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Copper-Catalyzed Aza-Michael Addition of 2-Aminobenzoate to β-Substituted α,β-Unsaturated Ketones: One-Pot Synthesis of 3-Carbonyl-2-Substituted Quinolin-4(1*H*)-ones

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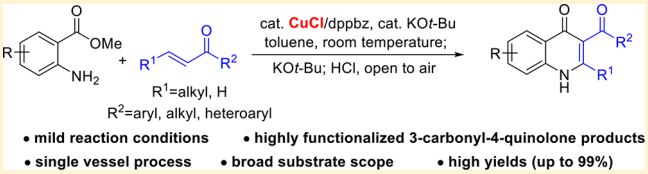
Supporting Information

ABSTRACT: We present a new and straightforward one-pot process for the synthesis of 3-carbonyl-4-quinolone derivatives through highly efficient Cu-catalyzed aza-Michael addition of 2-aminobenzoates to β-substituted α,β-unsaturated ketones/cyclization/mild oxidation reactions. A broad range of new versatile 3-carbonyl-quinolin-4(1*H*)-ones is prepared from readily available chemicals under mild reaction conditions with short reaction times, producing good to excellent yields (up to 99%).



INTRODUCTION

Quinolones are important scaffolds that are found in a variety of biologically active molecules and pharmaceuticals.[1] In particular, substitution and diversity in the quinolone moiety produces altered effects on their pharmacological and biological activities. Although quinoline core structures have been prepared by many classical syntheses including the Skraup, Friedländer, Combes, Conrad−Limpach, Doebner−von Miller, and Pfitzinger reactions,[2] the synthetic approaches for highly functionalized 3-carbonyl-2-substituted 4-quinolones have been less studied.[3] The acyl-substituted 4-quinolones serve as valuable building blocks for the synthesis of bioactive molecules and color chemicals (Figure 1).[4,5] In addition, they are readily transformed to structurally modified quinoline derivatives, which are ubiquitous in natural products and drugs. The frequently used methods for preparing 3-carbonyl-4-quinolones involve the thermal cyclization of β-anilinoacrylate derivatives prepared from the condensation of ethoxymethylene acetoacetate intermediates with anilines (the Gould−Jacobs reaction in pathway 1 of Scheme 1)[6] and the intramolecular ring closure of enaminoesters derived from reaction of β-ketonic enol ethers with methyl anthranilates (pathway 2).[7] However, the reactions were carried out under harsh reaction conditions including high temperatures and the use of high-boiling solvents, resulting in low to moderate yields of the products and the generation of side-products. In a recent report, Goggiamani and coworkers described a palladium-catalyzed intramolecular cyclocarbonylation of *N*-(2-iodoaryl)-enaminoes derived from addition of 2-iodoanilines to α,β-ynones using CO gas under reflux conditions, affording 2-substituted 3-aroyl-4-quinolones.[3a] Due to the significance and practical utilities of functionalized 3-carbonyl-4-quinolones, the development of a new and effective method is highly desirable.

The aza-Michael addition reaction of arylamines is one of the most useful and simplest protocols for synthesizing β-amino carbonyl compounds.[8] Recently, we described an efficient and mild catalytic conjugate addition of (hetero)aromatic amines to α,β-unsaturated olefins in the presence of a Cu catalyst based on an electron-donating Lewis base ligand. This reaction afforded versatile β-amino nitriles, β-amino sulfones, and β-amino carbonyl compounds with high efficiency and selectivity.[9] However, most of the substrate scopes were limited to terminal olefins bearing a nitrile and sulfonyl group. In addition, Gunnoe, Yamazaki, Kantam, and coworkers demonstrated the Cu-catalyzed aza-Michael addition of anilines or imidazoles to α,β-unsaturated carbonyl compounds in which the reactions were also specific to terminal alkenes or highly activated ethenetricarboxylates.[10] With a goal to develop a widely applicable aza-Michael addition reaction using a low-cost and environmentally benign copper catalyst, we decided to investigate Cu-catalyzed amine conjugate addition to more sterically demanding β-substituted α,β-unsaturated ketones with 2-aminobenzoates, affording functional β-amino carbonyl compounds. Encouraged by our previous results, we intended to utilize the catalytic protocol for the synthesis of novel and highly functionalized 3-carbonyl-2-substituted 4-quinolones in a single vessel, as shown in pathway 3 of Scheme 1.

In this study, we developed a new and easy method for a one-pot synthesis of biologically and synthetically valuable 3-carbonyl-4-quinolones through Cu-catalyzed aza-Michael addition, followed by base-mediated cyclization and oxidation in mild reaction conditions. The commercially available and readily obtainable 2-aminobenzoates were efficiently added to the β-substituted α,β-unsaturated ketones in the presence of 5

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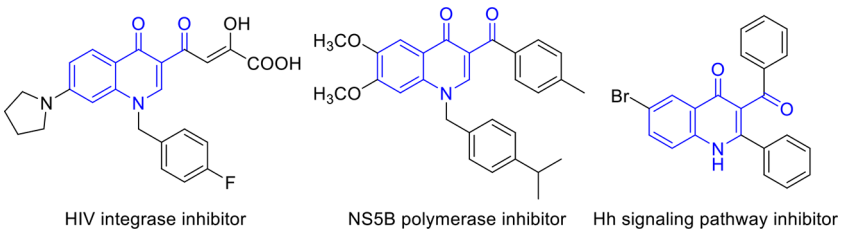
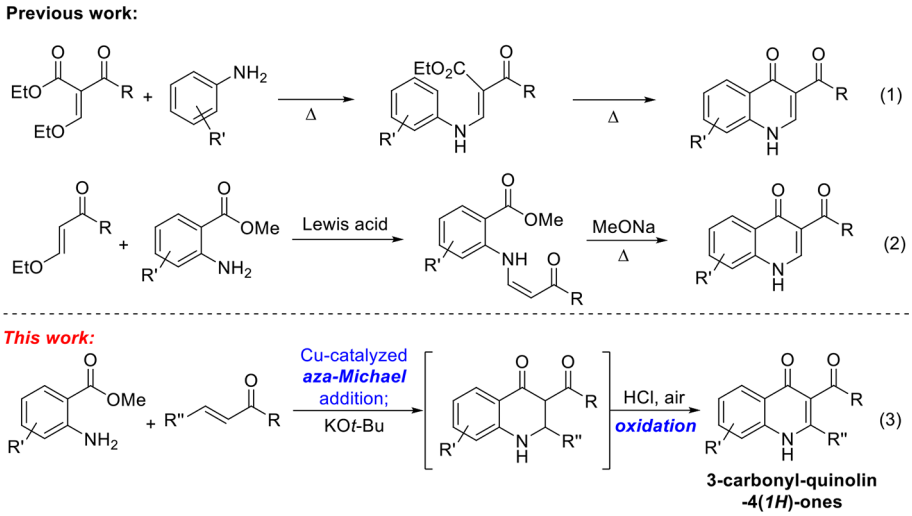


Figure 1. Bioactive 3-carbonyl-4-quinolone derivatives.

Scheme 1. Methods for Preparation of 3-Carbonyl-Substituted Quinolin-4(1*H*)-ones

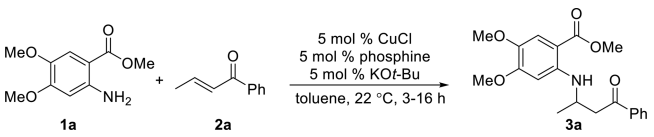


mol % CuCl, phosphine, and KO*t*-Bu, which in situ generated Cu-amido catalytic species,[11] at room temperature. After direct treatment with KO*t*-Bu, the resulting *β*-amino ketone products were cyclized to form 3-carbonyl-2,3-dihydroquinolin-4(1*H*)-one intermediates. These subsequently underwent dehydrogenation in acidic and open air conditions at ambient temperatures within 1 h, providing the oxidized 3-carbonyl-quinolin-4(1*H*)-ones with high efficiency. In previous reports, a few oxidation conditions for the transformation of 2,3-dihydroquinolin-4(1*H*)-ones to quinolin-4(1*H*)-ones have been studied, such as the use of thallium(III)-tosylate,[12] the use of a (diacetoxyiodo)benzene oxidant and base,[13] the use of I_2 in dimethyl sulfoxide,[14] and the use of palladium on C with H_2 and NaOH.[15] Most of these oxidation reactions should be performed under heating conditions. In contrast, we explored the first example of the oxidation of 3-carbonyl-2,3-dihydroquinolin-4(1*H*)-one to 3-carbonyl-quinolin-4(1*H*)-one in both mild and simple reaction conditions.

RESULTS AND DISCUSSION

We began our investigation by establishing the optimal conditions for the catalytic aza-Michael addition of methyl 2-aminobenzoate **1a** to (*E*)-1-phenylbut-2-en-1-one (**2a**). On the basis of our previous studies, we examined the necessity of CuCl, phosphine ligand, and KO*t*-Bu. As shown in Table 1, there is no reaction without CuCl or KO*t*-Bu. When the addition of **1a** to **2a** was carried out in the presence of only 5 mol % KO*t*-Bu or a mixture of 5 mol % CuCl and KO*t*-Bu, the *β*-substituted *α*,*β*-unsaturated ketone **2a** was completely decomposed, and the *β*-amino ketone product **3a** was not obtained (<2% of **3a**, entries 3 and 4). However, the use of a phosphine ligand combined with CuCl and KO*t*-Bu produced

Table 1. Optimization of the Cu-Catalyzed Aza-Michael Addition of 1a to 2a[a]



1a 2a 3a

entry	CuCl (mol %)	phosphine	KO*t*-Bu (mol %)	time (h)	conv (%)[b]	yield (%)[b]
1	0	no	0	16	<2	<2
2	5	no	0	16	<2	<2
3	0	no	5	16	>98	<2
4	5	no	5	16	>98	<2
5	5	PPh_3	5	3	<2	<2
6	5	PCy_3	5	3	14	10
7	5	dppe	5	3	42	40
8	5	dppp	5	3	62	60
9	5	dppb	5	3	37	36
10	5	binap	5	3	35	33
11	5	DPEphos	5	3	25	24
12	5	dppbz	5	3	>98	>98

[a]Reaction conditions: aminobenzoate **1a** (0.36 mmol), **2a** (0.30 mmol), CuCl (0.015 mmol), phosphine (0.015 mmol), KO*t*-Bu (0.015 mmol), and toluene (0.2 M) under N_2. [b]Determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard.

the desired product **3a** (entries 6−12). These findings explain that the in situ generated CuO*t*-Bu complex based on phosphine may play an important role in the formation of Cu-amido catalytic species for promoting aryl amine addition to *α*,*β*-unsaturated ketone **2a**. As a result of evaluating a variety of phosphines including monodentate and bidentate ligands,[16]

