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(4 + 2) cyclization of aza-*o*-quinone methides with azlactones: construction of biologically important dihydroquinolinone frameworks†

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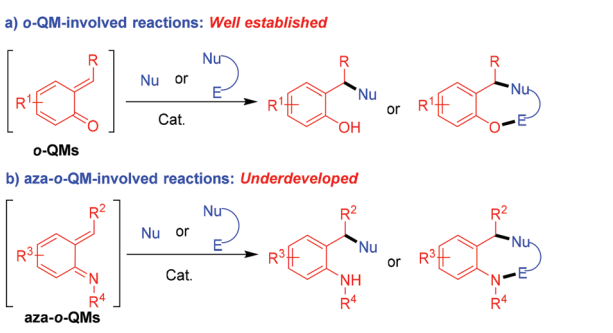
A base-promoted (4 + 2) cyclization of aza-*o*-quinone methides (aza-*o*-QMs) *in situ* generated from *N*-(*o*-chloromethyl)aryl amides was established. In this approach, azlactones were utilized as competent two-atom reaction partners to undergo (4 + 2) cyclization with aza-*o*-QMs, which afforded a series of dihydroquinolinone derivatives in overall good yields (up to 98%). This protocol has not only advanced the development of aza-*o*-QM-involved reactions, but also offered a useful method for constructing biologically important dihydroquinolinone frameworks.

Introduction

Heterocyclic compounds, especially nitrogenous and oxygenous heterocycles are widely distributed in biologically important natural products and synthetic pharmaceuticals.[1] So, developing efficient methods toward the construction of heterocyclic scaffolds has become an important goal in the community of synthetic chemistry and medicinal chemistry.[2] In recent years, *ortho*-quinone methides (*o*-QMs) have been proven to be versatile building blocks for the construction of oxygenous heterocyclic frameworks.[3,4] As illustrated in Scheme 1a, both 1,4-addition reactions and (4 + *n*) cyclizations of *o*-QMs have been well established, and lots of phenol derivatives and oxygen-containing heterocycles have been synthesized efficiently.[5,6]

However, in sharp contrast, aza-*o*-QMs, a class of analogues of *o*-QMs, have received far less attention from the synthetic community in spite of the fact that aza-*o*-QMs should be convenient building blocks for constructing nitrogenous heterocyclic skeletons.[7] Consequently, both 1,4-addition reactions and (4 + *n*) cyclizations of aza-*o*-QMs are underdeveloped (Scheme 1b). Therefore, there is great demand to develop reactions involving aza-*o*-QM for the construction of biologically important nitrogenous heterocyclic frameworks.

In this context, *N*-(*ortho*-chloromethyl)aryl amides have been recognized as a class of important precursors of aza-*o*-QMs because they can easily transform into aza-*o*-QMs in the presence of a base, thus undergoing cyclization reactions to construct nitrogenous scaffolds (Scheme 2).[8–11] Nevertheless, most of the (4 + *n*) cyclizations involving aza-*o*-QMs *in situ* generated from *N*-(*o*-chloromethyl)aryl amides are confined to (4 + 1) and (4 + 3) cyclizations (eqn (1) and (2)),[8,9] which provide robust methods for the construction of five-membered and seven-membered nitrogenous heterocyclic frameworks. In contrast, (4 + 2) cyclizations of such aza-*o*-QMs have been rarely reported (eqn (3)) although this type of cyclization could construct six-membered nitrogenous cyclic skeletons,[10] which are frequently found in bioactive molecules. This might be ascribed to the challenges in finding suitable two-atom reaction partners for (4 + 2) cyclizations with such precursors of aza-*o*-QMs in the presence of a base.



Scheme 1 Comparison of reactions involving *o*-QM and aza-*o*-QM.

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†Electronic supplementary information (ESI) available: Original NMR spectra of products **3–5** and compound **I**. CCDC 2046973 for compound **3aa**. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0ob02388d

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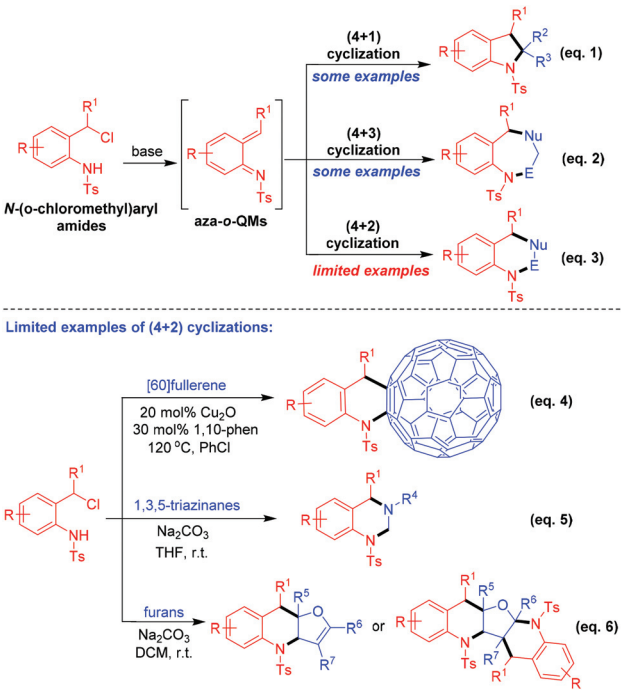
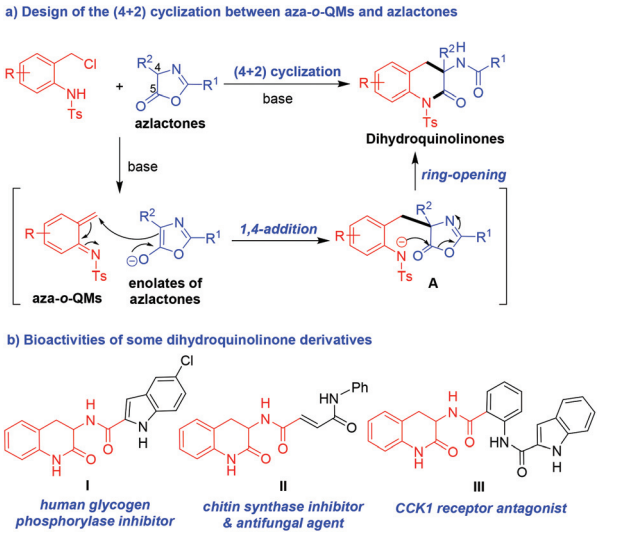


Scheme 2 Profile of (4 + *n*) cyclizations involving aza-*o*-QMs *in situ* generated from *N*-(*o*-chloromethyl)aryl amides.



Scheme 3 Design of the (4 + 2) cyclization of aza-*o*-QMs with azlactones for constructing biologically important dihydroquinolinone frameworks.

