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A copper-mediated cross-coupling approach for the synthesis of 3-heteroaryl quinolone and related analogues†

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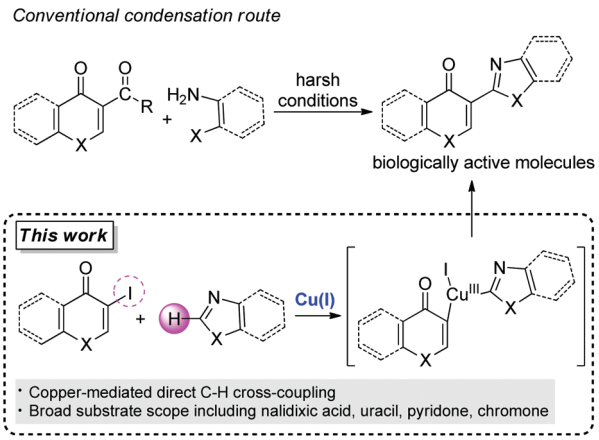
An efficient and practical method for the direct cross-coupling between quinolones and a range of azoles was developed *via* copper-mediated C–H functionalization. This synthetic strategy provides a convenient access to a variety of C3-heteroaryl quinolones, quinolinone, nalidixic acid, uracil, pyridone and chromone derivatives, which are prominent structural motifs in many biologically active compounds.

Introduction

The family of quinolones constitutes an important class of naturally occurring compounds and privileged medicinal scaffolds.[1] The characteristics of the substituents on a quinolone core profoundly affect the biological activity. Among them, 3-heteroaryl substituted quinolones have been extensively investigated because of their promising biological properties including antitumor, antiviral, and antibacterial activities.[2] Although significant synthetic contributions were made to introduce a range of heteroaryl groups into the quinolone core, the existing condensation route is often limited by a modest substrate scope, harsh conditions, multiple steps, or low chemical yield.[2] In this regard, the development of a more straightforward synthetic route to various heteroaryl-substituted quinolones would be highly desirable for the construction of scaffold focused chemical libraries.

In recent years, substantial advances have been made toward direct arylation and alkenylation of various azoles through direct transition metal-catalyzed functionalization of C–H bonds in heterocycles.[3] Despite advances in this type of cross-coupling, the applicable substrate scope of azole coupling partners remains limited to simple arenes.[4,5] Inspired by the recent progress in copper-based cross-coupling reactions,[5] we investigated the feasibility of the expeditious synthetic approach for the installation of azoles at the C3 position of quinolone scaffolds as depicted in Scheme 1. It is worth noting that transition metal-catalyzed cross-coupling reactions of azoles with enaminone or enolone systems are unprecedented. During these studies, we established a copper-mediated protocol which would present opportunities for the efficient construction of heteroaryl-substituted quinolones and related scaffolds, and herein we report the details of this study.



Scheme 1 Synthetic strategy for construction of 3-heteroaryl quinolone motif *via* copper-mediated C–H cross-coupling.

Results and discussion

For the initial screening, *N*-benzyl-quinolone **1a** and benzothiazole (**2a**) were used as model substrates; representative screening data for the cross-coupling reaction are listed in Table 1. We were pleased to observe that the corresponding product **3a** was obtained in a catalytic system comprising both $Pd(PPh_3)_4$ and CuI (Table 1, entry 1). This approach allows for the direct installation of benzothiazole at the C-3 position of the quinolone core. Further investigations of the reaction conditions revealed that the coupling reaction proceeded in

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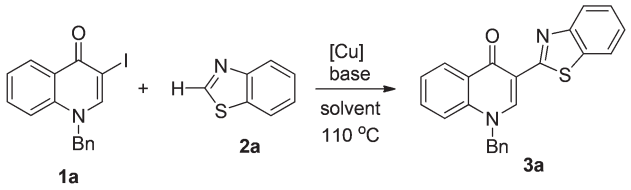
Table 1 Optimization of the coupling reaction of quinolone **1a** with benzothiazole (**2a**)[a]



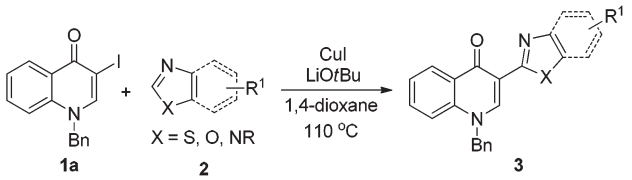
Entry	M (equiv.)	Base (equiv.)	Solvent	Yield[b] (%)
1	$Pd(PPh_3)_4$(0.025)/ CuI (2.0)	Cs_2CO_3 (2.0)	1,4-Dioxane	51%
2	CuI (2.0)	Cs_2CO_3 (2.0)	1,4-Dioxane	31%
3	CuI (2.0)	K_3PO_4 (2.0)	1,4-Dioxane	31%
4	CuI (2.0)	KO^{t}Bu (2.0)	1,4-Dioxane	Trace
5	CuI (2.0)	LiO^{t}Bu (2.0)	DCE	15%
6	CuI (2.0)	LiO^{t}Bu (2.0)	DME	44%
7	CuI (2.0)	LiO^{t}Bu (2.0)	1,4-Dioxane	65%
8	CuCl (2.0)	LiO^{t}Bu (2.0)	1,4-Dioxane	21%
9	CuBr (2.0)	LiO^{t}Bu (2.0)	1,4-Dioxane	15%
10	CuI (3.0)	LiO^{t}Bu (1.5)	1,4-Dioxane	75%
11	**CuI (3.0)**	**LiO^{t}Bu (1.2)**	**1,4-Dioxane**	**80%**
12	CuI (0.1)	LiO^{t}Bu (1.5)	1,4-Dioxane	41%
13	CuI (1.0)	LiO^{t}Bu (1.5)	1,4-Dioxane	60%