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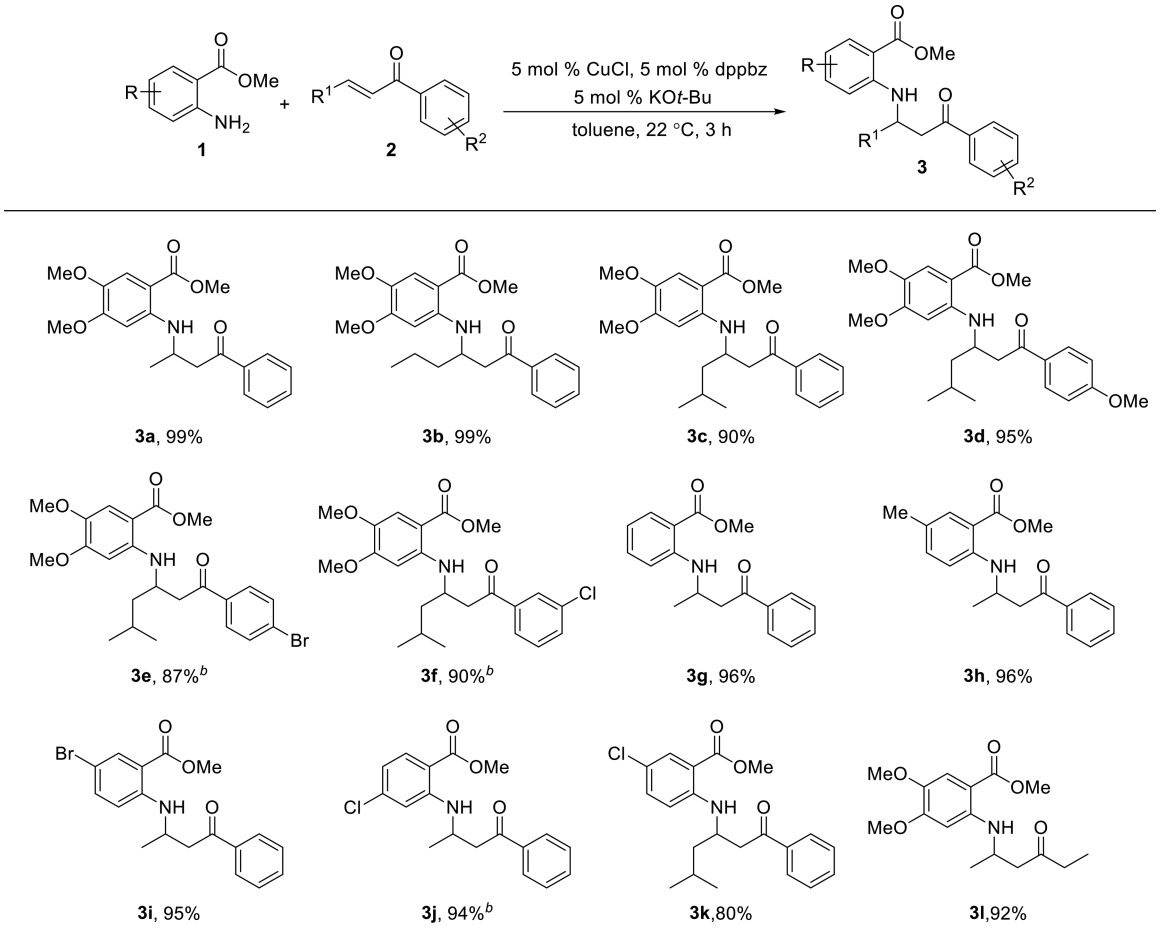
Table 2. Cu-Catalyzed Aza-Michael Addition of β-Substituted α,β-Unsaturated Ketones[a]



[a]Reaction conditions: 2-aminobenzoate **1** (0.36 mmol), α,β-unsaturated ketone **2** (0.30 mmol), CuCl (0.015 mmol), dppbz (0.015 mmol), KO*t*-Bu (0.015 mmol), and toluene (0.2 M) under N_2. Isolated yields after purification. [b]Reaction time was 5 h.

1,2-bis(diphenylphosphanyl)benzene (dppbz) was the most effective and generally applicable, furnishing the β-amino ketone **3a** in >98% yield (entry 12).

After determining the optimized reaction conditions, the scope of the Cu-catalyzed aza-Michael addition was investigated. A variety of β-substituted α,β-unsaturated ketones and readily accessible 2-aminobenzoates was examined. All transformations were performed at ambient temperature in the presence of 5 mol % CuCl, dppbz, and KO*t*-Bu. The results are illustrated in Table 2. The catalytic addition of methyl 2-amino-4,5-dimethoxybenzoate to α,β-unsaturated ketones bearing a methyl, propyl, or isobutyl substituent on the β-position of the keto group efficiently proceeded to complete the conversion within 3 h, giving the β-amino carbonyl compounds **3a**−**3c** with excellent yields (90−99%). Various alkene substrates with a methoxy, bromo, or chloro moiety attached on the aryl unit were smoothly converted to the desired products **3d**−**3f** with 87−95% yields. In addition, the methyl, bromo, or chloro substituent on the 2-aminobenzoate were well-tolerated in the Cu-catalyzed aza-Michael addition to afford **3g**−**3k** with excellent yields ranging from 80 to 96%. When (*E*)-hex-4-en-3-one was used as an alkyl enone substrate, the catalytic reaction was proceeded to complete conversion to provide 92% yield of the desired product **3l**. However, α,β-unsaturated ketones, including a sterically demanding aryl substituent on the β-position, were not suitable for the present system. Additions of **1a** to (*E*)-4-phenylbut-3-en-2-one or (*E*)-chalcone did not proceed (<2% conv).

To highlight the synthetic utility of the present catalytic system, we designed a new and highly efficient route for producing functionalized 3-carbonyl-2-substituted 4-quinolones using β-amino carbonyl products in a single vessel. As illustrated in Scheme 2, when the Michael adduct **3a** was treated with 3 equiv of KO*t*-Bu in toluene at room temperature, the cyclization reaction rapidly proceeded to complete conversion within 1 h, resulting in different products according to the quenching conditions. When the reaction was immediately quenched by the addition of water, only the 3-benzoyl-2,3-dihydroquinolin-4(1*H*)-one product **5a** was obtained in 98% yield, as was expected. In contrast, the addition of aqueous hydrochloric acid to the resulting reaction solution in open air conditions surprisingly delivered the oxidized 3-benzoyl-quinolin-4(1*H*)-one product **4a** within 1 h in 75% yield. To confirm whether the oxidation reaction indeed proceeded during the quenching process under the acidic and aerobic conditions, the isolated 2,3-dihydroquinolin-4(1*H*)-one **5a** was treated with 6 N HCl in toluene under open air conditions. It was found that dehydrogenation smoothly occurred to generate the desired 3-carbonyl-4-quinolone **4a** in 78% yield, as shown in Scheme 2. If the corresponding reaction with **5a** is performed under nitrogen conditions, the oxidation does not proceed (<5% **4a**). This result indicates that

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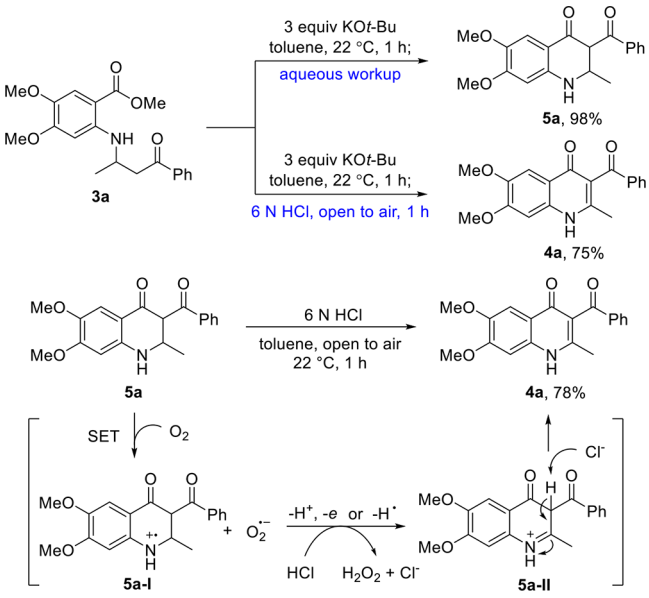
Scheme 2. Cyclization of β-Amino Ketone 3a Followed by Oxidation and Plausible Oxidation Mechanism



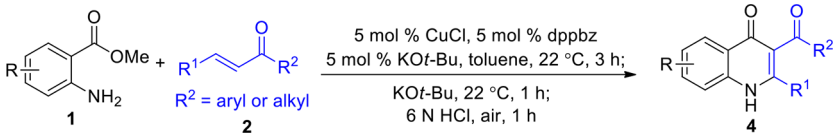
the oxidation reaction seems to be promoted by the presence of acid and air. Although further investigation for the mechanism of aerobic oxidation is necessary, it is likely to generate the radical cation intermediate **5a-I** via a single electron transfer (SET) from dihydroquinolinone **5a** to oxygen, followed by a further SET step to form the dihydroquinolinium **5a-II**. Subsequently, deprotonation occurs to furnish the quinolinone **4a**.[17]

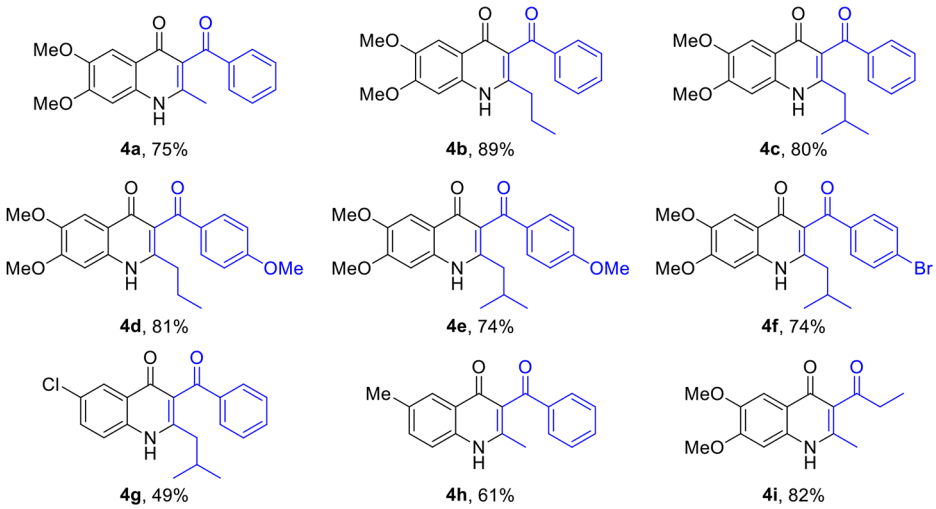
Because it is known that the keto−enol tautomerism between 4-quinolone and 4-hydroxyquinoline forms can proceed in certain solvents,[18] we decided to confirm the structure of our 3-benzoyl-4-quinolone **4a** using a 2D NMR (NOSEY) experiment. The NMR study disclosed that only 4-quinolone existed in the deuteriodimethyl sulfoxide solution. In addition, when methyl iodide was introduced to **4a** in DMF in the presence of potassium carbonate, the *N*-methylated 4-quinolone, rather than the *O*-alkylated product, was observed. Its structural assignment that was determined by the 2D NMR study was similar to the 3-benzoyl-quinolin-4(1*H*)-one product **4a**.[19]

On the basis of the above findings, we attempted an easy one-pot synthesis of 3-carbonyl-2-substituted 4-quinolones from readily available 2-aminobenzoates via aza-Michael addition/cyclization/oxidation sequential reactions, as depicted in Table 3. Various 2-aminobenzoates **1** were reacted with β-substituted α,β-unsaturated ketones **2** in the presence of a 5 mol % Cu catalyst. This reaction formed β-amino ketone intermediates, which were directly treated with KO*t*-Bu followed by the addition of 6 N HCl under open to air in a single vessel. All one-pot reactions were successfully performed in toluene under mild reaction conditions at room temperature and were completed within a total of 5 h, producing new and versatile 3-aroyl-2-substituted 4-quinolones **4a**−**4h**. In general, moderate to good yields were observed, except for the low yield of the product **4g** (49% yield) that was derived from 2-aminobenzoate substituted with a chloro group because of the sluggish oxidation reaction (Table 3). The one-pot process using (*E*)-hex-4-en-3-one was also efficient to synthesize 3-acyl-2-substituted 4-quinolone **4i** in 82% yield.

