JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

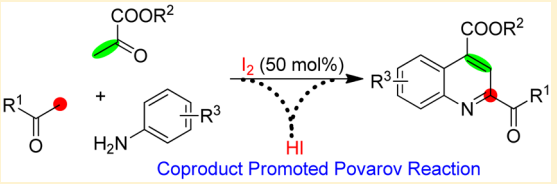
Coproduct Promoted Povarov Reaction: Synthesis of Substituted Quinolines from Methyl Ketones, Arylamines, and α-Ketoesters

Qinghe Gao, Shan Liu, Xia Wu, Jingjing Zhang, and Anxin Wu*

Key Laboratory of Pesticide & Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, Wuhan 430079, P. R. China

Supporting Information

ABSTRACT: A highly efficient I_2-catalyzed Povarov-type reaction of methyl ketones, arylamines, and α-ketoesters is developed. This reaction utilizes a catalytic amount of HI coproduct as a promoter for the synthesis of substituted quinolones. This simple procedure represents an interesting new form of reactivity for the Povarov reaction with good functional group compatibility.



The concept of an ideal synthesis is to bring together readily available fragments in a convergent manner using only carbon−hydrogen bond couplings to forge the requisite carbon−carbon and carbon−heteroatom bonds of the target compound.[1] In the pursuit of ideal synthesis, great attention is currently being given to domino, one-pot, and multicomponent reactions that allow the direct synthesis of complex molecules from simple substrates in a highly efficient manner.[2] Nevertheless, many reactions still suffer from issues, such as the simultaneous production of large amounts of byproducts with the desired product.[3] Recently, domino reactions have been designed to directly utilize a generated byproduct as a catalyst/cocatalyst for a subsequent reaction.[4] In 2008, Alaimo et al. first reported that the $InCl_3$ byproduct produced from a reduction step was internally recycled to catalyze a subsequent cycloaddition reaction. The reaction used 2 equiv of indium powder as the reducing agent and 5 equiv of an aldehyde to achieve a high overall yield.[4a] Subsequently, Tian and co-workers described an indirect method for utilization of the byproduct of TMSCl hydrolysis to construct protected β-amino esters/ketones. Water was used as a hydrolyzing agent to decompose the TMSCl and yield the secondary byproduct HCl that served as an active catalyst for the following two steps.[4b] The byproduct catalyzed strategy has also proven successful for the assembly of saturated ketones scaffolds. This involves Ph_3PO generated from a Wittig reaction being used as a catalyst for a following step.[4c] Despite these promising results, the byproduct catalyzed strategy is a young and relatively unexplored area of synthesis. Herein, we report our progress toward the direct synthesis of substituted quinolines using a coproduct promoted Povarov reaction in the absence of external additives.

Quinolines occur widely in natural products and are broadly used in medicinal chemistry, particularly as antiviral, anticancer, antituberculosis, and antimalarial agents.[5] Consequently, much attention has been focused toward developing more efficient and convenient strategies for the synthesis of substituted quinolines, through either construction or modification of quinoline rings. The Povarov reaction has become one of the most attractive protocols for quinoline preparation.[6] However, the substrate scope of these reactions is limited to preformed aldimines or aldehydes, and Povarov reactions that involve ketones are rare.[7] The Mancheño and Wang groups, independently and systematically, developed a versatile dehydrogenative Povarov/oxidation tandem reaction of α-amino carbonyl compounds (Scheme 1a).[8] Both Ji and Tamariz demonstrated an interesting route for the synthesis of 1,2-dihydroquinolines from an arylamine and two of the same enolizable ketones (Scheme 1b).[9] We reported in 2014 the first example of a formal [3 + 2 + 1] cycloaddition via the oxidative C_{sp^3}−H bonds of the methyl ketone, providing a series of quinoline derivatives (Scheme 1c).[10] However, to the best of our knowledge, no example of an I_2-catalyzed Povarov-type reaction of arylamine with two different kinds of ketones is reported (Scheme 1d), wherein the catalytic amount of HI coproduct serves as a promoter to accelerate the quinoline synthesis.

Initially, we optimized the procedure for the preparation of quinolines from phenylglyoxal (**1ac**) with *p*-toluidine (**2a**) and ethyl pyruvate (**3a**). There are also a few reports dealing with the use of α-oxo aldehydes as one of the partners in the Povarov reaction.[11] Rewardingly, the reaction proceeded smoothly over 1 h using 1.0 equiv of I_2 at 100 °C in DMSO to afford the Povarov cycloaddition product (**4a**) in 90% yield as a single regioisomer (Table 1, entry 1). The structure of this compound was unambiguously confirmed by X-ray crystallography analysis (Supporting Information, Figure S1). A control experiment was conducted without I_2, which gave the product in low yields of 24% (Table 1, entry 5). It is well-known that protic acids can also catalyze the Povarov-type reaction involving α-ketoesters. Considering the role of I_2 in the reaction, it is possible that trace amounts of HI, generated during the reaction, might be the actual catalyst for this process. Thus, some control experiments were performed using different

Received: April 9, 2015
Published: May 14, 2015

DOI: 10.1021/acs.joc.5b00785
J. Org. Chem. 2015, 80, 5984−5991

Scheme 1. Povarov Reactions Involving Ketones

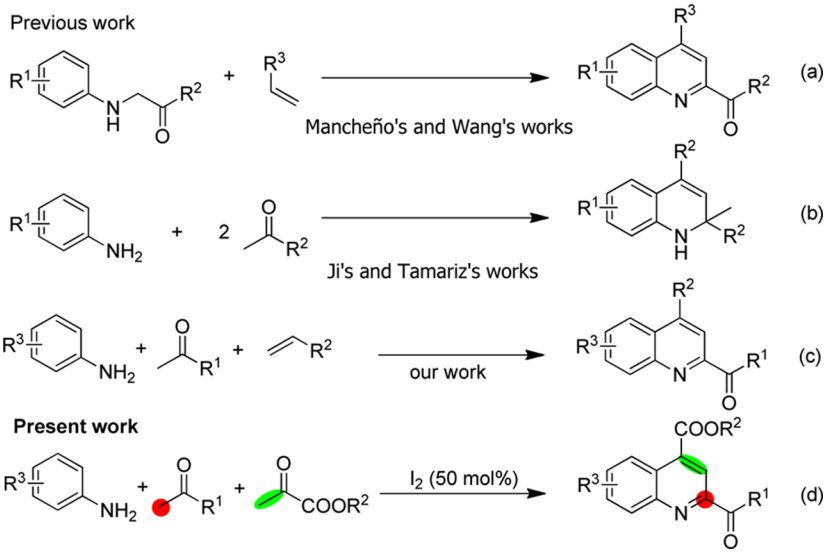
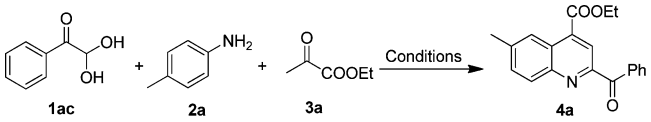


Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	temp (°C)	yield[b] (%)
1	I_2 (100%)	100	90
2	I_2 (50%)	100	90
3	I_2 (30%)	100	88
4	I_2 (10%)	100	88
5		100	24
6	I_2 (50%)	rt	36
7	I_2 (50%)	50	64
8	I_2 (50%)	70	66
9	I_2 (50%)	90	87
10	I_2 (50%)	110	91
11	I_2 (50%)	130	91
12	HI (1%)	110	78
13	HI (5%)	110	91
14	HI (10%)	110	91

[a]Reaction conditions: **1ac** (0.5 mmol), **2a** (0.5 mmol), **3a** (0.75 mmol), DMSO (2 mL). [b]Isolated yields.

amounts of HI (Table 1, entries 12−14). It can be seen that HI at 1 mol % was sufficient to catalyze the model reaction giving the product in a good yield at 110 °C after 1 h. Therefore, we considered the possibility of preparing **4a** via a byproduct catalyzed strategy by combining aromatic ketones with I_2, where HI is generated as a byproduct in the iodination and Kornblum oxidation steps.[12] After many screening experiments, we found that heating acetophenone (**1a**) in the presence of I_2 (50 mol %) at 130 °C for 40 min and then adding *p*-toluidine (**2a**) and ethyl pyruvate (**3a**) at 130 °C for another 1 h yielded the desired product in good yield (88%).

