Hz, 2H), 4.15-4.11 (m, 1H), 4.00 (d, J = 3.2 Hz, 1H), 3.63-3.57 (m, 1H), 2.89-2.82 (m, 3H), 1.96 (br s, 2H), 1.52-1.46 (m, 2H), 1.23 (s, 18H), 0.88 (t, J = 6.8 Hz, 3 H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 170.8, 142.1, 135.2, 128.7, 128.2, 127.5, 127.4, 126.7, 126.3, 125.0, 122.7, 48.3, 46.3, 40.8, 31.9, 30.5, 29.6, 29.5, 29.44, 29.38, 29.3 27.4, 26.9, 22.7, 21.5, 14.1. HRMS (ESI): *m*/*z* calcd. for $C_{29}H_{39}NO$ $[M + H]^+$ 418.3104, found 418.3091.

2-((3-Oxo-1-phenyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-2-yl)methyl)isoindoline-1,3-dione (5aa). Following procedure **A:** the reaction of **2a** (49.4 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (8:1 to 4:1) to afford **5aa** (35 mg, 43% yield) as white solid. R_f = 0.5 (PE/EtOAc 2:1). M. p. 215-217 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 8.0 Hz, 1H), 7.78-7.75 (m, 2H), 7.71-7.68 (m,

2H), 7.47 (d, J = 7.6 Hz, 1H), 7.33-7.27 (m, 2H), 7.12 (s, 5H), 6.14 (s, 1H), 4.49 (d, J = 6.0 Hz, 1H), 4.33 (dd, J_1 = 14.0 Hz, J_2 = 6.4 Hz, 1H), 4.26 (dd, J_1 = 14.0 Hz, J_2 = 8.8 Hz, 1H), 3.85-3.80 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 169.4, 168.1, 144.9, 139.6, 135.0, 134.1, 131.7, 130.4, 128.8, 127.5, 127.3, 124.4, 123.9, 123.3, 120.9, 114.0, 101.5, 54.3, 44.4, 38.0. HRMS (ESI): m/z calcd. for $C_{26}H_{19}N_2O_3$ $[M + H]^+$ 407.1390, found 407.1398.

2-((7-Methyl-3-oxo-1-phenyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-2-yl)methyl)isoindoline-1,3-dione (5ba). Following procedure **A:** the reaction of **2b** (52.2 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (8:1 to 4:1) to afford **5ba** (38 mg, 45% yield) as white solid. R_f = 0.5 (PE/EtOAc 2:1). M. p. 154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.0 Hz, 1H), 7.78-7.75 (m, 2H), 7.70-7.68 (m, 2H), 7.26 (s, 1H), 7.11 (s, 6H), 6.06 (s, 1H), 4.47 (d, J = 5.6 Hz, 1H), 4.32 (dd, J_1 = 14.0 Hz, J_2 = 6.4 Hz, 1H), 4.24 (dd, J_1 = 14.0 Hz, J_2 = 9.2 Hz, 1H), 3.83-3.78 (m, 1H), 2.43 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 169.2, 168.1, 145.0, 139.7, 135.3, 134.1, 134.0, 131.7, 128.8, 128.6, 127.5, 127.3, 125.1, 123.3, 120.9, 113.6, 101.3, 54.3, 44.4, 38.1, 21.6. HRMS (ESI): m/z calcd. for $C_{27}H_{21}N_2O_3$ $[M + H]^+$ 421.1547, found 421.1558.

2-((7-Methoxy-3-oxo-1-phenyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-2-yl)methyl)isoindoline-1,3-dione (5ca). Following procedure **A:** the reaction of **2c** (55.4 mg, 0.2 mmol) and **3a** (138 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (8:1 to 3:1) to afford **5ca** (46 mg, 53% yield) as white solid. R_f = 0.2 (PE/EtOAc 5:1). M. p. 230-231 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.8 Hz, 1H), 7.77-7.69 (m, 4H), 7.12 (s, 5H), 6.92 (d, J = 8.8 Hz, 2H), 6.07 (s, 1H), 4.47 (d, J = 5.6 Hz, 1H), 4.31 (dd, J_1 = 14.0 Hz, J_2 = 6.4 Hz, 1H), 4.24 (dd, J_1 = 14.0 Hz, J_2 = 8.8 Hz, 1H), 3.83-3.76 (m, 4H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 169.0, 168.1, 157.1, 145.8, 139.6, 136.1, 134.0, 131.7, 128.8, 127.5, 127.3, 125.1, 123.3, 114.6, 112.2, 104.0, 101.5, 55.7, 54.3, 44.4, 38.1. HRMS (ESI): m/z calcd. for $C_{27}H_{21}N_2O_4$ $[M + H]^+$ 437.1496, found 437.1505.

