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Sequential Oxidative Fragmentation and Skeletal Rearrangement of Peroxides for the Synthesis of Quinazolinone Derivatives

Akash S. Ubale, Moseen A. Shaikh, and Boopathy Gnanaprakasam*

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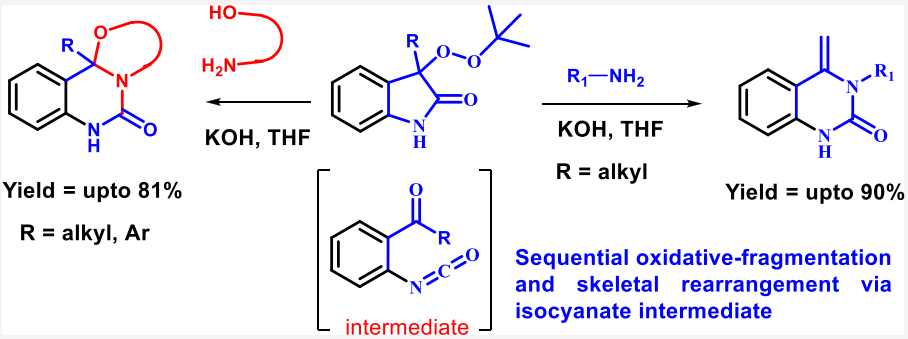

ABSTRACT: For the first time, the sequential reaction of peroxyoxindole that involves base-promoted oxidative fragmentation to isocyanate formation and primary amine or amino alcohol accelerated skeletal rearrangement to synthesize exo-olefinic-substituted quinazolinone or oxazoloquinazolinone is reported. The advantages of this new reaction include a broad substrate scope and transition-metal-free and room-temperature conditions. The formation of the isocyanate as a key intermediate that accelerates oxidative skeletal rearrangement has been confirmed by trapping experiments and spectroscopic evidence.

INTRODUCTION

Heterocycles are the most essential and important chemical entity in pharmaceuticals and agricultural applications.[1] A large number of alkaloids contain diverse heterocycles in the scaffold. Peroxide-functionalized heterocycles emerge as a vital intermediate in diverse oxidative transformations.[2] Moreover, the incorporation of peroxide functionality on the oxindole or substituted-2-oxindole derivatives makes them fascinating precursors for structurally distinct rearrangement reactions.[3] In general, peroxides are known to perform Baeyer−Villiger oxidation,[4] and the Hock process[5] to produce phenol from cumene hydroperoxide involving the migration of an aryl/alkyl group to an electron-deficient oxygen atom has been broadly studied under an acid source. Synthetically, the Kornblum−DeLaMare rearrangement[6] is an important rearrangement in organic peroxide for the production of ketones and alcohols under basic conditions (Scheme 1A).[6] On the basis of these rearrangements, the skeletal rearrangement of the peroxides to access biologically important intermediates is an attractive paradigm in organic synthesis. Recently, pioneering work on direct C−H peroxidation of 2-oxindole by a Cu catalyst and subsequent base-mediated fragmentation has been reported by Stoltz and co-workers (Scheme 1B).[7a] Subsequently, our group reported the rearrangement of C3-substituted 2-oxindole peroxide using a Lewis acid as well as a Brønsted acid (Scheme 1C).[7b−d] A few other rearrangements have also been reported by other research groups by using different heterocyclic peroxides.[7e−g]

Nitrogen-containing heterocyclic compounds such as C4-substituted quinazolinone[8] and quinazolinediones[9] exhibit a wide range of biological properties such as Na^+/Ca^{2+} exchange inhibitor,[10] anti-inflammatory,[11] anticancer,[12] antimalarial,[13] antidiabetic,[14] and antihypertensive[15] activities (Figure 1). Hence, it has a central role in drug development, medicinal chemistry, and corresponding drug-target relationships superintended for specific biological activity and drug action. In the literature, few pioneering methods have been reported for the synthesis of 4-methylene-3,4-dihydroquinazolin-2-ones.[16a,b] Gimeno et al. reported the Au(I)-complex-catalyzed synthesis of 4-methylene-3,4-dihydroquinazolin-2-ones from 1-(*o*-alkynylaryl) urea.[16c−e] Afterward, Barba and co-workers described the synthesis of 3-substituted 2-quinazolinones from the reaction of 2-aminoacetophenone and an electrogenerated cyanomethyl anion from acetonitrile reduction at a graphite electrode.[16f] Recently, to overcome the use of expensive catalysts or ligands,

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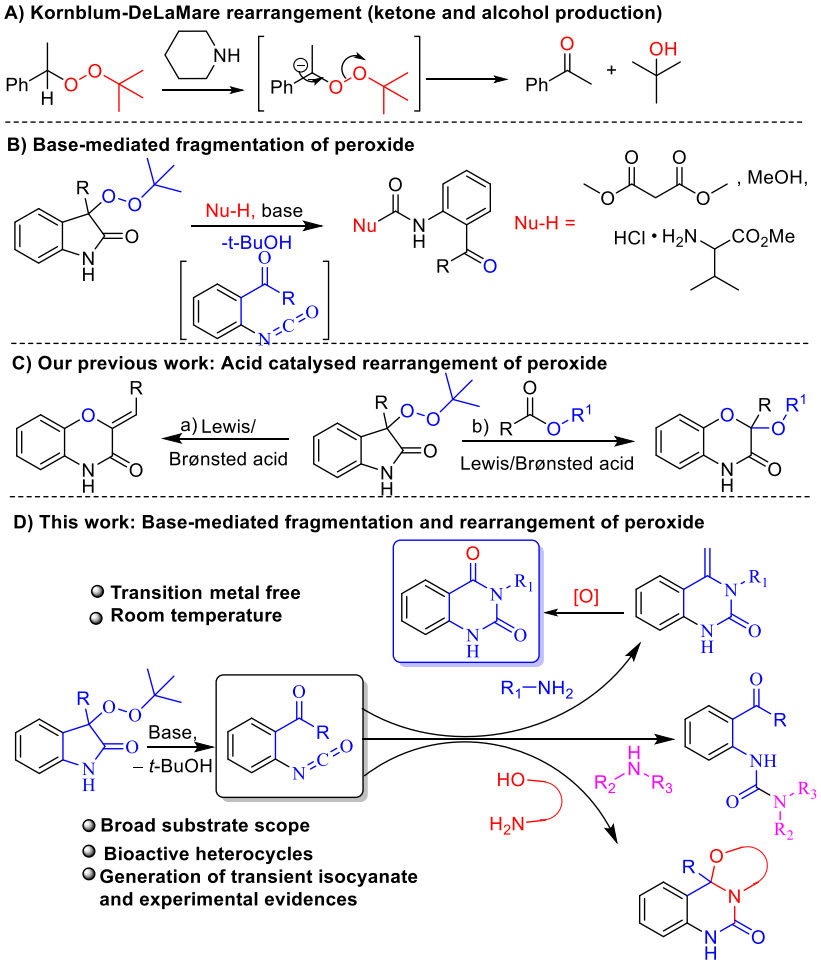
Scheme 1. State of the Art in a Rearrangement of Peroxide



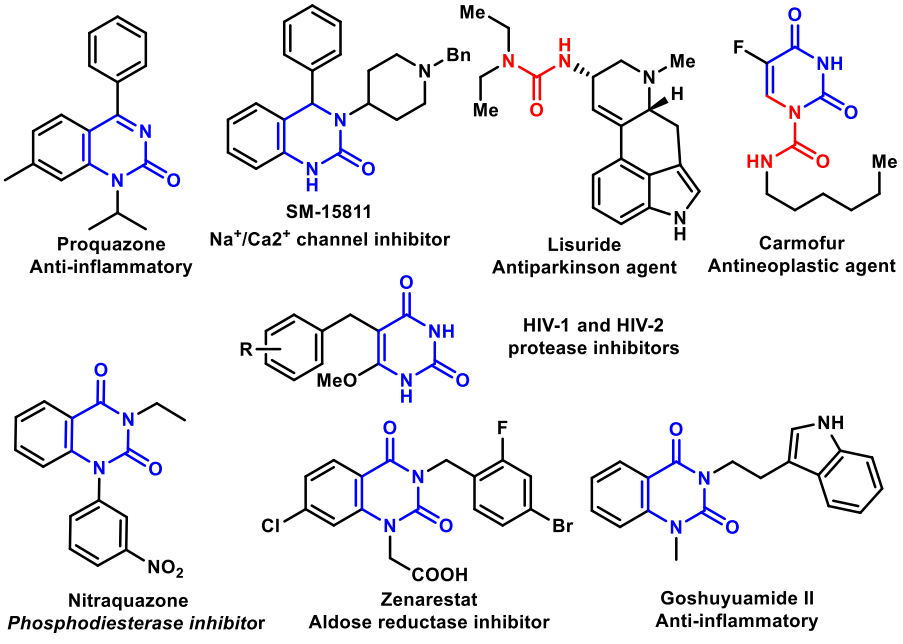


Figure 1. Pharmacologically active quinazolinone framework.

Ma and co-workers reported a variant protocol for the synthesis of 4-alkenylquinazolinons and 4-alkenylquinazolinthione by using catalytic amounts of NaOH under reflux.[17] Although there are pros and cons of the reported method for the quinazolinone derivatives, designing an attractive and newer approach for these heterocycles is an evergrowing paradigm in chemical synthesis.

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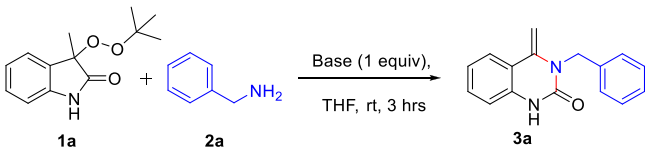
From the literature, it is evident that no peroxide rearrangement has been used for the construction of the quinazolinone derivatives. As a part of our research on the rearrangement of peroxides toward the synthesis of heterocycles (Scheme 1C),[7b−d] herein we report the transition-metal-free oxidative fragmentation of peroxyoxindole derivatives to synthesize bioactive quinazolinone derivatives in the presence of various amine nucleophiles. The present work includes the following features: (i) first report on quinazolinone using a peroxide via oxidative fragmentation and skeletal rearrangement; (ii) transition-metal-free and room-temperature reaction conditions; and (iii) efficient, broad substrate scope and high yield.