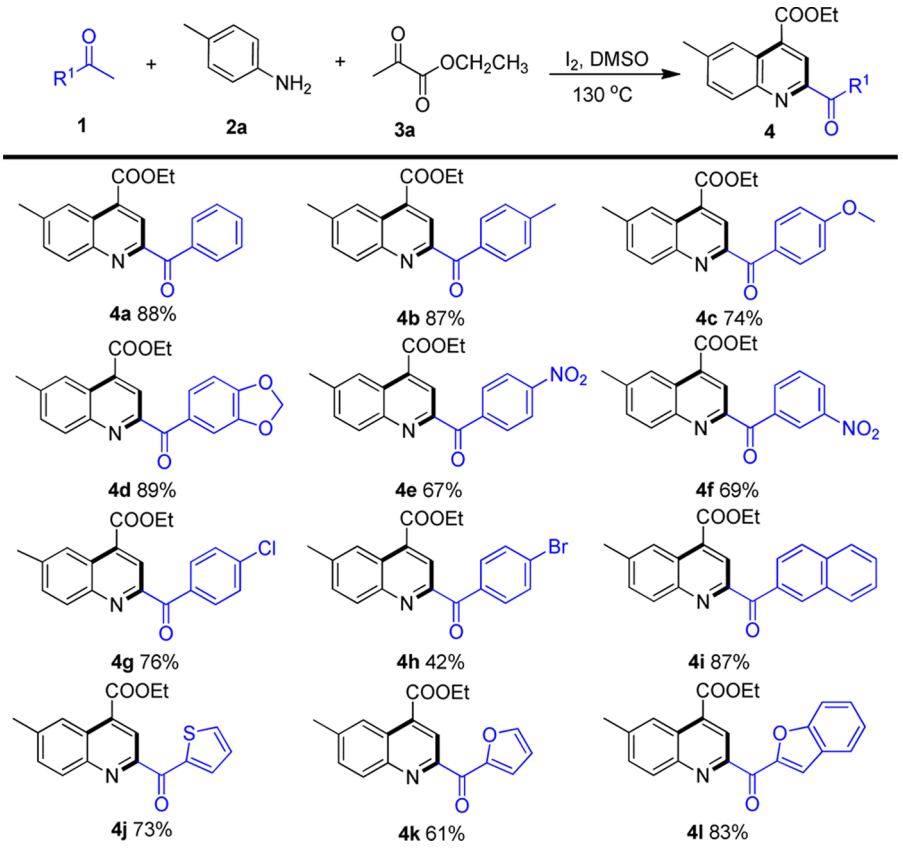
The efficient formation of the desired product prompted us to study the reaction scope further. The reaction demonstrated good tolerance of different aromatic ketone units (Scheme 2). Aryl methyl ketones bearing electron-neutral (e.g., 4-H), electron-rich (e.g., 4-Me, 4-OMe, 3,4-OCH_2O), and electron-deficient (e.g., 4-NO_2, 3-NO_2) phenyl rings were successfully converted to the corresponding products in moderate to good yields (67−89%; **4a−f**). Furthermore, the optimized conditions were mild enough to be compatible with a broad range of halogenated (e.g., 4-Cl, 4-Br) substrates (42−76%; **4g−h**), which allow the possibility of further functionalization. 2-Naphthyl methyl ketone also provided the expected product (**4i**) in 87% yield. Furthermore, the optimized conditions could be applied to various heteroaryl ketones, including thienyl, furanyl, and benzofuryl methyl ketones, which gave the corresponding products in moderate to good yields (61−83%; **4j−l**).

The scope and generality of the coproduct promoted Povarov reaction were tested with respect to various aromatic amines, and the desired products were obtained in satisfactory yields (Scheme 3). Interestingly, in the absence of any aniline substituent the quinoline product **4m** was isolated in good yield, which is different from the research results by our group and others.[11,12a,d] Both electron-rich and electron-deficient anilines could be smoothly converted to the desired products (56−94%; **4n−q**). In general, aromatic amines containing electron-rich groups showed better activities than those bearing electron-withdrawing groups. Notably, substrates bearing halogen substituents were well tolerated with the corresponding halo-substituted products being isolated in reasonable yields (48−68%; **4r−t**). 1-Naphthylamine and 2-naphthylamine were suitable for this protocol and gave **4u** and **4v** in 78% and 85% yields, respectively. Furthermore, methyl pyruvate was also a good substrate for the reaction. However, the yield decreased if the ester functional group was then changed to another electron-withdrawing group such as a phenyl (34%; **4x**), ketone (0%; **4y**), and carboxyl (0%; **4z**), indicating that ester substitution is optimal. It may be noted that the ester group can be transformed easily into other groups such as carboxyl or amide groups. We also performed the reaction on a gram scale and were pleased to find that the quinolone product **4a** was obtained in 84% yield (Scheme 4).

With the scope of the method established, the reaction mechanism was considered. Acetophenone (**1a**) was reacted with I_2 in DMSO at 130 °C to give phenylglyoxal (**1ab**), and the corresponding hydrated species (**1ac**) in quantitative yield (Scheme 5a). When the acetophenone substrate was replaced

DOI: 10.1021/acs.joc.5b00785
J. Org. Chem. 2015, 80, 5984−5991

Scheme 2. Scope of Methyl Ketones[a]



[a]Isolated yield.

with α-iodo acetophenone (**1aa**), which was identified as a probable precursor of α-ketoaldehyde (**1ab**), the desired product **4a** was obtained in good yields, both with I_2 (50 mol %) and without (Scheme 5b). When the reaction of **1ac** with ethyl pyruvate (**3a**) was performed under the standard conditions, the product **6** was not detected (Scheme 5c), suggesting that this reaction mechanism might be different from that of the modified Doebner−von Miller reaction. When *C*-acylimine (**5p**) was tested in the presence of HI, the desired product **4p** was formed in excellent yield. However, the Povarov adduct was isolated in poor yield when the reaction was conducted in the absence of HI (Scheme 5d), indicating that the catalytic amount of HI generated as a coproduct from the upstream iodination and Kornblum oxidation process may be responsible for the Povarov process.

On the basis of our findings and previous reports,[13] a possible mechanism can be proposed using acetophenone (**1a**), *p*-toluidine (**2a**), and ethyl pyruvate (**3a**) as the substrates (Scheme 6). The initial elimination of HI from **1a** by I_2 generates α-iodo ketone in situ, which is converted into phenylglyoxal and releases HI after the following Kornblum oxidation. The reaction of *p*-toluidine (**2a**) with the aldehyde group of **1ab** then gives the *C*-acylimine (**5a**). Next, the enolate quickly formed from the tautomerization of ketoester reacts with the activated *C*-acyl imine ion (**5a′**) in the presence of HI, which is formed as a coproduct from the upstream iodination and Kornblum oxidation process, to afford intermediate **A**. Subsequently the electron-rich benzene ring can add to the keto group to form intermediate **B**. Finally, **B** undergoes sequential dehydration and oxidative aromatization reactions to give the desired **4a**.

