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One-Pot Synthesis of 3-Hydroxyquinolin-2(1*H*)-ones from *N*-Phenylacetoacetamide via PhI(OCOCF$_3$)$_2$-Mediated α-Hydroxylation and H$_2$SO$_4$-Promoted Intramolecular Cyclization

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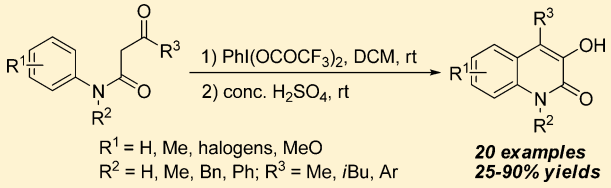
Supporting Information

ABSTRACT: A clean, one-pot synthesis of the biologically important 3-hydroxyquinolin-2(1*H*)-one compounds has been realized from the readily available *N*-phenylacetoacetamide derivatives through a PhI(OCOCF$_3$)$_2$-mediated α-hydroxylation and a H$_2$SO$_4$-promoted intramolecular condensation. The hydroxyl group in the generated α-hydroxylated intermediate can be well tolerated in the second H$_2$SO$_4$-promoted cyclization step.



3-Hydroxyquinolin-2(1*H*)-ones are a biologically important class of compounds that have attracted much attention in recent years.[1] For examples, naturally occurring viridicatin (**1**), viridicatol (**2**), and 3-*O*-methylviridicatin (**3**) (Figure 1), fungal

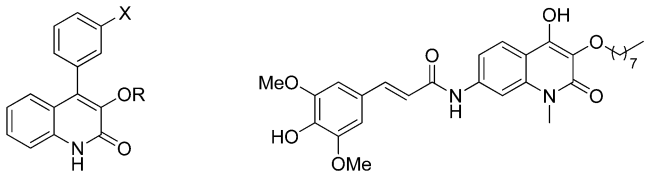


Figure 1. Representative 3-hydroxyquinolin-2(1*H*)-one compounds found in natural product and pharmaceutical agents.

metabolites isolated from penicillium species, have been reported to inhibit the replication of human immunodeficiency virus (HIV).[2] Furthermore, compounds containing the 3-hydroxyquinolin-2(1*H*)-one skeleton have also been intensively studied as pharmaceutical agents such as the antiallergenic agent, TA-270 (**4**) (Figure 1),[3] selective inhibitors of HIV-1 reverse transcriptase,[4] potent D-amino acid oxidase (DAAO) inhibitors,[5] and maxi-K channel openers with antibacterial activities.[6]

Although the significance of this class of compounds is obvious, only a few synthetic strategies have been developed for the construction of the skeleton. Among them, one of the methods was through ring expansion of isatin with aryldiazomethanes, but unfortunately the 3-hydroxyquinolin-2(1*H*)-one derivatives as products were formed in unsatisfactory yields (Figure 2, path a).[7] Huntress and co-workers[8] reported that 2-(*N*-chloroacetamino)-benzaldehyde, an intermediate from the reaction of 2-aminobenzaldehyde with chloroacetic anhydride, could be converted to 3-hydroxyquinolin-2(1*H*)-one in the

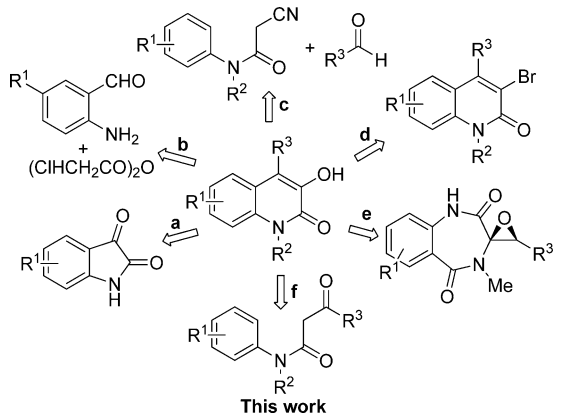


Figure 2. General strategies for the synthesis of the 3-hydroxyquinolin-2(1*H*)-one skeleton.

presence of a base and by heating under reflux (Figure 2, path b). Recently, an efficient synthesis of 3-hydroxy-4-arylquinolin-2(1*H*)-ones through a one-pot Knoevenagel condensation/epoxidation of cyanoacetanilides followed by decyanative epoxide-arene cyclization was reported by Kobayashi and Harayama (Figure 2, path c).[9] Another method utilized a Pd$_2$(dba)$_3$-catalyzed coupling reaction mediated by *tert*-butyl X-Phos; 3-hydroxyquinolin-2(1*H*)-one could be prepared from its bromo precursor in good yield (Figure 2, path d).[10] Finally, viridicatin and viridicatol could be transformed from cyclopenin and cyclopenol respectively through a decarboxylation/rearrangement process (Figure 2, path e).[11] Although the existing methods have their own merits in the preparation of certain 3-hydroxyquinolin-2(1*H*)-one derivative(s), the search for a general method that is applicable to the construction of

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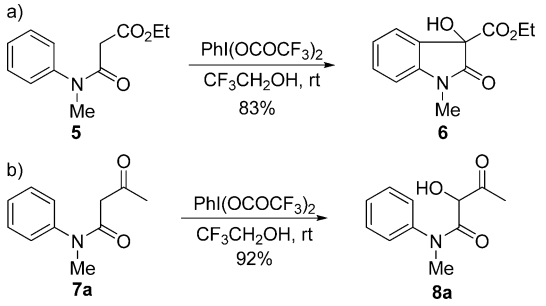
the 3-hydroxyquinolin-2(1*H*)-one ring bearing a variety of R^2 and R^3 substituents remains highly desirable. Herein, we report a new strategy developed for the convenient synthesis of variously functionalized 3-hydroxyquinolin-2(1*H*)-ones starting from the readily available *N*-phenylacetoacetamide substrates (Figure 2, path f). In a one-pot manner, the reactions proceed through a hypervalent iodine reagent-mediated α-hydroxylation and followed by a H_2SO_4-promoted intramolecular annulation step.

In our previous work, the reaction of phenyliodine bis(trifluoroacetate) (PIFA) with anilide **5** in CF_3CH_2OH was found to give 3-hydroxy-2-oxindole derivative **6** through an oxidative C−C bond formation and the subsequent oxidative hydroxylation (Scheme 1a).[12] However, when the terminal

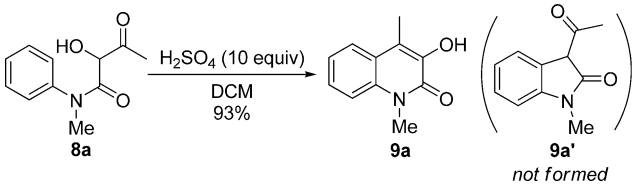
Scheme 1. Different Reaction Pathways of PIFA with Anilides Bearing Ethoxycarbonyl versus Acetyl Group



ethoxycarbonyl group in anilide **5** was changed to an acetyl group, the corresponding *N*-methyl-3-oxo-*N*-phenylbutanamide **7a** was, unexpectedly, converted predominantly to the uncyclized hydroxylated product **8a** under the same conditions, with no cyclized 3-hydroxy-2-oxindole product detected (Scheme 1b).

