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Radical Cation Salt-Promoted Catalytic Aerobic sp^3 C–H Oxidation: Construction of Quinoline-Fused Lactones and Lactams

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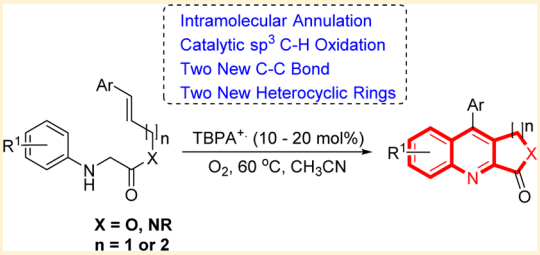
Supporting Information

ABSTRACT: A direct construction of quinoline-fused lactones and lactams was achieved by sp^3 C–H bond oxidation of *N*-aryl glycine esters and amides under catalytic radical cation salt-induced conditions. These polycyclic products are formed in a single step from readily accessible starting materials, and this method provides a new synthetic approach to this class of heterocycles.



Heterocycle-fused lactones and lactams represent interesting classes of natural and synthetic compounds that display a wide range of biological properties. Therefore, the development of streamlined protocols that allow access to these valuable molecules from relatively simple starting materials is a worthwhile endeavor. For example, derivatives of furo[3,4-*b*]quinolin-3(1*H*)-one have been used to synthesize quinoline-2-carboxamides **A**, which represent promising new radioligands for molecular imaging of the 18 kDa translocator protein (TSPO).[1] Furthermore, the group of Nicolaou has employed a lactone-fused analogue in their synthesis of the enediyne antibiotic uncialamycin (Figure 1, eq 1).[2] Quinoline-fused 2-pyran-1-one system **B** can be perceived as a class of analogues of the dihydroisocoumarin glucosides **C**, which have been extracted from the fungus *Cephalosporium* sp. AL031 and exhibit antibacterial and fungicidal properties (Figure 1, eq 2).[3] Additionally, quinoline-fused lactams are key intermediates to luotonin A, a cytotoxic alkaloid isolated from the Chinese medicinal plant *Peganum nigellastrum* that is active against murine leukemia cell line P-388 with an IC_{50} value of 1.8 mg·mL^{-1} (Figure 1, eq 3).[4]

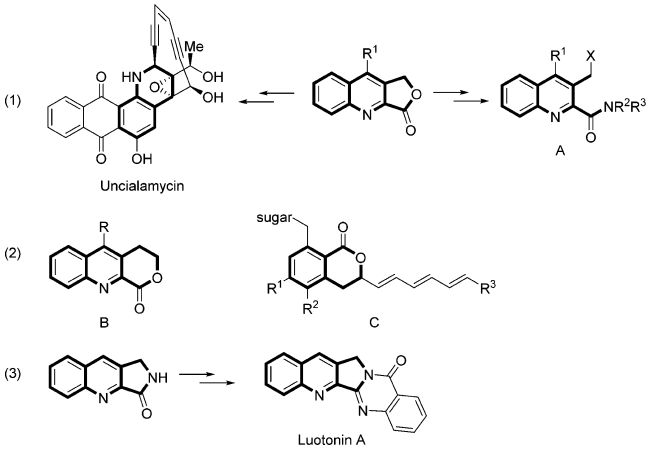


Figure 1. Heterocycle-fused lactones and lactams.

Quinoline-fused variants are important members of these classes of heterocycles, and several research groups have established protocols for constructing these scaffolds. Nevertheless, the development of new catalytic approaches still remains an active field of research, and efforts are validated by the multitude of possible synthetic and biological applications. A stepwise approach toward these heterocycles is usually employed in which quinoline formation occurs prior to a final lacton- or lactamization (Figure 2, eq 1).[1f,3b,4b] For example, van de Weghe reported an elegant approach involving a tandem intermolecular Povarov cyclization/lactonization or lactamiza-

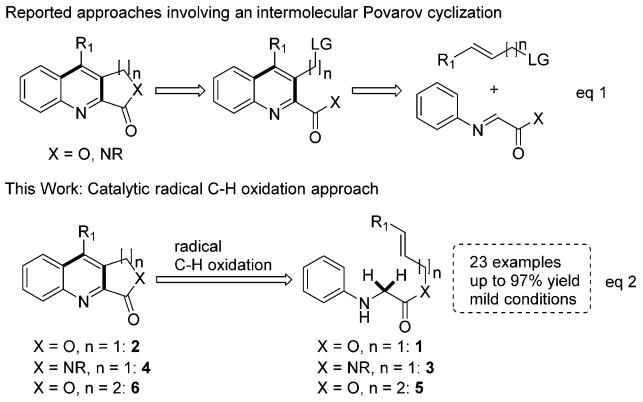


Figure 2. Synthetic disconnections in the synthesis of quinoline-fused lactones and lactams.

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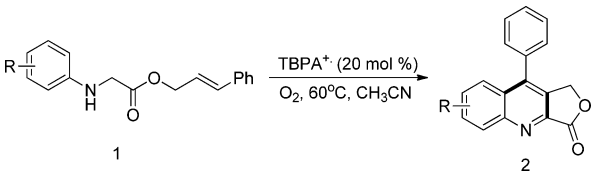
tion.[2c] However, this method requires a tedious synthetic route to obtain the desired starting materials that suffers from low yields. We hypothesized that both the heteroaromatic ring and either the lactone or lactam ring could be constructed via an intramolecular process involving the C−H oxidation/functionalization of readily accessible linear starting materials using the catalytic radical chemistry developed in our laboratory[5] (Figure 2, eq 2). This would represent a highly efficient approach that could inspire new synthetic disconnections in the synthesis of heterocycles.

We recently reported a catalytic radical-cation-initiated C−H functionalization of glycine derivatives with styrenes to build quinoline skeletons.[5] This method represented a novel approach to cross-dehydrogenative couplings (CDCs), avoiding using excess quantities of the oxidants (such as DDQ, TEMPO oxoammonium, and peroxides).[6] Preliminary results obtained during testing of the intramolecular variant suggested that our hypothesis concerning a one-step construction of quinoline-fused lactones and lactams was indeed feasible. Herein we report a novel method for the direct formation of heterocycle-fused lactones and lactams by catalytic aerobic oxidation of glycine derivatives **1**.

