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Metal-Free Intramolecular Amination: One-Pot Tandem Synthesis of 3-Substituted 4-Quinolones

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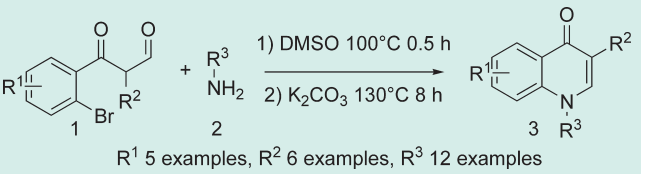
Supporting Information

ABSTRACT: 3-Substituted 4-quinolones were synthesized using a one-pot metal-free strategy in moderate to quantitative yields. Carried out in dimethylsulfoxide (DMSO) via a sequential addition of materials, the methodology is tolerant of a wide range of functional groups and applicable to library synthesis.



KEYWORDS: quinolones, metal-free, one-pot, intramolecular amination

INTRODUCTION

Since the finding of the antibacterial activities of Nalidixic Acid,[1] 3-substituted 4-quinolone have been extensively studied as a useful structural moiety for drug candidates. Apart from the numerous marketed drugs such as Ciprofloxacin, Levofloxacin, and Moxifloxacin, scientists have found a wide range of bioactive derivatives that exhibit antitumor,[2] antibacterial,[3] antiviral,[4] antitrypanosomal,[3f] and selective M1 positive allosteric modulating activities.[5] All these justify the effort to develop new efficient synthesis strategies for this structural moiety. However, existing synthesis methods for 3-substituted 4-quinolones usually require multi steps and laborious isolation of the intermediates,[6] rare substrates,[7] or protective groups[8] to furnish the reaction, and thus find limited application in library synthesis. With recent advances in chemistry, more efficient, mild, and diversity oriented reactions such as metal-catalyzed couplings, multicomponent reactions (MCRs), and combinatorial approaches have gained and will continue to gain much progress.[9] Numerous transition metal catalyzed amination of aromatic rings have been reported.[10] As part of our continuing effort at the construction of heterocycles via transition metal catalyzed reactions,[11] we set out to develop an efficient synthesis methodology for a quinolone library. Herein we report a serendipitous finding, an efficient one-pot metal-free combinatorial process (Figure 1) for the synthesis of 3-substituted 4-quinolones (chemset **3**) using amines (chemset **2**) and 3-(2-bromophenyl)-3-oxopropanal derivatives (chemset **1**).

RESULTS AND DISCUSSION

In the light of preceding works, we envisioned that the target molecule could be obtained via intramolecular cyclization/amination of the enamines (**i-2**) formed in situ (Figure 1). To study the proposed reaction, we first, on the basis of our previous work in CuI catalyzed reactions, carried out a series of reaction conditions screening and found that **i-1** undergoes cyclization in yields as good as reactions with no catalyst and ligand (Table 1 Entries 1−4). Chemset **1** could be obtained through a modified procedure under mild conditions.[12] Spectral data of chemset **1** showed typical aldehydic proton signals at about 9.5 ppm except for **1**{*4*} which exist solely in enolic form as evidenced by a doublet (enolic hydroxyl signal) at 14.61 ppm in $CDCl_3$ and a broad singlet at 11.18 ppm in deuterated DMSO. Bernini attempted to prepare 2-substituted 4-quinolones from enamine formed in situ via a copper catalyzed one-pot strategy, but evaporation of volatile materials was decisive and thus limited its application.[13] As Table 1 shows, our products could easily be obtained from β-ketonaldehydes and amines in DMSO in the presence of K_2CO_3 at 130 °C. DMSO was crucial for the present study, when other solvents were employed, no or trivial amount of product was observed (Table 1 Entries 5−8). The importance of preheating of substrates before the addition of base suggested a plausible reaction mechanism (Figure 1). And this was confirmed by thin layer chromatography (TLC) analysis of the reaction. Since chemset **1** and its Schiff base had the same R_f values, half an equivalent of aniline was employed, the aniline spot disappeared, and no product was detected before the addition of base. Addition of base promoted the enamine-imine transformation and further facilitated the dehydrobromination process to effect the cyclization reaction. While weaker base failed to function in either of the processes and stronger base triggered aldol condensation, K_2CO_3 proved to be the most suitable base (Table 1 Entries 9−10).

