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Triflic Anhydride Promoted Intramolecular Cyclization of *N*-Aryl Cinnamides: Access to Polysubstituted Quinolin-2(1*H*)-ones

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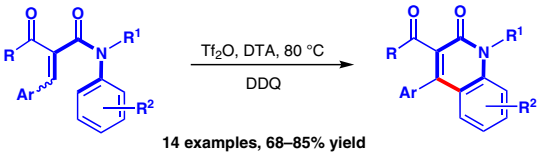

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Abstract A facile and efficient synthesis of polysubstituted quinolin-2(1*H*)-ones is developed via intramolecular cyclization of readily available *N*-aryl cinnamides promoted by triflic anhydride in *N*,*N*-dimethyl trifluoroacetamide (DTA) under mild conditions.

Key words C–C bond formation, cyclization reaction, heterocycles, quinolin-2(1*H*)-ones, triflic anhydride

Quinolin-2(1*H*)-ones and their analogues have drawn considerable interest from researchers as a result of their presence in numerous natural products and synthetic organic compounds, and due to their diverse and useful bioactivities.[1,2] For instance, some substituted quinolin-2(1*H*)-ones have been identified as angiotensin II receptor antagonists, antibiotics, antiplatelet agents and antitumor agents.[3] In addition, the utility of quinolin-2(1*H*)-ones as versatile building blocks for the synthesis of a wide variety of aza-heterocycles has directed extensive research toward the construction of the framework of such compounds.[4] To date, many synthetic approaches are available to access quinolin-2(1*H*)-ones and their derivatives, which include the classical acid-catalyzed Knorr synthesis,[5] the base-catalyzed Friedländer synthesis[6] and the metal-catalyzed heteroannulation of acyclic precursors.[7] Recently, some improved synthetic methods associated with microwaves[8] or irradiation[9] have also been reported. Nevertheless, the development of efficient and convenient synthetic approaches for such aza-heterocycles, in particular those with flexible substituent patterns, is still in demand.

During the course of our studies on the synthesis of highly valuable heterocycles based on β-oxo amide derivatives,[10] we successfully developed efficient syntheses of substituted pyrano[2,3-*b*]quinolines from enaminones mediated by triflic acid,[11] and substituted quinolin-2(1*H*)-ones from penta-2,4-dienamides mediated by concentrated aqueous H_2SO_4.[12] More recently, we achieved a facile synthesis of indeno[2,1-*c*]quinolin-6(7*H*)-ones from α-acetyl *N*-aryl cinnamides in the presence of polyphosphoric acid.[13] In connection with these previous investigations and our continued efforts on the synthesis of heterocycles through acid-mediated processes, we decided to examine the reactivity of α-acyl *N*-aryl cinnamides bearing different substituents toward triflic acid and various anhydrides. As a result of these studies, we developed a facile and efficient synthesis of substituted quinolin-2(1*H*)-ones and dihydroquinolin-2(1*H*)-ones in the presence of triflic anhydride under mild conditions. Herein, we report our experimental results.

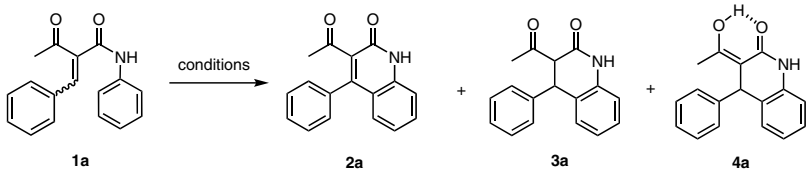
The substrates, *N*-aryl cinnamides **1**, were prepared by Knoevenagel condensation of commercially available β-oxo amides with aryl aldehydes in the presence of piperidine in acetic acid according to a reported procedure.[13] Next, we selected 2-benzylidene-3-oxo-*N*-phenylbutanamide (**1a**) as a model compound to investigate its reactivity under acidic conditions. Thus, the reaction of **1a** was first attempted in the presence of triflic acid (1.0 equiv) in *N*,*N*-dimethyl trifluoroacetamide (DTA) (5.0 mL) at 50 °C, but no reaction occurred as indicated by TLC (Table 1, entry 1). On treatment of **1a** with triflic anhydride (1.0 equiv) at 50 °C in DTA, the reaction proceeded to furnish a major product (45% yield) after work-up and purification by silica gel column chromatography, which was characterized as 3-acetyl-4-phenylquinolin-2(1*H*)-one (**2a**) (entry 2) on the basis of spectral and analytical data.

The optimization of the reaction conditions, including the reaction temperature, the solvent, the additive, and acidic reagents, was then investigated as shown in Table 1. When **1a** and Tf_2O (1.0 equiv) reacted in the presence of DTA at 80 °C, the yield of **2a** reached 79% (Table 1, entry 3).