Initially, we visualized the α-hydroxyl anilide **8a** to undergo cyclization under acidic dehydrative conditions to give the 2-oxindole product **9a′**.[13] But to our surprise, upon treatment of **8a** with concentrated H_2SO_4, an unexpected 3-hydroxyquinolin-2(1*H*)-one **9a** was instead achieved in an excellent 93% yield (Scheme 2).[14] The finding that the hydroxyl functionality

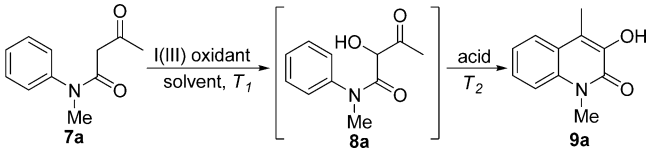
Scheme 2. Formation of 3-Hydroxy-1,4-dimethylquinolin-2(1*H*)-one



in α-hydroxyl anilide **8a** can be well tolerated in the acidic environment during the cyclization step opens the door to a new approach for the convenient construction of the biologically active 3-hydroxyquinolin-2(1*H*)-one compounds, that is, from the readily available *N*-phenylacetoacetamides through α-hydroxylation and the subsequent dehydrative cyclization.

In an effort to develop a one-pot protocol for the two-step reaction mentioned above, we used substrate **7a** to further screen for the optimal reaction conditions. Although CF_3CH_2OH (TFE) was a desirable solvent for the PIFA-mediated α-hydroxylation step, it was not efficient for the second step since only a trace amount of the desired product **9a** was obtained after conc. H_2SO_4 was added to the reaction mixture (Table 1, entry 1).

Table 1. Optimization of Reaction Conditions[a]



entry	oxidant	solvent	time 1	acid	time 2	yield (%)[b]
1	PIFA	TFE	2 h	H_2SO_4	1 h	trace
2[c]	**PIFA**	**DCM**	**10 min**	**H_2SO_4**	**15 min**	**88**
3	PIFA	toluene	10 min	H_2SO_4	15 min	72
4	PIFA	MeCN	1 h	H_2SO_4	2 h	<10
5	PIFA	EtOAc	10 min	H_2SO_4	2 h	ND[d]
6	PIDA	DCM	2 h	H_2SO_4	–	ND
7[e]	PIFA	DCM	10 min	PPA	3 h	52
8[f]	PIFA	DCM	10 min	$AlCl_3$	2 h	ND
9[f]	PIFA	DCM	10 min	$FeCl_3$	2 h	ND

[a]Reaction conditions: all reactions were carried out with the termination of the first step, by mixing **7a** (0.5 mmol) and oxidant (0.55 mmol) in solvent (2.5 mL) and then adding conc. H_2SO_4 (10 equiv) at rt unless otherwise stated. [b]Isolated overall yields over two steps. [c]**8a** could be obtained in 94% yield if isolated after the first step. [d]No desired product. [e]Reaction was performed at 100 °C after the evaporation of DCM and introduction of PPA (10 equiv). [f]3 equiv of Lewis acid was used.

Switching the solvent to the nonpolar DCM not only furnished the α-hydroxylated intermediate **8a** in a comparably excellent yield (94%) within a short period of reaction time (10 min) but also smoothly converted the intermediate **8a** to the desired cyclized product **9a**, separated in an overall 88% yield after the introduction of 10 equiv[15] of conc. H_2SO_4 to the reaction mixture (Table 1, entry 2). Further solvent screening showed that nonpolar toluene also worked well for this one-pot protocol, while other polar solvents including MeCN and EtOAc were not suitable, mainly because they were not effective for the second H_2SO_4-promoted dehydration step (Table 1, entries 4 and 5). The less potent PIDA, although effective for the *N*-unsubstituted anologs of **7a** to undergo α-acetoxylation,[16] was found to be ineffective for substrate **7a** in which the N-atom was substituted with a methyl group, to undergo α-hydroxylation (Table 1, entry 6). Polyphosphoric acid (PPA), which had been successively used for the dehydrative cyclization of acetoacetamide,[17] was also investigated in our reaction. However, the cyclization did not occur at room temperature, and raising the reaction temperature to 100 °C only afforded an overall 52% yield of the desired product (Table 1, entry 7). Lewis acids such as $AlCl_3$ and $FeCl_3$ (Table 1, entries 8 and 9) and other protonic acids including TFA and AcOH were also studied, but no desired cyclized product was observed in any of the cases (not shown).

With the optimized conditions established (Table 1, entry 2), the substrate scope of the reaction with regard to the substituents on the aromatic ring (R^1), on the nitrogen atom (R^2), and on the carbonyl moiety (R^3) of anilides **7** was investigated (Table 2). It seems that both the electron-donating and -withdrawing groups were tolerated in the process, as the desired products were obtained in good to excellent yields

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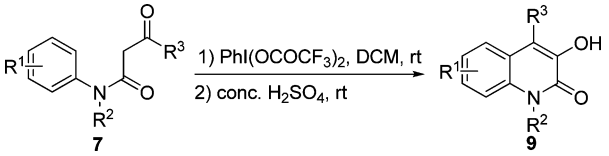
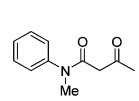
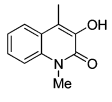
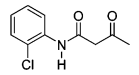
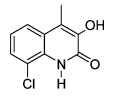
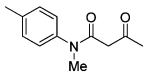
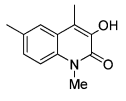
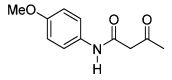
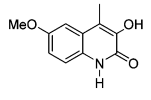
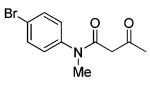
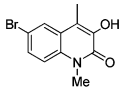
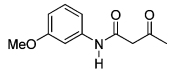
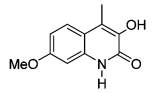
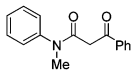
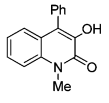
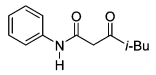
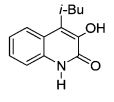
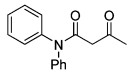
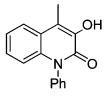
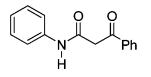
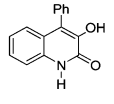
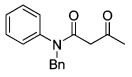
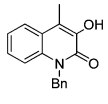
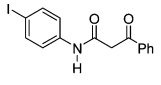
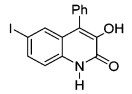
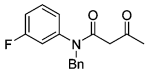
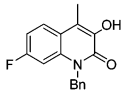
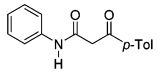
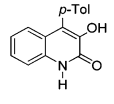
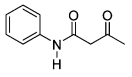
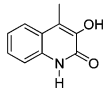
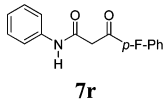
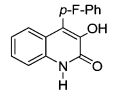
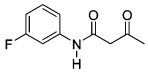
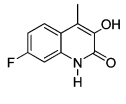
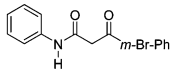
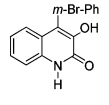
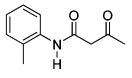
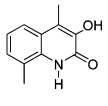
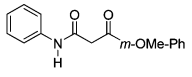
Table 2. Synthesis of 3-Hydroxyquinolin-2-(1*H*)-ones via *α*-Hydroxylation and Intramolecular Cyclization of *N*-Phenylacetoacetamide[a]