Next, we explored the efficiency and generality of this simple process. Thus, the scope of the one-pot reaction was further extended to different α,β-unsaturated carbonyl compounds and

Table 3. One-Pot Synthesis of 3-Carbonyl-2-Substituted 4-Quinolones[a]





[a]Reaction conditions: 2-aminobenzoate **1** (0.36 mmol), α,β-unsaturated ketone **2** (0.30 mmol), CuCl (0.015 mmol), dppbz (0.015 mmol), KO*t*-Bu (0.015 mmol), and toluene (0.2 M) under N_2. In the cyclization step, KO*t*-Bu (0.90 mmol) was added, followed by the addition of 6 N HCl (1 mL). Isolated yields after purification.

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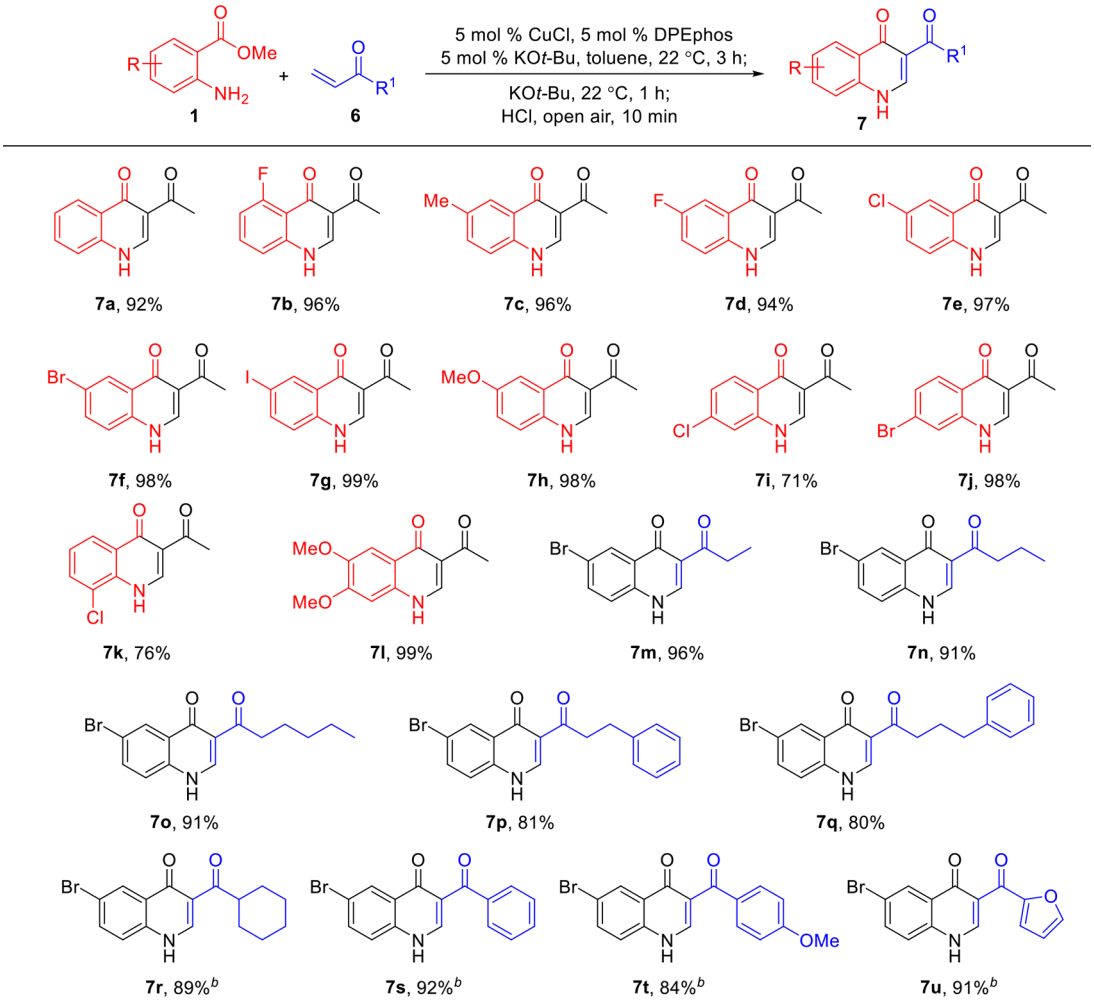
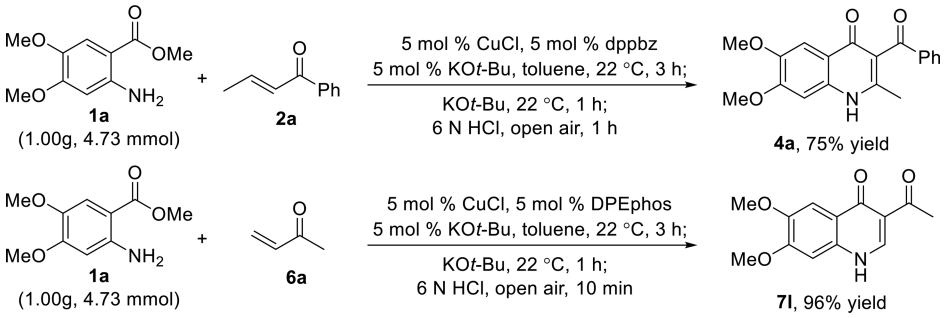
Table 4. One-Pot Synthesis of 3-Acyl-quinolin-4(1*H*)-ones[a]



[a]Reaction conditions: 2-aminobenzoate **1** (0.30 mmol), vinyl ketone **6** (0.36 mmol), CuCl (0.015 mmol), DPEphos (0.015 mmol), KO*t*-Bu (0.015 mmol), and toluene (0.2 M) under N_2. In the cyclization step, KO*t*-Bu (0.9 mmol) was added, followed by the addition of 6 N HCl (1 mL). Isolated yields after purification (trituration or recrystallization). [b]Dppbz used.

Scheme 3. Gram Scale Synthesis of 3-Carbonyl-4-quinolones 4a and 7l



a broad range of 2-aminobenzoates. The catalytic system also proved to be effective in promoting the aza-Michael addition to alkyl vinyl ketones or aryl vinyl ketones under the established conditions, which were transformed to a wide range of 3-acyl-4-quinolones with high efficiency and up to 99% yield, as demonstrated in Table 4. It is noteworthy that the one-pot process with vinyl ketone substrates is faster and more efficient than that with sterically demanding *β*-substituted *α*,*β*-unsaturated ketones. The oxidation of the in situ-generated 3-acyl-2,3-dihydroquinolin-4(1*H*)-ones during acidic workup was complete within 10 min, and the desired 3-acyl-quinolin-4(1*H*)-one products were easily purified by trituration or recrystallization (no silica gel column chromatography was required) in high yields. It is also noted that DPEphos ligand is more effective in catalyzing the conjugate addition with alkyl-substituted vinyl ketones than the dppbz ligand. The 2-aminobenzoates, bearing electron-donating methyl and methoxy or electron-withdrawing fluoro, chloro, bromo, and iodo

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substituents performed well in this catalytic process with methyl vinyl ketone to afford the corresponding 3-acyl-4-oxoquinolines **7a**−**7l** in 71−99% yields. Furthermore, we also examined the substrate scope with various alkyl vinyl ketones as Michael acceptors, including the ethyl, *n*-propyl, *n*-pentyl, phenethyl, and phenylpropyl groups. All groups were suitable for this one-pot reaction and smoothly reacted with methyl 2-amino-5-bromobenzoate, providing the desired 4-quinolones **7m**−**7q**, bearing a bromo unit on the phenyl ring, which can be further functionalized as useful building blocks through cross-coupling reactions, in high yields (80−96%). It was also found that the vinyl ketones, which have sterically demanding cyclohexyl, aryl, and furyl substituents, could efficiently take part in this transformation, affording the corresponding products **7r**−**7u** in 84−92% yields. These results indicate that the current reaction is a highly efficient way to synthesize a wide range of 3-acyl-4-quinolones.

This methodology also allowed the gram-scale one-pot synthesis of 3-cabonyl-4-quinolones with high efficiency, as shown in Scheme 3. The reactions of 1.00 g of 2-aminobenzoate **1a** with (*E*)-1-phenylbut-2-en-1-one (**2a**) and methyl vinyl ketone (**6a**) in the presence of 5 mol % Cu catalyst provided the corresponding 3-carbonyl-4-quinolones **4a** and **7l** in 75 and 96% yields, respectively. The Cu-catalyzed process was performed on a benchtop without using glovebox techniques. The facile one-pot process on gram-scale highlights a significant practical utility of this method.

CONCLUSIONS

In summary, we demonstrated a mild and efficient method for Cu-catalyzed aza-Michael addition of 2-aminobenzoates to *β*-substituted *α,β*-unsaturated ketones and successfully investigated the synthetic utility of the Michael adduct by developing a novel approach to highly functionalized 3-carbonyl-4-quinolones in a single vessel. Specifically, we suggested a new and efficient way to oxidize 3-carbonyl-2,3-dihydroquinolin-4(1*H*)-ones to 3-carbonyl-4-quinolones under mild reaction conditions. The use of easily accessible or commercially available substrates and inexpensive Cu catalysts, the applicability of the straightforward and mild one-pot process, the broad substrate scope, and the synthetic potential of the *β*-amino ketone and 3-carbonyl-4-quinolone products make this methodology very attractive and practical.

EXPERIMENTAL SECTION

General. Infrared (IR) spectra were recorded in reciprocal centimeters (cm^{-1}). Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts are reported in ppm from tetramethylsilane, with the solvent resonance as the internal standard ($CDCl_3$: δ 7.27 ppm and DMSO-d_6: 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR spectra were recorded on a 100 MHz spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.00 ppm and DMSO-d_6: 39.51 ppm). High-resolution mass spectra (HRMS) were obtained using an electrospray ionization (ESI) time-of-flight mass spectrometer. Melting points were determined using a melting point apparatus and are uncorrected. Unless otherwise noted, all reactions were carried out with distilled solvents under an atmosphere of dry N_2 in oven-dried (130 °C) glassware. Toluene was purified by distillation from sodium benzophenone ketyl immediately prior to use, unless otherwise specified. All workup and purification procedures were carried out with reagent grade solvents in air. A variety of vinyl ketones[20] and disubstituted *α,β*-unsaturated ketones[21] were prepared according to previously reported experimental procedures.

