JOC The Journal of Organic Chemistry

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Oxidative Radical Addition/Cyclization Cascade for the Construction of Carbonyl-Containing Quinoline-2,4(1*H*,3*H*)-Diones

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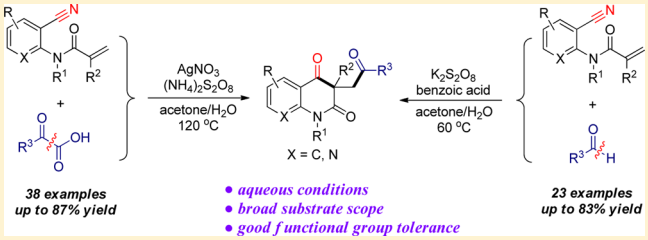
Supporting Information

ABSTRACT: Oxidative radical addition/cyclization cascade of *o*-cyanoarylacrylamides with α-keto acids as well as aldehydes is reported. This transformation exhibits a wide substrate scope and significant functional group tolerance and provides a convenient and highly efficient access to carbonyl-containing quinoline-2,4(1*H*,3*H*)-diones. A possible mechanism for the transformation is proposed.



INTRODUCTION

Quinoline-2,4-diones are well-known highly valuable heterocycles that are ubiquitous in pharmaceuticals and agrochemicals.[1] It has been shown that quinoline-2,4-dione derivatives possess antiplatelet, antibacterial, and herbicidal activities. Moreover, they serve as useful precursors for the preparation of novel molecules and natural products such as pyranoquinoline alkaloids.[2] In light of their biological and synthetic importance, numerous methods for the synthesis of these compounds have been developed.[3] However, these procedures generally involve multiple synthetic steps and/or complex substrates. Therefore, the development of an efficient and straightforward method for the synthesis of quinoline-2,4-dione derivatives is highly desirable.

Transition-metal-catalyzed decarboxylative coupling reactions have become one of the most powerful methods to construct C−C and C−heteroatom bonds in recent years because such reactions present many advantages, such as using readily available and stable carboxylic acids (or their salts) as substrate, high selectivity, and only produce nontoxic CO_2 as the side product.[4,5] In this context, decarboxylation of α-keto acids as acyl surrogates has attracted considerable research interest.[6−8] Since an inspiring breakthrough was reported by Gooßen and co-workers, who first demonstrated a palladium-catalyzed decarboxylative acylation of α-keto acid salts with aryl bromides to afford diaryl ketones,[6a] numerous decarboxylative acylations of aromatic C−H bonds with α-keto acids have been developed.[7] Moreover, the radical-mediated decarboxylative coupling and cascade reactions of α-keto acids with unsaturated substrates have also been achieved.[8] On the other hand, addition reactions to nitriles are efficient approaches for the synthesis of ketones. This addition reaction can be classified into two major types depending on the mechanism: (1) the insertions of cyano groups from Grignard reagents,[9a,b] lithium reagents,[9c] and transition-metal complexes,[10] and (2) the radical addition. Although radical additions to the polar cyano group are generally unfavorable processes due to the slowness and generating highly unstable iminyl radicals,[11] this radical addition might be successful if the unstable iminyl radical intermediate can be effectively trapped.[12] Many reports showed that the radical addition of cyano groups was carried out by metal reagents. However, most of the metal reagents are the early transition-metal complexes such as titanium,[12a,b] samarium,[12c,d] and manganese.[12e] As part of our ongoing interest in radical cyclizations,[13] herein, we present a novel Ag-catalyzed oxidative radical decarboxylative addition/cyclization cascade of α-keto acids with *o*-cyanoarylacrylamides for the synthesis of valuable carbonyl-containing quinoline-2,4(1*H*,3*H*)-diones in which the cyclization was accomplished by an intramolecular addition of the carbon radical to the nitrile (Scheme 1). In addition, these quinoline-2,4(1*H*,3*H*)-diones could be also achieved through a similar cascade when α-keto acids was replaced by aldehydes.

RESULTS AND DISCUSSION

Initially, anthranilonitrile-derived *N*-(2-cyanophenyl)-*N*-methylmethacrylamide **1a** and readily available phenylglyoxylic acid **2a** were shosen as the model substrates to optimize reaction conditions for the decarboxylative addition/cyclization. When acrylamide **1a** was treated with 3.0 equiv of phenylglyoxylic acid in the presence of 10 mol % of Ag_2CO_3 and 1.0 equiv of $K_2S_2O_8$ in THF/H_2O (1:1) at 120 °C, to our delight, the reaction proceeded smoothly and afforded the desired quinoline-2,4-dione **3a** in 46% yield (Table 1, entry 1). After an extensive solvent screening, acetone/H_2O (1:1) was shown to be the optimal solvent for this reaction, providing the desired product in moderate yield (Table 1, entries 2−4). When the loading of Ag_2CO_3 was decreased to 5 mol %, the yield of **3a** improved to

Received: January 29, 2016
Published: March 3, 2016

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DOI: 10.1021/acs.joc.6b00210
J. Org. Chem. 2016, 81, 2920−2929

Scheme 1. Oxidative Radical Addition/Cyclization Cascade

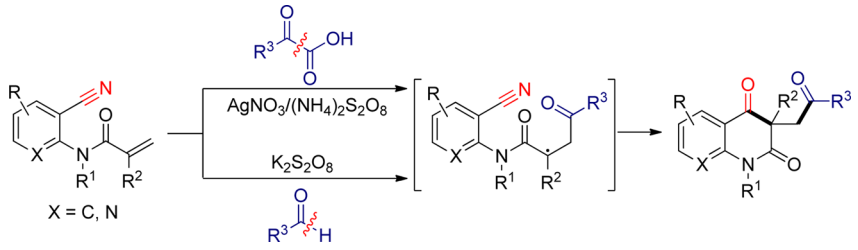
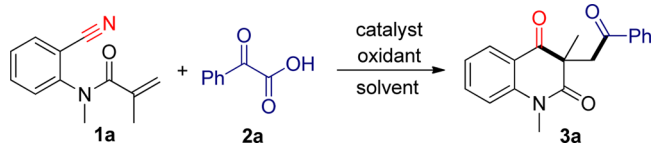


Table 1. Reaction Conditions Screening[a]



entry	catalyst (mol %)	oxidant	solvent (v/v)	yield[b] (%)
1	Ag_2CO_3 (10)	$K_2S_2O_8$	THF/H_2O (1:1)	46
2	Ag_2CO_3 (10)	$K_2S_2O_8$	CH_3CN/H_2O (1:1)	63
3	Ag_2CO_3 (10)	$K_2S_2O_8$	dioxane/H_2O (1:1)	58
4	Ag_2CO_3 (10)	$K_2S_2O_8$	acetone/H_2O (1:1)	64
5	Ag_2CO_3 (5)	$K_2S_2O_8$	acetone/H_2O (1:1)	66
6	Ag_2O (5)	$K_2S_2O_8$	acetone/H_2O (1:1)	67
7	$AgNO_3$ (5)	$K_2S_2O_8$	acetone/H_2O (1:1)	68
8	AgOAc (5)	$K_2S_2O_8$	acetone/H_2O (1:1)	60
9	AgF (5)	$K_2S_2O_8$	acetone/H_2O (1:1)	59
10	CuCl (5)	$K_2S_2O_8$	acetone/H_2O (1:1)	16
11	CuBr (5)	$K_2S_2O_8$	acetone/H_2O (1:1)	17
12	$CuCl_2$ (5)	$K_2S_2O_8$	acetone/H_2O (1:1)	23
13	$CuBr_2$ (5)	$K_2S_2O_8$	acetone/H_2O (1:1)	26
14	$Cu(OAc)_2$ (5)	$K_2S_2O_8$	acetone/H_2O (1:1)	29
15	**$AgNO_3$ (5)**	**$(NH_4)_2S_2O_8$**	**acetone/H_2O (1:1)**	**74**
16	$AgNO_3$ (5)	oxone	acetone/H_2O (1:1)	0
17	$AgNO_3$ (5)	TBHP	acetone/H_2O (1:1)	0
18	$AgNO_3$ (5)	DTBP	acetone/H_2O (1:1)	0
19	$AgNO_3$ (5)	TBPB	acetone/H_2O (1:1)	24
20	$AgNO_3$ (5)	BPO	acetone/H_2O (1:1)	36
21[c]	$AgNO_3$ (5)	$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	55
22	$AgNO_3$ (5)		acetone/H_2O (1:1)	0
23		$(NH_4)_2S_2O_8$	acetone/H_2O (1:1)	37

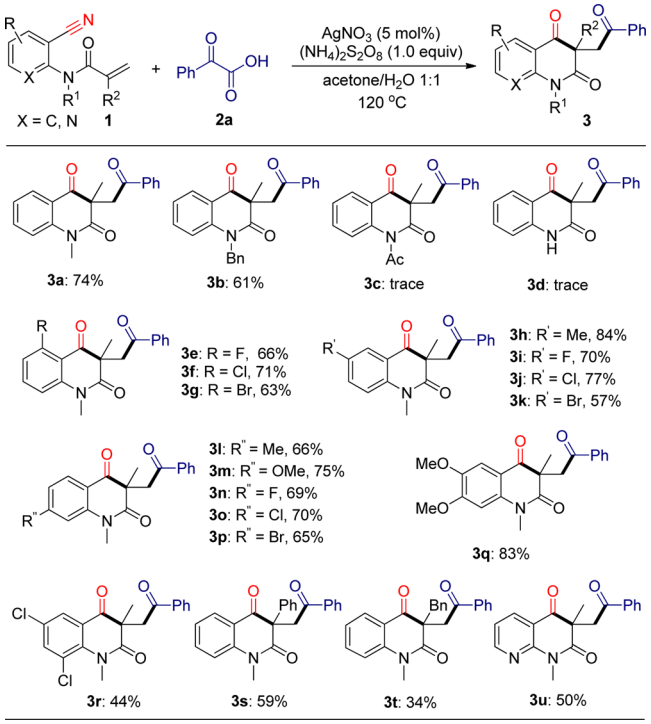
[a]Reaction conditions: **1a** (0.30 mmol), **2a** (0.90 mmol), catalyst, and oxidant (1.0 equiv) in solvent (3.0 mL) at 120 °C for 12 h under N_2. [b]Isolated yield. [c]100 °C