Increasing the reaction temperature or the amount of Tf_2O had no significant influence on the yield of **2a** or the reaction time (entries 4 and 5). However, a decrease in the amount of Tf_2O to 0.8 equivalents resulted in a lower yield of **2a** (entry 6). A complex mixture was formed when trifluoroacetic anhydride (TFAA) or acetic anhydride (Ac_2O) was employed (entries 7 and 8). Interestingly, the reaction of **1a** and Tf_2O (1.0 equiv) proceeded smoothly in DTA under nitrogen at 80 °C, as indicated by TLC results, to furnish, instead of **2a**, a pair of inseparable products, which were characterized as 3-acetyl-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (**3a**) and 3-(1-hydroxyethylidene)-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (**4a**) on the basis of the NMR and mass spectra (entry 9) (see the Supporting Information). In the ^{1}H NMR spectrum, **3a** displays two characteristic doublets at 3.94 and 4.72 ppm, which might be assigned to the adjacent 3-H and 4-H of the quinolin-2(1*H*)-one ring, respectively, and the resonance signal of the amide N–H appears at 8.21 ppm. By contrast, **4a** displays a characteristic singlet at 4.90 ppm assigned to 4-H of the quinolin-2(1*H*)-one ring, the resonance signal of hydroxy O–H appears at 14.54 ppm due to the formation of a hydrogen bond, and that for the amide N–H is shifted to 7.69 ppm. With the establishment of the structures of **3a** and **4a**, it is not difficult to conclude that quinolin-2(1*H*)-one **2a** is derived from dihydroquinolin-2(1*H*)-ones **3a** and **4a** via an oxidation process. Considering all the above results, and in particular that no reaction was observed in the presence of triflic acid (as shown in Table 1, entry 1), triflic anhydride acts as a promoter for the intramolecular cyclization of *N*-aryl cinnamides **1** and the subsequent oxidation.[14]

It is worth noting that when the reaction of **1a** with triflic anhydride was conducted in the absence of DTA in toluene at 80 °C, only a mixture of **3a** and **4a** was obtained, even on prolonging the reaction time (Table 1, entry 10). Next, two separate experiments were performed involving treatment of **1a** with triflic anhydride (1.0 equiv) and DTA (1.0 equiv) in toluene at 80 °C (entries 11 and 12). These experiments revealed that the reaction formed a mixture of compounds **2a**, **3a** and **4a** within 12 hours, and that both **3a** and **4a** could be completely converted into compound **2a** when the reaction time was extended to 24 hours. These results suggest that DTA plays an important role in assisting the oxidation of 3,4-dihydroquinolin-2(1*H*)-ones **3a** and **4a** to the corresponding quinolin-2(1*H*)-one **2a**, which is beyond that of a solvent. To further promote this transformation,

Table 1 Reaction of **1a** under Different Conditions[a]



Entry	Reagent (equiv)	Additive (equiv)	Solvent	Temp (°C)	Time (h)	Yield (%)[b]	
						2a	**3a** + **4a**
1	TfOH (1.0)	–	DTA	50	24	no reaction	
2	Tf_2O (1.0)	–	DTA	50	24	45	–
3	Tf_2O (1.0)	–	DTA	80	19	79	–
4	Tf_2O (1.0)	–	DTA	100	17	76	–
5	Tf_2O (1.2)	–	DTA	80	16	74	–
6	Tf_2O (0.8)	–	DTA	80	24	68	–
7	TFAA (1.0)	–	DTA	80	24	mixture	
8	Ac_2O (1.0)	–	DTA	80	24	mixture	
9	Tf_2O (1.0)	–	DTA	80	7	0	85 (1:2)[c]
10	Tf_2O (1.0)	–	toluene	80	12	0	82 (1:2)
11	Tf_2O (1.0)	DTA (1.0)	toluene	80	12	29	54 (1:3)
12	Tf_2O (1.0)	DTA (1.0)	toluene	80	24	76	0
13	**Tf_2O (1.0)**	**DDQ (1.0)**	**DTA**	**80**	**4**	**81**	**0**
14	Tf_2O (1.0)	DDQ (1.0)	toluene	80	6	75	0

[a] Reaction conditions: **1a** (1.0 mmol), additive (1.0 mmol), solvent (5.0 mL), under air.
[b] Yield of isolated product. Data in parentheses refers to the ratio of **3a**/**4a** determined by ^{1}H NMR spectroscopy.
[c] Reaction under N_2.

we investigated the reaction of **1a** with triflic anhydride in the presence of DDQ (1.0 equiv) in DTA or toluene at 80 °C (entries 13 and 14). It was observed that the reaction time could be dramatically reduced to several hours in both cases.

Using the optimized conditions (see Table 1, entry 13), a series of reactions of α-acetyl *N*-aryl cinnamides **1** was carried out and some of the results are listed in Table 2. It was found that the reactions of α-acetyl *N*-aryl cinnamides **1b–g** bearing different electron-donating groups R^2 and R^3 proceeded efficiently to afford the corresponding quinolin-2(1*H*)-ones **2b–g** in good to high yields (Table 2, entries 2–7). The investigation revealed that α-acetyl *N*-aryl cinnamides **1h** and **1i** bearing electron-withdrawing R^3 groups (Cl and NO_2) could be converted into the corresponding quinolin-2(1*H*)-ones **2h** and **2i** under identical reaction conditions (entries 8 and 9). The validity of this quinolin-2(1*H*)-one synthesis was evaluated by employing α-acetyl *N*-aryl tertiary cinnamides **1j**,**k** and α-benzoyl *N*-aryl secondary cinnamides **1l–n** as the substrates (entries 10–14). It should be mentioned that the structure of **2a** was further confirmed by single-crystal X-ray analysis and from its spectral and analytical data (Figure 1).