Representative Experimental Procedure for Cu-Catalyzed Aza-Michael Addition of 2-Aminobenzoate to *β*-Substituted *α,β*-Unsaturated Ketones. *Methyl 4,5-Dimethoxy-2-((4-oxo-4-phenylbutan-2-yl)amino)benzoate (**3a**).* Methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol), CuCl (1.50 mg, 0.0150 mmol), dppbz (6.70 mg, 0.0150 mmol), and KO*t*-Bu (1.70 mg, 0.0150 mmol) were added to a vial (8 mL) charged with a magnetic bar in the glovebox. The vial was sealed with a cap (phenolic open top cap with gray PTFE/silicone) and was removed from the glovebox. Then, the vial was purged with N_2 gas for 5 min, and toluene (0.7 mL) was added. After being premixed for 10 min, a solution of (*E*)-1-phenylbut-2-en-1-one (43.9 mg, 0.300 mmol) in toluene (0.8 mL) was added to the mixture, which was allowed to stir at room temperature for 3 h. After that time period, the reaction was quenched by adding a saturated aqueous solution of NH_4Cl (1 mL) and was washed with EtOAc (3 × 3 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified using silica gel column chromatography (hexanes:EtOAc = 4:1) to produce the desired *β*-amino product **3a** (106.5 mg, 0.298 mmol, 99% yield) as a bright greenish solid. mp 166−167 °C; IR (neat): 3318 (w), 1683 (s), 1608 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.96 (dd, *J* = 7.3, 1.3 Hz, 2H), 7.78 (br s, 1H), 7.58 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.47 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.37 (s, 1H), 6.33 (s, 1H), 4.33−4.31 (m, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.82 (s, 3H), 3.31 (dd, *J* = 16.5, 4.3 Hz, 1H), 3.16 (dd, *J* = 16.5, 7.9 Hz, 1H), 1.38 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.9, 168.6, 155.5, 147.2, 139.3, 137.0, 133.2, 128.6, 128.0, 113.8, 101.1, 95.0, 56.4, 55.6, 51.0, 45.3, 44.9, 21.3; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{24}NO_5$ 358.1654, Found 358.1641.

*Methyl 4,5-Dimethoxy-2-((1-oxo-1-phenylhexan-3-yl)amino)-benzoate (**3b**).* Compound **3b** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-1-phenylhex-2-en-1-on (52.3 mg, 0.300 mmol) in 99% yield (114.5 mg, 0.297 mmol) as a greenish oil. IR (neat): 3325 (w), 1645 (s), 1616 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.93 (dd, *J* = 7.3, 1.3 Hz, 2H), 7.77 (br s, 1H), 7.53 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.42 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.34 (s, 1H), 6.34 (s, 1H), 4.28−4.19 (m, 1H), 3.85 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H), 3.24−3.12 (m, 2H), 1.70−1.62 (m, 2H), 1.51−1.42 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.3, 168.7, 155.5, 147.8, 139.2, 137.1, 133.2, 128.6, 128.0, 113.8, 101.0, 95.0, 56.4, 55.6, 51.0, 49.1, 44.1, 38.1, 19.2, 13.8; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{22}H_{28}NO_5$ 386.1967, Found 386.1962.

*Methyl 4,5-Dimethoxy-2-((5-methyl-1-oxo-1-phenylhexan-3-yl)-amino)benzoate (**3c**).* Compound **3c** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-5-methyl-1-phenylhex-2-en-1-one (56.5 mg, 0.300 mmol) in 90% yield (108.3 mg, 0.271 mmol) as a greenish oil. IR (neat): 3425 (w), 1710 (s), 1685 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.93 (dd, *J* = 7.3, 1.5 Hz, 2H), 7.74 (br s, 1H), 7.56 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.45 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.35 (s, 1H), 6.37 (s, 1H), 4.32−4.22 (m, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 3.81 (s, 3H), 3.22 (dd, *J* = 16.5, 4.3 Hz, 1H), 3.14 (dd, *J* = 16.5, 7.9 Hz, 1H), 1.85−1.78 (m, 1H), 1.66−1.59 (m, 1H), 1.53−1.46 (m, 1H), 0.95 (d, *J* = 7.3 Hz, 3H), 0.92 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.3, 168.6, 155.4, 147.6, 139.1, 137.0, 133.2, 128.6, 128.0, 113.6, 100.8, 94.7, 56.3, 55.6, 51.0, 47.4, 45.4, 44.5, 24.8, 23.1, 21.8; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{30}NO_5$ 400.2124, Found 400.2120.

*Methyl 4,5-Dimethoxy-2-((1-(4-methoxyphenyl)-5-methyl-1-oxo-hexan-3-yl)amino)benzoate (**3d**).* Compound **3d** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-1-(4-methoxyphenyl)-5-methylhex-2-en-1-one (65.5 mg, 0.300 mmol) in 95% yield (122.8 mg, 0.286 mmol) as a greenish oil. IR (neat): 3345 (w), 1696 (s), 1618 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.91 (dd, *J* = 7.0, 1.9 Hz, 2H), 7.71 (br s, 1H), 7.34 (s, 1H), 6.90 (dd, *J* = 7.0, 1.9 Hz, 2H), 6.36 (s, 1H), 4.30−4.20 (m, 1H),

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3.86 (s, 3H), 3.84 (s, 3H), 3.82 (s, 3H), 3.79 (s, 3H), 3.14 (dd, J = 16.3, 4.6 Hz, 1H), 3.07 (dd, J = 16.3, 6.9 Hz, 1H), 1.88−1.74 (m, 1H), 1.64−1.57 (m, 1H), 1.51−1.44 (m, 1H), 0.94 (d, J = 7.0 Hz, 3H), 0.90 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.9, 168.7, 163.7, 155.6, 147.8, 139.1, 130.4, 130.3, 113.8, 113.7, 100.8, 94.9, 56.4, 55.7, 55.3, 51.1, 47.7, 45.5, 44.2, 24.9, 23.2, 21.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{32}NO_6$ 430.2230, Found 430.2230.

*Methyl 2-((1-(4-Bromophenyl)-5-methyl-1-oxohexan-3-yl)-amino)-4,5-dimethoxybenzoate (**3e**).* Compound **3e** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-1-(4-bromophenyl)-5-methylhex-2-en-1-one (80.2 mg, 0.300 mmol) in 87% yield (125.3 mg, 0.262 mmol) as a sticky oil. IR (neat): 3248 (w), 1686 (s), 1621 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78 (d, J = 8.5 Hz, 2H), 7.77 (br s, 1H), 7.58 (d, J = 8.5 Hz, 2H), 7.34 (s, 1H), 6.34 (s, 1H), 4.32−4.21 (m, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 3.81 (s, 3H), 3.16 (dd, J = 16.3, 4.9 Hz, 1H), 3.11 (dd, J = 16.3, 6.6 Hz, 1H), 1.85−1.75 (m, 1H), 1.66−1.56 (m, 1H), 1.50−1.46 (m, 1H), 0.95 (d, J = 6.6 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.6, 168.8, 155.5, 147.6, 139.3, 135.9, 132.0, 129.7, 128.5, 113.6, 101.0, 94.9, 56.4, 55.7, 51.2, 47.7, 45.5, 44.5, 24.9. 23.2, 21.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{29}BrNO_5$ 478.1229, Found 478.1229.

*Methyl 2-((1-(3-Chlorophenyl)-5-methyl-1-oxohexan-3-yl)-amino)-4,5-dimethoxybenzoate (**3f**).* Compound **3f** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-1-(3-chlorophenyl)-5-methylhex-2-en-1-one (66.8 mg, 0.300 mmol) in 90% yield (117.6 mg, 0.271 mmol) as a greenish oil. IR (neat): 3412 (w), 1673 (s), 1612(s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.89 (s, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.53 (d, J = 7.8 Hz, 1H), 7.39 (dd, J = 7.8, 7.5 Hz, 1H), 7.34 (s, 1H), 6.36 (s, 1H), 4.27 (br s, 1H), 3.89 (s, 3H), 3.84 (s, 3H), 3.81 (s, 3H), 3.22 (dd, J = 16.6, 4.6 Hz, 1H), 3.12 (dd, J = 16.6, 6.6 Hz, 1H), 1.85−1.75 (m, 1H), 1.66−1.60 (m, 2H), 1.51−1.43 (m, 1H), 0.95 (d, J = 6.6 Hz, 3H), 0.93 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.6, 169.1, 155.8, 147.9, 139.0, 135.3, 133.5, 130.3, 128.6, 128.5, 126.5, 114.0, 101.3, 95.1, 56.7, 56.0, 51.5, 47.8, 45.8, 45.0, 25.2, 23.5, 22.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{29}ClNO_5$ 434.1734, Found 434.1732.

*Methyl 2-((4-Oxo-4-phenylbutan-2-yl)amino)benzoate (**3g**).* Compound **3g** was synthesized from methyl 2-aminobenzoate (54.4 mg, 0.360 mmol) and (*E*)-1-phenylbut-2-en-1-one (43.9 mg, 0.300 mmol) in 96% yield (85.9 mg, 0.289 mmol) as a greenish oil. IR (neat): 3356 (w), 1663 (s), 1633 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00−7.95 (m, 3H), 7.92 (dd, J = 8.0, 1.5 Hz, 1H), 7.86 (br s, 1H), 7.57 (dd, J = 8.0, 8.0 Hz, 1H), 7.46 (dd, J = 7.7, 7.7 Hz, 2H), 6.78 (d, J = 8.0 Hz, 1H), 6.59 (dd, J = 7.7, 7.7 Hz, 1H), 4.39−4.28 (m, 1H), 3.80 (s, 3H), 3.35 (dd, J = 16.8, 3.9 Hz, 1H), 3.16 (dd, J = 16.8, 8.4 Hz, 1H), 1.36 (d, J = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.8, 169.2, 149.9, 137.1, 134.8, 133.3, 131.9, 128.7, 128.2, 114.7, 111.7, 110.1, 51.4, 44.9, 44.3, 21.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{20}NO_3$ 298.1443, Found 298.1443.

*Methyl 5-Methyl-2-((4-oxo-4-phenylbutan-2-yl)amino)benzoate (**3h**).* Compound **3h** was synthesized from methyl 2-amino-5-methylbenzoate (59.5 mg, 0.360 mmol) and (*E*)-1-phenylbut-2-en-1-one (43.9 mg, 0.300 mmol) in 96% yield (90.0 mg, 0.289 mmol) as a yellow oil. IR (neat): 3386 (w), 1673 (s), 1611 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78 (d, J = 7.3 Hz, 2H), 7.57 (br s, 1H), 7.50 (br, 1H), 7.37 (dd, J = 7.4, 7.4 Hz, 1H), 7.27 (dd, J = 7.7, 7.7 Hz, 2H), 7.01 (dd, J = 8.5, 2.0 Hz, 1H), 6.56 (d, J = 8.5 Hz, 1H), 4.17−4.12 (m, 1H), 3.68 (s, 3H), 3.16 (dd, J = 16.7, 4.0 Hz, 1H), 2.95 (dd, J = 16.7, 8.3 Hz, 1H), 2.06 (s, 3H), 1.20 (d, J = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.7, 169.0, 147.9, 135.7, 133.0, 131.5, 128.5, 127.9, 123.5, 116.7, 111.7, 109.9, 51.1, 44.8, 44.3, 21.0, 19.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}NO_3$ 312.1600, Found 312.1604.