RESULTS AND DISCUSSION

To establish a base-mediated oxidative fragment and skeletal rearrangement to 4-methylene-3-substituted quinazolinone, initial optimization was performed with peroxides **1a** and **2a**. Control experiments **1a** and **2a** in the absence of base at room temperature or 60 °C in THF solvent did not produce the desired product **3a** (Table 1, entries 1 and 2). Hence, base has a

Table 1. Optimization of Reaction Conditions[a]



entry	base	solvent	yield (%) of **3a**
1		THF	no reaction
2[b]		THF	no reaction
3	Na_2CO_3	THF	25
4	K_2CO_3	THF	no reaction
5	Cs_2CO_3	THF	74
6	NaOH	THF	77
7	KOH	THF	87
8	*t*-BuOK	THF	75
9	*t*-BuOLi	THF	82
10[c]	KOH	THF	27
11[d]	KOH	THF	55
12	KOH	DCM	67
13	KOH	EtOH	78
14	KOH	*t*-BuOH	55
15	KOH	H_2O	no reaction
16	KOH	EtOAc	76
17	KOH	ACN	80

[a]Reaction conditions: base (0.35 mmol), compound **1a** (0.35 mmol), compound **2a** (0.42 mmol), and solvent (2 mL) were stirred at room temperature for 3 h. [b]At 60 °C. [c]0.2 equiv of base used. [d]0.5 equiv of base used. The mentioned yields are isolated yields.

decisive role in the oxidative fragmentation of the peroxide. When this reaction was performed in the presence of Na_2CO_3, product **3a** was obtained in 25% yield (Table 1, entry 3). Next, K_2CO_3 failed to give **3a** (Table 1, entry 4). Interestingly, the reaction works well in the presence of Cs_2CO_3 and provided product **3a** in 74% yield. Furthermore, we screened a variety of bases for this reaction. Notably, the addition of NaOH results in a slight improvement in the yield of product **3a** to 77% yield (Table 1, entry 6). An excellent yield was obtained for **3a** in the case of KOH as a base (Table 1, entry 7). Other bases such as KO*t*Bu and LiO*t*Bu are also efficient to form the product **3a** in 75 and 82% yields, respectively (Table 1, entries 8 and 9). From our survey of bases, KOH is found to be the best base for this transformation. Furthermore, by decreasing the KOH quantity, a decrease in yield was observed (Table 1, entries 10 and 11). Next, varieties of solvents were tested to enhance the product yield of **3a**, but no improvement was detected (Table 1, entries 12−17). In the case of water, there was no detection of desired product **3a**. From this experimental study, THF is established to be the best solvent for this conversion to provide **3a** in 87% yield after 3 h (Table 1, entry 7). Product **3a** was characterized by spectroscopic techniques and single-crystal XRD (Figure 2).

Next, we started our studies to generalize the substrate scope for quinazolinone derivatives. Initially, electron-rich benzyl amines such as 2-Me, 4-Me, 4-OMe, 3,4-OMe, 2,3,4-OMe, and 4-Ph afforded a 64−90% yield of products **3b−3g** (Scheme 2). Afterward, in the presence of an electron-withdrawing substituent such as 4-F, 3-Br, or 4-CF_3 on benzyl amines, moderate to good yields of corresponding products **3h−3j** were provided (Scheme 2). Gratifyingly, heteroaryl amines were well tolerated under optimized experimental conditions. 2-Picolylamine, tryptamine, and furfuryl amine were successfully converted to **3k**, **3l**, and **3m** in 58, 61, and 67% yields, respectively. Furthermore, the scope of the reaction was analyzed with primary aliphatic amines. When cyclopropyl, methyl, ethyl, hexyl, and octyl amines were used under standard optimized conditions, products **3n−3r** were isolated in moderate to good yields (Scheme 2). Additionally, propargylamine and allylamine provided corresponding products **3s** and **3t** in 65 and 61% yields, respectively. Notably, 3-methoxyphenethylamine provided quinazolinone product **3u** in 65% yield. Similarly, the reaction of 3-butyl-3-(*tert*-butylperoxy)-indolin-2-one **1c** with **2a** afforded product **3v** as an exclusive E isomer in 21% yield. Furthermore, the reaction of peroxide **1d** with 4-methoxybenzylamine **2d** afforded **3w** as an E/Z mixture in 50% yield. A reaction of peroxide **1b** with **2d** led to product **3x** in 63% yield. Furthermore, this reaction with primaquine bisphosphate amine afforded the respective product **3y** in 45% yield. However, the reaction of **1a** with aniline, 4-methoxy aniline, or tryptophan led to a complicated reaction mixture that could not be separated by column chromatography. Remarkably, the reaction of **1a′** with amines preceded instinctively to give the desired derivatives of the 4-methylene-3-substituted quinazolinone in 58−85% yields (Scheme 3). To our delight, a gram-scale reaction was also successfully performed with **1a** (1.0 g, 4.25 mmol) and **2a** under optimized conditions to afford a 65% yield of product **3a**.

In contrast to primary amines, the reaction of peroxyoxindole with secondary amine-based nucleophiles generates a variety of urea derivatives (Scheme 4). Thus, the reaction of **1a** and secondary amine having different substitutions such as −N(Me)$_2$, −N(iPr)$_2$, and −N(iBu)$_2$ under the above standard reaction condition by using KOH (1 equiv) for 2 h afforded urea derivatives **6a−6c** in moderate to good yields (Scheme 4). Moreover, pyrrolidine and morpholine afforded 80 and 71% yields of products **6d** and **6e**, respectively.

Next, we have extended this concept to the molecular reconstruction of the peroxyoxindole by using amino alcohols. For instance, the reaction of peroxyoxindole **1a** with 1.5 equiv of KOH and ethanolamine **8a** at room temperature afforded tricyclic compound **9a** in 81% isolated yield. To outspread the substrate scope, this reaction was performed with other amino alcohols to afford products **9b−9g** in moderate to good yields (Scheme 5).

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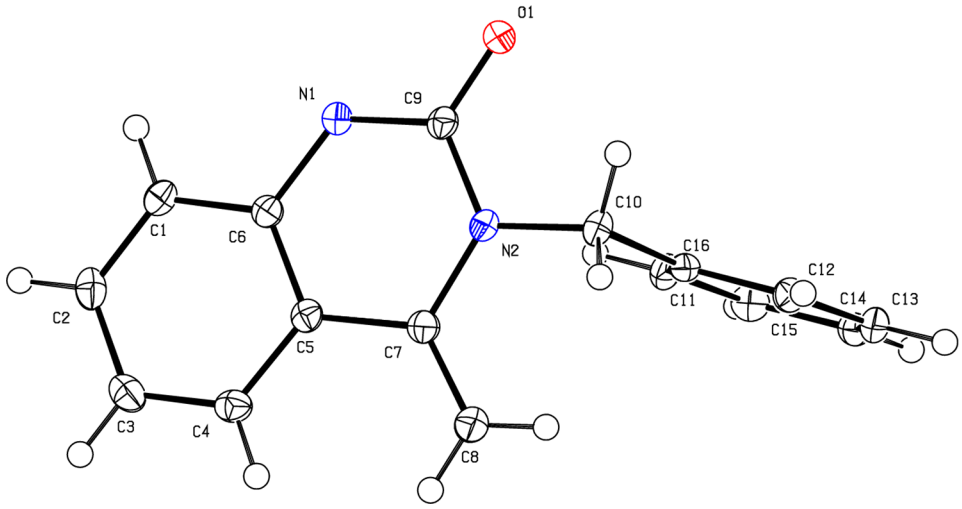

Figure 2. ORTEP crystal structure of **3a** showing thermal ellipsoids at the 50% probability level.

Likewise, the formation of other tricyclic compounds from peroxyoxindole derivatives also progressed well in the presence of chiral amino alcohols to afford as a diastereomeric mixture [**9h** (*de* = 97%):**9h′** (*de* = 90%, dr = 3.4:1), [**9i** (*de* = 94%):**9i′** (*de* = 95%, dr = 2.4:1), and [(**9j** (*de* 94%):**9j′** (*de* = 84%, dr = 1.3:1] in good yields. The stereochemistry and structure of compound **9h** was confirmed using single-crystal XRD (Figure 3). Moreover, the stereochemistry of all of the other tricyclic compounds (**9h, 9h′, 9i, 9i′**, and **9j, 9j′**) was comparatively dispensed on the basis of the crystal structure of **9h**.