66% (Table 1, entry 5). Different Ag and Cu catalysts (e.g., Ag_2O, $AgNO_3$, AgOAc, AgF, CuCl, CuBr, $CuCl_2$, $CuBr_2$, and $Cu(OAc)_2$) were screened; $AgNO_3$ gave the best results (Table 1, entries 5−14). In addition, other oxidants such as $(NH_4)_2S_2O_8$, oxone, *tert*-butyl hydroperoxide (TBHP, anhydrous, about 5.5 M in decane), di-*tert*-butyl peroxide (DTBP), *tert*-butyl peroxybenzoate (TBPB), and benzoyl peroxide (BPO) were also tested, and the results indicate that $(NH_4)_2S_2O_8$ was the most efficient oxidant for this reaction, providing **3a** in 74% yield. (Table 1, entries 15−20). Decreasing the temperature negatively affected the reaction (Table 1, entry 21). Control experiments showed that no reaction occurred in the absence of $(NH_4)_2S_2O_8$, whereas, in the absence of $AgNO_3$, product **3a** could form in the presence of $(NH_4)_2S_2O_8$, albeit with a much lower yield (Table 1, entries 22, 23).

With the optimized conditions in hand, the scope of *o*-cyanoarylacrylamides was investigated. As depicted in Table 2, the *N*-methyl and *N*-benzyl substituted substrates gave the desired products in moderate to good yields (**3a**, **3b**), whereas the reactions of *N*-acetyl and N-H derivatives failed (**3c**, **3d**). The substrates with both electron-donating and electron-withdrawing groups at the phenyl ring could be successfully converted into the quinoline-2,4-diones in moderate to good yields (**3e**−**3p**). Notably, halo functional groups such as F, Cl, and Br were well-tolerated in the reaction, which provided opportunities for modification at the halogenated positions. No steric effect on the phenyl ring was observed in this transformation because the *ortho*-substituted acrylamides gave comparable yields (**3e**−**3g**). Multisubstituted amides were also reacted well with phenylglyoxylic acid, and the expected products **3q** and **3r** were obtained in 83% and 44% yields, respectively. The substitute effect at the α-position (R^2) of the acrylamides was next explored, and it was found that two α-sustitutents, phenyl and benzyl, were compatible with this decarboxylative addition/cyclization reaction, affording the desired products **3s** and **3t** in moderate

DOI: 10.1021/acs.joc.6b00210
J. Org. Chem. 2016, 81, 2920−2929

Table 2. Scope of *o*-Cyanoarylacrylamides[a,b]

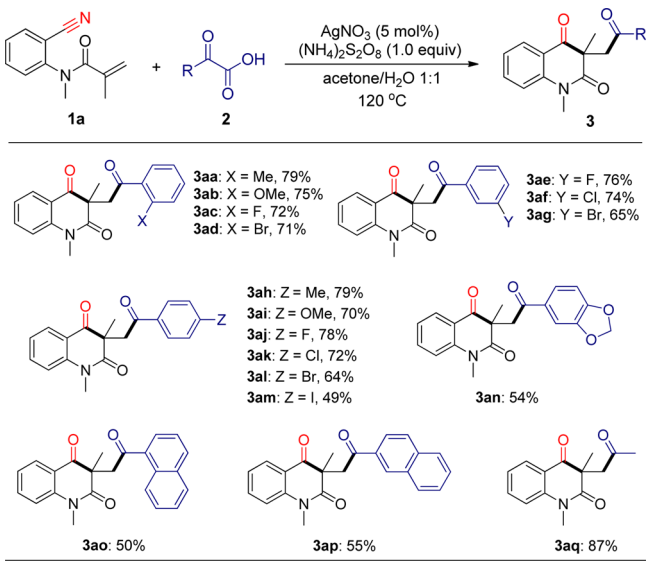


[a]All the reactions were carried out in the presence of 0.30 mmol of **1**, 3.0 equiv of **2a**, 5 mol % $AgNO_3$, and 1.0 equiv of $(NH_4)_2S_2O_8$ in 3.0 mL of acetone/H_2O (1:1) at 120 °C under N_2. [b]Yield of the isolated product.

yields. Heterocyclic substrate pyridineacrylamide also underwent the reaction smoothly, affording product **3u** in 50% yield.

We next studied the reaction of *N*-(2-cyanophenyl)-*N*-methylmethacrylamide **1a** with various α-keto acids under the optimized conditions (Table 3). Phenylglyoxylic acids bearing an

Table 3. Scope of α-Keto Acids[a,b]

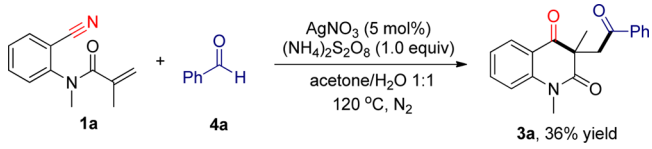


[a]All the reactions were carried out in the presence of 0.30 mmol of **1a**, 3.0 equiv of **2**, 5 mol % $AgNO_3$, and 1.0 equiv of $(NH_4)_2S_2O_8$ in 3.0 mL of acetone/H_2O (1:1) at 120 °C under N_2. [b]Yield of the isolated product.

electron-withdrawing group or an electron-donating group, such as Me, MeO, F, Cl, Br, or I, at the aryl ring were consistent with the optimized conditions, and the corresponding products **3aa**–**3am** were obtained in moderate to good yields. It is noteworthy that *o*-substituted phenylglyoxylic acids turned out to be compatible (**3aa**–**3ad**). The acetal functionality was also well-tolerated (**3an**). Besides phenyl substitution, α- and β-naphthyloxoacetic acids are all suitable substrates, albeit in moderate yields (**3ao**, **3ap**). The reaction is not limited to aromatic α-keto acids; pyruvic acid also provided the corresponding quinoline-2,4-dione **3aq** in good yield.

Aldehydes are readily available and are bulk scale raw chemicals in industry. Acylation using aldehydes as acyl precursors through a $C(sp^2)$–H bond cleavage mode are considered as atom-efficient processes.[14] We postulated that the above transformation might also be achieved if α-keto acids were replaced by aldehydes. Gratifyingly, benzaldehyde successfully underwent the addition/cyclization reaction with *N*-(2-cyanophenyl)-*N*-methylmethacrylamide under the optimized conditions, furnishing the desired quinoline-2,4-dione in 36% yield. (Scheme 2)

Scheme 2. Oxidative Addition/Cyclization of Benzaldehyde

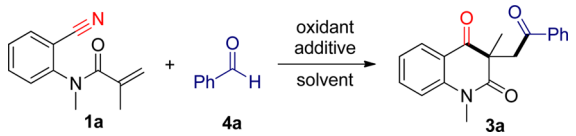


In order to explore this cascade reaction, we next optimized the reaction conditions, and the catalyst demonstrated entirely no efficiency to this transformation (Table 4, entry 1). The oxidant loading and effect of benzaldehyde stoichiometry were also examined (Table 4, entries 2–5), and the results indicate that using 4.0 equiv of aldehyde with 2.0 equiv of oxidant led to the desired product in moderate yield. When the substrate concentration was decreased to 0.05 M, the yield of **3a** improved to 66% yield (Table 4, entriy 6). Different reaction temperatures were also investigated, and the best result was obtained at 60 °C (Table 4, entries 7, 8). This reaction could occur in the presence of other oxidants such as $K_2S_2O_8$ and BPO, while the reactivity of $K_2S_2O_8$ was better than BPO, to afford the desired product **3a** in 72% yield (Table 4, entries 8–13). No reaction occurred when oxone, DTBP, and TBPB were used. We postulated that this cascade reaction was favored in acidic conditions because, in the transformation, imine hydrolysis might be involved. Several acids such as benzoic acid, TsOH·H_2O, and AcOH were tested. Benzoic acid was proved to be the best additive, and the appropriate amount of it was 15 mol % (Table 4, entries 14–18). Different solvents were screened, and, among them, acetone/H_2O (1:1) exhibited unmatched efficacy for the transformation (Table 4, entries 15, 19–21).

Under the above obtained optimum reaction conditions, we set out to explore the substrate scope for the oxidative addition/cyclization of aldehydes with *o*-cyanoarylacrylamides, and representative results are listed in Table 5. Initially, *o*-cyanoarylacrylamides were examined. An investigation into different N-protection groups showed that the electron-donating groups, methyl and benzyl, are suitable for this reaction (**3a**, **3c**). The substrates with electron-withdrawing or electron-donating groups were all well-tolerated, and the corresponding quinoline-2,4-diones were obtained in moderate to good yields (**3f**–**3p**).

