EurJOC
European Journal of Organic Chemistry

Chemistry Europe
European Chemical Societies Publishing

Accepted Article

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.202001128

Link to VoR: https://doi.org/10.1002/ejoc.202001128

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Site-Selective C–H Amidation of 2-Aryl Quinazolinones Using Nitrene Surrogates

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Dedicated to Prof. Pierre H. Dixneuf for his outstanding contribution to organometallic chemistry and catalysis

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Abstract: The site-selective modifications of quinazolinones constitute a pivotal topic in drug discovery and material science. Herein, we describe the rhodium(III)-catalyzed C–H amidation of 2-aryl quinazolin-4(3*H*)-ones with a range of nitrene surrogates including dioxazolones, organic azides, and *N*-methoxyamides. Complete site-selectivity and functional group tolerance are observed. Notably, the large-scale reaction and late-stage functionalization highlight the synthetic potential of the developed protocol. Combined mechanistic investigations elucidate a plausible reaction mechanism of this process.

Introduction

The carbon-nitrogen (C–N) bond is one of the most fundamental links in various pharmaceuticals and biologically relevant molecules.[1] Representative approaches to realize the C–N bond formation include the Ullmann[2] and Buchwald-Hartwig[3] cross-coupling reactions under transition-metal catalysis. However, from a synthetic point of view, these approaches have intrinsic drawbacks including the requirement for prefunctionalized aryl(pseudo) halides as starting materials. In the past decades, the transition-metal-catalyzed C–H amination has been a central theme to realize the direct access of C–N bonds.[4] In this context, various amidation agents such as chloramines, organic azides, hydroxylamines, dioxazolones, and anthranils have been employed for the generation of nitrene intermediates.

2-Aryl quinazolin-4(3*H*)-one motif is among the ubiquitous core found in natural products, pharmaceuticals, and advanced organic materials such as bouchardatin, luotonin A, methaqualone, and photoredox catalysts.[5] Moreover, *ortho*-aminated 2-aryl quinazolin-4(3*H*)-ones displayed interesting biological profiles including topoisomerase I inhibition and antitumoral activity (Figure 1).[6] The unmasked quinazolin-4(3*H*)-one framework possesses integral structural features with inherent directing group capability and amide-iminol tautomerism. Due to the biological importance and structural feasibility of 2-aryl quinazolin-4(3*H*)-ones, recent efforts have been made towards the transition-metal-catalyzed C−H functionalization of 2-aryl quinazolin-4(3*H*)-ones, leading to the C−X and C−C bond forming reactions.[7]

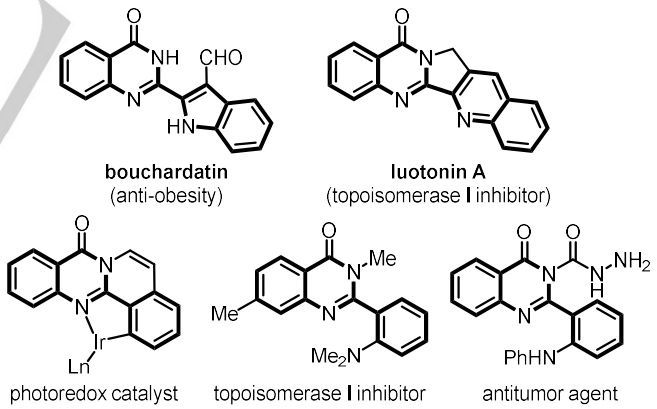
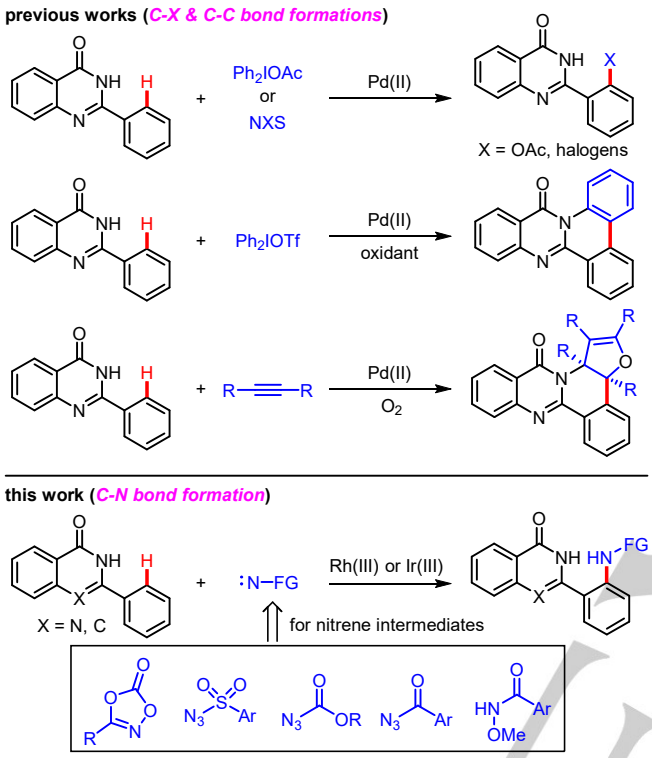


Figure 1. Selected examples of bioactive and advanced organic molecules containing 2-aryl quinazolinone motif.

For examples, the quinazolinone-directed C−H acetoxylation and halogenation have been independently reported by Yadav[7a] and Dabiri (Scheme 1).[7b] Hong demonstrated the direct construction of quinazolino-phenanthridinones through the Pd(II)-catalyzed two-fold C–H functionalization of 2-aryl quinazolin-4(3*H*)-ones.[7c] In addition, Cui described an elegant literature for the synthesis of fused polyheterocycles through sequential [4+2] and [3+2] cycloadditions between 2-aryl quinazolinones and internal alkynes.[7d] However, the transition-metal-catalyzed C−N bond forming reactions using 2-aryl quinazolin-4(3*H*)-ones have been rarely explored.[8] In

continuation of our recent works on the catalytic C−N bond forming reactions,[9] we herein describe the Rh(III)- and Ir(III)-catalyzed C–H amidation of a range of 2-aryl quinazolin-4(3*H*)-ones with easily accessible nitrene surrogates such as dioxazolones, organic azides, and *N*-methoxyamides. Notably, the large-scale reaction and late-stage C–H amidations of complex molecules demonstrate the synthetic utility of our developed method.

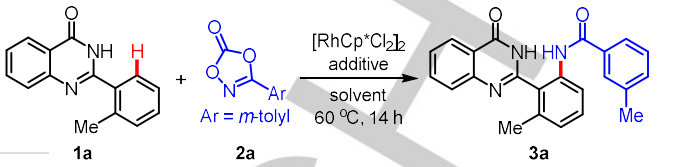


Scheme 1. C–H functionalization of 2-aryl quinazolinones.

Results and Discussion

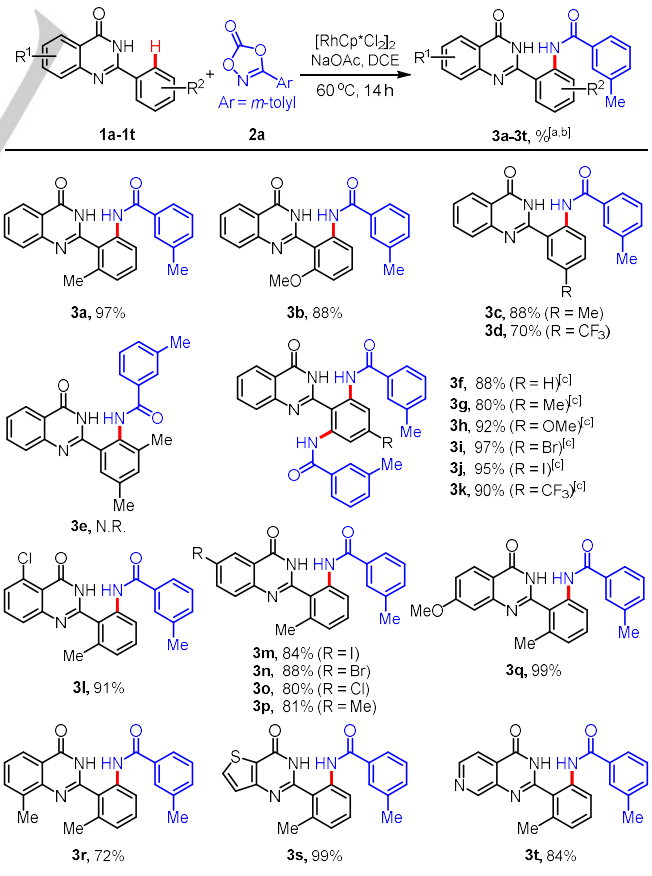
Optimization study was initiated by the coupling of 2-(*o*-tolyl)quinazolin-4(3*H*)-one (**1a**) with 3-(*m*-tolyl)-1,4,2-dioxazol-5-one (**2a**) under Rh(III) catalysis (Table 1). A cationic Rh(III) catalyst afforded the desired product **3a** in a moderate yield (57%), as shown in entry 1. Treatment of a cationic Rh(III) catalyst in the presence of NaOAc displayed the significantly improved formation of **3a** (Table 1, entry 2). Notably, a neutral Rh(III) species generated from $[RhCp^*Cl_2]_2$ and NaOAc also catalyzed the coupling reaction of **1a** and **2a**, furnishing the desired product **3a** in 81% yield (Table 1, entry 3). In addition, the amidated adduct **3a** was formed in an almost quantitative yield (99%) in the presence of a stoichiometric amount of NaOAc (Table 1, entry 5). However, exchanging NaOAc into other acetate sources such as KOAc and LiOAc was less effective in this transformation (Table 1, entries 6 and 7). Screening of solvents indicated that DCE was a most effective solvent in this reaction (Table 1, entries 8−10). Gratifyingly, this reaction was comparable with 1 mol % of $[RhCp^*Cl_2]_2$ to give **3a** in 97% yield (Table 1, entry 11). Finally, it should be noted that other transition-metal catalysts such as $Pd(OAc)_2$, $[RuCl_2(p\text{-cymene})]_2$, $[Cp^*Co(CO)I_2]$, and $[IrCp^*Cl_2]_2$ were found to be unreactive under the optimized reaction conditions (data not shown).

