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Synthesis of Quinolinones with Palladium-Catalyzed Oxidative Annulation between Acrylamides and Arynes

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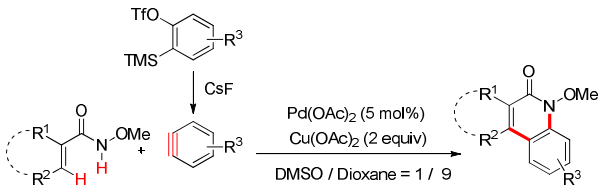


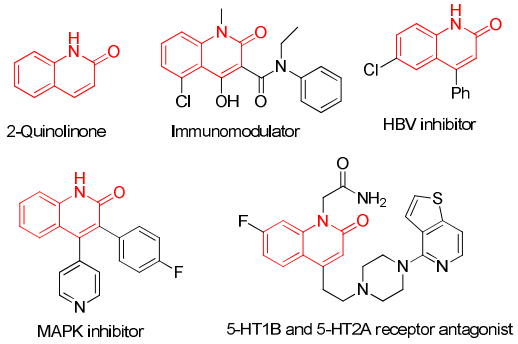
Abstract: An unprecedented palladium-catalyzed oxidative annulation of acrylamides with benzyne precursors has been successfully developed. By using this mild "N-H activation/Heck reaction" method, a wide variety of quinolinones were conveniently prepared in one step with high efficiency.

2-Quinolinones represent an important class of heterocycles prevalent in a number of natural alkaloids, biologically active compounds as well as pharmaceuticals.[1] They have been reported with various important bioactivities, such as antiviral, antibiotic, anticancer, and antihypertensive activities (Scheme 1).[2] For example, 3,4-diarylquinolinone containing a pyridine moiety is a promising lead compound as potent and selective p38αMAP kinase inhibitors (IC_{50} = 1.8 μm).[2c] Importantly, quinolinones are also useful building blocks in organic synthesis and this skeleton has also been utilized to design fluorescent probes.[3]

The development of new synthetic methods toward this heterocycle has remained a long-lasting interest in the past decade.[4] Recently, various transition-metal-catalyzed cross-coupling/cyclization cascade reactions have been developed.[5] For example, in 2003, the Larock group reported an elegant palladium-catalyzed three-component cyclization of 2-iodoanilines, internal alkynes and CO.[5b] Most of these methods start from a preactivated arylhalides, which need to be prepared in advance. Transition-metal-

catalyzed oxidative annulation from easily available starting materials with direct C-H functionalization represents an attractive synthetic strategy for the synthesis of quinolinone structure. However, this activation pathway is still very limited in the literature.[6]

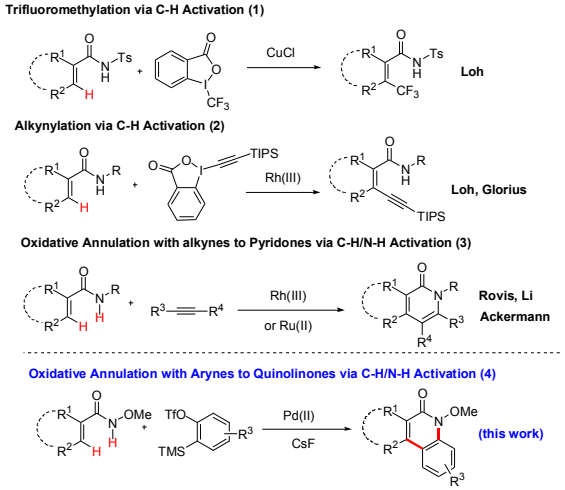
Scheme 1. Natural products and bioactive pharmaceuticals containing quinolinones



Directing group assisted C-H functionalization reactions have been attracting increasing attentions from the synthetic community in recent years. Electron-rich alkenes such as enamides have been widely exploited in direct C-H functionalization reactions.[7,8] In contrast, the electron-deficient alkenes are more elusive because the rate-limiting electrophilic metallation step favors the electron-rich substrates. To date, only very limited examples have been reported (Scheme 2).[9] Loh and Glorius have reported the direct trifluoromethylation and alkynylation of acrylamides with hypervalent iodonium reagents in the presence of copper(I) or rhodium(III)-catalyst (eq 1, 2). Li and Rovis demonstrated a rhodium(III)-catalyzed C-H/N-H activation of acrylamides, leading to the pyridines skeletons in one step. Ackermann et al developed similar oxidative annulation reactions between acrylamides and internal alkynes with ruthenium catalyst (eq 3). Arynes[10] are strained alkynes, and the oxidative annulation of acrylamides with arynes would generate quinolinone structure in one step (eq 4). However the high reactivity of