In summary, we have developed a coproduct promoted Povarov reaction for the synthesis of substituted quinolines from methyl ketones, arylamines, and α-ketoesters. HI, generated in situ from the iodination and Kornblum oxidation steps, served as a promoter for the following Povarov step, without the need of any additives. This reaction presents an interesting new form of reactivity for the Povarov reaction with good functional group compatibility.

EXPERIMENTAL SECTION

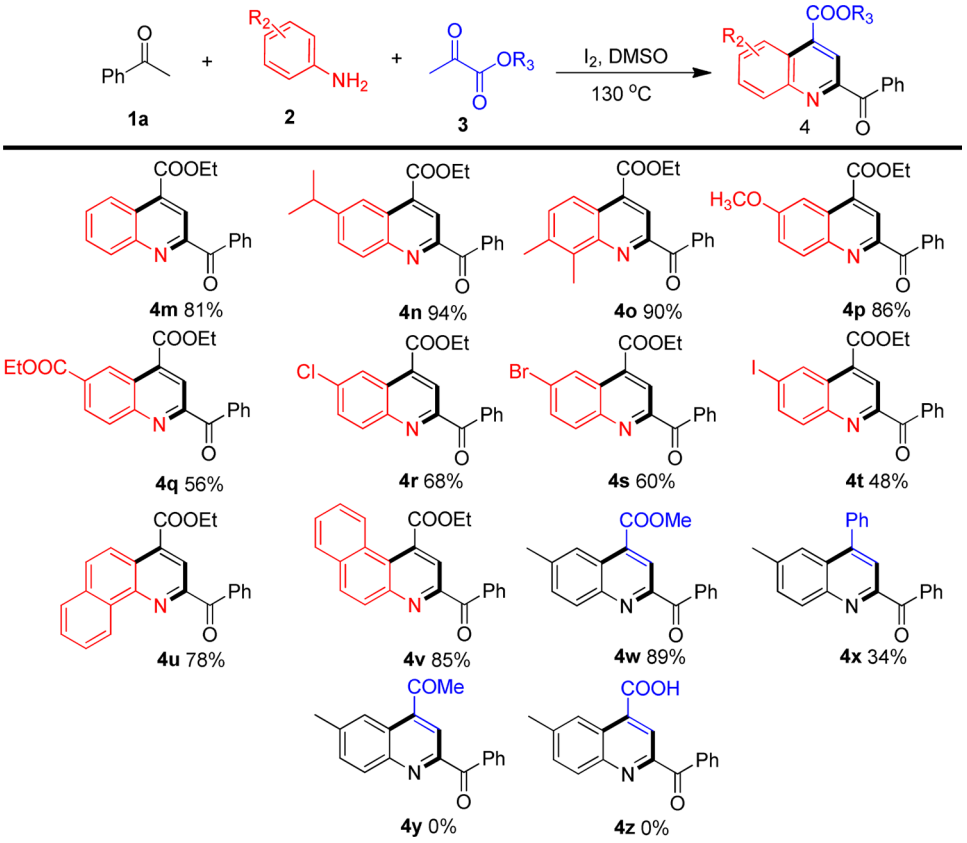
General Information. IR spectra were recorded as KBr pellets with absorption in cm^{-1}. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6. HRMS were obtained on a 7.0T FTMS equipped with ESI.

General Procedure for the Synthesis of 4 (4a as an example). A sealed tube was charged with acetophenone (**1a**) (60 mg, 0.5 mmol) and iodine (63.5 mg, 50 mol %) at room temperature, and then dried solvent DMSO (2 mL) was added. The resulting mixture was stirred at 130 °C; after disappearance of the reactant (monitored by TLC), *p*-toluidine (**2a**) (53.5 mg, 0.5 mmol) and ethyl pyruvate (**3a**) (87 mg, 0.75 mmol) were added at 130 °C, reacting for another 1 h. After the reaction completed, 50 mL of water were added to the mixture, followed by extraction with EtOAc 3 times. The extract was washed with a $Na_2S_2O_3$ solution, dried over anhydrous Na_2SO_4, and evaporated. The residue was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford **4a**.

*Ethyl 2-Benzoyl-6-methylquinoline-4-carboxylate (**4a**).* Light yellow solid; 140.3 mg (yield 88%); mp 111−113 °C; IR (KBr): 1719, 1654, 1595, 1341, 1234 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ (ppm) 8.45 (s, 1H), 8.38 (s, 1H), 8.13 (d, J = 7.2 Hz, 2H), 8.04 (d, J

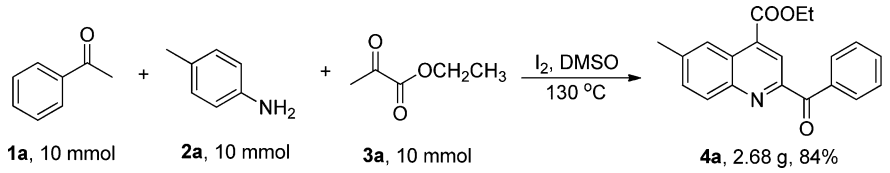
DOI: 10.1021/acs.joc.5b00785
J. Org. Chem. 2015, 80, 5984−5991

Scheme 3. Scope of Anilines and α-Ketoesters[a]



[a]Isolated yield

Scheme 4. Scaled up for the Gram Scale



= 9.0 Hz, 1H), 7.73 (t, *J* = 7.2 Hz, 2H), 7.59 (t, *J* = 7.8 Hz, 2H), 4.49 (q, *J* = 7.2 Hz, 2H), 2.57 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm) 192.4, 165.2, 152.8, 145.5, 140.6, 135.6, 135.2, 133.2, 132.9, 130.9, 130.3, 128.2, 124.9, 123.9, 121.1, 61.9, 21.82, 14.0; HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{18}NO_3$: 320.1281; found: 320.1280.

*Ethyl 6-Methyl-2-(4-methylbenzoyl)quinoline-4-carboxylate (**4b**).* Yellow solid; 144.8 mg (yield 87%); mp 104−107 °C; IR (KBr): 1723, 1659, 1608, 1343, 1237 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.63 (s, 1H), 8.56 (s, 1H), 8.18−8.11 (m, 3H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 2H), 4.53 (q, *J* = 7.2 Hz, 2H), 2.61 (s, 3H), 2.45 (s, 3H), 1.49 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.6, 166.0, 153.4, 146.3, 144.0, 140.5, 135.3, 133.3, 132.5, 131.5, 130.7, 128.9, 125.8, 124.3, 122.0, 61.9, 22.3, 21.7, 14.3; HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{19}NNaO_3$: 356.1257; found: 356.1256.