Table 1. Optimization of reaction conditions.[a]



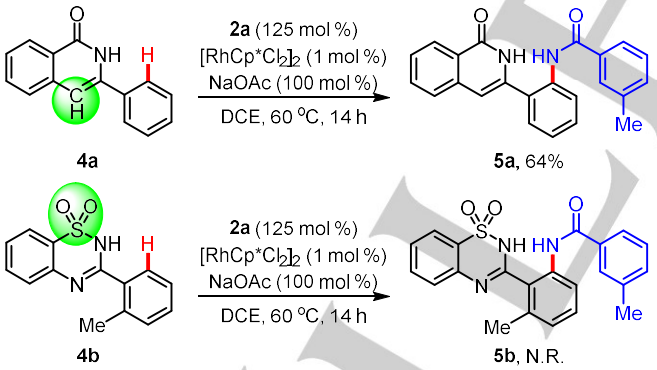
entry	catalyst (mol %)	additive (mol %)	solvent	yield[b]
1	$[Cp^*RhCl_2]_2$ (2.5)	$AgSbF_6$ (10)	DCE	57
2	$[Cp^*RhCl_2]_2$ (2.5)	$AgSbF_6$ (10), NaOAc (30)	DCE	93
3	$[Cp^*RhCl_2]_2$ (2.5)	NaOAc (30)	DCE	81
4	$[Cp^*RhCl_2]_2$ (2.5)	NaOAc (50)	DCE	93
5	$[Cp^*RhCl_2]_2$ (2.5)	NaOAc (100)	DCE	99
6	$[Cp^*RhCl_2]_2$ (2.5)	KOAc (100)	DCE	76
7	$[Cp^*RhCl_2]_2$ (2.5)	LiOAc (100)	DCE	58
8	$[Cp^*RhCl_2]_2$ (2.5)	NaOAc (100)	THF	85
9	$[Cp^*RhCl_2]_2$ (2.5)	NaOAc (100)	toluene	91
10	$[Cp^*RhCl_2]_2$ (2.5)	NaOAc (100)	MeOH	13
11	**$[Cp^*RhCl_2]_2$ (1)**	**NaOAc (100)**	**DCE**	**97**
12[c]	$[Cp^*RhCl_2]_2$ (2.5)	NaOAc (100)	DCE	51

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.25 mmol), $[RhCp^*Cl_2]_2$ (quantity noted), additive (quantity noted), solvent (1 mL) at 60 °C for 14 h under air in pressure tubes. [b] Yield isolated by flash column chromatography. [c] The reaction was carried out at room temperature.



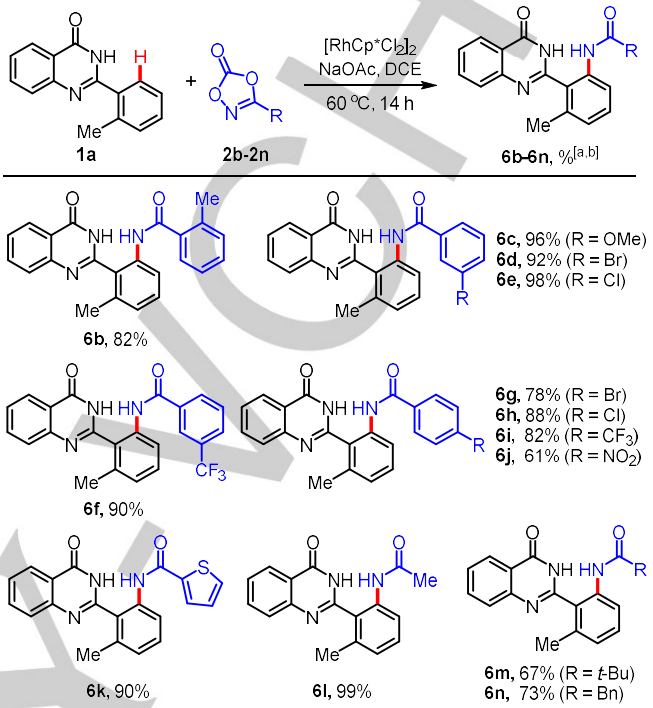
Scheme 2. Scope of 2-aryl quinazolinones. [a] Reaction conditions: **1a**–**1t** (0.2 mmol), **2a** (0.25 mmol), $[RhCp^*Cl_2]_2$ (1 mol %), NaOAc (100 mol %), DCE (1 mL) at 60 °C for 14 h under air in pressure tubes. [b] Yield isolated by flash column chromatography. [c] **2a** (0.5 mmol, 2.5 equiv.) was used.

To evaluate the substrate scope of this reaction, a range of 2-aryl quinazolinones **1b**–**1t** were reacted with dioxazolone **2a** under the optimized reaction conditions (Scheme 2). 2-Aryl quinazolinones **1b**–**1d** with *ortho*- and *meta*-substituents on the aryl ring were smoothly coupled with **2a** to afford the corresponding amidated products **3b**–**3d** in good to high yields. It is noted that the complete site-selectivity at less hindered positions was detected in case of *meta*-substituted substrates. However, a sterically congested 3,5-disubstituted compound **1e** led to no formation of amidated adduct **3e**, and most of starting material **1e** was recovered under the current reaction conditions. In addition, *para*-substituted 2-aryl quinazolinones **1f**–**1k** participated in the amidation reaction to afford bis-amidated products **3f**–**3k** in high yields under the slightly modified reaction conditions. Meanwhile, the scope of quinazolinone motif has been evaluated under the standard reaction conditions. To our delight, the current protocol could be applied to the C5-, C6-, C7-, and C8-substituted 2-aryl quinazolinones **1l**–**1r**, providing the desired products **3l**–**3r** in good to high yields. The site-selective C–H amidation of 2-aryl quinazolin-4(3*H*)-ones on the *ortho*-position of aryl ring was confirmed by the X-ray crystallographic data of product **3m** (CCDC2002612**,** see the Supporting Information for details). It is noteworthy that the tolerance of iodo and bromo groups (**3i**, **3j**, **3m** and **3n**) can provide a versatile synthetic handle for further cross-coupling reactions. Furthermore, we were pleased to observe the C–H amidation reaction of heterocycle-containing substrates to afford the corresponding products **3s** (99%) and **3t** (84%), respectively.



Scheme 3. C–H amidation of isoquinolone and benzothiadiazine dioxide.

Isoquinolone as a structural isostere of quinazolinone is a key motif found in a range of bioactive natural products.[10] Consequently, the structural modifications of isoquinolones are among recent intensive topic in organic and medicinal chemistry.[11] Thus, the reaction of isoquinolone **4a** with **2a** were subjected under the standard reaction conditions (Scheme 3). To our pleasure, our desired product **5a** was formed in 64% yield. It is mentioned that no formation of bis-amidated adduct was observed. Given functional similarities between carboxamide and sulfonamide, we anticipated that benzothiadiazine dioxide can also undergo the C–H amidation reaction. However, this reaction between **4b** and **2a** was found to be unsuccessful to deliver **5b** under the current reaction conditions.