The survey of the literature only revealed very limited examples of (4 + 2) cyclizations of aza-*o*-QMs *in situ* generated from *N*-(*o*-chloromethyl)aryl amides (eqn (4)–(6)).[10] In these cases, compatible two-atom reaction partners were discovered for (4 + 2) cyclizations of aza-*o*-QMs. For example, Wang's group utilized [60]fullerene as an electron-rich olefin (eqn (4));[10a] Liu's group employed 1,3,5-triazinanes as equivalents of two-atom reaction partners (eqn (5));[10b] Mo, Lu and co-workers used substituted furans as electron-rich arenes (eqn (6)).[10c] In spite of these elegant works, (4 + 2) cyclizations of aza-*o*-QMs *in situ* generated from *N*-(*o*-chloromethyl)aryl amides are still rather underdeveloped. Thus, it is highly valuable to find other competent two-atom reaction partners and to develop (4 + 2) cyclizations of such aza-*o*-QMs.

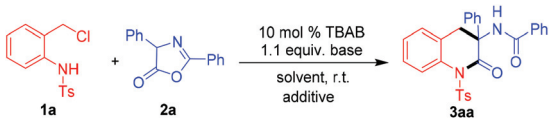
To achieve this goal, and with our long-lasting efforts in constructing heterocyclic frameworks,[12] we designed a base-promoted (4 + 2) cyclization of this class of aza-*o*-QMs, wherein azlactones were selected as suitable two-atom reaction partners (Scheme 3a). This design was based on the consideration that azlactone can utilize its C4,C5-reactivity to serve as two-atom synthons and perform (2 + *n*) cyclizations.[13–15] In addition, azlactones can be promoted by a base *via* deprotonation to generate the enolates of azlactones. As illustrated in Scheme 3a, in the presence of a base, the enolates of azlactones would undergo 1,4-addition with aza-*o*-QMs which are generated from *N*-(*o*-chloromethyl)aryl amides, thus affording intermediates **A**. Then, intermediates **A** would undergo an intramolecular aminolysis of the ester group and a ring-opening reaction, thus accomplishing the (4 + 2) cyclization and constructing the dihydroquinolinone scaffold.

It should be noted that the dihydroquinolinone scaffold exists in many bioactive compounds (Scheme 3b).[16] For instance, compound **I** is a human glycogen phosphorylase inhibitor;[16a] compound **II** is a chitin synthase inhibitor and an antifungal agent;[16b] and compound **III** is a CCK1 receptor antagonist.[16c] So, the designed (4 + 2) cyclization of aza-*o*-QMs with azlactones could provide a useful protocol for the construction of biologically important dihydroquinolinone frameworks.

Results and discussion

Based on this design, the reaction of *N*-(*o*-chloromethyl)aryl amide **1a** with azlactone **2a** was utilized as a model reaction to testify the feasibility of our design (Table 1). As expected, in the presence of caesium carbonate as a base, the two substrates of **1a** and **2a** smoothly underwent the designed (4 + 2) cyclization to generate the dihydroquinolinone derivative **3aa** in a good yield of 77% (entry 1). Because caesium carbonate belongs to an inorganic base, to increase its effect in organic solvent (acetonitrile), *tetra*-butylammonium bromide (TBAB) as a phase-transfer catalyst was added to the reaction mixture, which indeed increased the yield to 87% (entry 2). Then, the evaluation of different solvents such as tetrahydrofuran, dichloromethane and toluene revealed that no other solvents were better than acetonitrile in terms of yield (entries 3–5 *vs.* entry 2). Next, different bases including an organic base (NEt_3) and inorganic bases ($NaHCO_3$ and Na_2CO_3) were evaluated for this reaction (entries 6–8), and it was discovered that these bases were inferior to caesium carbonate in promoting the reaction (entries 6–8 *vs.* entry 2). Subsequently, the reagent ratio was carefully modulated (entries 9–13), and it was found that suitably increasing the amount of azlactone **2a** could

Table 1 Optimization of reaction conditions[a]



Entry	Solvent	Base	1a : 2a	Additive	Yield[b] (%)
1[c]	CH_3CN	Cs_2CO_3	1 : 1.5	—	77
2	CH_3CN	Cs_2CO_3	1 : 1.5	—	87
3	THF	Cs_2CO_3	1 : 1.5	—	85
4	CH_2Cl_2	Cs_2CO_3	1 : 1.5	—	85
5	Toluene	Cs_2CO_3	1 : 1.5	—	44
6	CH_3CN	NEt_3	1 : 1.5	—	84
7	CH_3CN	$NaHCO_3$	1 : 1.5	—	44
8	CH_3CN	Na_2CO_3	1 : 1.5	—	51
9	CH_3CN	Cs_2CO_3	1 : 2	—	90
10	CH_3CN	Cs_2CO_3	1 : 3	—	91
11	CH_3CN	Cs_2CO_3	1.5 : 1	—	81
12	CH_3CN	Cs_2CO_3	2 : 1	—	90
13	CH_3CN	Cs_2CO_3	3 : 1	—	87
14	CH_3CN	Cs_2CO_3	1 : 3	Na_2SO_4	93
15	CH_3CN	Cs_2CO_3	1 : 3	$MgSO_4$	98
16	CH_3CN	Cs_2CO_3	1 : 3	3 Å MS	91
17	CH_3CN	Cs_2CO_3	1 : 3	4 Å MS	91
18	CH_3CN	Cs_2CO_3	1 : 3	5 Å MS	92

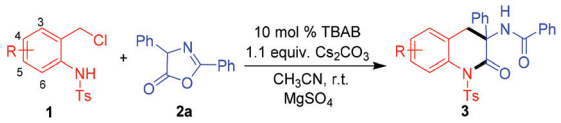
[a] Unless indicated otherwise, the reaction was carried out on a 0.1 mmol scale at room temperature (r.t.) in a solvent (1 mL) without or with an additive (100 mg) for 3 h. [b] Determined by ^1H NMR. [c] In the absence of TBAB.

further improve the yield to 91% (entry 10). Finally, some additives such as anhydrous sulfates and different molecular sieves (MS) were added to the reaction system (entries 14–18), and it was revealed that the addition of magnesium sulfate could greatly enhance the yield to 98% (entry 15). So, the reaction conditions as illustrated in entry 15 were chosen as the optimal conditions for this (4 + 2) cyclization.

After establishing the optimal reaction conditions, we studied the generality of the (4 + 2) cyclization between *N*-(*o*-chloromethyl)aryl amides **1** and azlactones **2**. First, the substrate scope of *N*-(*o*-chloromethyl)aryl amides **1** was investigated (Table 2). It was discovered that a range of *N*-(*o*-chloromethyl)aryl amides **1** bearing a methyl group or a chloro-group at different positions of the phenyl ring could successfully participate in the (4 + 2) cyclization with azlactone **2a**, which generated dihydroquinolinone derivatives **3** in high isolated yields (84%–98%), which demonstrated that this reaction was amenable to various *N*-(*o*-chloromethyl)aryl amides **1**.