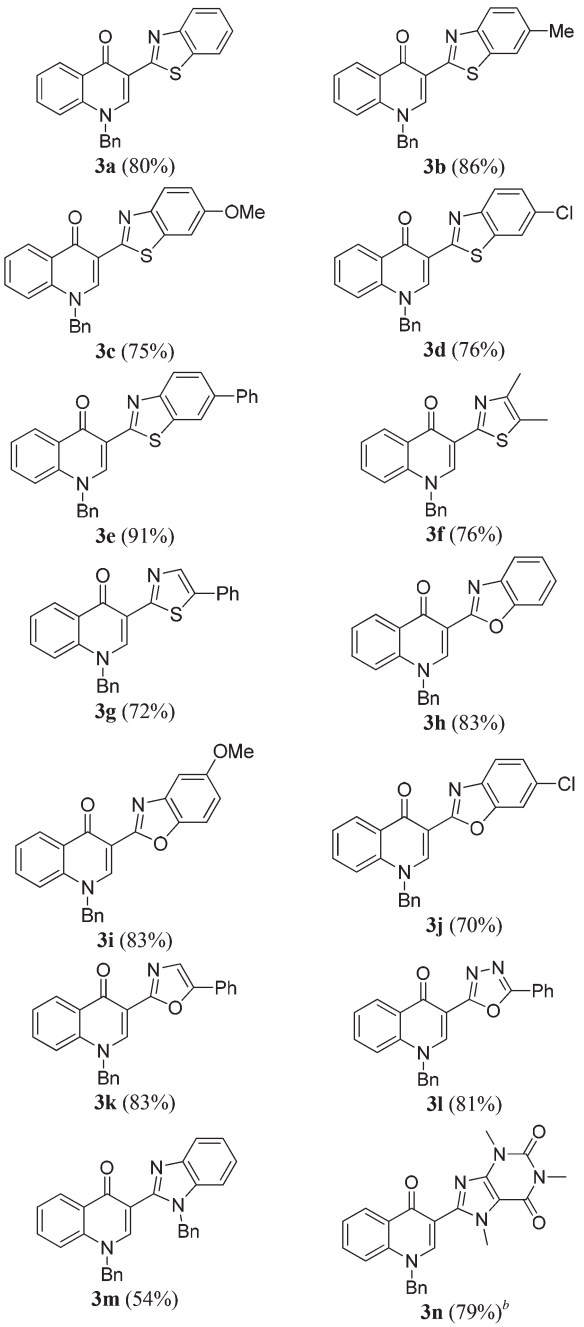
[a] Reactions were conducted with quinolone (0.1 mmol), benzothiazole (0.15 mmol), CuX, and base in solvent (1 mL) at 110 °C for 20 h under N_2. [b] Isolated yield. DCE = 1,2-dichloroethane, DME = 1,2-dimethoxyethane.

the absence of a Pd catalyst, and the reaction conditions consisting of CuI and Cs_2CO_3 in 1,4-dioxane at 110 °C allowed the isolation of the 3-heteroaryl quinolone product **3a**, albeit only in 31% yield (entry 2). A systematic investigation of more reactive reaction conditions was conducted by testing various copper sources, bases, ligands, solvents, and temperatures. LiO^{t}Bu proved to be the most efficient base while the more strongly basic KO^{t}Bu gave no positive effect (entries 3–4 and 7). Among the Cu species screened, CuI was the most effective for promoting the reactions (entries 7–9). The choice of solvent was critical for the reaction efficiency, and the yield increased further to 65% in 1,4-dioxane (entries 5–7). Interestingly, variations in the amount of base present influenced the reaction outcomes, and a lower yield of the isolated product **3a** was observed with an excess of base, presumably as a result of decomposition of the starting substrate (entries 7 and 10). After screening a variety of bases, we found that the use of 1.2 equiv. LiO^{t}Bu gave the best product yields with minimal by-product formation (entry 11). The loading of lower amounts of CuI (entries 12 and 13) resulted in lower conversion rates. Under the optimized reaction conditions, the cross-coupling of **1a** (1 equiv.) and **2a** (1.5 equiv.) in the presence of CuI (3 equiv.) and LiO^{t}Bu (1.2 equiv.) in 1,4-dioxane at 110 °C afforded the product **3a** in the highest yield (80%).

To diversify the 3-heteroaryl quinolone derivatives, the coupling reaction studies were extended to include a range of azole substrates. The protocol was found to be applicable to the reactions of the synthetically useful azole-based substrates, and Table 2 outlines the substrate scope of the cross-coupling

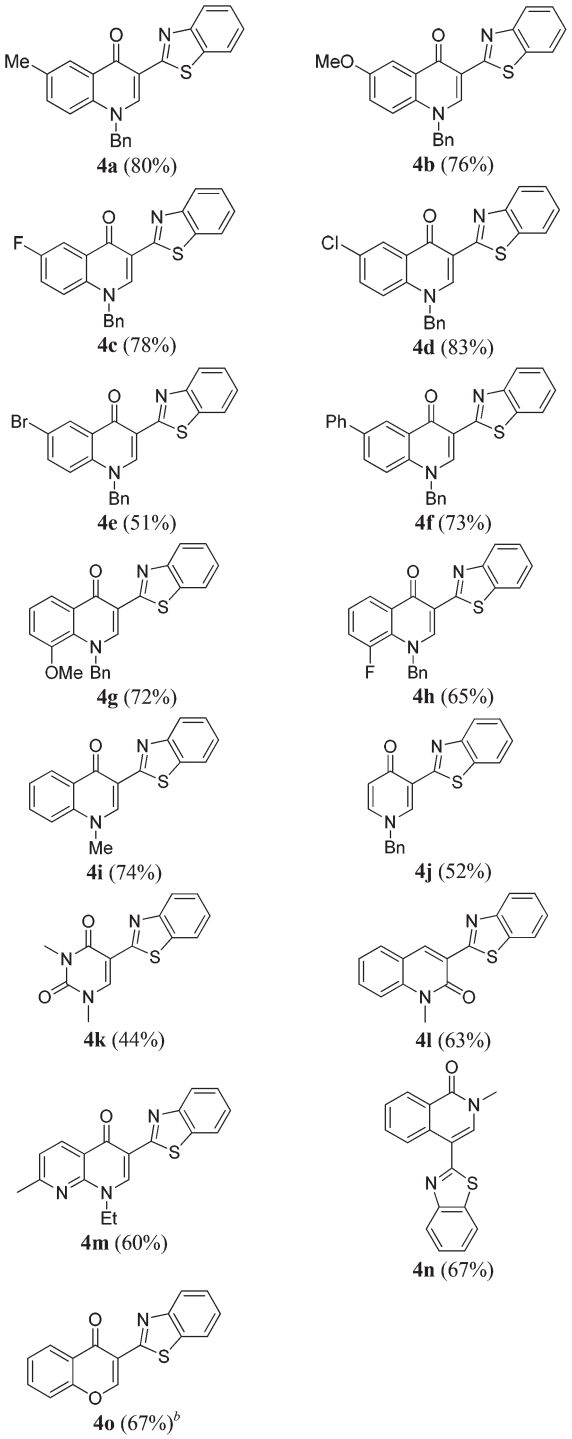
Table 2 Copper-mediated direct cross-coupling of quinolone with various azoles[a]