7-Methoxy-3-oxo-1-phenyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-2-yl)methyl benzoate (5cb).

Following procedure **A:** the reaction of **2c** (55.4 mg, 0.2 mmol) and **3b** (124 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (10:1 to 5:1) to afford **5cb** (25 mg, 32% yield) as white solid. R_f = 0.2 (PE/EtOAc 10:1). M. p. 137-138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, J = 8.8 Hz, 1H), 7.87 (d, J = 7.6 Hz, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.38-7.31 (m, 7H), 7.00 (s, 1H), 6.96 (d, J = 8.8 Hz, 1H), 6.21 (s, 1H), 4.89 (dd, J_1 = 11.6 Hz, J_2 = 3.6 Hz, 1H), 4.80 (dd, J_1 = 11.6 Hz, J_2 = 4.8 Hz, 1H), 4.59 (d, J = 5.6 Hz, 1H), 3.86 (s, 3H), 3.49-3.45 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 168.8, 166.2, 157.2, 145.7, 140.1, 136.3, 133.3, 129.7, 129.4, 129.1, 128.4, 127.8, 127.6, 125.2, 114.6, 112.3, 104.0, 101.9, 62.3, 56.7, 55.7, 42.9. HRMS (ESI): *m*/*z* calcd. for $C_{26}H_{22}NO_4$ $[M + H]^+$ 412.1543, found 412.1544.

1-(3,4-Dimethoxyphenyl)-9-methyl-2-propyl-1*H*-pyrrolo[1,2-*a*]indol-3(2*H*)-one (5dc). Following procedure **A:** the reaction of **2d** (64 mg, 0.2 mmol) and **3c** (96 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (15:1 to 6:1) to afford **5dc** (36 mg, 50% yield) as colorless liquid. R_f = 0.3 (PE/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J = 7.6 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.35-7.29 (m, 2H), 6.82 (s, 2H), 6.70 (s, 1H), 4.20 (d, J = 4.8 Hz, 1H), 3.89 (s, 3H), 3.81 (s, 3H), 3.11-3.06 (m, 1H), 2.06-1.99 (m, 1H), 1.89 (s, 3H), 1.86-1.79 (m, 1H), 1.59-1.50 (m, 2H), 0.94 (t, J = 7.2 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 172.8, 149.4, 148.2, 140.3, 136.2, 133.5, 130.1, 123.8, 123.6, 119.9, 118.8, 113.8, 111.2, 110.2, 109.7, 57.4, 56.0, 55.9, 44.9, 33.3, 20.0, 14.0, 8.0. HRMS (ESI): *m*/*z* calcd. for $C_{23}H_{26}NO_3$ $[M + H]^+$ 364.1907, found 364.1897.

2-Cyclobutyl-1-(3,4-dimethoxyphenyl)-9-methyl-1*H*-pyrrolo[1,2-*a*]indol-3(2*H*)-one (5de). Following procedure **A:** the reaction of **2d** (64 mg, 0.2 mmol) and **3e** (103 mg, 0.6 mmol) was performed at 60 °C for 36 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (20:1 to 13:1) to afford **5de** (30 mg, 40% yield) as colorless liquid. R_f = 0.5 (PE/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 7.6 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.34-7.28 (m, 2H),

6.82 (d, J = 8.4 Hz, 1H), 6.79 (t, J = 8.4 Hz, 1H), 6.67 (s, 1H), 4.18 (d, J = 3.2 Hz, 1H), 3.88 (s, 3H), 3.81 (s, 3H), 3.08 (dd, J_1 = 8.4 Hz, J_2 = 4.8 Hz, 1H), 2.91-2.81 (m, 1H), 2.24-1.93 (m, 5H), 1.90 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 171.9, 149.4, 148.2, 140.2, 136.2, 133.8, 130.1, 123.8, 123.6, 119.9, 118.8, 113.8, 111.3, 110.3, 109.6, 61.9, 56.0, 55.9, 43.4, 37.8, 26.8, 26.2, 18.8, 8.1. HRMS (ESI): m/z calcd. for $C_{24}H_{26}NO_3$ $[M + H]^+$ 376.1907, found 376.1896.

