The synthesis of 3,4-disubstituted dihydroquinolin-2(1*H*)-one under metal-free conditions in aqueous solution

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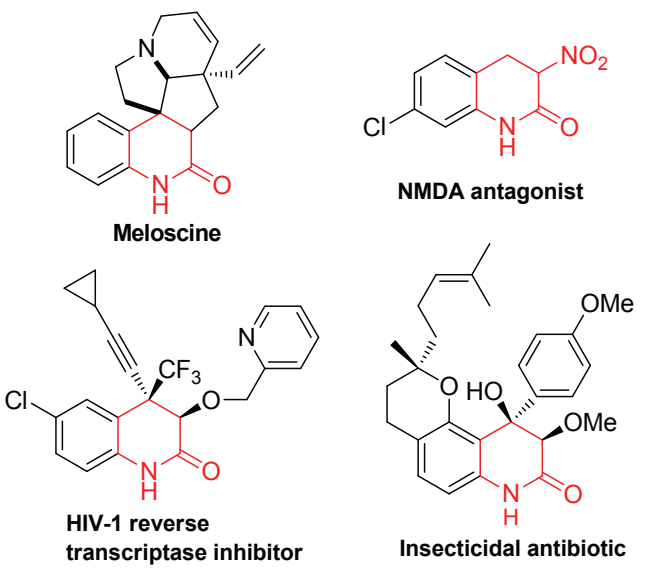
A novel route toward 3,4-disubstituted dihydroquinolin-2(1*H*)-ones *via* radical process has been developed in aqueous solution without metals. This method offers a new and simple route for the synthesis of skeleton of dihydroquinolin-2(1*H*)-one in one step.

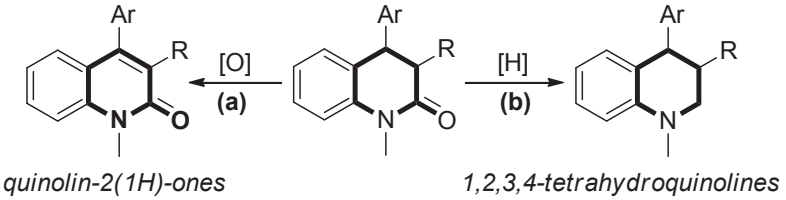
Keywords: dihydroquinolin-2(1*H*)-one, metal-free conditions, aqueous solution

The 3,4-disubstituted dihydroquinolin-2(1*H*)-one unit is an important component of pharmacologically and biologically active compounds, and its derivatives are found in many natural products and pharmaceuticals which have cardiovascular, anti-inflammatory and phosphodiesterase inhibitory activities (Scheme 1).[1–3] Moreover, the 3,4-dihydroquinolin-2(1*H*)-one unit is not only very important in pharmaceuticals, but is also a good synthetic block for 1,2,3,4-tetrahydroquinolines and quinolin-2(1*H*)-ones (Scheme 2).[4] As a result, the development of a simple and highly efficient method for construction of 3,4-dihydroquinolin-2(1*H*)-one is desirable. Generally, the preparation of a 3,4-dihydroquinolin-2(1*H*)-one system involves the Friedel–Crafts cyclisation[5–7], and palladium[8–9] or rhodium[10] catalysed reactions. Recently, other methods such as Ugi/acrylanilide [6π]-photocyclisations, intermolecular tandem reactions and Mn-mediated intramolecular cyclisations have also been developed.[11–14] Despite their efficiencies, most of them are catalysed by metals, or require harsh reaction conditions involving strong acid or base, or the use of complicated compounds as substrates. Radical reactions have been widely applied in organic synthesis, especially in cyclisation reactions.[15,16] However, radical tandem cyclisation for constructing 3,4-disubstituted dihydroquinolin-2(1*H*)-ones remains rare. Recently, we have reported a silver-catalysed approach for the synthesis of 3,4-dihydroquinolin-2(1*H*)-ones.[17] As a logical extension of the catalytic method, we now report a new approach to the 3,4-disubstituted dihydroquinolin-2(1*H*)-ones under metal-free condition.



Scheme 1 Some drugs containing 3,4-dihydroquinolin-2-one structure.