With this protocol in hand we next studied the scope of the reaction. R^3 affected the reaction significantly, with electron rich aromatics giving yields higher than its electron poor counterparts (Table 2 Entries 1−10) and alkyl substituents (Table 2 Entries 11−12). Unlike R^3, R^1 and R^2 did not have much impact on the outcomes of the reaction. Good yields were obtained with both electron donating and attracting substitutents (Table 2 Entries 13-21). Yields decreased as the steric hindrance grew larger (Table 2 Entries 3, 16, 17). Unexpectedly, our attempt to expand

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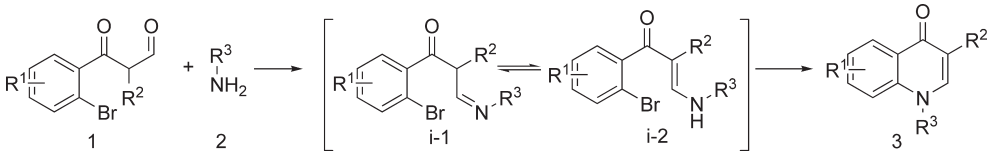


Figure 1. Construction of quinolone structure moiety.

Table 1. Screening of Reaction Conditions

entry	catalyst	ligand	base	solvent	yield[a] (%)
1	CuI	1,10-phenanthroline	K_2CO_3	DMSO	95[b]
2	CuI	DMEDA	K_2CO_3	DMSO	96[b]
3	CuI	L-proline	K_2CO_3	DMSO	94[b]
4			K_2CO_3	DMSO	95[b]/94.8[c]/85[d]
5			K_2CO_3	toluene	nd[d,e]
6			K_2CO_3	methanol	nd[d,e]
7			K_2CO_3	dioxane	nd[d,e]
8			K_2CO_3	DMF	trace[d]
9			KOH	DMSO	40[d,e]
10			Na_2CO_3	DMSO	30[d,e]

[a] Isolated yield. [b] 0.05 mmol Schiff base, 5% equiv CuI, 10% equiv ligand, 2 equiv base, 3 mL of DMSO, 130 °C. [c] 1 and 2 were heated in DMSO at 90 °C for 0.5 h before the addition of 1 equiv of base. [d] All components were heated together. [e] Not detected.

the scope to the synthesis of 2-methyl-4-quinolone led to the isolation of 2-methylchromone in 60% yield when 2-bromobenzoylacetone and aniline were employed as the starting materials (Figure 2). This result was in good accordance with Bernini's report that enamine of ketones could not be formed in DMSO alone.[13] Successful completion of the present protocol may be accounted for by the stronger reactivity of aldehyde than ketones and the activated bromine by adjacent carbonyl group.

CONCLUSION

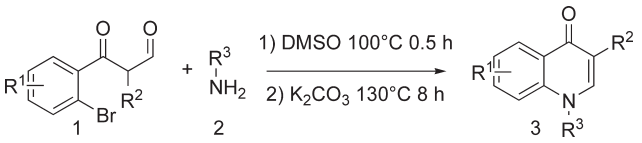
A copper-free tandem strategy using easily obtained β-ketonaldehydes and amines as starting material for the synthesis of 3-substituted 4-quinolones is reported. The strategy gives 3-substituted quinolones in up to 97.5% yield without isolation of intermediates, and is tolerant of a wide range of functional groups and applicable to library synthesis.