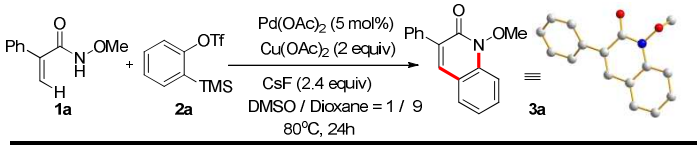
aryne intermediates ready to many side reactions, and also the difficulties in C-H activation of electron-deficient acrylamides, make this transformation very challenging. We wish to report our recent efforts on the efficient synthesis of quinolinone derivatives via a palladium-catalyzed oxidative annulation of electron-deficient acrylamides with benzyne precursors.[11,12]

Scheme 2. C-H activation of electron-deficient alkenes



To achieve the challenging transformation, we optimized the reaction conditions employing acrylamide **1a** and benzyne precursor **2a** as model substrates (Table 1). After a detailed study of different reactions parameters, the oxidative annulation of **1a** with **2a**

Table 1. Optimization of Reaction Conditions



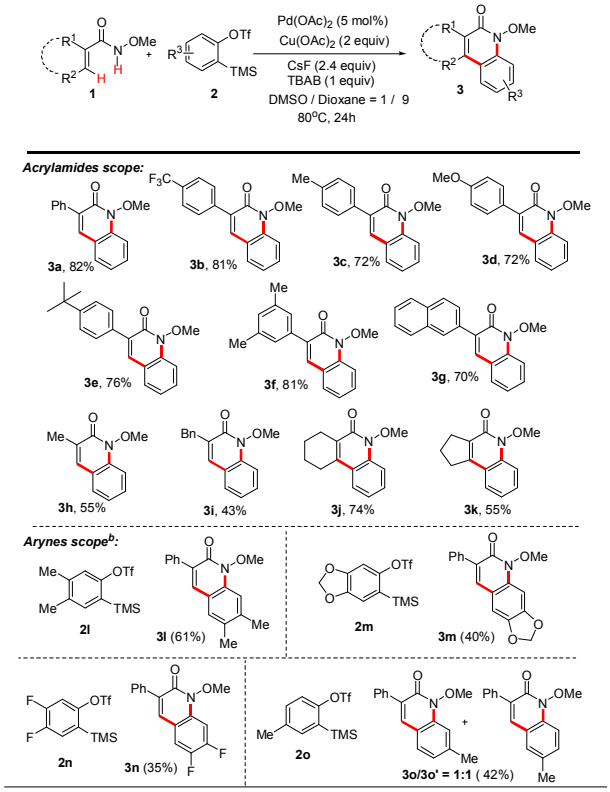
entry	variation from the standard conditions	isolated yields (%)
1	none	82
2	$[Cp^*RhCl_2]_2$ instead of $Pd(OAc)_2$	0
3	$[RuCl_2(p\text{-cymene})]_2$ instead of $Pd(OAc)_2$	0
4	$Pd(PPh_3)_4$ instead of $Pd(OAc)_2$	65
5	$K_2S_2O_8$ instead of $Cu(OAc)_2$	10
6	AgOAc instead of $Cu(OAc)_2$	36
7	Dioxane instead of Dioxane/DMSO	72
8	DMF instead of Dioxane/DMSO	68
9	without of TBAB	10
10	K_2CO_3 instead of TBAB	32
11	adding Ph_3P (10 mol)	70
12	TBAF instead of CsF	40
13	without $Pd(OAc)_2$	0

Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (5 mol%), $Cu(OAc)_2$ (0.4 mmol), CsF (0.48 mmol), TBAB (0.2 mmol), 4Å molecular sieve (100 mg), solvent (1 mL), 24 h. TBAB = tetra-*n*-butylammonium-bromide, TBAF = tetra-*n*-butylammonium-fluoride.