To understand the reaction pathway for the formation of 4-methylene-3-substituted quinazolinone, we have performed several experiments using peroxyoxindole (Scheme 6). The reaction of *N*-methylated peroxyoxindole **1aa** has been proven to be chemically inactive under optimized reaction conditions (Scheme 6,(i)). This experiment suggests that the abstraction of proton from oxindole nitrogen was a crucial step for this transformation. To identify the intermediate in this reaction, a trapping experiment was performed with other nucleophiles. Hence, we reacted peroxyoxindole **1a** with alcohol **2aa**, which gave carbamate **6g** in 53% yield (Scheme 6,(ii)). This reaction confirmed the generation of isocyanate intermediate **B**, and this in-situ-generated isocyanate intermediate was trapped by alcohol **2aa**. From this experimental observation, we hypothesized that after deprotonation at oxindole nitrogen, an isocyanate intermediate was formed. Furthermore, in the absence of an external nucleophile, peroxyoxindole **1a** undergoes intramolecular cyclization to afford 4-hydroxyquinolinone **7a** (Scheme 6,(iii)).[7a]

On the basis of experimental observations and literature precedents,[7a] we have proposed the two possible pathways shown in Scheme 7. In pathway (a), we envision the complete elimination of *t*-BuOOH from peroxyoxindole **1a** that would lead to *N*-alkylated product **4a** *via* intermediate **A** (Scheme 7, pathway a). But pathway (a) failed to deliver product **4a**. However, in pathway (b), peroxyoxindole **1a** is followed by Kornblum−DeLaMare rearrangement,[6] similar to 4-oxa-Grob fragmentation,[18] and Stoltz's group reported oxidative fragmentation.[7a] Pathway (b) allowed the fragmentation of the C2−C3 bond and elimination of *tert*-butyl alcohol to the simultaneous formation of ketone, and isocyanate is an intermediate (**B**) generated in situ (Scheme 7, pathway (b)). The **B** intermediate was highly unstable even in the absence of amine and was not able to be isolated from the reaction, which immediately gave cyclized product **3a**. To confirm the isocyanate as the intermediate, we have performed the reaction of 2-amino acetophenone and benzylisocyanate in the presence or absence of KOH, resulting in product **3a** (Scheme 6, entry (vi)). Furthermore, this intermediate (**B**) was also confirmed by a trapping experiment with different secondary amine/oxygen-based nucleophiles (Schemes 4 and 6, entry (ii)). The isocyanate formation in the reaction was also confirmed by the in situ analysis of IR and HRMS (SI Figures S3 and S1). In the case of product **9**, intermediate **B** undergoes a reaction with a primary amine/amino alcohol to obtain urea derivative **C**/**C′**. Furthermore, intermediate **C** containing a nitrogen atom is highly unstable (not able to isolate from the reaction mixture), undergoing a rapid intramolecular reaction with ketone to form the **D**/**D′** hemiaminol intermediate. Interestingly, intermediate **C′** was isolated from the reaction of peroxide **1a** and 3-amino-1-propanol and performed the cyclization in the presence of KOH to give product **9a** (Scheme 6, entry (v)). Finally, the dehydration of **D** afforded product **3a**. Afterward, iminium cation **E** formed upon dehydration of **D′** to facilitate another intramolecular addition reaction (i.e., oxygen attack over the iminium cation to generate **9a** (Scheme 7).

Next, the application of a 4-methylene-3-substituted quinazolinone derivative has been investigated for the synthesis of 3-substituted quinazoline-2,4-diones by an oxidation reaction. This oxidation has been performed using **3a** and **3p** with $CuCl_2$ and TBHP.[19] After the reaction was complete, corresponding products **10a** and **10b** were isolated in 78 and 69% yields (Scheme 8). Moreover, the synthesized quinazoline-2,4-diones can be employed as valuable precursors in the synthesis of various bioactive molecules.[9]

CONCLUSIONS

We have developed a novel transition-metal-free sequential oxidative fragmentation and rearrangement of peroxyoxindole for the synthesis of 4-methylene-3-substituted quinazolinone derivatives in the presence of a varieties of amine and hydroxyl nucleophiles. This reaction was easily achieved by inexpensive benchtop KOH base under ambient condition and synthesized a large number of quinazolinone derivatives in good to excellent yields. A plausible mechanism has been proposed on the basis of the experimental results, and previous literature studies involved

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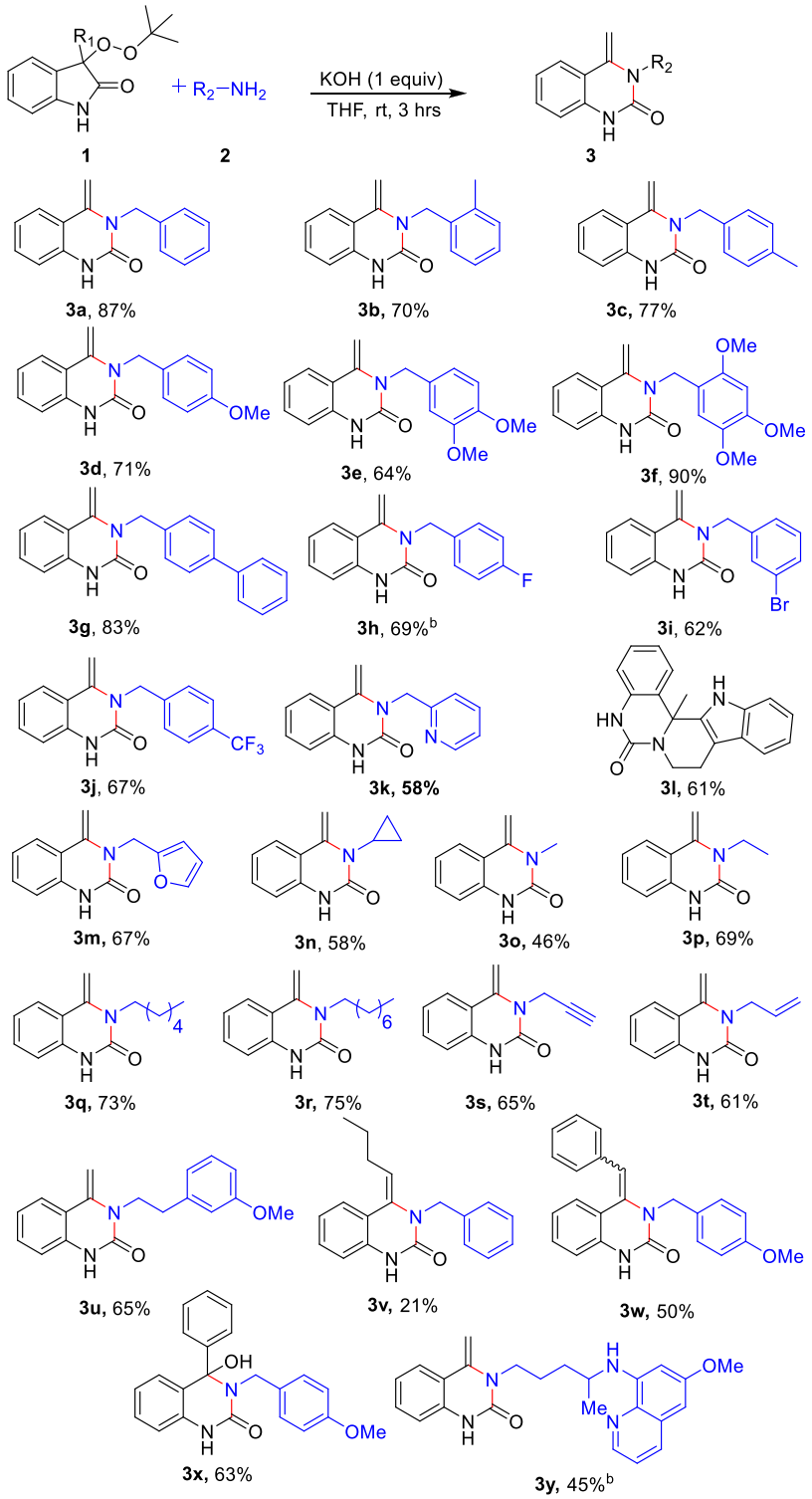
Scheme 2. Substrate Scope for Quinazolinone Derivatives[a]



[a]Reaction conditions: KOH (19 mg, 0.35 mmol, 1 equiv), peroxy compound **1** (0.35 mmol, 1 equiv), and amines **2** (0.42 mmol, 1.2 equiv) in THF (2 mL) were stirred at room temperature for 3 h. [b]2 equiv of base was used. The mentioned yields are isolated yields. For product **3v**, 3-butyl-3-(*tert*-butylperoxy)indolin-2-one has been used. For product **3w**, 3-benzyl-3-(*tert*-butylperoxy)indolin-2-one has been used. For **3x**, 3-phenyl-3-(*tert*-butylperoxy)indolin-2-one has been used.

the fragmentation of peroxyoxindole via deprotanation to form isocyanate as the key step in the formation of quinazolinone derivatives.

EXPERIMENTAL SECTION

General Information and Data Collection. The amines, 2-oxindole, amino alcohols, KOH, cupric chloride, and *tert*-butyl hydroperoxide (TBHP) 5.0−6.0 M in decane solution were purchased from Sigma-Aldrich. All of the solvents used in the reactions were dry

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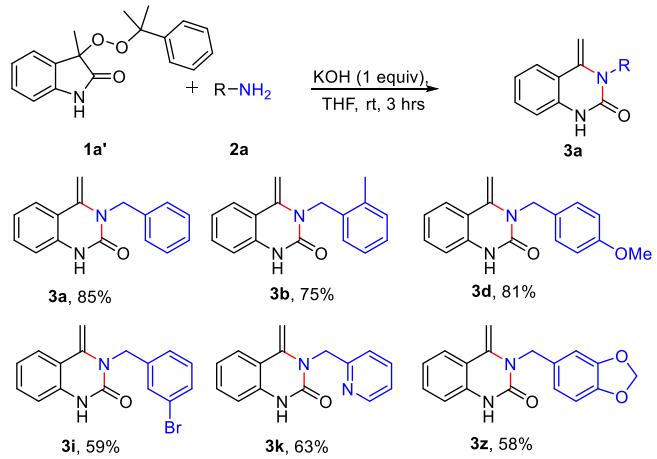
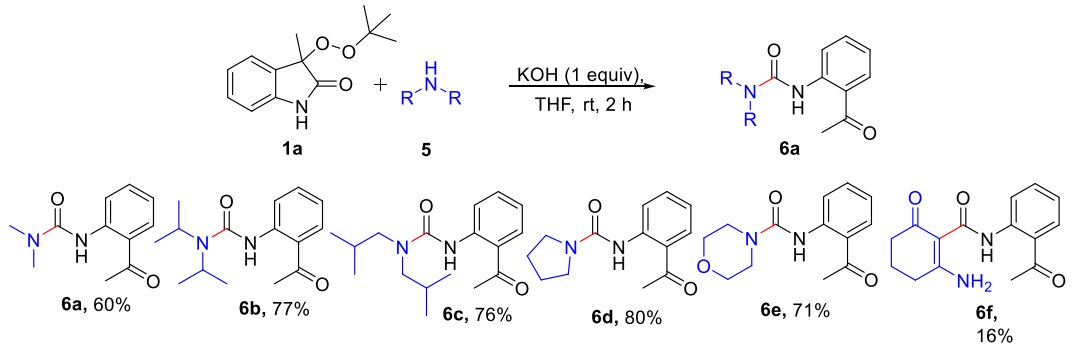
Scheme 3. Substrate Scope for Quinazolinone Derivatives[a]



[a]Reaction conditions: KOH (19 mg, 0.35 mmol, 1 equiv), peroxy compound **1a′** (0.35 mmol, 1 equiv), and amine **2a** (0.42 mmol, 1.2 equiv) in THF (2 mL) were stirred at room temperature for 3 h. The mentioned yields are isolated yields.