DOI: 10.1021/acs.joc.6b00210
J. Org. Chem. 2016, 81, 2920–2929

Table 4. Optimization of the Addition/Cyclization Conditions[a]



entry	oxidant (equiv)	additive (mol %)	solvent	temp. (°C)	yield[b] (%)
1[c,d]	$(NH_4)_2S_2O_8$ (1.0)		acetone/H_2O (1:1)	120	44
2[c,d]	$(NH_4)_2S_2O_8$ (2.0)		acetone/H_2O (1:1)	120	54
3[c,d]	$(NH_4)_2S_2O_8$ (3.0)		acetone/H_2O (1:1)	120	41
4[c]	$(NH_4)_2S_2O_8$ (2.0)		acetone/H_2O (1:1)	120	63
5[c,e]	$(NH_4)_2S_2O_8$ (2.0)		acetone/H_2O (1:1)	120	62
6	$(NH_4)_2S_2O_8$ (2.0)		acetone/H_2O (1:1)	120	66
7	$(NH_4)_2S_2O_8$ (2.0)		acetone/H_2O (1:1)	80	69
8	$(NH_4)_2S_2O_8$ (2.0)		acetone/H_2O (1:1)	60	69
9	$K_2S_2O_8$ (2.0)		acetone/H_2O (1:1)	60	72
10	oxone (2.0)		acetone/H_2O (1:1)	60	0
11	BPO (2.0)		acetone/H_2O (1:1)	60	42
12	DTBP (2.0)		acetone/H_2O (1:1)	60	0
13	TBPB (2.0)		acetone/H_2O (1:1)	60	0
14	$K_2S_2O_8$ (2.0)	benzoic acid (10)	acetone/H_2O (1:1)	60	73
15	**$K_2S_2O_8$ (2.0)**	**benzoic acid (15)**	**acetone/H_2O (1:1)**	**60**	**80**
16	$K_2S_2O_8$ (2.0)	benzoic acid (20)	acetone/H_2O (1:1)	60	65
17	$K_2S_2O_8$ (2.0)	TsOH·H_2O (15)	acetone/H_2O (1:1)	60	65
18	$K_2S_2O_8$ (2.0)	AcOH (15)	acetone/H_2O (1:1)	60	62
19	$K_2S_2O_8$ (2.0)	benzoic acid (15)	THF/H_2O (1:1)	60	trace
20	$K_2S_2O_8$ (2.0)	benzoic acid (15)	CH_3CN/H_2O (1:1)	60	72
21	$K_2S_2O_8$ (2.0)	benzoic acid (15)	dioxane/H_2O (1:1)	60	26

[a]Reaction conditions: **1a** (0.30 mmol), **4a** (4.0 equiv), oxidant, and additive in solvent (6.0 mL) for 24 h under N_2. [b]Isolated yield. [c]3.0 mL of solvent. [d]3.0 equiv of aldehyde was used. [e]5.0 equiv of aldehyde was used.

However, the steric hindrance effect was obvious on the transformation reactivity. The substrates with substituents at an *ortho* site of the cyano group exhibited lower reactivity, and it produced relatively lower yields (**3f**, **3g**). When R^2 was replaced by −Ph or $-CH_2OAc$, the reaction proceeded smoothly in moderate yields as well (**3s**, **3v**). Pyridineacrylamide was also compatible with this addition/cyclization, affording product **3u** in 71% yield. The scope of aldehydes was also examined. The benzaldehydes with electron-donating or electron-withdrawing groups were all well-tolerated (**3aa**−**3al**). Gratifyingly, aliphatic aldehydes, such as valeraldehyde, phenylpropyl aldehyde, and cyclopropanecarboxaldehyde, were suitable for the reaction, providing the corresponding quinoline-2,4-diones in moderate to good yields (**3ar**−**3at**).

Several radical-trapping experiments were carried out to investigate the mechanism for this oxidative cascade reaction (Scheme 3). The reactions of *N*-(2-cyanophenyl)-*N*-methylmethacrylamide with phenylglyoxylic acid as well as benzaldehyde were performed in the presence of radical scavenger, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or 1,1-diphenylethylene, under the standard conditions, and no reaction was observed, even after longer reaction times. In addition, when diene **5** was employed instead of *N*-(2-cyanophenyl)-*N*-methylmethacrylamide, cyclized product **6** was obtained in 33% yield. These results indicate that the transformation may involve a radical intermediate process.

A possible mechanism for this transformation is proposed in Scheme 4 on the basis of the experimental results above and the previous reports. First, oxidation of Ag(I) by persulfate generates the Ag(II) intermediate, which then abstracts a single electron from carboxylate to provide the carboxyl radical. The fast decarboxylation of the carboxyl radical gives the corresponding nucleophilic acyl radical **A**.[15] This acyl radical can also be generated from aldehydes in the presence of peroxides.[14a−e] Potassium peroxydisulfate may decompose to sulfate radical anion upon heating,[16] which then abstracts a hydrogen atom from aldehyde to generate the acyl radical **A**. Subsequently, addition of the acyl radical to the carbon−carbon double bond of **1a** leads to alkyl radical **B**. Intramolecular addition of the alkyl radical to the nitrile affords imine radical **C**, which then undergoes H-abstraction to give the imine **D**.[12f,g] Finally, imine is hydrolyzed by H_2O to provide the desired product **3a**.

CONCLUSIONS

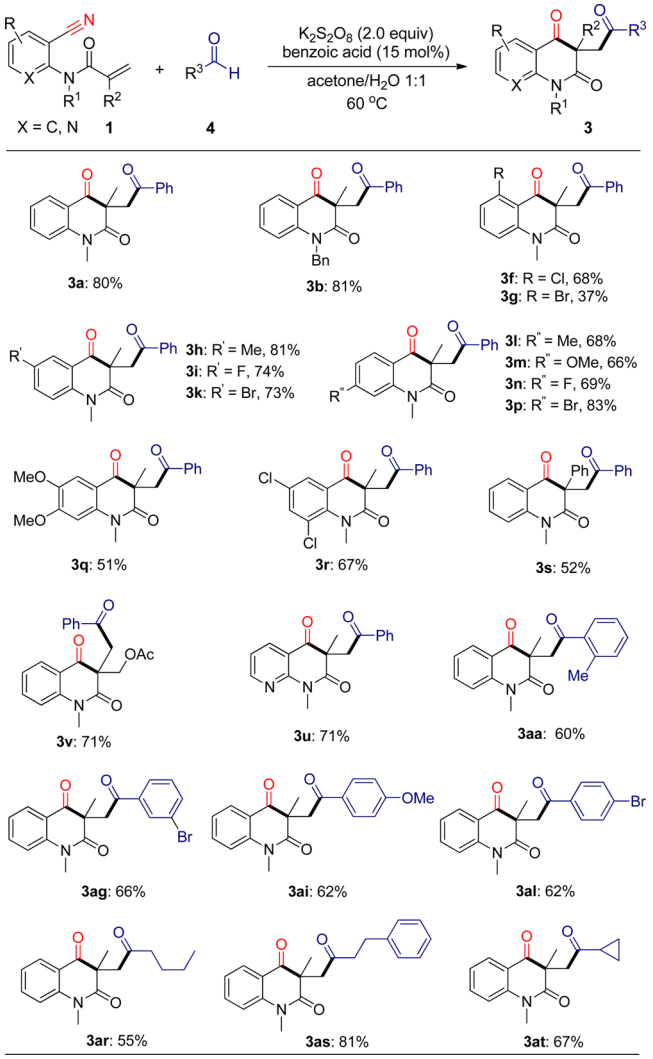
In conclusion, we have developed a novel Ag-catalyzed oxidative radical decarboxylative addition/cyclization of α-keto acids with *o*-cyanoarylacrylamides in which the cyclization was accomplished by an intramolecular addition of the carbon radical to the nitrile. This transformation is characterized by its good functional group tolerance, wide substrate scope, and utilizing readily available reagents, thus providing a convenient and highly efficient access to carbonyl-containing quinoline-2,4(1*H*,3*H*)-diones. Furthermore, a similar oxidative radical cascade of aldehydes with *o*-cyanoarylacrylamides was also developed. Further mechanistic investigation and the synthetic applications of this transformation are underway in our laboratory.

EXPERIMENTAL SECTION

General Information. All purchased chemicals were used without further purification. All the starting *o*-cyanoarylacrylamides and α-keto acids are known compounds and were synthesized according to known procedures.[13e,17] Column chromatography was carried out on silica gel

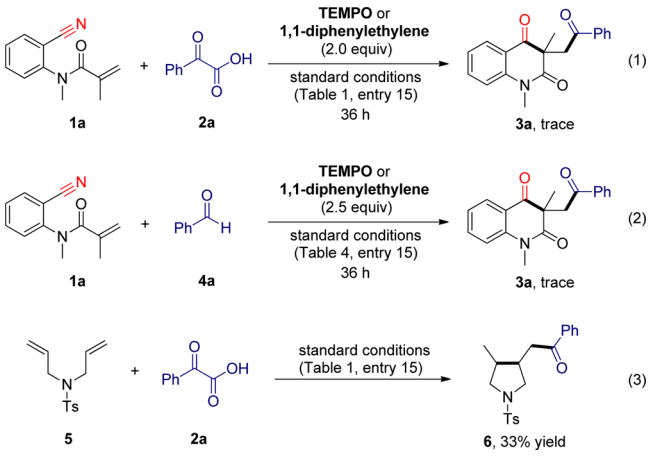
DOI: 10.1021/acs.joc.6b00210
J. Org. Chem. 2016, 81, 2920−2929

Table 5. Substrate Scope[a,b]



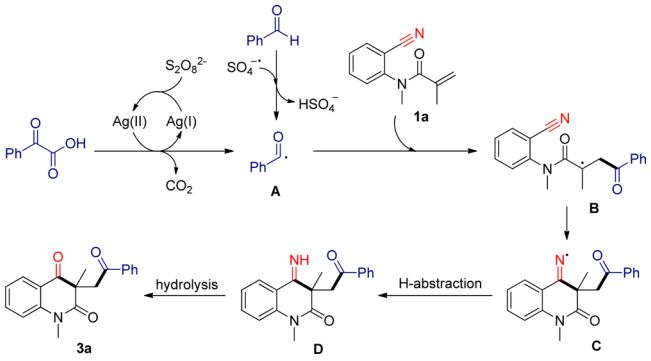
[a]All the reactions were carried out in the presence of 0.30 mmol of **1**, 4.0 equiv of **4**, 2.0 equiv of $K_2S_2O_8$, and 15 mol % benzoic acid in 6.0 mL of acetone/H_2O (1:1) at 60 °C under N_2. [b]Yield of the isolated product.