We found that the previously reported optimal conditions[5a] employing 20 mol % tris(4-bromophenyl)aminium hexachloroantimonate ($TBPA^{+\bullet}$) and O_2 (1 atm) at 60 °C led to the efficient formation of the desired quinoline-fused lactone **2**. With these conditions in hand, we applied them to a diverse array of *N*-aryl glycine cinnamyl ester derivatives, and the results are compiled in Table 1. This study revealed that

Table 1. Intramolecular Cyclization of *N*-Aryl Glycine Cinnamyl Esters[a]



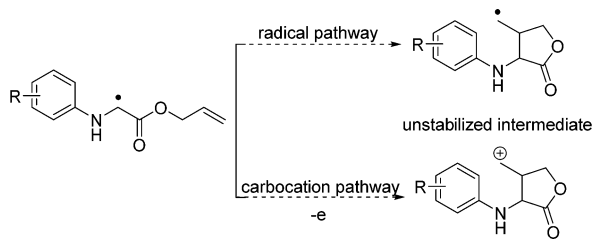
1 2

entry	R	time (h)	product	yield (%)[b]
1	*p*-Br	72	**2a**	92
2	*p*-Cl	72	**2b**	97
3	*p*-F	72	**2c**	72
4	H	36	**2d**	49
5	*p*-Me	12	**2e**	91[c]
6	*p*-MeO	12	**2f**	85[c]
7	*p*-OH	24	**2g**	83[c]
8	*o*-Me	36	**2h**	20

[a]Reaction conditions: **1** (0.5 mmol), $TBPA^{+\bullet}$ (20 mol %), O_2 (1 atm), 60 °C. [b]Isolated yields. [c]The reaction was carried out in the presence of 10 mol % $TBPA^{+\bullet}$.

substituted *N*-aryl glycine cinnamyl esters containing both electron-withdrawing and -donating groups were transformed to the desired products in moderate to excellent yields. However, electron-withdrawing groups were found to cause a decrease in reaction rate (entries 1−3), presumably because the electron-withdrawing group increases the difficulty of oxidation. In the absence of a substituent at the *para* position of the aniline, a diminution in the yield was obtained (entries 4 and 8). This is in accordance with our previously reported intermolecular variant.[5] One reason for the observed yield attenuation is that coupling can occur at the *para* position of the aniline during oxidation.[7] A free phenol group was also tolerated, leading to the desired product in 83% yield, thus implying that these mild oxidation condition are amenable to the synthesis of more complicated compounds without requiring tedious protection−deprotection of fragile functional groups (entry 7). The reaction conditions were also tested using *N*-aryl glycine allyl esters, but no desired product was isolated, suggesting that stability of the radical or carbocation intermediate is crucial for the success of this reaction (Scheme 1).

Scheme 1. Reaction of Glycine Allyl Esters



To determine the generality of this protocol, we turned our attention toward the construction of quinoline-fused lactams using the optimized conditions (Table 2). All of the tested *N*-aryl glycine cinnamyl amides exhibited good reactivity, affording the quinoline-fused lactams in good to excellent yields. Bulky amide *N*-protecting groups, including *tert*-butyl and isopropyl, gave better results than the corresponding *n*-butyl analogues (entry 1 vs entries 2 and 3). This might be due to the fact that large *N*-protecting groups provide a larger population of the reactive rotamer (Scheme 2). When the group is large, the cinnamyl group is closer to the desired reactive radical, which favors intramolecular annulation. The effect of the substituent on cinnamyl group was also examined, and the results show that an electron-donating group increased the annulation yield (entries 4 and 5). Otherwise, an electron-withdrawing group (4-Br) reduced the yield to 66% or 70%, depending on the *N*-protecting group (entries 6 and 7), which supports the existence of an electron-deficient intermediate. One reviewer presented a reasonable reason for the substituent effect in Table 2, and we agree with him. The results in Table 1 show that increasing electron donation on the *N*-aryl group of the glycine ester accelerates the reaction, presumably because the rate-limiting step is sp^3 C−H bond oxidation, not the cyclization. However, when a powerful electron-donating group is connected to the aniline, the oxidation process is no longer rate-limiting, and increased electron donation on the cinnamyl group renders the alkene more nucleophilic, accelerating closure to give the electron-deficient radical **A** (see Scheme 4). All of these results support that an electron transfer may indeed be the pathway to radical intermediate **A**. The reaction of *N*,*N*-dicinnamylamide also occurred smoothly, leaving one *N*-cinnamyl group unchanged (entry 9). This implies that the C−H bond adjacent to the aniline nitrogen is more active than the C−H bond adjacent to the amide group as a result of higher resonance stabilization. Even the benzyl C−H bond adjacent to the amide nitrogen does not disturb the oxidation process, showing good selectivity under the oxidation conditions (entry 8).

Having succeeded in constructing quinoline-fused five-membered lactones and lactams, we wanted to explore the possibility of forming six-membered lactones (Table 3). The

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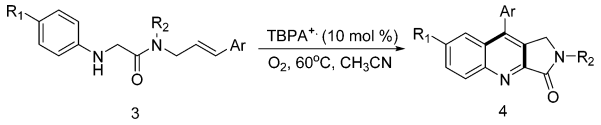
Table 2. Intramolecular Cyclization of Glycine Amides[a]



3 4

entry	R^1	R^2	Ar	time (h)	product	yield (%)[b]
1	OMe	*n*-Bu	Ph	20	**4a**	72
2	OMe	*t*-Bu	Ph	12	**4b**	93
3	OMe	*i*-Pr	Ph	19	**4c**	83
4	OMe	Ph	Ph	20	**4d**	70
5	OMe	Ph	*p*-$MeOC_6H_4$	12	**4e**	94
6	OMe	Ph	*p*-BrC_6H_4	24	**4f**	66
7	OMe	2,4-dimethylphenyl	*p*-BrC_6H_4	24	**4g**	70
8	OMe	CH_2Ph	Ph	16	**4h**	70
9	OMe	cinnamyl	Ph	14	**4i**	64
10	Br	*t*-Bu	Ph	24	**4j**	62

[a]Reaction conditions: **3** (0.5 mmol), $TBPA^{+\bullet}$ (10 mol %), O_2 (1 atm), 60 °C. [b]Isolated yields.