2-Cyclohexyl-1-(3,4-dimethoxyphenyl)-9-methyl-1*H*-pyrrolo[1,2-*a*]indol-3(2*H*)-one (5dg). Following procedure **A:** the reaction of **2d** (64 mg, 0.2 mmol) and **3g** (120 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (20:1 to 10:1) to afford **5dg** (42 mg, 52% yield) as white solid. R_f = 0.5 (PE/EtOAc 10:1). M. p. 148-149 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J = 7.6 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.34-7.28 (m, 2H), 6.81 (d, J = 8.4 Hz, 1H), 6.78 (d, J = 8.4 Hz, 1H), 6.66 (s, 1H), 4.33 (d, J = 3.6 Hz, 1H), 3.88 (s, 3H), 3.80 (s, 3H), 3.06 (t, J = 4.0 Hz, 1H), 2.13-2.07 (m, 1H), 1.90 (s, 3H), 1.77-1.72 (m, 4H), 1.43-1.21 (m, 6H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 172.4, 149.4, 148.1, 140.8, 136.3, 134.4, 129.9, 123.8, 123.5, 119.9, 118.8, 113.9, 111.2, 110.3, 109.4, 63.3, 56.0, 55.8, 41.3, 40.0, 30.3, 28.8, 26.5, 26.2, 26.1, 8.0. HRMS (ESI): m/z calcd. for $C_{26}H_{30}NO_3$ $[M + H]^+$ 404.2220, found 404.2221.

1-(3,4-Dimethoxyphenyl)-9-methyl-2-(1-tosylpiperidin-4-yl)-1*H*-pyrrolo[1,2-*a*]indol-3(2*H*)-one (5dh). Following procedure **A:** the reaction of **2d** (64 mg, 0.2 mmol) and **3h** (257 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (6:1 to 2:1) to afford **5dh** (45 mg, 40% yield) as white solid. R_f = 0.5 (PE/EtOAc 1:1). M. p. 205-207 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06-8.04 (m, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.45-7.43 (m, 1H), 7.33 (d, J = 7.6 Hz, 4H), 6.79 (dd, J_1 = 17.6 Hz, J_2 = 8.4 Hz, 2H), 6.63 (s, 1H, 4.28 (d, J = 4.0 Hz, 1H), 3.88-3.80 (m, 8H), 3.11 (t, J = 4.0 Hz, 1H), 2.44 (s, 3H), 2.25 (t, J = 11.2 Hz, 2H), 2.10-2.02 (m, 1H), 1.87 (s, 3H), 1.76-1.59 (m, 4H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 171.2, 149.5, 148.3, 143.6, 140.2, 136.3, 133.7, 133.0, 129.9, 129.6, 127.7, 124.1, 123.7, 120.1, 118.9, 113.8, 111.3, 110.08, 110.05, 61.7,

56.0, 55.9, 46.5, 46.2, 40.8, 37.0, 29.2, 26.7, 21.5, 7.9. HRMS (ESI): *m*/*z* calcd. for $C_{32}H_{35}N_2O_5S$ [M + H]$^+$ 559.2261, found 559.2247.