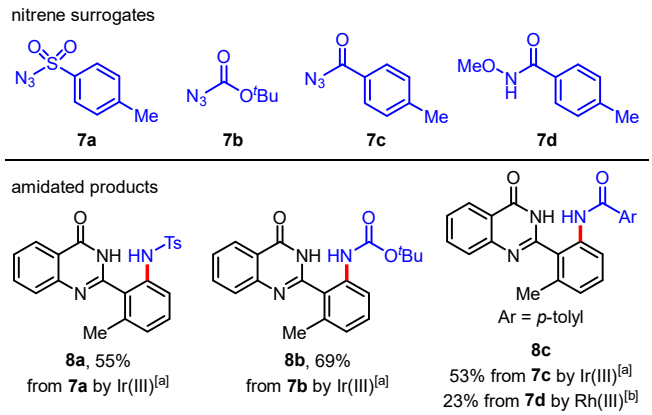


Scheme 4. Scope of dioxazolones. [a] Reaction conditions: **1a** (0.2 mmol), **2b**–**2n** (0.25 mmol), $[RhCp^*Cl_2]_2$ (1 mol %), NaOAc (100 mol %), DCE (1 mL) at 60 °C for 14 h under air in pressure tubes. [b] Yield isolated by flash column chromatography.

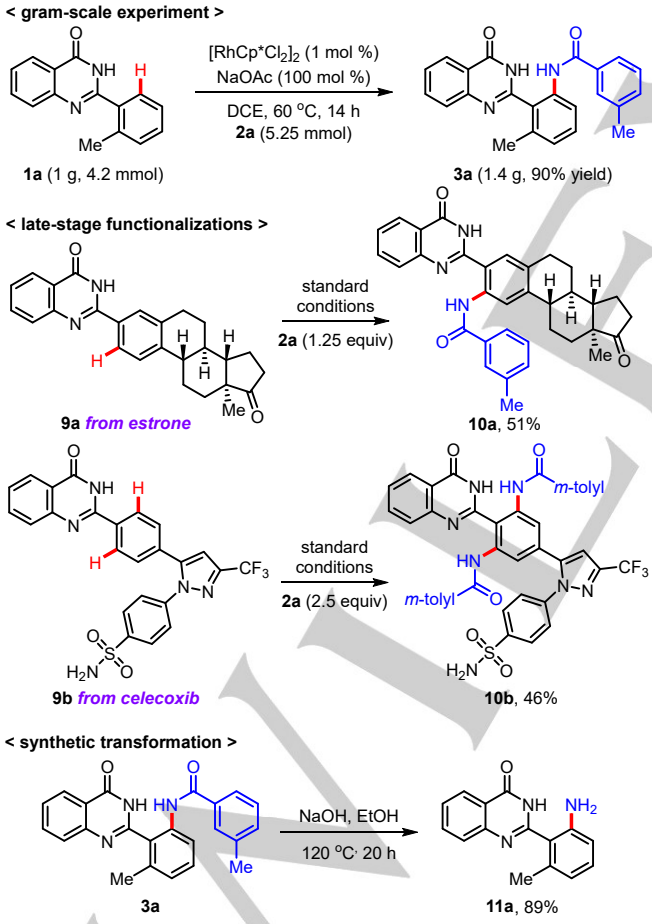
With successful screening data of quinazolinones in hand, the scope of dioxazolones **2b**–**2n** was examined (Scheme 4). Regardless of electronic and steric effects on aromatic ring, a range of dioxazolones **2b**–**2j** were successfully coupled with **1a**, providing **6b**–**6j** in good to high yields. Notably, dioxazolone **2j** with a NO_2 group, which is often problematic in the C–H functionalization event, was also tolerable in this transformation. Additionally, heterocycle-containing dioxazolone **2k** was also compatible to afford **6k** in 90% yield. Furthermore, this process is not limited with (hetero)aryl-substituted dioxazolones. Alkyl-substituted dioxazolones **2l**–**2n** also reacted with **1a** to furnish the corresponding products **6l**–**6n** in good to high yields.

Next, we envisioned that this protocol could be extended to the C–H amidation reactions by using well-defined nitrene surrogates. To our delight, tosyl azide **7a** was smoothly coupled with **1a** at room temperature to provide **8a** in 55% yield under cationic Ir(III) catalysis (Scheme 5). It should be mentioned that neutral or cationic Rh(III) catalysts was found to be ineffective in this reaction, and the chemical yield of **8a** can be improved by further optimization of reaction conditions. Additionally, BOC azide **7b** also proved to be an amenable substrate under cationic Ir(III) catalysis, furnishing the desired product **8b** in 69% yield. Moreover, C–H amidated adduct **8c** was obtained from acyl azide **7c** and *N*-methoxyamide **7d**, respectively, under cationic Ir(III) or Rh(III) catalysis. It is noted that nitrene surrogates **7a**–**7d** were less reactive or unreactive with neutral

Ir(III) or Rh(III) catalysts under otherwise identical reaction conditions.

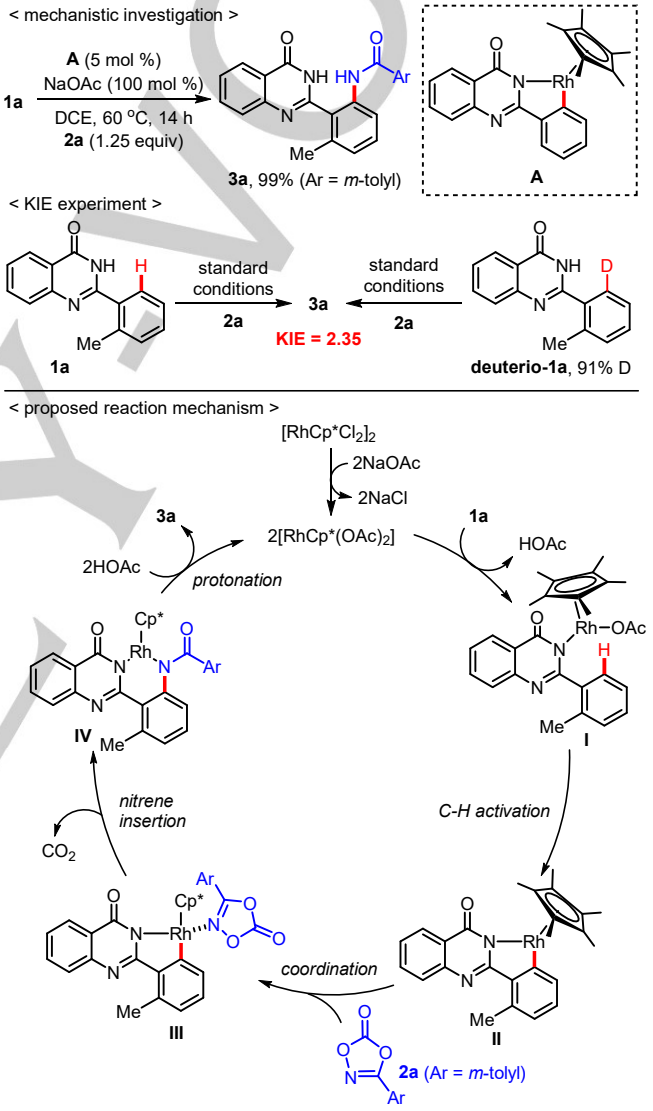


Scheme 5. Amidation by other nitrene surrogates. [a] Reaction conditions: **1a** (0.2 mmol), **7a**–**7c** (0.25 mmol), $[IrCp^*Cl_2]_2$ (2.5 mol %), $AgNTf_2$ (10 mol %), DCE (1 mL) at room temperature for 20 h under air in pressure tubes. [b] Reaction conditions: **1a** (0.2 mmol), **7d** (0.25 mmol), $[RhCp^*Cl_2]_2$ (2.5 mol %), $AgSbF_6$ (10 mol %), NaOAc (30 mol %), DCE (1 mL) at 100 °C for 20 h under air in pressure tubes.



Scheme 6. Gram-scale experiment, late-stage functionalizations and synthetic transformation.

To demonstrate the synthetic utility of the developed method, the gram-scale experiment and late-stage functionalizations were performed (Scheme 6). The reaction of **1a** (1 g, 4.2 mmol) with **2a** was successfully carried out, providing 1.4 g of **3a** in 90% yield. The late-stage C–H amidation reactions of quinazolinone derivatives **9a** and **9b** derived from estrone and celecoxib afforded the corresponding adducts **10a** (51%) and **10b** (46%), respectively. To highlight the synthetic applicability of synthesized products, the deprotection of an *N*-aroyl group on **3a** was performed under basic hydrolysis conditions, and aniline adduct **11a** was obtained in 89% yield.



Scheme 7. Mechanistic investigation, KIE experiment, and proposed reaction mechanism.

To gain mechanistic insight, the reaction of **1a** with **2a** in the presence of rhodacycle complex **A** was performed (Scheme 7). We were pleased to observe the formation of **3a** in an almost quantitative yield (99%), suggesting that the catalytic cycle might be initiated by the formation of rhodacycle complex. A kinetic isotope effect (KIE) experiment between **1a** and **deuterio-1a** resulted in a k_H/k_D value of 2.35, thus revealing that C–H

cleavage might be involved in the rate-limiting step of this process. Based on preliminary mechanistic investigation and reported literatures,[12] a plausible reaction pathway is depicted. A monomeric [RhCp*$(OAc)_2$] as an active catalyst can be generated from $[RhCp^*Cl_2]_2$ by the ligand exchange of NaOAc.[13] The formation of intermediate **I** assisted by NaOAc followed by C–H activation can take place to deliver rhodacycle **II**. In this stage, dioxazolone **2a** can coordinate into **II** to give intermediate **III**, which can undergo migratory insertion to afford N-Rh(III)-N species **IV** with release of CO_2 gas. Protonation of **IV** provides the desired product **3a** and a recyclable [RhCp*$(OAc)_2$] catalyst.