EXPERIMENTAL SECTION

DMSO was dried over CaH_2 and distilled. Melting points were determined without correction on an XT5 digital melting-point apparatus purchased from Beijing Keyi Elec-opti Instrument Factory. ^{1}H NMR and ^{13}C NMR spectra were obtained from a solution in $CDCl_3$ or DMSO with tetramethylsilane (TMS) as internal standard using a Varian Inova 400/101 MHz (^{1}H/^{13}C) or 300/75 MHz (^{1}H/^{13}C) spectrometer, δ in parts per million (ppm), and J in hertz (Hz). IR data were recorded on ProStar LC240 using KBr tablets, wavenumbers in cm^{-1}. HRMS analyses were carried out using a time-of-flight mass spectrometry (TOF-MS) or Saturan2200 (ESI) instrument.

General Procedure for the Synthesis of Chemset 1. A solution of the ketone (2 mmol) in DMF (3 mL) was added to a solution of $POCl_3$ (3.5 equiv) in DMF (2 mL) at 0 °C under nitrogen, and the mixture was stirred at room temperature for

Table 2. Synthesis of 3-Substituted 4-Quinolones



entry	R^1	R^2	R^3	product	yield[a] (%)
1	H	Ph	Ph	3{*1,1*}	95
2	H	Ph	4-$OMeC_6H_4$	3{*1,2*}	97.5
3	H	Ph	2-MeC_6H_4	3{*1,3*}	77
4	H	Ph	4-FC_6H_4	3{*1,4*}	87.3
5	H	Ph	2,4-$Cl_2C_6H_3$	3{*1,5*}	56
6	H	Ph	1-naphthyl	3{*1,6*}	84
7	H	Ph	3,4-$OCH_2OC_6H_3$	3{*1,7*}	95
8	H	Ph	4-MeC_6H_4	3{*1,8*}	82
9	H	Ph	3-$NO_2C_6H_4$	3{*1,9*}	52
10	H	Ph	2-pyridyl	3{*1,10*}	40
11	H	Ph	cyclopropyl	3{*1,11*}	63
12	H	Ph	benzyl	3{*1,12*}	51.2
13	H	4-MeC_6H_4	Ph	3{*2,1*}	80.3
14	4,5-OCH_2O	Ph	Ph	3{*3,1*}	70
15	H	Me	Ph	3{*4,1*}	97
16	3-Me	Ph	Ph	3{*5,1*}	52
17	H	2-ClC_6H_4	Ph	3{*6,1*}	65
18	H	4-FC_6H_4	Ph	3{*7,1*}	65.2
19	H	4-ClC_6H_4	Ph	3{*8,1*}	82
20	5-MeO	Ph	Ph	3{*9,1*}	68
21	H	3,5-$Me_2C_6H_3$	Ph	3{*10,1*}	84
22	5-F	Ph	Ph	3{*11,1*}	85

[a] Isolated yield.

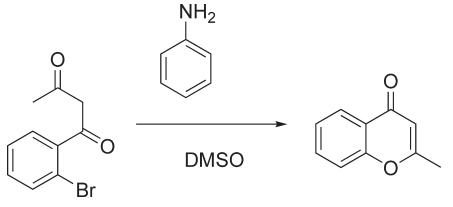


Figure 2. Isolation of 2-methylchromone.

3 h, poured into water, basified with $NaHCO_3$, heated at 80 °C for 0.5 h, and then separated between EtOAc and water. The organic layer was dried over Na_2SO_4, filtered, evaporated, and run through column chromatography to give chemset **1**.

General Procedure for the Synthesis of Chemset 3. A mixture of chemset **1** (0.5 mmol) and chemset **2** (0.55 mmol) were stirred at 90−100 °C for 0.5 h in DMSO under N_2, then

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K_2CO_3 (0.5 mmol) was added and stirred at 130 °C for another 8 h. The reaction mixture was separated between EtOAc (3 × 20 mL) and 30 mL of water. The organic layer was dried over Na_2SO_4, filtered, evaporated under vacuum, and purified by column chromatography to give chemset **3**.