Scheme 2. Rotamerization of Glycine Amide

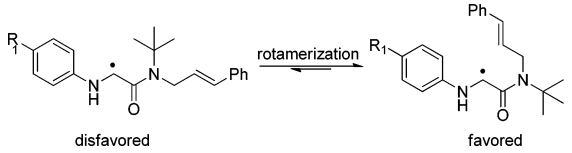
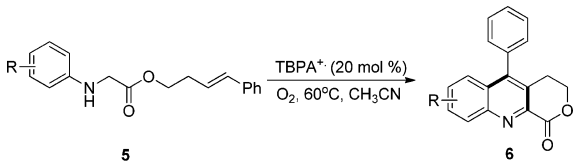


Table 3. Construction of Six-Membered Lactones[a]



5 6

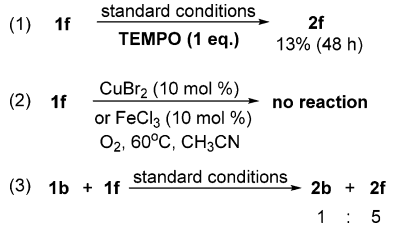
entry	R	time (h)	product	yield (%)[b]
1	*p*-Br	72	**6a**	97
2	*p*-Cl	72	**6b**	75[d]
3	*p*-OCH_3	72	**6c**	92[c]
4	*p*-OH	24	**6d**	83[c]
5	*o*-OCH_3	36	**6e**	49[c]

[a]Reaction conditions: **3** (0.5 mmol), $TBPA^{+\bullet}$ (20 mol %), O_2 (1 atm), 60 °C [b]Isolated yields. [c]The reaction was carried out in the presence of 10 mol % $TBPA^{+\bullet}$. [d]Under reflux.

results show that the desired 3,4-dihydro-1*H*-pyrano[3,4-*b*]quinolin-1-one skeleton can also be built efficiently. The substituent on aniline does not affect the efficiency of the reaction, providing the polycyclic products in high yields.

To probe the reaction mechanism, some control experiments were conducted (Scheme 3). In the presence of the radical inhibitor TEMPO (1 equiv), the reaction was inhibited, and

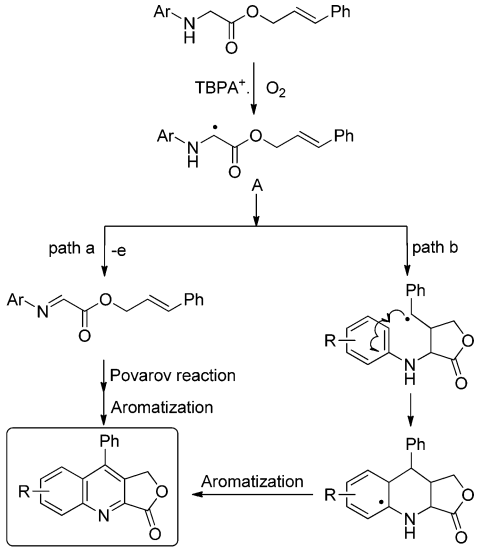
Scheme 3. Control Experiments



only a 13% yield of the desired product was isolated after 48 h (eq 1), which suggested that radical intermediates might be involved. Other oxidants, such as Cu(II) and Fe(III), were used to initiate this reaction, but no reaction occurred, implying that $TBPA^{+\bullet}$ is crucial to induce the oxidation of the sp^3 C−H bond in glycine derivatives (eq 2). A rate study was conducted to confirm the electronic effects on glycine esters. The standard reaction conditions were applied to a mixture of **1b** and **1f** (eq 3). The ratio of the desired products is **2b**:**2f** = 1:5, showing that electron-donating groups accelerate the oxidation of the sp^3 C−H bond. These results also supported the involvement of an electron-deficient intermediate.

On the basis of the results of our group and others,[5,7] a plausible mechanism is proposed (Scheme 4). The sp^3 C−H

Scheme 4. Proposed Mechanism of Radical-Cation-Prompted Intramolecular Annulation



bond adjacent to the anilino group is oxidized by $TBPA^{+\bullet}$ in the presence of O_2, yielding radical intermediate **A**, which can be further oxidized to the corresponding glycine imine (Scheme 4, path a). Then a radical cation salt-induced Povarov reaction can occur[8] to provide the quinoline derivative. However, another pathway might also be operative (Scheme 4, path b), in

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which radical intermediate **A** adds to the double bond directly, followed by radical addition to the phenyl group. After further oxidation and aromatization, the quinolino lactones or lactams are obtained. At this stage, neither of the two pathways can be fully ruled out.

In conclusion, we have demonstrated an efficient synthesis of quinoline-fused lactones and lactams using a radical cation salt-prompted sp^3 C−H aerobic oxidation. The catalytic aerobic oxidation of glycine esters and amides was screened for a broad range of substrates. This approach provides one-step access to these biologically and synthetically relevant core structures from simple starting materials. The mild reaction conditions, good functional group tolerance, and high efficiency will allow for further applications in the synthesis of complicated natural products.

EXPERIMENTAL SECTION

Typical Procedure for the $TBPA^{+\bullet}$-Induced Reaction of *N*-Aryl Glycine Cinnamyl Esters. A solution of **1** (0.5 mmol) in CH_3CN (5 mL) was mixed fully and then flushed with O_2 (continuing to flush until the reaction was complete), followed by addition of $TBPA^{+\bullet}$ (20 mol %) at 60 °C. After completion of the reaction as monitored by TLC (by UV visualization), the reaction was quenched by the addition of a saturated solution of Na_2CO_3 in MeOH (10 mL). The mixture was poured into a separatory funnel with the addition of excess DCM (10 mL), and the crude organic solution was extracted three times with water to remove inorganic salts. The organic phase was then dried over anhydrous magnesium sulfate and filtered, and the solvent was removed under reduced pressure. The products were separated by silica gel column chromatography, eluting with petroleum ether/acetone (10:1 v/v).

*7-Bromo-9-phenylfuro[3,4-b]quinolin-3(1H)-one (**2a**).* Compound **2a** was isolated in 92% yield (156 mg, colorless crystals); mp 168−171 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 9.1 Hz, 1H), 8.04 (d, J = 2.1 Hz, 1H), 7.91 (dd, J = 9.1, 2.1 Hz, 1H), 7.73−7.58 (m, 3H), 7.50−7.41 (m, 2H), 5.40 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 149.2, 144.6, 143.1, 134.3, 133.1, 132.8, 129.9, 129.5, 128.9, 128.7, 127.9, 125.5, 124.2, 67.7; EI-MS m/z (relative intensity) 341 (99.3%), 339 (100%), 312 (12.6%), 310 (11.9%), 284 (64.7%), 282 (68.0%), 232 (11.3%), 216 (19.2%), 203 (39.3%), 176 (16.4%); IR (KBr, neat, cm^{-1}) ν 3057, 2965, 2915, 2851, 1779, 1574, 1482, 1439, 1378, 1262, 1134, 1049, 1006; HRMS (ESI) calcd for $C_{17}H_{10}BrNO_2$ + H^+ 339.9973, found 339.9976.