Then, the substrate scope of azlactones **2** was investigated by their reaction with *N*-(*o*-chloromethyl)aryl amide **1a** under standard reaction conditions (Table 3). In general, a variety of azlactones **2** bearing different R^1/R^2 substituents could smoothly take part in the (4 + 2) cyclization, which gave rise to dihydroquinolinone derivatives **3** with structural diversity in moderate to good yields (60%–87%). In detail, R^2 groups could be substituted phenyl (entries 1 and 2), phenyl (entries 3–6) and ester (entries 7–14) groups. Moreover, R^1 groups could be a wide range of phenyl groups bearing electronically different substituents at *ortho*-, *meta*-, and *para*-positions (entries 3–6

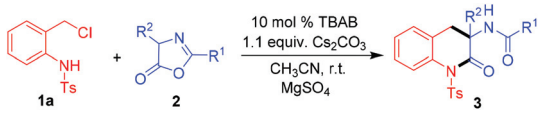
Table 2 Substrate scope of *N*-(*o*-chloromethyl)aryl amides **1**[a]



Entry	R (1)	3	Yield[b] (%)
1	H (**1a**)	**3aa**	92
2	6-Me (**1b**)	**3ba**	86
3	5-Cl (**1c**)	**3ca**	91
4	4-Me (**1d**)	**3da**	84
5	4-Cl (**1e**)	**3ea**	98
6	3-Me (**1f**)	**3fa**	91
7	3-Cl (**1g**)	**3ga**	88

[a] The reaction was carried out on a 0.1 mmol scale in CH_3CN (1 mL) with $MgSO_4$ (100 mg) as an additive for 3 h, and the molar ratio of **1** : **2a** was 1 : 3. [b] Isolated yield.

Table 3 Substrate scope of azlactones **2**[a]



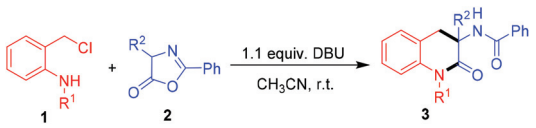
Entry	R^1/R^2 (2)	3	Yield[b] (%)
1	Ph/*o*-ClC_6H_4 (**2b**)	**3ab**	79
2	Ph/*p*-ClC_6H_4 (**2c**)	**3ac**	87
3	*o*-FC_6H_4/Ph (**2d**)	**3ad**	78
4	*m*-ClC_6H_4/Ph (**2e**)	**3ae**	75
5	*p*-ClC_6H_4/Ph (**2f**)	**3af**	77
6	*p*-$MeOC_6H_4$/Ph (**2g**)	**3ag**	81
7	Ph/CO_2Et (**2h**)	**3ah**	85
8	*o*-FC_6H_4/CO_2Et (**2i**)	**3ai**	60
9	*o*-MeC_6H_4/CO_2Et (**2j**)	**3aj**	62
10	*m*-ClC_6H_4/CO_2Et (**2k**)	**3ak**	81
11	*p*-$CF_3C_6H_4$/CO_2Et (**2l**)	**3al**	81
12	*p*-MeC_6H_4/CO_2Et (**2m**)	**3am**	75
13[c]	Me/CO_2Et (**2n**)	**3an**	78
14[c,d]	Me/CO_2Et (**2n**)	**3hn**	82

[a] The reaction was carried out on a 0.1 mmol scale in CH_3CN (1 mL) with $MgSO_4$ (100 mg) as an additive for 3 h, and the molar ratio of **1a**:**2** was 1 : 3. [b] Isolated yield. [c] The molar ratio of **1a** : **2n** was 1 : 1.2. [d] Using *N*-Boc-protected **1h** as a reactant.

and 8–12). More importantly, an aliphatic methyl group could serve as a suitable R^1 group for substrate **2n**, which successfully participated in the (4 + 2) cyclizations with **1a** and *N*-Boc-protected **1h** to give products **3an** and **3hn** in high yields (entries 13 and 14). So, this (4 + 2) cyclization could be applicable to a series of azlactones **2**.

To further improve the generality of the substrate scope, we utilized azlactones **2** bearing alkyl (R^2) groups as substrates in the (4 + 2) cyclization (Table 4). Initially, the reaction of *N*-Ts-protected amide **1a** with benzyl-substituted azlactone **2o** was performed under standard conditions, which could undergo the desired (4 + 2) cyclization to give product **3ao** albeit with a low yield of 40% (entry 1). To improve the yield, *N*-Boc-protected amide **1h** was utilized as a reaction partner for azlactone

Table 4 Application of azlactones **2** bearing alkyl (R^2) groups as substrates in the reaction[a]



Entry	R^1 (**1**)	R^2 (**2**)	**3**	Yield[b] (%)
1[c]	Ts (**1a**)	Bn (**2o**)	**3ao**	40
2	Boc (**1h**)	Bn (**2o**)	**3ho**	75
3	Boc (**1h**)	Me (**2p**)	**3hp**	82
4	Boc (**1h**)	i-Pr (**2q**)	**3hq**	58
5	Boc (**1h**)	Allyl (**2r**)	**3hr**	73

[a] The reaction was carried out on a 0.1 mmol scale with 1.1 equiv. DBU in CH_3CN (1 mL) at r.t. for 3 h, and the molar ratio of **1** : **2** was 1 : 1.2. [b] Isolated yield. [c] Catalyzed by 10 mol% TBAB and 1.1 equiv. Cs_2CO_3 in CH_3CN (1 mL) with $MgSO_4$ (100 mg) as an additive at r.t. for 3 h, and the molar ratio of **1a** : **2o** was 1 : 1.2.

2o under modified reaction conditions, which smoothly underwent (4 + 2) cyclization to afford product **3ho** in a good yield of 75% (entry 2). Furthermore, it was revealed that the (4 + 2) cyclization could tolerate azlactones **2p–2r** bearing different alkyl (R^2) groups such as methyl, iso-propyl and allyl groups, which generated products **3hp–3hr** in moderate to good yields (entries 3–5).

The structures of dihydroquinolinone derivatives **3** were determined based on their ^{1}H NMR, ^{13}C NMR, IR and HR MS spectra. In addition, the structure of product **3aa** was confirmed by X-ray analysis of its single crystal (Fig. 1).[17]

To examine whether the reaction could be scaled up or not, two one-mmol-scale reactions of *N*-Ts-protected amide **1a** with azlactone **2a** and *N*-Boc-protected amide **1h** with azlactone **2n** were carried out under standard conditions (Scheme 4, eqn (7) and (8)). These (4 + 2) cyclization reactions smoothly occurred to give products **3aa** and **3hn** in good yields, which were comparable to those of the small-scale reactions (Table 2, entry 1; Table 3, entry 14). These results demonstrated that this (4 + 2) cyclization reaction could be scaled up without sacrifice of the yield. In addition, the deprotection of the *N*-Ts group in product **3aa** could be successfully performed with the action of samarium(II) iodide, generating NH-unprotected product **4** in a good yield of 70% (Scheme 4, eqn (9)).

Finally, to demonstrate the utility of this methodology, the synthesis of the bioactive molecule (compound **I**, in Scheme 3b) was performed by using **3hn** as a starting material (Scheme 5). In brief, the deprotection of the *N*-Boc group in **3hn** generated compound **5** in a high yield of 85%. Then, compound **5** underwent decarboxylation reaction to give an intermediate product **6**, which directly reacted with 5-chloroindole-2-carboxylic acid without isolation to afford compound **I** as an inhibitor of human glycogen phosphorylase in a total yield of 72% over three steps.