2-(Dec-9-en-1-yl)-1-(3,4-dimethoxyphenyl)-9-methyl-1*H*-pyrrolo[1,2-*a*]indol-3(2*H*)-one (5dj). Following procedure **B:** the reaction of **2d** (64 mg, 0.2 mmol) and **3j** (219.6 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (15:1 to 6:1) to afford **5dj** (43 mg, 47% yield) as colorless liquid. R_f = 0.5 (PE/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 6.8 Hz, 1H), 7.45 (d, *J* = 6.8 Hz, 1H), 7.34-7.29 (m, 2H), 6.82 (s, 2H), 6.70 (s, 1H), 5.85-5.75 (m, 1H), 4.98 (d, *J* = 17.2 Hz, 1H), 4.92 (d, *J* = 10.4 Hz, 1H), 4.20 (d, *J* = 4.0 Hz, 1H), 3.89 (s, 3H), 3.81 (s, 3H), 3.09-3.05 (m, 1H), 2.05-2.00 (m, 3H), 1.89-1.82 (m, 4H), 1.36-1.26 (m, 12H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 172.7, 149.4, 148.2, 140.3, 139.2, 136.2, 133.5, 130.1, 123.8, 123.6, 119.9, 118.8, 114.1, 113.8, 111.2, 110.2, 109.7, 57.6, 56.0, 55.9, 44.8, 33.8, 31.0, 29.5, 29.34, 29.31, 29.0, 28.9, 26.6, 8.1. HRMS (ESI): *m*/*z* calcd. for $C_{30}H_{38}NO_3$ [M + H]$^+$ 460.2846, found 460.2836.

1-(3,4-Dimethoxyphenyl)-9-methyl-2-undecyl-1*H*-pyrrolo[1,2-*a*]indol-3(2*H*)-one (5dk). Following procedure **B:** the reaction of **2d** (64 mg, 0.2 mmol) and **3k** (199 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (20:1 to 10:1) to afford **5dk** (59 mg, 62% yield) as colorless liquid. R_f = 0.5 (PE/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 6.8 Hz, 1H), 7.35-7.28 (m, 2H), 6.82 (s, 2H), 6.70 (s, 1H), 4.20 (d, *J* = 4.8 Hz, 1H), 3.89 (s, 3H), 3.81 (s, 3H), 3.09-3.05 (m, 1H), 2.06-1.97 (m, 1H), 1.89-1.80 (m, 4H), 1.29-1.24 (m, 18H), 0.88 (t, *J* = 6.8 Hz). ^{13}C NMR (176 MHz, $CDCl_3$): δ 172.7, 149.4, 148.2, 140.3, 136.2, 133.5, 130.1, 123.8, 123.6, 119.9, 118.8, 113.8, 111.2, 110.2, 109.6, 57.6, 56.0, 55.9, 44.8, 31.9, 31.1, 29.59, 29.58, 29.53, 29.51, 29.4, 29.3, 26.6, 22.7, 14.1, 8.1. HRMS (ESI): *m*/*z* calcd. for $C_{31}H_{42}NO_3$ [M + H]$^+$ 476.3159, found 476.3160.

1-(4-Bromophenyl)-9-methyl-2-undecyl-1*H*-pyrrolo[1,2-*a*]indol-3(2*H*)-one (5ek). Following procedure **B:** the reaction of **2e** (68 mg, 0.2 mmol) and **3k** (199 mg, 0.5 mmol) was performed at 50 °C

for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (200:1 to 100:1) to afford **5ek** (73 mg, 74% yield) as colorless liquid. R_f = 0.5 (PE/EtOAc 0:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 7.2 Hz, 1H), 7.47-7.44 (m, 3H), 7.35-7.28 (m, 2H), 7.11 (d, J = 8.0 Hz, 2H), 4.21 (d, J = 4.0 Hz, 1H), 3.05-3.00 (m, 1H), 2.05-1.97 (m, 1H), 1.88-1.79 (m, 4H), 1.24 (s, 18H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 172.3, 140.4, 139.5, 136.1, 132.1, 130.1, 129.2, 123.9, 123.8, 121.1, 118.8, 113.9, 109.9, 57.6, 44.4, 31.9, 31.2, 29.6, 29.5, 29.4, 29.34, 29.31, 26.6, 22.7, 14.1, 8.1. HRMS (ESI): m/z calcd. for $C_{29}H_{37}BrNO$ $[M + H]^+$ 494.2053, found 494.2064.