7 **9**

entry	anilide **7**	product **9**	time[b]	yield (%)[c]	entry	anilide **7**	product **9**	time[b]	yield (%)[c]
1	 **7a**	 **9a**	15 min	88	11	 **7k**	 **9k**	3 h	40
2	 **7b**	 **9b**	15 min	90	12	 **7l**	 **9l**	2 h	35
3	 **7c**	 **9c**	30 min	72	13	 **7m**	 **9m**	2 h	30
4	 **7d**	 **9d**	2 h	25	14	 **7n**	 **9n**	3 h	64
5	 **7e**	 **9e**	2 h	82	15	 **7o**	 **9o (1)**	3 h	60
6	 **7f**	 **9f**	1.5 h	79	16	 **7p**	 **9p**	5 h	65
7	 **7g**	 **9g**	2 h	67	17	 **7q**	 **9q**	3 h	75
8	 **7h**	 **9h**	3 h	70	18	 **7r**	 **9r**	3 h	78
9	 **7i**	 **9i**	3 h	74	19	 **7s**	 **9s**	3 h	60
10	 **7j**	 **9j**	2 h	50	20	 **7t**	**9t**	3 h	40

[a]General conditions: (1) Substrate **1** (0.5 mmol), PIFA (0.55 mmol) in DCM (2.5 mL) at rt for 12 min; (2) Conc. H_2SO_4 (266 μL), rt. [b]Time for the second step. [c](1) Purified via silica gel column chromatography; (2) Isolated yields over two steps.

(Table 2, entries 2 and 3). When the R^3 group in **7a** was replaced with a phenyl group, the corresponding **7d** also underwent cyclization to give product **9d**, but in a much lower yield (Table 2, entry 4). On the other hand, when the methyl

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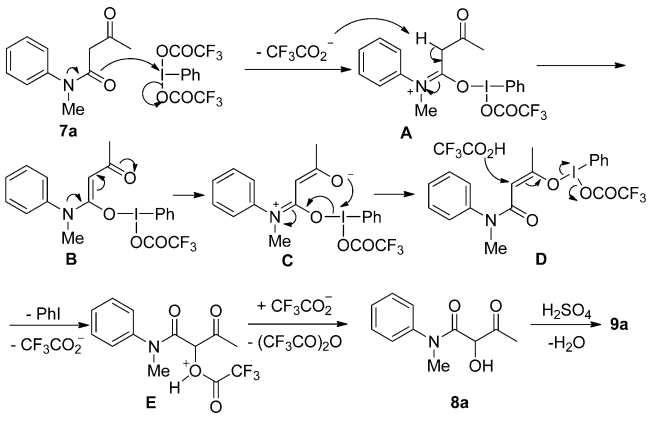
group on the N-atom in **7a** was changed to the bulkier phenyl or benzyl group, the reaction was not affected and the cyclized product could be obtained in good yields (Table 2, entries 5–7).

Our next step was to examine the reactions with a series of *N*-unsubstituted 3-hydroxyquinolin-2-(1*H*)-ones, as the product structure resembles that of viridicatin. As summarized in Table 2, the method was also applicable to the synthesis of a variety of 3-hydroxyquinolin-2-(1*H*)-ones with a free NH moiety (entries 8–20). Specifically, for the substrates bearing no substitution or electron-withdrawing group on the aromatic ring, the reaction afforded the cyclized products in satisfactory yields (Table 2, entries 8 and 9). However, when the sterically hindered *ortho*-substituted substrates were applied, the yields obtained were relatively lower (Table 2, entries 10 and 11). Especially, when the substrates bearing a methoxy group on the aromatic ring, the reaction afforded the desired product in much lower yields (Table 2, entries 12 and 13), which is probably due to the formation of an array of unidentified byproducts as a result of overoxidations of the electron-rich aromatic ring. When the R^3 group in **7h** was replaced with a isobutyl group, the reaction gave the desired product **9n** in a satisfactory yield (Table 2, entry 14). Subjecting substrate **7o** to the reaction conditions smoothly afforded the biologically active Viridicatin (**1**) in 60% yield (Table 2, entry 15), which is quite different from the case in regard to the reaction of **7d** in terms of the effect of the phenyl group on the reaction yield. Using the same approach, other Viridicatin derivatives bearing various substitutions were also conveniently synthesized in satisfactory yields (Table 2, entries 16–19). Although in a relatively lower yield, 3-hydroxyquinolin-2-(1*H*)-one **9t**, the precursor of viridicatol **2**, was achieved from the readily available substrate **7t** using this method. It is worth noting that the obtained compound **9t** can readily undergo demethylation in the presence of BBr_3 to afford viridicatol **2** in a satisfactory 80% yield.[18] Thus, both the naturally occurring viridicatin **1** and viridicatol **2** can be efficiently and concisely obtained by this one-pot approach.

Based on the mechanism[12] described for the PIFA-mediated synthesis of 3-hydroxy-2-oxindoles and spirooxindoles from anilides, we propose a mechanistic sequence for the α-hydroxylation step (Scheme 3). First, the reaction of **7a** with PIFA gives the iminium salt **A**, which turns into the enamine intermediate **B** after losing a proton. Considering the fact that no cyclized 3-hydroxy-2-oxindole product was produced from **7a**, as opposed to **5**, we postulated that the relatively more potent electron-withdrawing carbonyl group of the acetyl moiety in **B** probably facilitates the conversion of **B** into its ylide salt **C**. With the nucleophilic attack by the enolate on the iodine(III) center, intermediate **C** was concerted into the highly electrophilic enolate **D**.[19] Further nucleophilic attack of the trifluoroacetic acid on the sp^2 carbon center of **D** realizes the trifluoroacetoxylation of intermediate **E**, along with the generation of phenyl iodide and the trifluoroacetate anion. Since water was found to be unnecessary for the α-hydroxylation step, we propose here that the trifluoroacetate anion acts as a nucleophile to attack the electron-deficient carbonyl center of the trifluoroacetate moiety in **E**, which then undergoes the elimination of one molecule of trifluoroacetic anhydride to give α-hydroxyl *N*-phenylacetoacetamide intermediate **8a**.