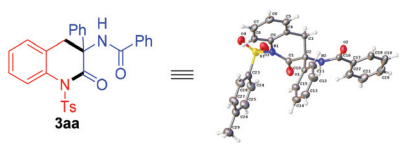
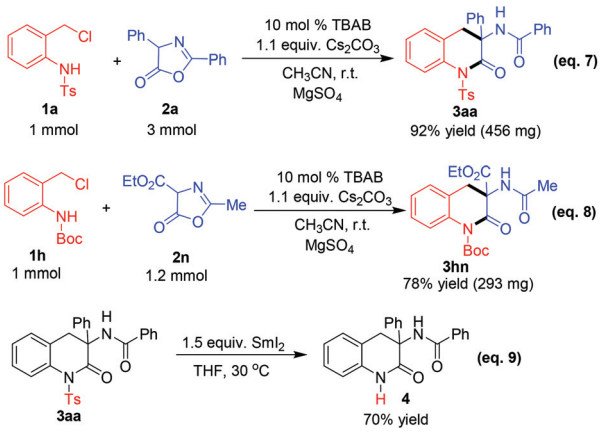
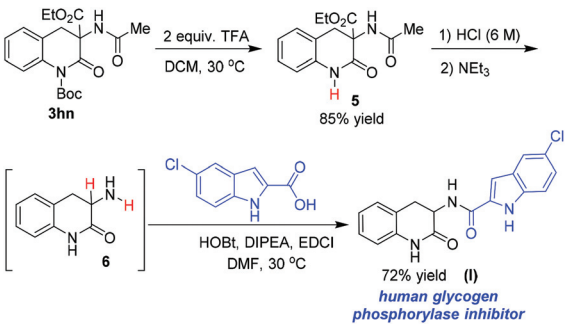


Fig. 1 X-ray single-crystal structure of **3aa**.



Scheme 4 One-mmol-scale reactions and deprotection of *N*-Ts.



Scheme 5 Synthesis of bioactive molecules.

Conclusions

In summary, we have established a base-promoted (4 + 2) cyclization of aza-*o*-QMs *in situ* generated from *N*-(*o*-chloromethyl) aryl amides, which utilized azlactones as competent two-atom reaction partners. By this approach, a series of dihydroquinolinone derivatives were synthesized in overall good yields. This reaction has not only enriched the research contents of aza-*o*-QM-involved reactions, but also provided a useful protocol for constructing biologically important dihydroquinolinone frameworks.

Experimental

General information

^{1}H and ^{13}C NMR spectra were measured at 400 and 100 MHz, respectively. The solvents used for NMR spectroscopy were $CDCl_3$ and DMSO-d_6, using tetramethylsilane as the internal

reference. HRMS (ESI) was determined using a HRMS/MS instrument. The X-ray source used for the single crystal X-ray diffraction analysis of compound **3aa** was MoKα (λ = 0.71073), and the thermal ellipsoid was drawn at the 30% probability level. Analytical grade solvents for column chromatography were distilled before use. All commercially available starting materials were used directly. Substrates **1** and **2** were synthesized according to the literature methods.[8,13]

Typical procedure for the synthesis of products 3

N-(*o*-Chloromethyl)aryl amides **1** (0.1 mmol), azlactones **2** (0.3 mmol), Cs_2CO_3 (0.11 mmol), TBAB (0.01 mmol) and $MgSO_4$ (100 mg) were added to a reaction tube. Then, CH_3CN (1 mL) was added to the reaction mixture, which was stirred at r.t. for 3 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was directly purified through preparative thin layer chromatography on silica gel to afford pure products **3**.

Characterization of products 3

***N*-(2-Oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3aa).** Yield: 92% (45.6 mg); white solid; m.p. 190–192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.0 Hz, 2H), 7.64 (d, J = 7.2 Hz, 2H), 7.57–7.52 (m, 2H), 7.48–7.43 (m, 1H), 7.40–7.34 (m, 4H), 7.33–7.30 (m, 1H), 7.27–7.23 (m, 2H), 7.20–7.15 (m, 2H), 7.14–7.07 (m, 3H), 4.50 (d, J = 15.6 Hz, 1H), 3.47 (d, J = 16.0 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 165.8, 145.5, 136.3, 135.0, 134.3, 134.2, 131.8, 129.7, 128.8, 128.7, 128.6, 128.4, 128.0, 127.6, 127.2, 127.1, 127.0, 123.4, 63.2, 33.8, 21.9; IR (KBr): 3406, 3027, 1698, 1508, 1476, 1375, 741, 698, 616 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{24}N_2O_4S + Na)^+$ requires m/z 519.1349, found m/z 519.1340.

***N*-(8-Methyl-2-oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3ba).** Yield: 86% (43.9 mg); white solid; m.p. 147–149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 7.6 Hz, 2H), 7.48–7.43 (m, 2H), 7.38–7.33 (m, 4H), 7.27–7.25 (m, 2H), 7.16–7.06 (m, 5H), 7.02–7.00 (d, 1H), 4.46 (d, J = 15.6 Hz, 1H), 3.10 (d, J = 15.6 Hz, 1H), 2.44 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 165.5, 145.7, 136.0, 135.7, 135.0, 134.4, 133.7, 131.7, 130.5, 130.4, 129.5, 128.5, 128.2, 128.1, 127.7, 127.0, 126.9, 126.2, 64.2, 33.9, 21.8, 20.0; IR (KBr): 3404, 1670, 1508, 1475, 1363, 764, 699, 668 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{26}N_2O_4S + Na)^+$ requires m/z 533.1505, found m/z 533.1508.

***N*-(7-Chloro-2-oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3ca).** Yield: 91% (48.2 mg); white solid; m.p. 141–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.0 Hz, 2H), 7.63–7.61 (m, 3H), 7.49–7.41 (m, 2H), 7.41–7.33 (m, 4H), 7.25–7.19 (m, 3H), 7.16–7.13 (m, 4H), 4.42 (d, J = 15.6 Hz, 1H), 3.52 (d, J = 15.6 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 165.9, 145.7, 135.9, 135.0, 134.8, 134.1, 132.8, 131.8, 129.7, 129.5, 128.8, 128.6, 128.5, 127.0, 126.9, 126.3, 123.4, 63.1, 33.4, 21.8; IR (KBr): 3588, 1730, 1508, 1476, 1173, 747, 668, 564 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{23}ClN_2O_4S + Na)^+$ requires m/z 553.0959, found m/z 553.0967.

***N*-(6-Methyl-2-oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3da).** Yield: 84% (42.8 mg); white solid; m.p. 222–224 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 7.6 Hz, 2H), 7.57 (s, 1H), 7.48–7.41 (m, 2H), 7.39–7.32 (m, 4H), 7.28–7.27 (m, 1H), 7.17–7.08 (m, 4H), 6.98 (d, J = 8.4 Hz, 1H), 4.44 (d, J = 15.6 Hz, 1H), 3.43 (d, J = 15.6 Hz, 1H), 2.47 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 165.7, 145.3, 137.0, 136.3, 135.2, 134.3, 131.7, 129.6, 129.1, 128.7, 128.5, 128.3, 128.0, 127.7, 127.1, 127.0, 123.2, 63.2, 33.7, 21.8, 21.0; IR (KBr): 3567, 1701, 1664, 1498, 1275, 764, 750, 668, 559 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{26}N_2O_4S + Na)^+$ requires m/z 533.1505, found m/z 533.1510.