Scheme 3. Radical-Trapping Experiments



(200−400 mesh). Melting points were determined without correction on a digital melting-point apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz, respectively. IR spectra were recorded on an FT-IR, and wavenumbers are given in cm^{-1}. High-resolution mass spectra (HRMS) were recorded on an LC-TOF spectrometer using electrospray ionization (ESI) techniques.

Scheme 4. Proposed Mechanism



General Procedure I: Synthesis of Carbonyl-Containing Quinoline-2,4(1*H*,3*H*)-Diones from *α*-Keto Acids and *o*-Cyanoarylacrylamides. A mixture of *o*-cyanoarylacrylamide **1** (0.30 mmol), *α*-keto acid **2** (0.90 mmol), $AgNO_3$ (0.015 mmol), and $(NH_4)_2S_2O_8$ (0.30 mmol) in acetone/H_2O [3.0 mL, 1/1 (v/v)] was heated under nitrogen at 120 °C for 12 h. Upon completion as shown by TLC, the reaction mixture was cooled to room temperature, and then aqueous Na_2CO_3 (1.0 M, 3.0 mL) was added. After stirring for a further 5 min, the reaction mixture was extracted with ethyl acetate (3 × 5.0 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated in vacuum. The residue was purified by flash chromatography on silica gel with petroleum ether/EtOAc as the eluent to afford the desired product **3**.

General Procedure II: Synthesis of Carbonyl-Containing Quinoline-2,4(1*H*,3*H*)-Diones from Aldehydes and *o*-Cyanoarylacrylamides. A mixture of *o*-cyanoarylacrylamide **1** (0.30 mmol), aldehyde **4** (1.20 mmol), benzoic acid (0.045 mmol), and $K_2S_2O_8$ (0.60 mmol) in acetone/H_2O [6.0 mL, 1/1 (v/v)] was heated under nitrogen at 60 °C for 24 h. Upon completion as shown by TLC, the reaction mixture was cooled to room temperature and extracted with ethyl acetate (3 × 5.0 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated in vacuum. The residue was purified by flash chromatography on silica gel with petroleum ether/EtOAc as the eluent to afford the desired product **3**.

*1,3-Dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4(1H,3H)-dione (**3a**).* The title compound was isolated as a white solid (general procedure I: 68.0 mg, 74% yield; general procedure II: 73.9 mg, 80% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 147−149 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 7.4 Hz, 1H), 7.94 (d, J = 7.4 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.0 Hz, 1H), 7.43 (t, J = 7.3 Hz, 2H), 7.25 (d, J = 8.3 Hz, 1H), 7.19 (t, J = 7.3 Hz, 1H), 4.13−4.04 (m, 2H), 3.51 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 196.5, 173.9, 143.3, 135.8, 135.7, 133.4, 128.5, 128.33, 128.29, 122.8, 119.6, 114.9, 53.4, 46.9, 29.8, 24.5; IR (KBr, cm^{-1}) υ 2968, 1691, 1674, 1657, 1599, 1387, 1344, 1292, 1222, 754, 554; HRMS (TOF-ESI) calc. for $C_{19}H_{17}NO_3$ (M + H)$^+$, 308.1281; found, 308.1287.

*1-Benzyl-3-methyl-3-(2-oxo-2-phenylethyl)quinoline-2,4(1H,3H)-dione (**3b**).* The title compound was isolated as a white solid (general procedure I: 70.6 mg, 61% yield; general procedure II: 92.8 mg, 81% yield) after flash chromatography (petroleum ether/EtOAc, 6:1); mp 170−172 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J = 7.7 Hz, 1H), 7.97 (d, J = 7.9 Hz, 2H), 7.56−7.53 (m, 1H), 7.48−7.42 (m, 3H), 7.35−7.31 (m, 4H), 7.25−7.24 (m, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.08 (d, J = 8.4 Hz, 1H), 5.34 (s, 2H), 4.20−4.09 (m, 2H), 1.56 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 196.3, 174.3, 142.4, 136.2, 135.8, 135.7, 133.5, 128.9, 128.5, 128.4, 128.3, 127.2, 126.2, 122.9, 119.8, 115.9, 53.6, 47.0, 46.0, 24.6; IR (KBr, cm^{-1}) υ 2927, 1666, 1599, 1489, 1379, 1319, 1253, 1221, 1185, 1110, 754, 530; HRMS (TOF-ESI) calc. for $C_{25}H_{21}NO_3$ (M + H)$^+$, 384.1594; found, 384.1599.

DOI: 10.1021/acs.joc.6b00210
J. Org. Chem. 2016, 81, 2920−2929

*5-Fluoro-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3e**).* The title compound was isolated as a white solid (general procedure I: 64.2 mg, 66% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 194−196 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95−7.94 (m, 2H), 7.60−7.54 (m, 2H), 7.44 (t, J = 7.7 Hz, 2H), 7.05 (d, J = 8.5 Hz, 1H), 6.91−6.85 (m, 1H), 4.09−4.00 (m, 2H), 3.51 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 193.7, 173.4, 163.7 (d, J_{C-F} = 266.0 Hz), 144.5, 136.0 (d, J_{C-F} = 11.8 Hz), 135.7, 133.5, 128.5, 128.3, 111.0 (d, J_{C-F} = 21.6 Hz), 110.7 (d, J_{C-F} = 2.4 Hz), 109.3 (d, J_{C-F} = 8.6 Hz), 54.3, 46.2, 30.6, 24.2; IR (KBr, cm^{-1}) υ 2911, 1667, 1635, 1473, 1343, 1221, 1193, 1011, 838, 799, 698, 575; HRMS (TOF-ESI) calc. for $C_{19}H_{16}FNO_3$ (M + Na)$^+$, 348.1006; found, 348.1010.

*5-Chloro-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3f**).* The title compound was isolated as a white solid (general procedure I: 72.4 mg, 71% yield; general procedure II: 69.5 mg, 68% yield) after flash chromatography (petroleum ether/EtOAc, 4:1); mp 184−186 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96−7.94 (m, 2H), 7.57−7.54 (m, 1H), 7.49 (t, J = 8.2 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.22 (dd, J = 8.0, 0.7 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 4.07−3.96 (m, 2H), 3.52 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.5, 194.1, 173.0, 145.1, 136.0, 135.9, 134.3, 133.4, 128.5, 128.3, 126.4, 117.4, 113.9, 54.5, 45.6, 30.8, 23.6; IR (KBr, cm^{-1}) υ 2929, 1667, 1581, 1453, 1339, 1284, 1222, 1138, 1201, 817, 745, 638, 535; HRMS (TOF-ESI) calc. for $C_{19}H_{16}ClNO_3$ (M + H)$^+$, 342.0891; found, 342.0882.

*5-Bromo-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3g**).* The title compound was isolated as a white solid (general procedure I: 73.3 mg, 63% yield; general procedure II: 42.8 mg, 37% yield) after flash chromatography (petroleum ether/EtOAc, 4:1); mp 181−183 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, J = 7.3 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46−7.38 (m, 4H), 7.23 (d, J = 8.3 Hz, 1H), 4.07−3.96 (m, 2H), 3.51 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.5, 194.2, 172.8, 145.2, 135.8, 134.5, 133.4, 130.0, 128.5, 128.2, 123.5, 118.4, 114.6, 54.2, 45.6, 30.9, 23.4; IR (KBr, cm^{-1}) υ 2926, 1668, 1601, 1585, 1462, 1340, 1222, 1112, 1031, 983, 795, 690; HRMS (TOF-ESI) calc. for $C_{19}H_{16}BrNO_3$ (M + H)$^+$, 386.0386; found, 386.0386.

*1,3,6-Trimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4(1H,3H)-dione (**3h**).* The title compound was isolated as a white solid (general procedure I: 81.2 mg, 84% yield; general procedure II: 77.6 mg, 81% yield) after flash chromatography (petroleum ether/EtOAc, 4:1); mp 158−160 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95−7.93 (m, 2H), 7.87 (s, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.47−7.41 (m, 3H), 7.15 (d, J = 8.5 Hz, 1H), 4.12−4.03 (m, 2H), 3.50 (s, 3H), 2.37 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 196.7, 173.7, 141.2, 136.6, 135.7, 133.4, 132.5, 128.5, 128.30, 128.25, 119.3, 114.9, 53.3, 46.9, 29.8, 24.5, 20.3; IR (KBr, cm^{-1}) υ 2923, 1658, 1602, 1465, 1340, 1219, 1107, 820, 770, 686, 525; HRMS (TOF-ESI) calc. for $C_{20}H_{19}NO_3$ (M + H)$^+$, 322.1438; found, 322.1440.