Conclusion

In conclusion, we have described the site-selective modifications of quinazolinones via the rhodium(III)-catalyzed C−H amidation reactions of 2-aryl quinazolinones with dioxazolones, organic azides, and *N*-methoxyamides as nitrene surrogates. This method can be also applied into the C−N bond forming reactions of isoquinolone as a quinazolinone isostere. Broad functional group tolerance, large-scale reaction, and late-stage C−H functionalizations demonstrate the synthetic potential of the developed method. Preliminary mechanistic investigations elucidate a plausible reaction mechanism of this process.

Experimental Section

General procedure and characterization data for the amidation of 2-aryl quinazolin-4(3*H*)-ones with dioxazolones (3a–3t, 5a and 6b–6n): To an oven-dried sealed tube charged with 2-(*o*-tolyl)quinazolin-4(3*H*)-one (**1a**) (47.3 mg, 0.2 mmol, 100 mol %), $[Cp^*RhCl_2]_2$ (1.2 mg, 0.002 mmol, 1 mol %) and NaOAc (16.4 mg, 0.2 mmol, 100 mol %) were added 3-(*m*-tolyl)-1,4,2-dioxazol-5-one (**2a**) (44.3 mg, 0.25 mmol, 125 mol %) and DCE (1 mL) under air at room temperature. The reaction mixture was allowed to stir at 60 °C for 14 h, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 1:1) to afford **3a** (71.6 mg) in 97% yield.

3-Methyl-*N*-(3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (3a): 71.6 mg (97%); white solid; mp = 235.9–236.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.31 (br, 1H), 10.14 (s, 1H), 8.31 (d, *J* = 7.2 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.86–7.78 (m, 2H), 7.57–7.54 (m, 2H), 7.46 (s, 1H), 7.27–7.22 (m, 3H), 6.88 (d, *J* = 7.6 Hz, 1H), 2.40 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 162.3, 152.1, 148.1, 138.3, 136.8, 136.1, 134.9, 134.2, 132.7, 130.8, 128.5, 127.5, 127.4, 126.9 (two carbons overlap), 126.8, 124.4, 123.9, 121.0, 120.1, 21.2, 20.6; IR (KBr) υ 3068, 1675, 1601, 1529, 1466, 1296, 1267, 1210, 1140, 941, 770 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{20}N_3O_2$ $[M+H]^+$ 370.1550, found 370.1549.

***N*-(3-Methoxy-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)-3-methylbenzamide (3b):** 67.9 mg (88%); brown solid; mp = 248.9–251.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.15 (s, 1H), 10.74 (s, 1H), 8.53 (d, *J* = 8.4 Hz, 1H), 8.32 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.81–7.76 (m, 3H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 8.4 Hz, 2H), 7.38–7.36 (m, 2H), 6.84 (d, *J* = 8.4 Hz, 1H), 4.01 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 161.1, 157.9, 151.3, 147.3, 140.9, 138.4, 135.6, 134.7, 133.0, 132.7, 128.5, 127.9, 127.3, 126.7, 126.5, 124.8, 121.1, 115.4, 107.8, 160.5, 56.5, 21.4; IR (KBr) υ 2922, 2853, 1678, 1606, 1592, 1561, 1477, 1460, 1234, 1137, 1014 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{20}N_3O_3$ $[M+H]^+$ 386.1499, found 386.1499.

3-Methyl-*N*-(4-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (3c): 65.1 mg (88%); yellow solid; mp = 255.4–258.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.88 (s, 1H), 10.95 (s, 1H), 8.80 (d, *J* = 8.4 Hz, 1H), 8.34 (d, *J* = 7.6 Hz, 1H), 7.87–7.72 (m, 5H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.43–7.37 (m, 3H), 2.46 (s, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 162.7, 152.2, 147.4, 138.4, 137.2, 135.6, 135.2, 133.6, 133.2, 132.6, 128.5, 128.0, 127.6, 127.5, 126.7, 126.6, 124.7, 123.1, 122.1, 118.3, 21.4, 20.9; IR (KBr) υ 2922, 2853, 1674, 1613, 1586, 1523, 1477, 1408, 1282, 1189, 1038, 971, 808 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{20}N_3O_2$ $[M+H]^+$ 370.1550, found 370.1550.

3-Methyl-*N*-(2-(4-oxo-3,4-dihydroquinazolin-2-yl)-4-(trifluoromethyl)phenyl)benzamide (3d): 59.5 mg (70%); white solid; mp = 268.2–270.3 °C; ^{1}H NMR (700 MHz, DMSO-d_6) δ 8.97 (d, *J* = 9.1 Hz, 1H), 8.83 (s, 1H), 8.10–8.07 (m, 3H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* = 5.6 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.49–7.45 (m, 2H), 7.35 (s, 1H), 2.47 (s, 3H); ^{13}C NMR (175 MHz, DMSO-d_6) δ 165.4, 153.6, 147.4, 143.1, 139.8, 138.2, 134.7, 132.6, 132.2, 131.7, 128.6, 128.0, 126.8, 125.9, 125.7, 125.1, 124.5 (q, J_{C-F} = 268.9 Hz), 124.4, 124.1, 123.4, 121.6, 120.2, 20.8; IR (KBr) υ 2957, 2922, 2853, 1681, 1611, 1582, 1531, 1467, 1414, 1338, 1315, 1273, 1171, 1108, 960 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{17}F_3N_3O_2$ $[M+H]^+$ 424.1268, found 424.1268.

***N,N'*-(2-(4-Oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene)bis(3-methylbenzamide) (3f):** 86.0 mg (88%); white solid; mp = 225.1–227.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$/CD_3OD = 10:1 v/v) δ 8.14 (d, *J* = 7.6 Hz, 1H), 7.83–7.72 (m, 4H), 7.59–7.56 (m, 4H), 7.47–7.43 (m, 2H), 7.24–7.19 (m, 4H), 2.25 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$/CD_3OD = 10:1 v/v) δ 166.6, 166.5, 162.3, 150.5, 138.4, 136.6, 136.5, 134.8, 133.9, 133.8, 132.8, 131.9, 128.5, 128.4, 127.7, 127.5, 126.9, 126.5, 124.3, 121.2, 121.1, 120.7, 118.3, 21.1; IR (KBr) υ 2957, 2922, 2853, 1678, 1657, 1604, 1471, 1448, 1416, 1332, 1294, 1268, 1158, 925 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{25}N_4O_3$ $[M+H]^+$ 489.1921, found 489.1922.

***N,N'*-(5-Methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene)bis(3-methylbenzamide) (3g):** 80.3 mg (80%); white solid; mp = 209.3–211.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.46 (s, 1H), 10.11 (s, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.72–7.69 (m, 2H), 7.58–7.52 (m, 6H), 7.47–7.43 (m, 1H), 7.17–7.11 (m, 4H), 2.23 (s, 3H), 2.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 162.7, 150.5, 148.0, 142.9, 138.4, 136.3, 134.9, 133.9, 132.7, 128.5, 127.6, 127.4, 127.0, 126.5, 124.3, 122.2, 120.5, 115.8, 21.6, 21.1; IR (KBr) υ 3272, 2923, 2853, 1670, 1589, 1565, 1515, 1466, 1438, 1276, 1199, 1132, 1039, 944, 821 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{27}N_4O_3$ $[M+H]^+$ 503.2078, found 503.2078.

***N,N'*-(5-Methoxy-2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene)bis(3-methylbenzamide) (3h):** 95.5 mg (92%); white solid; mp = 233.8–234.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.44 (s, 1H), 10.24 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.71–7.70 (m, 2H), 7.56–7.53 (m, 4H), 7.47 (s, 2H), 7.45–7.41 (m, 1H), 7.17–7.11 (m, 4H), 3.74 (s, 3H), 2.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 162.9, 162.0, 150.6, 148.0, 138.4, 138.1, 134.8, 134.0, 132.8, 128.4, 127.7, 127.2, 126.9, 126.5, 124.3, 120.4, 110.3, 106.8, 55.5, 21.1; IR (KBr) υ 3060, 2925, 1671, 1604, 1589, 1536, 1467, 1278, 1206, 1161, 1085, 1049, 969, 946, 852,

807 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{27}N_4O_4$ $[M+H]^+$ 519.2027, found 519.2027.