We first selected *N*-methyl-*N*-phenylcinnamamide (**1a**) and pentane-2,4-dione (**2**) as substrates to investigate the reaction conditions. The results were summarised in Table 1. Based on our previous work, the $AgNO_3$–$K_2S_2O_8$ catalytic system was firstly examined at 100 °C in CH_3CN/H_2O solution and product **3** was isolated in 65% yield (Table 1, entry 1). Ag_2O as catalyst gave a similar result under the same condition (Table 1, entry 2). Unexpectedly, the reaction still proceeded well when changing the silver metal to copper metal (Table 1, entries 3 and 4). This did not happen in our previous work on the synthesis of 3,4-dihydroquinolin-2(1*H*)-ones. So we considered that the metal does not play a key role in this transformation. We were pleased to find that $K_2S_2O_8$ itself displayed catalytic effect in this transformation with 56% product yield (Table 1, entry 5). We next examined $(NH_4)_2S_2O_8$ as oxidant under the same conditions, it still showed a catalytic effect but the yield decreased to 39% (Table 1, entry 6). No reaction occurred in the absence of oxidant (Table 1, entry 7). When other oxidants such as BOP, TBHP and H_2O_2 were tested under the same conditions, no reaction occurred (Table 1, entries 8–10). Improving the amount of $K_2S_2O_8$, the yield increased slightly (Table 1, entry 13). However, the product was not obtained in acetone/H_2O or EtOAc/H_2O using $K_2S_2O_8$ as oxidant which demonstrated solvent also played an important role (Table 1, entries 11 and 12).



Scheme 2 Utility of 3,4-dihydroquinolin-2(1*H*)-ones.

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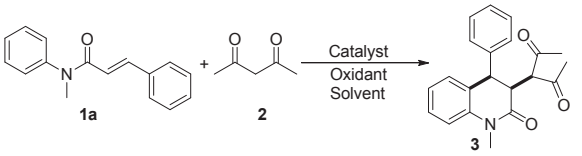
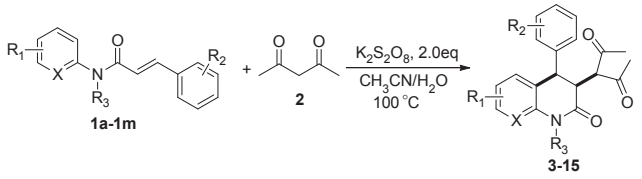
Table 1 Effect of solvents, catalysts and oxidants in the new reaction[a]



Entry	Catalyst	Oxidant	Solvent	Yield /%[b]
1	$AgNO_3$	$K_2S_2O_8$	CH_3CN/H_2O	65
2	Ag_2O	$K_2S_2O_8$	CH_3CN/H_2O	58
3	CuCl	$K_2S_2O_8$	CH_3CN/H_2O	44
4	CuI	$K_2S_2O_8$	CH_3CN/H_2O	51
5	–	$K_2S_2O_8$	CH_3CN/H_2O	56
6	–	$(NH_4)_2S_2O_8$	CH_3CN/H_2O	39
7	–	–	CH_3CN/H_2O	0
8	–	BPO	CH_3CN/H_2O	0
9	–	TBHP	CH_3CN/H_2O	0
10	–	H_2O_2	CH_3CN/H_2O	0
11	–	$K_2S_2O_8$	Acetone/H_2O	trace
12	–	$K_2S_2O_8$	EtOAc/H_2O	0
13[c]	–	$K_2S_2O_8$	CH_3CN/H_2O	70
14[d]	–	$K_2S_2O_8$	CH_3CN/H_2O	63

[a]Catalyst (20 mol%), **1a** (1.0 mmol), **2** (2.0 mmol) and oxidant (1.0 equiv.) in 3 mL of the indicated solvent/H_2O (1 : 1) at 100 °C for 15 h. TBHP, tert-butyl-hydroperoxide; DTBP, tert-butyl-peroxide; BPO, benzoyl peroxide.
[b]Isolated yields.
[c]$K_2S_2O_8$ (2.0 equiv.).
[d]$K_2S_2O_8$ (3.0 equiv.).