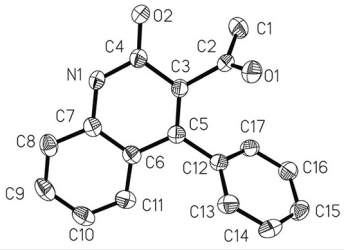
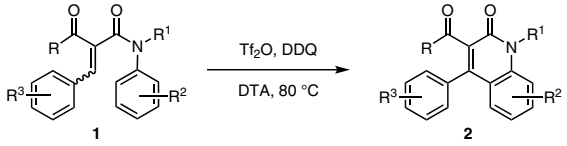


Figure 1 ORTEP drawing of **2a**

To gain insight into the mechanism of this transformation, a separate experiment was carried out by treatment of an isolated mixture of **3a** and **4a** with DDQ in DTA at 80 °C, and quinolin-2(1*H*)-one **2a** was exclusively obtained in 87% yield. On the basis of all the obtained experimental results, a plausible mechanism for the reaction of *N*-aryl cinnamide **1** with Tf_2O/DTA is proposed as depicted in Scheme 1. The substrate *N*-aryl cinnamide **1** reacts with Tf_2O in DTA to generate a very reactive iminium triflate **A**,[15,16] followed by an intramolecular nucleophilic addition reaction to form intermediates **B** and **B′**.[17] The hydrolysis of intermediates **B** and **B′** gives rise to a mixture of **3** and **4**, which can be oxidized to give quinolin-2(1*H*)-one **2**. In the presence of

Table 2 Synthesis of Substituted Quinolin-2(1*H*)-ones **2** from *N*-Aryl Cinnamides **1**[a]

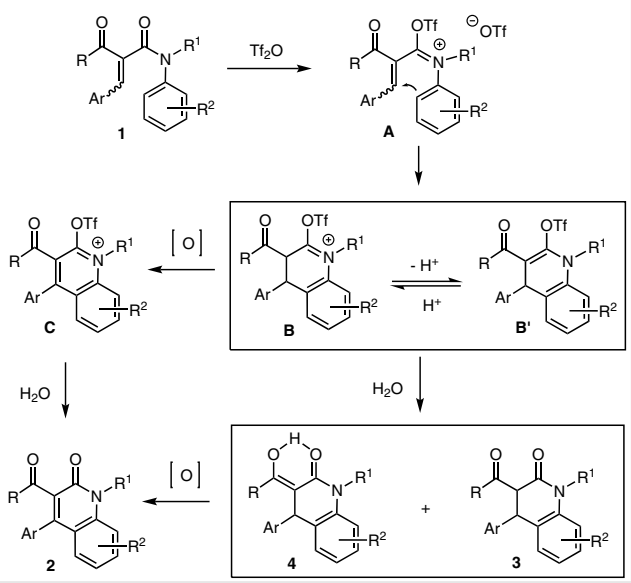


1 **2**

Entry	Substrate	R	R^1	R^2	R^3	Product	Time (h)	Yield (%)[b]
1	**1a**	Me	H	H	H	**2a**	4.0	81
2	**1b**	Me	H	2-Me	H	**2b**	3.5	77
3	**1c**	Me	H	4-Me	H	**2c**	3.5	83
4	**1d**	Me	H	4-Me	4-Me	**2d**	4.0	85
5	**1e**	Me	H	2-Me	4-Me	**2e**	4.5	68
6	**1f**	Me	H	H	2-Me	**2f**	3.5	75
7	**1g**	Me	H	H	4-MeO	**2g**	4.0	80
8	**1h**	Me	H	H	4-Cl	**2h**	3.5	76
9	**1i**	Me	H	H	3-O_2N	**2i**	3.0	77
10	**1j**	Me	Me	H	H	**2j**	4.0	84
11	**1k**	Me	Me	H	4-Cl	**2k**	5.0	82
12	**1l**	Ph	H	H	H	**2l**	4.0	80
13	**1m**	Ph	H	Me	H	**2m**	7.0	74
14	**1n**	Ph	H	H	4-MeO	**2n**	4.0	83

[a] Reaction conditions: **1** (1.0 mmol), Tf_2O (1.0 mmol), DDQ (1.0 mmol), DTA (5.0 mL), 80 °C.
[b] Yield of isolated product.

DDQ, intermediates **B** and **B′** quickly undergo oxidation to form triflate **C**, which is hydrolyzed during the work-up process to afford the final product **2**.



Scheme 1 A plausible mechanism for the cyclization reaction of *N*-aryl cinnamides **1**

In summary, a facile and efficient synthesis of polysubstituted quinolin-2(1*H*)-ones **2** is developed via triflic anhydride promoted intramolecular cyclization of readily available *N*-aryl cinnamides **1**. The ready availability of the substrates, mild reaction conditions, metal-catalyst-free, simple procedure, good to high yields and synthetic potential of the products makes this novel protocol very attractive. Further work on the mechanism of the reaction and the utilization and extension of the scope of the methodology is currently under investigation in our laboratory.

All reagents were purchased from commercial sources and used without purification, unless otherwise indicated. The products were purified by column chromatography over Haiyang silica gel (200–400 mesh). Compounds **2a**,**c**,**g**,**h**,**j** are known and were identified by ^{1}H NMR, ^{13}C NMR, IR spectroscopy and mass spectrometry. The data are in good agreement with those reported in the literature. Melting points were determined using a Perkin-Elmer PE-2400 instrument and are uncorrected. IR spectra (KBr) were recorded on a Shimadzu FTIR-8400S FTIR spectrophotometer in the range of 400–4000 cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-300 (or Varian Inova-400) spectrometers at 25 °C at 300 MHz (or 400 MHz) and 100 MHz, respectively, with TMS as the internal standard. Mass spectra were recorded on a Bruker Daltonics-Autoflex III Smartbeam MALDI TOF mass spectrometer.