***N,N'*-(5-Bromo-2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene)bis(3-methylbenzamide) (3i):** 110.1 mg (97%); white solid; mp = 269.8–272.3 °C; ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$ = 10:1 v/v) δ 8.18 (d, *J* = 8.0 Hz, 1H), 8.10–8.09 (m, 2H), 7.79–7.78 (m, 2H), 7.62–7.58 (m, 3H), 7.51–7.47 (m, 1H), 7.29–7.24 (m, 5H), 2.29 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3/CD_3OD$ = 10:1 v/v) δ 166.5, 162.2, 150.2, 147.7, 138.6, 137.7, 137.6, 135., 133.6, 133.5, 133.1, 128.6, 128.5, 127.9, 127.8, 126.9, 126.7, 125.8, 124.4, 123.5, 12.9, 116.2, 21.2; IR (KBr) υ 2920, 2852, 1672, 1599, 1563, 1509, 1462, 1376, 1268 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{24}BrN_4O_3$ $[M+H]^+$ 567.1026, found 567.1027.

***N,N'*-(5-Iodo-2-(4-oxo-3,4-dihydroquinazolin-2-yl)-1,3-phenylene)bis(3-methylbenzamide) (3j):** 116.8 mg (95%); yellow solid; mp = 243.2–244.8 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.15 (s, 1H), 7.99 (s, 1H), 7.71–7.74 (m, 2H), 7.56–7.53 (m, 4H), 7.46 (s, 1H), 7.20–7.19 (m, 2H), 7.18–7.16 (m, 2H), 2.19 (s, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 166.5, 160.3, 160.2, 156.0, 141.4, 138.7, 137.6, 135.2, 133.5, 133.2, 130.6, 128.7, 128.0, 127.8, 126.9, 124.4, 110.1, 105.7, 21.2; IR (KBr) υ 2954, 2921, 2853, 1665, 1591, 1560, 1524, 1466, 1419, 1295, 1267, 1220, 1149, 944, 808 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{24}IN_4O_3$ $[M+H]^+$ 615.0888, found 615.0888.

***N,N'*-(2-(4-Oxo-3,4-dihydroquinazolin-2-yl)-5-(trifluoromethyl)-1,3-phenylene)bis(3-methylbenzamide) (3k):** 100.2 mg (90%); white solid; mp = 254.3–257.2 °C; ^{1}H NMR (700 MHz, DMSO-d_6) δ 12.68 (s, 1H), 10.98 (br, 2H), 8.35 (s, 2H), 8.14 (d, *J* = 9.1 Hz, 1H), 7.89 (t, *J* = 7.7 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.67–7.64 (m, 4H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.39–7.36 (m, 4H), 2.32 (s, 3H); ^{13}C NMR (175 MHz, DMSO-d_6) δ 166.1, 162.2, 150.6, 148.6, 138.9, 138.3, 134.9, 134.8, 133.0, 131.1 (q, J_{C-F} = 31.6 Hz), 128.9, 128.4, 127.6, 127.4, 126.4, 125.3, 124.0 (q, J_{C-F} = 270.5 Hz), 122.1, 120.6, 115.6, 21.3; IR (KBr) υ 3056, 2923, 2854, 1674, 1602, 1577, 1505, 1434, 1355, 1290, 1268, 1165, 1128, 1105, 947, 875 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{24}F_3N_4O_3$ $[M+H]^+$ 557.1795, found 557.1796.

***N*-(2-(5-Chloro-4-oxo-3,4-dihydroquinazolin-2-yl)-3-methylphenyl)-3-methylbenzamide (3l):** 73.5 mg (91%); yellow solid; mp = 220.1–222.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.05 (br, 1H), 10.10 (s, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.72–7.66 (m, 2H), 7.57–7.50 (m, 3H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.28–7.22 (m, 3H), 6.98 (d, *J* = 7.6 Hz, 1H), 2.44 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 130.6, 152.8, 150.3, 138.4, 136.9, 136.2, 134.8, 134.4, 134.2, 132.7, 131.2, 130.2, 128.6, 127.5, 127.1, 126.1, 124.3, 123.1, 120.3, 118.2, 21.3, 20.7; IR (KBr) υ 3061, 2923, 1672, 1592, 1536, 1463, 1410, 1296, 1267, 1197, 1129, 967, 894, 816, 737 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}ClN_3O_2$ $[M+H]^+$ 404.1160, found 404.1160.

***N*-(2-(6-Iodo-4-oxo-3,4-dihydroquinazolin-2-yl)-3-methylphenyl)-3-methylbenzamide (3m):** 83.2 mg (84%); light yellow solid; mp = 139.8–141.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.65 (br, 1H), 9.92 (s, 1H), 8.61 (d, *J* = 2.0 Hz, 1H), 8.04–7.95 (m, 2H), 7.48–7.42 (m, 3H), 7.28–7.21 (m, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.76 (d, *J* = 7.6 Hz, 1H), 2.32 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 160.7, 152.7, 147.3, 143.5, 138.3, 137.0, 135.7, 135.5, 133.8, 132.8, 130.6, 128.5 (two carbon overlap), 127.5, 127.1, 124.3, 124.2, 122.6, 120.4, 91.9, 21.2, 20.5; IR (KBr) υ 3058, 2925, 1675, 1593, 1530, 1460, 1400, 1294, 1265, 1200, 1146, 1113, 941 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}IN_3O_2$ $[M+H]^+$ 496.0517, found 496.0518.

***N*-(2-(6-Bromo-4-oxo-3,4-dihydroquinazolin-2-yl)-3-methylphenyl)-3-methylbenzamide (3n):** 78.9 mg (88%); light yellow solid; mp = 224.8–227.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.62 (s, 1H), 9.91 (s, 1H), 8.41 (d, *J* = 2.4 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.86 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.43 (s, 1H), 7.28–7.21 (m, 2H), 7.12 (t, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 2.33 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 161.0, 152.5, 146.9, 138.4, 137.9, 137.0, 135.7, 133.8, 132.8, 130.7, 129.3, 128.6, 128.5, 127.5, 127.1, 124.3, 124.2, 122.4, 121.0, 120.4, 21.2, 20.5; IR (KBr) υ 3062, 2923, 2854, 1675, 1597, 1572, 1527, 1461, 1405, 1294, 1265, 1199, 1145, 1111, 941, 833 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}BrN_3O_2$ $[M+H]^+$ 448.0655, found 448.0656.

***N*-(2-(6-Chloro-4-oxo-3,4-dihydroquinazolin-2-yl)-3-methylphenyl)-3-methylbenzamide (3o):** 64.6 mg (80%); white solid; mp = 210.8–212.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.47 (br, 1H), 9.91 (s, 1H), 8.26 (d, *J* = 2.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.75–7.67 (m, 2H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.44 (s, 1H), 7.29–7.22 (m, 2H), 7.17 (t, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 2.35 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 161.2, 152.4, 146.6, 138.4, 136.9, 135.8, 135.2, 133.9, 133.3, 132.8, 130.8, 128.5, 128.4, 127.5, 127.1, 126.2, 124.2, 124.1, 122.1, 120.4, 21.2, 20.5; IR (KBr) υ 2922, 2853, 1678, 1602, 1572, 1532, 1463, 1410, 1328, 1295, 1202, 1146, 1119, 1073, 943, 879, 833 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}ClN_3O_2$ $[M+H]^+$ 404.1160, found 404.1160.

3-Methyl-*N*-(3-methyl-2-(6-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (3p): 62.1 mg (81%); pale yellow solid; mp = 245.7–247.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.36 (s, 1H), 10.16 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 8.09 (s, 1H), 7.68–7.61 (m, 2H), 7.55 (d, *J* = 6.4 Hz, 1H), 7.47 (s, 1H), 7.25–7.18 (m, 3H), 6.85 (d, *J* = 7.6 Hz, 1H), 2.52 (s, 3H), 2.37 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 162.3, 151.2, 146.1, 138.3, 137.8, 136.8, 136.3, 136.1, 134.2, 132.6, 130.6, 128.5, 127.5, 126.9, 126.7, 126.2, 124.3, 124.0, 120.7, 120.0, 21.3, 21.2, 20.6; IR (KBr) υ 3056, 2924, 1671, 1598, 1527, 1487, 1463, 1414, 1295, 1266, 1198, 1141, 1085, 832 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{22}N_3O_2$ $[M+H]^+$ 384.1707, found 384.1707.

***N*-(2-(7-Methoxy-4-oxo-3,4-dihydroquinazolin-2-yl)-3-methylphenyl)-3-methylbenzamide (3q):** 79.1 mg (99%); yellow solid; mp = 213.3–214.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.48 (s, 1H), 10.26 (s, 1H), 8.33–8.28 (m, 2H), 7.71 (d, *J* = 6.8 Hz, 1H), 7.61 (s, 1H), 7.42–7.36 (m, 3H), 7.26–7.23 (m, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 4.05 (s, 3H), 2.54 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 165.0, 162.0, 152.8, 150.3, 138.3, 136.8, 136.1, 134.3, 132.6, 130.8, 128.4, 128.3, 127.6, 126.9, 124.3, 124.1, 120.2, 117.1, 114.3, 107.9, 55.7, 21.2, 20.6; IR (KBr) υ 2952, 2922, 2854, 1731, 1666, 1599, 1565, 1529, 1458, 1358, 1292, 1269, 1209, 1172, 1099, 1024, 940, 836 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{22}N_3O_3$ $[M+H]^+$ 400.1656, found 400.1656.