1,3-Diphenylquinolin-4(1H)-one (3{1,1}). White solid, mp 209−211 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, J = 8.1 Hz, 1H), 7.82 (s, 1H), 7.71 (d, J = 7.7 Hz, 2H), 7.59 (m, 3H), 7.43 (m, 6H), 7.30 (t, J = 7.3 Hz, 1H), 7.03 (d, J = 8.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ175.97, 160.14, 142.02, 141.14, 135.36, 134.11, 131.71, 131.01, 128.80, 128.75, 128.35, 127.20, 126.80, 123.89, 121.92, 117.29, 116.45, 115.38, 114.78, 55.78; IR (KBr): 3048, 3036, 2936, 1616, 1580, 1549, 1497, 1477, 1368, 1325, 1256, 756, 696. HRMS (EI): M^+ calcd for $C_{21}H_{15}NO$ 297.1154. Found: 297.1154.

1-(4-Methoxyphenyl)-3-phenylquinolin-4(1H)-one (3{1,2}). Pale yellow solid, mp 124−127 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, J = 7.9 Hz, 1H), 7.81 (s, 1H), 7.71 (d, J = 7.6 Hz, 2H), 7.49 (t, J = 7.7 Hz, 1H), 7.43−7.33 (m, 5H), 7.30 (t, J = 7.3 Hz, 1H), 7.08 (d, J = 8.6 Hz, 2H), 7.02 (d, J = 8.5 Hz, 1H), 3.90 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$): δ 175.97, 160.14, 142.02, 141.14, 135.36, 134.11, 131.71, 128.80, 128.75, 128.35, 127.20, 126.80, 123.89, 121.92, 117.29, 115.38, 55.78. IR (KBr): 3063, 3048, 3009, 2970, 2932, 2833, 1624, 1609, 1585, 1508, 1325, 1246, 1024, 775. HRMS (EI): M^+ calcd for $C_{22}H_{17}NO_2$ 327.1259. Found: 327.1260.

3-Phenyl-1-o-tolylquinolin-4(1H)-one (3{1,3}). Pale yellow solid, mp 138−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (d, J = 8.1 Hz, 1H), 7.78−7.70 (m, 3H), 7.54−7.28 (m, 9H), 6.80 (d, J = 8.5 Hz, 1H), 2.10 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 176.09, 141.25, 140.47, 140.09, 136.18, 135.32, 132.05, 131.93, 130.11, 128.81, 128.38, 128.34, 128.03, 127.38, 127.26, 126.84, 123.99, 122.31, 116.85, 17.34. IR (KBr): 3053, 3024, 1624, 1587, 1479, 1327, 766. HRMS (EI): M^+ calcd for $C_{22}H_{17}NO$ 311.1310. Found: 311.1310.

1-(4-Fluorophenyl)-3-phenylquinolin-4(1H)-one (3{1,4}). Pale yellow solid, mp 223−225 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, J = 8.0 Hz, 1H), 7.77 (s, 1H), 7.69 (d, J = 7.5 Hz, 2H), 7.51 (t, J = 7.6 Hz, 1H), 7.48−7.25 (m, 8H), 6.98 (d, J = 8.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 176.00, 164.02, 161.53, 141.49, 140.85, 137.41, 135.13, 131.92, 129.73, 129.64, 128.77, 128.40, 127.35, 127.35, 126.78, 126.16, 124.11, 122.30, 117.59, 117.36, 116.96. IR (KBr): 3049, 3038, 1618, 1582, 1508, 1477, 1223, 756. HRMS (EI): M^+ calcd for $C_{21}H_{14}$-FNO 315.1059. Found: 315.1059.

1-(2,4-Dichlorophenyl)-3-phenylquinolin-4(1H)-one (3{1,5}). Pale yellow solid, mp 145−147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, J = 8.0 Hz, 1H), 7.75−7.65 (m, 3H), 7.62 (s, 1H), 7.56−7.42 (m, 3H), 7.39 (t, J = 7.4 Hz, 3H), 7.30 (t, J = 7.3 Hz, 1H), 6.77 (d, J = 8.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 176.16, 140.76, 140.11, 137.00, 136.71, 134.88, 134.14, 132.21, 131.16, 131.06, 129.12, 128.81, 128.36, 127.43, 126.66, 124.25, 122.85, 116.29. IR (KBr): 3057, 3026, 2957, 2924, 1622, 1589, 1476, 1331, 760. HRMS (EI): M^+ calcd for $C_{21}H_{13}Cl_2NO$ 365.0374. Found: 365.0389.