Table 2 Direct synthesis of 3,4-disubstituted dihydroquinoline-2(1*H*)-one without metal[a]



Entry	X, R_1, R_2, R_3	Products	Yield/%[b]
1	X = C, R_1 = H, R_2 = H, R_3 = Me	**3**	70
2	X = C, R_1 = H, R_2 = *m*-OMe, R_3 = Me	**4**	73
3	X = C, R_1 = H, R_2 = *o*-Me, R_3 = Me	**5**	56
4	X = C, R_1 = H, R_2 = *o*-Br, R_3 = Me	**6**	69
5	X = C, R_1 = H, R_2 = *o*-Cl, R_3 = Me	**7**	58
6	X = C, R_1 = H, R_2 = *p*-F, R_3 = Me	**8**	43
7	X = C, R_1 = H, R_2 = *p*-Br, R_3 = Me	**9**	50
8	X = C, R_1 = H, R_2 = *p*-Cl, R_3 = Me	**10**	57
9	X = N, R_1 = H, R_2 = H, R_3 = Bz	**11**	46
10	X = C, R_1 = *p*-Cl, R_2 = H, R_3 = Me	**12**	72
11	X = C, R_1 = *p*-F, R_2 = H, R_3 = Me	**13**	51
12	X = C, R_1 = H, R_2 = H, R_3 = Et	**14**	75
13	X = C, R_1 = H, R_2 = H, R_3 = CH_2CH_2CN	**15**	64

[a]Reaction conditions: *N*-methyl-*N*-phenylcinnamamide (1.0 mmol), pentane-2,4-dione (2.0 mmol), $AgNO_3$ (0.2 mmol) and $K_2S_2O_8$ (2.0 mmol), heating to 100 °C for 15 h, CH_3CN/H_2O (V : V = 3 : 3 mL).
[b]Isolated yield.

The novel reactions were carried out under the optimised reaction conditions, and the results summarised in Table 2. As shown in Table 2, many 3,4-dihydroquinolin-2(1*H*)-ones could be obtained cleanly under metal-free condition. MeO, Cl, Br, F, and pyridine substituents in substrates **1** were compatible with the current condition. Electron-withdrawing and donating substituted groups, such as *o*-Cl(Br), *p*-Br(Cl, F), *m*-OMe and *o*-Me on the phenyl ring (**2**) of cinnamic acid do not influence the reactivity. The products were obtained in moderate yields (Table 2, **3**–**10**). For example, (*E*)-*N*-methyl-*N*-phenyl-3-(o-tolyl)acrylamide reacted with **2** to form the 3,4-dihydroquinoline-2(1*H*)-one **5** in 56% yield. Electron-withdrawing group on phenyl ring of substrate **1** also worked well in this transformation. For example, *N*-(4-fluorophenyl)-*N*-methylcinnamamide reacted with **2** to produce the product **13** in 51% yield. On changing the *N*-protecting group from Me to Et, Bz and CH_3CH_2CN, the reaction still proceeded well (Table 2, 11, 14 and 15). Unfortunately, the reaction did not work well under the optimised conditions when using 1-phenylbutane-1,3-dione and ethyl 3-oxobutanoate as substrate **2** (Table 1, 16 and 17). The reason for this is not clear at present.

In summary, we have developed a radical tandem cyclisation to synthesise 3,4-disubstituted dihydroquinoline-2(1*H*)-ones that have very important place in pharmaceutical field. Method worked in aqueous solution without a metal which eliminated the worries of metal contamination in the preparation of drugs. Further investigations of this method are ongoing in our laboratory.

Experimental

All experiments were carried out using a conical flask in the air. Cinnamic acids, thionyl chloride, aromatic secondary amines and pentane-2,4-dione were purchased from commercial suppliers and used as received unless otherwise noted. All solvents and other commercially available reagents were purchased from Acros or TCI companies and used directly. Reactions were monitored by TLC (Qingdao Haiyang Chemical Co. Ltd. Silica gel 60 F254). Products were detected using a UV-Vis lamp (254 nm). Column chromatography was performed on Qingdao Haiyang Chemical Co. Ltd. Gel 60 (200–300 mesh). The ^1H and ^{13}C NMR spectras were obtained on a Bruker 400 MHz NMR Fourier transform spectrometer. ^1H NMR data were reported as: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. ^{13}C NMR data were reported in terms of chemical shift (δ ppm) multiplicity, and coupling constant (Hz). The spectra are referenced against the internal solvent ($CDCl_3$, δ ^1H = 7.26 ppm, ^{13}C = 77.0 ppm; DMSO-d6, δ ^1H = 2.50 ppm, ^{13}C = 40.0 ppm). Data are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. ESI-MS spectra were recorded on a Bruker Esquire 3000.