3-Methyl-*N*-(3-methyl-2-(8-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (3r): 55.2 mg (72%); yellow solid; mp = 169.1–171.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.29 (s, 1H), 10.05 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 1H), 7.50–7.43 (m, 2H), 7.33–7.26 (m, 2H), 7.25–7.20 (m, 2H), 6.93 (d, *J* = 7.6 Hz, 1H), 2.61 (s, 3H), 2.41 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 162.8, 150.7, 146.7, 138.3, 136.7, 135.9, 135.7, 135.4, 134.5, 132.6, 130.6, 128.5, 127.3, 127.1, 126.9, 124.5, 124.4, 124.2, 121.0, 120.0, 21.0, 20.7, 17.6; IR (KBr) υ 2955, 1922, 1853, 1730, 1667, 1599, 1564, 1530, 1503, 1457, 1358, 1292, 1267, 1209, 1172, 1099, 941

cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{22}N_3O_2$ $[M+H]^+$ 384.1707, found 384.1707.

3-Methyl-*N*-(3-methyl-2-(4-oxo-3,4-dihydrothieno[3,2-*d*]pyrimidin-2-yl)phenyl)benzamide (3s): 74.4 mg (99%); white solid; mp = 220.1–222.2 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.59 (br, 1H), 9.84 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 5.6 Hz, 1H), 7.52 (d, *J* = 6.8 Hz, 1H), 7.45 (s, 1H), 7.36 (d, *J* = 5.6 Hz, 1H), 7.29–7.23 (m, 2H), 7.17 (t, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 2.34 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 158.4, 156.6, 153.5, 138.4, 137.1, 135.8, 135.2, 133.9, 132.7, 130.8, 128.5, 127.6, 127.2, 124.4, 124.3, 124.3, 122.2, 120.8, 21.2, 20.5; IR (KBr) υ 3058, 2922, 1668, 1605, 1587, 1513, 1464, 1418, 1294, 1269, 1132, 1088, 1043, 789 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{18}N_3O_2S$ $[M+H]^+$ 376.1114, found 376.1114.

3-Methyl-*N*-(3-methyl-2-(4-oxo-3,4-dihydropyrido[3,4-*d*]pyrimidin-2-yl)phenyl)benzamide (3t): 62.3 mg (84%); yellow solid; mp = 299.7–301.3 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.37 (br 1H), 9.79 (s, 1H), 9.20 (s, 1H), 8.73 (d *J* = 4.8 Hz, 1H), 8.09 (d, *J* = 5.2 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.53–7.47 (m, 2H), 7.29–7.28 (m, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 2.38 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 160.8, 154.0, 150.5, 147.0, 142.8, 138.7, 137.0, 135.8, 133.7, 133.1, 131.1, 128.7, 127.5, 127.4, 126.2, 124.4, 124.1, 120.9, 118.7, 21.3, 20.6; IR (KBr) υ 2922, 2853, 1679, 1602, 1511, 1460, 1423, 1320, 1293, 1263, 1196, 1169, 1142, 1078, 1033, 943 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{19}N_4O_2$ $[M+H]^+$ 371.1503, found 371.1503.

3-Methyl-*N*-(2-(1-oxo-1,2-dihydroisoquinolin-3-yl)phenyl)benzamide (5a): 45.4 mg (64%); yellow solid; mp = 134.1–135.3 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.45 (s, 1H), 9.05 (s, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.59–7.51 (m, 5H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.07–6.99 (m, 2H), 6.74 (s, 1H), 1.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 164.3, 138.3, 138.0, 137.8, 135.3, 133.9, 133.1, 132.4, 130.6, 130.1, 129.3, 128.4, 127.5, 127.3, 127.2, 126.5, 126.4, 126.3, 124.4, 124.1, 107.8, 20.9; IR (KBr) υ 3054, 2922, 2854, 1634, 1606, 1515, 1473, 1445, 1346, 1302, 1283, 1150, 1022, 938, 837 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}N_2O_2$ $[M+H]^+$ 355.1441, found 355.1440.

2-Methyl-*N*-(3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (6b): 60.6 mg (82%); white solid; mp = 225.8–227.1 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.59 (br, 1H), 9.35 (s, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 7.2 Hz, 1H), 7.77 (t, *J* =8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.38–7.31 (m, 2H), 7.28–7.25 (m, 2H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.10–7.04 (m, 2H), 2.40 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 162.0, 151.6, 148.0, 137.1, 136.9, 136.1, 135.3, 135.0, 131.4, 131.0, 130.5, 127.6, 127.5, 127.1, 126.9, 126.7, 125.7, 124.9, 121.0, 120.9, 20.5, 20.0; IR (KBr) υ 2952, 2925, 1854, 1675, 1605, 1524, 1466, 1296, 1266, 1137, 946, 739 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{20}N_3O_2$ $[M+H]^+$ 370.1550, found 370.1550.

2-Methyl-*N*-(3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (6c): 74.2 mg (96%); white solid; mp = 225.8–227.1 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.59 (br, 1H), 9.35 (s, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 7.2 Hz, 1H), 7.77 (t, *J* =8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.38–7.31 (m, 2H), 7.28–7.25 (m, 2H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.10–7.04 (m, 2H), 2.40 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 162.0, 151.6, 148.0, 137.1, 136.9, 136.1, 135.3, 135.0, 131.4, 131.0, 130.5, 127.6, 127.5, 127.1, 126.9, 126.7, 125.7, 124.9, 121.0, 120.9, 20.5, 20.0; IR (KBr) υ 2952, 2925, 2854, 1675, 1605, 1524, 1466, 1296, 1266, 1137, 946, 739 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{20}N_3O_2$ $[M+H]^+$ 370.1550, found 370.1550.

3-Bromo-*N*-(3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (6d): 80.0 mg (92%); white solid; mp = 228.7–229.3 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.62 (s, 1H), 10.28 (s, 1H), 8.31 (d, *J* = 8.8 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.88 (t, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.63–7.56 (m, 3H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 161.9, 151.8, 148.0, 136.7, 136.1, 135.3, 133.1, 131.9, 131.1, 128.6, 127.8, 127.3, 126.9, 126.8, 126.7, 123.7, 121.0, 120.3, 20.8; IR (KBr) υ 3058, 2923, 1671, 1601, 1533, 1466, 1416, 1294, 1266, 1139, 1070, 1009, 949, 840, 742 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}BrN_3O_2$ $[M+H]^+$ 434.0499, found 434.0500.

3-Chloro-*N*-(3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (6e): 76.5 mg (98%); yellow solid; mp = 233.8–234.9 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.80 (br, 1H), 10.44 (s, 1H), 8.29 (d, *J* = 7.6 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.89–7.83 (m, 2H), 7.74 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 9.2 Hz, 1H), 7.36–7.29 (m, 2H), 7.02 (d, *J* = 7.6 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 162.2, 151.7, 147.9, 136.7, 136.2, 136.1, 135.3, 134.8, 132.0, 131.1, 130.0, 127.8, 127.4, 127.1 (two carbons overlap), 126.8, 125.4, 123.5, 120.8, 120.2, 20.8; IR (KBr) υ 3064, 2920, 1673, 1601, 1567, 1534, 1466, 1419, 1294, 1258, 1134, 1071, 938, 776 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}ClN_3O_2$ $[M+H]^+$ 390.1004, found 390.1005.

***N*-(3-Methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)-3-(trifluoromethyl)benzamide (6f):** 76.3 mg (90%); white solid; mp = 234.1–236.1 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.18 (br, 1H), 10.39 (s, 1H), 8.27 (d, *J* = 7.2 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.00–7.98 (m, 2H), 7.84 (t, *J* = 8.0 Hz, 1H), 7.78–7.71 (m, 2H), 7.57–7.50 (m, 2H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 162.4, 151.8, 147.9, 136.9, 135.9, 135.3, 135.2, 131.3, 131.0, 130.7, 129.4, 128.5 (q, J_{C-F} = 3.4 Hz), 127.8, 127.5, 126.9, 126.7, 123.9, 123.6 (q, J_{C-F} = 3.4 Hz), 123.5 (q, J_{C-F} = 277.1 Hz), 120.7, 120.4, 20.7; IR (KBr) υ 3067, 2973, 2927, 1672, 1604, 1531, 1467, 1332, 1299, 1253, 1168, 1127, 1073, 939, 810 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{17}F_3N_3O_2$ $[M+H]^+$ 424.1267, found 424.1267.