Scheme 3. Proposed Mechanistic Pathway from 7a to 8a



In summary, we have demonstrated a new strategy for the construction of the 3-hydroxyquinolin-2(1*H*)-ones skeleton through the $PhI(OCOCF_3)_2$-mediated α-hydroxylation of *N*-phenylacetoacetamides, followed by H_2SO_4-promoted dehydrative cyclization reactions. The main advantages of this strategy are the ready availability of the substrates, a convenient one-pot protocol, the diversity of substitutions, and simple workup, and the most significant feature of this method is that it allows for a convenient access to the naturally occurring viridicatin and its derivatives. In view of the versatile biological activities associated with 3-hydroxyquinolin-2(1*H*)-one compounds, our method may find its application in exploring the synthesis of many other biologically potent compounds bearing various substituents on the benzene rings.

EXPERIENMENTAL SECTION

General Information. All reactions were stirred magnetically under an air atmosphere and performed in standard glassware heated at 80 °C for 3 h before use. Different substituted *N*-methylaniline,[20] *N*-benzyl aniline,[21] acetoacetic acid,[22] and 3-oxo-3-arylpropanoic acid[23] were synthesized according to the literature procedures. Other reagents and solvents were purchased as reagent grade and were used without further purification. Flash chromatography was performed on silica gel 200–300 m, and the eluent was a mixture of ethyl acetate (EA) and petroleum ether (PE). Thin layer chromatography (TLC) was performed on glass backed plates precoated with silica (GF254), which were developed using standard visualizing agents. ^1H and ^{13}C NMR spectra were recorded on a 600 or 400 MHz spectrometer at 25 °C. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: δ = 7.26 ppm for ^1H and $CDCl_3$: δ = 77.0 ppm for ^{13}C as well as DMSO-d_6: δ = 2.50 ppm for ^1H and DMSO-d_6: δ = 39.5 ppm for ^{13}C). High-resolution mass spectra (HRMS) were performed on a Q-TOF microspectrometer. Melting points were performed on recrystallized solids and recorded on a national standard melting point apparatus and are uncorrected.

General Procedures for the Preparation of Substrates. Procedure A.[12,24] Adapted from a previously reported procedure with some modifications. To a solution of *N*-substituted aniline (10 mmol) in DCM (50 mL) was added successively acetoacetic acid (0.51 g, 10 mmol) and DCC (2.06 g, 10 mmol). The reaction mixture was stirred at room temperature until TLC indicated the total consumption of the substrate. The mixture was filtrated through a short pad of silica gel, and the filtrate was evaporated to partially remove the solvent. The residue was treated with saturated aq. $NaHCO_3$ (50 mL) and extracted with EtOAc (50 mL × 3). The combined organic layer was dried with anhydrous Na_2SO_4. The solvent was removed under vacuum, and the crude product was purified by silica gel flash column chromatography.

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Procedure B:[25] A mixture of ethylacetoacetate (1.30 g, 10 mmol) and aniline (10 mmol) was taken into a round-bottom flask and refluxed under stirring for 24 h. The mixture was concentrated under vacuum, and then the crude product was purified by column chromatography using EA/PE to give acetoacetanilide **7**.

Procedure C.[26] Acetoacetanilide (10 mmol) was dissolved in aqueous sodium hydroxide solution (20% W/W, 6 mL). The resulting solution was externally cooled by an ice bath and stirred persistently. When the temperature of the solution reached 2 °C, aroylchloride (10 mmol) was added gradually while the temperature of the reaction mixture was kept below 5 °C. After all the acid chloride was added, the mixture was stirred for 0.5 h at 5 °C and for an additional 30 min at room temperature. The reaction mixture was then diluted with aqueous ammonium hydroxide solution (25% W/W, 1.5 mL) containing ammonium chloride (10 mmol) and stirred for 5 min. The resulting mixture was heated to 40−50 °C, left to stand overnight at room temperature, and filtered. The crude product was purified by column chromatography using EA/PE to give aroylacetanilides.

***N*-Methyl-3-oxo-*N*-phenylbutanamide (7a).**[27] By following the general procedure B, **7a** was purified by silica gel chromatography (EA/PE = 10/90). Yield: 50%, 0.956 g, colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (t, J = 7.2 Hz, 2H), 7.36 (t, J = 7.2 Hz, 1H), 7.20 (d, J = 7.2 Hz, 2H), 3.30 (s, 2H), 3.30 (s, 3H), 2.10 (s, 3H).

2-Hydroxy-*N*-methyl-3-oxo-*N*-phenylbutanamide (8a). By following the literature procedure,[12] **8a** was purified by silica gel chromatography (EA/PE = 15/85). Yield: 92%, 190 mg, yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (t, J = 7.2 Hz, 2H), 7.41 (t, J = 7.2 Hz, 1H), 7.26 (d, J = 7.2 Hz, 2H), 4.55 (s, 1H), 4.06 (br s, 1H), 3.36 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 203.9, 168.7, 141.9, 130.0, 128.7, 127.6, 75.2, 38.1, 26.0; HRMS (ESI) m/z calcd for $C_{11}H_{13}NO_3Na$ [M + Na^+] 230.0788, found 230.0793.

***N*-Methyl-3-oxo-*N*-*p*-tolylbutanamide (7b) and (*Z*)-3-Hydroxy-*N*-methyl-*N*-*p*-tolylbut-2-enamide (7b′).** By following general procedure A, a mixture of **7b** and **7b′** was purified by silica gel chromatography (EA/PE = 10/90). Yield: 80%, 1.642 g, (ketone/enol = 3.75: 1), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) major isomer (ketone) δ 7.21 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 3.30 (s, 2H), 3.28 (s, 3H), 2.38 (s, 3H), 2.11 (s, 3H); minor isomer (enol) δ 14.27 (s, 1H), 7.21 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 4.68 (s, 1H), 3.27 (s, 3H), 2.39 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 173.5, 171.9, 166.8, 141.0, 140.8, 138.3, 137.5, 130.5, 130.2, 127.1, 126.9, 88.9, 49.8, 37.3, 36.3, 30.3, 21.6, 21.0 (two peaks overlapped); HRMS (ESI) m/z calcd for $C_{12}H_{15}NO_2Na$ [M + Na^+] 228.1000, found 228.1007.

***N*-(4-Bromophenyl)-*N*-methyl-3-oxobutanamide (7c) and (*Z*)-*N*-(4-Bromophenyl)-3-hydroxyl -*N*-methylbut-2-enamide (7c′).** By following general procedure A, a mixture of **7c** and **7c′** was purified by silica gel chromatography (EA/PE = 10/90). Yield: 82%, 2.215 g, (ketone/enol = 2.5: 1), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) major isomer (ketone) δ 7.55 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 3.32 (s, 2H), 3.28 (s, 3H), 2.13 (s, 3H); minor isomer (enol) δ 14.18 (s, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 4.70 (s, 1H), 3.28 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 171.7, 166.4, 142.6, 142.4, 137.4, 133.1, 132.8, 130.2, 129.1, 129.0, 122.1, 88.6, 49.8, 37.3, 36.3, 30.4, 21.7; HRMS (ESI) m/z calcd for $C_{11}H_{12}{}^{79}BrNO_2Na$ [M + Na^+] 291.9944, found 291.9947.