Scheme 4. Synthesis of Urea Derivatives[a]



[a]Reaction conditions: KOH (0.35 mmol), compound **1** (0.35 mmol), compound **5** (0.42 mmol), and THF (2 mL) were stirred at room temperature for 2 h. The mentioned yields are isolated yields.

grade. The column chromatographic separation separations were achieved over 100−200 mesh size silica gel. Visualization completed with UV light, PMA, and CAM staining go along with the heating method. By using a Bruker or JEOL spectrometer, the ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. The following information was used in NMR follow-up experiments: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad; ddd, doublet of doublets of doublets. High-resolution mass spectra were recorded via a Waters Synapt G2 applying electrospray ionization (ESI). Infrared (ATR) spectra were obtained with a Bruker Alpha-E infrared spectrometer. HPLC analysis was performed using an Agilent 1200 infinity series HPLC system with a diode array detector. Diastereomeric excess values were determined by HPLC analysis on a Chiralpak IA (4.6 mm × 250 mm) column in comparison with authentic racemic material using *n*-heptane and isopropanol as eluents. Data were analyzed using Agilent OpenLAB software. The melting point was measured using the BUCHI M-560 melting-point instrument. All melting points were measured in an open glass capillary tube. Single-crystal diffraction analysis data were collected at 100 K with a Bruker Kappa Apex III CCD Duo diffractometer (operated at 1500 W power: 50 kV, 30 mA) using graphite monochromatic Mo Kα radiation and Cu Kα radiation. More information on crystal structures can also be obtained from the Cambridge Crystallographic Data Centre (CCDC) via deposition numbers 2053446 (**3a**) and 2053447 (**9h**).

*(A) General Experimental Procedure for the Synthesis 4-Methylene-3-Substituted Quinazolinone Derivatives (**3**).* In a 20 mL resealable vial, KOH (19 mg, 0.35 mmol, 1 equiv), peroxy compound (0.35 mmol, 1 equiv), and amine (0.42 mmol, 1.2 equiv) were added to THF (2 mL). Then the tube was sealed with a rubber septum, and the reaction mixture was kept at room temperature with stirring for 3 h. After the completion of the reaction, water was added, and the resulting mixture was extracted with ethyl acetate two times using 10 mL of solvent each time. The organic layers were combined and dried over Na_2SO_4. After removing the solvent under reduced pressure, the residue was purified by using column chromatography (EtOAc:*n*-hexane = 30:70 to 70:30).

*(B) Experimental Procedure for the Gram-Scale Synthesis of **3a**.* In a 20 mL resealable vial, KOH (238 mg, 4.25 mmol, 1 equiv), compound **1a** (1000 mg, 4.25 mmol, 1 equiv), and benzyl amine **2a** (546 mg, 5.1 mmol, 1.2 equiv) were added to THF (10 mL). Then the tube was sealed with a rubber septum, and the reaction mixture was kept at room temperature with stirring for 3 h. After the completion of the reaction, water was added, and the resulting mixture was extracted with ethyl acetate two times using 20 mL of solvent each time. The organic layers were combined and dried over Na_2SO_4. After removing the solvent under reduced pressure, the residue was purified by using column chromatography (EtOAc:*n*-hexane = 30:70) to afford 3-benzyl-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one **3a** (694 mg, 65%) as a white solid.

(C) General Experimental Procedure for the Synthesis of Urea Derivatives. In a 20 mL resealable vial, KOH (19 mg, 0.35 mmol, 1 equiv), compound **1a** (0.35 mmol, 1 equiv), and amine **5a** (0.42 mmol, 1.2 equiv) were added to THF (2 mL). Then the tube was sealed with a rubber septum, and the reaction mixture was kept at room temperature with stirring for 2 h. After the completion of the reaction, water was added, and the resulting mixture was extracted with ethyl acetate two

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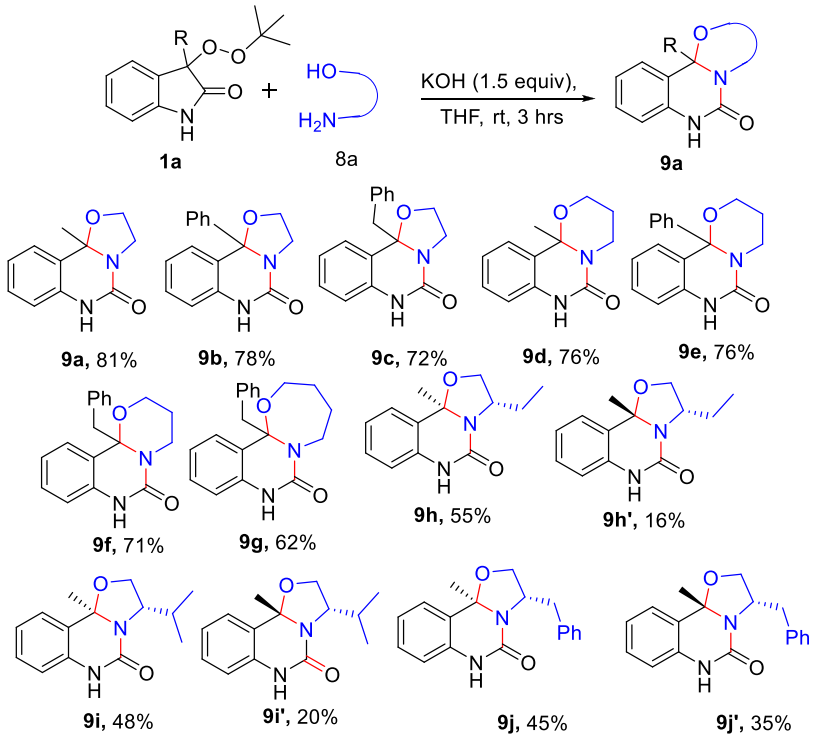
Scheme 5. Synthesis of a Polyheterocycle Scaffold[a]



[a]Reaction conditions: KOH (1.5 eq, 0.525 mmol), compound **1** (0.35 mmol), compound **8** (1.2 eq 0.42 mmol), and solvent (2 mL) were stirred at room temperature for 3 h. The mentioned yields are isolated yields.

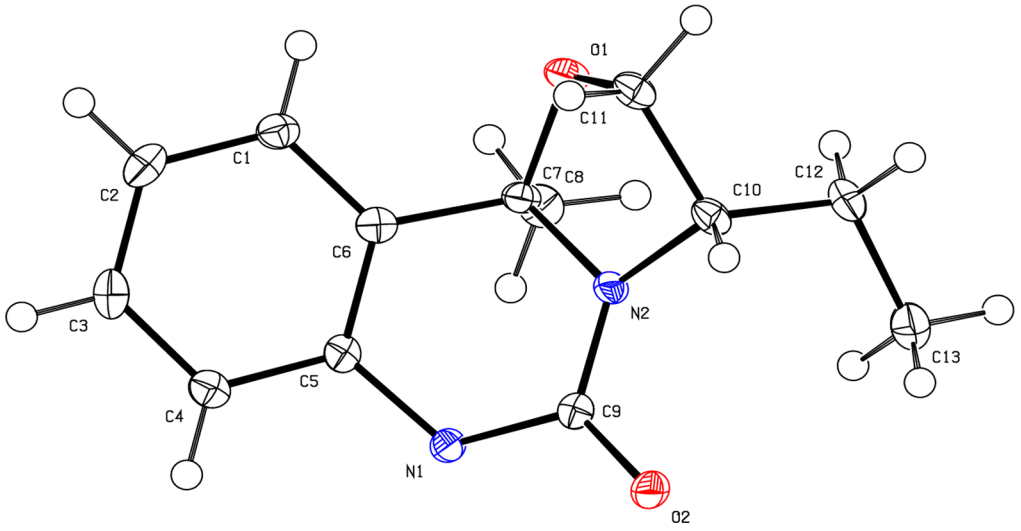


Figure 3. ORTEP crystal structure of **9h** showing thermal ellipsoids at the 50% probability level.

times using 10 mL of solvent each time. The organic layers were combined and dried over Na_2SO_4. After removing the solvent under reduced pressure, the residue was purified by using column chromatography (EtOAc:*n*-hexane = 20:80 to 50:50).

*(D) Experimental Procedure for the Synthesis Carbamates (**6g**).* In a 20 mL resealable vial, KOH (19 mg, 0.35 mmol, 1 equiv), compound **1a** (82 mg, 0.35 mmol, 1 equiv), and 2-methoxybenzyl alcohol **2aa** (58 mg, 0.42 mmol, 1.2 equiv) were added to THF (2 mL). Then the tube was sealed with a rubber septum, and the reaction mixture was kept at room temperature with stirring for 3 h. After the completion of the reaction, water was added, and the resulting mixture was extracted with ethyl acetate two times using 10 mL of solvent each time. The organic layers were combined and dried over Na_2SO_4. After removing the solvent under reduced pressure, the residue was purified by using column chromatography (EtOAc:*n*-hexane = 10:90).