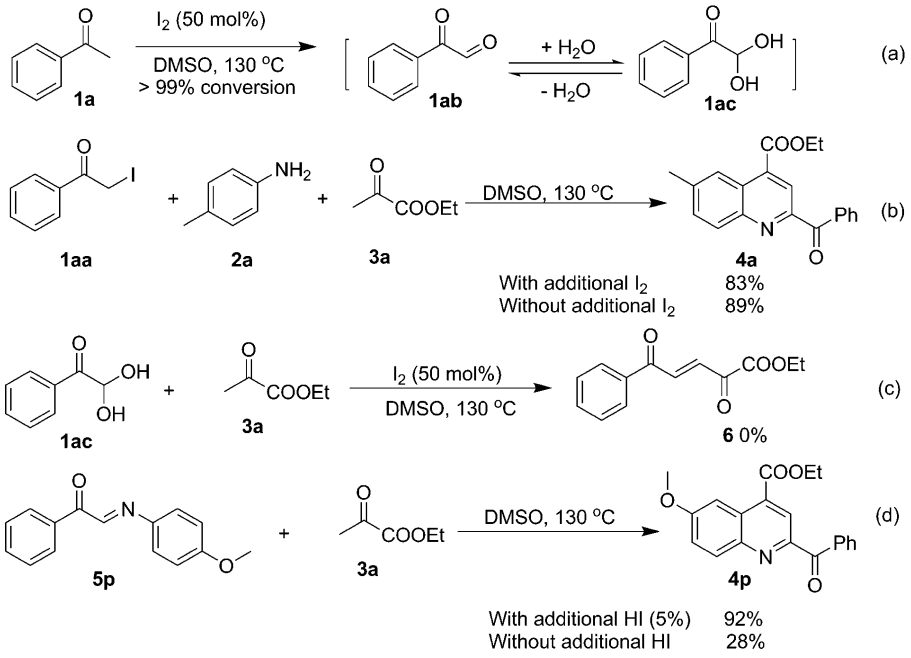
*Ethyl 2-(4-Methoxybenzoyl)-6-methylquinoline-4-carboxylate (**4c**).* White solid; 129 mg (yield 74%); mp 129−131 °C; IR (KBr): 1715, 1655, 1597, 1247 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.62 (s, 1H), 8.55 (s, 1H), 8.30 (d, *J* = 9.0 Hz, 2H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 9.0 Hz, 1H), 7.00 (d, *J* = 9.0 Hz, 2H), 4.53 (q, *J* = 7.2 Hz, 2H), 3.90 (s, 3H), 2.61 (s, 3H), 1.49 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.3, 165.9, 163.7, 153.8, 146.2, 140.4, 135.3, 133.8, 132.4, 130.5, 128.6, 125.7, 124.3, 122.1, 113.5, 61.9, 55.4, 22.2, 14.2; HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{19}NNaO_4$: 372.1206; found: 372.1206.

*Ethyl 2-(Benzo[d][1,3]dioxole-5-carbonyl)-6-methylquinoline-4-carboxylate (**4d**).* Yellow solid; 161.5 mg (yield 89%); mp 165−168 °C; IR (KBr): 1716, 1639, 1599, 1489, 1441, 1250 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.62 (s, 1H), 8.53 (s, 1H), 8.13 (d, *J* = 9.0 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.78 (s, 1H), 7.65 (d, *J* = 9.0 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.07 (s, 2H), 4.53 (q, *J* = 6.6 Hz, 2H), 2.61 (s, 3H), 1.49 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 190.8, 165.9, 153.6, 152.0, 147.7, 146.1, 140.5, 135.4, 132.5, 130.6, 130.2, 128.5, 125.7, 124.3, 122.1, 110.8, 107.8, 101.8, 61.9, 22.3, 14.2; HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}NO_5$: 364.1180; found: 364.1186.

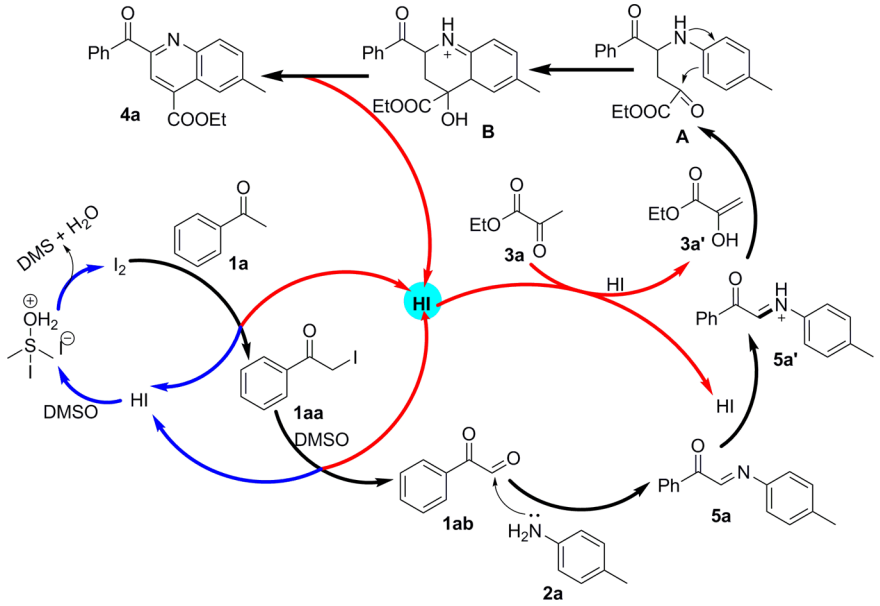
*Ethyl 6-Methyl-2-(4-nitrobenzoyl)quinoline-4-carboxylate (**4e**).* Light yellow solid; 121.9 mg (yield 67%); mp 174−176 °C; IR (KBr): 1728, 1673, 1620, 1518, 1348 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.67 (s, 1H), 8.64 (s, 1H), 8.41 (d, *J* = 8.4 Hz, 2H), 8.35 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 4.55 (q, *J* = 7.2 Hz, 2H), 2.63 (s, 3H), 1.51 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.2, 165.7, 151.6, 149.9, 146.3, 141.6, 141.2, 135.8, 132.9, 132.2, 130.7, 126.2, 124.5, 123.0, 121.7, 62.1, 22.4, 14.3; HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{16}N_2NaO_5$: 387.0951; found: 387.0951.

DOI: 10.1021/acs.joc.5b00785
J. Org. Chem. 2015, 80, 5984−5991

Scheme 5. Control Experiments



Scheme 6. Possible Mechanism



*Ethyl 6-Methyl-2-(3-nitrobenzoyl)quinoline-4-carboxylate (**4f**).* Light yellow solid; 125.6 mg (yield 69%); mp 145−146 °C; IR (KBr): 1720, 1659, 1611, 1529, 1349 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 9.24 (s, 1H), 8.68 (s, 1H), 8.64 (s, 1H), 8.61 (d, J = 7.2 Hz, 1H), 8.47 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 9.0 Hz, 1H), 7.72 (t, J = 7.8 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 4.55 (q, J = 7.2 Hz, 2H), 2.63 (s, 3H), 1.52 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 190.0, 165.7, 151.6, 147.9, 146.3, 141.5, 137.3, 136.8, 135.8, 132.9, 130.8, 129.2, 127.0, 126.6, 126.2, 124.5, 121.7, 62.1, 22.4, 14.3; HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{20}H_{16}N_2NaO_5$: 387.0951; found: 387.0959.

*Ethyl 2-(4-Chlorobenzoyl)-6-methylquinoline-4-carboxylate (**4g**).* Light yellow solid; 134.1 (yield 76%); mp 147−148 °C; IR (KBr): 1727, 1664, 1662, 1593, 1345 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): 8.63 (s, 1H), 8.60 (s, 1H), 8.23 (d, J = 8.4 Hz, 2H), 8.11 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.49 (d, J = 8.4 Hz, 2H), 4.54 (q, J = 7.2 Hz, 2H), 2.62 (s, 3H), 1.50 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.5, 165.8, 152.7, 146.2, 140.9, 139.6, 135.6, 134.3, 132.9, 132.7, 130.7, 128.4, 126.0, 124.4, 121.9, 62.0, 22.3, 14.3; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{17}ClNO_3$: 354.0892; found: 354.0894.