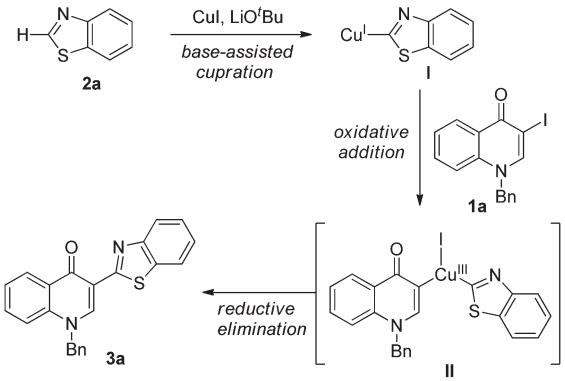


[a] Reactions were conducted with quinolone (0.1 mmol), azole (0.15–0.2 mmol), CuI (0.3 mmol), and LiO^{t}Bu (0.12–0.2 mmol) in 1,4-dioxane (1 mL) at 110 °C for 20 h under N_2. [b] Quinolone (0.1 mmol), caffeine (0.2 mmol), CuI (0.3 mmol), and LiO^{t}Bu (0.2 mmol) in DMF (1 mL) at 140 °C for 20 h under N_2. Isolated yield.

Table 3 Copper-mediated direct cross-coupling of various quinolones or related scaffolds with benzothiazole[a]



[a] Reactions were conducted with substrate (0.1 mmol), benzothiazole (0.15 mmol), CuI (0.3 mmol), and LiO^{t}Bu (0.12–0.15 mmol) in 1,4-dioxane (1 mL) at 110 °C for 20 h under N_2. [b] Substrate (0.1 mmol), benzothiazole (0.3 mmol), CuI (0.5 mmol), and LiO^{t}Bu (0.3 mmol) in 1,4-dioxane (1 mL) at 100 °C for 20 h under N_2. Isolated yield.



Scheme 2 Plausible reaction pathway.

reaction under the optimized reaction conditions. A broad range of azoles, including variously substituted benzothiazoles (**3a–3e**), thiazoles (**3f** and **3g**), benzoxazoles (**3h** and **3i**), oxazole (**3k**), oxadiazole (**3l**), and imidazole (**3m**) efficiently coupled with quinolone **1a** to afford the corresponding coupling products in good yields. Notably, caffeine reacted as a coupling partner with similar efficiencies under the slightly modified conditions (DMF, 140 °C) to afford the corresponding product **3n** in 79% yield.

Encouraged by the successful results, we next investigated the generality of this coupling reaction by extending it to a variety of quinolone and related substrates, as illustrated in Table 3. The present process was amenable to the presence of a variety of functional groups. For example, a relatively broad range of functional groups (*e.g.*, methyl, methoxy, fluoro, chloro, bromo, and phenyl groups) on the quinolone core were compatible with the cross-coupling conditions and provided moderate to good yields (**4a–4i**). Substitution of the electron-donating or -withdrawing group on the quinolone core had a little effect on the reaction efficiency. Expanding the scope from the bicyclic quinolone core to a monocyclic enaminone or uracil system was also possible, leading to the formation of **4j** and **4k**. For broad utility, we next investigated a series of experiments designed to explore the potential applicability to a series of heterocycles including quinolinone,[6] nalidixic acid,[7] pyridone[8] and chromone,[9] demonstrating that the reaction is highly flexible with respect to the substrate type to afford **4l**, **4m**, **4n**, and **4o** in modest to good yields.

We proposed a plausible mechanism for the cross-coupling between *N*-benzyl-quinolone **1a** and benzothiazole (**2a**) (Scheme 2). The reaction is initiated by the base-assisted cupration of benzothiazole (**2a**).[10] The Cu species **I** would then react with **1a** through the oxidative addition to afford copper species of higher oxidation state,[11] and the subsequent reductive elimination of **II** provides the desired coupled product **3a**.

Conclusions

In summary, we developed an efficient and versatile method for the copper-mediated direct cross-coupling reactions of a

range of azoles with quinolones, offering a promising alternative to classical procedures. This synthetic strategy was suitable for the swift construction of a variety of C3-heteroaryl quinolones, quinolinone, nalidixic acid, uracil, pyridone and chromone derivatives, which are prominent structural motifs in many biologically active compounds. Further studies toward broadening the scope to include related heterocycles and the development of catalytic variants are currently underway.

Experimental

General methods and materials

Unless stated otherwise, reactions were performed in flame-dried glassware under a positive pressure of nitrogen using freshly distilled solvents. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F_{254} plates and visualization on TLC was achieved by UV light (254 and 354 nm). Flash column chromatography was undertaken on silica gel (400–630 mesh). ^{1}H NMR was recorded on 400 MHz and chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for tetramethylsilane. The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet. Coupling constants, *J*, were reported in hertz (Hz). ^{13}C NMR was recorded at 100 MHz and was fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.0 ppm of chloroform-*d*. Mass spectral data were obtained using the EI method. Commercial grade reagents and solvents were used without further purification except as indicated below. 1,2-Dichloroethane and 1,2-dimethoxyethane were distilled from calcium hydride. Unless otherwise stated, all commercial reagents and solvents were used without additional purification.

General procedure (GP) for synthesis of 3-heteroaryl quinolones. Quinolone derivative (0.1 mmol), heteroarene (0.15–0.2 mmol), CuI (0.3 mmol) and LiO^tBu (0.12–0.2 mmol) were combined in 1,4-dioxane (1 mL) under N_2. The reaction mixture was heated to 110 °C with vigorous stirring. The reaction was monitored by TLC using ethyl acetate and toluene = 1 : 7 as the mobile phase. When the starting material disappeared, the reaction mixture was diluted with CH_2Cl_2 and the residue was extracted with aqueous NH_4Cl and aqueous $NaHCO_3$ (3 × 30 mL). The organic layer was dried over $MgSO_4$. After the removal of solvent, the residue was purified by flash chromatography (ethyl acetate and toluene = 1 : 7) on silica gel to give the desired product.

3-(Benzo[*d*]thiazol-2-yl)-1-benzylquinolin-4(1*H*)-one (3a). Compound **3a** was prepared (29.4 mg, 80% yield) according to GP from quinolone derivative (0.1 mmol). mp 214–216 °C. white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.55 (d, J = 0.8 Hz, 1H), 8.44–8.39 (m, 1H), 8.14–8.09 (m, 1H), 7.96 (dt, J = 8.0, 0.7 Hz, 1H), 7.78 (ddd, J = 8.7, 1.4, 0.6 Hz, 1H), 7.76–7.70 (m, 1H), 7.50 (dtd, J = 8.3, 6.9, 1.2 Hz, 2H), 7.41–7.35 (m, 1H), 7.35–7.31 (m, 2H), 7.31–7.25 (m, 3H), 5.90 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.8, 161.9, 151.7, 145.5, 139.2, 136.6, 135.5, 133.2, 129.4, 128.3, 127.1, 126.9, 126.7, 126.5, 125.7, 124.5, 122.4, 121.8, 118.6, 113.4, 56.4. HRMS (ESI$^+$) m/z calcd for $C_{23}H_{16}N_2NaOS^+$ [M + Na]$^+$: 391.0876, found: 391.0868.