Synthesis of substrate **1***; general procedure*

A 50 mL anhydrous flask was fitted with a magnetic stirrer bar, and cinnamic acid (5 mmol, 0.74 g) and $SOCl_2$ (5 mL) were added. After stirring at 60 °C for 3 h, the redundant $SOCl_2$ was evaporated under reduced pressure and the liquid was added dropwise into another flask containing *N*-methylaniline (10 mmol, 1.07 g) dissolved in anhydrous CH_2Cl_2 (20 mL). The mixture was stirred for 1 h at room temperature. The organic phase was then washed by HCl aqueous solution and K_2CO_3 aqueous solution, then dried by anhydrous Na_2SO_4. After evaporating the CH_2Cl_2, the *N*-methyl-*N*-phenylcinnamamide was obtained in 97% yield and used in the next step directly.

Synthesis of **3**–**15***; general procedure*

1 (1.0 mmol), **2** (2.0 mmol), $K_2S_2O_8$ (540 mg, 2.0 mmol) and a stirrer were added to a 50 mL tube and then CH_3CN (3 mL) and H_2O (3 mL) were added. The mixture was stirred at 100 °C for 15 h (monitored by TLC). The solution was then diluted by ethyl acetate (20 mL) and washed with a solution of K_2CO_3 and water, then dried by anhydrous Na_2SO_4. The crude mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 15 : 1–6 : 1, v/v) to give the products **3**–**15**.

3-(1-Methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydroquinolin-3-yl) pentane-2,4-dione (**3**): Yellow solid; m.p. 144–148 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.31 (m, 4H), 7.14–7.09 (m, 3H), 7.04 (dd, *J*=7.6 Hz,0.8 Hz,1H), 6.83 (d, *J*=7.2 Hz, 1H), 4.22 (d, *J*=8.4 Hz, 1H), 3.79 (t, *J*=7.6 Hz, 1H), 3.53 (d, *J*=7.2 Hz, 1H), 3.41 (s, 3H), 2.18 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.13, 202.87, 168.76, 139.69, 139.60, 129.16, 128.60, 128.44, 128.44, 128.33, 127.74, 127.25, 123.46, 114.90, 66.87, 48.87, 45.03, 30.14, 30.08, 29.95, 29.71. FT-IR ν/cm^{-1} (KBr): 1720, 1666, 1593, 1466, 1377, 1250, 744, 702. HRMS (ESI) calcd for $C_{21}H_{21}NO_3$ [M+H]$^+$:336.1594; found:336.1592.

3-(4-(3-Methoxyphenyl)-1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)pentane-2,4-dione (**4**): Yellow liquid: ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.36–7.26 (m, 1H),7.10 (d, *J*=8.4 Hz, 1H), 7.39 (t, *J*=7.2 Hz, 1H), 6.86 (dd, *J*=7.8 Hz, 2.4 Hz, 2H), 6.74 (d, *J*=8.0 Hz, 1H), 6.66 (s, 1H), 4.19 (d, *J*=8.8 Hz, 1H), 3.80 (s, 3H), 3.77 (t, *J*=7.2 Hz, 1H), 3.54 (t, *J*=7.2 Hz, 1H), 3.41 (s, 3H), 2.19 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.15, 202.84, 168.75, 160.13, 141.32, 139.57, 130.20, 128.58, 128.32, 127.14, 123.46, 120.68, 114.87, 114.36, 112.80, 66.70, 55.22, 48.77, 45.03, 30.07, 29.70. FT-IR ν/cm^{-1} (KBr): 1703, 1670, 1601, 1458, 1369, 1263, 1130, 1041, 762. HRMS (ESI) calcd for $C_{22}H_{23}NO_4$ [M+H]$^+$:366.1700; found:366.1697.