*Methyl 5-Bromo-2-((4-oxo-4-phenylbutan-2-yl)amino)benzoate (**3i**).* Compound **3i** was synthesized from methyl 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol) and (*E*)-1-phenylbut-2-en-1-one (43.9 mg, 0.300 mmol) in 95% yield (107 mg, 0.284 mmol) as a bright yellow solid. mp 155−156 °C. IR (neat): 3425 (w), 1683 (s), 1601 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.01 (d, J = 2.5 Hz, 1H), 7.95 (d, J = 7.8 Hz, 2H), 7.84 (br s, 1H), 7.58 (dd, J = 7.4, 7.4 Hz, 1H), 7.47 (dd, J = 7.8, 7.8 Hz, 2H), 7.40 (dd, J = 9.1, 2.5 Hz, 1H), 6.68 (d, J = 9.1 Hz, 1H), 4.30−4.26 (m, 1H), 3.86 (s, 3H), 3.30 (dd, J = 16.8, 4.3 Hz, 1H), 3.14 (dd, J = 16.8, 8.0 Hz, 1H), 1.36 (d, J = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.5, 168.1, 148.7, 137.3, 137.0, 134.1, 133.3, 128.7, 128.1, 113.5, 111.5, 105.9, 51.6, 44.7, 44.4, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}BrNO_3$ 376.0548, Found 376.0549.

*Methyl 4-Chloro-2-((4-oxo-4-phenylbutan-2-yl)amino)benzoate (**3j**).* Compound **3j** was synthesized from methyl 2-amino-4-chlorobenzoate (66.8 mg, 0.360 mmol) and (*E*)-1-phenylbut-2-en-1-one (43.9 mg, 0.300 mmol) in 94% yield (93.9 mg, 0.283 mmol) as a yellow solid. mp 176−177 °C. IR (neat): 3389 (w), 1676 (s), 1612 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.96 (dd, J = 7.3, 1.6 Hz, 2H), 7.95 (br s, 1H), 7.82 (d, J = 8.5 Hz, 1H), 7.58 (td, J = 7.3, 1.6 Hz, 1H), 7.47 (dd, J = 7.3, 7.3 Hz, 2H), 6.76 (d, J = 2.0 Hz, 1H), 6.54 (dd, J = 8.5, 2.0 Hz, 1H), 4.27−4.23 (m, 1H), 3.84 (s, 3H), 3.31 (dd, J = 16.9, 4.4 Hz, 1H), 3.15 (dd, J = 16.9, 8.0 Hz, 1H), 1.37 (d, J = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.6, 168.2, 148.5, 137.1, 134.7, 133.4, 131.2, 128.7, 128.1, 119.3, 113.2, 111.0, 51.7, 44.8, 44.5, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}ClNO_3$ 332.1053, Found 332.1054.

*Methyl 5-Chloro-2-((5-methyl-1-oxo-1-phenylhexan-3-yl)amino)-benzoate (**3k**).* Compound **3k** was synthesized from methyl 2-amino-5-chlorobenzoate (66.8 mg, 0.360 mmol) and (*E*)-5-methyl-1-phenylhex-2-en-1-one (56.5 mg, 0.300 mmol) in 80% yield (90.1 mg, 0.241 mmol) as a greenish oil. IR (neat): 3275 (w), 1655 (s), 1602 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.99 (d, J = 2.3 Hz, 1H), 7.92 (dd, J = 7.3, 1.5 Hz, 2H), 7.79 (br s, 1H), 7.55 (dd, J = 7.3, 7.3 Hz, 1H), 7.46 (dd, J = 7.8, 7.8 Hz, 2H), 7.38 (dd, J = 9.0, 2.3 Hz, 1H), 6.72 (d, J = 9.0 Hz, 1H), 4.33−4.22 (m, 1H), 3.84 (s, 3H), 3.20 (dd, J = 17.1, 4.6 Hz, 1H), 3.14 (dd, J = 17.1, 7.3 Hz, 1H), 1.87−1.75 (m, 1H), 1.62−1.47 (m, 2H), 0.95 (d, J = 6.6 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.8, 168.1, 149.2, 137.3, 134.0, 133.2, 132.5, 128.6, 128.0, 113.3, 111.3, 105.6, 51.6, 47.0, 45.0, 24.9, 23.2, 22.3, 21.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{25}ClNO_3$ 374.1523, Found 374.1519.

*Methyl 4,5-Dimethoxy-2-((4-oxohexan-2-yl)amino)benzoate (**3l**).* Compound **3l** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-hex-4-en-3-one (34.3 μL, 0.300 mmol) in 92% yield (85.8 mg, 0.276 mmol) as an ivory solid. mp 86−87 °C; IR (neat): 3078 (w), 1612 (s), 1566 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.66 (s, 1H), 7.36 (s, 1H), 6.27 (s, 1H), 4.13 (br s, 1H), 3.91 (s, 3H), 3.83 (s, 3H), 3.82 (s, 3H), 2.78 (dd, J = 16.1, 4.8 Hz, 1H), 2.56 (dd, J = 16.1, 7.3 Hz, 1H), 2.49−2.44 (m, 2H), 1.29 (d, J = 6.3 Hz, 3H), 1.04 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 210.6, 168.8, 155.4, 147.3, 139.3, 113.5, 101.1, 95.0, 56.4, 55.8, 51.2, 49.3, 44.7, 37.4, 21.3, 7.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{24}NO_5$ 310.1654, Found 310.1648.

Representative Experimental Procedure for the One-Pot Synthesis of 3-Aroyl-2-Substituted 4-Quinolones. *3-Benzoyl-6,7-dimethoxy-2-methylquinolin-4(1H)-one (**4a**).* In the glovebox, methyl 2-amino-4,5-dimethoxybenzoate (**1a**) (76.0 mg, 0.360 mmol), CuCl (1.50 mg, 0.0150 mmol), dppbz (6.70 mg, 0.0150 mmol), and KO*t*-Bu (1.70 mg, 0.0150 mmol) were added to a vial (8 mL) charged with a magnetic bar. The vial was sealed with a cap (phenolic open top cap with gray PTFE/silicone) and taken out of the glovebox. The vial was purged with N_2 gas for 5 min. Toluene (0.7 mL) was added to the mixture, which was allowed to premix for 10 min. Then, a solution of (*E*)-1-phenylbut-2-en-1-one (**2a**) (43.9 mg, 0.300 mmol) in toluene (0.8 mL) was added to the mixture, which was allowed to stir at room temperature for 3 h. After that time, KO*t*-Bu (101 mg, 0.900 mmol) was added, and the reaction was allowed to stir for an additional 1 h at 22 °C. In open air conditions, an aqueous solution of 6 N HCl (1.5 mL) was added to the resulting solution, which was allowed to stir for 1 h. The reaction was quenched by adding a saturated aqueous solution of K_2CO_3 (2 mL) and was washed with CH_2Cl_2 (3 × 2 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (MeOH:CH_2Cl_2 = 5:95) to afford the desired product **4a** (72.7 mg, 0.225 mmol, 75% yield) as a yellow solid.

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mp 252−253 °C; IR (neat): 3417 (w), 1664 (s), 1603 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 11.85 (s, 1H), 7.76 (d, J = 7.6 Hz, 2H), 7.59 (dd, J = 7.6, 7.6 Hz, 1H), 7.46 (dd, J = 7.6 7.6 Hz, 2H), 7.36 (s, 1H), 7.01 (s, 1H), 3.89 (s, 3H), 3.81 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.1, 171.8, 153.8, 147.8, 137.9, 135.5, 133.0, 128.9,128.6, 128.5, 118.6, 117.6, 104.1, 99.3, 55.8, 55.6, 17.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{18}NO_4$ 324.1236, Found 324.1235.

*3-Benzoyl-6,7-dimethoxy-2-propylquinolin-4(1H)-one (**4b**).* Compound **4b** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-1-phenylhex-2-en-1-one (52.3 mg, 0.300 mmol) in 89% yield (94.2 mg, 0.268 mmol) as a yellow solid. mp 248−249 °C; IR (neat): 3408 (w), 1644 (s), 1635 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.82 (s, 1H), 7.79 (d, J = 7.3 Hz, 2H), 7.61 (dd, J = 7.3, 7.3 Hz, 1H), 7.55 (s, 1H), 7.48 (dd, J = 7.3, 7.3 Hz, 2H), 7.32 (s, 1H), 3.91 (s, 3H), 3.84 (s, 3H), 2.58 (t, J = 7.3 Hz, 2H), 1.60 (qt, J = 7.3, 7.3 Hz, 2H), 0.82 (t, J = 7.3 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.3 172.3 153.8, 151.3, 147.5, 138.0, 135.7, 133.1, 128.9, 128.6, 118.5, 117.7, 104.1, 99.5, 55.8, 55.7, 32.9, 22.2, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{22}NO_4$ 352.1549, Found 352.1545.

*3-Benzoyl-2-isobutyl-6,7-dimethoxyquinolin-4(1H)-one (**4c**).* Compound **4c** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-5-methyl-1-phenylhex-2-en-1-one (56.5 mg, 0.300 mmol) in 80% yield (88.1 mg, 0.241 mmol) as a dark yellow solid. mp 257−258 °C; IR (neat): 3369 (w), 1687 (s), 1626 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.16 (s, 1H), 7.76 (d, J = 7.3 Hz, 2H), 7.58 (dd, J = 7.3, 7.3 Hz, 1H), 7.46 (dd, J = 7.3, 7.3 Hz, 2H), 7.41 (s, 1H), 7.25 (s, 1H), 3.90 (s, 3H), 3.82 (s, 3H), 2.49 (d, J = 6.6 Hz, 2H), 2.02−1.91 (m, 1H), 0.81 (d, J = 6.6 Hz, 6H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 197.2, 174.2, 153.3, 150.8, 147.0, 138.3, 135.3, 132.9, 128.9, 128.6, 118.8, 118.6, 104.2, 99.3, 55.7, 55.5, 33.1, 22.3, 13.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{24}NO_4$ 366.1705, Found 366.1703.

*6,7-Dimethoxy-3-(4-methoxybenzoyl)-2-propylquinolin-4(1H)-one (**4d**).* Compound **4d** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-1-(4-methoxyphenyl)hex-2-en-1-one (61.3 mg, 0.300 mmol) in 81% yield (93.1 mg, 0.244 mmol) as an ivory solid. mp 243−244 °C; IR (neat): 3423 (w), 1658 (s), 1614 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 11.69 (s, 1H), 7.73 (d, J = 8.8 Hz, 2H), 7.37 (s, 1H), 7.04 (s, 1H), 6.99 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H), 3.82 (s, 6H), 2.46 (t, J = 7.6 Hz, 2H), 1.57 (qt, J = 7.5, 7.5 Hz, 2H), 0.82 (t, J = 7.5 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 195.5, 174.0, 163.2, 153.3, 150.1, 146.9, 135.3, 131.5, 131.2, 119.2, 118.5, 113.9, 104.2, 99.3, 55.7, 55.6, 55.5, 33.1, 22.3, 13.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{24}NO_5$ 382.1654, Found 382.1649.