1-Benzyl-3-(6-methylbenzo[*d*]thiazol-2-yl)quinolin-4(1*H*)-one (3b). Compound **3b** was prepared (32.9 mg, 86% yield) according to GP from quinolone derivative (0.1 mmol). mp 234–236 °C. white solid. ^{1}H NMR (400 MHz, chloroform-d) δ 9.28 (s, 1H), 8.66–8.58 (m, 1H), 7.84 (d, J = 8.3 Hz, 1H), 7.79–7.74 (m, 1H), 7.57 (ddd, J = 8.6, 7.1, 1.6 Hz, 1H), 7.44 (ddd, J = 8.0, 7.1, 1.0 Hz, 1H), 7.41–7.37 (m, 1H), 7.36–7.26 (m, 4H), 7.21–7.16 (m, 2H), 5.55 (s, 2H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, chloroform-d) δ 174.6, 161.0, 149.4, 144.0, 138.9, 136.0, 134.5, 134.2, 132.6, 129.3, 128.5, 127.9, 127.4, 127.3, 126.0, 125.1, 121.4, 121.0, 116.8, 114.5, 57.7, 21.6. HRMS (ESI$^+$) m/z calcd for $C_{24}H_{18}N_2NaOS^+$ [M + Na]$^+$: 405.1032, found: 405.1038.

1-Benzyl-3-(6-methoxybenzo[*d*]thiazol-2-yl)quinolin-4(1*H*)-one (3c). Compound **3c** was prepared (29.8 mg, 75% yield) according to GP from quinolone derivative (0.1 mmol). mp 240–242 °C. White solid. ^{1}H NMR (400 MHz, chloroform-d) δ 9.34 (s, 1H), 8.61 (dd, J = 8.0, 1.6 Hz, 1H), 7.86 (d, J = 8.9 Hz, 1H), 7.58 (ddd, J = 8.6, 7.0, 1.7 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.43–7.38 (m, 3H), 7.37–7.26 (m, 2H), 7.22–7.16 (m, 2H), 7.08 (dd, J = 8.9, 2.6 Hz, 1H), 5.56 (s, 2H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, chloroform-d) δ 174.4, 160.1, 157.3, 148.1, 144.2, 138.9, 136.6, 134.4, 132.7, 129.3, 128.5, 127.5, 127.2, 126.1, 125.3, 121.6, 116.9, 116.1, 113.9, 103.8, 57.8, 55.9. HRMS (ESI$^+$) m/z calcd for $C_{24}H_{18}N_2NaO_2S^+$ [M + Na]$^+$: 421.0981, found: 421.0983.

1-Benzyl-3-(6-chlorobenzo[*d*]thiazol-2-yl)quinolin-4(1*H*)-one (3d). Compound **3d** was prepared (30.6 mg, 76% yield) according to GP from quinolone derivative (0.1 mmol). mp 250–252 °C. White solid. ^{1}H NMR (400 MHz, chloroform-d) δ 9.22 (s, 1H), 8.59 (dd, J = 8.0, 1.6 Hz, 1H), 7.92 (d, J = 2.1 Hz, 1H), 7.82 (d, J = 8.7 Hz, 1H), 7.57 (ddd, J = 8.6, 7.0, 1.6 Hz, 1H), 7.44 (ddd, J = 8.1, 7.1, 1.0 Hz, 1H), 7.39 (dd, J = 8.7, 2.1 Hz, 2H), 7.37–7.27 (m, 3H), 7.18 (d, J = 6.3 Hz, 2H), 5.54 (s, 2H). ^{13}C NMR (100 MHz, chloroform-d) δ 174.5, 162.3, 150.2, 144.0, 138.9, 137.2, 134.3, 132.6, 129.7, 129.3, 128.5, 127.4, 127.2, 126.5, 126.0, 125.1, 122.3, 121.1, 116.7, 114.2, 57.7. HRMS (ESI$^+$) m/z calcd for $C_{23}H_{15}ClN_2NaOS^+$ [M + Na]$^+$: 425.0486, found: 425.0493.

1-Benzyl-3-(6-phenylbenzo[*d*]thiazol-2-yl)quinolin-4(1*H*)-one (3e). Compound **3e** was prepared (40.4 mg, 91% yield) according to GP from quinolone derivative (0.1 mmol). mp 277–279 °C. White solid. ^{1}H NMR (400 MHz, chloroform-d) δ 9.30 (s, 1H), 8.68–8.61 (m, 1H), 8.18 (dd, J = 1.9, 0.6 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.74–7.65 (m, 3H), 7.59 (ddd, J = 8.6, 7.1, 1.7 Hz, 1H), 7.49–7.40 (m, 4H), 7.38–7.28 (m, 4H), 7.22–7.17 (m, 2H), 5.58 (s, 2H). ^{13}C NMR (100 MHz, chloroform-d) δ 174.6, 162.2, 150.6, 144.2, 140.9, 138.9, 137.5, 136.5, 134.4, 132.6, 129.3, 128.8, 128.5, 127.5, 127.4, 127.3, 127.2, 126.0, 125.7, 125.2, 121.5, 119.9, 116.8, 114.4, 57.7. HRMS (ESI$^+$) m/z calcd for $C_{29}H_{20}N_2NaOS^+$ [M + Na]$^+$: 467.1189, found: 467.1210.

1-Benzyl-3-(4,5-dimethylthiazol-2-yl)quinolin-4(1*H*)-one (3f). Compound **3f** was prepared (26.3 mg, 76% yield) according to GP from quinolone derivative (0.1 mmol). mp 164–167 °C. Yellow solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.06 (s, 1H), 8.59 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.54 (ddd, *J* = 8.6, 7.1, 1.7 Hz, 1H), 7.40 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 7.38–7.34 (m, 1H), 7.34–7.25 (m, 3H), 7.15 (dd, *J* = 7.8, 1.5 Hz, 2H), 5.51 (s, 2H), 2.40 (d, *J* = 0.8 Hz, 3H), 2.37 (d, *J* = 0.8 Hz, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 174.0, 156.0, 145.9, 141.9, 138.7, 134.7, 132.2, 129.2, 128.3, 127.4, 127.0, 126.6, 125.9, 124.6, 116.6, 115.0, 57.4, 14.6, 11.2. HRMS (ESI$^+$) *m*/*z* calcd for $C_{21}H_{19}N_2OS^+$ [M + H]$^+$: 347.1213, found: 347.1194.