***N*-Methyl-3-oxo-*N*,3-diphenylpropanamide (7d) and (*Z*)-3-Hydroxy-*N*-methyl-*N*,3-diphenylacrylamide (7d′).** By following general procedure A, a mixture of **7d** and **7d′** was purified by silica gel chromatography (EA/PE = 10/90). Yield: 82%, 2.077 g, (ketone/enol = 1: 1), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) isomer (ketone) δ 7.76−7.26 (m, 10H), 3.86 (s, 2H), 3.36 (s, 3H); isomer (enol) δ 14.69 (s, 1H), 7.76−7.26 (m, 10H), 5.39 (s, 1H), 3.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 172.1, 170.2, 167.1, 143.7, 143.4, 136.4, 134.6, 133.3, 130.6, 129.9, 129.8, 128.6 (two peaks overlapped), 128.3, 128.3, 127.8, 127.3, 127.3, 125.9, 86.9, 45.5, 37.4, 36.6; HRMS (ESI) m/z calcd for $C_{16}H_{15}NO_2Na$ [M + Na^+] 276.1000, found 276.1007.

3-Oxo-*N*,*N*-diphenylbutanamide (7e) and (*Z*)-3-Hydroxy-*N*,*N*-diphenylbut-2-enamide (7e′).[28] By following general procedure A, a mixture of **7e** and **7e′** was purified by silica gel chromatography (EA/PE = 10/90). Yield: 87%, 2.204 g, (ketone/enol = 3:2), white solid, mp 83−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) isomer (ketone) δ 7.39−7.20 (m, 10H), 3.48 (s, 2H), 2.14 (s, 3H); isomer (enol) δ 14.11 (s, 1H), 7.39−7.20 (m, 10H), 4.86 (s, 1H), 1.87 (s, 3H).

***N*-Benzyl-3-oxo-*N*-phenylbutanamide (7f) and (*Z*)-*N*-Benzyl-3-hydroxy-*N*-phenylbut-2-enamide (7f′):**[12] By following general procedure A, a mixture of **7f** and **7f′** was purified by silica gel chromatography (EA/PE = 10/90). Yield: 78%, 2.085 g, (ketone/enol = 2.5:1), white solid, mp 56−58 °C; ^{1}H NMR (400 MHz, $CDCl_3$) major isomer (ketone) δ 7.32−7.23 (m, 8H), 6.99−6.97 (m, 2H), 4.91 (s, 2H), 3.31 (s, 2H), 2.09 (s, 3H); minor isomer (enol) δ 14.31 (s, 1H), 7.32−7.23 (m, 8H), 7.03−7.00 (m, 2H), 4.91 (s, 2H), 4.64 (s, 1H), 1.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 174.4, 171.7, 166.7, 141.8, 137.5, 137.0, 129.7, 129.5, 128.8, 128.5, 128.4, 128.4, 127.9, 127.5, 127.4, 89.1, 53.0, 52.2, 50.1, 30.4, 21.7 (four carbon peaks were missing due to overlapping); HRMS (ESI) m/z calcd for $C_{17}H_{17}NNaO_2^+$ [M + Na^+] 290.1151, found 290.1156.

***N*-Benzyl-*N*-(3-fluorophenyl)-3-oxobutanamide (7g) and (*Z*)-*N*-benzyl-*N*-(3-fluorophenyl)-3-hydroxybut-2-enamide (7g′).** By following general procedure A, a mixture of **7g** and **7g′** was purified by silica gel chromatography (EA/PE = 10/90). Yield: 80%, 2.283 g, (ketone/enol = 2: 1), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) major isomer (ketone) δ 7.29−7.21 (m, 6H), 7.03 (t, J = 8.0 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.73 (d, J = 9.2 Hz, 1H), 4.90 (s, 2H), 3.34 (s, 2H), 2.13 (s, 3H); minor isomer (enol) δ 14.20 (s, 1H), 7.29−7.21 (m, 6H), 7.03 (t, J = 8.0 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 6.79 (d, J = 9.2 Hz, 1H), 4.90 (s, 2H), 4.67 (s, 1H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.0, 175.0, 171.6, 166.4, 162.8 (d, J_{C-F} = 247.8 Hz), 143.2 (d, J_{C-F} = 9.8 Hz), 137.1, 136.6, 130.8 (d, J_{C-F} = 8.9 Hz), 130.6 (d, J_{C-F} = 10.0 Hz), 128.7, 128.5, 128.3, 127.7, 127.5, 124.3 (d, J_{C-F} = 3.1 Hz), 115.8 (d, J_{C-F} = 21.8 Hz), 115.7 (d, J_{C-F} = 20.9 Hz), 114.9, 88.8, 53.0, 52.1, 50.0, 30.4, 21.8 (five carbon peaks were missing due to overlapping); HRMS (ESI) m/z calcd for $C_{17}H_{16}{}^{19}FNO_2Na$ [M + Na^+] 308.1057, found 308.1059.

3-Oxo-*N*-phenylbutanamide (7h).[25] By following general procedure B, **7h** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 44%, 0.779 g, white solid, mp 85−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (br s, 1H), 7.54 (d, J = 7.8 Hz, 2H), 7.33 (t, J = 7.8 Hz, 2H), 7.12 (t, J = 7.8 Hz, 1H), 3.59 (s, 2H), 2.33 (s, 3H).

***N*-(3-Fluorophenyl)-3-oxobutanamide (7i).**[29] By following general procedure A, **7i** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 86%, 1.678 g, white solid, mp 65−67 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.27 (br s, 1H), 7.52 (m, 1H), 7.30−7.24 (m, 1H), 7.18 (d, J = 12 Hz, 1H), 6.82 (ddd, J = 12, 2.4 Hz, 1H), 3.60 (s, 2H), 2.34 (s, 3H).

3-Oxo-*N*-*o*-tolylbutanamide (7j).[30] By following general procedure A, **7j** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 82%, 1.566 g, white solid, mp 105−106 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.16 (br s, 1H), 7.91 (d, J = 7.2 Hz, 1H), 7.21−7.18 (m, 2H), 7.06 (t, J = 7.2 Hz, 1H), 3.62 (s, 2H), 2.33 (s, 6H).

***N*-(2-Chlorophenyl)-3-oxobutanamide (7k).**[25] By following general procedure A, **7k** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 80%, 1.693 g, white solid, mp 105−107 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.60 (br s, 1H), 8.33 (d, J = 7.8 Hz, 1H), 7.38 (dd, J = 7.8, 1.2 Hz, 1H), 7.26 (td, J = 7.8, 1.2 Hz, 1H), 7.05 (td, J = 7.8, 1.2 Hz, 1H), 3.65 (s, 2H), 2.34 (s, 3H).