*6-Fluoro-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3i**).* The title compound was isolated as a white solid (general procedure I: 68.3 mg, 70% yield; general procedure II: 71.8 mg, 74% yield) after flash chromatography (petroleum ether/EtOAc, 4:1); mp 136−138 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94−7.93 (m, 2H), 7.74 (dd, J = 8.1, 3.1 Hz, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.40−7.36 (m, 1H), 7.23 (dd, J = 9.1, 4.0 Hz, 1H), 4.14−4.03 (m, 2H), 3.51 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 195.7, 173.5, 158.4 (d, J_{C-F} = 244.6 Hz), 139.7, 135.6, 133.6, 128.5, 128.3, 122.8 (d, J_{C-F} = 23.5 Hz), 120.8 (d, J_{C-F} = 6.1 Hz), 116.7 (d, J_{C-F} = 7.0 Hz), 114.0 (d, J_{C-F} = 23.2 Hz), 53.2, 47.2, 30.1, 24.4; IR (KBr, cm^{-1}) υ 2924, 1669, 1472, 1328, 1166, 1098, 1005, 774, 688, 621, 552; HRMS (TOF-ESI) calc. for $C_{19}H_{16}FNO_3$ (M + H)$^+$, 326.1187; found, 326.1187.

*6-Chloro-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3j**).* The title compound was isolated as a white solid (general procedure I: 78.5 mg, 77% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 160−162 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 2.6 Hz, 1H), 7.94−7.93 (m, 2H), 7.60 (dd, J = 8.9, 2.6 Hz, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.8 Hz, 2H), 7.20 (d, J = 8.9 Hz, 1H), 4.14−4.04 (m, 2H), 3.50 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 195.4, 173.6, 141.8, 135.53, 135.46, 133.6, 128.7, 128.6, 128.3, 127.8, 120.6, 116.6, 53.5, 47.2, 30.0, 24.3; IR (KBr, cm^{-1}) υ 2976, 1662, 1467,1428, 1333, 1187, 1137, 1106, 929, 758, 688, 562; HRMS (TOF-ESI) calc. for $C_{19}H_{16}ClNO_3$ (M + H)$^+$, 342.0891; found, 342.0894.

*6-Bromo-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3k**).* The title compound was isolated as a white solid (general procedure I: 66.5 mg, 57% yield; general procedure II: 84.9 mg, 73% yield) after flash chromatography (petroleum ether/EtOAc, 7:1); mp 183−184 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, J = 2.4 Hz, 1H), 7.93 (d, J = 7.4 Hz, 2H), 7.73 (dd, J = 8.8, 2.4 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.7 Hz, 2H), 7.13 (d, J = 8.9 Hz, 1H), 4.13−4.03 (m, 2H), 3.48 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 195.3, 173.5, 142.3, 138.3, 135.5, 133.6, 130.8, 128.5, 128.3, 120.8, 116.9, 115.9, 53.4, 47.2, 29.9, 24.3; IR (KBr, cm^{-1}) υ 2967, 1667, 1598, 1467, 1380, 1344, 1296, 1220, 1099, 1003, 757, 622, 524; HRMS (TOF-ESI) calc. for $C_{19}H_{16}BrNO_3$ (M + H)$^+$, 386.0386; found, 386.0394.

*1,3,7-Trimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4(1H,3H)-dione (**3l**).* The title compound was isolated as a white solid (general procedure I: 63.6 mg, 66% yield; general procedure II: 65.6 mg, 68% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 186−188 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97−7.93 (m, 3H), 7.56−7.53 (m, 1H), 7.42 (t, J = 7.7 Hz, 1H), 7.05 (s, 1H), 7.01 (d, J = 7.9 Hz, 1H), 4.10−4.03 (m, 2H), 3.51 (s, 3H), 2.48 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 196.2, 174.2, 147.2, 143.4, 135.7, 133.4, 128.5, 128.4, 128.3, 123.9, 117.4, 115.4, 53.3, 46.9, 29.8, 24.7, 22.4; IR (KBr, cm^{-1}) υ 1647, 1605, 1461, 1337, 1217, 1089, 797, 605, 523; HRMS (TOF-ESI) calc. for $C_{20}H_{19}NO_3$ (M + Na)$^+$, 344.1257; found, 344.1261.

*7-Methoxy-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3m**).* The title compound was isolated as a white solid (general procedure I: 75.9 mg, 75% yield; general procedure II: 67.2 mg, 66% yield) after flash chromatography (petroleum ether/EtOAc, 4:1); mp 121−122 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 8.6 Hz, 1H), 7.94 (d, J = 7.9 Hz, 2H), 7.53 (t, J = 7.3 Hz, 1H), 7.42 (t, J = 7.6 Hz, 2H), 6.72−6.69 (m, 2H), 4.05 (s, 2H), 3.90 (s, 3H), 3.48 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 195.0, 174.3, 165.7, 145.2, 135.7, 133.3, 130.6, 128.4, 128.2, 113.5, 108.1, 100.8, 55.6, 53.0, 46.7, 29.7, 24.8; IR (KBr, cm^{-1}) υ 2928, 1651, 1600, 1452, 1336, 1226, 1100, 1030, 839, 741, 541; HRMS (TOF-ESI) calc. for $C_{20}H_{19}NO_4$ (M + H)$^+$, 338.1387; found, 338.1390.

*7-Fluoro-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3n**).* The title compound was isolated as a white solid (general procedure I: 67.5 mg, 69% yield; general procedure II: 67.0 mg, 69% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 120−122 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (dd, J = 8.4, 6.8 Hz, 1H), 7.94 (d, J = 7.9 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 6.94 (dd, J = 10.9, 1.9 Hz, 1H), 6.89 (td, J = 8.2, 1.9 Hz, 1H), 4.12−4.04 (m, 2H), 3.49 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 195.0, 174.0, 167.5 (d, J_{C-F} = 255.3 Hz), 145.6 (d, J_{C-F} = 11.7 Hz), 135.6, 133.6, 131.0 (d, J_{C-F} = 11.2 Hz), 128.5, 128.3, 116.2, 110.2 (d, J_{C-F} = 22.1 Hz), 102.5 (d, J_{C-F} = 27.5 Hz), 53.4, 47.0, 30.0, 24.5; IR (KBr, cm^{-1}) υ 2968, 1669, 1606, 1589, 1469, 1334, 1223, 1096, 960, 600; HRMS (TOF-ESI) calc. for $C_{19}H_{16}FNO_3$ (M + H)$^+$, 326.1187; found, 326.1188.

*7-Chloro-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3o**).* The title compound was isolated as a white solid (general procedure I: 72.0 mg, 70% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 115−116 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.3 Hz, 1H), 7.93 (d, J = 7.4 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.42 (t, J = 6.9 Hz, 2H), 7.25 (s, 1H), 7.17 (d, J = 8.3 Hz, 1H), 4.13−4.04 (m, 2H), 3.49 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 195.4, 173.9, 144.3, 142.2, 135.5, 133.6, 129.8, 128.5, 128.3, 123.1, 118.0, 115.2, 53.5, 47.1, 31.0, 24.4; IR (KBr, cm^{-1}) υ 2956, 1667, 1596, 1461, 1431, 1378, 1330, 1291, 1100, 868, 760, 688; HRMS (TOF-ESI) calc. for $C_{19}H_{16}ClNO_3$ (M + Na)$^+$, 364.0711; found, 364.0716.

*7-Bromo-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3p**).* The title compound was isolated as a white solid (general procedure I: 75.2 mg, 65% yield; general procedure II: 95.8 mg,

DOI: 10.1021/acs.joc.6b00210
J. Org. Chem. 2016, 81, 2920−2929

83% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 140−141 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94−7.91 (m, 3H), 7.56 (t, J = 7.4 Hz, 1H), 7.45−7.42 (m, 3H), 7.34 (dd, J = 8.3, 1.6 Hz, 1H), 4.12−4.03 (m, 2H), 3.50 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 195.6, 173.9, 144.2, 135.5, 133.6, 130.9, 129.7, 128.5, 128.3, 126.1, 118.3, 118.2, 53.5, 47.2, 30.0, 24.4; IR (KBr, cm^{-1}) υ 2924, 1664, 1599, 1459, 1429, 1332, 1292, 1221, 1027, 907, 730, 533; HRMS (TOF-ESI) calc. for $C_{19}H_{16}BrNO_3$ (M + Na)$^+$, 408.0206; found, 408.0208.

*6,7-Dimethoxy-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4(1H,3H)-dione (**3q**).* The title compound was isolated as a white solid (general procedure I: 91.1 mg, 83% yield; general procedure II: 55.8 mg, 51% yield) after flash chromatography (petroleum ether/EtOAc, 2:1); mp 197−199 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (dd, J = 8.4, 1.2 Hz, 1H), 7.57−7.52 (m, 2H), 7.45−7.42 (m, 2H), 6.71 (s, 1H), 4.07 (s, 2H), 4.03 (s, 3H), 3.92 (s, 3H), 3.53 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.9, 195.3, 174.3, 155.5, 145.1, 139.5, 134.5, 133.4, 128.5, 128.3, 112.3, 109.1, 98.3, 56.3, 56.2, 52.9, 47.1, 29.9, 25.0; IR (KBr, cm^{-1}) υ 2927, 1679, 1645, 1068, 1481, 1425, 1306, 1249, 1031, 734, 563; HRMS (TOF-ESI) calc. for $C_{21}H_{21}NO_5$ (M + Na)$^+$, 390.1312; found, 390.1312.