*Ethyl 2-(4-Bromobenzoyl)-6-methylquinoline-4-carboxylate (**4h**).* Light yellow solid; 83.6 mg (yield 42%); mp 148−150 °C; IR (KBr): 1727, 1666, 1622, 1588, 1246 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.63 (s, 1H), 8.60 (s, 1H), 8.15 (d, J = 8.4 Hz, 2H), 8.12 (d, J = 9.0 Hz, 1H), 7.67 (d, J = 8.4 Hz, 3H), 4.54 (d, J = 7.2 Hz, 2H), 2.63 (s, 3H), 1.50 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.6, 165.8, 152.5, 146.2, 140.9, 135.5, 134.6, 132.9, 132.6, 131.4, 130.6, 128.3, 125.9, 124.4, 121.8, 61.9, 22.3, 14.2; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{17}BrNO_3$: 398.0386; found: 398.0386.

*Ethyl 2-(2-Naphthoyl)-6-methylquinoline-4-carboxylate (**4i**).* Yellow solid; 160.5 mg (yield 87%); mp 138−140 °C; IR (KBr): 1717, 1649, 1623, 1356, 1264 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.83 (s, 1H), 8.65 (s, 1H), 8.63 (s, 1H), 8.27−8.24 (m, 1H), 8.15 (d, J

DOI: 10.1021/acs.joc.5b00785
J. Org. Chem. 2015, 80, 5984−5991

= 8.4 Hz, 1H), 7.97−7.93 (m, 2H), 7.89 (d, J = 8.4 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.62−7.58 (m, 1H), 7.55−7.51 (m, 1H), 4.54 (q, J = 7.2 Hz, 2H), 2.62 (s, 3H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.8, 165.9, 153.3, 146.3, 140.6, 135.5, 135.4, 134.0, 133.2, 132.5, 132.3, 130.7, 129.8, 128.5, 127.9, 127.6, 126.5, 126.3, 125.8, 124.3, 122.0, 61.9, 22.3, 14.2; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{24}H_{20}NO_3$: 370.1438; found: 370.1438.

*Ethyl 6-Methyl-2-(thiophene-2-carbonyl)quinoline-4-carboxylate (**4j**)*. Yellow solid; 118.6 mg (yield 73%); mp 128−130 °C; IR (KBr): 1726, 1641, 1503, 1412, 1360 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.68 (s, 1H), 8.61 (s, 1H), 8.50 (d, J = 3.6 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 4.8 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.22 (t, J = 4.2 Hz, 1H), 4.52 (q, J = 7.2 Hz, 2H), 2.60 (s, 3H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 182.7, 165.8, 151.8, 146.2, 140.9, 139.3, 136.8, 135.3, 132.6, 130.3, 127.5, 126.2, 124.4, 121.0, 120.9, 61.9, 22.3, 14.2; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{16}NO_3S$: 326.0845; found: 326.0850.

*Ethyl 2-(furan-2-carbonyl)-6-methylquinoline-4-carboxylate (**4k**)*. Yellow solid; 94.2 mg (yield 61%); mp 140−142 °C; IR (KBr): 1727, 1650, 1466, 1270 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.69 (s, 1H), 8.62 (s, 1H), 8.29 (d, J = 3.6 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.80 (s, 1H), 7.70−7.65 (m, 1H), 6.70−6.66 (m, 1H), 4.53 (q, J = 7.2 Hz, 2H), 2.62 (s, 3H), 1.50 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 178.4, 165.9, 151.9, 150.9, 147.9, 146.5, 140.9, 135.3, 132.6, 130.6, 126.2, 124.8, 124.5, 121.0, 112.5, 61.9, 22.3, 14.2; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{16}NO_4$: 310.1074; found: 310.1075.

*Ethyl 2-(Benzofuran-2-carbonyl)-6-methylquinoline-4-carboxylate (**4l**)*. Yellow solid; 149 mg (yield 83%); mp 164−166 °C; IR (KBr): 1729, 1644, 1536, 1275 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.70 (s, 1H), 8.65 (s, 1H), 8.61 (s, 1H), 8.21 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.74−7.66 (m, 2H), 7.50 (t, J = 7.8 Hz, 1H), 7.33 (t, J = 7.4 Hz, 1H), 4.53 (q, J = 7.2 Hz, 2H), 2.61 (s, 3H), 1.50 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 180.1, 165.8, 155.8, 151.8, 150.7, 146.5, 141.1, 135.4, 132.7, 130.7, 128.7, 127.5, 126.3, 124.5, 123.8, 123.8, 121.0, 120.7, 112.4, 62.0, 22.3, 14.3; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{22}H_{18}NO_4$: 360.1230; found: 360.1236.

*Ethyl 2-Benzoylquinoline-4-carboxylate (**4m**)*. Yellow solid; 123.5 mg (yield 81%); mp 84−86 °C; IR (KBr): 1731, 1670, 1256 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.86 (d, J = 8.4 Hz, 1H), 8.62 (s, 1H), 8.25 (d, J = 8.4 Hz, 3H), 7.85−7.80 (m, 1H), 7.76 (t, J = 7.8 Hz, 1H), 7.66−7.62 (m, 1H), 7.53 (t, J = 7.8 Hz, 2H), 4.54 (q, J = 6.6 Hz, 2H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.9, 165.8, 154.1, 147.6, 136.4, 135.8, 133.2, 131.4, 131.0, 130.2, 130.0, 128.2, 125.8, 125.6, 121.9, 62.0, 14.3; HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{19}H_{15}NNaO_3$: 328.0944; found: 328.0946.

*Ethyl 2-Benzoyl-6-isopropylquinoline-4-carboxylate (**4n**)*. Brown oil; 163 mg (yield 94%); IR (KBr): 1725, 1663, 1343, 1237 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.71 (s, 1H), 8.62 (s, 1H), 8.24 (d, J = 7.8 Hz, 2H), 8.18 (d, J = 9.0 Hz, 1H), 7.75−7.72 (m, 1H), 7.64−7.59 (m, 1H), 7.53−7.48 (m, 2H), 4.54 (q, J = 7.2 Hz, 2H), 3.21−3.14 (m, 1H), 1.50 (t, J = 7.2 Hz, 3H), 1.38 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.9, 165.9, 153.1, 151.1, 146.5, 135.8, 135.5, 133.0, 131.3, 130.8, 130.0, 128.0, 125.9, 121.9, 121.8, 61.8, 34.6, 23.6, 14.2; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{22}H_{22}NO_3$: 348.1594; found: 348.1593.

*Ethyl 2-Benzoyl-7,8-dimethylquinoline-4-carboxylate (**4o**)*. White solid; 149.8 mg (yield 90%); mp 87−89 °C; IR (KBr): 1721, 1667, 1242 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.59 (s, 1H), 8.55 (d, J = 8.4 Hz, 1H), 8.31 (d, J = 7.8 Hz, 2H), 7.64−7.59 (m, 1H), 7.55−7.49 (m, 3H), 4.51 (q, J = 7.2 Hz, 2H), 2.69 (s, 3H), 2.50 (s, 3H), 1.48 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.8, 166.1, 152.1, 146.5, 138.2, 136.3(3), 136.2(9), 136.2(2), 132.9, 132.7, 131.5, 127.8, 124.2, 122.1, 120.4, 61.8, 20.5, 14.2, 13.8; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{21}H_{20}NO_3$: 334.1438; found: 334.1441.