3-(1-Methyl-2-oxo-4-(o-tolyl)-1,2,3,4-tetrahydroquinolin-3-yl) pentane-2,4-dione (**5**): Yellow solid m.p. 142–145 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.30 (m, 1H), 7.27–7.17 (m, 3H), 7.10 (dd, *J*=8.0 Hz,1H), 6.98–6.95 (m, 2H), 6.62 (d, *J*=7.6 Hz, 1H), 4.56 (d, *J*=6.4 Hz, 1H), 3.78 (dd, *J*=10.4 Hz, 6.4 Hz, 1H), 3.57 (d, *J*=6.4 Hz, 1H), 3.44 (s, 3H), 2.33 (s, 3H), 2.15 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.48, 203.04, 169.27, 139.85, 137.55, 137.00, 131.35, 128.16, 128.07, 127.92, 127.83, 127.68, 126.91, 123.43, 114.79, 66.09, 47.72, 40.89, 30.38, 30.18, 29.92, 19.65. FT-IR *ν*/cm^{-1} (KBr): 1705, 1668, 1595, 1369, 1136, 752, 723. HRMS (ESI) calcd for $C_{22}H_{23}NO_3$ [M+H]$^+$:350.1751; found: 350.1748.

3-(4-(2-Bromophenyl)-1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)pentane-2,4-dione (**6**): White solid m.p. 181–184 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, *J*=8.0 Hz, 1.2 Hz, 1H), 7.46 (dd, *J*=7.6 Hz, 1.6 Hz, 1H), 7.33–7.28 (m, 1H), 7.22 (m, 1H), 7.12–6.99 (m, 4H), 4.98 (d, *J*=7.2 Hz, 1H), 4.28 (dd, *J*=11 Hz, 6.8 Hz, 1H), 3.93 (d, *J*=10.4 Hz, 1H), 3.47 (s, 3H), 2.35 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.20, 200.72, 169.38, 139.50, 138.62, 133.74, 129.22, 129.01, 128.72, 128.63, 128.47, 127.89, 123.99, 123.79, 115.75, 67.63, 46.54, 41.28, 30.41, 30.18, 29.75. FT-IRν/cm^{-1} (KBr): 1709, 1668, 1595, 1469, 1371, 1020, 750. HRMS (ESI) calcd for $C_{21}H_{20}BrNO_3$ [M+H]$^+$:414.0699; found: 414.0695.

3-(4-(2-Chlorophenyl)-1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)pentane-2,4-dione (**7**): White solid m.p. 178–182 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J*=7.6 Hz, 2.0 Hz, 1H), 7.36–7.24 (m, 4H), 7.11 (d, *J*=7.6 Hz, 1H), 7.04–6.98 (m, 2H), 6.71 (d, *J*=7.6 Hz, 1H), 4.80 (d, *J*=10.0 Hz, 1H), 3.93 (dd, *J*=6.4 Hz, 2.0 Hz, 1H), 3.52 (d, *J*=6.4 Hz, 1H), 3.43 (s, 3H), 2.21 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.09, 202.50, 168.75, 13 9.74, 136.80, 134.82, 130.52, 130.29, 129.23, 128.39, 127.95, 127.74, 126.55, 123.46, 114.92, 66.27, 47.21, 42.13, 30.43, 30.14, 29.89; FT-IR *ν*/cm^{-1} (KBr): 1705, 1676, 150 9, 1471, 1369, 1259, 1041, 752. HRMS (ESI) calcd for $C_{21}H_{20}ClNO_3$ [M+H]$^+$:370.1204; found:370.1214.

3-(4-(4-fluorophenyl)-1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)pentane-2,4-dione (**8**): Yellow solid m.p. 144–148 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.34 (m, 1H), 7.12–7.02 (m, 6H), 6.85 (d, *J*=7.2 Hz, 1H), 4.19 (d, *J*=7.6 Hz, 1H), 3.76 (t, *J*=8.0 Hz, 1H), 3.56 (t, *J*=8.oHz, 1H), 3.39 (s, 3H), 2.19 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.77, 202.65, 168.44, 163.34, 160.89, 139.53, 135.59, 135.55, 129.91, 129.83, 128.69, 128.56, 126.67, 123.61, 116.11, 115.90, 115.06, 67.23, 48.97, 44.31, 30.33, 30.04, 29.54. FT-IR *ν*/cm^{-1} (KBr): 1707, 1664, 1504, 1375, 1225, 762, 667. HRMS (ESI) calcd for $C_{21}H_{20}FNO_3$ [M+H]$^+$:354.1500; found:354.1498.