*6,8-Dichloro-1,3-dimethyl-3-(2-oxo-2-phenylethyl)quinoline-2,4-(1H,3H)-dione (**3r**).* The title compound was isolated as a white solid (general procedure I: 49.9 mg, 44% yield; general procedure II: 75.7 mg, 67% yield) after flash chromatography (petroleum ether/EtOAc, 10:1); mp 181−183 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96−7.94 (m, 2H), 7.86 (d, J = 2.5 Hz, 1H), 7.65 (d, J = 2.5 Hz, 1H), 7.58 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 4.12−3.96 (m, 2H), 3.62 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5, 195.1, 174.4, 141.0, 137.3, 135.6, 133.6, 129.7, 128.6, 128.4, 126.6, 124.5, 123.5, 53.6, 47.0, 37.8, 23.1; IR (KBr, cm^{-1}) υ 2926, 1703, 1668, 1649, 1613, 1453, 1334, 1221, 885, 528; HRMS (TOF-ESI) calc. for $C_{19}H_{15}Cl_2NO_3$ (M + H)$^+$, 376.0502; found, 376.0503.

*1-Methyl-3-(2-oxo-2-phenylethyl)-3-phenylquinoline-2,4(1H,3H)-dione (**3s**).* The title compound was isolated as a white solid (general procedure I: 65.1 mg, 59% yield; general procedure II: 58.0 mg, 52% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 210−213 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (dd, J = 7.7, 1.3 Hz, 1H), 7.95 (d, J = 7.4 Hz, 2H), 7.59−7.53 (m, 2H), 7.43−7.40 (m, 2H), 7.34 (d, J = 7.5 Hz, 1H), 7.30−7.24 (m, 1H), 7.17 (d, J = 8.4 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 4.40−4.33 (m, 2H), 3.57 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 194.0, 171.5, 143.0, 135.7, 135.5, 133.5, 129.1, 128.5, 128.3, 128.1, 126.9, 122.9, 121.0, 114.9, 62.7, 48.5, 30.1; IR (KBr, cm^{-1}) υ 2920, 1642, 1548, 1462, 1390, 1310, 1215, 1161, 1085, 670; HRMS (TOF-ESI) calc. for $C_{24}H_{19}NO_3$ (M + H)$^+$, 370.1438; found, 370.1438.

*3-Benzyl-1-methyl-3-(2-oxo-2-phenylethyl)quinoline-2,4(1H,3H)-dione (**3t**).* The title compound was isolated as a white solid (general procedure I: 39.2 mg, 34% yield) after flash chromatography (petroleum ether/EtOAc, 7:1); mp 235−236 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95−7.92 (m, 3H), 7.56 (t, J = 7.4 Hz, 1H), 7.45−7.41 (m, 3H), 7.05 (t, J = 7.5 Hz, 1H), 7.01−6.98 (m, 3H), 6.91−6.89 (m, 2H), 6.83 (d, J = 8.4 Hz, 1H), 4.23−4.16 (m, 2H), 3.31 (s, 3H), 3.22−3.14 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 196.5, 172.7, 142.9, 135.7, 135.5, 133.8, 133.5, 129.5, 128.5, 128.4, 127.5, 127.2, 122.5, 121.5, 114.4, 58.7, 47.8, 46.3, 29.4; IR (KBr, cm^{-1}) υ 2934, 1659, 1603, 1497, 1368, 1217, 1193, 810, 759, 546; HRMS (TOF-ESI) calc. for $C_{25}H_{21}NO_3$ (M + H)$^+$, 384.1594; found, 384.1596.

*1,3-Dimethyl-3-(2-oxo-2-phenylethyl)-1,8-naphthyridine-2,4-(1H,3H)-dione (**3u**).* The title compound was isolated as a white solid (general procedure I: 46.0 mg, 50% yield; general procedure II: 65.8 mg, 71% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 146−147 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (dd, J = 4.7, 1.8 Hz, 1H), 8.30 (dd, J = 7.6, 1.8 Hz, 1H), 7.93 (d, J = 7.5 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.15 (dd, J = 7.6, 4.8 Hz, 1H), 4.17−4.02 (m, 2H), 3.64 (s, 3H), 1.49 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 196.1, 174.5, 154.4, 154.1, 136.8, 135.5, 133.7, 128.6, 128.4, 118.7, 114.9, 53.7, 47.3, 28.8, 24.4; IR (KBr, cm^{-1}) υ 2921, 1645, 1568, 1551, 1514, 1461, 1388, 720, 609, 517; HRMS (TOF-ESI) calc. for $C_{18}H_{16}N_2O_3$ (M + H)$^+$, 309.1234; found, 309.1235.

*(1-Methyl-2,4-dioxo-3-(2-oxo-2-phenylethyl)-1,2,3,4-tetrahydroquinolin-3-yl)methyl Acetate (**3v**).* The title compound was isolated as a white solid (general procedure II: 77.7 mg, 71% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 148−150 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.7 Hz, 1H), 7.91 (d, J = 8.2 Hz, 2H), 7.68−7.65 (m, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.7 Hz, 2H), 7.26 (d, J = 7.9 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 4.47−4.38 (m, 2H), 4.13−4.06 (m, 2H), 3.52 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.8, 194.3, 171.1, 169.7, 143.4, 136.0, 135.4, 133.7, 128.6, 128.3, 127.8, 122.9, 121.0, 114.9, 68.6, 57.1, 44.3, 30.0, 20.2; IR (KBr, cm^{-1}) υ 2921, 1643, 1569, 1464, 1381, 1227, 1014, 752, 608; HRMS (TOF-ESI) calc. for $C_{21}H_{19}NO_5$ (M + H)$^+$, 366.1336; found, 366.1336.

*1,3-Dimethyl-3-(2-oxo-2-(o-tolyl)ethyl)quinoline-2,4(1H,3H)-dione (**3aa**).* The title compound was isolated as a white solid (general procedure I: 76.0 mg, 79% yield; general procedure II: 57.5 mg, 60% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 126−128 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07−8.05 (m, 1H), 7.82 (d, J = 7.6 Hz, 1H), 7.67−7.63 (m, 1H), 7.37−7.34 (m, 1H), 7.28−7.22 (m, 2H), 7.21−7.18 (m, 2H), 4.04−3.96 (m, 2H), 3.51 (s, 3H), 2.38 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.4, 196.5, 173.9, 143.3, 138.5, 136.2, 135.8, 131.8, 131.6, 129.0, 128.3, 125.6, 122.8, 119.6, 114.9, 53.8, 49.1, 29.8, 24.5, 21.3; IR (KBr, cm^{-1}) υ 2929, 1699,1676, 1657,1608,1467, 1345, 1208, 1161, 1101, 788, 513; HRMS (TOF-ESI) calc. for $C_{20}H_{19}NO_3$ (M + H)$^+$, 322.1438; found, 322.1444.

*3-(2-(2-Methoxyphenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3ab**).* The title compound was isolated as a white solid (general procedure I: 76.1 mg, 75% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 156−157 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 7.6 Hz, 1H), 7.76−7.74 (m, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.48−7.45 (m, 1H), 7.24 (d, J = 8.4 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H), 6.93 (t, J = 7.5 Hz, 1H), 4.16−4.07 (m, 2H), 3.97 (s, 3H), 3.52 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.3, 196.8, 174.2, 159.7, 143.4, 135.7, 134.5, 131.1, 128.4, 125.7, 122.7, 120.4, 119.7, 114.8, 111.6, 55.5, 53.6, 52.5, 29.8, 24.4; IR (KBr, cm^{-1}) υ 2981, 1655, 1598, 1549, 1475, 1374, 1340, 1105, 1046, 807, 623, 534; HRMS (TOF-ESI) calc. for $C_{20}H_{19}NO_4$ (M + H)$^+$, 338.1387; found, 338.1390.

*3-(2-(2-Fluorophenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3ac**).* The title compound was isolated as a white solid (general procedure I: 70.5 mg, 72% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 121−123 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (dd, J = 7.7, 1.5 Hz, 1H), 7.81 (td, J = 7.7, 1.7 Hz, 1H), 7.68−7.65 (m, 1H), 7.54−7.50 (m, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.21−7.13 (m, 3H), 4.12−4.03 (m, 2H), 3.52 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.4, 195.6 (d, J_{C-F} = 4.1 Hz), 173.8, 162.6 (d, J_{C-F} = 256.6 Hz), 143.3, 135.8, 135.2 (d, J_{C-F} = 8.7 Hz), 130.8 (d, J_{C-F} = 1.5 Hz), 128.4, 126.6, 124.3 (d, J_{C-F} = 3.3 Hz), 122.9, 119.6, 116.7 (d, J_{C-F} = 23.7 Hz), 114.9, 53.6, 51.2 (d, J_{C-F} = 9.2 Hz), 29.8, 24.5; IR (KBr, cm^{-1}) υ 2923, 1653, 1603, 1470, 1345, 1298, 1225, 1105, 757, 672, 568; HRMS (TOF-ESI) calc. for $C_{19}H_{16}FNO_3$ (M + H)$^+$, 326.1187; found, 326.1190.