*(E) Experimental Procedure for the Synthesis of 1-(2-Acetylphenyl)-3-(3-hydroxypropyl)urea (**6i**).* In a 20 mL resealable vial, KOH (29.5 mg, 0.52 mmol, 1.5 equiv), peroxy compound **1a** (0.35 mmol, 1 equiv), and 3-aminopropan-1-ol (0.42 mmol, 1.2 equiv) were added to THF (2 mL). Then the tube was sealed with a rubber septum, and the reaction mixture was kept at room temperature with stirring for 20−30 min. Water was added to the reaction mixture, and the resulting mixture was extracted with ethyl acetate two times using 10 mL of solvent each time. The organic layers were combined and dried over Na_2SO_4. After removing the solvent under reduced pressure, the residue was purified by using column chromatography (EtOAc:*n*-hexane = 30:70 to 70:30).

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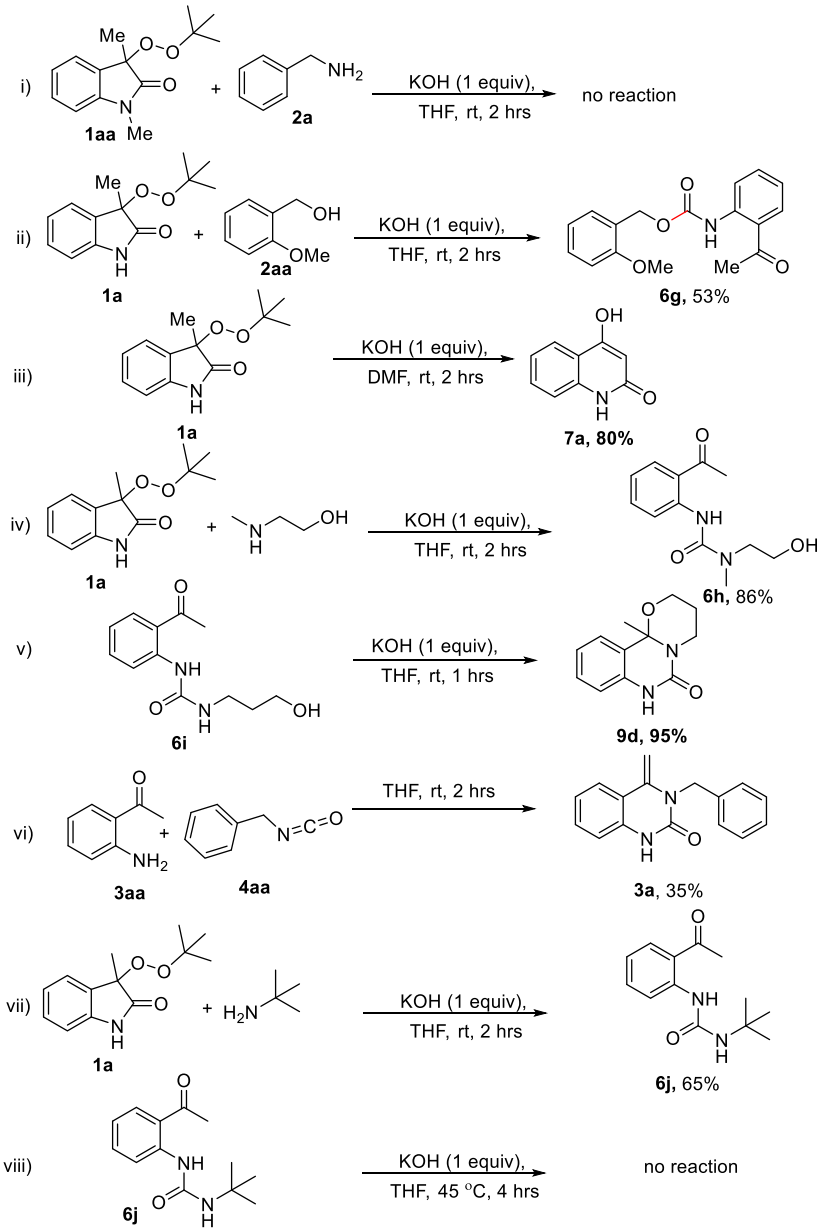
Scheme 6. Experiments for Mechanistic Studies



*(F) Experimental Procedure for the Synthesis 4-Hydroxyquinolin-2(1H)-one (**7a**).* Compound 7**a** was prepared according to the reported procedure by the Stoltz group.[7a] In a 20 mL resealable vial, KOH (19 mg, 0.35 mmol, 1 equiv) and compound **1a** (82 mg, 0.35 mmol, 1 equiv) were added to DMF (2 mL). Then the tube was sealed with a rubber septum, and the reaction mixture was kept at room temperature with stirring for 2 h. After the completion of the reaction, the resulting mixture was filtered through a plug of Celite and the filtrate was concentrated under reduced pressure. Finally, the residue was purified by using column chromatography (DCM:MeOH = 90:10).

*(G) General Experimental Procedure for the Synthesis of a Polyheterocycle Scaffold (**9**).* In a 20 mL resealable vial, KOH (29.5 mg, 0.52 mmol, 1.5 equiv), peroxy compound (0.35 mmol, 1 equiv), and amino alcohols (0.42 mmol, 1.2 equiv) were added to THF (2 mL). Then the tube was sealed with a rubber septum, and the reaction mixture was kept at room temperature with stirring for 3 h. After the completion of the reaction, water was added, and the resulting mixture was extracted with ethyl acetate two times using 10 mL of solvent each time. The organic layers were combined and dried over Na_2SO_4. After removing the solvent under reduced pressure, the residue was purified by using column chromatography (EtOAc:*n*-hexane = 30:70 to 70:30).

*(H) Experimental Procedure for the Oxidation of the 4-Methylene-3-Substituted Quinazolinone Derivative (**10**).* In a 50 mL round-bottomed flask, compound **3a** (0.25 mmol, 1 equiv), $CuCl_2$ (5 mol %), 2,2′-bipyridine (5 mol %), and 5.0−6.0 M *tert*-butyl hydroperoxide (TBHP) in decane solution (0.50 mmol, 2 equiv) were added to acetonitrile (2 mL). Then the round-bottomed flask was sealed using a rubber septum without maintaining any special conditions such as an inert atmosphere. The reaction mixture was kept at room temperature for 12 h. After the completion of the reaction, a volatile component was evaporated under vacuum. The residue was directly purified by silica gel chromatography (EtOAc:*n*-hexane = 30:70).

(I) Experimental Procedure for the Detection of the Isocyanate Intermediate Using HRMS Analysis. In a 20 mL resealable vial, compound **1b** (104 mg, 0.35 mmol, 1 equiv) and KOH (20 mg, 0.35 mmol, 1 equiv) were added at 0 °C in dry THF (2 mL). Then the tube was sealed with a rubber septum, and the reaction was performed under a nitrogen atmosphere. After 5 min, the reaction mixture was subjected to HRMS analysis. The presence of m/z = 224.0716 corresponds to isocyanate intermediate **B** (SI, Figure S1).

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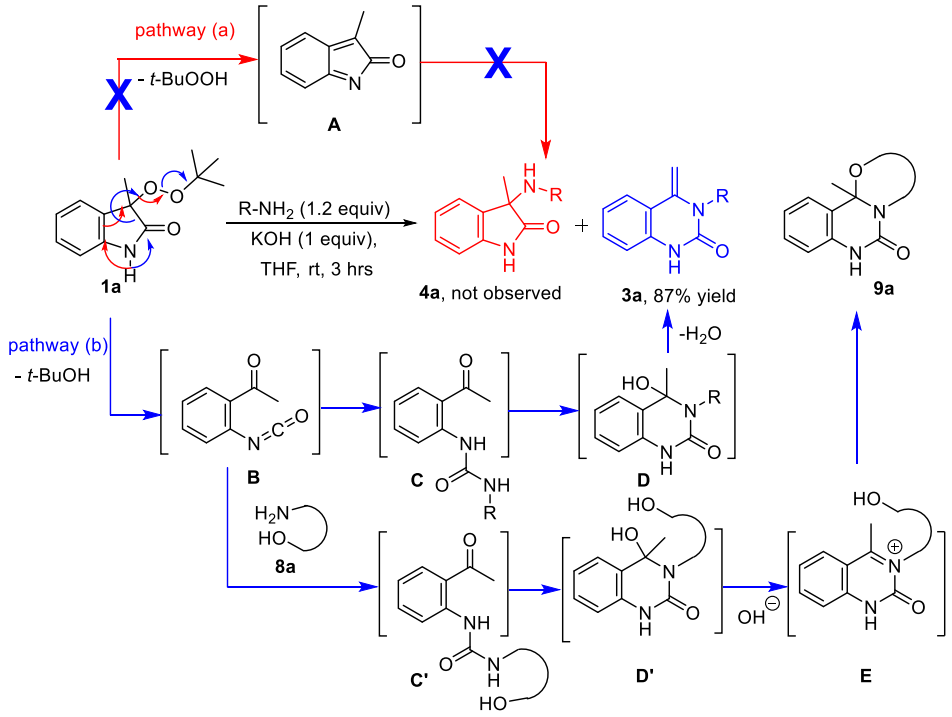
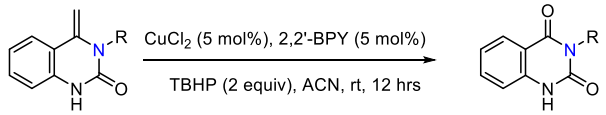
Scheme 7. Plausible Mechanism for Products 3a and 9a



Scheme 8. Oxidation of 4-Methylene-3-Substituted Quinazolinone Derivative[a]



R = $C_6H_5CH_2$, **3a**
R = CH_2CH_3 , **3p**

R = $C_6H_5CH_2$, (**10a**) =78%
R = CH_2CH_3, (**10b**) =69%

[a]Reaction conditions: compound **3a**/**3p** (0.25 mmol, 1 equiv), $CuCl_2$ (5 mol %), 2,2′-bipyridine (5 mol %), and TBHP (2 equiv) in 2 mL of acetonitrile were stirred at room temperature for 12 h.