***N*-(4-Methoxyphenyl)-3-oxobutanamide (7l).**[25] By following the general procedure B, **7l** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 45%, 0.932 g, white solid, mp 116−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (br s, 1H), 7.44 (d, J = 8.8 Hz, 2H), 7.85 (d, J = 8.8 Hz, 2H), 3.79 (s, 3H), 3.57 (s, 2H), 2.32 (s, 3H).

***N*-(3-Methoxyphenyl)-3-oxobutanamide (7m).**[29] By following the general procedure B, **7m** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 47%, 0.974 g, white solid, mp 76−77 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.07 (br s, 1H), 7.28 (s, 1H), 7.22 (t, J = 7.8 Hz, 1H), 7.04 (d, J = 7.8 Hz, 1H), 6.68 (d, J = 7.8 Hz, 1H), 3.81 (s, 3H), 3.59 (s, 2H), 2.33 (s, 3H).

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5-Methyl-3-oxo-*N*-phenylhexanamide (7n).[31] By following general procedure A, **7n** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 85%, 1.863 g, white solid, mp 90−92 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.18 (br s, 1H), 7.55 (d, J = 7.8 Hz, 2H), 7.32 (t, J = 7.8 Hz, 2H), 7.11 (t, J = 7.8 Hz, 1H), 3.53 (s, 2H), 2.45 (d, J = 6.6 Hz, 2H), 2.18 (m, 1H), 0.96 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.5, 163.5, 137.6, 129.0, 124.5, 120.1, 53.0, 49.4, 24.4, 22.4.

3-Oxo-*N*,3-diphenylpropanamide (7o).[31] By following general procedure A, **7o** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 89%, 2.219 g, white solid, mp 106−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (br s, 1H), 8.05 (d, J = 7.8 Hz, 2H), 7.65 (t, J = 7.8 Hz, 1H), 7.59 (d, J = 7.8 Hz, 2H), 7.53 (t, J = 7.8 Hz, 2H), 7.34 (t, J = 7.8 Hz, 2H), 7.13 (t, J = 7.8 Hz, 1H), 4.13 (s, 2H).

***N*-(4-Iodophenyl)-3-oxo-3-phenylpropanamide (7p).**[32] By following general procedure A, **7p** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 89%, 3.2499 g, white solid, mp 174−176 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.42 (br s, 1H), 8.02 (d, J = 7.8 Hz, 2H), 7.66−7.62 (m, 3H), 7.52 (t, J = 7.8 Hz, 2H), 7.38 (d, J = 7.8 Hz, 2H), 4.09 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.5, 163.7, 137.9, 137.4, 136.0, 134.5, 129.0, 128.6, 122.0, 87.8, 45.2.

3-Oxo-*N*-phenyl-3-*p*-tolylpropanamide (7q).[33] By following the general procedure A, **7q** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 90%, 2.279 g, white solid, mp 114−115 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.35 (br s, 1H), 7.92 (d, J = 7.8 Hz, 2H), 7.58 (d, J = 7.8 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.11 (t, J = 7.8 Hz, 1H), 4.07 (s, 2H), 2.43 (s, 3H).

3-(4-Fluorophenyl)-3-oxo-*N*-phenylpropanamide (7r).[34] By following general procedure C, **7r** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 49%, 1.260 g, white solid, mp 132−134 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.15 (br s, 1H), 8.07 (t, J = 7.8 Hz, 2H), 7.57 (d, J = 7.8 Hz, 2H), 7.33 (t, J = 7.8 Hz, 2H), 7.19 (t, J = 7.8 Hz, 2H), 7.13 (t, J = 7.8 Hz, 1H), 4.08 (s, 2H).

3-(3-Bromophenyl)-3-oxo-*N*-phenylpropanamide (7s).[26] By following general procedure A, **7s** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 88%, 2.799 g, white solid, mp 123−124 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.06 (br s, 1H), 8.17 (s, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.57 (d, J = 7.8 Hz, 2H), 7.41 (t, J = 7.8 Hz, 1H), 7.34 (t, J = 7.8 Hz, 2H), 7.13 (t, J = 7.8 Hz, 1H), 4.09 (s, 2H).

3-(3-Methoxyphenyl)-3-oxo-*N*-phenylpropanamide (7t).[35] By following the general procedure C, **7t** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 45%, 1.211 g, white solid, mp 97−99 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.28 (br s, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 7.8 Hz, 2H), 7.54 (d, J = 2.4 Hz, 1H), 7.42 (t, J = 7.8 Hz, 1H), 7.34 (t, J = 7.8 Hz, 2H), 7.18 (dd, J = 7.8, 2.4 Hz, 1H), 7.12 (t, J = 7.8 Hz, 1H), 4.11 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.4, 163.7, 160.1, 137.6, 137.4, 130.0, 129.0, 124.6, 121.3, 121.0, 120.2, 112.6, 55.5, 45.7; HRMS (ESI) m/z calcd for $C_{16}H_{15}NO_3Na$ [M + Na^+] 292.0944, found 292.0947.

General Procedure for the Preparation of the Products. To a solution of *N*-phenylacetoacetamide **7** (0.5 mmol) in DCM (2.5 mL) was added PIFA (237 mg, 0.55 mmol), and the reaction mixture was stirred at room temperature. Then conc. H_2SO_4 (266 μL) was added to the reaction mixture when TLC indicated the total consumption of the *N*-phenylacetoacetamide **7**. The reaction was monitored by TLC. The solution was diluted with cooled water (50 mL) until the complete consumption of **8** and extracted with EtOAc (50 mL × 3). The combined organic layer was dried with anhydrous Na_2SO_4. The solvent was removed under vacuum, and the crude product was purified by flash column chromatography on silica gel using a mixture of PE and EA as eluent to give the desired product.

3-Hydroxy-1,4-dimethylquinolin-2(1*H*)-one (9a). By following the general procedure, **9a** was purified by silica gel chromatography (EA/PE = 5/95). Yield: 88%, 83 mg, white solid, mp 209−210 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.09 (br s, 1H), 7.67 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 7.2 Hz, 1H), 7.46 (t, J = 7.2 Hz, 1H), 7.29 (d, J = 7.2 Hz, 1H), 3.71 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 157.5, 142.0, 134.1, 126.7, 123.6, 122.4, 121.7, 118.1, 114.4, 29.6, 10.5; HRMS (ESI) m/z calcd for $C_{11}H_{11}NO_2Na$ [M + Na^+] 212.0682, found 212.0687.