*7-Chloro-9-phenylfuro[3,4-b]quinolin-3(1H)-one (**2b**).* Compound **2b** was isolated in 97% yield (143 mg, colorless crystals); mp 154−158 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 9.1 Hz, 1H), 7.86 (d, J = 2.2 Hz, 1H), 7.77 (dd, J = 9.1, 2.3 Hz, 1H), 7.68−7.58 (m, 3H), 7.45 (dd, J = 7.8, 1.6 Hz, 2H), 5.40 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 148.7, 144.3, 143.0, 135.6, 133.1, 132.7, 132.5, 131.5, 129.7, 129.4, 128.7, 128.3, 124.4, 67.7; EI-MS m/z (relative intensity) 297 (12.8%), 295 (45.8%), 268 (5.0%), 266 (12.9%), 240 (20.1%), 238 (52.1%), 203 (11.3%), 85 (64.6%), 71 (74.3%), 57 (100%); IR (KBr, neat, cm^{-1}) ν 3051, 2920, 2848, 1774, 1676, 1486, 1447, 1368, 1342, 1270, 1132, 1054, 1008; HRMS (ESI) calcd for $C_{17}H_{10}ClNO_2$ + H^+ 296.0478, found 296.0488.

*7-Fluoro-9-phenylfuro[3,4-b]quinolin-3(1H)-one (**2c**).* Compound **2c** was isolated in 72% yield (100 mg, colorless crystals); mp 150−152 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, J = 9.2, 5.6 Hz, 1H), 7.76−7.56 (m, 4H), 7.56−7.39 (m, 3H), 5.41 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 162.3 (d, J = 253.1 Hz), 147.7, 143.9 (d, J = 2.9 Hz), 143.3 (d, J = 6.4 Hz), 134.0 (d, J = 9.6 Hz), 133.0 (d, J = 9.4 Hz), 129.7, 129.5, 129.1, 129.0, 128.6, 121.4 (d, J = 26.5 Hz), 109.1 (d, J = 23.7 Hz), 67.6; EI-MS m/z (relative intensity) 279 (79.7%), 250 (29.6%), 234 (12.2%), 222 (100%); IR (KBr, neat, cm^{-1}) ν 2919, 2854, 1769, 1705, 1634, 1578, 1507, 1458, 1225, 1126, 1048, 1013; HRMS (ESI) calcd for $C_{17}H_{10}FNO_2$ + H^+ 280.0774, found 280.0786.

*9-Phenylfuro[3,4-b]quinolin-3(1H)-one (**2d**).* Compound **2d** was isolated in 49% yield (64 mg, colorless oil); R_f 0.20 ($v_{PE}/v_{acetone}$ = 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 8.5 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.86 (ddd, J = 8.4, 6.8, 1.4 Hz, 1H), 7.70−7.56 (m, 4H), 7.46 (dd, J = 7.8, 1.6 Hz, 2H), 5.40 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 150.6, 144.2, 143.9, 133.5, 132.2, 131.3, 130.6, 129.5, 129.3, 129.3, 128.8, 127.8, 125.7, 67.7; EI-MS m/z (relative intensity) 261 (100%), 241 (19.9%), 232 (24.5%), 216 (17.3%), 204 (91.7%), 121 (46.6%); IR (KBr, neat, cm^{-1}) ν 2953, 2926, 2847, 1775, 1578, 1458, 1112, 1056; HRMS (ESI) calcd for $C_{17}H_{11}NO_2$ + H^+ 262.0868, found 262.0876.

*7-Methyl-9-phenylfuro[3,4-b]quinolin-3(1H)-one (**2e**).* Compound **2e** was isolated in 91% yield (125 mg, colorless crystals); mp 142−143 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, J = 8.6, 2.7 Hz, 1H), 7.67 (d, J = 8.7 Hz, 1H), 7.65−7.54 (m, 4H), 7.49−7.41 (m, 2H), 5.35 (s, 2H), 2.51 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 168.8, 149.3, 143.3, 142.9, 140.0, 133.7, 133.1, 132.5, 131.0, 129.4, 129.3, 128.8, 127.9, 124.3, 67.8, 22.1; IR (KBr, neat, cm^{-1}) ν 3051, 2920, 2848, 1781, 1578, 1505, 1447, 1375, 1132, 1048, 1021; HRMS (ESI) calcd for $C_{18}H_{13}NO_2$ + H^+ 276.1025, found 276.1026.

*7-Methoxy-9-phenylfuro[3,4-b]quinolin-3(1H)-one (**2f**).* Compound **2f** was isolated in 85% yield (124 mg, colorless oil); R_f 0.20 ($v_{PE}/v_{acetone}$ = 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 9.3 Hz, 1H), 7.68−7.54 (m, 3H), 7.54−7.42 (m, 3H), 7.10 (d, J = 2.7 Hz, 1H), 5.35 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.0, 160.1, 147.0, 141.9, 141.7, 133.9, 133.1, 132.9, 129.5, 129.4 (two ^{13}C), 128.6, 123.9, 102.9, 67.7, 55.6; IR (KBr, neat, cm^{-1}) ν 3058, 2927, 2854, 1774, 1617, 1505, 1460, 1420, 1368, 1290, 1224, 1126, 1047, 1021; HRMS (ESI) calcd for $C_{18}H_{13}NO_3$ + H^+ 292.0974, found 292.0980.

*7-Hydroxy-9-phenylfuro[3,4-b]quinolin-3(1H)-one (**2g**).* Compound **2g** was isolated in 83% yield (115 mg, colorless crystals); mp 218.0−220.0 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 3:1); ^{1}H NMR (400 MHz, acetone-d_6) δ 8.17 (d, J = 9.2 Hz, 1H), 7.70−7.52 (m, 6H), 7.17 (d, J = 2.6 Hz, 1H), 5.43 (s, 1H); ^{13}C NMR (101 MHz, acetone-d_6) δ 169.4, 159.2, 146.8, 142.5, 141.7, 135.0, 134.5, 133.5, 130.5, 123.0, 129.9, 129.8, 124.2, 107.0, 68.3; EI-MS m/z (relative intensity) 277 (100%), 248 (17.0%), 220 (88.6%); IR (KBr, neat, cm^{-1}) ν 3445, 3051, 2914, 2848, 1761, 1610, 1518, 1460, 1387, 1244, 1126, 1047, 1014; HRMS (ESI) calcd for $C_{17}H_{11}NO_3$ + H^+ 278.0817, found 278.0828.