(J) Experimental Procedure for the Observation of the Isocyanate Intermediate Using IR Analysis. In a 20 mL resealable vial, compound **1b** (104 mg, 0.35 mmol, 1 equiv) and KOH (20 mg, 0.35 mmol, 1 equiv) were added at 0 °C to dry THF (2 mL). Then the tube was sealed with a rubber septum, and the reaction was performed under a nitrogen atmosphere. After 5 min, the IR spectrum was recorded for the reaction mixture (Figure S3). Then 4-methoxybenzylamine **2d** (48 mg, 0.35 mmol, 1 equiv) was added to the reaction mixture, and the IR spectrum was recorded after 10 min (Figure S4). The IR spectra indicate the disappearance of the isocyanate peak. Interestingly, after 2 h the complete disappearance of the isocyanate peak was noticed (Figure S5).

*(K) Analytical Data for the Product. 3-Benzyl-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3a**).* Prepared according to general procedure A, using benzylamine (45 mg, 0.42 mmol) to afford 3-benzyl-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3a**) (76 mg, 87% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 198−201 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.28 (s, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.35−7.20 (m, 6H), 6.99−6.91 (m, 2H), 5.00 (s, 2H), 4.81 (d, J = 2.3 Hz, 1H), 4.12 (d, J = 2.3 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 150.1, 139.7, 137.0, 135.6, 130.1, 128.4, 126.7, 126.3, 123.9, 122.1, 115.9, 114.6, 85.2, 45.8. IR (neat): 1453, 1685, 2919, 3207 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{16}H_{15}N_2O$ $(M + H)^+$ 251.1184, found 251.1184. Crystals of compound **3a** were grown using dichloromethane and petroleum ether (2:1) as a solvent by slow evaporation. A needle-shaped single crystal was mounted on a loop by applying a small amount of paraffin oil. Crystal data for compound **3a**: $C_{16}H_{15}N_2O$, M = 249.28, monoclinic, space group $P21/n$ with a = 10.4745(5) Å, b = 5.5284(2) Å, c = 21.446(1) Å, α = 90°, β = 101.990(1)°, γ = 90°, V = 1214.79(9) Å^3, T = 296(2) K, R1 = 0.0490, wR2 = 0.1282 on observed data, z = 4, D_{calcd} = 1.363 g cm^{-3}, $F(000)$ = 524, absorption coefficient = 0.127 mm^{-1}, λ = 0.71073 Å, 3014 reflections collected on a Bruker APEX-II CCD single-crystal diffractometer, and 2362 observed reflections ($I \geq 2\sigma(I)$). The largest difference peak and hole are 0.875 and −0.267 eÅ^{-3}, respectively

*3-(2-Methylbenzyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3b**).* Prepared according to general procedure A, using 2-methylbenzylamine (51 mg, 0.42 mmol) to afford 3-(2-methylbenzyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3b**) (65 mg, 70% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 249−252 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.23 (s, 1H), 7.56 (d, J = 7.4 Hz, 1H), 7.25−7.20 (m, 1H), 7.16−7.12 (m, 1H), 7.09−7.01 (m, 2H), 6.94−6.86 (m, 3H), 4.88 (s, 2H), 4.73 (d, J = 2.4 Hz, 1H), 3.87 (d, J = 2.4 Hz, 1H), 2.29 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 149.9, 139.9, 135.6, 134.7, 133.8, 130.0, 126.3, 125.7, 124.1, 123.8, 122.0, 115.9, 114.6, 84.8, 44.3, 18.6. IR (neat): 1502, 1694, 2919, 3358 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{17}N_2O$ $(M + H)^+$ 265.1341, found 265.1349.

*3-(4-Methylbenzyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3c**).* Prepared according to general procedure A, using 4-methylbenzylamine (59 mg, 0.42 mmol) to afford 3-(4-methylbenzyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3c**) (71 mg, 77% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 183−186 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.51 (d, J = 7.9 Hz, 1H), 7.24−7.19 (m, 3H), 7.13 (d, J = 8.0 Hz, 2H), 6.98 (t, J = 7.7 Hz, 1H), 6.77 (d, J = 7.9 Hz, 1H), 5.08 (s, 2H), 4.78 (d, J = 2.6 Hz, 1H), 4.24 (d, J = 2.6 Hz, 1H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 140.2, 136.7, 134.9, 133.5, 130.2, 129.4, 126.5, 124.1, 122.9, 117.1, 114.7, 86.5, 47.1, 21.2. IR (neat): 1508, 1630, 1979, 2921, 3204 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{17}N_2O$ $(M + H)^+$ 265.1341, found 265.1339.

*3-(4-Methoxybenzyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3d**).* Prepared according to general procedure A, using 4-

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methoxybenzylamine (58 mg, 0.42 mmol) to afford 3-(4-methoxybenzyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3d**) (70 mg, 71% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 175−185 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.51 (d, J = 7.9 Hz, 1H), 7.24−7.21 (m, 3H), 7.00−6.95 (m, 1H), 6.89−6.84 (m, 2H), 6.80 (d, J = 8.0 Hz, 1H), 5.06 (s, 2H), 4.79 (d, J = 2.6 Hz, 1H), 4.26 (d, J = 2.6 Hz, 1H), 3.78 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.8, 151.8, 140.2, 135.0, 130.2, 128.7, 127.9, 124.0, 122.8, 117.1, 114.9, 114.2, 86.2, 55.4, 46.7. IR (neat): 1464, 1521, 1696, 2917, 3131 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{17}N_2O_2$ $(M + H)^+$ 281.1290, found 281.1297.

*3-(3,4-Dimethoxybenzyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3e**).* Prepared according to general procedure A, using 3,4-dimethoxybenzylamine (70 mg, 0.42 mmol) to afford 3-(3,4-dimethoxybenzyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3e**) (70 mg, 64% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 209−211 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.25−7.22 (m, 1H), 7.01−6.96 (m, 1H), 6.89−6.79 (m, 4H), 5.06 (s, 2H), 4.80 (d, J = 2.6 Hz, 1H), 4.29 (d, J = 2.6 Hz, 1H), 3.85 (d, J = 2.7 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.8, 151.8, 149.3, 148.2, 140.3, 135.0, 130.2, 129.2, 124.0, 122.9, 118.8, 117.0, 114.8, 111.2, 110.0, 86.3, 56.0, 47.2. IR (neat): 1513, 1632, 1679, 2954, 3441 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{18}H_{19}N_2O_3$ $(M + H)^+$ 311.1395, found 311.1388.

*4-Methylene-3-(2,4,5-trimethoxybenzyl)-3,4-dihydroquinazolin-2(1H)-one (**3f**).* Prepared according to general procedure A, using 3,4,5-trimethoxybenzylamine (83 mg, 0.42 mmol) to afford 4-methylene-3-(2,4,5-trimethoxybenzyl)-3,4-dihydroquinazolin-2(1*H*)-one (**3f**) (107 mg, 90% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 225−227 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.27−7.21 (m, 1H), 7.02−6.97 (m, 1H), 6.83−6.77 (m, 1H), 6.51 (s, 2H), 5.03 (s, 2H), 4.81 (d, J = 2.6 Hz, 1H), 4.28 (d, J = 2.7 Hz, 1H), 3.81 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.6, 151.7, 140.4, 137.0, 134.9, 132.5, 130.3, 124.1, 123.0, 117.0, 114.8, 103.4, 86.7, 61.0, 56.2, 47.8. IR (neat): 1460, 1519, 1651, 2925, 3273 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{19}H_{20}N_2O_4$ $(M + H)^+$ 341.1501, found 341.1505.

*3-([1,1′-Biphenyl]-4-ylmethyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3g**).* Prepared according to general procedure A, using 4-phenylbenzylamine (77 mg, 0.42 mmol) to afford 3-([1,1′-biphenyl]-4-ylmethyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3g**) (95 mg, 83% yield) as a faint yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 228−231 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.30 (s, 1H), 7.62 (t, J = 7.2 Hz, 5H), 7.45 (t, J = 7.6 Hz, 2H), 7.38−7.26 (m, 4H), 6.96 (dd, J = 14.1, 7.7 Hz, 2H), 5.05 (s, 2H), 4.85 (d, J = 2.0 Hz, 1H), 4.18 (d, J = 2.1 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 150.1, 139.9, 139.7, 138.7, 136.3, 135.6, 130.2, 128.9, 127.3, 127.0, 126.8, 126.5, 123.9, 122.1, 115.9, 114.6, 85.3, 45.5. IR (neat): 1514, 1696, 1743 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{22}H_{19}N_2O$ $(M + H)^+$ 327.1497, found 327.1490.

*3-(4-Fluorobenzyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3h**).* Prepared according to general procedure A, using 4-fluorobenzylamine (53 mg, 0.42 mmol) to afford 3-(4-fluorobenzyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3h**) (65 mg, 69% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 180−183 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (s, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.29 (dd, J = 8.3, 5.2 Hz, 2H), 7.24 (*t*, J = 7.7 Hz, 1H), 7.05−6.97 (m, 3H), 6.83−6.79 (m, 1H), 5.09 (s, 2H), 4.79 (d, J = 2.8 Hz, 1H), 4.20 (d, J = 2.8 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.4, (d, J = 243.5 Hz), 151.9 (d, J = 6.5 Hz), 140.2, 135.0, 132.3 (d, J = 2.5 Hz), 130.3, 128.2 (d, J = 7.9 Hz), 124.0, 122.9, 116.9, 115.7, 115.5, 115.0 (d, J = 1.3 Hz), 86.2, 46.7. IR (neat): 1507, 1678, 2921 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{16}H_{14}FN_2O$ $(M + H)^+$ 269.1090, found 269.1084.