gave quinolinone **3a** in 82% yield under the standard conditions: $Pd(OAc)_2$ (5 mol%), $Cu(OAc)_2$ (2 equiv), and CsF (2.4 equiv) in dioxane and DMSO mixed solvent at 80 ^oC for 24 h (entry 1). The structure of **3a** was unambiguously characterized by single crystal X-ray analysis. The choice of palladium catalyst was crucial for the reaction. Replacing $Pd(OAc)_2$ with the mostly used Rh(III) or Ru(II) catalysts, no desired product was observed and the starting **1a** remained intact (entries 2, 3). Using other palladium catalyst such as $Pd(PPh_3)_4$ could generate the product in a little lower 65% isolated yield (entry 4). As to oxidants, $K_2S_2O_8$ gave very low yield (entry 5) and AgOAc gave only 36% yield (entry 6). Other solvents also resulted in decreased yield (entries 7, 8). TBAB is a very important additive and its removal greatly decreased the yield (entries 9, 10). Adding

extra triphenylphosphine ligand did not help the reaction (entry 11). Replacing of CsF by TBAF lowered the yield (entry 12). TBAF is more soluble in organic solvents and thus could generate benzyne intermediate instantly. These results indicate that the rate of benzyne generation should synchronize with that of the rate-limiting C-H activation. No product was formed without palladium catalyst (entry 13).

Table 2. Palladium-catalyzed annulation of various acrylamides with aryne precursors for the synthesis of quinolinones.[a]

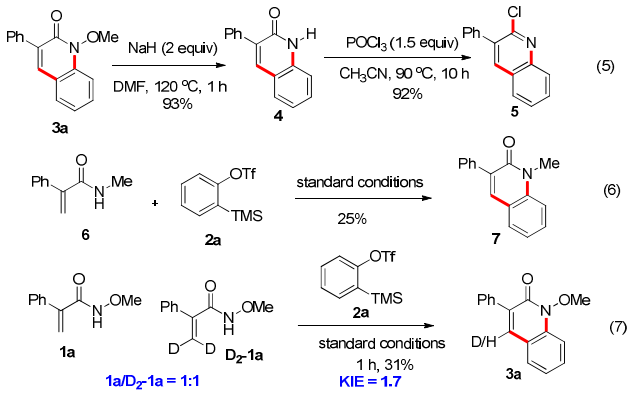


[a]*Reaction conditions:* **1** (0.2 mmol), **2** (0.4 mmol), $Pd(OAc)_2$ (5 mol%), $Cu(OAc)_2$ (0.4 mmol), CsF (0.48 mmol), TBAB (0.2 mmol), solvent (1 mL), 4Å molecular sieve (100 mg), 24 h, isolated yields. [b]$Pd(OAc)_2$ (10 mol%), the solution of **2** in 1.5 mL solvent was added slowly with syringe pump in 15 h.

With the optimized conditions, the oxidative annulation of benzyne with a range of acrylamides was tested (Table 2). Benzyne reacted with a variety of acrylamides bearing

aromatic or alkyl substituents, leading to the formation of quinolinone **3** in good yields (**3a**-**3k**). Different aromatic substituents bearing electron-donating group or electron-withdrawing group at the α-position of the acrylamides does not affect the reaction, and everyone afforded 3-aryl quinolinones in very good yields (**3a**-**3g**). Acrylamides with alkyl group at the α-position proceeded in moderate yields (**3h**, **3i**). Cyclic substrates could also react efficiently to furnish desired fused quinolinones in moderate to good yields (**3j**, **3k**). However, trying to extend this reaction to the more challenging cinnamide and crotonyl amide was not successful.

The reaction scope with regard of different arynes were also examined (Table 2). We need to inject the aryne precursors solution slowly into the reaction system to obtain good yields of the corresponding annulation products. For substituted arynes, bearing both electron-donating group and electron-withdrawing group could all react with acrylamide **1a**, generating the corresponding quinolinones in low to moderate yields of 35–61% (**3l**-**3n**). For unsymmetric aryne **2o**, a 1/1 regioisomers mixture was obtained, which very importantly, indicated the formation of aryne intermediate in the reaction.