9-Methyl-1-(4-(trifluoromethyl)phenyl)-2-undecyl-1*H*-pyrrolo[1,2-*a*]indol-3(2*H*)-one (5fk). Following procedure **B:** the reaction of **2f** (65.8 mg, 0.2 mmol) and **3k** (199 mg, 0.5 mmol) was performed at 50 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (200:1 to 100:1) to afford **5fk** (61 mg, 63% yield) as colorless liquid. R_f = 0.5 (PE/EtOAc 0:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J = 7.2 Hz, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 7.2 Hz, 1H), 7.37-7.32 (m, 4H), 4.32 (d, J = 4.4 Hz, 1H), 3.08-3.04 (m, 1H), 2.08-1.99 (m, 1H), 1.91-1.81 (m, 4H), 1.24 (s, 18H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 172.1, 145.4, 139.2, 136.1, 130.1, 129.7 (q, $^2J_{CF}$ = 32.6 Hz), 127.9, 126.0 (q, $^3J_{CF}$ = 3.7 Hz), 124.00, 123.99 (q, $^1J_{CF}$ = 271.9 Hz), 123.9, 118.9, 113.9, 110.1, 57.6, 44.7, 31.9, 31.3, 29.6, 29.5, 29.44, 29.35, 29.3, 26.6, 22.7, 14.1, 8.1. HRMS (ESI): m/z calcd. for $C_{30}H_{37}F_3NO$ $[M + H]^+$ 484.2822, found 484.2835.

2-Cyclohexyl-9-methyl-1-phenyl-1*H*-pyrrolo[1,2-a]indol-3(2*H*)-one (5gg). Following procedure **A:** the reaction of **2g** (52 mg, 0.2 mmol) and **3g** (120 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (200:1 to 100:1) to afford **5gg** (41 mg, 60% yield) as colorless liquid. R_f = 0.4 (PE/EtOAc 0:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J = 7.2 Hz, 1H), 7.44 (d, J = 7.6 Hz, 1H), 7.33-7.23 (m, 5H), 7.19 (d, J = 7.6 Hz, 2H), 4.37 (d, J = 2.8 Hz, 1H), 3.06 (t, J = 3.2 Hz, 1H), 2.11 (br s, 1H), 1.88 (s, 3H), 1.79-1.72 (m, 4H), 1.41-1.20 (m, 6H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 172.3, 142.1, 140.8, 136.3, 129.9, 128.9, 127.5, 127.1,

123.8, 123.5, 118.7, 113.8, 109.3, 63.4, 41.5, 40.2, 30.4, 28.8, 26.4, 26.2, 26.1, 8.0. HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{26}NO$ $[M + H]^+$ 344.2009, found 344.2004.

1-(3,4-Dimethoxyphenyl)-9-phenyl-2-undecyl-1*H*-pyrrolo[1,2-*a*]indol-3(2*H*)-one (5hk). Following procedure **B:** the reaction of 2**h** (76.6 mg, 0.2 mmol) and **3k** (240 mg, 0.6 mmol) was performed at 60 °C for 12 h. The crude product was purified by silica gel flash chromatography using PE/EtOAc (15:1 to 8:1) to afford **5hk** (70 mg, 65% yield) as colorless liquid. R_f = 0.5 (PE/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.41-7.33 (m, 2H), 7.26-7.19 (m, 5H), 6.72 (s, 2H), 6.58 (s, 1H), 4.38 (d, *J* = 3.2 Hz, 1H), 3.82 (s, 3H), 3.68 (s, 3H), 3.14-3.12 (m, 1H), 2.08-1.99 (m, 1H), 1.90-1.81 (m, 1H), 1.24 (s, 18H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 173.3, 149.2, 148.1, 140.8, 134.2, 134.0, 132.6, 130.4, 128.5, 128.3, 126.8, 124.4, 124.1, 120.0, 119.7, 115.9, 114.1, 111.2, 110.3, 57.6, 55.8, 55.8, 45.3, 31.9, 31.6, 29.6, 29.52, 29.47, 29.4, 29.3, 26.7, 22.6, 14.1. HRMS (ESI): *m*/*z* calcd. for $C_{36}H_{44}NO_3$ $[M + H]^+$ 538.3316, found 538.3307.

ASSOCIATED CONTENT

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

X-ray crystallographic data of **4aa** and **5ba**, gram-scale preparation and mechanism study, copies of ^{1}H and ^{13}C NMR spectra and cif files of **4aa** and **5ba**.