3-Hydroxy-1,4,6-trimethylquinolin-2(1*H*)-one (9b). By following the general procedure, **9b** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 90%, 92 mg, white solid, mp 198−200 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.01 (s, 1H), 7.46 (s, 1H), 7.37 (d, J = 6.8 Hz, 1H), 7.27 (d, J = 6.8 Hz, 1H), 3.67 (s, 3H), 2.39 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.8, 142.5, 132.7, 131.9, 128.3, 124.0, 122.1, 118.4, 114.9, 30.1, 21.0, 11.0; HRMS (ESI) m/z calcd for $C_{12}H_{13}NO_2Na$ [M + Na^+] 226.0838, found 226.0843.

6-Bromo-3-hydroxy-1,4-dimethylquinolin-2(1*H*)-one (9c). By following the general procedure, **9c** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 72%, 97 mg, white solid, mp 212−214 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.17 (br s, 1H), 3.81 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 142.3, 133.2, 129.8, 126.5, 124.4, 117.5, 116.3, 115.8, 30.3, 10.8; HRMS (ESI) m/z calcd for $C_{11}H_{10}{}^{79}BrNO_2Na$ [M + Na^+] 289.9787, found 289.9791.

3-Hydroxy-1-methyl-4-phenylquinolin-2(1*H*)-one (9d):[9] By following the general procedure, **9d** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 25%, 32 mg, white solid, mp 200−202 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (t, J = 7.2 Hz, 2H), 7.52−7.39 (m, 6H), 7.26−7.19 (m, 1H), 7.18 (br s, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 140.9, 134.5, 133.0, 130.0, 128.6, 128.3, 127.3, 126.2, 123.3, 123.1, 122.1, 114.2, 30.5.

3-Hydroxy-4-methyl-1-phenylquinolin-2(1*H*)-one (9e). By following the general procedure, **9e** was purified by silica gel chromatography (EA/PE = 25/75). Yield: 82%, 103 mg, white solid, mp 184−185 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.20 (br s, 1H), 7.74−7.72 (m, 1H), 7.64 (t, J = 7.8 Hz, 2H), 7.57 (t, J = 7.8 Hz, 1H), 7.34 (d, J = 7.8 Hz, 2H), 7.27−7.23 (m, 2H), 6.49 (d, J = 7.8 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 157.5, 142.3, 137.5, 135.4, 130.3, 128.9, 128.8, 126.4, 123.7, 122.6, 121.7, 119.2, 115.2, 10.7; HRMS (ESI) m/z calcd for $C_{16}H_{13}NO_2Na$ [M + Na^+] 274.0838, found 274.0839.

1-Benzyl-3-hydroxy-4-methylquinolin-2(1*H*)-one (9f). By following the general procedure, **9f** was purified by silica gel chromatography (EA/PE = 20/80). Yield: 79%, 105 mg, white solid, mp 177−179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.0 Hz, 1H), 7.39−7.21 (m, 8H), 7.16 (br s, 1H), 5.66 (s, 2H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 141.5, 136.0, 133.6, 128.9, 127.4, 127.2, 126.6, 124.1, 123.1, 122.8, 119.3, 115.5, 46.7, 10.9; HRMS (ESI) m/z calcd for $C_{17}H_{15}NO_2Na$ [M + Na^+] 288.0995, found 288.0998.

1-Benzyl-7-fluoro-3-hydroxy-4-methylquinolin-2(1*H*)-one (9g). By following the general procedure, **9g** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 67%, 95 mg, white solid, mp 202−204 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, J = 9.2, 6.0 Hz, 1H), 7.34 (t, J = 7.2 Hz, 2H), 7.28 (t, J = 7.2 Hz, 1H) 7.22 (d, J = 7.2 Hz, 2H), 7.07 (br s, 1H), 7.04−7.00 (m, 2H), 5.59 (s, 2H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8 (d, J_{C-F} = 244.0 Hz), 159.2, 140.8, 135.3, 134.8 (d, J_{C-F} = 10.0 Hz), 129.0, 127.7, 126.5 (two peaks overlapped), 125.7 (d, J_{C-F} = 10.0 Hz), 119.2 (d, J_{C-F} = 8.5 Hz), 111.1 (d, J_{C-F} = 22.4 Hz), 102.2 (d, J_{C-F} = 26.8 Hz), 47.0, 11.1; HRMS (ESI) m/z calcd for $C_{17}H_{14}{}^{19}FNO_2Na$ [M + Na^+] 306.0901, found 306.0903.

3-Hydroxy-4-methylquinolin-2(1*H*)-one (9h). By following the general procedure, **9h** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 70%, 62 mg, white solid, mp 249−250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.97 (br s, 1H), 9.08 (br s, 1H), 7.59 (d, J = 7.8 Hz, 1H), 7.33 (t, J = 7.8 Hz, 1H), 7.27 (d, J = 7.8 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.8, 142.2, 132.7, 126.5, 123.2, 122.4, 121.2, 120.0, 115.1, 10.4; HRMS (ESI) m/z calcd for $C_{10}H_9NO_2Na$ [M + Na^+] 198.0531, found 198.0540.

7-Fluoro-3-hydroxy-4-methylquinolin-2(1*H*)-one (9i). By following the general procedure, **9i** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 74%, 72 mg, white solid,

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mp 249−252 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.05 (br s, 1H), 9.14 (br s, 1H), 7.62 (s, 1H), 7.05−7.04 (m, 2H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.5 (d, J_{C-F} = 240.9 Hz), 158.0, 142.1, 134.0 (d, J_{C-F} = 10.8 Hz), 125.2, 119.3, 118.1, 109.8 (d, J_{C-F} = 21.2 Hz), 101.0 (d, J_{C-F} = 25.7 Hz), 10.6; HRMS (ESI) m/z calcd for $C_{10}H_8{}^{19}FNO_2Na$ [M + Na$^+$] 216.0431, found 216.0436.

3-Hydroxy-4,8-dimethylquinolin-2(1*H*)-one (9j). By following the general procedure, **9j** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 50%, 47 mg, white solid, mp 230−232 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.12 (br s, 1H), 9.11 (br s, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.19 (d, J = 7.8 Hz, 1H), 7.11 (t, J = 7.8 Hz, 1H), 2.44 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 158.2, 142.5, 131.3, 127.9, 123.2, 121.8, 121.3, 121.2, 119.7, 17.5, 10.7; HRMS (ESI) m/z calcd for $C_{11}H_{11}NO_2Na$ [M + Na$^+$] 212.0682, found 212.0682.

8-Chloro-3-hydroxy-4-methylquinolin-2(1*H*)-one (9k). By following the general procedure, **9k** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 40%, 42 mg, white solid, mp 224−226 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.26 (br s, 1H), 9.48 (br s, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.21 (t, J = 7.8 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 157.9, 143.5, 129.3, 126.6, 123.1, 122.7, 122.5, 119.4, 118.4, 10.8; HRMS (ESI) m/z calcd for $C_{10}H_8{}^{35}ClNO_2Na$ [M + Na$^+$] 232.0136, found 232.0137.