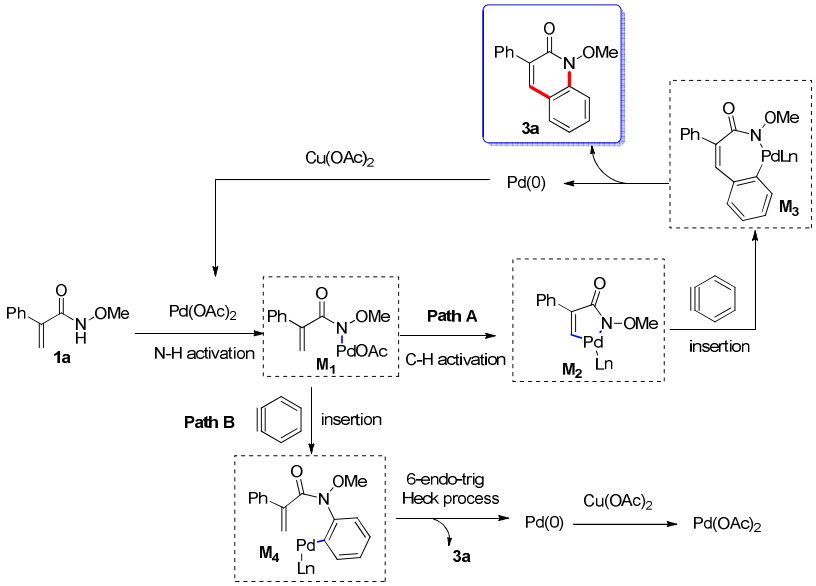


The methoxy group on the nitrogen atom serves as a very important protecting group.[13] Notably, it could be easily removed by NaH to give free quinolinone **4** in 93% yield.[14] This product was further transformed into important 2-choloroquinoline **5** in 92%

yield in the presence of $POCl_3$ (eq 5).[6c] The oxidative annulation of N-methyl acrylamide **6** with **2a** gave quinolinone **7** in 25% yield under the standard conditions (eq. 6).[15] On the other hand, very tiny product (<5%) was observed in the standard reaction of dimethyl but-2-ynedioate with **2a**. No reaction occurred between diphenylacetylene and **2a,** showing the importance of strain releasing.

Since this reaction occurs with C-H functionalization, an intermolecular KIE experiment was conducted. A KIE value of 1.7 was observed (eq 6). This value is much lower than that of other C-H functionalization reactions, indicating that maybe the C-H cleavage is not involved in the rate-determing step.[9,11,12]

Scheme 3. Possible reaction pathways



On the basis of these experiments and literature precedents, two possible reaction pathways were proposed in Scheme 3. Sequential N-H and C-H activation of acrylamide **1a** to form the five-membered palladacycle $\mathbf{M_2}$. Subsequent benzyne insertion and reductive elimination would generate the product **3a** and Pd(0), which was reoxidized to Pd(II) by $Cu(OAc)_2$ (Path A). On the other hand, the aminopalladation of intermediate $\mathbf{M_1}$

to benzyne would form the palladium intermediate **M_4**, which went through a Heck type reaction: insertion to the electron-deficient double bond and subsequent β-hydrogen elimination would also produce the target product (pathway B). Even though pathway A cannot be excluded, pathway B is more likely because of the following aspects: 1) Electrophilic palladation of the electron-deficient alkene is difficult to form the proposed palladacycle **M_2**. No similar metal complex was reported so far to our knowledge. Actually, all our efforts trying to synthesize this palladacycle were not successful and only palladium black was observed either under acid or basic condition. 2) In a recent related work from Jeganmohan group the N-arylated product was observed under many conditions.[11a] These results indicated the fromation of **M_4** is very possible. The intramolecular C-H activation to form a seven membered palladium intermediate from M_4 is not easy, but another 6-endo-trig addition/subsequent β-hydrogen elimination sequence forms the final product **3a**. Similar 6-endo-trig, but not 5-exo-trig pathway was also observed in an early intramolecular Heck reaction from Dankwardt.[16] For the cyclic substrates, the direct syn-insertion and syn-β-hydrogen elmination could not form the target products **3j** and **3k**. The subsequent double bond migration is needed.[16a]

In summary, we have developed the first palladium-catalyzed strain releasing oxidative annulation between acrylamides and arynes. Application of this protocol led to the concise and flexible synthesis of quinolinones, which cannot easily be accessed by other methods. This approach reprents a new direction for the transition-metal chemistry of benzynes.