1-(Naphthalen-1-yl)-3-phenylquinolin-4(1H)-one (3{1,6}). Pale yellow solid, mp 115−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (dd, J = 6.2, 3.3 Hz, 1H), 8.07 (d, J = 8.1 Hz, 1H), 8.00 (d, J = 8.3 Hz, 1H), 7.85 (s, 1H), 7.72 (d, J = 7.3 Hz, 2H), 7.60 (m, 3H), 7.44 (t, J = 7.6 Hz, 1H), 7.41−7.31 (m, 5H), 7.25 (dd, J = 12.9, 5.3 Hz, 1H), 6.70 (dd, J = 6.1, 3.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): 176.15, 142.06, 141.28, 137.45, 135.14, 134.62, 131.92, 130.41, 130.07, 128.73, 128.28, 128.18, 127.36, 127.18, 127.14, 126.69, 126.17, 125.83, 123.97, 122.18, 122.13, 117.41. IR (KBr): 3055, 3028, 1620, 1589, 1476, 1321, 762. HRMS (EI): M^+ calcd for $C_{25}H_{17}NO$ 347.1310. Found: 347.1309.

1-(Benzo[d][1,3]dioxol-5-yl)-3-phenylquinolin-4(1H)-one (3{1,7}). White solid, mp 173−175 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, J = 7.5 Hz, 1H), 7.80 (s, 1H), 7.70 (d, J = 7.5 Hz, 2H), 7.52 (m, 1H), 7.40 (m, 3H), 7.31 (t, J = 7.4 Hz, 1H), 7.08 (d, J = 8.5 Hz, 1H), 6.98 (d, J = 7.9 Hz, 1H), 6.96−6.89 (m, 2H), 6.13 (d, J = 4.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 176.03, 148.98, 148.55, 141.83, 141.07, 135.31, 135.18, 131.81, 128.79, 128.39, 127.30, 127.28, 126.81, 123.99, 122.09, 121.30, 117.24, 109.13, 108.64, 102.42. IR (KBr): 3044, 3032, 1618, 1603, 1576, 1487, 1229, 1036, 750. HRMS (EI): M^+ calcd for $C_{22}H_{15}NO_3$ 341.1052. Found: 341.1069.

3-Phenyl-1-p-tolylquinolin-4(1H)-one (3{1,8}). Pale yellow solid, mp 164−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, J = 8.1 Hz, 1H), 7.80 (s, 1H), 7.75−7.64 (m, 2H), 7.54−7.43 (m, 1H), 7.44−7.27 (m, 8H), 7.03 (d, J = 8.5 Hz, 1H), 2.48 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$): 176.00, 141.79, 140.89, 139.78, 138.90, 135.37, 131.69, 130.93, 128.77, 128.34, 127.37, 127.23, 127.19, 126.82, 123.92, 122.00, 117.28, 21.33. IR (KBr): 3057, 3028, 2957, 2922, 1622, 1603, 1584, 1514, 1479, 1327, 1254, 758. HRMS (EI): M^+ calcd for $C_{22}H_{17}NO$ 311.1310. Found: 311.1313.

1-(3-Nitrophenyl)-3-phenylquinolin-4(1H)-one (3{1,9}). Pale yellow solid, mp 229−230 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (dd, J = 8.1, 1.4 Hz, 1H), 8.46−8.40 (m, 1H), 8.37 (s, 1H), 7.89−7.83 (m, 2H), 7.76 (s, 1H), 7.66 (d, J = 7.3 Hz, 2H), 7.58−7.51 (m, 1H), 7.40 (dt, J = 11.1, 7.6 Hz, 3H), 7.31 (t, J = 7.3 Hz, 1H), 6.96 (d, J = 8.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 173.37, 146.70, 139.69, 137.97, 137.57, 132.01, 131.38, 129.63, 128.91, 126.13, 125.77, 125.02, 124.93, 124.06, 121.89, 121.77, 120.55, 120.42, 113.72. IR (KBr): 3078, 3026, 2957, 2924, 2855, 1626, 1609, 1587, 1528, 1477, 1350, 750. HRMS (EI): M^+ calcd for $C_{21}H_{14}N_2O_3$ 342.1004. Found: 342.1008.