3-Hydroxy-6-methoxy-4-methylquinolin-2(1*H*)-one (9l). By following the general procedure, **9l** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 35%, 36 mg, white solid, mp 225−227 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.87 (br s, 1H), 9.06 (br s, 1H), 7.21 (d, J = 8.8 Hz, 1H), 7.03 (d, J = 2.4 Hz, 1H), 6.98 (dd, J = 8.8, 2.4 Hz, 1H), 3.81 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.8, 155.1, 143.7, 127.7, 122.7, 119.5, 116.8, 115.2, 106.3, 55.9, 11.1; HRMS (ESI) m/z calcd for $C_{11}H_{11}NO_3Na$ [M + Na$^+$] 228.0631, found 228.0634.

3-Hydroxy-7-methoxy-4-methylquinolin-2(1*H*)-one (9m). By following the general procedure, **9m** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 30%, 31 mg, white solid, mp 221−223 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.82 (br s, 1H), 8.75 (br s, 1H), 7.51−7.45 (m, 1H), 6.83−6.80 (m, 2H), 3.77 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 158.1, 140.8, 134.3, 124.4, 119.8, 115.1, 110.4, 98.5, 55.1, 10.5 (one carbon peaks was missing due to overlapping); HRMS (ESI) m/z calcd for $C_{11}H_{11}NO_3Na$ [M + Na$^+$] 228.0631, found 228.0634.

3-Hydroxy-4-isobutylquinolin-2(1*H*)-one (9n). By following the general procedure, **9n** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 64%, 70 mg, white solid, mp 192−193 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.03 (br s, 1H), 9.01 (br s, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.32 (t, J = 7.8 Hz, 2H), 7.19 (t, J = 7.8 Hz, 1H), 2.72 (d, J = 7.2 Hz, 2H), 1.97 (m, 1H), 0.93 (s, 6H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 157.8, 143.2, 133.1, 126.1, 123.3, 122.8, 122.0, 120.8, 115.3, 33.1, 27.8, 22.5; HRMS (ESI) m/z calcd for $C_{13}H_{15}NO_2Na$ [M + Na$^+$] 240.0995, found 240.0998.

Viridicatin (9o).[9] By following the general procedure, **9o** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 60%, 72 mg, white solid, mp 268−269 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.23 (br s, 1H), 9.20 (br s, 1H), 7.53−7.42 (m, 7H), 7.10−7.04 (m, 2H).

3-Hydroxy-6-iodo-4-phenylquinolin-2(1*H*)-one (9p). By following the general procedure, **9p** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 65%, 118 mg, white solid, mp >300 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.34 (br s, 1H), 9.48 (br s, 1H), 7.63−7.47 (m, 4H), 7.34 (d, 2H), 7.29 (s, 1H), 7.18 (d, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 158.1, 143.2, 134.5, 133.2, 132.6, 132.1, 129.8, 128.5, 127.9, 123.4, 122.7, 117.5, 85.7; HRMS (ESI) m/z calcd for $C_{15}H_{10}{}^{127}INNaO_2{}^+$ [M + Na$^+$] 385.9648, found 385.9655.

3-Hydroxy-4-*p*-tolylquinolin-2(1*H*)-one (9q). By following the general procedure, **9q** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 75%, 95 mg, white solid, mp 240−242 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.22 (br s, 1H), 9.13 (br s, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.34−7.32 (m, 3H), 7.23 (d, J = 7.8 Hz, 2H), 7.11−7.06 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 158.2, 142.4, 136.9, 133.2, 130.7, 129.7, 128.9, 126.3, 124.4, 123.9, 122.1, 121.0, 115.2, 20.9; HRMS (ESI) m/z calcd for $C_{16}H_{13}NNaO_2{}^+$ [M + Na$^+$] 274.0838, found 274.0841.

4-(4-Fluorophenyl)-3-hydroxyquinolin-2(1*H*)-one (9r). By following the general procedure, **9r** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 78%, 100 mg, white solid, mp 242−245 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.24 (br s, 1H), 9.29 (br s, 1H), 7.40−7.32 (m, 6H), 7.10−7.05 (m, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 161.58 (d, J_{C-F} = 91.2 Hz), 159.17, 142.66, 133.13, 131.44 (d, J_{C-F} = 31.8 Hz), 129.92 (d, J_{C-F} = 12 Hz), 126.47, 124.14, 122.91, 122.18, 120.82, 115.35, 115.24 (d, J_{C-F} = 35.8 Hz); HRMS (ESI) m/z calcd for $C_{15}H_{10}{}^{19}FNNaO_2{}^+$ [M + Na$^+$] 278.0588, found 278.0592.

4-(3-Bromophenyl)-3-hydroxyquinolin-2(1*H*)-one (9s). By following the general procedure, **9s** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 60%, 95 mg, white solid, mp 220−222 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.27 (br s, 1H), 9.43 (br s, 1H), 7.66 (d, J = 7.8 Hz, 1H), 7.55 (s, 1H), 7.49 (t, J = 7.8 Hz, 1H), 7.36−7.33 (m, 3H), 7.10 (t, J = 7.8 Hz, 1H), 7.04 (d, J = 7.8 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 158.1, 142.7, 136.2, 133.1, 132.4, 130.6, 130.5, 129.0, 126.5, 124.0, 122.4, 122.3, 121.6, 120.5, 115.3; HRMS (ESI) m/z calcd for $C_{15}H_{10}{}^{79}BrNNaO_2{}^+$ [M + Na$^+$] 337.9787, found 337.9789.

3-Hydroxy-4-(3-methoxyphenyl)quinolin-2(1*H*)-one (9t):[36] By following the general procedure, **9t** was purified by silica gel chromatography (EA/PE = 30/70). Yield: 40%, 54 mg, white solid, mp 239−240 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.21 (br s, 1H), 9.18 (br s, 1H), 7.43 (t, J = 7.8 Hz, 1H), 7.36−7.31 (m, 2H), 7.08 (d, J = 3.6 Hz, 2H), 7.02 (d, J = 7.8 Hz, 1H), 6.90−6.88 (m, 2H), 3.79 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 159.7, 158.7, 142.8, 135.6, 133.6, 129.9, 126.9, 124.9, 124.3, 122.6, 122.5, 121.3, 115.9, 115.7, 113.6, 55.6; HRMS (ESI) m/z calcd for $C_{16}H_{13}NNaO_3{}^+$ [M + Na$^+$] 290.0788, found 290.0791.

2 (Viridicatol):[9] Yield: 80%, 41 mg, white solid, mp 268−271 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.19 (br s, 1H), 9.50 (br s, 1H), 9.12 (br s, 1H), 7.34−7.28 (m, 3H), 7.11−7.07 (m, 2H), 6.82 (d, J = 7.8 Hz, 1H), 6.72 (d, J = 7.8 Hz, 2H).

■ ASSOCIATED CONTENT

Supporting Information

Spectral data for all synthesized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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