1-Benzyl-3-(5-phenylthiazol-2-yl)quinolin-4(1*H*)-one (3g). Compound **3g** was prepared (28.4 mg, 72% yield) according to GP from quinolone derivative (0.1 mmol). mp 242–244 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.08 (s, 1H), 8.61 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.99 (s, 1H), 7.72–7.63 (m, 2H), 7.56 (ddd, *J* = 8.6, 7.0, 1.6 Hz, 1H), 7.47–7.36 (m, 4H), 7.36–7.25 (m, 4H), 7.17 (dd, *J* = 7.9, 1.7 Hz, 2H), 5.50 (s, 2H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 174.1, 159.7, 142.3, 138.8, 136.7, 134.5, 132.5, 132.2, 129.3, 129.1, 128.5, 127.8, 127.4, 127.0, 126.5, 126.0, 124.9, 116.7, 115.1, 57.6. HRMS (ESI$^+$) *m*/*z* calcd for $C_{25}H_{18}N_2NaOS^+$ [M + Na]$^+$: 417.1032, found: 417.1029.

3-(Benzo[*d*]oxazol-2-yl)-1-benzylquinolin-4(1*H*)-one (3h). Compound **3h** was prepared (29.2 mg, 83% yield) according to GP from quinolone derivative (0.1 mmol). mp 210–212 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.88 (s, 1H), 8.62 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.77–7.68 (m, 1H), 7.65–7.60 (m, 1H), 7.60–7.53 (m, 1H), 7.46–7.40 (m, 1H), 7.35 (dd, *J* = 7.7, 5.9 Hz, 3H), 7.32 (dd, *J* = 6.7, 2.6 Hz, 3H), 7.22–7.17 (m, 2H), 5.48 (s, 2H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 173.8, 161.1, 150.5, 146.7, 141.1, 139.1, 134.3, 132.7, 129.4, 128.6, 128.5, 128.0, 126.0, 125.3, 124.6, 124.5, 119.3, 116.6, 110.9, 109.0, 57.5. HRMS (ESI$^+$) *m*/*z* calcd for $C_{23}H_{16}N_2NaO_2^+$ [M + Na]$^+$: 375.1104, found: 375.1093.

1-Benzyl-3-(5-methoxybenzo[*d*]oxazol-2-yl)quinolin-4(1*H*)-one (3i). Compound **3i** was prepared (31.7 mg, 83% yield) according to GP from quinolone derivative (0.1 mmol). mp 204–206 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.77 (s, 1H), 8.57 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.49 (ddd, *J* = 8.6, 7.0, 1.7 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 1H), 7.39–7.34 (m, 1H), 7.34–7.25 (m, 4H), 7.20–7.13 (m, 3H), 6.87 (dd, *J* = 8.9, 2.5 Hz, 1H), 5.44 (s, 2H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 173.7, 161.7, 157.2, 146.5, 145.1, 142.2, 138.9, 134.3, 132.6, 129.3, 128.5, 128.4, 127.8, 126.0, 125.1, 116.6, 112.8, 110.8, 109.0, 102.5, 57.4, 55.9. HRMS (ESI$^+$) *m*/*z* calcd for $C_{24}H_{18}N_2NaO_3^+$ [M + Na]$^+$: 405.1210, found: 405.1214.

1-Benzyl-3-(6-chlorobenzo[*d*]oxazol-2-yl)quinolin-4(1*H*)-one (3j). Compound **3j** was prepared (27.1 mg, 70% yield) according to GP from quinolone derivative (0.1 mmol). mp 255–257 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.82 (s, 1H), 8.63–8.57 (m, 1H), 7.62 (dd, *J* = 8.5, 0.5 Hz, 1H), 7.59–7.57 (m, 1H), 7.57–7.53 (m, 1H), 7.42 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1H), 7.39–7.31 (m, 4H), 7.29 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.21–7.17 (m, 2H), 5.47 (s, 2H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 173.6, 161.6, 150.5, 146.6, 140.3, 139.0, 134.2, 132.8, 130.0, 129.4, 128.6, 128.4, 127.9, 126.0, 125.3, 125.1, 119.9, 116.6, 111.2, 108.5, 57.5. HRMS (ESI$^+$) *m*/*z* calcd for $C_{23}H_{15}ClN_2NaO_2^+$ [M + Na]$^+$: 409.0714, found: 409.0716.

1-Benzyl-3-(5-phenyloxazol-2-yl)quinolin-4(1*H*)-one (3k). Compound **3k** was prepared (31.4 mg, 83% yield) according to GP from quinolone derivative (0.1 mmol). mp 200–203 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.87 (s, 1H), 8.60 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.81–7.73 (m, 2H), 7.56 (ddd, *J* = 8.6, 7.1, 1.6 Hz, 1H), 7.46–7.37 (m, 4H), 7.39–7.34 (m, 2H), 7.34–7.28 (m, 3H), 7.24–7.16 (m, 2H), 5.48 (s, 2H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 173.6, 158.7, 150.9, 144.9, 139.0, 134.5, 132.4, 129.3, 128.8, 128.5, 128.3, 128.1, 127.6, 126.0, 124.8, 124.2, 122.4, 116.5, 109.8, 57.3. HRMS (ESI$^+$) *m*/*z* calcd for $C_{25}H_{18}N_2NaO_2^+$ [M + Na]$^+$: 401.1260, found: 401.1248.

1-Benzyl-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinolin-4(1*H*)-one (3l). Compound **3l** was prepared (30.7 mg, 81% yield) according to GP from quinolone derivative (0.1 mmol). mp 189–191 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.78 (s, 1H), 8.58 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.17 (dd, *J* = 7.5, 2.2 Hz, 2H), 7.59 (ddd, *J* = 8.6, 7.1, 1.6 Hz, 1H), 7.53–7.46 (m, 3H), 7.44 (ddd, *J* = 8.0, 7.1, 0.9 Hz, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.38–7.28 (m, 3H), 7.22–7.16 (m, 2H), 5.47 (s, 2H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 173.3, 164.8, 162.7, 145.6, 139.4, 134.2, 132.8, 131.4, 129.4, 128.9, 128.7, 128.2, 127.6, 127.1, 126.2, 125.3, 124.2, 116.7, 106.6, 57.4. HRMS (ESI$^+$) *m*/*z* calcd for $C_{24}H_{17}N_3NaO_2^+$ [M + Na]$^+$: 402.1213, found: 402.1211.