3-Phenyl-1-(pyridin-2-yl)quinolin-4(1H)-one (3{1,10}). Pale yellow solid, mp 210−211 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00−7.91 (m, 1H), 7.81 (dd, J = 8.1, 1.5 Hz, 1H), 7.22 (td, J = 7.8, 1.9 Hz, 1H), 6.94 (dd, J = 8.2, 1.1 Hz, 2H), 6.81−6.69 (m, 3H), 6.64 (t, J = 7.6 Hz, 3H), 6.59−6.47 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 176.31, 153.45, 150.41, 140.45, 139.44, 135.16, 131.87, 128.92, 128.32, 127.43, 127.33, 126.68, 124.37, 124.29, 122.72, 121.60, 116.53. IR (KBr): 3051, 1618, 1607, 1580, 1553, 1481, 1470, 1437, 1317, 752. HRMS (EI): M^+ calcd for $C_{22}H_{14}N_2O$ 298.1106. Found: 298.1105.

1-Cyclopropyl-3-phenylquinolin-4(1H)-one (3{1,11}). Pale yellow solid, mp 180−182 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.6 Hz, 1H), 7.85 (s, 1H), 7.65 (t, J = 7.8 Hz, 3H), 7.39 (m, 3H), 7.29 (t, J = 7.4 Hz, 1H), 3.54−3.37 (m, 1H), 1.27 (q, J = 6.4 Hz, 2H), 1.12−1.01 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): 175.87, 141.42, 140.88, 135.63, 131.81, 128.73, 128.29, 127.30, 127.05, 126.90, 123.80, 121.76, 116.07, 33.86, 8.36. IR (KBr): 3069, 3017, 1620, 1609, 1578, 1483, 1329, 754. HRMS (EI): M^+ calcd for $C_{18}H_{15}NO$ 261.1154. Found: 261.1155.

1-Benzyl-3-phenylquinolin-4(1H)-one (3{1,12}). White solid, mp 169−171 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (dd, J = 8.1, 1.3 Hz, 1H), 7.86 (s, 1H), 7.76−7.67 (m, 2H), 7.61−7.51 (m, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.35 (m, 6H), 7.19 (d, J = 7.0 Hz, 2H), 5.40 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): 175.98, 142.61, 139.47,

135.39, 135.25, 132.06, 129.26, 128.76, 128.35, 128.30, 127.61, 127.53, 127.17, 126.08, 123.80, 122.15, 116.03, 56.62. IR (KBr): 3049, 3028, 1626, 1611, 1580, 1555, 1491, 756. HRMS (EI): M^+ calcd for $C_{22}H_{17}NO$ 311.1310. Found: 311.1310.

1-Phenyl-3-p-tolylquinolin-4(1H)-one (3{2,1}). Pale yellow solid, mp 173−174 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, J = 8.0 Hz, 1H), 7.81 (s, 1H), 7.60 (m, 5H), 7.47 (m, 3H), 7.38 (t, J = 7.5 Hz, 1H), 7.22 (d, J = 7.7 Hz, 2H), 7.03 (d, J = 8.5 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 176.11, 141.50, 141.30, 140.72, 136.96, 132.31, 131.69, 130.41, 129.57, 129.08, 128.62, 127.69, 127.29, 126.73, 123.91, 122.10, 117.14, 21.32. IR (KBr): 3057, 3044, 1626, 1612, 1597, 1477, 1329, 1258, 758. HRMS (EI): M^+ calcd for $C_{22}H_{17}NO$ 311.1310. Found: 311.1312.