4-Bromo-*N*-(3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (6g): 67.8 mg (78%); white solid; mp = 227.3–228.5 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.69 (s, 1H), 10.28 (s, 1H), 8.31 (d, *J* = 8.8 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.88 (t, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.63–7.56 (m, 3H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 162.0, 151.8, 148.0, 136.7, 136.1, 135.3, 133.1, 131.9, 131.1, 128.6, 127.8, 127.3, 126.9, 126.8, 126.7, 123.7, 120.9, 120.3, 20.8; IR (KBr) υ 3064, 2922, 1671, 1600, 1534, 1466, 1416, 1294, 1262, 1139, 1070, 1009, 950, 841 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}BrN_3O_2$ $[M+H]^+$ 434.0499, found 434.0499.

4-Chloro-*N*-(3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (6h): 68.7 mg (88%); white solid; mp = 237.1–238.7 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.89 (s, 1H), 10.27 (s, 1H), 8.30 (d, *J* = 7.6 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.89–7.85 (m, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.8 Hz, 2H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.34–7.27 (m, 3H), 6.97 (d, *J* = 7.6 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 162.1, 151.9, 148.0, 138.3, 136.8, 136.1, 135.2, 132.7,

131.0, 128.9, 128.4, 127.7, 127.3, 126.9, 126.7, 123.8, 120.9, 120.3, 20.7; IR (KBr) υ 2957, 2923, 2854, 1671, 1598, 1565, 1534, 1465, 1293, 1262, 1210, 1137, 1092, 1013, 950, 844 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}ClN_3O_2$ $[M+H]^+$ 390.1004, found 390.1005.

***N*-(3-Methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)-4-(trifluoromethyl)benzamide (6i):** 69.5 mg (82%); white solid; mp = 220.5–223.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.08 (br, 1H), 10.39 (s, 1H), 8.29 (d, *J* = 7.2 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.89–7.85 (m, 3H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.62–7.56 (m, 3H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 162.3, 151.9, 147.8, 137.5, 137.0, 135.9, 135.3, 133.7, 133.4, 131.1, 127.8, 127.5 (two carbons overlap), 127.3, 126.9, 126.6, 125.7 (q, J_{C-F} = 3.4 Hz), 124.0, 123.5 (q, J_{C-F} = 271.1 Hz), 120.5, 119.4, 20.7; IR (KBr) υ 3070, 2971, 2924, 1671, 1603, 1534, 1466, 1323, 1300, 1262, 1167, 1126, 1066, 1063, 951, 856, 766 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{17}F_3N_3O_2$ $[M+H]^+$ 424.1267, found 424.1267.

***N*-(3-Methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)-4-nitrobenzamide (6j):** 48.8 mg (61%); light yellow solid; mp = 250.1–251.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.56 (s, 1H), 8.30 (d, *J* = 7.5 Hz, 1H), 8.82 (d, *J* = 9.0 Hz, 2H), 7.95–7.89 (m, 3H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 7.5 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 163.0, 161.9, 161.8, 151.8, 149.8, 139.9, 136.8, 136.0, 135.5, 131.4, 128.2, 128.1, 127.9, 127.0, 126.5, 123.9, 123.6, 120.9, 120.5, 20.8; IR (KBr) υ 3066, 2923, 2854, 1671, 1601, 1524, 1466, 1345, 1295, 1262, 1139, 1107, 1012, 951, 851 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}N_4O_4$ $[M+H]^+$ 401.1244, found 401.1245.

***N*-(3-Methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)thiophene-2-carboxamide (6k):** 65.1 mg (90%); light yellow solid; mp = 232.1–233.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.09 (s, 1H), 9.95 (s, 1H), 8.34 (d, *J* = 7.6 Hz, 1H), 8.21 (d, *J* = 8.4 Hz, 1H), 7.88–7.85 (m, 2H), 7.61–7.57 (m, 1H), 7.47–7.46 (m, 2H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.05–7.01 (m, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.8, 171.5, 159.7, 151.6, 139.1, 136.3, 136.1, 135.2, 131.2, 130.9, 128.7, 127.8, 127.7, 127.2, 127.1, 126.9, 123.4, 121.0, 120.4, 20.8; IR (KBr) υ 2923, 2854, 1668, 1600, 1530, 1465, 1421, 1330, 1295, 1262, 1138, 1109, 946, 856 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{16}N_3O_2S$ $[M+H]^+$ 362.0958, found 362.0958.

***N*-(3-Methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)acetamide (6l):** 58.1 mg (99%); light yellow solid; mp = 185.3–187.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.99 (s, 1H), 8.86 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.78–7.74 (m, 2H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.28–7.24 (m, 2H), 7.02 (d, *J* = 7.6 Hz, 1H), 2.30 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 162.3, 151.7, 148.2, 136.9, 135.6, 134.9, 130.6, 127.1, 127.0, 126.7, 125.1, 121.3, 121.0, 24.3, 20.2; IR (KBr) υ 3055, 2963, 2933, 1681, 1603, 1521, 1461, 1416, 1328, 1294, 1262, 1163, 1114, 939 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{16}N_3O_2$ $[M+H]^+$ 294.1237, found 294.1238.

***N*-(3-Methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)pivalamide (6m):** 45.0 mg (67%); white solid; mp = 202.8–204.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (br, 1H), 9.19 (s, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.82 (t, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 2.38 (s, 3H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 161.9, 151.7, 148.0, 136.5, 136.1, 135.0, 130.8, 127.5, 127.1, 127.0, 126.8, 124.9, 121.0, 120.9, 39.6, 27.4, 20.4; IR (KBr) υ 3057, 2964, 2932, 1677, 1603, 1525, 1466, 1416, 1328, 1294, 1265, 1163, 1135, 938, 777 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{22}N_3O_2$ $[M+H]^+$ 336.1707, found 336.1706.

***N*-(3-Methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)-2-phenylacetamide (6n):** 54.0 mg (73%); white solid; mp = 220.5–223.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.59 (s, 1H), 8.29 (d, *J* = 8.8 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.85 (s, 1H), 7.79 (t, *J* = 8.4 Hz, 1H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 6.93 (d, *J* = 7.2 Hz, 2H), 6.83 (t, *J* = 7.2 Hz, 2H), 6.77–6.73 (m, 1H), 3.51 (s, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 162.0, 151.0, 148.2, 136.7, 135.0, 134.6, 133.4, 130.5, 128.9, 128.7, 127.8, 127.4, 127.3, 126.8, 126.5, 125.4, 121.1, 120.6, 44.6, 19.7; IR (KBr) υ 3071, 2916, 1671, 1603, 1522, 1468, 1410, 1328, 1291, 1136, 1071, 1033, 943 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{20}N_3O_2$ $[M+H]^+$ 370.1550, found 370.1551.

General procedure and characterization data for the Ir(III)-catalyzed C–H amidation (8a–8c): To an oven-dried sealed tube charged with 2-(*o*-tolyl)quinazolin-4(3*H*)-one (**1a**) (47.3 mg, 0.2 mmol, 100 mol %), $[IrCp^*Cl_2]_2$ (4.0 mg, 0.005 mmol, 2.5 mol %) and $AgNTf_2$ (7.8 mg, 0.02 mmol, 10 mol %) were added nitrene surrogate (**7a**–**7c**) (0.25 mmol, 125 mol %) and DCE (1 mL) under air at room temperature. The reaction mixture was allowed to stir at room temperature for 20 h under air, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 1:2) to afford **8a** (44.7 mg) in 55% yield.

General procedure and characterization data for the Rh(III)-catalyzed C–H amidation (8c): To an oven-dried sealed tube charged with 2-(*o*-tolyl)quinazolin-4(3*H*)-one (**1a**) (47.3 mg, 0.2 mmol, 100 mol %), $[RhCp^*Cl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), NaOAc (5.0 mg, 0.005 mmol, 2.5 mol %) and $AgSbF_6$ (6.9 mg, 0.02 mmol, 10 mol %) were added *N*-methoxy-4-methylbenzamide (**7d**) (41.3 mg, 0.25 mmol, 125 mol %) and DCE (1 mL) under air at room temperature. The reaction mixture was allowed to stir at 100 °C for 20 h under air, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 1:1) to afford **8c** (17.0 mg) in 23% yield.

4-Methyl-*N*-(3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzenesulfonamide (8a): 44.7 mg (55%); white solid; mp = 199.5–201.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.72 (s, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.58–7.52 (m, 2H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.22–7.16 (m, 3H), 6.93 (d, *J* = 8.0 Hz, 2H), 2.31 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 150.3, 147.7, 144.3, 136.5, 135.8, 135.3, 135.2, 131.2, 129.6 (two carbons overlap), 129.1, 127.8, 127.5, 126.6, 126.5 (two carbons overlap), 126.3, 124.3, 120.6, 21.5, 20.4; IR (KBr) υ 2922, 2853, 1671, 1600, 1464, 1386, 1331, 1293, 1265, 1161, 1090, 1021, 970, 940, 870, 812 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{20}N_3O_3S$ $[M+H]^+$ 406.1220, found 406.1221.