3-Acetyl-4-phenylquinolin-2(1*H*)-one (2a);[6e,8d] Typical Procedure

To a solution of Tf_2O (282 mg, 1.0 mmol) in DTA (5.0 mL) was added **1a** (265 mg, 1.0 mmol) and DDQ (227 mg, 1.0 mmol) with stirring at 0 °C for 30 min. The mixture was then heated at 80 °C for 4 h. The resulting mixture was poured into saturated aqueous NaCl solution (30 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were washed with H_2O, dried over anhydrous $MgSO_4$, filtered, and evaporated in vacuo. The crude product was purified by flash silica gel chromatography (PE–EtOAc, 3:1) to give product **2a**.

Yield: 213 mg (81%); white solid; mp 242–245 °C.

IR (KBr): 2997, 2881, 2847, 1709, 1657, 1595, 1481, 1431, 1374, 1344, 761, 700, 659 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.23 (s, 3 H), 7.14 (t, *J* = 7.2 Hz, 1 H), 7.28–7.37 (m, 4 H), 7.48–7.54 (m, 4 H), 11.19 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.7, 115.6, 118.8, 121.9, 126.6, 127.5, 127.9, 128.0, 130.4, 131.8, 133.3, 137.3, 148.0, 160.6, 200.9.

MS (MALDI-TOF): *m*/*z* = 286.1 [M + Na]$^+$.

Colorless crystal, *M* = 263.28, monoclinic, *P*21/*c*, *a* = 12.6491(18) Å, *b* = 7.0985(10) Å, *c* = 15.060(2) Å, *α* = 90.00°, *β* = 97.09°, *γ* = 90.00°, *V* = 1341.9(3) Å^3, *Z* = 4, *T* = 273 K, F000 = 552.0, F000′ = 552.25, *R* = 0.0461 (2211), *wR*2 = 0.1262 (2647). CCDC 1033852 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

3-Acetyl-8-methyl-4-phenylquinolin-2(1*H*)-one (2b)

Yield: 213 mg (77%); white solid; mp 244–246 °C.

IR (KBr): 3156, 3108, 3021, 1712, 1632, 1593, 1472, 1444, 1371, 770, 755, 705 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.26 (s, 3 H), 2.53 (s, 3 H), 7.04 (t, *J* = 7.8 Hz, 1 H), 7.12 (d, *J* = 7.8 Hz, 1 H), 7.29–7.32 (m, 2 H), 7.38 (d, *J* = 6.9 Hz, 1 H), 7.46–7.48 (m, 3 H), 9.74 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.3, 30.5, 118.9, 121.3, 123.1, 125.0, 127.4, 127.7, 127.9, 131.6, 131.8, 133.7, 135.8, 148.3, 159.9, 200.7.

MS (MALDI-TOF): *m*/*z* = 300.3 [M + Na]$^+$.

3-Acetyl-6-methyl-4-phenylquinolin-2(1*H*)-one (2c)[6f]

Yield: 230 mg (83%); yellow solid; mp 260–262 °C.

IR (KBr): 2970, 2911, 2824, 1711, 1645, 1498, 1473, 1416, 1376, 818, 783, 705 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 6 H), 7.01 (s, 1 H), 7.31–7.35 (m, 4 H), 7.48–7.51 (m, 3 H), 12.16 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.1, 30.7, 115.5, 118.8, 126.0, 127.5, 127.8, 128.0, 131.6, 131.8, 131.9, 133.5, 135.3, 147.7, 160.4, 201.1.

MS (MALDI-TOF): *m*/*z* = 300.2 [M + Na]$^+$.

3-Acetyl-6-methyl-4-(*p*-tolyl)quinolin-2(1*H*)-one (2d)

Yield: 247 mg (85%); yellow solid; mp 262–264 °C.

IR (KBr): 2973, 2918, 2848, 1705, 1648, 1598, 1472, 1375, 1351, 825 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 3 H), 2.29 (s, 3 H), 2.44 (s, 3 H), 7.06 (s, 1 H), 7.20 (d, *J* = 8.1 Hz, 2 H), 7.28–7.37 (m, 4 H), 11.77 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.1, 20.4, 30.8, 115.5, 118.9, 126.0, 127.9, 128.2, 130.4, 131.5, 131.8, 135.3, 137.8, 147.9, 150.4, 201.3.

MS (MALDI-TOF): *m*/*z* = 314.2 [M + Na]$^+$.

3-Acetyl-8-methyl-4-(*p*-tolyl)quinolin-2(1*H*)-one (2e)

Yield: 197 mg (68%); white solid; mp 273–276 °C.

IR (KBr): 3151, 3093, 2992, 1710, 1628, 1567, 1472, 1445, 1370, 857, 794, 764 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3 H), 2.43 (s, 3 H), 2.50 (s, 3 H), 7.04 (t, *J* = 7.5 Hz, 1 H), 7.14–7.20 (m, 4 H), 7.29 (s, 1 H), 7.36 (d, *J* = 7.2 Hz, 1 H), 9.32 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2, 20.3, 30.6, 119.0, 121.3, 122.8, 125.1, 127.9, 128.2, 130.6, 131.5, 131.8, 135.8, 137.7, 148.4, 159.8, 200.8.

MS (MALDI-TOF): *m*/*z* = 292.3 $[M + H]^+$.

3-Acetyl-4-(*o*-tolyl)quinolin-2(1*H*)-one (2f)

Yield: 207 mg (75%); yellow solid; mp 212–215 °C.