5,7-Diphenyl-[1,3]dioxolo[4,5-g]quinolin-8(5H)-one (3{3,1}). Pale yellow solid, mp 274−276 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.71 (s, 2H), 7.69 (s, 1H), 7.66−7.53 (m, 3H), 7.47−7.34 (m, 4H), 7.33−7.24 (m, 1H), 6.39 (s, 1H), 6.02 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): 174.74, 151.63, 145.84, 141.74, 140.40, 137.97, 135.38, 130.48, 129.72, 128.84, 128.33, 127.61, 127.19, 122.68, 121.49, 104.20, 102.08, 96.51. IR (KBr): 3075, 3057, 2909, 1634, 1584, 1493, 1468, 1236, 1030, 694. HRMS (EI): M^+ calcd for $C_{22}H_{15}NO_3$ 341.1052. Found: 341.1049.

3-Methyl-1-phenylquinolin-4(1H)-one (3{4,1}). White solid, mp 169−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (d, J = 8.1 Hz, 1H), 7.63−7.47 (m, 4H), 7.47−7.34 (m, 3H), 7.29 (t, J = 7.5 Hz, 1H), 6.96 (d, J = 8.6 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 178.12, 141.55, 141.05, 140.49, 131.31, 130.27, 129.34, 127.68, 126.54, 123.32, 118.45, 116.99, 13.86. IR (KBr): 3048, 3011, 1628, 1589, 1553, 1483, 1371, 1308, 762, 694. HRMS (EI): M^+ calcd for $C_{16}H_{13}NO$ 235.0997. Found: 235.0995.

8-Methyl-1,3-diphenylquinolin-4(1H)-one (3{5,1}). Pale yellow solid, mp 189−191 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, J = 7.7 Hz, 1H), 7.78 (s, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.55−7.42 (m, 3H), 7.42−7.26 (m, 7H), 1.78 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 176.33, 145.55, 144.64, 139.89, 136.24, 135.12, 129.90, 128.74, 128.34, 127.26, 127.09, 126.93, 125.79, 124.35, 121.48, 22.41. IR (KBr): 3061, 3022, 1618, 1578, 1562, 1479, 1308, 770, 696. HRMS (EI): M^+ calcd for $C_{22}H_{17}NO$ 311.1310. Found: 311.1310.

3-(2-Chlorophenyl)-1-phenylquinolin-4(1H)-one (3{6,1}). Pale yellow solid, mp 164−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, J = 8.0 Hz, 1H), 7.79 (s, 1H), 7.65−7.37 (m, 9H), 7.32−7.23 (m, 2H), 7.08 (d, J = 8.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 175.61, 143.22, 141.30, 140.99, 134.15, 133.92, 132.74, 131.99, 130.43, 129.83, 129.66, 129.05, 127.67, 127.31, 126.71, 124.23, 120.44, 120.02, 117.37. IR (KBr): 3051, 3030, 3013, 1630, 1601, 1587, 1557, 1479, 1331, 764, 745, 704. HRMS (EI): M^+ calcd for $C_{21}H_{14}ClNO$ 331.0764. Found: 331.0764.

3-(4-Fluorophenyl)-1-phenylquinolin-4(1H)-one (3{7,1}). Pale yellow solid, mp 199−201 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, J = 8.0 Hz, 1H), 7.79 (s, 1H), 7.71−7.55 (m, 5H), 7.53−7.43 (m, 3H), 7.39 (t, J = 7.5 Hz, 1H), 7.08 (t, J = 8.7 Hz, 2H), 7.03 (d, J = 8.6 Hz, 1H).^{13}C NMR (75 MHz, $CDCl_3$): 176.31, 164.48, 161.20, 156.30, 153.04, 133.86, 130.84, 130.73, 127.87, 126.48, 125.46, 124.59, 124.53, 118.19, 115.75, 115.46. IR (KBr): 3048, 1620, 1576, 1555, 1510, 1479, 1327, 1225, 835, 756, 694, 532. HRMS (EI): M^+ calcd for $C_{21}H_{14}NO$ 315.1059. Found: 315.1058.