*3-(2-(2-Bromophenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3ad**).* The title compound was isolated as a yellow solid (general procedure I: 82.7 mg, 71% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 173−175 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09−8.05 (m, 1H), 7.66−7.63 (m, 1H), 7.60−7.58 (m, 2H), 7.36 (t, J = 7.5 Hz, 1H), 7.30−7.29 (m, 1H), 7.23 (d, J = 8.4 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 4.05−3.97 (m, 2H), 3.51 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.8, 196.1, 173.4, 143.2, 139.3, 135.9, 133.9, 132.0, 129.3, 128.3, 127.2, 122.8, 119.5, 119.1, 114.9, 53.9, 49.5, 29.8, 24.6; IR (KBr, cm^{-1}) υ 2924, 1693, 1659, 1602, 1473, 1378, 1351, 1298, 1214, 1102, 756, 620; HRMS (TOF-ESI) calc. for $C_{19}H_{16}BrNO_3$ (M + H)$^+$, 386.0386; found, 386.0389.

*3-(2-(3-Fluorophenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3ae**).* The title compound was isolated as a white solid (general procedure I: 73.9 mg, 76% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 147−148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.7, 1.6 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.68−7.65 (m, 1H), 7.62−7.59 (m, 1H), 7.45−7.40 (m, 1H), 7.28−7.24 (m,

DOI: 10.1021/acs.joc.6b00210
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2H), 7.22−7.19 (m, 1H), 4.08−4.00 (m, 2H), 3.52 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.7, 196.4, 173.7, 162.7 (d, J_{C-F} = 248.0 Hz), 143.3, 137.7, 136.0, 130.2 (d, J_{C-F} = 7.4 Hz), 128.4, 124.1, 123.0, 120.5 (d, J_{C-F} = 21.4 Hz), 115.1, 115.0 (d, J_{C-F} = 22.2 Hz), 114.9, 53.5, 46.8, 29.9, 24.5; IR (KBr, cm^{-1}) υ 2922, 1669, 1593, 1472, 1342, 1246, 1166, 1100, 884, 758, 681; HRMS (TOF-ESI) calc. for $C_{19}H_{16}FNO_3$ $(M + H)^+$, 326.1187; found, 326.1188.

*3-(2-(3-Chlorophenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3af**).* The title compound was isolated as a white solid (general procedure I: 75.8 mg, 74% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 152−154 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, J = 7.7, 1.4 Hz, 1H), 7.91 (s, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.67−7.63 (m, 1H), 7.51 (d, J = 7.9 Hz, 1H), 7.37 (t, J = 7.9 Hz, 1H), 7.24 (d, J = 8.4 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H). 4.08−4.00 (m, 2H), 3.50 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.6, 196.2, 173.6, 143.2, 137.1, 135.9, 134.7, 133.3, 129.8, 128.3, 128.2, 126.3, 122.9, 119.4, 114.9, 53.4, 46.6, 29.8, 24.4; IR (KBr, cm^{-1}) υ 2931, 1651, 1601, 1472, 1380, 1301, 1103, 1021, 840, 764, 525; HRMS (TOF-ESI) calc. for $C_{19}H_{16}ClNO_3$ $(M + H)^+$, 342.0891; found, 342.0894.

*3-(2-(3-Bromophenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3ag**).* The title compound was isolated as a white solid (general procedure I: 75.6 mg, 65% yield; general procedure II: 76.5 mg, 66% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 132−134 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 9.0 Hz, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.66 (t, J = 8.5 Hz, 1H), 7.31 (t, J = 7.9 Hz, 1H), 7.24 (d, J = 8.4 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 4.08−3.99 (m, 2H), 3.50 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.5, 196.2, 173.6, 143.2, 137.3, 136.2, 135.9, 131.3, 130.1, 128.3, 126.8, 122.9, 122.8, 119.5, 114.9, 53.5, 46.6, 29.8, 24.5; IR (KBr, cm^{-1}) υ 2922, 1681, 1639, 1618, 1568, 1464, 1209, 1101, 771, 521; HRMS (TOF-ESI) calc. for $C_{19}H_{16}BrNO_3$ $(M + H)^+$, 386.0386; found, 386.0389.

*1,3-Dimethyl-3-(2-oxo-2-(p-tolyl)ethyl)quinoline-2,4(1H,3H)-dione (**3ah**).* The title compound was isolated as a white solid (general procedure I: 75.9 mg, 79% yield) after flash chromatography (petroleum ether/EtOAc, 6:1); mp 132−134 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.7, 1.6 Hz, 1H), 7.84 (d, J = 8.2 Hz, 2H), 7.67−7.64 (m, 1H), 7.25−7.18 (m, 4H), 4.11−4.02 (m, 2H), 3.51 (s, 3H), 2.39 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.4, 196.6, 173.9, 144.3, 143.3, 135.8, 133.2, 129.2, 128.4, 128.3, 122.8, 119.6, 114.9, 53.4, 46.9, 29.8, 24.5, 21.7; IR (KBr, cm^{-1}) υ 2929, 1699, 1676, 1657, 1608, 1467, 1345, 1208, 1161, 1101, 788, 513; HRMS (TOF-ESI) calc. for $C_{20}H_{19}NO_3$ $(M + H)^+$, 322.1438; found, 322.1444.

*3-(2-(4-Methoxyphenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3ai**).* The title compound was isolated as a white solid (general procedure I: 71.1 mg, 70% yield; general procedure II: 62.3 mg, 63% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 145−148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (dd, J = 7.7, 1.5 Hz, 1H), 7.92 (d, J = 8.8 Hz, 2H), 7.68−7.64 (m, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 6.90 (d, J = 8.8 Hz, 2H), 4.09−4.00 (m, 2H), 3.86 (s, 3H), 3.52 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.6, 196.3, 174.0, 163.8, 143.3, 135.8, 130.7, 128.9, 128.4, 122.8, 119.6, 114.9, 113.6, 55.4, 53.4, 46.8, 29.9, 24.4; IR (KBr, cm^{-1}) υ 2922, 1643, 1568, 1550, 1514, 1463, 1384, 1137, 1105, 756; HRMS (TOF-ESI) calc. for $C_{20}H_{19}NO_4$ $(M + H)^+$, 338.1387; found, 338.1389.

*3-(2-(4-Fluorophenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3aj**).* The title compound was isolated as a white solid (general procedure I: 76.3 mg, 78% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 161−163 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.7, 1.2 Hz, 1H), 7.97 (dd, J = 8.7, 5.5 Hz, 2H), 7.68−7.65 (m, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.10 (t, J = 8.6 Hz, 2H), 4.09−4.00 (m, 2H), 3.52 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.5, 196.2, 173.8, 166.0 (d, J_{C-F} = 255.3 Hz), 143.3, 135.9, 132.2, 131.0 (d, J_{C-F} = 9.4 Hz), 128.4, 122.9, 119.5, 115.6 (d, J_{C-F} = 21.9 Hz), 114.9, 53.5, 46.7, 29.8, 24.5; IR (KBr, cm^{-1}) υ 2962, 1657, 1600, 1475, 1383, 1342, 1224, 1104, 843, 759, 557; HRMS (TOF-ESI) calc. for $C_{19}H_{16}FNO_3$ $(M + H)^+$, 326.1187; found, 326.1191.

*3-(2-(4-Chlorophenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3ak**).* The title compound was isolated as a white solid (general procedure I: 73.8 mg, 72% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 110−112 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.7, 1.4 Hz, 1H), 7.88 (d, J = 8.5 Hz, 2H), 7.69−7.65 (m, 1H), 7.41 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 8.5 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 4.08−4.00 (m, 2H), 3.52 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.7, 196.4, 173.8, 143.3, 139.9, 135.9, 134.1, 129.7, 128.9, 128.4, 122.9, 119.5, 114.9, 53.5, 46.7, 29.9, 24.5; IR (KBr, cm^{-1}) υ 2975, 1657, 1602, 1471, 1381, 1344, 1298, 1219, 1103, 1088, 1004, 858, 629; HRMS (TOF-ESI) calc. for $C_{19}H_{16}ClNO_3$ $(M + H)^+$, 342.0891; found, 342.0894.

*3-(2-(4-Bromophenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3al**).* The title compound was isolated as a white solid (general procedure I: 73.7 mg, 64% yield; general procedure II: 71.7 mg, 62% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 134−136 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.7, 1.3 Hz, 1H), 7.81 (d, J = 8.5 Hz, 2H), 7.70−7.66 (m, 1H), 7.58 (d, J = 8.5 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.21 (t, J = 7.5 Hz, 1H)., 4.08−3.99 (m, 2H), 3.52 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.9, 196.4, 173.8, 143.3, 136.0, 134.5, 131.9, 129.8, 128.7, 128.4, 123.0, 119.6, 114.9, 53.5, 46.7, 29.9, 24.5; IR (KBr, cm^{-1}) υ 2917, 1683, 1655, 1602, 1471, 1382, 1298, 1218, 1068, 792, 643, 534; HRMS (TOF-ESI) calc. for $C_{19}H_{16}BrNO_3$ $(M + H)^+$, 386.0386; found, 386.0387.

*3-(2-(4-Iodophenyl)-2-oxoethyl)-1,3-dimethylquinoline-2,4-(1H,3H)-dione (**3am**).* The title compound was isolated as a white solid (general procedure I: 63.9 mg, 49% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 186−187 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.7, 1.5 Hz, 1H), 7.80 (d, J = 8.5 Hz, 2H), 7.68−7.64 (m, 3H), 7.25 (d, J = 8.4 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 4.06−3.97 (m, 2H), 3.51 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.2, 196.4, 173.7, 143.3, 137.9, 135.9, 135.0, 129.6, 128.4, 122.9, 119.5, 114.9, 101.6, 53.5, 46.6, 29.9, 24.5; IR (KBr, cm^{-1}) υ 2920, 1682, 1643, 1591, 1468, 1380, 1295, 1098, 992, 791, 687, 518; HRMS (TOF-ESI) calc. for $C_{19}H_{16}INO_3$ $(M + H)^+$, 434.0248; found, 434.0249.