*2-Isobutyl-6,7-dimethoxy-3-(4-methoxybenzoyl)quinolin-4(1H)-one (**4e**).* Compound **4e** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-1-(4-methoxyphenyl)-5-methylhex-2-en-1-one (65.5 mg, 0.300 mmol) in 74% yield (88.2 mg, 0.223 mmol) as a bright ivory solid. mp 253−254 °C; IR (neat): 3385 (w), 1675 (s), 1628 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 11.16 (s, 1H), 7.73 (d, J = 8.7 Hz, 2H), 7.37 (s, 1H), 7.07 (s, 1H), 6.98 (d, J = 8.7 Hz, 2H), 3.90 (s, 3H), 3.82 (s, 6H), 2.42 (d, J = 7.6 Hz, 2H), 1.92 (m, 1H), 0.80 (d, J = 6.6 Hz, 6H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 195.4, 174.0, 163.2, 153.3, 149.5, 147.0, 135.3, 131.5, 131.2, 119.6, 118.2, 113.8, 104.2, 99.3, 55.7, 55.6, 55.5, 28.0, 22.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{26}NO_5$ 396.1811, Found 396.1810.

*3-(4-Bromobenzoyl)-2-isobutyl-6,7-dimethoxyquinolin-4(1H)-one (**4f**).* Compound **4f** was synthesized from methyl 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-1-(4-bromophenyl)-5-methylhex-2-en-1-one (80.1 mg, 0.300 mmol) in 74% yield (99.1 mg, 0.223 mmol) as a dark yellow solid. mp 235−236 °C; IR (neat): 3432 (w), 1695 (s), 1613 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.74 (s, 1H), 7.72−7.67 (m, 4H), 7.53 (s, 1H), 7.33 (s, 1H), 3.91 (s, 3H), 3.84 (s, 3H), 2.56 (d, J = 7.6 Hz, 2H), 1.98−1.92 (m, 1H), 0.82 (d, J = 6.5 Hz, 6H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 195.4, 172.4, 153.8, 151.2, 147.6, 137.2, 135.6, 131.6, 130.8, 126.9, 118.3, 117.8, 104.1, 99.6, 55.8, 55.6, 28.2, 21.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{23}BrNO_4$ 444.0810, Found 444.0805.

*3-Benzoyl-6-chloro-2-isobutylquinolin-4(1H)-one (**4g**).* Compound **4g** was synthesized from methyl 2-amino-5-chlorobenzoate (66.8 mg, 0.360 mmol) and (*E*)-5-methyl-1-phenylhex-2-en-1-one (56.5 mg, 0.300 mmol) in 49% yield (50.3 mg, 0.148 mmol) as a yellow solid. mp 215−216 °C; IR (neat): 3373 (w), 1682 (s), 1621 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.04 (s, 1H), 7.95 (d, J = 2.3 Hz, 1H), 7.79 (d, J = 7.5 Hz, 2H), 7.76 (dd, J = 8.8, 2.3 Hz, 1H), 7.70 (d, J = 8.8 Hz, 1H), 7.61 (dd, J = 7.5, 7.5 Hz, 1H), 7.47 (dd, J = 7.5, 7.5 Hz, 2H), 2.48 (d, J = 6.6 Hz, 2H), 2.00−1.91 (m, 1H), 0.82 (d, J = 6.5 Hz, 6H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 197.0, 175.2, 151.4, 138.2, 137.7, 133.7, 133.2, 133.0, 128.9, 128.6, 124.7, 124.2, 119.8, 118.3, 28.1, 22.0, 20.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{19}ClNO_2$ 340.1104, Found 340.1103.

*3-Benzoyl-2,6-dimethylquinolin-4(1H)-one (**4h**).* Compound **4h** was synthesized from methyl 2-amino-5-methylbenzoate (59.5 mg, 0.360 mmol) and (*E*)-1-phenylbut-2-en-1-one (43.8 mg, 0.300 mmol) in 61% yield (51.0 mg, 0.184 mmol) as a dark yellow solid. mp 223−224 °C. IR (neat): 3413 (w), 1674 (s), 1624 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 11.95 (s, 1H), 7.81 (s, 1H), 7.77 (d, J = 7.5 Hz, 2H), 7.60 (d, J = 7.5 Hz, 1H), 7.54 (dd, J = 8.5, 1.9 Hz, 2H), 7.50 (d, J = 8.5 Hz, 2H), 2.40 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 197.1, 174.9, 148.7, 138.1, 137.7, 133.8, 133.2, 133.1, 129.1, 128.7, 124.8, 124.3, 119.5, 118.2, 20.8, 17.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{16}NO_2$ 278.1181, Found 278.1176.

*6,7-Dimethoxy-2-methyl-3-propionylquinolin-4(1H)-one (**4i**).* Compound **4i** was synthesized from 2-amino-4,5-dimethoxybenzoate (76.0 mg, 0.360 mmol) and (*E*)-hex-4-en-3-one (34.3 μL, 0.300 mmol) in 82% yield (67.7 mg, 0.246 mmol) as a yellow solid. mp 248−249 °C; IR (neat): 3340 (w), 1696 (s), 1674 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 11.75 (s, 1H), 7.46(s, 1H), 6.96 (s, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 2.92 (q, J = 7.3 Hz, 2H), 2.34 (s, 3H), 1.02 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 207.1, 175.3, 154.2, 149.3, 148.0, 135.1, 120.6, 119.4, 101.4, 98.9, 56.1, 56.0, 37.4, 19.5, 8.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}NO_4$ 276.1236, Found 276.1231.

*3-Benzoyl-6,7-dimethoxy-2-methyl-2,3-dihydroquinolin-4(1H)-one (**5a**).* Methyl 4,5-dimethoxy-2-((4-oxo-4-phenylbutan-2-yl)-amino)benzoate (**3a**) (85.9 mg, 0.300 mmol) and KO*t*-Bu (101 mg, 0.900 mmol) were added to a vial (8 mL) charged with a magnetic bar. The vial was sealed with a cap (phenolic open top cap with gray PTFE/silicone) and was purged with N_2 gas. Toluene (1.5 mL) was added to the mixture, which was allowed to stir at room temperature for 1 h. The resulting solution was quenched by adding water (1 mL) and was washed with CH_2Cl_2 (3 × 2 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (CH_2Cl_2:MeOH = 95:5) to produce the 2,3-dihydroquinolin-4(1*H*)-one **5a** (95.8 mg, 0.294 mmol, 98% yield) as a yellow solid. mp 233−234 °C; IR (neat): 3331 (w), 1694 (s), 1635 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 8.02 (d, J = 7.5 Hz, 2H), 7.66 (dd, J = 7.5, 7.5 Hz, 1H), 7.54 (dd, J = 7.5, 7.5 Hz, 2H), 6.98 (s, 1H), 6.73 (s, 1H), 6.35 (s, 1H), 4.57 (d, J = 10.8 Hz, 1H), 4.05−3.96 (m, 1H), 3.78 (s, 3H), 3.65 (s, 3H), 1.14 (d, J = 5.6 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 199.3, 189.4, 156.3, 149.1, 141.8, 138.0, 133.6, 128.9, 128.7, 109.8, 107.1, 97.8, 59.6, 55.6, 55.6, 51.3, 19.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{20}NO_4$ 326.1392, Found 326.1385.

*3-Benzoyl-6,7-dimethoxy-1,2-dimethylquinolin-4(1H)-one (**Me-4a**).* 3-Benzoyl-6,7-dimethoxy-2-methylquinolin-4(1*H*)-one (**4a**) (32.3 mg, 0.100 mmol), NaH (60% in mineral oil, 6.00 mg, 0.150 mmol), and DMF (1 mL) were added to a vial (4 mL) charged with a magnetic bar. The mixture was allowed to stir at room temperature for 1 h under N_2 gas. Then, methyl iodide (18.6 μL, 0.300 mmol) was added to the mixture, which was allowed to stir at 80 °C for 4 h. The reaction was quenched by adding water (1 mL) and was washed with CH_2Cl_2 (3 × 1 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified using silica gel column chromatography (Hexanes:EtOAc = 1:3) to produce the desired product (29.4 mg, 0.0872 mmol, 87%

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yield) as an ivory solid. mp 175−176 °C; IR (neat): 1684 (s), 1607 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 7.80 (d, J = 8.2 Hz, 2H), 7.62 (dd, J = 7.4, 7.4 Hz, 1H), 7.49 (dd, J = 7.4, 7.4 Hz, 2H), 7.49 (s, 1H), 7.23 (s, 1H), 3.99 (s, 3H), 3.83 (s, 3H), 3.82, (s, 3H), 2.32 (S, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 197.7, 173.0, 153.4, 148.4, 146.8, 137.9, 137.3, 133.4, 129.2, 128.9, 121.1, 119.8, 104.8, 99.3, 54.6, 54.5, 35.4, 18.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}NO_4$ 338.1392, Found 338.1391.

Representative Experimental Procedure for One-Pot Synthesis of 3-Acyl Quinolin-4(1*H*)-ones. *General Procedure A.* In the glovebox, methyl 2-amino-6-fluorobenzoate (50.8 mg, 0.300 mmol), CuCl (1.50 mg, 0.0150 mmol), DPEphos (8.10 mg, 0.0150 mmol), and KO*t*-Bu (1.70 mg, 0.0150 mmol) were added to a vial (8 mL) charged with a magnetic bar. The vial was sealed with a cap (phenolic open top cap with gray PTFE/silicone) and taken out of the glovebox. The vial was purged with N_2 gas for 5 min. Toluene (1.5 mL) was added to the mixture, which was allowed to premix for 10 min. Then, methyl vinyl ketone (25.0 μL, 0.360 mmol) was added to the reaction solution. After stirring at room temperature for 3 h, KO*t*-Bu (101 mg, 0.900 mmol) was added, and the reaction was allowed to stir for an additional 1 h at 22 °C. The resulting solution was quenched with an aqueous solution of 6 N HCl (1 mL) and allowed to stir for 10 min in open air conditions. The organic layers were washed with CH_2Cl_2 (3 × 2 mL), combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was recrystallized from dichloromethane and diethyl ether to afford the desired product **7b** (59.3 mg, 0.289 mmol, 96% yield) as an ivory solid.