Experimental Section:

General Details. All NMR spectras were recorded on 400 MHz spectrometer. High-resolution mass spectrometry (HRMS) were measured in positive-ion mode on a Q-TOF instrument with an ESI ion source. Routine monitoring of the reaction was performed by TLC using precoated silica gel plates. All the reagents and solvents were used directly. Acrylamides and deuterated substrates were prepared according to reported procedures.[9d,17]

Typical Procedure for the Synthesis of Substituted Quinolinone (3). A mixture of $Pd(OAc)_2$ (2.24 mg, 0.01 mmol, 5 mmol%) , $Cu(OAc)_2$ (72.7 mg, 0.4 mmol), **1a** (35.4 mg, 0.2 mmol) , CsF (73.0 mg, 0.48 mmol) ,TBAB (64.4 mg, 0.2 mmol) and 4Å molecular sieve (100 mg) were dissolved in a mixed solvent of dioxane (0.9 mL) and DMSO (0.1 mL), **2a** (119.2 mg, 2 equiv) was added to the reaction system. The resulting mixture was stirred at 80℃ until the reaction was completed (monitored by TLC). The reaction mixture was filtered and evaporated under reduced pressure and purified by column chromatography (silica gel) with petroleum ether/ethyl acetate (10:1) to give the pure product **3a** (41.2 mg, 82%).

3-Phenyl-1*H*-quinolin-2-one (4). NaH (0.6 mmol, 60%) was added into a stirred solution of 1-methoxy-3-phenyl-1*H*-quinolin-2-one **3a** (0.2 mmol) in DMF (1 mL) and the resulting mixture was heated at 120 ℃for 0.5-1.0 h. After the reaction was completed, the reaction mixture was allowed to cool down to room temperature, and washed with H_2O (16 mL), extracted with CH_2Cl_2 (10 mL x 3). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel) with petroleum ether/ethyl acetate (2:1) to give the White solid **4** (41.1 mg, 93%)[14]: mp 227-228 ℃. ^{1}H NMR (400 MHz, D_6-DMSO) δ 7.14-7.18 (m, 1H), 7.30-7.42 (m, 4H), 7.45-7.49 (m, 1H), 7.69-7.74 (m, 3H), 8.07(s, 1H), 11.92(s, 1H).

2-Chloro-3-phenyl-quinoline (5). Phosphorous oxychloride ($POCl_3$) (0.24 mmol) was added into a solution of 3-phenyl-1*H*-quinolin-2-one (**4**) (0.2 mmol) in CH_3CN (3.0 mL). The reaction mixture was heated to reflux at 90 °C for 10 h. After the reaction mixture

was cooled to room temperature, ice water was poured and extracted with ethyl acetate. The organic layer was separated, dried with Na_2SO_4, and concentrated under the reduced pressure. The residue was purified on column chromatography (silica gel) with petroleum ether/ethyl acetate (10:1) to give the yellow solid **5** (44.4 mg, 92%)[6c]: mp 54-55 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.54 (m, 6H), 7.56-7.60 (m, 1H), 7.73-7.77 (m, 1H), 7.82-7.84 (m, 1H), 8.06-8.10 (m, 1H).

1-Methyl-3-phenyl-1*H*-quinolin-2-one (7). A mixture of $Pd(OAc)_2$ (2.24 mg, 0.01 mmol, 5 mmol%) , $Cu(OAc)_2$ (72.7 mg, 0.4 mmol), N-methyl acrylamide (32.2 mg, 0.2 mmol) , CsF (73.0 mg, 0.48 mmol) ,TBAB (64.4 mg, 0.2 mmol) and 4Å molecular sieve (100 mg) were dissolved in a mixed solvent of dioxane (0.9 mL) and DMSO (0.1 mL), **2a** (119.2 mg, 2 equiv) was added to the reaction system. The resulting mixture was stirred at 80℃ until the reaction was completed (monitored by TLC). The reaction mixture was filtered and evaporated under reduced pressure and purified by column chromatography (silica gel) with petroleum ether/ethyl acetate (8:1) to give the liquid product **6** (11.8 mg, 25%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 7.37-7.50 (m, 5H), 7.57-7.62 (m, 2H)，7.70-7.72 (m, 2H), 7.80 (s, 1H).

Intermolecular isotope effect of the palladium-catalyzed oxidative annulation between 1a and [d]-1a with 2a. A mixture of $Pd(OAc)_2$ (3.36 mg, 0.015 mmol, 5 mmol %), **1a** (53.1 mg, 0.30 mmol), **[D2]-1a** (53.7 mg, 0.30 mmol), $Cu(OAc)_2$ (108.9 mg, 0.6 mmol), CsF (54 mg, 0.36 mmol) and TBAB (96.7 mg, 0.3 mmol) were dissolved in a mixed solvent of dioxane (0.9 mL) and DMSO (0.1 mL). **2a** (89.4 mg, 0.30 mmol) was added to the reaction system. The resulting mixture was stirred at 80^0C for 1h. The reaction mixture was filtered, evaporated under reduced pressure and purified by column chromatography (silica gel) to give **3a**/**[d_1]-3a** (23.3 mg, 31% yield) as a white solid