***tert*-Butyl (3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)carbamate (8b):** 48.5 mg (69%); white solid; mp = 202.3–204.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 8.29 (d, *J* = 7.6 Hz, 1H), 7.83–7.75 (m, 3H), 7.64 (s, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 2.33 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 153.4, 151.4, 148.4, 136.7, 136.3, 134.9,

130.8, 127.5, 127.4, 126.6, 126.3, 124.9, 121.0, 120.2, 80.9, 28.2, 20.4; IR (KBr) υ 2975, 2925, 1729, 1672, 1603, 1520, 1469, 1366, 1294, 1246, 1156, 1081, 945, 880 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{22}N_3O_3$ $[M+H]^+$ 352.1656, found 352.1655.

4-Methyl-*N*-(3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (8c): 39.2 mg (53%) from **7c**, 17.0 mg (23%) from **7d**; light yellow solid; mp = 241.4–243.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 1H), 10.15 (s, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.89–7.80 (m, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.93 (d, *J* = 7.2 Hz, 2H), 2.43 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 161.8, 151.8, 148.1, 142.6, 136.5, 136.4, 135.1, 131.4, 131.1, 129.3, 127.6, 127.1 (two carbons overlap), 127.0, 126.9, 123.7, 121.0, 120.4, 21.4, 20.7; IR (KBr) υ 3068, 2918, 1673, 1603, 1566, 1530, 1466, 1416, 1295, 1263, 1187, 1138, 1021, 948, 839 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{20}N_3O_2$ $[M+H]^+$ 370.1550, found 370.1550.

General procedure and characterization data for the late-stage functionalizations (10a and 10b): To an oven-dried sealed tube charged with 2-aryl quinazolinones derived from drug molecules (**9a**) (0.2 mmol, 100 mol %), $[Cp^*RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol %) and NaOAc (16.4 mg, 0.2 mmol, 100 mol %) were added 3-(*m*-tolyl)-1,4,2-dioxazol-5-one (**2a**) (44.3 mg, 0.25 mmol, 125 mol %) and DCE (1 mL) under air at room temperature. The reaction mixture was allowed to stir at 60 °C for 14 h, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 1:2) to afford **10a** (54.3 mg) in 51% yield.

3-Methyl-*N*-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-3-(4-oxo-3,4-dihydroquinazolin-2-yl)-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-2-yl)benzamide (10a): 54.3 mg (51%); white solid; mp = 303.5–304.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.93 (s, 1H), 11.40 (s, 1H), 8.87 (s, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 7.87–7.86 (m, 2H), 7.80 (t, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68 (s, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.42–7.37 (m, 2H), 2.91–2.88 (m, 2H), 2.55–2.48 (m, 2H), 2.44 (s, 3H), 2.29–2.25 (m, 1H), 2.18–2.11 (m, 1H), 2.07–1.96 (m, 3H), 1.64–1.57 (m, 3H), 1.49–1.44 (m, 3H), 0.88 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 198.6, 166.1, 162.9, 152.3, 147.6, 145.3, 138.4, 137.4, 135.5, 135.1, 132.7, 131.8, 128.5, 128.0, 127.8, 127.2, 126.7, 126.6, 126.5, 124.7, 118.9, 116.1, 50.5, 47.9, 44.9, 37.8, 35.8, 31.5, 29.7, 28.8, 26.3, 25.6, 21.4, 13.8; IR (KBr) υ 3201, 3153, 3056, 2921, 1738, 1667, 1607, 1557, 1523, 1405, 1331, 1280, 1251, 1212, 1083, 956, 901 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{34}N_3O_3$ $[M+H]^+$ 532.2595, found 532.2595.

***N,N'*-(2-(4-Oxo-3,4-dihydroquinazolin-2-yl)-5-(1-(4-sulfamoylphenyl)-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)-1,3-phenylene)bis(3-methylbenzamide) (10b):** 71.6 mg (46%); white solid; mp = 281.5–283.4 °C; ^{1}H NMR (500 MHz, CD_3OD) δ 8.16 (d, *J* = 7.5 Hz, 1H), 7.99 (d, *J* = 8.5 Hz, 2H), 7.91 (s, 2H), 7.82 (t, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.63–7.59 (m, 6H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.35–7.29 (m, 4H), 7.11 (s, 1H), 2.32 (s, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 168.6, 152.9, 149.6, 145.5, 145.3, 145.1, 144.8, 142.9, 139.8, 139.1, 135.8, 135.4, 134.0, 132.9, 129.6, 129.0, 128.6, 128.5, 128.0, 127.3, 127.1, 125.8, 123.7, 123.6 (q, J_{C-F} = 280.6 Hz), 122.2, 121.5, 119.8, 107.9, 107.8, 21.3; IR (KBr) υ 3048, 2922, 2856, 1688, 1675, 1652, 1640, 1515, 1467, 1341, 1267, 1176, 1136, 936, 824 cm^{-1}; HRMS (ESI) calcd for $C_{40}H_{31}F_3N_7O_5S$ $[M+H]^+$ 778.2054, found 778.2054.

General procedure and characterization data for the removal of *N*-aroyl group (11a): To an oven-dried sealed tube charged with 3-methyl-*N*-(3-methyl-2-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl)benzamide (**3a**) (73.9mg, 0.2 mmol, 100 mol %) and EtOH (2 mL) and added NaOH (448.0 mg, 11.2 mmol, 56 equiv.) under air at room temperature. The reaction mixture was allowed to stir at 120 °C for 20 h, and cooled to room temperature. The reaction was quenched with H_2O and the mixture was extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc = 2:1) to afford 44.8 mg of **11a** in 89% yield.

2-(2-Amino-6-methylphenyl)quinazolin-4(3*H*)-one (11a): 44.8 mg (89%); yellow solid; mp = 175.7–177.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 (br, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.77–7.71 (m, 2H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 4.20 (br, 2H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 152.2, 148.8, 145.0, 136.9, 134.6, 130.8, 127.4, 127.0, 126.4, 120.9, 120.7, 119.6, 114.2, 20.0; IR (KBr) υ 3056, 2927, 2924, 1668, 1604, 1560, 1466, 1442, 1333, 1289, 1265, 1139, 940, 874 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}N_3O$ $[M+H]^+$ 252.1131, found 252.1132.

General procedure and characterization data for the synthesis of rhodacycle A: A mixture of 2-phenylquinazolin-4(3*H*)-one (**1f**) (44.5 mg, 0.2 mmol, 100 mol %), $[Cp^*RhCl_2]_2$ (61.8 mg, 0.1 mmol, 50 mol %), NaOAc (65.7 mg, 0.8 mmol, 400 mol %) and DCE (1 mL) were weighted in a Schlenk tube equipped with a stir bar under nitrogen. The reaction mixture was stirred at 60 °C under nitrogen for overnight, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc = 1:1) to afford 38.8 mg of rhodacycle **A** in 42% yield.

Rhodacycle A: 38.8 mg (42%); dark brown solid; mp = 237.5–239.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36–8.31 (m, 2H), 8.00 (d, *J* = 7.5 Hz, 1H), 7.92 (d, *J* = 7.5 Hz, 1H), 7.85 (t, *J* = 7.0 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 1.55 (s, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.4, 159.5, 159.4, 146.9, 138.1, 137.7, 135.4, 132.2, 127.7, 126.9, 126.8, 125.2, 123.2, 120.4, 96.5, 96.4, 9.5; IR (KBr) υ 2920, 2852, 1698, 1666, 1606, 1586, 1536, 1509, 1468, 1454, 1376, 1324, 1292, 1163, 1127, 1023, 943, 862, 770 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{24}N_2ORh$ $[M+H]^+$ 459.0938, found 459.0938.

Acknowledgements

This work was supported by the National Research Foundation of Korea (NRF) and funded by the Korea government (MSIFP) (Nos. 2018R1C1B6005607, 2019R1A4A2001451 and 2020R1A2C3005357).

Keywords: Amidation • C–H functionalization • Dioxazolones • Quinazolinoes • Rhodium

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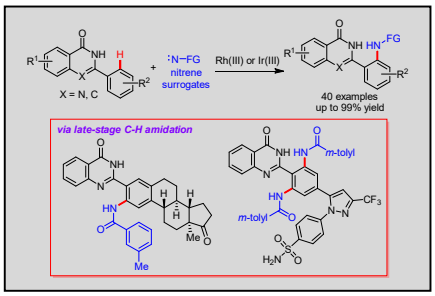
Entry for the Table of Contents

Key Topic: C–H Amidation



The site-selective C–H amidation of 2-aryl quinazolin-4(3*H*)-ones with dioxazolones under rhodium(III) catalysis is described. Gram-scale reaction, late-stage C–H functionalization, and synthetic transformations highlight the potential of the developed method.