AUTHOR INFORMATION

Corresponding Author

dudm@bit.edu.cn

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

We are grateful for financial support from National Natural Science Foundation of China (Grant No. 21272024). We also thank Analysis & Testing Center of Beijing Institute of Technology for the measurement of NMR and mass spectrometry.

REFERENCES

(1) (a) Tominaga, M.; Tone, H.; Nakagawa, K.; Takada, K.; Hoshino, Y.; Watanabe, K. Syntheses and β-Adrenergic Blocking Activities of Carbostyril Derivatives. *Chem. Pharm. Bull*. **1981**, *29*, 2166-2181. (b) Saxton, J. E. Recent Progress in the Chemistry of the Monoterpenoid Indole Alkaloids. *Nat. Prod. Rep*. **1995**, *12*, 385-411. (c) Zeni, G.; Larock, R. C. Synthesis of Heterocycles via Palladium-Catalyzed Oxidative Addition. *Chem. Rev*. **2006**, *106*, 4644-4680. (d) Candeias, N. R.; Branco, L. C.; Gois, P. M. P.; Afonso, C. A. M.; Trindade, A. F. More Sustainable Approaches for the Synthesis of *N*-Based Heterocycles. *Chem. Rev*. **2009**, *109*, 2703-2802.

(2) Selected examples of methods for synthesis of dihydroquinolinone derivatives, see: (a) Zhang, L.; Sonaglia, L.; Stacey, J.; Lautens, M. Multicomponent Multicatalyst Reactions $(MC)^2R$: One-Pot Synthesis of 3,4-Dihydroquinolinones. *Org. Lett*. **2013**, *15*, 2128-2131. (b) Yan, J.-X.; Li, H.; Liu, X.-W.; Shi, J.-L.; Wang, X.; Shi, Z.-J. Palladium-Catalyzed C(sp^3)-H Activation: A Facile Method for the Synthesis of 3,4-Dihydroquinolinone Derivatives. *Angew. Chem. Int. Ed*. **2014**, *53*, 4945-4949. (c) Mai, W.-P.; Wang, J.-T.; Yang, L.-R.; Yuan, J.-W.; Xiao, Y.-M.; Mao, P.; Qu, L.-B. Silver-Catalyzed Radical Tandem Cyclization for the Synthesis of 3,4-Disubstituted Dihydroquinolin-2(1*H*)-ones. *Org. Lett*. **2014**, *16*, 204-207.

(3) Selected examples of methods for synthesis of pyrrolo[1,2-*a*]indole derivatives, see: (a) Kusama, H.; Takaya, J.; Iwasawa, N. A Facile Method for the Synthesis of Polycyclic Indole Derivatives: the Generation and Reaction of Tungsten-Containing Azomethine Ylides. *J. Am. Chem. Soc*. **2002**, *124*, 11592-11593. (b) Ikemoto, H.; Yoshino, T.; Sakata, K.; Matsunaga, S.; Kanai, M. Pyrroloindolone Synthesis via a Cp^*Co^{III}-Catalyzed Redox-Neutral Directed C–H Alkenylation/Annulation Sequence. *J. Am. Chem. Soc*. **2014**, *136*, 5424-5431; (c) Xu, H.-D.; Jia, Z.-H.; Xu, K.; Zhou, H.; Shen, M.-H. One-Pot Protocol to Functionalized Benzopyrrolizidine Catalyzed Successively by $Rh_2(OAc)_4$ and $Cu(OTf)_2$: a Transition Metal–Lewis Acid Catalysis Relay. *Org. Lett*. **2015**, *17*, 66-69.

(4) (a) Alabaster, C. T.; Bell, A. S.; Campbell, S. F.; Ellis, P.; Henderson, C. G.; Morris, D. S.; Roberts, D. A.; Ruddock, K. S.; Samuels, G. M. R.; Stefaniak, M. H. 2(1*H*)-Quinolinones with Cardiac Stimulant Activity. 2. Synthesis and Biological Activities of 6-(*N*-Linked, Five-Membered Heteroaryl) Derivatives. *J. Med. Chem*. **1989**, *32*, 575-583. (b) Zhang, X.; Mu, T.; Zhan, F.; Ma, L.; Liang, G. Total Synthesis of (-)-Isatisine A. *Angew. Chem., Int. Ed.* **2011**, *50*, 6164-6166. (c) Zeldin, R. M.; Toste, F. D. Synthesis of Flinderoles B and C by a Gold-Catalyzed Allene Hydroarylation. *Chem. Sci*. **2011**, *2*, 1706-1709.