1-Benzyl-3-(1-benzyl-1*H*-benzo[*d*]imidazol-2-yl)quinolin-4(1*H*)-one (3m). Compound **3m** was prepared (23.8 mg, 54% yield) according to GP from quinolone derivative (0.1 mmol). Pale yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.54 (dd, *J* = 8.1, 1.6 Hz, 1H), 8.28 (s, 1H), 7.78 (d, *J* = 7.0 Hz, 1H), 7.55 (ddd, *J* = 8.7, 7.1, 1.6 Hz, 1H), 7.39 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1H), 7.32 (td, *J* = 6.4, 5.9, 3.1 Hz, 2H), 7.29–7.25 (m, 3H), 7.25–7.18 (m, 2H), 7.17–7.09 (m, 3H), 7.03–6.94 (m, 4H), 5.63 (s, 2H), 5.35 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.4, 162.8, 151.0, 148.3, 143.4, 139.6, 137.9, 136.7, 136.4, 133.1, 129.3, 128.9, 128.3, 127.7, 127.2, 126.8, 126.7, 125.1, 122.7, 122.2, 119.4, 118.2, 112.8, 111.1, 55.7, 47.9. HRMS (ESI$^+$) *m*/*z* calcd for $C_{30}H_{24}N_3O^+$ [M + H]$^+$: 442.1914, found: 442.1932.

8-(1-Benzyl-4-oxo-1,4-dihydroquinolin-3-yl)-1,3,7-trimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione (3n). Compound **3n** was prepared (33.8 mg, 79% yield) according to GP from quinolone derivative (0.1 mmol). mp 291–294 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.53–8.47 (m, 1H), 8.24 (s, 1H), 7.60 (ddd, *J* = 8.7, 7.1, 1.7 Hz, 1H), 7.43 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1H), 7.40–7.35 (m, 2H), 7.35–7.29 (m, 2H), 7.19 (dd, *J* = 8.0, 1.5 Hz, 2H), 5.44 (s, 2H), 4.00 (s, 3H), 3.56 (s, 3H), 3.40 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 174.2, 155.3, 151.7, 148.7, 148.0, 147.0, 139.4, 134.3, 132.9, 129.4, 128.6, 127.5, 127.4, 126.1, 125.1, 116.6, 111.2, 108.9, 57.3, 34.2, 29.7, 28.0. HRMS (ESI$^+$) *m*/*z* calcd for $C_{24}H_{21}N_5NaO_3^+$ [M + Na]$^+$: 450.1537, found: 450.1541.

3-(Benzo[*d*]thiazol-2-yl)-1-benzyl-6-methylquinolin-4(1*H*)-one (4a). Compound **4a** was prepared (30.6 mg, 80% yield) according to GP from quinolone derivative (0.1 mmol). mp

192–194 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.32 (s, 1H), 8.39 (dd, *J* = 1.6, 0.7 Hz, 1H), 8.00–7.93 (m, 2H), 7.46 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.39–7.34 (m, 2H), 7.34–7.25 (m, 4H), 7.17 (dd, *J* = 7.9, 1.5 Hz, 2H), 5.53 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 174.4, 162.2, 150.9, 143.9, 136.8, 135.6, 135.4, 134.5, 134.0, 129.2, 128.4, 127.1, 126.7, 126.0, 126.0, 124.1, 121.7, 121.3, 116.8, 113.7, 57.7, 21.0. HRMS (ESI$^+$) *m*/*z* calcd for $C_{24}H_{18}N_2NaOS^+$ [M + Na]$^+$: 405.1032, found: 405.1042.

3-(Benzo[*d*]thiazol-2-yl)-1-benzyl-6-methoxyquinolin-4(1*H*)-one (4b). Compound **4b** was prepared (30.3 mg, 76% yield) according to GP from quinolone derivative (0.1 mmol). mp 224–226 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.25 (s, 1H), 8.00 (d, *J* = 3.0 Hz, 1H), 7.99–7.93 (m, 2H), 7.46 (ddd, *J* = 8.2, 7.1, 1.3 Hz, 1H), 7.38–7.25 (m, 5H), 7.19–7.12 (m, 3H), 5.53 (s, 2H), 3.91 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 174.0, 162.2, 157.2, 151.5, 143.0, 135.8, 134.5, 133.3, 129.3, 128.6, 128.5, 125.9, 125.9, 124.0, 123.1, 121.7, 121.5, 118.5, 113.4, 106.5, 57.9, 55.8. HRMS (ESI$^+$) *m*/*z* calcd for $C_{24}H_{18}N_2NaO_2S^+$ [M + Na]$^+$: 421.0981, found: 421.0980.

3-(Benzo[*d*]thiazol-2-yl)-1-benzyl-6-fluoroquinolin-4(1*H*)-one (4c). Compound **4c** was prepared (30.1 mg, 78% yield) according to GP from quinolone derivative (0.1 mmol). mp 244–246 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.25 (s, 1H), 8.22 (dd, *J* = 8.7, 3.0 Hz, 1H), 7.99–7.95 (m, 1H), 7.95–7.91 (m, 1H), 7.46 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H), 7.40–7.30 (m, 5H), 7.29–7.24 (m, 1H), 7.16 (dd, *J* = 8.0, 1.5 Hz, 2H), 5.53 (s, 2H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 173.7, 161.6, 161.1, 158.6, 151.1, 144.1, 135.6, 135.3, 134.1, 129.4, 129.0, 128.9, 128.7, 126.1, 125.9, 124.3, 121.7, 121.6, 121.2, 121.0, 119.3, 119.2, 113.7, 112.3, 112.1, 58.1. HRMS (ESI$^+$) *m*/*z* calcd for $C_{23}H_{15}FN_2NaOS^+$ [M + Na]$^+$: 409.0781, found: 409.0774.

3-(Benzo[*d*]thiazol-2-yl)-1-benzyl-6-chloroquinolin-4(1*H*)-one (4d). Compound **4d** was prepared (33.4 mg, 83% yield) according to GP from quinolone derivative (0.1 mmol). mp 268–270 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.12 (s, 1H), 8.47 (d, *J* = 2.5 Hz, 1H), 7.95 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.87 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.44 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.39 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.35 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.30 (ddd, *J* = 7.8, 7.0, 0.9 Hz, 3H), 7.24 (dd, *J* = 5.0, 4.1 Hz, 1H), 7.16–7.07 (m, 2H), 5.47 (s, 2H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 173.3, 161.2, 151.4, 144.1, 137.1, 135.7, 134.0, 132.7, 131.4, 129.4, 128.6, 128.2, 126.7, 126.0, 125.9, 124.2, 121.7, 121.6, 118.5, 114.6, 57.9. HRMS (ESI$^+$) *m*/*z* calcd for $C_{23}H_{15}ClN_2NaOS^+$ [M + Na]$^+$: 425.0486, found: 425.0479.