IR (KBr): 2990, 2878, 2839, 1711, 1642, 1597, 1479, 1430, 1357, 755 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3 H), 2.35 (s, 3 H), 7.03 (d, *J* = 7.8 Hz, 1 H), 7.12 (t, *J* = 6.9 Hz, 2 H), 7.28–7.44 (m, 4 H), 7.54 (t, *J* = 8.1 Hz, 1 H), 12.08 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.8, 30.4, 115.5, 118.7, 122.1, 124.9, 126.3, 127.5, 128.0, 129.2, 130.5, 131.5, 133.0, 135.2, 137.2, 148.3, 160.6, 200.3.

MS (MALDI-TOF): *m*/*z* = 300.2 $[M + Na]^+$.

3-Acetyl-4-(4-methoxyphenyl)quinolin-2(1*H*)-one (2g)[8e]

Yield: 234 mg (80%); white solid; mp 257–259 °C.

IR (KBr): 2965, 2882, 2834, 1705, 1653, 1608, 1498, 1429, 1377, 818, 766 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.29 (s, 3 H), 3.88 (s, 3 H), 7.01 (d, *J* = 8.0 Hz, 2 H), 7.14 (t, *J* = 7.2 Hz, 1 H), 7.27 (d, *J* = 8.4 Hz, 2 H), 7.34 (d, *J* = 8.0 Hz, 1 H), 7.47 (d, *J* = 8.0 Hz, 1 H), 7.53 (t, *J* = 7.2 Hz, 1 H), 12.80 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.9, 55.6, 114.4, 116.1, 119.7, 122.7, 126.6, 127.5, 130.7, 131.6, 133.9, 138.9, 147.3, 159.8, 159.9, 202.2.

MS (MALDI-TOF): *m*/*z* = 316.2 $[M + Na]^+$.

3-Acetyl-4-(4-chlorophenyl)quinolin-2(1*H*)-one (2h)[6f,8e]

Yield: 226 mg (76%); white solid; mp 260–262 °C.

IR (KBr): 2994, 2884, 2847, 1707, 1652, 1486, 1378, 817, 760 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 7.13 (t, *J* = 8.0 Hz, 1 H), 7.19 (d, *J* = 8.0 Hz, 1 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.41–7.43 (m, 2 H), 7.46 (s, 1 H), 7.53 (t, *J* = 8.0 Hz, 1 H), 12.53 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 32.0, 116.2, 119.2, 122.9, 127.5, 129.0, 131.2, 131.8, 133.6, 133.9, 134.0, 139.0, 146.5, 159.7, 202.1.

MS (MALDI-TOF): *m*/*z* = 320.2 $[M + Na]^+$.

3-Acetyl-4-(3-nitrophenyl)quinolin-2(1*H*)-one (2i)

Yield: 237 mg (77%); white solid; mp 233–236 °C.

IR (KBr): 2997, 2885, 2853, 1700, 1673, 1530, 1481, 1351, 765 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.47 (s, 3 H), 7.10 (d, *J* = 6.0 Hz, 1 H), 7.19 (t, *J* = 9.0 Hz, 1 H), 7.42 (d, *J* = 9.0 Hz, 1 H), 7.60 (t, *J* = 6.0 Hz, 1 H), 7.69–7.74 (m, 2 H), 8.20 (s, 1 H), 8.35–8.37 (m, 1 H), 11.62 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 31.9, 116.2, 119.0, 123.1, 124.0 (2 C), 127.5, 130.7, 132.0, 134.1, 136.0, 136.4, 139.1, 145.7, 148.2, 159.7, 202.1.

MS (MALDI-TOF): *m*/*z* = 331.2 $[M + Na]^+$.

3-Acetyl-1-methyl-4-phenylquinolin-2(1*H*)-one (2j)[7i]

Yield: 232 mg (84%); light yellow solid; mp 179–180 °C.

IR (KBr): 2983, 2940, 1710, 1632, 1371, 767, 706 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3 H), 3.80 (s, 3 H), 7.16 (t, *J* = 6.0 Hz, 1 H), 7.28–7.32 (m, 3 H), 7.43–7.48 (m, 4 H), 7.61 (t, *J* = 6.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.4, 30.4, 113.2, 119.6, 121.3, 127.5, 127.6, 127.8, 128.1, 130.3, 132.0, 133.1, 138.6, 145.3, 158.3, 200.7.

MS (MALDI-TOF): *m*/*z* = 278.1 $[M + H]^+$.

3-Acetyl-4-(4-chlorophenyl)-1-methylquinolin-2(1*H*)-one (2k)

Yield: 255 mg (82%); yellow solid; mp 172–174 °C.

IR (KBr): 3083, 3000, 2938, 1710, 1640, 1373, 1316, 822, 767 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3 H), 3.80 (s, 3 H), 7.18 (t, *J* = 6.0 Hz, 1 H), 7.23–7.26 (m, 3 H), 7.44–7.47 (m, 3 H), 7.63 (t, *J* = 6.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.5, 30.4, 113.4, 119.4, 121.5, 127.4, 127.8, 129.5, 130.6, 131.6, 134.1, 138.7, 144.3, 158.3, 200.5.

MS (MALDI-TOF): *m*/*z* = 312.1 $[M + H]^+$.

3-Benzoyl-4-phenylquinolin-2(1*H*)-one (2l)

Yield: 260 mg (80%); white solid; mp 251–252 °C.