1-Methoxy-3-phenyl-1*H*-quinolin-2-one (3a). White solid (41.2 mg, 82%)：mp 126-128 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (s, 3H), 7.26-7.30 (m, 1H), 7.38-7.47 (m, 3H)，7.61-7.66 (m, 3H), 7.74-7.76 (m, 2H), 7.81(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

62.7, 111.6, 119.7, 122.9, 128.3, 128.4, 128.5, 128.9, 130.8, 133.5, 135.7, 135.8, 137.4, 157.3; IR (neat): ν (cm^{-1}) 3038, 2933, 2862, 1721, 1650, 1596, 1263, 1172, 1061, 1036, 991, 848, 729, 674, 543; HRMS (ESI, m/z) calcd for $C_{16}H_{13}NO_2$ (M+H): 252.1019, found 252.1022. The CCDC number for the cystal of **3a** is 1037415.

1-Methoxy-3-(4-trifluoromethyl-phenyl)-1*H*-quinolin-2-one (3b). Yellow liquid (51.7 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (s, 3H), 7.29-7.33 (m, 1H), 7.64-7.71 (m, 5H), 7.85-7.89 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.8, 111.8, 119.4, 123.2, 125.2 (q, J_{C-F} = 3.7 Hz, C), 128.7, 129.2, 130.1, 130.4, 131.4, 131.9, 136.6, 137.7, 139.4 (d, J_{C-F} = 1.4 Hz, C), 156.9; IR (neat): ν (cm^{-1}) 3041, 2933, 2857, 1725, 1660, 1587, 1268, 1150, 1055, 991, 852, 766, 703, 568, 548; HRMS (ESI, m/z) calcd for $C_{17}H_{12}F_3NO_2$ (M+H): 320.0893, found 320.0892.

1-Methoxy-3-p-tolyl-1*H*-quinolin-2-one (3c). Yellow liquid (38.2 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 4.12 (s, 3H),7.23-7.27 (m, 3H), 7.57-7.65 (m, 5H), 7.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 62.7, 111.5, 119.7, 122.9, 128.3, 128.7, 129.0, 130.5, 132.9, 133.3, 135.2, 137.2, 138.3, 157.3; IR(neat): ν (cm^{-1}) 3027, 2933, 2855, 1719, 1645, 1594, 1259, 1180, 1055, 960, 882, 819, 745, 657, 573, 515; HRMS (ESI, m/z) calcd for $C_{17}H_{15}NO_2$ (M+H): 266.1176, found 266.1177.

1-Methoxy-3-(4-methoxy-phenyl)-1*H*-quinolin-2-one (3d). Yellow liquid (38.6 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3H), 4.13 (s, 3H), 6.96-6.98 (m, 2H), 7.24-7.28 (m, 1H), 7.57-7.63 (m, 3H), 7.71-7.75 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 62.7, 111.6, 113.8, 119.8, 122.9, 128.3, 130.1, 130.3, 130.4, 132.9, 134.7, 137.1, 157.4, 159.8; IR(neat): ν (cm^{-1}) 3068, 2927, 2860, 1717, 1667, 1582, 1257, 1162, 1073, 1052, 981, 862, 743, 652, 510; HRMS (ESI, m/z) calcd for $C_{17}H_{15}NO_3$ (M+H): 282.1125, found 282.1112.

3-(4-tert-Butyl-phenyl)-1-methoxy-1*H*-quinolin-2-one (3e). Yellow liquid (46.7 mg, 76%). ^{1}HNMR (400 MHz, $CDCl_3$) δ 1.34 (s, 9H), 4.12 (s, 3H), 7.24-7.25 (m, 1H), 7.45-7.47 (m, 2H), 7.58-7.63 (m, 3H) 7.68-7.70 (m, 2H), 7.79 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.6, 62.6, 111.5, 119.7, 122.8, 125.2, 128.3, 128.5, 130.5, 132.9, 133.3, 135.2, 137.3, 151.4, 157.3; IR(neat): ν (cm^{-1}) 3466, 2959, 1708, 1651, 1604, 1274, 1206,

1112, 1065, 960, 871, 839, 745, 647, 526; HRMS (ESI, m/z) calcd for $C_{20}H_{21}NO_2$ (M+H): 308.1651, found 308.1649.