*5-Methyl-9-phenylfuro[3,4-b]quinolin-3(1H)-one (**2h**).* Compound **2h** was isolated in 20% yield (28 mg, colorless oil); R_f 0.20 ($v_{PE}/v_{acetone}$ = 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.5 Hz, 1H), 7.58 (d, J = 6.7 Hz, 1H), 7.55−7.41 (m, 4H), 7.39−7.33 (m, 2H), 5.27 (s, 2H), 2.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 149.8, 143.8, 142.9, 139.5, 133.9, 132.1, 130.5, 129.3, 129.1, 129.0, 128.8, 127.8, 123.6, 67.61, 18.6; EI-MS m/z (relative intensity) 275 (100%), 241 (49.0%), 229 (63.0%), 202 (24.3%), 166 (36.4%), 120 (87.6%); IR (KBr, neat, cm^{-1}) ν 2967, 2911, 2855, 1769, 1486, 1260, 1076, 1013; HRMS (ESI) calcd for $C_{18}H_{13}NO_2$ + H^+ 276.1025, found 276.1030.

*2-Butyl-7-methoxy-9-phenyl-1H-pyrrolo[3,4-b]quinolin-3(2H)-one (**4a**).* Compound **4a** was isolated in 72% yield (125 mg, colorless crystals); mp 180−183 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 9.3 Hz, 1H), 7.66−7.52 (m, 3H), 7.48 (d, J = 6.8 Hz, 2H), 7.40 (dd, J = 9.3, 2.0 Hz, 1H), 7.01 (s, 1H), 4.32 (s, 2H), 3.76 (s, 3H), 3.68 (t, J = 7.5 Hz, 2H), 1.64 (dt, J = 15.2, 7.6 Hz, 2H), 1.44−1.30 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 158.8, 148.8, 145.6, 141.5, 134.7, 132.3, 129.1, 128.9, 128.8, 128.6, 122.2, 103.4, 55.4, 47.1, 42.8, 30.1, 20.0, 13.7; EI-MS m/z (relative intensity) 346 (100%), 294 (43.2%), 265 (25.5%), 250 (42.9%), 214 (13.3%); IR (KBr, neat, cm^{-1}) ν 3051, 2959, 2927, 2861, 1702, 1617, 1578, 1512, 1460, 1414, 1264, 1224, 1119, 1028; HRMS (ESI) calcd for $C_{22}H_{22}N_2O_2$ + H^+ 347.1760, found 347.1761.

*2-(tert-Butyl)-7-methoxy-9-phenyl-1H-pyrrolo[3,4-b]quinolin-3(2H)-one (**4b**).* Compound **4b** was isolated in 93% yield (161 mg, colorless crystals); mp 172−176 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 9.3 Hz, 1H), 7.57−7.43 (m,

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3H), 7.40−7.34 (m, 2H), 7.32 (dd, J = 9.3, 2.6 Hz, 1H), 6.93 (t, J = 6.7 Hz, 1H), 4.29 (s, 2H), 3.67 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 158.7, 149.8, 145.7, 141.3, 134.7, 132.3, 129.1, 128.8, 128.8, 128.7, 128.4, 122.1, 103.3, 55.3, 55.0, 45.4, 27.8; EI-MS m/z (relative intensity) 346 (26.1%), 331 (22.8%), 290 (21.6%), 173 (88.5%), 171 (100%), 151 (51.1%), 108 (62.8%); IR (KBr, neat, cm^{-1}) ν 3051, 2979, 2920, 1695, 1584, 1493, 1447, 1395, 1264, 1224; HRMS (ESI) calcd for $C_{22}H_{22}N_2O_2$ + H^+ 347.1760, found 347.1768.

*2-Isopropyl-7-methoxy-9-phenyl-1H-pyrrolo[3,4-b]quinolin-3(2H)-one (**4c**).* Compound **4c** was isolated in 83% yield (138 mg, colorless crystals); mp 177−179 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 9.3 Hz, 1H), 7.66−7.53 (m, 3H), 7.47 (d, J = 6.8 Hz, 2H), 7.42 (dd, J = 9.3, 2.5 Hz, 1H), 7.01 (d, J = 2.4 Hz, 1H), 4.85 (m, 1H), 4.27 (s, 2H), 3.77 (s, 3H), 1.29 (d, J = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 158.8, 149.1, 145.6, 141.6, 134.7, 132.3, 129.1, 128.8, 128.8, 128.7, 128.6, 122.2, 103.3, 55.3, 43.0, 42.1, 20.4; EI-MS m/z (relative intensity) 332 (100%), 317 (65.1%), 303 (16.8%), 290 (23.0%), 261 (13.8%), 246 (48.5%); IR (KBr, neat, cm^{-1}) ν 3051, 2973, 2927, 1696, 1624, 1505, 1460, 1414, 1230, 1119, 1028; HRMS (ESI) calcd for $C_{21}H_{20}N_2O_2$ + H^+ 333.1603, found 333.1611.

*7-Methoxy-2,9-diphenyl-1H-pyrrolo[3,4-b]quinolin-3(2H)-one (**4d**).* Compound **4d** was isolated in 70% yield (128 mg, colorless crystals); mp 232−233 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 9.3 Hz, 1H), 7.87 (dd, J = 8.7, 1.0 Hz, 2H), 7.69−7.55 (m, 3H), 7.51 (dd, J = 8.0, 1.4 Hz, 2H), 7.41 (ddd, J = 15.3, 9.0, 1.9 Hz, 3H), 7.20−7.11 (m, 1H), 7.03 (d, J = 2.7 Hz, 1H), 4.77 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 159.2, 148.4, 146.1, 141.7, 139.3, 134.6, 132.5, 129.3, 129.2, 129.1, 129.1, 128.8, 128.1, 125.0, 122.7, 119.5, 103.4, 55.5, 48.1; EI-MS m/z (relative intensity) 366 (100%), 337 (24.8%), 293 (7.9%), 247 (11.1%), 204 (9.7%), 71 (38.8%), 57 (53.8%); IR (KBr, neat, cm^{-1}) ν 3058, 2927, 2842, 1702, 1610, 1505, 1460, 1382, 1296, 1244, 1171, 1028; HRMS (ESI) calcd for $C_{24}H_{18}N_2O_2$ + H^+ 367.1447, found 367.1460.

*7-Methoxy-9-(4-methoxyphenyl)-2-phenyl-1,2-dihydro-3H-pyrrolo[3,4-b]quinolin-3-one (**4e**).* Compound **4e** was isolated in 94% yield (186 mg, colorless crystals); R_f 0.20 ($v_{PE}/v_{acetone}$ = 4:1); mp 227−230 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 9.2 Hz, 1H), 7.89 (d, J = 7.7 Hz, 2H), 7.46−7.37 (m, 5H), 7.23−7.06 (m, 4H), 4.79 (s, 2H), 3.95 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 160.1, 159.0, 148.3, 145.9, 141.6, 139.2, 132.3, 130.2, 129.4, 129.0, 128.2, 126.5, 124.9, 122.5, 119.3, 114.7, 103.4, 55.4 (two ^{13}C), 48.1; EI-MS m/z (relative intensity) 396 (8.7%), 353 (20.7%), 266 (18.9%), 201 (26.3%), 158 (59.3%), 147 (100%), 121 (30.5%); IR (KBr, neat, cm^{-1}) ν 3058, 2926, 2847, 1705, 1613, 1507, 1450, 1394, 1295, 1239, 1176, 1133, 1027; HRMS (ESI) calcd for $C_{25}H_{20}N_2O_3$ + H^+ 397.1552, found 397.1561.