IR (KBr): 3019, 2999, 1673, 1635, 1591, 1471, 1374, 839, 749, 690 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.13 (t, *J* = 7.2 Hz, 2 H), 7.28–7.33 (m, 6 H), 7.36 (d, *J* = 7.5 Hz, 2 H), 7.49 (t, *J* = 7.5 Hz, 2 H), 7.84 (d, *J* = 7.2 Hz, 2 H), 11.64 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 115.8, 118.9, 121.9, 126.4, 127.2, 127.4, 127.7, 128.2 (2 C), 129.8, 130.3, 132.3, 133.0, 136.2, 137.5, 149.4, 161.0, 193.5.

MS (MALDI-TOF): *m*/*z* = 348.2 $[M + Na]^+$.

3-Benzoyl-6-methyl-4-phenylquinolin-2(1*H*)-one (2m)

Yield: 251 mg (74%); white solid; mp 255–257 °C.

IR (KBr): 2997, 2915, 1676, 1641, 1593, 1500, 1373, 818, 766, 697 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.28 (s, 3 H), 7.03 (s, 1 H), 7.18–7.24 (m, 3 H), 7.29–7.35 (m, 6 H), 7.49 (t, *J* = 7.2 Hz, 1 H), 7.81 (d, *J* = 7.2 Hz, 2 H), 12.52 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.0, 115.7, 118.8, 125.7, 127.2, 127.4, 127.6, 128.2 (2 C), 129.7, 131.5, 131.8, 132.2, 133.1, 135.6, 136.3, 149.2, 160.8, 193.7.

MS (MALDI-TOF): *m*/*z* = 362.2 $[M + Na]^+$.

3-Benzoyl-4-(4-methoxyphenyl)quinolin-2(1*H*)-one (2n)

Yield: 295 mg (83%); light yellow solid; mp 264–266 °C.

IR (KBr): 2955, 2934, 1676, 1625, 1504, 1476, 1377, 833, 753 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.77 (s, 3 H), 6.82 (d, *J* = 6.0 Hz, 2 H), 7.11–7.19 (m, 3 H), 7.28 (s, 1 H), 7.36 (t, *J* = 7.2 Hz, 3 H), 7.44–7.52 (m, 2 H), 7.83 (d, *J* = 6.0 Hz, 2 H), 11.96 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 54.2, 112.7, 115.8, 119.2, 121.8, 125.1, 126.4, 127.4, 128.2, 129.6, 129.8, 130.2, 132.3, 136.2, 137.5, 149.3, 158.8, 161.0, 193.7.

MS (MALDI-TOF): *m*/*z* = 356.3 $[M + H]^+$.

3-Acetyl-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (3a) and 3-(1-Hydroxyethylidene)-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (4a)

Yield: 225 mg (85%); yellow solid.

IR (KBr): 3202, 3040, 3022, 1642, 1597, 1488, 1434, 1314, 895, 757 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ (**3a** + **4a**) = 1.99 (s, 3 H), 2.25 (s, 3 H), 3.94 (d, *J* = 7.4 Hz, 1 H), 4.72 (d, *J* = 7.4 Hz, 1 H), 4.90 (s, 1 H), 6.74 (d, *J* = 8.0 Hz, 1 H), 6.81 (d, *J* = 8.0 Hz, 1 H), 6.94–6.96 (m, 1 H), 6.97–6.99 (m, 1 H), 7.10–7.19 (m, 3 H), 7.10–7.26 (m, 6 H), 7.25–7.26 (m, 4 H), 7.31–7.33 (m, 1 H), 7.69 (s, 1 H), 8.21 (s, 1 H), 14.54 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (**3a** + **4a**) = 18.3, 29.1, 43.1, 43.7, 60.3, 97.8, 114.4, 114.7, 122.4, 122.9, 124.4, 124.7, 125.6, 125.8, 126.4, 126.6, 127.0, 127.2, 127.8, 127.9, 128.0, 133.7, 134.8, 139.2, 145.3, 167.0, 169.4, 174.2, 201.4.

MS (MALDI-TOF): *m*/*z* = 288.2 $[M + Na]^+$.

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Supporting Information

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References

(1) (a) Chung, H. S.; Woo, W. S. *J. Nat. Prod.* **2001**, *64*, 1579. (b) Ito, C.; Itoigawa, M.; Furukawa, A.; Hirano, T.; Murata, T.; Kaneda, N.; Hisada, Y.; Okuda, K.; Furukawa, H. *J. Nat. Prod.* **2004**, *67*, 1800. (c) Grabley, S.; Thiericke, R. *Drug Discovery from Nature*; Springer-Verlag: Berlin, **1999**, 124. (d) He, J.; Lion, U.; Sattler, I.; Gollmick, F. A.; Grabley, S.; Cai, J.; Meiner, M.; Schaumann, K.; Dechert, U.; Krohn, M. *J. Nat. Prod.* **2005**, *6*, 1397.

(2) (a) Cheng, P.; Zhang, Q.; Ma, Y. B.; Jiang, Z. Y.; Zhang, X. M.; Zhang, F. X. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3787. (b) Guo, L. J.; Wei, C. X.; Jia, J. H.; Zhao, L. M.; Quan, Z. S. *Eur. J. Med. Chem.* **2009**, *44*, 954. (c) Marzano, C.; Chilin, A.; Baccichetti, F.; Bettio, F.; Guiotto, A.; Miolo, G.; Bordin, F. *Eur. J. Med. Chem.* **2004**, *39*, 411. (d) Sliskovic, D. R.; Picard, J. A.; Roark, W. H.; Roth, B. D.; Ferguson, E.; Krause, B. R.; Newton, R. S.; Sekerke, C.; Shaw, M. K. *J. Med. Chem.* **1991**, *34*, 367. (e) Patel, M.; McHugh, R. J.; Cordova, B. C.; Klabe, R. M.; Bacheler, L. T.; Erickson-Viitanen, S.; Rodger, J. D. *Bioorg. Med. Chem. Lett.* **2011**, *11*, 1943.