3-(3,5-Dimethyl-phenyl)-1-methoxy-1*H*-quinolin-2-one (3f). Yellow liquid (43.1 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 6H), 4.12 (s, 3H), 7.02 (s, 1H), 7.23-7.27 (m, 1H), 7.35 (s, 2H), 7.58-7.62 (m, 3H), 7.76 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 62.7, 111.5, 119.7, 122.3, 122.8, 126.6, 128.3, 130.1, 130.6, 135.5, 135.7, 137.3, 137.7, 157.4; IR(neat): *v* (cm^{-1}) 3052, 2946, 2855, 1717, 1658, 1653, 1260, 1168, 1067, 1022, 972, 854, 736, 663, 526; HRMS (ESI, m/z) calcd for $C_{18}H_{17}NO_2$ (M+H): 280.1338, found 280.1338.

1-Methoxy-3-naphthalen-2-yl-1*H*-quinolin-2-one (3g). Yellow liquid (42.1 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (s, 3H), 7.24-7.29 (m, 1H), 7.47-7.49 (m, 2H), 7.60-7.66 (m, 3H), 7.83-7.91 (m, 5H), 8.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.8, 111.6, 119.7, 123.0, 126.1, 126.4, 126.5, 127.5, 127.7, 128.2, 128.4, 128.5, 130.8, 133.1, 133.2, 133.2, 133.3, 136.1, 137.4, 157.4; IR(neat): *v* (cm^{-1}) 3052, 2922, 1724, 1645, 1595, 1268, 1189, 1118, 1063, 963, 892, 812, 737, 636, 511; HRMS (ESI, m/z) calcd for $C_{20}H_{15}NO_2$ (M+H): 302.1176, found 302.1175

1-Methoxy-3-methyl-1*H*-quinolin-2-one (3h). Yellow liquid (20.1 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 3H), 4.08 (s, 3H), 7.19-7.24 (m, 1H), 7.50-7.57 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.3, 62.7, 111.5, 119.7, 122.7, 127.5, 129.8, 131.3, 134.9, 136.9, 158.5; IR(neat): *v* (cm^{-1}) 3043, 2942, 2851, 1712, 1643, 1582, 1264, 1153, 1071, 991, 957, 840, 726, 691, 536; HRMS (ESI, m/z) calcd for $C_{11}H_{11}NO_2$ (M+H): 190.0863, found 190.0870.

3-Benzyl-1-methoxy-1*H*-quinolin-2-one (3i). Yellow liquid (22.8 mg, 43%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (s, 2H), 4.11 (s, 3H), 7.17-7.21 (m, 2H), 7.25-7.33 (m, 5H), 7.44-7.46 (m, 1H), 7.53-7.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.5, 62.8, 111.5, 119.6, 122.7, 126.5, 127.9, 128.6, 129.5, 130.1, 134.8, 134.8, 136.9, 138.7, 157.9; IR(neat): *v* (cm^{-1}) 3052, 2927, 2871, 1715, 1662, 1593, 1257, 1168, 1082, 982, 953, 854, 734, 680, 527; HRMS (ESI, m/z) calcd for $C_{17}H_{15}NO_2$ (M+H): 266.1176, found 266.1167.

1-Methoxy-7,8,9,10-tetrahydro-5*H*-phenanthridin-6-one (3j). Yellow liquid (33.9 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.79-1.89 (m, 4H), 2.69 (t, *J* = 6.0 Hz, 2H), 2.85 (t, *J* = 6.4 Hz, 2H), 4.08 (s, 3H), 7.23-7.27 (m, 1H), 7.51-7.55 (m, 1H), 7.59 (d, *J* = 8.3 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 21.9, 24.3, 25.5, 62.7, 111.6, 120.4, 122.4, 123.5, 129.5, 129.8, 135.9, 141.4, 157.7; IR(neat): *v* (cm^{-1}) 3067, 2958, 2844, 1718, 1663, 1581, 1251, 1183, 1062, 1027, 982, 857, 745, 692, 558; HRMS (ESI, m/z) calcd for $C_{14}H_{15}NO_2$ (M+H): 230.1176, found 230.1184.