*9-(4-Bromophenyl)-7-methoxy-2-phenyl-1,2-dihydro-3H-pyrrolo-[3,4-b]quinolin-3-one (**4f**).* Compound **4f** was isolated in 66% yield (147 mg, colorless crystals); mp 225−229 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.8 Hz, 1H), 7.84 (d, J = 7.6 Hz, 2H), 7.79 (d, J = 6.9 Hz, 2H), 7.49−7.32 (m, 5H), 7.22−7.11 (m, 1H), 6.96 (s, 1H), 4.72 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 159.3, 148.2, 145.9, 140.4, 139.1, 133.4, 132.6, 132.4, 130.6, 129.1, 128.8, 128.0, 125.0, 123.5, 122.8, 119.3, 103.0, 55.5, 47.9; EI-MS m/z (relative intensity) 446 (26.5%), 444 (27.0%), 417 (6.2%), 415 (6.8%), 365 (2.0%), 289 (2.5%), 203 (3.5%), 183 (6.9%), 161 (2.7%), 149 (3.7%), 147 (3.3%), 77 (7.7%), 44 (100%); IR (KBr, neat, cm^{-1}) ν 3058, 2918, 2853, 2224, 1708, 1622, 1589, 1496, 1470, 1391, 1305, 1232, 1173, 1139, 1067, 1028; HRMS (ESI) calcd for $C_{24}H_{17}BrN_2O_2$ + H^+ 445.0552, found 445.0541.

*9-(4-Bromophenyl)-2-(2,4-dimethylphenyl)-7-methoxy-1,2-dihydro-3H-pyrrolo[3,4-b]quinolin-3-one (**4g**).* Compound **4g** was isolated in 70% yield (166 mg, colorless crystals); mp 231−233 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.6 Hz, 1H), 7.72 (d, J = 6.2 Hz, 2H), 7.48 (d, J = 8.0 Hz, 1H), 7.38−7.37 (m, 2H), 7.12 (s, 2H), 7.10−6.99 (m, 2H), 4.63 (s, 2H), 3.82 (s, 3H), 2.33 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 159.4, 148.1, 145.9, 140.5, 138.4, 135.7, 134.1, 133.5, 132.7, 132.5, 132.0, 130.5, 129.3, 128.6, 127.5, 126.7, 123.4, 122.9, 103.1, 55.6, 50.5, 21.0, 18.2; EI-MS m/z (relative intensity) 474 (5.9%), 472 (6.3%), 268 (13.6%), 184 (3.7%), 169 (2.2%), 167 (2.0%), 139 (3.5%), 77 (4.6%), 71 (10.8%), 44 (100%); IR (KBr, neat, cm^{-1}) ν 2919, 2853, 1708, 1622, 1589, 1510, 1457, 1411, 1239, 1028; HRMS (ESI) calcd for $C_{26}H_{21}BrN_2O_2$ + H^+ 473.0865, found 473.0874.

*2-Benzyl-7-methoxy-9-phenyl-1H-pyrrolo[3,4-b]quinolin-3(2H)-one (**4h**).* Compound **4h** was isolated in 70% yield (133 mg, colorless crystals); mp 212−214 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 9.3 Hz, 1H), 7.60−7.46 (m, 3H), 7.40 (m, 3H), 7.27 (m, 5H), 6.97 (s, 1H), 4.86 (s, 2H), 4.20 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 158.9, 148.3, 145.6, 141.7, 136.4, 134.5, 132.3, 129.0, 128.9, 128.8, 128.8, 128.7, 128.2, 127.7, 122.3, 103.4, 55.4, 47.0, 46.7; EI-MS m/z (relative intensity) 380 (33.9%), 330 (29.4%), 315 (17.3%), 246 (17.7%), 161 (20.1%), 71 (70.5%), 57 (100%); IR (KBr, neat, cm^{-1}) ν 3052, 2926, 1705, 1620, 1577, 1507, 1457, 1408, 1218, 1028; HRMS (ESI) calcd for $C_{25}H_{20}N_2O_2$ + H^+ 381.1603, found 381.1609.

*2-Cinnamyl-7-methoxy-9-phenyl-1H-pyrrolo[3,4-b]quinolin-3(2H)-one (**4i**).* Compound **4i** was isolated in 64% yield (130 mg, colorless crystals); mp 242−246 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 9.3 Hz, 1H), 7.63−7.49 (m, 3H), 7.49−7.38 (m, 3H), 7.38−7.16 (m, 5H), 7.00 (d, J = 2.4 Hz, 1H), 6.59 (d, J = 15.8 Hz, 1H), 6.23 (dt, J = 15.6, 6.6 Hz, 1H), 4.47 (d, J = 6.2 Hz, 2H), 4.33 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 158.9, 148.4, 145.6, 141.7, 136.0, 134.6, 133.8, 132.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.5, 127.9, 126.4, 123.6, 122.3, 103.4, 55.3, 46.8, 45.2; EI-MS m/z (relative intensity) 406 (100%), 345 (24.0%), 291 (60.2%), 247 (56.4%), 219 (13.6%), 204 (36.0%), 168 (38.4%); IR (KBr, neat, cm^{-1}) ν 2960, 2919, 2847, 1698, 1613, 1500, 1408, 1288, 1218 1028; HRMS (ESI) calcd for $C_{27}H_{22}N_2O_2$ + H^+ 407.1760, found 407.1771.

*7-Bromo-2-(tert-butyl)-9-phenyl-1H-pyrrolo[3,4-b]quinolin-3(2H)-one (**4j**).* Compound **4j** was isolated in 62% yield (122 mg, colorless crystals); mp 239−242 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 9.0 Hz, 1H), 7.78−7.66 (m, 2H), 7.66−7.55 (m, 3H), 7.43 (d, J = 6.6 Hz, 2H), 4.43 (s, 2H), 1.59 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 152.3, 148.0, 142.3, 133.7, 133.7, 132.4, 130.6, 129.2, 128.8, 128.7, 128.1, 124.3, 121.3, 55.3, 45.4, 27.7; EI-MS m/z (relative intensity) 396 (0.1%), 394 (0.1%), 326 (80.0%), 279 (9.0%), 234 (16.7%), 232 (16.4%), 167 (38.1%), 149 (100%); IR (KBr, neat, cm^{-1}) ν 3056, 2966, 2918, 2849, 1697, 1596, 1490, 1442, 1389, 1262, 1082, 1024; HRMS (ESI) calcd for $C_{21}H_{19}BrN_2O$ + H^+ 395.0759, found 395.0759.