***N*-(6-Chloro-2-oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3ea).** Yield: 98% (51.9 mg); white solid; m.p. 149–151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.8 Hz, 1H), 7.47–7.42 (m, 1H), 7.42–7.33 (m, 5H), 7.27–7.29 (m, 2H), 7.19–7.12 (m, 4H), 4.33 (d, J = 15.6 Hz, 1H), 3.59 (d, J = 15.6 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 166.0, 145.7, 135.9, 134.9, 134.1, 132.8, 132.2, 131.8, 129.8, 129.7, 128.9, 128.7, 128.6, 128.3, 127.5, 127.0, 126.9, 124.6, 63.3, 33.8, 21.8; IR (KBr): 3446, 1730, 1665, 1481, 1174, 749, 666, 566 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{23}ClN_2O_4S + Na)^+$ requires m/z 553.0959, found m/z 553.0973.

***N*-(5-Methyl-2-oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3fa).** Yield: 91% (46.4 mg); white solid; m.p. 207–209 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 7.56 (s, 1H), 7.50–7.42 (m, 1H), 7.40–7.33 (m, 5H), 7.23–7.17 (m, 2H), 7.15–7.09 (m, 3H), 7.09–6.99 (m, 2H), 4.64 (d, J = 15.6 Hz, 1H), 3.25 (d, J = 16.0 Hz, 1H), 2.48 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 165.8, 145.4, 136.3, 135.6, 135.5, 134.3, 134.1, 131.8, 129.6, 128.8, 128.7, 128.5, 128.4, 128.3, 127.0, 126.9, 126.7, 121.4, 63.5, 29.9, 21.8, 19.8; IR (KBr): 3650, 1701, 1670, 1473, 1265, 748, 668, 570 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{26}N_2O_4S + Na)^+$ requires m/z 533.1505, found m/z 533.1498.

***N*-(5-Chloro-2-oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3ga).** Yield: 88% (46.6 mg); white solid; m.p. 123–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.48–7.42 (m, 2H), 7.41–7.33 (m, 4H), 7.32–7.27 (m, 3H), 7.23 (d, J = 8.0 Hz, 1H), 7.20–7.14 (m, 3H), 7.13–7.08 (m, 1H), 4.82 (d, J = 16.4 Hz, 1H), 3.45 (d, J = 16.0 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 165.9, 145.7, 135.9, 135.3, 134.7, 134.1, 133.0, 131.8, 129.7, 128.9, 128.8, 128.7, 128.6, 127.7, 127.0, 126.9, 126.8, 122.1, 63.5, 30.5, 21.9; IR (KBr): 3588, 1734, 1655, 1475, 1274, 764, 668, 568 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{23}ClN_2O_4S + Na)^+$ requires m/z 553.0959, found m/z 553.0967.

***N*-(3-(2-Chlorophenyl)-2-oxo-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3ab).** Yield: 79% (41.9 mg); white solid; m.p. 228–230 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.4

Hz, 2H), 7.71–7.59 (m, 4H), 7.49–7.42 (m, 1H), 7.39–7.31 (m, 4H), 7.25–7.12 (m, 5H), 7.08–7.02 (m, 1H), 6.97–6.91 (m, 1H), 4.46 (d, J = 15.6 Hz, 1H), 3.53 (d, J = 16.0 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 166.0, 145.3, 135.8, 134.7, 134.3, 132.8, 132.1, 131.8, 131.5, 131.2, 129.7, 129.5, 128.9, 128.6, 128.4, 128.2, 127.6, 127.1, 127.0, 126.0, 123.6, 63.9, 34.2, 21.8; IR (KBr): 3537, 1731, 1655, 1476, 1173, 751, 656, 562 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{23}ClN_2O_4S + H)^+$ requires m/z 531.1140, found m/z 531.1143.

***N*-(3-(4-Chlorophenyl)-2-oxo-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3ac).** Yield: 87% (46.1 mg); white solid; m.p. 156–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.4 Hz, 2H), 7.69–7.62 (m, 3H), 7.61–7.54 (m, 1H), 7.50–7.43 (m, 1H), 7.42–7.31 (m, 5H), 7.25–7.14 (m, 4H), 7.07 (d, J = 8.8 Hz, 2H), 4.56 (d, J = 15.6 Hz, 1H), 3.35 (d, J = 15.6 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 165.7, 136.0, 134.3, 134.0, 133.4, 131.9, 129.7, 128.7, 128.6, 128.5, 127.6, 127.3, 127.0, 123.5, 62.4, 33.5, 21.9; IR (KBr): 3447, 1727, 1663, 1478, 1173, 750, 652, 556 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{23}ClN_2O_4S + H)^+$ requires m/z 531.1140, found m/z 531.1154.

2-Fluoro-*N*-(2-oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3ad). Yield: 78% (40.1 mg); white solid; m.p. 154–156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 13.2 Hz, 1H), 7.94 (d, J = 8.4 Hz, 2H), 7.88–7.79 (m, 1H), 7.58–7.53 (m, 1H), 7.44–7.39 (m, 1H), 7.36 (d, J = 8.4 Hz, 2H), 7.31–7.27 (m, 2H), 7.22–7.15 (m, 3H), 7.15–7.11 (m, 3H), 7.08–7.01 (m, 1H), 4.34 (d, J = 15.6 Hz, 1H), 3.60 (d, J = 15.6 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 161.8, 160.6 (J = 247.0 Hz), 145.4, 135.1, 134.2, 133.6 (J = 9.2 Hz), 131.7, 131.6, 129.7, 129.6, 128.9, 128.6, 128.4, 127.8, 127.4, 127.2, 127.0, 124.6 (J = 3.2 Hz), 123.4, 121.1 (J = 11.4 Hz), 116.1 (J = 24.7 Hz), 63.7, 34.0, 21.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.3; IR (KBr): 3403, 1705, 1670, 1478, 1173, 751, 698, 563 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{23}FN_2O_4S + H)^+$ requires m/z 515.1436, found m/z 515.1441.

3-Chloro-*N*-(2-oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3ae). Yield: 75% (39.8 mg); white solid; m.p. 165–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 2H), 7.62–7.58 (m, 1H), 7.58–7.53 (m, 1H), 7.50–7.48 (m, 2H), 7.44–7.36 (m, 3H), 7.33–7.27 (m, 2H), 7.25–7.22 (m, 2H), 7.21–7.15 (m, 2H), 7.14–7.08 (m, 3H), 4.41 (d, J = 15.6 Hz, 1H), 3.53 (d, J = 15.6 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 164.5, 145.5, 136.1, 136.0, 134.8, 134.7, 134.1, 131.8, 129.8, 129.6, 128.8, 128.7, 128.5, 128.4, 127.7, 127.4, 127.1, 127.0, 125.0, 123.3, 63.4, 33.7, 21.9; IR (KBr): 3397, 1725, 1664, 1490, 1173, 749, 562 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{23}ClN_2O_4S + Na)^+$ requires m/z 553.0959, found m/z 553.0957.