1,2,3,5-tetrahydro-cyclopenta[c]quinolin-4-one (3k). Yellow liquid (23.6 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60-2.71 (m, 2H), 3.44 (t, *J* = 7.2 Hz, 2H), 3.54 (t, *J* = 7.6 Hz, 2H), 4.52 (s, 3H), 7.67-7.95 (m, 1H), 7.95-8.05(m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8, 31.0, 32.0, 62.9, 112.1, 118.3, 122.5, 125.2, 129.9, 134.0, 137.4, 149.6, 156.6; IR(neat): *v* (cm^{-1}) 3063, 2938, 2849, 1724, 1651, 1588, 1243, 1180, 1059, 1023, 976, 851, 735, 678, 547; HRMS (ESI, m/z) calcd for $C_{13}H_{13}NO_2$ (M+H): 216.1019, found 216.1017.

1-Methoxy-6,7-dimethyl-3-phenyl-1*H*-quinolin-2-one (3l). Yellow liquid (34.1 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.42 (s, 3H), 4.11 (s, 3H), 7.33-7.44 (m, 5H), 7.71-7.74 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 20.7, 62.6, 112.1, 117.9, 128.1, 128.2, 128.5, 128.8, 131.8, 132.1, 135.4, 135.7, 136.2, 140.9, 157.2; IR(neat): *v* (cm^{-1}) 3048, 2936, 2861, 1718, 1647, 1572, 1268, 1182, 1091, 973, 962, 861, 747, 663, 521; HRMS (ESI, m/z) calcd for $C_{18}H_{17}NO_2$ (M+H): 280.1338, found 280.1339.

1-Methoxy-7-phenyl-5H-[1,3]dioxolo[4,5-g]quinolin-6-one (3m). Yellow liquid (23.6 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (s, 3H), 6.05 (s, 2H), 6.97 (s, 1H), 7.08 (s, 1H), 7.34-7.35 (m, 1H), 7.39-7.43 (m, 2H), 7.64 (s, 1H), 7.70-7.72 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.7, 92.7, 102.0, 105.9, 114.0, 128.0, 128.2, 128.7, 130.5, 134.7, 135.4, 136.0, 144.3, 151.3, 157.0; IR(neat): *v* (cm^{-1}) 3063, 2917, 2870, 1714, 1645, 1588, 1247, 1185, 1065, 996, 871, 829, 735, 657, 510; HRMS (ESI, m/z) calcd for $C_{17}H_{13}NO_4$ (M+H): 296.0923, found 296.0914.

6,7-Difluoro-1-methoxy-3-phenyl-1*H*-quinolin-2-one (3n). Yellow liquid (20.1 mg, 35%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (s, 3H), 7.38-7.45 (m, 5H), 7.68-7.70 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.9, 100.9 (d, J_{C-F} = 46.6 Hz, C), 115.6 (d, J_{C-F} = 4.2 Hz, C), 115.7, 115.8 (d, J_{C-F} = 4.4 Hz, C), 128.4, 128.7, 128.8, 134.0, 134.3, 134.3, 135.2, 147.8, 156.9; IR(neat): ν (cm^{-1}) 3047, 2922, 2849, 1729, 1656, 1578, 1274, 1143, 1059, 996, 845, 824, 745, 694, 526; HRMS (ESI, m/z) calcd for $C_{16}H_{11}F_2NO_2$ (M+H): 288.0836, found 288.0831.

1-Methoxy-6-methyl-3-phenyl-1*H*-quinolin-2-one and 1-Methoxy-7-methyl-3-phenyl-1*H*-quinolin-2-one (3o/3o' = 1/1). Yellow liquid (22.3 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 2.52 (s, 3H), 4.11 (s,3H), 4.12 (s, 3H), 7.07-7.09 (m, 1H), 7.35-7.45 (m, 9H), 7.50-7.52 (m, 2H), 7.72-7.75 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 22.4, 62.7, 111.5, 111.5, 117.5, 119.7, 124.4, 128.1, 128.2, 128.2, 128.2, 128.3, 128.3, 128.8, 128.9, 132.1, 132.5, 133.3, 135.4, 135.6, 135.7, 136.0, 136.0, 137.4, 141.7, 157.1, 157.4; IR(neat): ν (cm^{-1}) 3042, 2925, 2853, 1714, 1653, 1597, 1258, 1142, 1058, 958, 841, 808, 725, 686, 514; HRMS (ESI, m/z) calcd for $C_{17}H_{15}NO_2$ (M+H): 266.1181, found 266.1171.

Supporting Information

Full experiment detail, ^{1}H and ^{13}C NMR spectra and HRMS data. This material is available free of charge via the Internet at http://pubs.acs.org.

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