*7-Bromo-5-phenyl-3,4-dihydro-1H-pyrano[3,4-b]quinolin-1-one (**6a**).* Compound **6a** was isolated in 97% yield (172 mg, colorless crystals); mp 162−166 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 9.0 Hz, 1H), 7.83 (d, J = 9.0 Hz, 1H), 7.70 (s, 1H), 7.65−7.53 (m, 3H), 7.36−7.25 (m, 2H), 4.55 (t, J = 5.8 Hz, 2H), 3.04 (t, J = 5.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 146.4, 146.0, 143.4, 134.1, 133.7, 132.8, 130.0, 129.6, 129.2, 129.1, 128.0, 124.1, 66.9, 26.6; EI-MS m/z (relative intensity) 355 (99.1%), 353 (100%), 297 (34.1%), 295 (35.2%), 230 (23.5%), 216 (48.2%); IR (KBr, neat, cm^{-1}) ν 3058, 2953, 2920, 1741, 1486, 1290, 1178; HRMS (ESI) calcd for $C_{18}H_{12}BrNO_2$ + H^+ 354.0130, found 354.0140.

*7-Chloro-5-phenyl-3,4-dihydro-1H-pyrano[3,4-b]quinolin-1-one (**6b**).* Compound **6b** was isolated in 75% yield (116 mg, colorless crystals); mp 170−171 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 9.0 Hz, 1H), 7.61 (d, J = 9.0 Hz, 1H), 7.57−7.46 (m, 3H), 7.44 (s, 1H), 7.23 (d, J = 7.5 Hz, 2H), 4.47 (t, J = 5.8 Hz, 2H), 2.96 (t, J = 5.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 146.1, 146.1, 143.2, 135.5, 134.1, 132.7, 131.0, 130.0, 129.2, 129.1, 129.1, 124.6, 66.8, 26.5; EI-MS m/z (relative intensity) 311 (33.0%), 309 (100%), 266 (4.0%), 264 (12.4%), 253 (25.2%), 251 (82.4%), 230 (25.4%), 216 (50.5%); IR (KBr, neat, cm^{-1}) ν 3058, 2920, 2848, 1738, 1486, 1283, 1178, 1087, 1021; HRMS (ESI) calcd for $C_{18}H_{12}ClNO_2$ + H^+ 310.0635, found 310.0641.

*7-Methoxy-5-phenyl-3,4-dihydro-1H-pyrano[3,4-b]quinolin-1-one (**6c**).* Compound **6c** was isolated in 92% yield (140 mg, colorless

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oil); R_f 0.20 ($v_{PE}/v_{acetone}$ = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 9.3 Hz, 1H), 7.57 (dq, J = 14.1, 6.9 Hz, 3H), 7.41 (dd, J = 9.2, 2.2 Hz, 1H), 7.31 (d, J = 7.0 Hz, 2H), 6.75 (d, J = 2.0 Hz, 1H), 4.53 (t, J = 5.7 Hz, 2H), 3.74 (s, 3H), 3.00 (t, J = 5.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 160.0, 144.9, 144.3, 140.5, 135.2, 132.9, 130.2, 129.5, 129.1, 129.0, 128.7, 123.0, 103.3, 66.9, 55.4, 26.6; EI-MS m/z (relative intensity) 305 (100%), 247 (40.9%), 232 (34.9%), 204 (26.3%); IR (KBr, neat, cm^{-1}) ν 3051, 2920, 2848, 1741, 1617, 1493, 1460, 1414, 1296, 1224, 1172, 1087, 1028; HRMS (ESI) calcd for $C_{19}H_{15}NO_3$ + H^+ 306.1130, found 306.1141.

*7-Hydroxy-5-phenyl-3,4-dihydro-1H-pyrano[3,4-b]quinolin-1-one (**6d**).* Compound **6d** was isolated in 83% yield (121 mg, colorless crystals); mp 210−212 °C; R_f 0.20 ($v_{PE}/v_{acetone}$ = 2:1); ^{1}H NMR (400 MHz, acetone-d_6) δ 8.12 (d, J = 9.1 Hz, 1H), 7.70−7.54 (m, 3H), 7.48 (d, J = 9.1 Hz, 1H), 7.41 (d, J = 7.7 Hz, 2H), 6.81 (s, 1H), 4.55 (t, J = 5.7 Hz, 2H), 3.01 (t, J = 5.7 Hz, 2H); ^{13}C NMR (101 MHz, acetone-d_6) δ 166.1, 161.6, 147.5, 146.8, 144.1, 139.1, 136.0, 133.8, 133.6, 132.9, 132.4, 132.0, 126.1, 110.0, 70.2, 30.0; EI-MS m/z (relative intensity) 291 (92.7%), 246 (14.3%), 233 (100%), 204 (16.3%); IR (KBr, neat, cm^{-1}) ν 3451, 3058, 2920, 2848, 1729, 1617, 1467, 1244, 1184, 1021; HRMS (ESI) calcd for $C_{18}H_{13}NO_3$ + H^+ 292.0974, found 292.0978.