4-Chloro-*N*-(2-oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3af). Yield: 77% (40.8 mg); white solid; m.p. 174–176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.4 Hz, 2H), 7.70–7.62 (m, 3H), 7.59–7.55 (m, 1H), 7.50–7.44 (m, 1H), 7.40–7.32 (m, 5H), 7.24–7.17 (m, 4H), 7.07 (d, J = 8.8 Hz, 2H), 4.56 (d, J = 15.6 Hz, 1H), 3.35 (d, J = 15.6 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 164.8, 145.5, 138.0, 136.2, 134.9, 134.1, 132.6, 129.6, 128.8, 128.7, 128.5, 128.4, 127.8, 127.4, 127.1, 127.0, 123.3, 63.3, 33.7, 21.8; IR (KBr): 3502, 1731, 1655, 1474, 1362, 1173, 750, 562 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{23}ClN_2O_4S + H)^+$ requires m/z 531.1140, found m/z 531.1148.

4-Methoxy-*N*-(2-oxo-3-phenyl-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3ag). Yield: 81% (42.6 mg); white solid; m.p. 118–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 7.57–7.52 (m, 1H), 7.46 (s, 1H), 7.37 (d, J = 8.0 Hz, 2H), 7.33–7.28 (m, 1H), 7.25–7.23 (m, 1H), 7.20–7.15 (m, 2H), 7.13–7.07 (m, 3H), 6.85 (d, J = 8.8 Hz, 2H), 4.48 (d, J = 16.0 Hz, 1H), 3.80 (s, 3H), 3.49 (d, J = 15.6 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 165.3, 162.4, 145.4, 136.2, 135.2, 134.2, 129.6, 128.8, 128.7, 128.3, 128.0, 127.3, 127.2, 127.0, 126.5, 123.3, 113.7, 63.1, 55.5, 33.9, 21.8; IR (KBr): 3565, 1729, 1660, 1474, 1174, 750, 560 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{26}N_2O_5S + H)^+$ requires m/z 527.1635, found m/z 527.1633.

Ethyl 3-benzamido-2-oxo-1-tosyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (3ah). Yield: 85% (41.8 mg); white solid; m.p. 158–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.4 Hz, 2H), 7.71–7.69 (m, 3H), 7.54–7.48 (m, 1H), 7.44–7.32 (m, 5H), 7.28–7.20 (m, 3H), 4.01–3.85 (m, 2H), 3.60 (q, J = 15.2 Hz, 2H), 2.46 (s, 3H), 0.83 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 166.5, 166.4, 145.4, 136.0, 134.8, 133.2, 132.1, 129.6, 128.9, 128.8, 128.6, 127.7, 127.2, 126.8, 126.3, 122.9, 65.2, 62.7, 34.3, 21.8, 13.4; IR (KBr): 3447, 1734, 1654, 1489, 1260, 749, 575 cm^{-1}; ESI FTMS exact mass calcd for $(C_{26}H_{24}N_2O_6S + H)^+$ requires m/z 493.1428, found m/z 493.1432.

Ethyl 3-(2-fluorobenzamido)-2-oxo-1-tosyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (3ai). Yield: 60% (30.6 mg); white solid; m.p. 153–155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.0 Hz, 2H), 7.93–7.86 (m, 1H), 7.80–7.67 (m, 2H), 7.52–7.43 (m, 1H), 7.36–7.34 (m, 3H), 7.25–7.17 (m, 3H), 7.15–7.06 (m, 1H), 4.04–3.85 (m, 2H), 3.68 (d, J = 15.2 Hz, 1H), 3.46 (d, J = 15.2 Hz, 1H), 2.45 (s, 3H), 0.82 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 166.2, 162.4, 160.8 (J = 248.7 Hz), 145.2, 136.0, 135.1, 134.0 (J = 9.3 Hz), 132.0, 129.5, 129.0, 128.6, 127.8, 126.6, 125.9, 124.8, 124.7, 122.9, 120.0 (J = 11.3 Hz), 116.1 (J = 24.7 Hz), 65.5, 62.7, 34.7, 21.8, 13.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.1; IR (KBr): 3567, 1734, 1613, 1480, 1363, 1175, 751, 576 cm^{-1}; ESI FTMS exact mass calcd for $(C_{26}H_{23}FN_2O_6S + H)^+$ requires m/z 511.1334, found m/z 511.1352.

Ethyl 3-(2-methylbenzamido)-2-oxo-1-tosyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (3aj). Yield: 62% (31.4 mg); white solid; m.p. 156–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.4 Hz, 1H), 7.40–7.34 (m, 2H), 7.33–7.27 (m, 3H), 7.26–7.20 (m, 2H), 7.20–7.12 (m, 2H), 6.78 (s, 1H), 4.02–3.84 (m, 2H), 3.70 (d, J = 14.8 Hz, 1H), 3.49 (d, J = 14.8 Hz, 1H), 2.43 (s, 3H), 2.25 (s, 3H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz,) δ 169.3, 166.7, 166.3, 145.5, 145.4, 136.8, 136.0, 135.0, 134.9, 131.1, 130.5, 129.6, 129.2, 128.8, 127.8, 127.0, 126.8, 126.2, 125.8, 123.1, 65.4, 62.6, 34.5, 21.8, 19.7, 13.5; IR (KBr): 3367, 1732, 1664, 1488, 1363, 1189, 743,

576 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{26}N_2O_6S + Na)^+$ requires *m*/*z* 529.1404, found *m*/*z* 529.1396.

Ethyl 3-(3-chlorobenzamido)-2-oxo-1-tosyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (3ak). Yield: 81% (42.6 mg); white solid; m.p. 198–200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.63–7.61 (m, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.37–7.32 (m, 3H), 7.30–7.28 (m, 1H), 7.25–7.18 (m, 2H), 4.00–3.81 (m, 2H), 3.62 (d, *J* = 15.2 Hz, 1H), 3.48 (d, *J* = 14.8 Hz, 1H), 2.44 (s, 3H), 0.81 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 166.5, 165.4, 145.5, 136.0, 135.0, 134.9, 134.8, 132.2, 130.0, 129.7, 129.0, 128.8, 127.9, 127.7, 126.8, 126.0, 125.9, 125.3, 122.9, 65.4, 62.8, 34.5, 21.8, 13.5; IR (KBr): 3567, 1731, 1655, 1527, 1489, 1363, 1175, 749, 575 cm^{-1}; ESI FTMS exact mass calcd for $(C_{26}H_{23}ClN_2O_6S + Na)^+$ requires *m*/*z* 549.0857, found *m*/*z* 549.0861.

Ethyl 2-oxo-1-tosyl-3-(4-(trifluoromethyl)benzamido)-1,2,3,4-tetrahydroquinoline-3-carboxylate (3al). Yield: 81% (45.4 mg); white solid; m.p. 182–184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.76–7.63 (m, 3H), 7.41–7.33 (m, 3H), 7.31–7.27 (m, 1H), 7.24–7.20 (m, 1H), 4.00–3.86 (m, 2H), 3.60 (s, 2H), 2.46 (s, 3H), 0.83 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 165.2, 145.4, 135.3 (*J* = 116.5 Hz), 129.6, 128.3 (*J* = 97.2 Hz), 126.8, 126.0, 125.7 (*J* = 3.8 Hz), 122.9, 65.3, 62.9, 34.3, 21.8, 13.4; IR (KBr): 3566, 1724, 1656, 1534, 1489, 1326, 1173, 749, 654 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{23}F_3N_2O_6S + Na)^+$ requires *m*/*z* 583.1121, found *m*/*z* 583.1119.