*Ethyl 2-Benzoyl-6-methoxyquinoline-4-carboxylate (**4p**)*. Light yellow solid; 144 mg (yield 86%); mp 98−100 °C; IR (KBr): 1712, 1668, 1618, 1477, 1250 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.69 (s, 1H), 8.33−8.30 (m, 1H), 8.24 (d, J = 7.8 Hz, 2H), 8.11 (d, J = 9.0 Hz, 1H), 7.64−7.60 (m, 1H), 7.64−7.49 (t, 2H), 7.46−7.42 (m, 1H), 4.52 (q, J = 7.2 Hz, 2H), 4.00 (s, 3H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.7, 165.9, 160.8, 151.3, 143.9, 136.0, 133.5, 132.9, 132.5, 131.3, 128.0, 127.7, 123.4, 122.7, 103.1, 61.8, 55.6, 14.2; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{20}H_{18}NO_4$: 336.1230; found: 336.1232.

*Diethyl 2-Benzoylquinoline-4,6-dicarboxylate (**4q**)*. Light yellow solid; 105.5 mg (yield 56%); mp 118−121 °C; IR (KBr): 1714, 1657, 1596, 1284, 1234 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 9.60−9.58 (m, 1H), 8.65 (s, 1H), 8.44−8.40 (m, 1H), 8.29 (d, J = 9.0 Hz, 1H), 8.24 (d, J = 7.8 Hz, 2H), 7.69−7.64 (m, 1H), 7.55 (t, J = 7.8 Hz, 2H), 4.58 (q, J = 7.2 Hz, 2H), 4.50 (q, J = 6.6 Hz, 2H), 1.53 (t, J = 7.2 Hz, 3H), 1.48 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.6, 165.9, 165.3, 155.9, 149.2, 137.7, 135.4, 133.5, 131.4, 131.3, 131.2, 129.8, 128.4, 128.3, 125.0, 122.6, 62.4, 61.7, 14.4, 14.3; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{22}H_{20}NO_5$: 378.1336; found: 378.1339.

*Ethyl 2-Benzoyl-6-chloroquinoline-4-carboxylate (**4r**)*. Yellow solid; 115.2 mg (yield 68%); mp 108−110 °C; IR (KBr): 1718, 1657, 1597, 1449, 1342, 1239 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.96 (s, 1H), 8.66 (s, 1H), 8.22 (d, J = 8.4 Hz, 2H), 8.18 (d, J = 9.0 Hz, 1H), 7.78−7.74 (m, 1H), 7.65 (t, J = 7.2 Hz, 1H), 7.55−7.51 (m, 2H), 4.54 (q, J = 7.2 Hz, 2H), 1.50 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.5, 165.2, 154.2, 146.0, 136.5, 135.6, 135.2, 133.3, 132.4, 131.3, 128.2, 126.4, 124.8, 122.9 (× 2), 62.3, 14.3; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{19}H_{15}ClNO_3$: 340.0735; found: 340.0741.

*Ethyl 2-Benzoyl-6-bromoquinoline-4-carboxylate (**4s**)*. Brown solid; 115 mg (yield 60%); mp 94−96 °C; IR (KBr): 1725, 1667, 1596, 1446, 1238 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 9.15−9.11 (m, 1H), 8.65 (s, 1H), 8.22 (d, J = 7.8 Hz, 2H), 8.10 (d, J = 9.0 Hz, 1H), 7.92−7.88 (m, 1H), 7.65 (t, J = 7.2 Hz, 1H), 7.56−7.51 (m, 2H), 4.54 (q, J = 7.2 Hz, 2H), 1.50 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.5, 165.2, 154.3, 146.2, 135.5, 135.1, 134.0, 133.3, 132.4, 131.3, 128.2, 128.1, 126.8, 125.1, 122.9, 62.3, 14.3; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{19}H_{15}BrNO_3$: 384.0230; found: 384.0237.

*Ethyl 2-Benzoyl-6-iodoquinoline-4-carboxylate (**4t**)*. Yellow solid; 103.4 mg (yield 48%); mp 113−114 °C; IR (KBr): 1723, 1668, 1594, 1443, 1342, 1235 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 9.36−9.34 (m, 1H), 8.63 (s, 1H), 8.22 (d, J = 7.2 Hz, 2H), 8.10−8.06 (m, 1H), 7.94 (d, J = 9.0 Hz, 1H), 7.68−7.63 (m, 1H), 7.53 (t, J = 7.8 Hz, 2H), 4.54 (q, J = 7.2 Hz, 2H), 1.50 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.5, 165.3, 154.6, 146.6, 139.3, 135.7, 134.9, 134.8, 133.3, 132.3, 131.4, 128.3, 127.2, 122.8, 97.5, 62.3, 14.3; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{19}H_{15}INO_3$: 432.0091; found: 432.0091.

*Ethyl 2-benzoylbenzo[h]quinoline-4-carboxylate (**4u**)*. Yellow solid; 138.4 mg (yield 78%); mp 96−98 °C; IR (KBr): 1721, 1666, 1599, 1369, 1341, 1236 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 9.13 (d, J = 7.8 Hz, 1H), 8.77 (s, 1H), 8.72 (d, J = 9.6 Hz, 1H), 8.33 (d, J = 7.8 Hz, 2H), 8.01 (d, J = 9.0 Hz, 1H), 7.94 (d, J = 7.8 Hz, 1H), 7.77−7.66 (m, 3H), 7.58 (t, J = 7.8 Hz, 2H), 4.56 (q, J = 7.2 Hz, 2H), 1.52 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.9, 166.1, 152.1, 146.1, 136.2(9), 136.2(7), 133.3, 132.9, 131.6, 131.5, 129.0, 128.1, 127.8, 125.2, 125.1(1), 125.0(7), 122.5, 122.4, 122.2, 62.13, 14.30; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{23}H_{18}NO_3$: 356.1281; found: 356.1288.

*Ethyl 3-Benzoylbenzo[f]quinoline-1-carboxylate (**4v**)*. Yellow solid; 150.8 mg (yield 85%); mp 120−122 °C; IR (KBr): 1737, 1658, 1596, 1372, 1330, 1262 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.32 (d, J = 8.4 Hz, 1H), 8.30 (s, 1H), 8.26 (d, J = 7.8 Hz, 2H), 8.07−8.00 (m, 2H), 7.94 (d, J = 8.4 Hz, 1H), 7.71−7.64 (m, 1H), 7.65−7.59 (m, 2H), 7.51 (t, J = 7.8 Hz, 2H), 4.60 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.4, 169.8, 153.1, 147.8, 139.3, 135.7, 133.2, 133.0, 132.3, 131.3, 128.9, 128.4(3), 128.3(5), 128.0, 127.5, 126.8, 126.2, 122.5, 120.5, 62.6, 13.8; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{23}H_{18}NO_3$: 356.1281; found: 356.1281.