3-(4-(4-Bromophenyl)-1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)pentane-2,4-dione (**9**): Yellow liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.46 (m, 2H), 7.39–7.35 (m, 1H), 7.12 (d, *J*=8.4 Hz, 1H), 7.06–6.99 (m, 3H), 6.85 (m, *J*=7.2 Hz, 1H), 4.16 (d, *J*=7.6 Hz, 1H), 3.75 (t, *J*=7.6 Hz, 1H), 3.55 (d, *J*=8.0 Hz, 1H), 3.43 (s, 1H), 3.39 (s, 3H), 2.20 (s, 1H), 2.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.74, 202.58, 168.30, 139.52, 138.98, 132.23, 129.95, 128.70, 128.67, 126.19, 123.67, 121.60, 115.10, 67.13, 48.69, 44.47, 30.35, 30.04, 29.62. FT-IR *ν*/cm^{-1} (KBr): 1703, 1670, 1603, 1489, 1371, 1138, 1074, 1012, 810, 760. HRMS (ESI) calcd for $C_{21}H_{20}BrNO_3$ [M+H]$^+$:414.0699; found:414.0695.

3-(4-(4-Chlorophenyl)-1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)pentane-2,4-dione (**10**): Yellow solid m.p. 139–142 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.34 (m, 1H), 7.33–7.30 (m, 2H), 7.12 (d, *J*=8.0 Hz, 1H), 7.07–7.02 (m, 3H), 6.85 (m, *J*=7.6 Hz, 1H), 4.18 (d, *J*=7.6 Hz, 1H), 3.75 (t, *J*=7.6 Hz, 1H), 3.55 (d, *J*=8.0 Hz, 1H), 3.39 (s, 1H), 2.20 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 202.74, 202.59, 168.33, 139.52, 138.45, 133.50, 129.60, 128.70, 128.65, 126.28, 123.66, 115.10, 67.14, 48.76, 44.40, 30.33, 30.03, 29.59. FT-IR *ν*/cm^{-1} (KBr): 1703, 1670, 1603, 1493, 1371, 1138, 1095, 1016, 760. HRMS (ESI) calcd for $C_{21}H_{20}ClNO_3$ [M+H]$^+$:370.1204; found:370.1202.

3-(1-Benzyl-2-oxo-4-phenyl-1,2,3,4-tetrahydro-1,8-naphthyridin-3-yl)pentane-2,4-dione (**11**): White solid m.p. 143–148 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J*=3.6 Hz, 1H), 7.47 (d, *J*=7.6 Hz, 2H), 7.36–7.23 (m, 7H), 7.10–7.04 (m, 3H), 6.91 (dd, *J*=12.4 Hz, 4.8 Hz, 1H), 5.51 (q, *J*=14.0 Hz, 1H), 4.28 (d, *J*=10.0 Hz, 1H), 3.84 (dd, *J*=6.8H z,5.8 Hz,1H), 3.58 (d, *J*=5.6 Hz, 1H), 2.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.89, 202.69, 169.16, 150.62, 146.84, 138.93, 137.77, 136.67, 129.37, 128.59, 128.49, 128.21, 128.10, 127. 03, 122.69, 118.91, 66.40, 48.63, 43.93, 43.86, 30.30, 29.93. FT-IR *ν*/cm^{-1} (KBr):1705, 1658, 1587, 1442, 1209, 766, 704. HRMS (ESI) calcd for $C_{24}H_{24}N_2O_3$ [M+H]$^+$:370.1204; found:370.1202.