Ethyl 3-(4-methylbenzamido)-2-oxo-1-tosyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (3am). Yield: 75% (38.0 mg); white solid; m.p. 210–212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.39–7.31 (m, 3H), 7.26–7.15 (m, 5H), 3.99–3.80 (m, 2H), 3.58 (q, *J* = 15.2 Hz, 2H), 2.45 (s, 3H), 2.38 (s, 3H), 0.82 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 166.6, 166.5, 145.4, 142.7, 136.0, 134.8, 130.4, 129.6, 129.3, 129.0, 128.9, 127.7, 127.3, 126.8, 126.4, 123.0, 65.2, 62.7, 34.4, 21.8, 21.6, 13.5; IR (KBr): 3566, 1724, 1656, 1534, 1489, 1326, 1173, 749, 654 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{26}N_2O_6S + Na)^+$ requires *m*/*z* 529.1404, found *m*/*z* 529.1391.

Ethyl 3-acetamido-2-oxo-1-tosyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (3an). Yield: 78% (33.5 mg); white solid; m.p. 126–128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 12.0 Hz, 1H), 7.37–7.30 (m, 3H), 7.22–7.16 (m, 2H), 6.63 (s, 1H), 3.91–3.80 (m, 2H), 3.49–3.33 (m, 2H), 2.43 (s, 3H), 1.94 (s, 3H), 0.79 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 166.7, 145.3, 136.2, 135.0, 129.7, 128.7, 128.6, 127.8, 126.7, 125.9, 122.7, 65.1, 62.5, 34.6, 23.1, 21.8, 13.4; IR (KBr): 3367, 1731, 1665, 1535, 1148, 754, 574 cm^{-1}; ESI FTMS exact mass calcd for $(C_{21}H_{22}N_2O_6S–H)^-$ requires *m*/*z* 429.1126, found *m*/*z* 429.1128.

1-(*tert*-Butyl) 3-ethyl 3-acetamido-2-oxo-3,4-dihydroquinoline-1,3(2*H*)-dicarboxylate (3hn). Yield: 82% (30.8 mg); white solid; m.p. 55–57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.18 (m, 2H), 7.14–7.08 (m, 1H), 7.03 (s, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 2H), 3.99 (d, *J* = 16.0 Hz, 1H), 3.30 (d, *J* = 16.0 Hz, 1H), 2.07 (s, 3H), 1.61 (s, 9H), 1.00 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 166.3, 163.9, 150.8, 135.0, 128.8, 127.5, 125.1, 123.6, 116.3, 86.1, 62.4, 62.1, 34.3, 27.6, 23.4, 13.7; IR (KBr): 3177, 1747, 1668, 1504, 1146, 753, 454 cm^{-1}; ESI FTMS exact mass calcd for $(C_{19}H_{24}N_2O_6 + Na)^+$ requires *m*/*z* 399.1526, found *m*/*z* 399.1530.

***N*-(3-Benzyl-2-oxo-1-tosyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (3ao).** Yield: 40% (20.4 mg); white solid; m.p. 164–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97–7.89 (m, 3H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.51–7.44 (m, 2H), 7.42–7.32 (m, 6H), 7.15–7.09 (m, 1H), 7.07–6.98 (m, 3H), 6.74 (d, *J* = 8.0 Hz, 2H), 4.14 (d, *J* = 16.0 Hz, 1H), 3.43 (d, *J* = 16.0 Hz, 1H), 3.15 (d, *J* = 12.0 Hz, 1H), 2.49 (d, *J* = 16.0 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 166.8, 145.4, 136.2, 134.9, 134.7, 134.5, 131.7, 129.8, 129.6, 129.3, 128.8, 128.6, 128.2, 127.9, 127.6, 127.3, 127.1, 126.9, 123.2, 62.0, 36.1, 35.4, 21.8; IR (KBr): 3403, 1707, 1663, 1507, 1147, 743, 572 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{26}N_2O_4S + Na)^+$ requires *m*/*z* 533.1505 found *m*/*z* 533.1497.

***tert*-Butyl 3-benzamido-3-benzyl-2-oxo-3,4-dihydroquinoline-1(2*H*)-carboxylate (3ho).** Yield: 75% (34.2 mg); white solid; m.p. 123–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.66 (m, 2H), 7.53–7.46 (m, 1H), 7.44–7.38 (m, 3H), 7.37–7.30 (m, 2H), 7.21–7.13 (m, 4H), 7.11–7.05 (m, 2H), 6.98 (d, *J* = 8.0 Hz, 1H), 4.40 (d, *J* = 16.0 Hz, 1H), 3.70 (d, *J* = 16.0 Hz, 1H), 3.32 (d, *J* = 16.0 Hz, 1H), 2.90 (d, *J* = 16.0 Hz, 1H), 1.68 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 167.1, 151.6, 135.4, 135.3, 134.9, 131.6, 130.2, 129.6, 128.6, 128.0, 127.0, 126.9, 125.1, 123.6, 116.1, 86.0, 60.2, 37.1, 36.4, 27.7; IR (KBr): 3399, 1761, 1696, 1663, 1510, 1176, 756, 700, 453 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{28}N_2O_4 + Na)^+$ requires *m*/*z* 479.1941, found *m*/*z* 479.1938.

***tert*-Butyl 3-benzamido-3-methyl-2-oxo-3,4-dihydroquinoline-1(2*H*)-carboxylate (3hp).** Yield: 82% (31.2 mg); white solid; m.p. 142–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89–7.82 (m, 2H), 7.79 (s, 1H), 7.55–7.48 (m, 1H), 7.47–7.41 (m, 2H), 7.32–7.25 (m, 2H), 7.16–7.11 (m, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 4.17 (d, *J* = 16.0 Hz, 1H), 3.21 (d, *J* = 16.0 Hz, 1H), 1.64 (s, 9H), 1.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 166.4, 151.2, 135.4, 134.7, 131.7, 129.5, 128.6, 127.6, 127.0, 125.0, 123.9, 116.2, 86.0, 55.9, 36.2, 27.7, 19.8; IR (KBr): 3334, 1763, 1663, 1499, 1147, 750, 453 cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{24}N_2O_4 + Na)^+$ requires *m*/*z* 403.1628, found *m*/*z* 403.1621.

***tert*-Butyl 3-benzamido-3-isopropyl-2-oxo-3,4-dihydroquinoline-1(2*H*)-carboxylate (3hq).** Yield: 58% (23.7 mg); white solid; m.p. 39–41 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88–7.84 (m, 2H), 7.63 (s, 1H), 7.55–7.49 (m, 1H), 7.48–7.42 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.28–7.24 (m, 1H), 7.15–7.09 (m, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 4.54 (d, *J* = 16.0 Hz, 1H), 3.36 (d, *J* = 16.0 Hz, 1H), 2.10–1.99 (m, 1H), 1.63 (s, 9H), 1.06 (d, *J* = 8.0 Hz, 3H), 0.91 (d, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 166.8, 151.3, 135.6, 135.2, 131.6, 129.3, 128.6, 127.7, 127.0, 124.9, 123.5, 115.7, 85.9, 62.0, 33.5, 31.9, 27.6, 17.6, 17.4; IR (KBr): 3393, 1763, 1669, 1515, 1370, 1244, 1147, 752, 629 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{28}N_2O_4 + Na)^+$ requires *m*/*z* 431.1941, found *m*/*z* 431.1925.