(5) Liu, J.-F.; Jiang, Z.-Y.; Wang, R.-R.; Zheng, Y.-T.; Chen, J.-J.; Zhang, X.-M.; Ma, Y.-B. Isatisine A, a Novel Alkaloid with an Unprecedented Skeleton from Leaves of Isatis Indigotica. *Org. Lett*. **2007**, *9*, 4127-4129.

(6) (a) Vepsalainen, J.; Auriola, S.; Tukiainen, M.; Ropponen, N.; Callaway, J. C. Isolation and Characterization of Yuremamine, a New Phytoindole. *Planta Med*. **2005**, *71*, 1053-1057. (b) Dethe, D. H.; Boda, R.; Das, S. $Cu(OTf)_2$ Catalysed [6+2] Cycloaddition Reaction For the Synthesis of Highly Substituted Pyrrolo[1,2-a]indoles: Rapid Construction of the Yuremamine Core. *Chem. Commun*. **2013**, *49*, 3260-3262.

(7) (a) Ito, C.; Itoigawa, M.; Otsuka, T.; Tokuda, H.; Nishino, H.; Furukawa, H. Constituents of Boronia pinnata. *J. Nat. Prod.* **2000**, *63*, 1344-1348. (b) Ito, C.; Kondo, Y.; Wu, T.-S.; Furukawa, H. Chemical Constituents of Glycosmis Citrifolia (WILLD.) LINDL. Structures of Four New Acridones and Three New Quinolone Alkaloids. *Chem. Pharm. Bull*. **2000**, *48*, 65-70. (c) Elmegeed, G. A.; Baiuomy, A. R.; Abdel-Salam, O. M. E. Evaluation of the Anti-inflammatory and Anti-nociceptive Activities of Novel Synthesized Melatonin Analogues. *Eur. J. Med. Chem*. **2007**, *42*, 1285-1292.

(8) Selected examples of alkyl radical involved in construction of complicated molecule scaffolds: (a) Zhou, S.-z.; Bommezijn, S.; Murphy, J. A. Formal Total Synthesis of (±)-Vindoline by Tandem Radical Cyclization. *Org. Lett*. **2002**, *4*, 443-445. (b) Taniguchi, T.; Tanabe, G.; Muraoka, O.; Ishibashi, H. Total Synthesis of (±)-Stemonamide and (±)-Isostemonamide Using a Radical Cascade. *Org. Lett*. **2008**, *10*, 197-199. (c) Nicolaou, K. C.; Ellery, S. P.; Chen, J. S. Samarium Diiodide Mediated Reactions in Total Synthesis. *Angew. Chem. Int. Ed*. **2009**, *48*, 7140-7165.

(9) Selected reviews of alkyl halides as radical precursor, see: (a) Ryu, L.; Sonoda, N. Tandem Radical Reactions of Carbon Monoxide, Isonitriles, and Other Reagent Equivalents of the Geminal Radical Acceptor/Radical Precursor Synthon. *Chem. Rev*. **1996**, *96*, 177-194. (b) Rossi, R. A.; Pierini, A. B.; Penenory, A. B. Nucleophilic Substitution Reactions by Electron Transfer. *Chem. Rev*. **2003**, *103*, 71-168. (c) Nicolaou, K. C.;

Edmonds, D J.; Bulger, P. G. Cascade Reactions in Total Synthesis. *Angew. Chem. Int. Ed*. **2006**, *45*, 7134-7186.

(10) Related reviews of aliphatic acid as radical precursor, see: (a) Rodriguez, N.; Goossen, L. J. Decarboxylative Coupling Reactions: A Modern Strategy for C–C Bond Formation. *Chem. Sov. Rev*. **2011**, *40*, 5030-5048. (b) Zheng, Q.-Z.; Jiao, N. Ag-Catalyzed C–H/C–C Bond Functionalization. *Chem. Sov. Rev*. **2016**, *45*, 4590-4627. (c) Fang, G.; Cong, X.; Zanoni, G.; Liu, Q.; Bi, X. Silver-Based Radical Reactions: Development and Insights. *Adv.Synth. Catal*. **2017**, *359*, 1422-1502.