(3) (a) Forbis, R. M.; Rinehart, K. L. *J. Am. Chem. Soc.* **1973**, *95*, 5003. (b) Nadzan, A. M.; Rinehart, K. L. Jr.; Sokolski, W. T. *J. Antibiot.* **1977**, *30*, 523. (c) Beier, N.; Labitzke, E.; Mederski, W. W. K. R.; Radunz, H.-E.; Rauschenbach-Ruess, K.; Schneider, B. *Heterocycles* **1994**, *39*, 117. (d) Chen, K.; Kuo, S. C.; Hsieh, M. C.; Mauger, A.; Lin, C. M.; Hamel, E.; Lee, K. H. *J. Med. Chem.* **1997**, *40*, 2266. (e) Huang, L. J.; Heieh, M. C.; Teng, C. M.; Lee, K. H.; Kuo, S. C. *Bioorg. Med. Chem.* **1998**, *6*, 1657.

(4) (a) Familoni, O. B.; Kaye, P. T.; Klaas, P. *Chem. Commun.* **1998**, 2563. (b) Glasnov, T. N.; Stadlbauer, W.; Kappe, C. O. *J. Org. Chem.* **2005**, *70*, 3864. (c) Bach, T.; Bergmann, H.; Grosch, B.; Harms, K. *J. Am. Chem. Soc.* **2002**, *124*, 7982. (d) Kumabe, R.; Nishino, H. *Tetrahedron Lett.* **2004**, *45*, 703. (e) Carrër, A.; Brion, J.-D.; Messaoudi, S.; Alami, M. *Adv. Synth. Catal.* **2013**, *355*, 2044. (f) Wu, Y.-L.; Chuang, C.-P.; Lin, P.-Y. *Tetrahedron* **2000**, *56*, 6029. (g) Battistuzzi, G.; Bernini, R.; Cacchi, S.; Salve, I. D.; Fabrizi, G. *Adv. Synth. Catal.* **2007**, *349*, 297.

(5) (a) Kulkarni, B. A.; Ganesan, A. *Chem. Commun.* **1998**, 785. (b) Li, K.; Foresee, L. N.; Tunge, J. A. *J. Org. Chem.* **2005**, *70*, 2881. (c) Kuethe, J. T.; Wong, A.; Davies, I. W. *Org. Lett.* **2003**, *5*, 3975. (d) Inglis, S. R.; Stojkoski, C.; Branson, K. M.; Cawthray, J. F.; Fritz, D.; Wiadrowski, E.; Ryke, M. S.; Booker, G. W. *J. Med. Chem.* **2004**, *47*, 5405. (e) Fourquez, J. M.; Godard, A.; Marsais, F.; Quéguiner, G. *J. Heterocycl. Chem.* **1995**, *32*, 1165. (f) Coppolar, G. M.; Hardtmann, G. E. *J. Heterocycl. Chem.* **1979**, *16*, 1605. (g) Iyobe, A.; Uchida, M.; Kamata, K.; Hotei, Y.; Kusama, H.; Harada, H. *Chem. Pharm. Bull.* **2001**, *49*, 822.

(6) (a) Hewawasam, P.; Fan, W.; Knipe, J.; Moon, S. L.; Boissard, C. G.; Gribkoff, V. K.; Starrett, J. E. Jr. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1779. (b) Ismaili, L.; Nadaradjane, A.; Nicod, L.; Guyon, C.; Xicluna, A.; Robert, J.; Refouvelet, B. *Eur. J. Med. Chem.* **2008**, *43*, 1270. (c) Marcaccini, S.; Pepino, R.; Pozo, M. C.; Basurto, S.; García-Valverde, M.; Torrobab, T. *Tetrahedron Lett.* **2004**, *45*, 3999. (d) Grzegożek, M. *J. Heterocycl. Chem.* **2008**, *45*, 1879. (e) Schejn, A.; Balan, L.; Falk, V.; Aranda, L.; Medjahdi, G.; Schneider, R. *CrystEngComm* **2014**, *16*, 4493. (f) Vijayalakshmi, S.; Ragunath, L.; Rajendran, S. P. *Heterocycl. Commun.* **2001**, *7*, 177.

(7) (a) Cortese, N. A.; Ziegler, C. B. Jr.; Hrnjez, B. J.; Heck, R. F. *J. Org. Chem.* **1978**, *43*, 2952. (b) Kadnikov, D. V.; Larock, R. C. *J. Org. Chem.* **2004**, *69*, 6772. (c) Terpko, M. O.; Heck, R. F. *J. Am. Chem. Soc.* **1979**, *101*, 5281. (d) Tsuritani, T.; Yamamoto, Y.; Kawasaki, M.; Mase, T. *Org. Lett.* **2009**, *11*, 1043. (e) Manley, P. J.; Bilodeau, M. T. *Org. Lett.* **2004**, *6*, 2433. (f) Minville, J.; Poulin, J.; Dufresne, C.; Sturino, C. F. *Tetrahedron Lett.* **2008**, *49*, 3677. (g) Jung, J. C.; Oh, S.; Kim, W. K.; Park, W. K.; Kong, J. Y.; Park, O. S. *J. Heterocycl. Chem.* **2003**, *40*, 617. (h) Yang, H.; Guo, L.-N.; Duan, X.-H. *RSC Adv.* **2014**, *4*, 52986. (i) Mai, W.-P.; Sun, G.-C.; Wang, J.-T.; Song, G.; Mao, P.; Yang, L.-R.; Yuan, J.-W.; Xiao, Y.-M.; Qu, L.-B. *J. Org. Chem.* **2014**, *79*, 8094.