*3-(3-Bromobenzyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3i**).* Prepared according to general procedure A, using 3-bromobenzylamine (78 mg, 0.42 mmol) to afford 3-(3-bromobenzyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3i**) (71 mg, 62% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 196−198 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.52 (d, J = 7.7 Hz, 1H), 7.45 (s, 1H), 7.38 (dt, J = 7.5, 1.6 Hz, 1H), 7.28−7.167 (m, 4H), 7.03−6.99 (m, 1H), 6.80 (dd, J = 8.0, 0.9 Hz, 1H), 5.08 (s, 2H), 4.80 (d, J = 2.8 Hz, 1H), 4.17 (d, J = 2.9 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.6, 140.2, 139.1, 134.9, 130.4, 130.4, 130.3, 129.6, 125.2, 124.1, 123.0, 123.0, 116.9, 114.9, 86.5, 46.9. IR (neat): 1521, 1695, 2847, 3260 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{16}H_{14}BrN_2O$ $(M + H)^+$ 329.0289, found 329.0294.

*4-Methylene-3-(4-(trifluoromethyl)benzyl)-3,4-dihydroquinazolin-2(1H)-one (**3j**).* Prepared according to general procedure A, using 4-(trifluoromethyl)benzylamine (74 mg, 0.42 mmol) to afford 4-methylene-3-(4-(trifluoromethyl)benzyl)-3,4-dihydroquinazolin-2(1*H*)-one (**3j**) (75 mg, 67% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 180−182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 7.61 (d, J = 8.2 Hz, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.28−7.24 (m, 1H), 7.03 (t, J = 7.4 Hz, 1H), 6.85 (d, J = 7.9 Hz, 1H), 5.20 (s, 2H), 4.82 (d, J = 2.8 Hz, 1H), 4.15 (d, J = 2.8 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.0, 140.9, 140.2, 134.9, 130.4, 129.5 (q, J = 32.0 Hz), 127.9 (q, J = 42.6 Hz), 125.7 (q, J = 3.4 Hz), 124.2 (q, J = 271.5 Hz), 124.0, 123.1, 116.7, 115.1, 86.3, 47.0. IR (neat): 1325, 1496, 1680, 2923 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{14}F_3N_2O$ $(M + H)^+$ 319.1058, found 319.1050.

*4-Methylene-3-(pyridin-2-ylmethyl)-3,4-dihydroquinazolin-2(1H)-one (**3k**).* Prepared according to general procedure A, using 2-picolylamine (45 mg, 0.42 mmol) to afford 4-methylene-3-(pyridin-2-ylmethyl)-3,4-dihydroquinazolin-2(1*H*)-one (**3k**) (51 mg, 58% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 173−176 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.58 (ddd, J = 4.9, 1.7, 0.9 Hz, 1H), 7.62 (td, J = 7.7, 1.8 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.29−7.22 (m, 2H), 7.17 (dd, J = 6.9, 5.4 Hz, 1H), 6.99 (t, J = 7.7 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 5.24 (s, 2H), 4.78 (d, J = 2.8 Hz, 1H), 4.25 (d, J = 2.8 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.0, 151.6, 149.4, 140.2, 137.0, 134.9, 130.3, 124.0, 123.0, 122.2, 120.7, 117.0, 114.9, 86.7, 49.5. IR (neat): 1439, 1676, 2922, 3213 cm^{-1}. HRMS (ESI-TOF)m/z calculated for $C_{15}H_{14}N_3O$ $(M + H)^+$ 252.1137, found 252.1138.

*14b-Methyl-8,9,14,14b-tetrahydroindolo[2′,3′:3,4]pyrido[1,2-c]-quinazolin-6(5H)-one (**3l**).* Prepared according to general procedure A, using tryptamine (67 mg, 0.42 mmol) to afford 14b-methyl-8,9,14,14b-tetrahydroindolo[2′,3′:3,4]pyrido[1,2-*c*]quinazolin-6(5*H*)-one (**3l**) (65 mg, 61% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 50:50). MP = 175−178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.55 (d, J = 7.8 Hz, 1H), 7.45−7.41 (m, 2H), 7.25−7.21 (m, 3H), 7.16 (t, J = 7.4 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1H), 6.80 (dd, J = 7.7, 3.4 Hz, 1H), 4.82−4.75 (m, 1H), 3.26 (ddd, J = 12.9, 10.9, 4.7 Hz, 1H), 2.93−2.79 (m, 2H), 1.85 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.6, 136.2, 136.0, 134.3, 128.7, 126.9, 125.3, 123.9, 122.6, 122.5, 120.1, 118.8, 114.7, 111.1, 110.7, 58.8, 38.6, 26.8, 21.1. IR (neat): 1520, 1657, 2900 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{19}H_{18}N_3O$ $(M + H)^+$ 304.1450, found 304.1457.

*3-(Furan-2-ylmethyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3m**).* Prepared according to general procedure A, using furfurylamine (41 mg, 0.42 mmol) to afford 3-(furan-2-ylmethyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3m**) (57 mg, 67% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 180−183 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.36−7.30 (m, 1H), 7.22 (t, J = 7.2 Hz, 1H), 6.97 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 8.0 Hz, 1H), 6.33 (d, J = 1.7 Hz, 2H), 5.07 (s, 2H), 4.84 (d, J = 2.7 Hz, 1H), 4.49 (d, J = 2.7 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.7, 150.3, 141.7, 140.2, 134.9, 130.1, 123.8, 122.7, 116.9, 115.0, 110.4, 108.0, 85.4, 40.5. IR (neat): 1520, 1696, 3612 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{14}H_{13}N_2O_2$ $(M + H)^+$ 241.0977, found 241.0981.

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*3-Cyclopropyl-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3n**).* Prepared according to general procedure A, using cyclopropylamine (24 mg, 0.42 mmol) to afford 3-cyclopropyl-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3n**) (40 mg, 58% yield) as a black solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 145−147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 7.50 (d, J = 7.3 Hz, 1H), 7.25−7.20 (m, 1H), 7.00−6.95 (m, 1H), 6.86−6.83 (m, 1H), 4.89 (d, J = 1.6 Hz, 1H), 4.72 (d, J = 1.6 Hz, 1H), 2.66−2.60 (m, 1H), 1.16−1.09 (m, 2H), 0.79−0.74 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.0, 141.8, 135.2, 129.8, 123.9, 122.6, 118.2, 114.7, 88.4, 26.1, 10.3. IR (neat): 1415, 1517, 1683, 2922, 3214, cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{13}N_2O$ (M + H)$^+$ 201.1028, found 201.1033.

*3-Methyl-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3o**).* Prepared according to general procedure A, using methylamine (13 mg, 0.42 mmol) to afford 3-methyl-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3o**) (28 mg, 46% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 155−157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.00 (t, J = 7.3 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 4.82 (d, J = 2.3 Hz, 1H), 4.26 (d, J = 2.3 Hz, 1H), 3.29 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.5, 141.8, 135.0, 130.2, 123.9, 122.7, 116.8, 114.9, 84.3, 30.6. IR (neat): 1454, 1559, 1637, 2924, 3344 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{10}H_{11}N_2O$ (M + H)$^+$ 175.0871, found 175.0878.

*3-Ethyl-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3p**).* Prepared according to general procedure A, using ethylamine (19 mg, 0.42 mmol) to afford 3-ethyl-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3p**) (45 mg, 69% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 159−162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.27−7.22 (m, 1H), 7.01−6.95 (m, 1H), 6.81 (d, J = 8.0 Hz, 1H), 4.83 (d, J = 2.5 Hz, 1H), 4.32 (d, J = 2.5 Hz, 1H), 3.93 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.2, 140.1, 135.3, 130.1, 124.0, 122.6, 117.1, 114.8, 84.0, 38.4, 11.3. IR (neat): 1441, 1495, 1654, 2924, 3204 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{11}H_{13}N_2O$ (M + H)$^+$ 189.1028, found 189.1030.

*3-Hexyl-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3q**).* Prepared according to general procedure A, using hexylamine (43 mg, 0.42 mmol) to afford 3-hexyl-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3q**) (63 mg, 73% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 1H), 7.55 (d, J = 7.8 Hz, 1H), 7.26−7.22 (m, 1H), 7.00−6.96 (m, 1H), 6.84 (dd, J = 8.1, 0.9 Hz, 1H), 4.82 (d, J = 2.4 Hz, 1H), 4.28 (d, J = 2.5 Hz, 1H), 3.85 (t, J = 7.7 Hz, 2H), 1.74−1.67 (m, 2H), 1.43−1.31 (m, 6H), 0.90 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.6, 140.3, 135.4, 130.0, 123.9, 122.5, 117.0, 114.9, 84.0, 43.4, 31.7, 26.8, 25.6, 22.7, 14.2. IR (neat): 1424, 1497, 1629, 1684, 2929, 3202 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{15}H_{21}N_2O$ (M + H)$^+$ 245.1654, found 245.1651.

*4-Methylene-3-octyl-3,4-dihydroquinazolin-2(1H)-one (**3r**).* Prepared according to general procedure A, using octylamine (54 mg, 0.42 mmol) to afford 4-methylene-3-octyl-3,4-dihydroquinazolin-2(1*H*)-one (**3r**) (71 mg, 75% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1H), 7.54 (dd, J = 8.1, 1.1 Hz, 1H), 7.25−7.20 (m, 1H), 7.00−6.95 (m, 1H), 6.83 (dd, J = 7.9, 0.8 Hz, 1H), 4.82 (d, J = 2.5 Hz, 1H), 4.28 (d, J = 2.5 Hz, 1H), 3.87−3.80 (m, 2H), 1.74−1.66 (m, 2H), 1.33−1.25 (m, 10H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.4, 140.3, 135.3, 130.0, 123.9, 122.5, 117.0, 114.8, 84.1, 43.5, 31.9, 29.4, 29.4, 27.1, 25.6, 22.7, 14.2. IR (neat): 1433, 1679, 2921, 3204 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{25}N_2O$ (M + H)$^+$ 273.1967, found 273.1971.