*9-Methoxy-5-phenyl-3,4-dihydro-1H-pyrano[3,4-b]quinolin-1-one (**6e**).* Compound **6e** was isolated in 49% yield (75 mg, colorless oil); R_f 0.20 ($v_{PE}/v_{acetone}$ = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.44 (m, 3H), 7.35−7.18 (m, 3H), 7.10−7.06 (m, 2H), 4.52 (t, J = 5.8 Hz, 1H), 4.11 (s, 1H), 3.01 (t, J = 5.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 156.5, 146.5, 141.7, 140.3, 135.2, 129. 8, 129.7, 129.2, 128.9, 128.7, 117.4, 107.6, 66.8, 56.1, 26.7; EI-MS m/z (relative intensity) 304 (100%), 276 (18.8%), 258 (52.0%), 230 (33.3%); IR (KBr, neat, cm^{-1}) ν 3182, 2914, 2848, 1735, 1624, 1512, 1211, 1159, 1021; HRMS (ESI) calcd for $C_{19}H_{15}NO_3$ + H^+ 306.1130, found 306.1144.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H NMR and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Cappelli, A.; Anzini, M.; Vomero, S.; De Benedetti, P. G.; Menziani, M. C.; Giorgi, G.; Manzoni, C. *J. Med. Chem.* **1997**, *40*, 2910. (b) Matarrese, M.; Moresco, R. M.; Cappelli, A.; Anzini, M.; Vomero, S.; Simonello, P.; Verza, E.; Magni, F.; Sudati, F.; Soloviev, D.; Todde, S.; Carpinelli, A.; Kienle, M. G.; Fazio, F. *J. Med. Chem.* **2001**, *44*, 579. (c) Anzini, M.; Cappelli, A.; Vomero, S.; Seeber, M.; Menziani, M. C.; Langer, T.; Hagen, B.; Manzoni, C.; Bourguignon, J.-J. *J. Med. Chem.* **2001**, *44*, 1134. (d) Cappelli, A.; Mohr, G. P.; Galleli, A.; Giuliani, G.; Anzini, M.; Vomero, S.; Fresta, M.; Porcu, P.; Maciocco, E.; Concas, A.; Biggio, G.; Donati, A. *J. Med. Chem.* **2003**, *46*, 3568. (e) Cappelli, A.; Matarrese, M.; Moresco, R. M.; Valenti, S.; Anzini, M.; Vomero, S.; Turolla, E. A.; Belloli, S.; Simonelli, P.; Filannino, M. A.; Lecchi, M.; Fazio, F. *Bioorg. Med. Chem.* **2006**, *14*, 4055. (f) Stevenson, L.; Tavares, A. A. S.; Brunet, A.; McGonagle, F. I.; Dewar, D.; Pimlott, S. L.; Sutherland, A. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 954.

(2) (a) Nicolaou, K. C.; Zhang, H.; Chen, J. S.; Crawford, J. J.; Pasunoon, L. *Angew. Chem., Int. Ed.* **2007**, *46*, 4704. (b) Nicolaou, K. C.; Chen, J. S.; Zhang, H.; Montero, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 185. (c) Desrat, S.; van de Weghe, P. *J. Org. Chem.* **2009**, *74*, 6728.

(3) (a) Bi, Y. B.; Bi, X. B.; Zhao, Q. R.; Chen, Y. T.; Xie, J. L. *Helv. Chim. Acta* **2004**, *87*, 2890. (b) Sall, C.; Desbois, N.; Paquelet, S.; Camacho, J. R.; Chezal, J. M.; Teulade, J.-C.; Blache, Y. *Tetrahedron Lett.* **2008**, *49*, 1301.

(4) (a) Ma, Z. Z.; Hano, Y.; Nomura, T.; Chen, Y. J. *Heterocycles* **1997**, *46*, 541. (b) Osborne, D.; Stevenson, P. J. *Tetrahedron Lett.* **2002**, *43*, 5469. (c) Tseng, M.-C.; Chu, Y.-W.; Tsai, H.-P.; Lin, C.-M.; Hwang, J.; Chu, Y.-H. *Org. Lett.* **2011**, *13*, 920. (d) Twin, H.; Batey, R. A. *Org. Lett.* **2004**, *6*, 4913. (e) Zhou, H.-B.; Liu, G.-S.; Yao, Z.-J. *J. Org. Chem.* **2007**, *72*, 6270. (f) Ju, Y.; Liu, F.; Li, C.-Z. *Org. Lett.* **2009**, *11*, 3582. (g) Mhaske, S. B.; Argade, N. P. *J. Org. Chem.* **2004**, *69*, 4563.

(5) (a) Jia, X.-D.; Peng, F.-F.; Qing, C.; Huo, C.-D.; Wang, X.-C. *Org. Lett.* **2012**, *14*, 4030. (b) Jia, X.-D.; Wang, Y.-X.; Peng, F.-F.; Huo, C.-D.; Yu, L.-L.; Wang, X.-C. *J. Org. Chem.* **2013**, *78*, 9450. (c) Jia, X.-D.; Wang, Y.-X.; Peng, F.-F.; Huo, C.-D.; Yu, L.-L.; Liu, J.; Wang, X.-C. *Adv. Synth. Catal.* **2014**, *356*, 1210.

(6) Recent developments on CDC reactions: (a) Chandrasekharam, M.; Chiranjeevi, B.; Gupta, K. S. V.; Sridhar, B. *J. Org. Chem.* **2011**, *76*, 10229. (b) Park, S. J.; Price, J. R.; Todd, M. H. *J. Org. Chem.* **2012**, *77*, 949. (c) Zhao, M.; Wang, F.; Li, X. *Org. Lett.* **2012**, *14*, 1412. (d) Wang, P.; Rao, H.; Hua, R.; Li, C.-J. *Org. Lett.* **2012**, *14*, 902. (e) Correiaa, C. A.; Li, C.-J. *Adv. Synth. Catal.* **2010**, *352*, 1446. (f) Zhao, L.; Li, C.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 7075. (g) Xie, J.; Huang, Z.-Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 10181. (h) Wang, P.; Rao, H.; Hua, R.; Li, C.-J. *Org. Lett.* **2012**, *14*, 902. (i) Guin, S.; Rout, S. K.; Banerjee, A.; Nandi, S.; Patel, B. K. *Org. Lett.* **2012**, *14*, 5294.

(7) (a) Richter, H.; Mancheño, O. G. *Org. Lett.* **2011**, *13*, 6066. (b) Rohlmann, R.; Stopka, T.; Richter, H.; Mancheño, O. G. *J. Org. Chem.* **2013**, *78*, 6050.

(8) (a) Jia, X.-D.; Lin, H.-C.; Huo, C.-D.; Zhang, W.; Lü, J.-M.; Yang, L.; Zhao, G.-Y.; Liu, Z.-L. *Synlett* **2003**, 1707. (b) Jia, X.-D.; Han, B.; Zhang, W.; Jin, X.-L.; Liu, Z.-L. *Synthesis* **2006**, 2831. (c) Jia, X.-D.; Qing, C.; Huo, C.-D.; Peng, F.-F.; Wang, X.-C. *Tetrahedron Lett.* **2012**, *53*, 7140. (d) Jia, X.-D.; Peng, F.-F.; Qing, C.; Huo, C.-D.; Wang, Y.-X.; Wang, X.-C. *Tetrahedron Lett.* **2013**, *54*, 4950. (e) Jia, X.-D.; Ren, Y.; Huo, C.-D.; Wang, W.-J.; Chen, X.-N.; Xu, X.-L.; Wang, X.-C. *Tetrahedron Lett.* **2010**, *51*, 6779. (f) Han, B.; Jia, X.-D.; Jin, X.-L.; Zhou, Y.-L.; Yang, L.; Liu, Z.-L.; Yu, W. *Tetrahedron Lett.* **2006**, *47*, 3545.