3-(Benzo[*d*]thiazol-2-yl)-1-benzyl-6-bromoquinolin-4(1*H*)-one (4e). Compound **4e** was prepared (22.8 mg, 51% yield) according to GP from quinolone derivative (0.1 mmol). mp 254–256 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.22 (s, 1H), 8.71 (d, *J* = 2.3 Hz, 1H), 7.97 (ddd, *J* = 7.9, 1.3, 0.6 Hz, 1H), 7.95–7.89 (m, 1H), 7.60 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.46 (ddd, *J* = 8.2, 7.1, 1.3 Hz, 1H), 7.39–7.28 (m, 4H), 7.27–7.22 (m, 1H), 7.15 (dd, *J* = 7.9, 1.5 Hz, 2H), 5.51 (s, 2H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 173.2, 161.3, 151.1, 144.3, 137.6, 135.6, 135.5, 134.0, 130.0, 129.4, 128.7, 128.5, 126.1, 126.0, 124.3, 121.7, 121.6, 119.1, 118.7, 114.6, 57.9. HRMS (ESI$^+$) *m*/*z* calcd for $C_{23}H_{15}BrN_2NaOS^+$ [M + Na]$^+$: 468.9981, found: 468.9980.

3-(Benzo[*d*]thiazol-2-yl)-1-benzyl-6-phenylquinolin-4(1*H*)-one (4f). Compound **4f** was prepared (32.4 mg, 73% yield) according to GP from quinolone derivative (0.1 mmol). mp 283–284 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.19 (s, 1H), 8.83 (d, *J* = 2.2 Hz, 1H), 8.01–7.96 (m, 1H), 7.95–7.90 (m, 1H), 7.76 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.67–7.61 (m, 2H), 7.49–7.39 (m, 4H), 7.38–7.26 (m, 5H), 7.22–7.15 (m, 2H), 5.53 (s, 2H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 174.6, 162.2, 144.3, 139.1, 138.1, 138.0, 135.4, 134.4, 131.5, 129.4, 129.0, 128.6, 128.0, 127.5, 127.1, 126.2, 126.1, 125.2, 124.4, 121.8, 121.2, 117.6, 57.9. HRMS (ESI$^+$) *m*/*z* calcd for $C_{29}H_{20}N_2NaOS^+$ [M + Na]$^+$: 467.1189, found: 467.1206.

3-(Benzo[*d*]thiazol-2-yl)-1-benzyl-8-methoxyquinolin-4(1*H*)-one (4g). Compound **4g** was prepared (28.7 mg, 72% yield) according to GP from quinolone derivative (0.1 mmol). mp 256–258 °C. White solid. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.12 (s, 1H), 8.28 (dd, *J* = 8.1, 1.4 Hz, 1H), 8.00–7.92 (m, 2H), 7.45 (ddd, *J* = 8.2, 7.2, 1.3 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.34 (ddd, *J* = 8.1, 7.2, 1.2 Hz, 1H), 7.31–7.25 (m, 2H), 7.23–7.19 (m, 1H), 7.07 (ddd, *J* = 9.2, 8.0, 1.3 Hz, 3H), 5.90 (s, 2H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 173.9, 161.9, 150.1, 146.7, 137.3, 135.8, 130.3, 129.8, 128.7, 127.6, 125.8, 125.5, 125.5, 124.0, 121.6, 121.4, 119.7, 114.8, 113.9, 62.1, 56.2. HRMS (ESI$^+$) *m*/*z* calcd for $C_{24}H_{18}N_2NaO_2S^+$ [M + Na]$^+$: 421.0981, found: 421.0991.

3-(Benzo[*d*]thiazol-2-yl)-1-benzyl-8-fluoroquinolin-4(1*H*)-one (4h). Compound **4h** was prepared (25.1 mg, 65% yield) according to GP from quinolone derivative (0.1 mmol). mp 245–247 °C. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.36 (s, 1H), 8.29 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.10 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.96 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.60 (ddd, *J* = 14.8, 7.9, 1.7 Hz, 1H), 7.56–7.45 (m, 2H), 7.43–7.36 (m, 1H), 7.40–7.30 (m, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 7.20 (dd, *J* = 7.5, 1.5 Hz, 2H), 5.91 (d, *J* = 2.9 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.8, 172.8, 161.3, 153.4, 151.8, 150.9, 147.3, 137.5, 135.7, 129.8, 129.2, 128.9, 128.8, 128.1, 126.5, 126.3, 126.2, 126.1, 124.6, 123.1, 123.0, 122.2, 122.0, 120.4, 120.2, 113.9, 60.5, 60.4. HRMS (ESI$^+$) *m*/*z* calcd for $C_{23}H_{15}FN_2NaOS^+$ [M + Na]$^+$: 409.0781, found: 409.0776.

3-(Benzo[*d*]thiazol-2-yl)-1-methylquinolin-4(1*H*)-one (4i). Compound **4i** was prepared (21.6 mg, 74% yield) according to GP from quinolone derivative (0.1 mmol). mp 302–304 °C. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.25 (s, 1H), 8.45–8.40 (m, 1H), 8.06 (ddd, *J* = 7.9, 1.3, 0.7 Hz, 1H), 7.95 (ddd, *J* = 8.1, 1.1, 0.6 Hz, 1H), 7.87–7.83 (m, 2H), 7.57 (ddd, *J* = 8.0, 4.6, 3.4 Hz, 1H), 7.48 (ddd, *J* = 8.2, 7.2, 1.3 Hz, 1H), 7.36 (ddd, *J* = 8.1, 7.2, 1.1 Hz, 1H), 4.10 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.7, 162.1, 151.9, 145.5, 140.1, 135.6, 133.1, 126.9, 126.5, 126.3, 125.4, 124.3, 122.1, 121.8, 117.9, 113.2, 41.6. HRMS (ESI$^+$) *m*/*z* calcd for $C_{17}H_{12}N_2NaOS^+$ [M + Na]$^+$: 315.0563, found: 315.0548.