3-(6-Chloro-1-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)pentane-2,4-dione (**12**): White solid m.p. 173–175 °C: ^{1}H NMR (400 MHz, CDCl3) δ 7.42–7.35 (m, 3H), 7.33 (m, 1H), 7.14 (dd, *J*=7.6 Hz, 1.6 Hz, 2H), 7.02 (d, *J*=8.8 Hz, 1H), 6.76 (dd, *J*=1.8 Hz, 0.8 Hz, 1H), 4.22 (d, *J*=9.6 Hz, 1H), 3.75 (dd, *J*=9.4 Hz, 6.8 Hz, 1H), 3.49 (t, *J*=7.6 Hz, 1H), 3.39 (s, 3H), 2.17 (d, *J*=5.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.10, 202.66, 168.54, 13 8.81, 138.31, 129.42, 128.67, 128.45, 128.34, 128.14, 128.12, 116.08, 66.39, 48.53, 44.87, 30.22, 29.97. FT-IR ν/cm^{-1} (KBr): 1707, 1672, 1493, 1410, 1371, 1246, 1136, 818, 710. HRMS (ESI) calcd for $C_{21}H_{20}ClNO_3$ [M+H]$^+$:370.1204; found:370.1202.

3-(6-Fluoro-1-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)pentane-2,4-dione (**13**): White solid m.p. 155–159 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.33 (m, 3H), 7.15 (dd, *J*=7.6 Hz, 1.6 Hz, 2H), 7.04 (d, *J*=4.8 Hz, 2H), 6.51 (dd, *J*=9.2 Hz, 1.2 Hz, 1H), 4.24 (d, *J*=10.0 Hz, 1H), 3.75 (dd, *J*=9.6 Hz, 7.8 Hz, 1H), 3.50 (t, *J*=6.8 Hz, 1H), 3.40 (s, 3H), 2.16 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.14, 202.75, 168.50, 159.99, 157.57, 138.85, 135.87, 129.38, 128.52, 128.10, 116.07, 115.99, 115.66, 115.42, 114.66, 11 4.44, 66.40, 48.54, 44.97, 30.36, 30.22, 29.97. FT-IR *ν*/cm^{-1} (KBr): 1705, 1670, 1504, 1360, 1157, 814. HRMS (ESI) calcd for $C_{21}H_{20}FNO_3$ [M+H]$^+$:354.1500; found:354.1497.

3-(1-Ethyl-2-oxo-4-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)pentane-2,4-dione (**14**): White solid m.p. 128–131 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.26 (m, 4H), 7.15–7.10 (m, 3H), 7.05 (dd, *J*=7.6 Hz, 0.8 Hz, 1H), 6.90 (d, *J*=7.2 Hz, 1H), 4.14 (d, *J*=6.8 Hz, 1H), 4.04 (dd, *J*=9.4 Hz, 2.8 Hz, 2H), 3.80 (dd, *J*=8.6 Hz, 2.8 Hz, 1H), 3.60 (d, *J*=8.8 Hz, 1H), 2.20 (s, 3H), 2.13 (s, 3H), 1.28 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.72, 202.69, 167.89, 139.93, 138.51, 129.25, 129.00, 128.45, 128.24, 127.57, 126.86, 123.42, 114.91, 67.71, 48.85, 45.17, 37.72, 30.44, 29.25, 12.63. FT-IR *ν*/cm^{-1} (KBr): 1707, 1655, 1603, 1496, 1466, 1388, 769, 704. HRMS (ESI) calcd for $C_{22}H_{23}NO_3$ [M+H]$^+$:350.1751; found:350.1748.

3-(2,4-Dioxopentan-3-yl)-2-oxo-4-phenyl-3,4-dihydroquinolin-1(2H)-yl)propanenitrile (**15**): White solid m.p. 126–128 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.31 (m, 4H), 7.17–7.05 (m, 4H), 6.90 (d, *J*=7.6 Hz, 1H), 4.33–4.11 (m, 3H), 3.81 (t, *J*=0.8 Hz, 1H), 3.53 (d, *J*=0.8 Hz, 1H), 2.76 (t, *J*=7.2 Hz, 2H), 2.18 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.75, 202.49, 16 8.88, 139.28, 137.86, 129.49, 129.23, 128.76, 128.27, 127.89, 127.26, 124.29, 117.35, 114.53, 66.98, 48.59, 45.03, 39.08, 30.30, 29.63, 15.94. FT-IR *ν*/cm^{-1} (KBr): 1701, 1668, 1599, 1462, 1367, 1169, 748. HRMS (ESI) calcd for $C_{23}H_{22}N_2O_3$ [M+H]$^+$:375.1703; found:375.1700.

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