*3-(2-(Benzo[d][1,3]dioxol-5-yl)-2-oxoethyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3an**).* The title compound was isolated as a white solid (general procedure I: 57.3 mg, 54% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 144−146 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.7, 1.5 Hz, 1H), 7.68−7.64 (m, 1H), 7.59 (dd, J = 8.2, 1.7 Hz, 1H), 7.35 (d, J = 1.6 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.19 (t, J = 7.2 Hz, 1H), 6.83 (d, J = 8.2 Hz, 1H), 6.02 (s, 2H), 4.05−3.97 (m, 2H), 3.51 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.5, 195.8, 173.9, 152.0, 148.0, 143.3, 135.8, 130.6, 128.3, 124.9, 122.8, 119.5, 114.9, 108.0, 107.8, 101.8, 53.5, 46.7, 29.8, 24.4; IR (KBr, cm^{-1}) υ 2917, 1657, 1601, 1454, 1343, 1251, 1104, 1034, 928, 755, 615; HRMS (TOF-ESI) calc. for $C_{20}H_{17}NO_5$ $(M + H)^+$, 352.1179; found, 352.1184.

*1,3-Dimethyl-3-(2-(naphthalen-1-yl)-2-oxoethyl)quinoline-2,4-(1H,3H)-dione (**3ao**).* The title compound was isolated as a white solid (general procedure I: 53.1 mg, 50% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 154−158 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.50−8.48 (m, 1H), 8.11 (dd, J = 7.7, 1.5 Hz, 1H), 8.07 (d, J = 7.1 Hz, 1H), 7.98 (d, J = 8.2 Hz, 1H), 7.83 (dd, J = 6.8, 2.4 Hz, 1H), 7.70−7.66 (m, 1H), 7.52−7.48 (m, 3H), 7.27 (d, J = 8.5 Hz, 1H), 7.22 (t, J = 7.5 Hz, 1H), 4.22−4.11 (m, 2H), 3.56 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.9, 196.6, 174.0, 143.4, 135.9, 134.4, 133.8, 133.0, 130.1, 128.4, 128.3, 128.2, 127.9, 126.4, 125.9, 124.3, 122.9, 119.7, 115.0, 54.0, 49.7, 29.9, 24.5; IR (KBr, cm^{-1}) υ 2921, 1655, 1465, 1378, 1173, 1095, 752, 677, 609; HRMS (TOF-ESI) calc. for $C_{23}H_{19}NO_3$ $(M + H)^+$, 358.1438; found, 358.1441.

*1,3-Dimethyl-3-(2-(naphthalen-2-yl)-2-oxoethyl)quinoline-2,4-(1H,3H)-dione (**3ap**).* The title compound was isolated as a white solid (general procedure I: 58.8 mg, 55% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); mp 137−139 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.08 (dd, J = 7.7, 1.6 Hz, 1H), 7.94−7.91 (m, 3H), 7.82 (d, J = 8.4 Hz, 3H), 7.67−7.60 (m, 1H), 7.58−7.50 (m, 2H), 7.25−7.22 (m, 2H), 7.18 (t, J = 7.5 Hz, 1H), 4.28−4.19 (m, 2H), 3.51 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 196.5, 173.9, 143.3, 135.8, 135.7, 133.0, 132.3, 130.2, 129.5, 128.5, 128.3, 127.7, 126.7, 123.7, 122.8, 119.5, 114.9, 53.5, 47.0, 29.8, 24.5; IR (KBr, cm^{-1}) υ 2924, 1650, 1599, 1466, 1381, 1169, 1099, 818, 759, 631, 534; HRMS (TOF-ESI) calc. for $C_{23}H_{19}NO_3$ $(M + H)^+$, 358.1438; found, 358.1442.

DOI: 10.1021/acs.joc.6b00210
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*1,3-Dimethyl-3-(2-oxopropyl)quinoline-2,4(1H,3H)-dione (**3aq**).* The title compound was isolated as a white solid (general procedure I: 63.8 mg, 87% yield) after flash chromatography (petroleum ether/EtOAc, 7:1); mp 206−208 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (dd, J = 7.7, 1.5 Hz, 1H), 7.66−7.63 (m, 1H), 7.22−7.17 (m, 2H), 3.53 (s, 2H), 3.48 (s, 3H), 2.15 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.3, 196.4, 173.7, 143.2, 135.8, 128.2, 122.8, 119.5, 114.8, 53.2, 50.9, 29.7, 28.8, 24.3; IR (KBr, cm^{-1}) υ 2936, 1694, 1652, 1598, 1471, 1379, 1298, 1104, 1040, 768, 658; HRMS (TOF-ESI) calc. for $C_{14}H_{15}NO_3$ (M + H)$^+$, 246.1125; found, 246.1127.

*1,3-Dimethyl-3-(2-oxohexyl)quinoline-2,4(1H,3H)-dione (**3ar**).* The title compound was isolated as a white solid (general procedure II: 47.6 mg, 55% yield) after flash chromatography (petroleum ether/EtOAc, 6:1); mp 145−147 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J = 7.7, 1.5 Hz, 1H), 7.66−7.62 (m, 1H), 7.22−7.16 (m, 2H), 3.51 (s, 2H), 3.48 (s, 3H), 2.43 (t, J = 7.5 Hz, 2H), 1.53−1.47 (m, 2H), 1.34 (s, 3H), 1.31−1.24 (m, 2H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.1, 196.6, 173.8, 143.3, 135.8, 128.3, 122.8, 119.5, 114.9, 53.2, 50.2, 41.4, 29.8, 25.6, 24.4, 22.2, 13.8; IR (KBr, cm^{-1}) υ 2974, 1656, 1465, 1423, 1384, 1228, 1046, 878, 756, 678; HRMS (TOF-ESI) calc. for $C_{17}H_{21}NO_3$ (M + H)$^+$, 288.1594; found, 288.1599.

*1,3-Dimethyl-3-(2-oxo-4-phenylbutyl)quinoline-2,4(1H,3H)-dione (**3as**).* The title compound was isolated as a white solid (general procedure II: 81.5 mg, 81% yield) after flash chromatography (petroleum ether/EtOAc, 6:1); mp 110−112 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.7 Hz, 1H), 7.65−7.62 (m, 1H), 7.26 (t, J = 7.5 Hz, 2H), 7.22−7.16 (m, 3H), 7.12 (d, J = 7.5 Hz, 2H), 3.52 (s, 2H), 3.48 (s, 3H), 2.83−2.74 (m, 4H), 1.34 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.8, 196.4, 173.7, 143.2, 140.7, 135.9, 128.4, 128.2, 128.1, 126.0, 122.8, 119.4, 114.9, 53.3, 50.0, 43.3, 29.8, 29.3, 24.4; IR (KBr, cm^{-1}) υ 2925, 1695, 1658, 1603, 1474, 1378, 1351, 1298, 1199, 1099, 756; HRMS (TOF-ESI) calc. for $C_{21}H_{21}NO_3$ (M + H)$^+$, 336.1594; found, 336.1598.

*3-(2-Cyclopropyl-2-oxoethyl)-1,3-dimethylquinoline-2,4(1H,3H)-dione (**3at**).* The title compound was isolated as a white solid (general procedure II: 54.8 mg, 67% yield) after flash chromatography (petroleum ether/EtOAc, 6:1); mp 164−165 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J = 7.7, 1.6 Hz, 1H), 7.65−7.61 (m, 1H), 7.21−7.16 (m, 2H), 3.67 (s, 2H), 3.48 (s, 3H), 2.00−1.96 (m, 1H), 1.36 (s, 3H), 1.00−0.93 (m, 2H), 0.89−0.87 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.6, 196.5, 173.8, 143.3, 135.8, 128.3, 122.8, 119.5, 114.8, 53.2, 50.8, 29.8, 24.4, 20.0, 11.03, 10.95; IR (KBr, cm^{-1}) υ 2922, 1645, 1468, 1387, 1346, 1088, 974, 895, 761, 619; HRMS (TOF-ESI) calc. for $C_{16}H_{17}NO_3$ (M + H)$^+$, 272.1281; found, 272.1285.

*2-(4-Methyl-1-tosylpyrrolidin-3-yl)-1-phenylethanone (**6**).* The title compound is an inseparable mixture. This mixture was isolated as a white solid (general procedure I: 35.1 mg, 33% yield) after flash chromatography (petroleum ether/EtOAc, 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89−7.84 (m, 2H), 7.73−7.70 (m, 2H), 7.59−7.56 (m, 1H), 7.48−7.44 (m, 2H), 7.33−7.27 (m, 2H), 3.68−3.39 (m, 2H), 3.11−1.87 (m, 9H), 0.97−0.82 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.4, 198.3, 143.4, 143.3, 136.6, 136.5, 133.9, 133.3, 133.3, 129.6, 128.7, 128.6, 127.91, 127.85, 127.6, 127.4, 54.3, 54.2, 53.2, 52.0, 41.2, 41.0, 38.7, 37.1, 36.5, 35.1, 21.50, 21.47, 16.4, 13.5; IR (KBr, cm^{-1}) υ 2921, 1641, 1514, 1461, 1390, 1159, 1049; HRMS (TOF-ESI) calc. for $C_{20}H_{23}NO_3S$ (M + H)$^+$, 358.1471; found, 358.1474.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00210.

^{1}H NMR and ^{13}C NMR spectra of new compounds (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for financial support from the National Natural Science Foundation of China (21402071) and Kunming University of Science and Technology (KKSY201426046).

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