3-(Benzo[*d*]thiazol-2-yl)-1-benzylpyridin-4(1*H*)-one (4j). Compound **4j** was prepared (16.6 mg, 52% yield) according to GP

from pyridone derivative (0.1 mmol). mp 218–220 °C. White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.10 (d, J = 2.3 Hz, 1H), 8.13–8.06 (m, 1H), 7.99 (dd, J = 7.5, 2.3 Hz, 1H), 7.95 (d, J = 8.1 Hz, 1H), 7.49 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.41 (d, J = 4.3 Hz, 4H), 7.40–7.31 (m, 2H), 6.55 (d, J = 7.5 Hz, 1H), 5.40 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.3, 161.2, 151.5, 141.3, 141.2, 136.9, 135.7, 129.5, 128.8, 128.2, 126.5, 124.7, 122.4, 122.0, 120.8, 119.4, 59.5. HRMS (ESI$^+$) m/z calcd for $C_{19}H_{14}N_2NaOS^+$ [M + Na]$^+$: 341.0719, found: 341.0697.

5-(Benzo[*d*]thiazol-2-yl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (4k). Compound **4k** was prepared (11.9 mg, 44% yield) according to GP from pyrimidinedione derivative (0.1 mmol). mp 227–229 °C. White solid. ^{1}H NMR (400 MHz, chloroform-d) δ 8.69 (s, 1H), 7.98–7.89 (m, 2H), 7.47 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.36 (ddd, J = 8.1, 7.2, 1.1 Hz, 1H), 3.59 (s, 3H), 3.48 (s, 3H). ^{13}C NMR (100 MHz, chloroform-d) δ 161.4, 159.8, 151.7, 150.8, 143.2, 135.5, 126.3, 124.6, 121.9, 121.6, 107.4, 37.8, 28.4. HRMS (ESI$^+$) m/z calcd for $C_{13}H_{11}N_3NaO_2S^+$ [M + Na]$^+$: 296.0464, found: 296.0424.

3-(Benzo[*d*]thiazol-2-yl)-1-methylquinolin-2(1*H*)-one (4l). Compound **4l** was prepared (18.4 mg, 63% yield) according to GP from quinolone derivative (0.1 mmol). mp 249–251 °C. Yellow solid. ^{1}H NMR (400 MHz, chloroform-d) δ 9.10 (s, 1H), 8.08 (dd, J = 8.2, 0.9 Hz, 1H), 7.97 (dd, J = 7.9, 0.9 Hz, 1H), 7.85–7.76 (m, 1H), 7.65 (ddd, J = 8.6, 7.2, 1.5 Hz, 1H), 7.50 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.45–7.35 (m, 2H), 7.31 (ddd, J = 8.0, 7.2, 1.0 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, chloroform-d) δ 161.8, 160.5, 152.1, 140.0, 137.8, 136.9, 132.1, 130.5, 126.1, 124.9, 123.4, 123.0, 122.6, 121.7, 120.1, 114.3, 30.0. HRMS (ESI$^+$) m/z calcd for $C_{17}H_{12}N_2NaOS^+$ [M + Na]$^+$: 315.0563, found: 315.0533.

3-(Benzo[*d*]thiazol-2-yl)-1-ethyl-7-methyl-1,8-naphthyridin-4-(1*H*)-one (4m). Compound **4m** was prepared (19.3 mg, 60% yield) according to GP from quinolone derivative (0.1 mmol). mp 273–275 °C. White solid. ^{1}H NMR (400 MHz, chloroform-d) δ 9.25 (s, 1H), 8.70 (d, J = 8.1 Hz, 1H), 7.99–7.92 (m, 2H), 7.46 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.34 (ddd, J = 8.1, 7.2, 1.1 Hz, 1H), 7.26 (d, J = 8.1 Hz, 1H), 4.61 (d, J = 7.2 Hz, 2H), 2.66 (s, 3H), 1.55 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, chloroform-d) δ 174.7, 162.9, 161.8, 151.1, 148.1, 143.0, 136.3, 135.5, 126.0, 124.1, 121.7, 121.5, 121.1, 119.6, 114.9, 46.9, 25.2, 15.4. HRMS (ESI$^+$) m/z calcd for $C_{18}H_{15}N_3NaOS^+$ [M + Na]$^+$: 344.0828, found: 344.0821.

4-(Benzo[*d*]thiazol-2-yl)-2-methylisoquinolin-1(2*H*)-one (4n). Compound **4n** was prepared (19.6 mg, 67% yield) according to GP from quinolone derivative (0.1 mmol). mp 142–144 °C. White solid. ^{1}H NMR (400 MHz, chloroform-d) δ 8.71 (ddd, J = 8.3, 1.2, 0.6 Hz, 1H), 8.51 (ddd, J = 8.1, 1.5, 0.6 Hz, 1H), 8.10 (ddd, J = 8.2, 1.2, 0.6 Hz, 1H), 7.90 (ddd, J = 8.0, 1.3, 0.6 Hz, 1H), 7.74 (ddd, J = 8.4, 7.1, 1.5 Hz, 1H), 7.71 (s, 1H), 7.56 (ddd, J = 8.2, 7.1, 1.2 Hz, 1H), 7.52 (ddd, J = 8.3, 7.2, 1.3 Hz, 1H), 7.41 (ddd, J = 8.0, 7.2, 1.2 Hz, 1H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, chloroform-d) δ 163.7, 162.1, 153.8, 135.9, 134.3, 134.0, 132.9, 128.1, 127.7, 126.4, 125.5, 125.4, 124.8, 123.1, 121.3, 111.9, 37.4. HRMS (ESI$^+$) m/z calcd for $C_{17}H_{12}N_2NaOS^+$ [M + Na]$^+$: 315.0563, found: 315.0551.

3-(Benzo[*d*]thiazol-2-yl)-4*H*-chromen-4-one (4o). Compound **4o** was prepared (18.7 mg, 67% yield) according to GP from chromone derivative (0.1 mmol). mp 233–235 °C. White solid. ^{1}H NMR (400 MHz, chloroform-d) δ 9.29 (s, 1H), 8.40–8.32 (m, 1H), 8.02 (ddd, J = 8.2, 1.2, 0.7 Hz, 1H), 7.97 (ddd, J = 8.0, 1.3, 0.7 Hz, 1H), 7.74 (ddd, J = 8.7, 7.1, 1.7 Hz, 1H), 7.57 (ddd, J = 8.5, 1.1, 0.5 Hz, 1H), 7.49 (dddd, J = 8.3, 7.2, 3.9, 1.2 Hz, 2H), 7.38 (ddd, J = 8.1, 7.1, 1.1 Hz, 1H). ^{13}C NMR (100 MHz, chloroform-d) δ 174.8, 158.6, 156.6, 155.9, 151.5, 136.0, 134.3, 126.3, 126.2, 126.2, 124.8, 123.8, 122.4, 121.6, 118.4, 118.2. HRMS (ESI$^+$) m/z calcd for $C_{16}H_9NNaO_2S^+$ [M + Na]$^+$: 302.0246, found: 302.0221.

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