DOI: 10.1021/acs.joc.5b00785
J. Org. Chem. 2015, 80, 5984−5991

*Methyl 2-Benzoyl-6-methylquinoline-4-carboxylate (**4w**).* Light yellow solid; 135.7 mg (yield 89%); mp 100−102 °C; IR (KBr): 1728, 1663, 1579, 1352, 1241 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.63 (s, 1H), 8.60 (s, 1H), 8.24 (d, J = 7.8 Hz, 2H), 8.13 (d, J = 8.4 Hz, 1H), 7.68−7.61 (m, 2H), 7.54−7.49 (m, 2H), 4.06 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.9, 166.3, 153.1, 146.3, 140.8, 135.9, 135.0, 133.1, 132.6, 131.4, 130.7, 128.1, 125.8, 124.3, 122.1, 52.7, 22.3; HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{19}H_{15}NNaO_3$: 328.0944; found: 328.0945.

*(6-Methyl-4-phenylquinolin-2-yl)(phenyl)methanone (**4x**).*[11] Light yellow solid; 54.9 mg (yield 34%); mp 125−128 °C; IR (KBr): 1653, 1442, 1357, 1248 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.26 (d, J = 7.8 Hz, 2H), 8.16 (d, J = 8.4 Hz, 1H), 8.02 (s, 1H), 7.75 (s, 1H), 7.62 (d, J = 7.8 Hz, 2H), 7.58−7.55 (m, 4H), 7.52 (t, J = 7.2 Hz, 3H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 193.9, 153.4, 148.8, 145.9, 138.8, 137.9, 136.3, 132.9, 132.2, 131.4, 130.6, 129.5, 128.6, 128.5, 128.1, 127.4, 124.5, 121.1, 22.0; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{23}H_{18}NO$: 324.1383; found: 324.1384.

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR spectra of compounds **4**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00785.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: chwuax@mail.ccnu.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (Grant 21272085, 21472056).

■ REFERENCES

(1) (1) (a) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960. (b) Zhou, L. H.; Lu, W. J. *Chem.—Eur. J.* **2014**, *20*, 634. (c) Ferrer, S.; Muratore, M. E.; Echavarren, A. M. *ChemCatChem* **2015**, *7*, 228. (d) Kang, F. A.; Lanter, J. C.; Cai, C. Z.; Sui, Z. H.; Murray, W. V. *Chem. Commun.* **2010**, *46*, 1347. (e) Wender, P. A. *Nat. Prod. Rep.* **2014**, *31*, 433. (f) Harrison, T. J.; Ho, S.; Leighton, J. L. *J. Am. Chem. Soc.* **2011**, *133*, 7308. (g) Gaich, T.; Baran, P. S. *J. Org. Chem.* **2010**, *75*, 4657.

(2) For representative reviews, see: (a) Cioc, R. C.; Ruijter, E.; Orru, R. V. A. *Green Chem.* **2014**, *16*, 2958. (b) Zhu, J. P.; Bienaymé, H. *Multicomponent Reactions*; Wiley-VCH: Weinheim, 2005. (c) Zhu, J. P.; Wang, Q.; Wang, M. X. *Multicomponent Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, 2015. (d) Tietze, L. F. *Domino Reactions*; Wiley-VCH: Weinheim, 2014. (e) Shindoh, N.; Takemoto, Y.; Takasu, K. *Chem.—Eur. J.* **2009**, *15*, 12168.

(3) For representative references, see: (a) Wu, J. C.; Song, R. J.; Wang, Z. Q.; Huang, X. C.; Xie, Y. X.; Li, J. H. *Angew. Chem., Int. Ed.* **2012**, *51*, 3453. (b) Tang, R. Y.; Guo, X. K.; Xiang, J. N.; Li, J. H. *J. Org. Chem.* **2013**, *78*, 11163. (c) Chen, J. B.; Liu, B.; Liu, D. F.; Liu, S.; Cheng, J. *Adv. Synth. Catal.* **2012**, *354*, 2438. (d) Li, L. T.; Huang, J.; Li, H. Y.; Wen, L. J.; Wang, P.; Wang, B. *Chem. Commun.* **2012**, *48*, 5187. (e) Wu, W. L.; Su, W. P. *J. Am. Chem. Soc.* **2011**, *133*, 11924. For representative reviews, see: (f) Swamy, K. C. K.; Kumar, N. N. B.; Balaraman, E.; Kumar, K. V. P. P. *Chem. Rev.* **2009**, *109*, 2551. (g) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863. (h) Fresneda, P. M.; Molina, P. *Synlett* **2004**, 1. (i) But, T. Y. S.; Toy, P. H. *Chem.—Asian J.* **2007**, *2*, 1340. (j) Gololobov, Y. G.; Kasukhin, L. F. *Tetrahedron* **1992**, *48*, 1353. (k) Ye, L. W.; Zhou; Tang, J. Y. *Chem. Soc. Rev.* **2008**, *37*, 1140.

(4) (a) Alaimo, P. J.; O'Brien, R.; Johnson, A. W.; Slauson, S. R.; O'Brien, J. M.; Tyson, E. L.; Marshall, A.-L.; Ottinger, C. E.; Chacon, J. G.; Wallace, L.; Paulino, C. Y.; Connell, S. *Org. Lett.* **2008**, *10*, 5111. (b) Yang, B. L.; Weng, Z. T.; Yang, S. J.; Tian, S. K. *Chem.—Eur. J.* **2010**, *16*, 718. (c) Cao, J. J.; Zhou, F.; Zhou, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 4976. (d) Li, H. H.; Dong, D. J.; Jin, Y. H.; Tian, S. K. *J. Org. Chem.* **2009**, *74*, 9501. (e) Zhu, Y. P.; Gao, Q. H.; Lian, M.; Yuan, J. J.; Liu, M. C.; Zhao, Q.; Yang, Y.; Wu, A. X. *Chem. Commun.* **2011**, *47*, 12700. (f) Liu, C. R.; Ding, L. H. *Org. Biomol. Chem.* **2015**, *13*, 2251. (g) Portalier, F.; Bourdreux, F.; Marrot, J.; Moreau, X.; Coeffard, V.; Greck, C. *Org. Lett.* **2013**, *15*, 5642. (h) Teng, Y.; Lu, J.; Toy, P. H. *Chem. Asian. J.* **2012**, *7*, 351. (i) Chen, L.; Du, Y.; Zeng, X. P.; Shi, T. D.; Zhou, F.; Zhou, J. *Org. Lett.* **2015**, *17*, 1557. (j) Zhu, F.; Xu, P. W.; Zhou, F.; Wang, C. H.; Zhou, J. *Org. Lett.* **2015**, *17*, 972. (k) Zhou, J. *Multicatalyst system in asymmetric catalysis*; John Wiley & Sons: NJ, 2015.

(5) (a) Musiol, R.; Jampilek, J.; Kralova, K.; Richardson, D. R.; Kalinowski, D.; Podeszwa, B.; Finster, J.; Niedbala, H.; Palka, A.; Polanski, J. *Bioorg. Med. Chem.* **2007**, *15*, 1280. (b) Michael, J. P. *Nat. Prod. Rep.* **2007**, *24*, 223. (c) Kaur, K.; Jain, M.; Reddy, R. P.; Jain, R. *Eur. J. Med. Chem.* **2010**, *45*, 3245. (d) Musiol, R.; Serda, M.; Hensel-Bielowka, S.; Polanski, J. *Curr. Med. Chem.* **2010**, *17*, 1960. (e) Solomon, V. R.; Lee, H. *Curr. Med. Chem.* **2011**, *18*, 1488. (f) Michael, J. P. *Nat. Prod. Rep.* **2008**, *25*, 166. (g) Chen, S.; Chen, R.; He, M.; Pang, R.; Tan, Z.; Yang, M. *Bioorg. Med. Chem.* **2009**, *17*, 1948. (h) Lilienkampf, A.; Mao, J.; Wan, B.; Wang, Y.; Franzblau, S. G.; Kozikowski, A. P. *J. Med. Chem.* **2009**, *52*, 2109. (i) Gakhar, G.; Ohira, T.; Shi, A.; Hua, D. H.; Nguyen, T. A. *Drug Dev. Res.* **2008**, *69*, 526. (j) Kong, L. K.; Zhou, Y. Y.; Huang, H.; Yang, Y.; Liu, Y. Y.; Li, Y. Z. *J. Org. Chem.* **2015**, *80*, 1275.