***tert*-Butyl 3-allyl-3-benzamido-2-oxo-3,4-dihydroquinoline-1(2*H*)-carboxylate (3hr).** Yield: 73% (29.6 mg); white solid; m.p. 96–98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86–7.81 (m, 2H), 7.64 (s, 1H), 7.54–7.49 (m, 1H), 7.47–7.42 (m, 2H), 7.30–7.25 (m, 2H), 7.16–7.10 (m, 1H), 6.90 (d, J = 8.0 Hz, 1H), 5.75–5.59 (m, 1H), 5.09–5.00 (m, 2H), 4.20 (d, J = 16.0 Hz, 1H), 3.29 (d, J = 16.0 Hz, 1H), 3.20–3.10 (m, 1H), 2.36–2.27 (m, 1H), 1.64 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 166.6, 151.3, 135.3, 134.7, 131.7, 131.5, 129.5, 128.6, 127.9, 126.9, 124.9, 123.4, 119.9, 115.9, 85.9, 59.1, 36.0, 35.8, 27.6; IR (KBr): 3399, 1763, 1664, 1511, 1368, 1244, 1147, 754, 574 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{26}N_2O_4 + Na)^+$ requires m/z 429.1785, found m/z 429.1779.

Procedure for one-mmol-scale reactions

N-(*o*-Chloromethyl)aryl amide **1a** (295.0 mg, 1 mmol), azlactone **2a** (711.0 mg, 3.0 mmol), Cs_2CO_3 (358.4 mg, 1.1 mol), TBAB (32.2 mg, 0.1 mmol) and $MgSO_4$ (1.0 g) were added into a reaction bottle. Then, CH_3CN (10 mL) was added to the reaction mixture, which was stirred at r.t. for 3 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (PE : DCM = 1 : 1) to afford the pure product **3aa** (456.0 mg, 92% yield).

N-(*o*-Chloromethyl)aryl amide **1h** (241.0 mg, 1 mmol), azlactone **2n** (205.2 mg, 1.2 mmol), Cs_2CO_3 (358.4 mg, 1.1 mol), TBAB (32.2 mg, 0.1 mmol) and $MgSO_4$ (1.0 g) were added into a reaction bottle. Then, CH_3CN (10 mL) was added to the reaction mixture, which was stirred at r.t. for 3 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (PE : EA = 2 : 1) to afford the pure product **3hn** (293.3 mg, 78% yield).

Procedure for the synthesis of product 4 and characterization data

Under an argon atmosphere, **3aa** (0.1 mmol) and the solution of SmI_2 (1.5 mL) in anhydrous THF (1 mol L^{-1}) were added into a flame-dried Schlenk tube. The reaction mixture was stirred at 30 °C for 3 h. After the completion of the reaction which was indicated by TLC, the mixture was directly purified through preparative thin layer chromatography on silica gel (PE : EA = 2 : 1) to afford the pure product **4**.

***N*-(2-Oxo-3-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)benzamide (4).** Yield: 70% (23.9 mg); white solid; m.p. 251–253 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.19 (s, 1H), 7.87–7.79 (m, 2H), 7.56–7.48 (m, 3H), 7.46–7.40 (m, 2H), 7.36 (d, J = 8.0 Hz, 1H), 7.22–7.15 (m, 3H), 7.14–7.09 (m, 1H), 7.08–7.02 (m, 1H), 6.67 (d, J = 8.0 Hz, 1H), 4.77 (d, J = 16.0 Hz, 1H), 3.60 (d, J = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 166.1, 137.3, 135.3, 134.6, 131.8, 128.7, 128.5, 128.4, 128.3, 127.8, 127.2, 127.1, 124.3, 123.4, 115.5, 59.9, 34.8; IR (KBr): 3234, 1686, 1658, 1596, 1479, 1372, 1296, 695, 564 cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{18}N_2O_2 + Na)^+$ requires m/z 365.1260, found m/z 365.1249.

Procedure for the synthesis of bioactive compound I and characterization data of compounds 5 and I

The solution of **3hn** (0.1 mmol) in anhydrous DCM (1 mL) was added into a flame-dried Schlenk tube under an argon atmosphere. Then, TFA (0.2 mmol) was added to the reaction mixture, which was stirred at 30 °C for 3 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was directly purified through preparative thin layer chromatography on silica gel (PE : EA = 2 : 1) to afford the pure product **5**.

Compound **5** (0.1 mmol) and HCl (1 mL, 6 M) were added into a sealed tube and heated to reflux for 6 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was quenched with NEt_3 and extracted with ethyl acetate three times. The combined organic layers were dried and concentrated under reduced pressure to give a crude product.

The crude product was dissolved in DMF (1 mL) containing 5-chloroindole-2-carboxylic acid (0.12 mmol), EDCI (0.12 mmol), HOBt (0.12 mmol). The reaction mixture was stirred at 30 °C for 5 h before being partitioned between water and EA. The organic layers were washed with water, saturated aqueous $NaHCO_3$ and dried over Na_2SO_4. The solution was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (EA) to afford the pure product **I**.

Ethyl 3-acetamido-2-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (5). Yield: 85% (23.5 mg); white solid; m.p. 141–143 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.54 (s, 1H), 8.34 (s, 1H), 7.18–7.10 (m, 2H), 6.96–6.81 (m, 2H), 4.02–3.88 (m, 2H), 3.44–3.35 (m, 2H), 1.86 (s, 3H), 0.94 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.1, 168.3, 165.5, 137.5, 128.4, 127.9, 122.9, 121.8, 115.3, 62.0, 61.4, 34.8, 22.9, 14.1; IR (KBr): 3431, 1737, 1698, 1597, 1545, 1434, 1281, 1027, 822, 761 cm^{-1}; ESI FTMS exact mass calcd for $(C_{14}H_{16}N_2O_4 + Na)^+$ requires m/z 299.1002, found m/z 299.1003.

5-Chloro-*N*-(2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide (I). Yield: 72% (24.4 mg); yellow solid; m.p. 168–170 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (s, 1H), 10.42 (s, 1H), 8.94–8.78 (m, 1H), 7.74 (s, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.25–7.16 (m, 4H), 6.98–6.88 (m, 2H), 4.83–4.71 (m, 1H), 3.23–3.02 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.2, 161.3, 138.1, 135.5, 133.4, 128.7, 128.1, 124.8, 124.1, 122.9, 122.8, 121.3, 115.7, 114.5, 103.1, 48.5, 31.9; IR (KBr): 3219, 1690, 1653, 1558, 1321, 1259, 1026, 758 cm^{-1}; ESI FTMS exact mass calcd for $(C_{18}H_{14}ClN_3O_2–H)^-$ requires m/z 338.0702, found m/z 338.0701.

Conflicts of interest

There are no conflicts to declare.

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