3-(4-Chlorophenyl)-1-phenylquinolin-4(1H)-one (3{8,1}). Pale yellow solid, mp 204−206 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (dd, J = 8.1, 1.4 Hz, 1H), 7.81 (s, 1H), 7.75−7.54 (m, 5H), 7.55−7.42 (m, 3H), 7.43−7.30 (m, 3H), 7.03 (d, J = 8.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 175.82, 141.44, 141.32, 140.75, 133.75, 132.96, 131.94, 130.48, 130.01, 129.74, 128.46, 127.66, 127.22, 126.71, 124.20, 120.84, 117.28. IR (KBr): 3063, 3034, 3009, 2956, 2924, 2855, 1622, 1611, 1584, 1555, 1493, 11090, 864, 829, 760, 704. HRMS (EI): M^+ calcd for $C_{21}H_{14}ClNO$ 331.0764. Found: 331.0766.

6-Methoxy-1,3-diphenylquinolin-4(1H)-one (3{9,1}). Pale yellow solid, mp 157−169 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 2.9 Hz, 1H), 7.79 (s, 1H), 7.72 (d, J = 7.7 Hz, 2H), 7.64−7.52 (m, 3H), 7.48−7.35 (m, 4H), 7.29 (t, J = 6.9 Hz, 1H), 7.12 (dd, J = 9.3, 2.9 Hz, 1H), 6.98 (d, J = 9.3 Hz, 1H), 3.93 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): 175.32, 156.57, 141.55, 140.84, 135.53, 135.40, 130.35, 129.56, 128.79, 128.33, 127.96, 127.61, 127.13, 122.56, 121.07, 118.91, 106.05, 55.87. IR (KBr): 3049, 2965, 2938, 2837, 1607, 1578, 1553, 1491, 1368, 1325, 1036, 808, 779, 698, 579. HRMS (EI): M^+ calcd for $C_{22}H_{17}NO_2$ 327.1259. Found: 327.1254.

3-(3,5-Dimethylphenyl)-1-phenylquinolin-4(1H)-one (3{10,1}). White solid, mp 218−220 °C. ^{1}H NMR (400 MHz, CDCl3): δ 8.59 (d, J = 8.0 Hz, 1H), 7.81 (s, 1H), 7.60 (m, 3H), 7.48 (m, 3H), 7.38 (t, J = 7.5 Hz, 1H), 7.33 (s, 2H), 7.03 (d, J = 8.5 Hz, 1H), 6.96 (s, 1H), 2.35 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): 176.10, 141.58, 141.52, 140.75, 137.82, 135.12, 131.70, 130.43, 129.58, 129.04, 127.73, 127.35, 126.81, 126.61, 123.94, 122.44, 117.14, 77.48, 77.16, 76.84, 21.50. IR (KBr): 3044, 3013, 3001, 2916, 1622, 1586, 1553, 1479, 1339, 754. HRMS (EI): M^+ calcd for $C_{23}H_{19}NO$ 325.1467. Found: 325.1468.

6-Fluoro-1,3-diphenylquinolin-4(1H)-one (3{11,1}). Pale yellow solid, mp 121−123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (dd, J = 9.1, 2.7 Hz, 1H), 7.81 (s, 1H), 7.67 (d, J = 7.4 Hz, 2H), 7.59 (dq, J = 13.3, 6.5 Hz, 3H), 7.44 (d, J = 7.0 Hz, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.29 (d, J = 7.4 Hz, 1H), 7.25−7.17 (m, 1H), 7.03 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): 175.09, 160.58, 158.14, 141.63, 141.19, 137.24, 134.90, 130.50, 129.80, 128.70, 128.34, 128.12, 127.51, 127.38, 127.32, 126.72, 121.38, 120.53, 120.28, 119.57, 119.50, 111.73, 111.50. IR (KBr): 3061, 3040, 2961, 2924, 1692, 1614, 1580, 1562, 1487, 1325, 1254, 820, 698, 579. HRMS (EI): M^+ calcd for $C_{21}H_{14}FNO$ 315.1059. Found: 315.1062.

Spectral data for 2-methyl-4-chromone, see ref 14.

■ ASSOCIATED CONTENT

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

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