General Procedure B. In the glovebox, methyl 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol), CuCl (1.50 mg, 0.0150 mmol), dppbz (6.70 mg, 0.0150 mmol), and KO*t*-Bu (1.70 mg, 0.0150 mmol) were added to a vial (8 mL) charged with a magnetic bar. The vial was sealed with a cap (phenolic open top cap with gray PTFE/silicone) and taken out of the glovebox. The vial was purged with N_2 gas for 5 min. Toluene (0.7 mL) was added to the mixture, which was allowed to mix for 10 min. Then, a solution of 1-cyclohexylprop-2-en-1-one (41.4 mg, 0.300 mmol) in toluene (0.8 mL) was added to the mixture, which was allowed to stir at room temperature for 3 h. After that time, KO*t*-Bu (101 mg, 0.900 mmol) was added to the reaction solution, which was allowed to stir for an additional 1 h at 22 °C. The resulting solution was quenched with an aqueous solution of 6 N HCl (1 mL) and allowed to stir for 10 min in open air conditions. The organic layers were washed with CH_2Cl_2 (3 × 2 mL), combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was recrystallized from dichloromethane and diethyl ether to afford the desired product **7r** (89.3 mg, 0.267 mmol, 89% yield) as an ivory solid.

*3-Acetylquinolin-4(1H)-one (**7a**).* Compound **7a** was synthesized according to general procedure A using methyl 2-aminobenzoate (38.8 μL, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in 92% yield (51.9 mg, 0.277 mmol) as an ivory solid. This compound has been previously reported, and spectral data match described.[1f] mp 252−253 °C. IR (neat): 3442 (w), 1643 (s), 1615 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.67 (br s, 1H), 8.51 (s, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.73 (dd, J = 8.0, 7.2 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.44 (dd, J = 8.0, 7.2 Hz, 1H), 2.61 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.6, 175.4, 144.2, 139.2, 132.7, 127.9, 125.9, 125.0, 119.0, 117.7, 31.1.

*3-Acetyl-5-fluoroquinolin-4(1H)-one (**7b**).* Compound **7b** was synthesized according to general procedure A using methyl 2-amino-6-fluorobenzoate (50.8 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in 96% yield (59.3 mg, 0.289 mmol) as an ivory solid. mp 216−217 °C; IR (neat): 3376 (w), 1630 (s), 1618 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.56 (br s, 1H), 8.41 (s, 1H), 7.69−7.64 (m, 1H), 7.40 (d, J = 8.3 Hz, 1H), 7.11 (dd, J = 8.1, 8.0 Hz, 1H), 2.55 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.5, 174.7, 162.6, 160.0, 144.0, 141.6 (d, J = 3.3 Hz), 133.5 (d, J = 10.7 Hz), 119.4, 115.1 (d, J = 4.2 Hz), 111.5 (d, J = 21.5 Hz), 31.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_9FNO_2$ 206.0617, Found 206.0618.

*3-Acetyl-6-methylquinolin-4(1H)-one (**7c**).* Compound **7c** was synthesized according to general procedure A using methyl 2-amino-5-methylbenzoate (49.6 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in 96% yield (57.8 mg, 0.287 mmol) as a dark yellow solid. mp 207−208 °C; IR (neat): 3384 (w), 1648 (s), 1624 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.56 (br s, 1H), 8.47 (s, 1H), 8.02 (s, 1H), 7.55 (s, 2H), 2.61 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 200.0, 175.4, 143.8, 137.3, 134.8, 134.1, 127.8, 125.3, 119.0, 117.5, 31.2, 20.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{12}NO_2$ 202.0868, Found 202.0868.

*3-Acetyl-6-fluoroquinolin-4(1H)-one (**7d**).* Compound **7d** was synthesized according to general procedure A using methyl 2-amino-5-fluorobenzoate (50.7 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) as an ivory solid in 94% yield (58.1 mg, 0.283 mmol). mp 207−208 °C; IR (neat): 3411 (w), 1635 (s), 1620 (s), 1616 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.53 (br s, 1H), 8.52 (s, 1H), 8.20 (d, J = 8.8 Hz, 1H), 7.67 (d, J = 2.0 Hz, 1H), 7.45 (dd, J = 8.8, 2.0 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.6, 174.7 (d, J = 2.5 Hz), 160.8, 158.4, 144.3, 136.1, 122.0 (d, J = 8.3 Hz), 121.3 (d, J = 24.8 Hz), 117.1, 110.3 (d, J = 23.2 Hz), 31.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_9FNO_2$ 206.0617, Found 206.0618.

*3-Acetyl-6-chloroquinolin-4(1H)-one (**7e**).* Compound **7e** was synthesized according to general procedure A using methyl 2-amino-5-chlorobenzoate (55.7 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in 97% yield (64.5 mg, 0.291 mmol) as a yellow solid. mp 243−244 °C; This compound has been previously reported, and spectral data match described.[1f] IR (neat): 3411 (w), 1642 (s), 1606 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.68 (br s, 1H), 8.52 (d, J = 6.7 Hz, 1H), 8.12 (s, 1H), 7.75 (dd, J = 8.7, 2.2 Hz, 1H), 7.66 (dd, J = 8.8, 2.2 Hz, 1H), 2.60 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.3, 174.2, 144.6, 137.8, 132.6, 129.7, 129.1, 124.8, 121.4, 117.8, 31.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_9ClNO_2$ 222.0322, Found 222.0328.

*3-Acetyl-6-bromoquinolin-4(1H)-one (**7f**).* Compound **7f** was synthesized according to general procedure A using methyl 2-amino-5-bromobenzoate (69.0 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in 98% yield (78.2 mg, 0.294 mmol) as a yellow solid. This compound has been previously reported, and spectral data match described.[22] mp 287−288 °C; IR (neat): 3421 (w), 1636 (s), 1613 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.66 (br s, 1H), 8.52 (s, 1H), 8.29 (d, J = 2.0 Hz, 1H), 7.87 (dd, J = 8.8, 2.0 Hz, 1H), 7.60 (d, J = 8.8 Hz, 1H), 2.60 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.4, 174.2, 144.7, 138.2, 135.4, 129.4, 128.1, 121.6, 118.1, 117.9, 31.1.

*3-Acetyl-6-iodoquinolin-4(1H)-one (**7g**).* Compound **7g** was synthesized according to general procedure A using methyl 2-amino-5-iodobenzoate (83.1 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in 99% yield (93.3 mg, 0.298 mmol) as an ivory solid. mp 293−294 °C; IR (neat): 3433 (w), 1660 (s), 1622 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.64 (br s, 1H), 8.54 (d, J = 6.5 Hz, 1H), 8.50 (d, J = 2.1 Hz, 1H), 8.01 (dd, J = 8.6, 2.1 Hz, 1H), 7.46 (d, J = 8.6 Hz, 1H), 2.60 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.3, 174.0, 144.6, 140.8, 140.7, 138.5, 134.3, 121.4, 121.3, 118.1, 31.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_9INO_2$ 313.9678, Found 313.9678.

*3-Acetyl-6-methoxyquinolin-4(1H)-one (**7h**).* Compound **7h** was synthesized according to general procedure A using methyl 2-amino-5-methoxybenzoate (54.4 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in 98% yield (63.6 mg, 0.293 mmol) as a bright yellow solid. mp 210−211 °C; IR (neat): 3453 (w), 1648 (s), 1620 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.69 (br s, 1H), 8.46 (s, 1H), 7.65 (d, J = 2.7 Hz, 1H), 7.62 (d, J = 8.8 Hz, 1H), 7.36 (dd, J = 8.8, 2.7 Hz, 1H), 3.86 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.6, 174.7, 156.8, 142.7, 133.5, 129.1, 122.2, 120.6, 116.7, 105.8, 55.4, 30.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{12}NO_3$ 218.0817, Found 218.0815.

*3-Acetyl-7-chloroquinolin-4(1H)-one (**7i**).* Compound **7i** was synthesized according to general procedure A using methyl 2-amino-4-chlorobenzoate (55.7 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in 71% yield (47.2 mg, 0.213 mmol) as a yellow solid. This compound has been previously reported, and

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spectral data match described.[1f] mp 260−261 °C; IR (neat): 3321 (m), 1660 (s), 1633 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.52 (br s, 1H), 8.51 (s, 1H), 8.20 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 1.7 Hz, 1H), 7.45 (dd, J = 8.8, 1.7 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.5, 174.9, 144.9, 140.0, 137.2, 128.2, 126.6, 125.3, 118.4, 118.2, 31.0.

*3-Acetyl-7-bromoquinolin-4(1H)-one (**7j**).* Compound **7j** was synthesized according to general procedure A using methyl 2-amino-4-bromobenzo ate (69.0 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in 98% yield (78.5 mg, 0.295 mmol) as a yellow solid. mp 263−264 °C; IR (neat): 3415 (w), 1644 (s), 1619 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.48 (br s, 1H), 8.51 (d, J = 6.6 Hz, 1H), 8.10 (d, J = 8.7 Hz, 1H), 7.80 (d, J = 1.5 Hz, 1H), 7.56 (dd, J = 8.5, 1.7 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.2, 174.8, 144.7, 140.0, 128.0, 127.8, 126.8, 125.8, 121.1, 118.2, 30.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_9BrNO_2$ 265.9817, Found 265.9811.

*3-Acetyl-8-chloroquinolin-4(1H)-one (**7k**).* Compound **7k** was synthesized according to general procedure A using methyl 2-amino-3-chlorobenzoate (55.7 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in 76% yield (50.8 mg, 0.229 mmol) as an ivory solid. mp 257−258 °C; IR (neat): 3332 (w), 1666 (s), 1640 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.66 (br s, 1H), 8.54 (s, 1H), 8.14 (d, J = 2.5 Hz, 1H), 7.77 (dd, J = 8.8, 2.5 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 2.60 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 196.3, 174.2, 144.6, 137.9 132.7, 129.7, 129.1, 124.8, 121.4, 117.9, 31.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_9ClNO_2$ 222.0322, Found 222.0321.

*3-Acetyl-6,7-dimethoxyquinolin-4(1H)-one (**7l**).* Compound 7l was synthesized according to general procedure A using methyl 2-amino-4,5-dimethoxybenzoate (63.4 mg, 0.300 mmol) and methyl vinyl ketone (25.0 μL, 0.360 mmol) in >98% yield (74.2 mg, 0.300 mmol) as an ivory solid. mp 230−231 °C; IR (neat): 3432 (w), 1648 (s), 1620 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.36 (br s, 1H), 8.43 (d, J = 4.6 Hz, 1H), 7.60 (s, 1H), 7.08 (s, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 197.5, 173.7, 153.7, 148.0, 142.7, 134.9, 121.0, 116.4, 104.8, 100.1, 56.0, 55.7, 30.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{14}NO_4$ 248.0923, Found 248.0929.

*6-Bromo-3-propionylquinolin-4(1H)-one (**7m**).* Compound **7m** was synthesized according to general procedure B using methyl 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol) and ethyl vinyl ketone (29.7 μL, 0.300 mmol) in 96% yield (81.0 mg, 0.289 mmol) as a yellow solid. mp 240−241 °C; IR (neat): 3421 (m), 1646 (s), 1611 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.66 (br s, 1H), 8.56 (d, J = 6.1 Hz, 1H), 8.30 (s, 1H), 7.89 (dd, J = 8.8, 2.4 Hz, 1H), 7.62 (d, J = 7.2 Hz, 1H), 3.10 (q, J = 7.2 Hz, 2H), 2.60 (t, J = 7.2 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 199.4, 173.8, 144.4, 138.0, 135.2, 129.3, 127.9, 121.4, 117.7, 117.6, 35.6, 8.01; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{11}BrNO_2$ 279.9973, Found 279.9977.