(6) For representative reviews, see: (a) Kouznetsov, V. V. *Tetrahedron* **2009**, *65*, 2721. (b) Glushkov, V. A.; Tolstikov, A. G. *Russ. Chem. Rev.* **2008**, *77*, 137. (c) Sridharan, V.; Suryavanshi, P. A.; Menendez, J. C. *Chem. Rev.* **2011**, *111*, 7157. (d) Masson, G.; Lalli, C.; Benohoud, M.; Dagousset, G. *Chem. Soc. Rev.* **2013**, *42*, 902. (e) Jiang, X. X.; Wang, R. *Chem. Rev.* **2013**, *113*, 5515. (f) Fochi, M.; Caruana, L.; Bernardi, L. *Synthesis* **2014**, *46*, 135. For representative references, see: (g) Sundararajan, G.; Prabagaran, N.; Varghese, B. *Org. Lett.* **2001**, *3*, 1973. (h) Shindoh, N.; Tokuyama, H.; Takemoto, Y.; Takasu, K. *J. Org. Chem.* **2008**, *73*, 7451. (i) Akiyama, T.; Morita, H.; Fuchibe, K. *J. Am. Chem. Soc.* **2006**, *128*, 13070. (j) Liu, H.; Dagousset, G.; Masson, G.; Retailleau, P.; Zhu, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 4598. (k) Xie, M. S.; Chen, X. H.; Zhu, Y.; Gao, B.; Lin, L. L.; Liu, X. H.; Feng, X. M. *Angew. Chem., Int. Ed.* **2010**, *49*, 3799. (l) Dagousset, G.; Zhu, J. P.; Masson, G. *J. Am. Chem. Soc.* **2011**, *133*, 14804. (m) Caruana, L.; Fochi, M.; Ranieri, S.; Mazzanti, A.; Bernardi, L. *Chem. Commun.* **2013**, *49*, 880. (n) Chen, Z. L.; Wang, B. L.; Wang, Z. B.; Zhu, G. Y.; Sun, J. W. *Angew. Chem., Int. Ed.* **2013**, *52*, 2027. (o) Chen, M.; Sun, N.; Liu, Y. H. *Org. Lett.* **2013**, *15*, 5574.

(7) Shi, F.; Xing, G. J.; Zhu, R. Y.; Tan, W.; Tu, S. J. *Org. Lett.* **2013**, *15*, 128.

(8) (a) Richter, H.; Mancheño, O. G. *Org. Lett.* **2011**, *13*, 6066. (b) Rohlmann, R.; Stopka, T.; Richter, H.; Mancheño, O. G. *J. Org. Chem.* **2013**, *78*, 6050. (c) Jia, X. D.; Peng, F. F.; Qing, C.; Huo, C. D.; Wang, X. C. *Org. Lett.* **2012**, *14*, 4030. (d) Jia, X. D.; Wang, Y. X.; Peng, F. F.; Huo, C. D.; Yu, L. L.; Liu, J.; Wang, X. C. *J. Org. Chem.* **2013**, *78*, 9450. (e) Liu, J.; Wang, Y. X.; Yu, L. L.; Huo, C. D.; Wang, X. C.; Jia, X. D. *Adv. Synth. Catal.* **2014**, *356*, 3214. (f) Huo, C. D.; Yuan, Y.; Wu, M. X.; Jia, X. D.; Wang, X. C.; Chen, F. J.; Tang, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 13544. (g) Liu, J.; Liu, F.; Zhu, Y. Z.; Ma, X. G.; Jia, X. D. *Org. Lett.* **2015**, *17*, 1409.

(9) (a) Zhang, J. C.; Ji, J. X. *ACS Catal.* **2011**, *1*, 1360. (b) Hu, X. Y.; Zhang, J. C.; Wei, W.; Ji, J. X. *Tetrahedron Lett.* **2011**, *52*, 2903. (c) Gutiérrez, R. U.; Correa, H. C.; Bautista, R.; Vargas, J.; Jerezano, A. V.; Delgado, F.; Tamariz, J. *J. Org. Chem.* **2013**, *78*, 9614.

(10) (a) Gao, Q. H.; Liu, S.; Wu, X.; Wu, A. X. *Org. Lett.* **2014**, *16*, 4582.

(11) (a) Bunescu, A.; Wang, Q.; Zhu, J. P. *Org. Lett.* **2014**, *16*, 1756. (b) Kobayshi, S.; Nagayama, S. *J. Am. Chem. Soc.* **1996**, *118*, 8977.

DOI: 10.1021/acs.joc.5b00785
J. Org. Chem. 2015, 80, 5984−5991

(c) Lucchini, V.; Prato, M.; Scorrano, G.; Tecilla, P. *J. Org. Chem.* **1988**, *53*, 2251. (d) Wei, W.; Wen, J. W.; Yang, D. S.; Sun, X. J.; You, J. M.; Suo, Y. R.; Wang, H. *Tetrahedron* **2013**, *69*, 10747.

(12) (a) Gao, M.; Yang, Y.; Wu, Y. D.; Deng, C.; Shu, W. M.; Zhang, D. X.; Cao, L. P.; She, N. F.; Wu, A. X. *Org. Lett.* **2010**, *12*, 4026. (b) Zhu, Y. P.; Lian, M.; Jia, F. C.; Liu, M. C.; Yuan, J. J.; Gao, Q. H.; Wu, A. X. *Chem. Commun.* **2012**, *48*, 9086. (c) Gao, Q. H.; Fei, Z.; Zhu, Y. P.; Lian, M.; Jia, F. C.; Liu, M. C.; She, N. F.; Wu, A. X. *Tetrahedron* **2013**, *69*, 22. (d) Gao, Q. H.; Wu, X.; Liu, S.; Wu, A. X. *Org. Lett.* **2014**, *16*, 1732. (e) Gao, Q. H.; Liu, S.; Wu, X.; Wu, A. X. *Tetrahedron Lett.* **2014**, *55*, 6403.

(13) (a) Luo, C. S.; Huang, Y. *J. Am. Chem. Soc.* **2013**, *135*, 8193. (b) Zhu, Y. W.; Qian, J. L.; Yi, W. B.; Cai, C. *Tetrahedron Lett.* **2013**, *54*, 638. (c) Waldmann, H.; Karunakar, G. V.; Kumar, K. *Org. Lett.* **2008**, *10*, 2159. (d) Zhang, B. Q.; Luo, Y.; He, Y. H.; Guan, Z. *Tetrahedron* **2014**, *70*, 1961. (e) Wu, X.; Gao, Q. H.; Liu, S.; Wu, A. X. *Org. Lett.* **2014**, *16*, 2888. (f) Liu, S.; Gao, Q. H.; Wu, X.; Zhang, J. J.; Ding, K. R.; Wu, A. X. *Org. Biomol. Chem.* **2015**, *13*, 2239.

DOI: 10.1021/acs.joc.5b00785
J. Org. Chem. 2015, 80, 5984−5991