(8) (a) Lange, J. H. M.; Verveer, P. C.; Osnabrug, S. J. M.; Visser, G. M. *Tetrahedron Lett.* **2001**, *42*, 1367. (b) Razzaq, T.; Kappe, C. O. *Tetrahedron Lett.* **2007**, *48*, 2513. (c) Jia, C.; Dong, Y.; Tu, S.; Wang, G. *Tetrahedron* **2007**, *63*, 892. (d) Subashini, R.; Khan, F.-R. N. *Monatsh. Chem.* **2012**, *143*, 485. (e) Acker, T. M.; Khatri, A.; Vance, K. M.; Slabber, C.; Bacsa, J.; Snyder, J. P.; Traynelis, S. F.; Liotta, D. C. *J. Med. Chem.* **2013**, *56*, 6434.

(9) Horaguchi, T.; Hosokawa, N.; Tanemura, K.; Suzuki, T. *J. Heterocycl. Chem.* **2002**, *39*, 61.

(10) For our recent work, see: (a) Pan, W.; Dong, D.; Wang, K.; Zhang, J.; Wu, R.; Xiang, D.; Liu, Q. *Org. Lett.* **2007**, *9*, 2421. (b) Xiang, D.; Wang, K.; Liang, Y.; Zhou, G.; Dong, D. *Org. Lett.* **2008**, *10*, 345. (c) Xiang, D.; Xin, X.; Liu, X.; Zhang, R.; Yang, J.; Dong, D. *Org. Lett.* **2012**, *14*, 644. (d) Zhang, D.; Zhang, Q.; Zhang, N.; Zhang, R.; Liang, Y.; Dong, D. *Chem. Commun.* **2013**, *49*, 7358. (e) Zhou, F.; Liu, X.; Zhang, N.; Liang, Y.; Zhang, R.; Xin, X.; Dong, D. *Org. Lett.* **2013**, *15*, 5786. (f) Zhang, Q.; Liu, X.; Xin, X.; Zhang, R.; Liang, Y.; Dong, D. *Chem. Commun.* **2014**, *50*, 15378.

(11) Xiang, D.; Xin, X.; Liu, X.; Kumar, S.; Dong, D. *Synlett* **2011**, 2187.

(12) Liu, X.; Xin, X.; Xiang, D.; Zhang, R.; Kumar, S.; Zhou, F.; Dong, D. *Org. Biomol. Chem.* **2012**, *10*, 5643.

(13) Liu, X.; Zhang, Q.; Zhang, D.; Xin, X.; Zhang, R.; Zhou, F.; Dong, D. *Org. Lett.* **2013**, *15*, 776.

(14) (a) Maas, G.; Stang, P. J. *J. Org. Chem.* **1981**, *46*, 1606. (b) Nenajdenko, V. G.; Vertelezkij, P. V.; Koldobskij, A. B.; Alabugin, I. V.; Balenkova, E. S. *J. Org. Chem.* **1997**, *62*, 2483.

(15) For reviews on iminium triflate, see: (a) Baraznenok, I. L.; Nenajdenko, V. G.; Balenkova, E. S. *Tetrahedron* **2000**, *56*, 3077. (b) Snider, B. B. *Chem. Rev.* **1988**, *88*, 793. (c) Madelaine, C.; Valerio, V.; Maulide, N. *Chem. Asian J.* **2011**, *6*, 2224.

(16) For selected examples on iminium triflate, see: (a) Barbaro, G.; Battaglia, A.; Bruno, C.; Giorgianni, P.; Guerrini, A. *J. Org. Chem.* **1996**, *61*, 8480. (b) DeRoy, P. L.; Charette, A. B. *Org. Lett.* **2003**, *5*, 4163. (c) Zheng, X.; Kerr, M. A. *Org. Lett.* **2006**, *8*, 3777. (d) Barbe, G.; Charette, A. B. *J. Am. Chem. Soc.* **2008**, *130*, 18. (e) Cui, S.; Wang, J.; Wang, Y. *J. Am. Chem. Soc.* **2008**, *130*, 13526. (f) Pelletier, G.; Bechara, W. S.; Charette, A. B. *J. Am. Chem. Soc.* **2010**, *132*, 12817. (g) Xiao, K.-J.; Luo, J.-M.; Ye, K.-Y.; Wang, Y.; Huang, P.-Q. *Angew. Chem. Int. Ed.* **2010**, *49*, 3037. (h) Wang, A.-E.; Chang, Z.; Sun, W.-T.; Huang, P.-Q. *Org. Lett.* **2015**, *17*, 732.

(17) (a) Kaiser, D.; Maulide, N. *J. Org. Chem.* **2016**, *81*, 44221. (b) Falmagne, J. B.; Escudero, J.; Taleb-Saharaoui, S.; Ghosez, L. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 879. (c) Movassaghi, M.; Hill, M. D. *J. Am. Chem. Soc.* **2006**, *128*, 14254. (d) Movassaghi, M.; Hill, M. D.; Ahmad, O. K. *J. Am. Chem. Soc.* **2007**, *129*, 10096. (e) Wezeman, T.; Zhong, S.; Nieger, M.; Bräse, S. *Angew. Chem. Int. Ed.* **2016**, *55*, 3823.