*6-Bromo-3-butyrylquinolin-4(1H)-one (**7n**).* Compound **7n** was synthesized according to general procedure B using methyl 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol) and hex-1-en-3-one (35.1 μL, 0.300 mmol) in 91% yield (80.6 mg, 0.274 mmol) as a yellow solid. mp 250−251 °C; IR (neat): 3321 (w), 1649 (s), 1607 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.79 (br s, 1H), 8.52 (s, 1H), 8.28 (d, J = 2.2 Hz, 1H), 7.86 (dd, J = 8.8, 2.2 Hz, 1H), 7.62 (d, J = 8.7 Hz, 1H), 3.05 (t, J = 7.1 Hz, 2H), 1.60−1.53 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 198.9, 173.9, 144.6, 138.2, 135.3, 129.4, 128.0, 121.6, 117.9, 117.8, 44.5, 17.1, 13.9.; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}BrNO_2$ 294.0130, Found 294.0124.

*6-Bromo-3-hexanoylquinolin-4(1H)-one (**7o**).* Compound **7o** was synthesized according to general procedure B using methyl 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol) and oct-1-en-3-one (45.5 μL, 0.300 mmol) in 91% yield (88.3 mg, 0.274 mmol) as a bright yellow solid. mp 228−229 °C; IR (neat): 3416 (m), 1661 (s), 1605 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.73 (br s, 1H), 8.55 (d, J = 6.6 Hz, 1H), 8.29 (d, J = 2.2 Hz, 1H), 7.88 (dd, J = 8.8, 2.2 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 3.07 (t, J = 7.3 Hz, 1H), 1.56 (d, J = 7.1 Hz, 2H), 1.30−1.27 (m, 4H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 199.0, 173.9, 144.5, 138.1, 135.2, 129.4, 128.0, 121.5, 117.8, 117.7, 42.4, 31.1, 23.4, 22.0, 13.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}BrNO_2$ 322.0443, Found 322.0456.

*6-Bromo-3-(3-phenylpropanoyl)quinolin-4(1H)-one (**7p**).* Compound **7p** was synthesized according to general procedure B using methyl 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol) and 5-phenylpent-1-en-3-one (48.1 mg, 0.300 mmol) in 81% yield (86.9 mg, 0.244 mmol) as a yellow solid. mp 264−265 °C; IR (neat): 3382 (m), 1643 (s), 1605 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.74 (br s, 1H), 8.59 (d, J = 6.8 Hz, 1H), 8.30 (s, 1H), 7.89 (dd, J = 8.9, 1.4 Hz, 1H), 7.63 (d, J = 8.9 Hz, 1H), 7.30−7.27 (m, 4H), 7.21−7.18 (m, 1H), 3.41 (t, J = 7.6 Hz, 2H), 2.89 (t, J = 7.6 Hz, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 198.6, 173.9, 153.5, 147.8, 142.8, 141.9, 134.7, 128.4, 128.3, 125.8, 121.4, 116.3, 105.1, 100.0, 44.1, 29.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{15}BrNO_2$ 356.0286, Found 356.0295.

*6-Bromo-3-(4-phenylbutanoyl)quinolin-4(1H)-one (**7q**).* Compound **7q** was synthesized according to general procedure B using methyl 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol) and 6-phenylhex-1-en-3-one (52.3 mg, 0.300 mmol) in 80% yield (89.2 mg, 0.241 mmol) as a yellow solid. mp 249−250 °C; IR (neat): 3389 (w), 1640 (s), 1613 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.68 (br s, 1H), 8.56 (d, J = 6.8 Hz, 1H), 8.29 (d, J = 2.0 Hz, 1H), 7.87 (dd, J = 8.6, 2.0 Hz, 1H), 7.60 (d, J = 8.6 Hz, 1H), 7.29−7.25 (m, 2H), 7.30−7.15 (m, 3H), 3.11 (t, J = 7.2 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H), 1.89−1.85 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 198.7, 173.9, 144.7, 142.1, 138.1, 135.3, 129.4, 128.4, 128.3, 128.0, 125.8, 121.5, 117.8, 117.7, 42.0, 34.7, 25.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{17}BrNO_2$ 370.0443, Found 370.0431.

*6-Bromo-3-(cyclohexanecarbonyl)quinolin-4(1H)-one (**7r**).* Compound **7r** was synthesized according to general procedure B using 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol) and 1-cyclohexylprop-2-en-1-one (41.5 mg, 0.300 mmol) in 89% yield (89.3 mg, 0.267 mmol) as an ivory solid. mp 267−268 °C; IR (neat): 3432 (w), 1653 (s), 1615 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.68 (br s, 1H), 8.52 (d, J = 6.6 Hz, 1H), 8.32 (d, J = 2.2 Hz, 1H), 7.88 (dd, J = 8.8, 2.2 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 1.86−1.60 (m, 11H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 202.1, 173.6, 144.9, 138.0, 135.2, 128.0, 121.4, 120.8, 117.6, 117.3, 45.6, 32.3, 28.2, 25.7, 25.5, 24.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}BrNO_2$ 334.0443, Found 334.0446.

*3-Benzoyl-6-bromoquinolin-4(1H)-one (**7s**).* Compound **7s** was synthesized according to general procedure B using 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol) and 1-phenylprop-2-en-1-one (39.6 mg, 0.300 mmol) in 92% yield (90.7 mg, 0.276 mmol) as a yellow solid. mp 234−235 °C; IR (neat): 2938 (m), 1638 (s), 1615 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.66 (br s, 1H), 8.38 (d, J = 6.5 Hz, 1H), 8.20 (d, J = 2.0 Hz, 1H), 7.91 (s, 1H), 7.90 (dd, J = 8.8, 2.0 Hz, 1H), 7.73 (d, J = 7.6 Hz, 2H), 7.46 (dd J = 7.6, 7.6 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 194.2, 173.3, 143.6, 138.5, 138.3, 135.3, 132.5, 128.5, 127.7, 127.6, 121.5, 121.4, 119.8, 117.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{11}BrNO_2$ 327.9973, Found 327.9968.

*6-Bromo-3-(4-methoxybenzoyl)quinolin-4(1H)-one (**7t**).* Compound **7t** was synthesized according to general procedure B using methyl 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol) and 1-(4-methoxyphenyl)prop-2-en-1-one (48.7 mg, 0.300 mmol) in 84% yield (90.6 mg, 0.253 mmol) as a yellow solid. mp 254−255 °C; IR (neat): 3392 (w), 1649(s), 1616 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.56 (br s, 1H), 8.33 (d, J = 6.3 Hz, 1H), 8.21 (d, J = 2.3 Hz, 1H), 7.90 (dd, J = 8.8, 2.3 Hz, 1H), 7.74 (d, J = 7.6 Hz, 2H), 7.64 (d, J = 8.8 Hz, 1H), 6.99 (d, J = 8.8 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 192.5, 173.2, 162.9, 142.9, 138.5, 135.1, 131.8, 130.8, 128.4, 127.7, 121.5, 120.5, 117.1, 113.4, 55.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{13}BrNO_3$ 358.0079, Found 358.0084.

*6-Bromo-3-(furan-2-carbonyl)quinolin-4(1H)-one (**7u**).* Compound **7u** was synthesized according to general procedure B using 2-amino-5-bromobenzoate (82.8 mg, 0.360 mmol) and 1-(furan-2-yl)prop-2-en-1-one (36.6 mg, 0.300 mmol) in 91% yield (87.2 mg, 0.274 mmol) as an ivory solid. mp 255−256 °C; IR (neat): 3413 (w),

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1630(s), 1616 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 12.61 (br s, 1H), 9.27 (s, 1H), 8.37 (d, J = 6.3 Hz, 1H), 8.24 (d, J = 1.7 Hz, 1H), 7.98 (s, 1H), 7.64 (d, J = 8.8 Hz, 1H), 7.33 (d, J = 3.2 Hz, 1H), 6.70 (d, J = 3.2 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 180.1, 172.9, 152.6, 147.7, 143.0, 138.5, 135.4, 128.4, 127.8, 121.5, 120.1, 119.7, 117.4, 112.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_9BrNO_3$ 317.9766, Found 317.9772.

Experimental Procedures for the One-Pot, Gram Scale Synthesis of 3-Carbonyl-4-quinolones. *3-Benzoyl-6,7-dimethoxy-2-methylquinolin-4(1H)-one (**4a**).* Methyl 2-amino-4,5-dimethoxybenzoate (**1a**) (1.00 g, 4.73 mmol), CuCl (23.5 mg, 0.237 mmol), dppbz (106 mg, 0.237 mmol), and KO*t*-Bu (26.6 mg, 0.237 mmol) were added to a round-bottom flask (100 mL) charged with a magnetic bar, which was sealed with a rubber septum. The flask was purged with N_2 gas for 5 min. Toluene (21.7 mL) was added to the mixture, which was allowed to premix for 10 min. Then, a solution of (*E*)-1-phenylbut-2-en-1-one (**2a**) (831 mg, 5.68 mmol) in toluene (2 mL) was added to the reaction solution. After the mixture was stirred for 3 h at room temperature, KO*t*-Bu (1.59 g, 14.2 mmol) was added, and the reaction was allowed to stir for an additional 1 h at 22 °C. In open air conditions, an aqueous solution of 6 N HCl (16 mL) was added to the resulting solution, which was allowed to stir for 1 h. The reaction was quenched by adding a saturated aqueous solution of K_2CO_3 (16 mL) and was washed with CH_2Cl_2 (3 × 30 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (MeOH:CH_2Cl_2 = 5:95) to afford the desired product **4a** (1.15 g, 3.56 mmol, 75% yield) as a yellow solid.

*3-Acetyl-6,7-dimethoxyquinolin-4(1H)-one (**7l**).* Methyl 2-amino-4,5-dimethoxybenzoate (**1a**) (1.00 g, 4.73 mmol), CuCl (23.5 mg, 0.237 mmol), DPEphos (128 mg, 0.237 mmol), and KO*t*-Bu (26.6 mg, 0.237 mmol) were added to a round-bottom flask (100 mL) charged with a magnetic bar. The round-bottom flask was sealed with a rubber septum and purged with N_2 gas for 5 min. Toluene (23.7 mL) was added to the mixture, which was allowed to premix for 10 min. Then, methyl vinyl ketone (**6a**) (473 μL, 5.68 mmol) was added to the reaction solution. After the mixture was stirred for 3 h at room temperature, KO*t*-Bu (1.59 g, 14.2 mmol) was added, and the reaction was allowed to stir for an additional 1 h at 22 °C. The resulting solution was quenched with an aqueous solution of 6 N HCl (16 mL) and allowed to stir for 10 min in open air conditions. The organic layers were washed with CH_2Cl_2 (3 × 30 mL), combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was recrystallized from dichloromethane and diethyl ether to afford the desired product **7l** (1.12 g, 4.53 mmol, 96% yield) as an ivory solid.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b03162.

^1H NMR and ^{13}C NMR spectra for all products (PDF)

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Notes

The authors declare no competing financial interest.

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