(11) Selected examples of redox-active as radical precursor, see: (a) Qin, T.; Cornella, J.; Li, C.; Malins, L. R.; Edwards, J. T.; Kawamura, S.; Maxwell, B. D.; Eastgate, M. D.; Baran, P. S. A General Alkyl-Alkyl Cross-Coupling Enabled by Redox-Active Esters and Alkylzinc Reagents. *Science* **2016**, *352*, 801-805. (b) Huihui, K. M. M.; Caputo, J. A.; Melchor, Z.; Olivares, A. M.; Spiewak, A. M.; Johnson, K. A.; DiBenedetto, T. A.; Kim, S.; Ackerman, L. K.; Weix, D. J. Decarboxylative Cross-Electrophile Coupling of *N*-Hydroxyphthalimide Esters with Aryl Iodides. *J. Am. Chem. Soc*. **2016**, *138*, 5016-5019.

(12) Reviews of peresters (or peroxides) as initiators and oxidants: (a) Debien, L.; Quiclet-Sire, B.; Zard, S. Z. Allylic Alcohols: Ideal Radical Allylating Agents?. *Acc. Chem. Res*. **2015**, *48*, 1237-1253. (b) Bayeh, L.; Tambar, U. K. Catalytic Asymmetric Intermolecular Allylic Functionalization of Unactivated Internal Alkenes. *ACS Catal*. **2017**, *7*, 8533-8543.

(13) (a) Spantulescu, M. D.; Jain, R. P.; Derksen, D. J.; Vederas, J. C. Photolysis of Diacyl Peroxides: A Radical-Based Approach for the Synthesis of Functionalized Amino Acids. *Org. Lett*. **2003**, *5*, 2963-2965. (b) Spantulescu, M. D.; Boudreau, M. A.; Vederas, J. C. Retention of Configuration in Photolytic Decarboxylation of Peresters to Form Chiral Acetals and Ethers. *Org. Lett*. **2009**, *11*, 645-648. (c) Rueda-Becerril, M.; Sazepin, C. C.; Leung, J. C. T.; Okbinoglu, T.; Kennepohl, P.; Paquin, J.-F.; Sammis, G. M. Fluorine Transfer to Alkyl Radicals. *J. Am. Chem. Soc*. **2012**, *134*, 4026-4029.

(14) (a) Jian, W.; Ge, L.; Jiao, Y.; Qian, B.; Bao, H. Iron-Catalyzed Decarboxylative Alkyl Etherification of Vinylarenes with Aliphatic Acids as the Alkyl Source. *Angew. Chem. Int. Ed*. **2017**, *56*, 3650-3654. (b) Babu, K. R.; Zhu, N.; Bao, H. Iron-Catalyzed C–H Alkylation of Heterocyclic C–H Bonds. *Org. Lett*. **2017**, *19*, 46-49. (c) Qian, Bo.; Chen, S.; Wang, T.; Zhang, X.; Bao, H. Iron-Catalyzed Carboamination of Olefins: Synthesis of Amines and Disubstituted β-Amino Acids. *J. Am. Chem. Soc*. **2017**, 139, 13076-13082. (d) Ye,

C.; Li, Y.; Bao, H. Copper-Catalyzed Decarboxylative Alkylation of Terminal Alkynes. *Adv. Synth. Catal.* **2017**, *359*, 3720-3724. (e) Zhu, X.; Ye, C.; Li, Y.; Bao, H. Iron-Catalyzed Radical Decarboxylative Oxyalkylation of Terminal Alkynes with Alkyl Peroxides. *Chem. - Eur. J.* **2017**, *23*, 10254-10258.

(15) Cui, Z.; Du, D.-M. Decarboxylative Synthesis of Functionalized Oxindoles via An Iron-Initiated Radical Chain Process and Application in Constructing Diverse Fused-Indoline Heterocycles. *Adv. Synth. Catal.* **2018**, *360*, 93-99.

(16) CCDC 1819937 (for **4aa**) and 1819940 (for **5ba**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.