*4-Methylene-3-(prop-2-yn-1-yl)-3,4-dihydroquinazolin-2(1H)-one (**3s**).* Prepared according to general procedure A, using propargylamine (23.13 mg, 0.42 mmol) to afford 4-methylene-3-(prop-2-yn-1-yl)-3,4-dihydroquinazolin-2(1*H*)-one (**3s**) (45 mg, 65% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 170−172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.59 (d, J = 7.9 Hz, 1H), 7.28−7.25 (m, 1H), 7.02 (t, J = 7.7 Hz, 1H), 6.79 (d, J = 7.9 Hz, 1H), 4.96 (d, J = 3.0 Hz, 1H), 4.65 (d, J = 2.4 Hz, 2H), 4.54 (d, J = 3.0 Hz, 1H), 2.24 (t, J = 2.4 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.4, 139.6, 134.6, 130.3, 124.1, 123.1, 117.0, 114.8, 86.1, 78.1, 77.1, 71.7, 33.2. IR (neat): 1462, 1521, 1686, 3284 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{11}N_2O$ (M + H)$^+$ 199.0871, found 199.0873.

*3-Allyl-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3t**).* Prepared according to general procedure A, using allylamine (28 mg, 0.42 mmol) to afford 3-allyl-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3t**) (42 mg, 61% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 127−130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.26−7.22 (m, 1H), 6.99 (dd, J = 7.9, 7.4 Hz, 1H), 6.84 (d, J = 7.8 Hz, 1H), 5.93−5.84 (m, 1H), 5.30−5.21 (m, 2H), 4.83 (d, J = 2.5 Hz, 1H), 4.52−4.51 (m, 2H), 4.32 (d, J = 2.3 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.5, 140.4, 135.1, 132.0, 130.1, 123.9, 122.7, 117.0, 116.7, 115.0, 85.5, 46.1. IR (neat): 1496, 1654, 2923, 3242 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{13}N_2O$ (M + H)$^+$ 201.1028, found 201.1027.

*3-(3-Methoxyphenethyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3u**).* Prepared according to general procedure A, using 3-methoxyphenethylamine (52.92 mg, 0.42 mmol) to afford 3-(3-methoxyphenethyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3u**) (67 mg, 65% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 128−130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.58 (d, J = 7.3 Hz, 1H), 7.28−7.22 (m, 2H), 7.03−6.99 (m, 1H), 6.93−6.85 (m, 2H), 6.78 (dd, J = 8.2, 1.7 Hz, 2H), 4.90 (d, J = 2.6 Hz, 1H), 4.43 (d, J = 2.7 Hz, 1H), 4.10−4.04 (m, 2H), 3.80 (s, 3H), 3.01−2.97 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.9, 150.9, 140.6, 140.2, 135.1, 130.2, 129.7, 124.1, 122.8, 121.2, 117.0, 114.7, 114.6, 112.0, 84.6, 55.3, 44.9, 32.0. IR (neat): 1517, 1680, 2927, 3616 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{18}H_{19}N_2O_2$ (M + H)$^+$ 295.1446, found 295.1456.

*(E)-3-Benzyl-4-butylidene-3,4-dihydroquinazolin-2(1H)-one (**3v**).* Prepared according to general procedure A, using benzylamine (45 mg, 0.42 mmol) to afford (*E*)-3-benzyl-4-butylidene-3,4-dihydroquinazolin-2(1*H*)-one (**3v**) (22 mg, 21% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 122−124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.39 (d, J = 7.9 Hz, 1H), 7.31−7.28 (m, 4H), 7.24−7.21 (m, 2H), 7.01−6.97 (m, 1H), 6.79 (dd, J = 7.9, 0.8 Hz, 1H), 5.04 (s, 2H), 4.99 (t, J = 7.1 Hz, 1H), 2.28 (q, J = 7.2 Hz, 2H), 1.38−1.29 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.5, 137.5, 136.8, 133.0, 129.1, 128.6, 127.1, 126.9, 126.6, 121.7, 118.4, 114.1, 112.7, 48.2, 30.6, 23.9, 13.7. IR (neat): 1448, 1500, 1669, 2922, 3211 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{19}H_{21}N_2O$ (M + H)$^+$ 293.1654, found 293.1660.

*(E/Z)-4-Benzylidene-3-(4-methoxybenzyl)-3,4-dihydroquinazolin-2(1H)-one (**3w**).* Prepared according to general procedure A, using 4-methoxybenzylamine (58 mg, 0.42 mmol) to afford (*E*/*Z*)-4-benzylidene-3-(4-methoxybenzyl)-3,4-dihydroquinazolin-2(1*H*)-one (**3w**) (62 mg, 50% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 236−238 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.21 (s, 1H), 7.49 (d, J = 7.4 Hz, 1H), 7.39−7.35 (m, 4H), 7.29−7.27 (m, 3H), 7.24−7.20 (m, 3H), 7.14−7.10 (m, 3H), 7.04−7.00 (m, 2H), 6.89−6.83 (m, 5H), 6.77 (t, J = 7.2 Hz, 2H), 6.67−6.62 (m, 3H), 6.31 (s, 1H), 6.08 (s, 1H), 5.13 (s, 2H), 4.70 (s, 2H), 3.79 (s, 3H), 3.70 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.7, 154.4, 152.9, 137.3, 136.6, 136.2, 135.3, 134.3, 134.1, 129.9, 129.8, 129.4, 129.2, 128.9, 128.8, 128.8, 128.6, 128.5, 128.4, 127.9, 127.2, 126.7, 123.0, 122.8, 121.8, 121.6, 117.0, 114.4, 114.4, 114.2, 113.8, 113.6, 111.8, 109.7, 55.4, 55.2, 49.5, 47.4. IR (neat): 1454, 1509, 1678, 2918 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{23}H_{21}N_2O_2$ (M + H)$^+$ 357.1603, found 357.1604.

*4-Hydroxy-3-(4-methoxybenzyl)-4-phenyl-3,4-dihydroquinazolin-2(1H)-one (**3x**).* Prepared according to general procedure A, using 4-methoxybenzylamine (48 mg, 0.35 mmol) to afford 4-hydroxy-3-(4-

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methoxybenzyl)-4-phenyl-3,4-dihydroquinazolin-2(1*H*)-one (**3x**) (80 mg, 63% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 70:30). MP = 140−143 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 7.40−7.38 (m, 1H), 7.28 (t, J = 7.5 Hz, 2H), 7.23−7.19 (m, 2H), 7.16−7.11 (m, 1H), 7.08 (d, J = 8.6 Hz, 2H), 6.97 (d, J = 7.7 Hz, 1H), 6.86−6.79 (m, 2H), 6.70 (d, J = 8.7 Hz, 2H), 4.30 (d, J = 15.1 Hz, 1H), 4.12 (d, J = 15.0 Hz, 1H), 3.67 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 157.5, 152.0, 145.6, 134.8, 132.0, 128.9, 128.6, 128.0, 127.7, 127.5, 125.8, 124.9, 120.9, 113.3, 112.8, 87.6, 54.9, 45.2. IR (neat): 1456, 1540, 1607, 1656, 2922, 2853 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{22}H_{20}N_2O_3Na$ (M + Na)$^+$ 383.1372, found 383.1382.

3-(4-((6-Methoxyquinolin-8-yl)amino)pentyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3y**). Prepared according to general procedure A, using primaquine (109 mg, 0.42 mmol) to afford 3-(4-((6-methoxyquinolin-8-yl)amino)pentyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3y**) (64 mg, 45% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 60:40). MP = 90−93 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 8.50 (dd, J = 4.2, 1.6 Hz, 1H), 7.90 (dd, J = 8.3, 1.6 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.29−7.25 (m, 1H), 7.21−7.17 (m, 1H), 6.95−6.91 (m, 1H), 6.79 (d, J = 7.9 Hz, 1H), 6.31 (q, J = 2.5 Hz, 2H), 6.03 (s, 1H), 4.76 (d, J = 2.5 Hz, 1H), 4.24 (d, J = 2.6 Hz, 1H), 3.86 (s, 3H), 3.73−3.60 (m, 2H), 1.92−1.81 (m, 4H), 1.72−1.67 (m, 1H), 1.30 (d, J = 6.3 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.5, 151.5, 145.1, 144.3, 140.1, 135.5, 135.2, 134.8, 130.1, 130.0, 123.9, 122.6, 121.9, 116.9, 114.8, 96.8, 91.7, 84.4, 55.3, 48.0, 43.2, 34.0, 22.4, 20.6. IR (neat): 1453, 1519, 1661, 2956 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{24}H_{27}N_4O_2$ (M + H)$^+$ 403.2134, found 403.2134.

3-(Benzo[d][1,3]dioxol-5-ylmethyl)-4-methylene-3,4-dihydroquinazolin-2(1H)-one (**3z**). Prepared according to general procedure A, using piperonylamine (64 mg, 0.42 mmol) to afford 3-(benzo[*d*][1,3]-dioxol-5-ylmethyl)-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one (**3z**) (60 mg, 58% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 173−175 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.31−7.25 (m, 1H), 6.98−6.91 (m, 2H), 6.83 (dd, J = 9.0, 4.7 Hz, 2H), 6.74 (dd, J = 8.0, 1.4 Hz, 1H), 5.97 (s, 2H), 4.90 (s, 2H), 4.82 (d, J = 2.3 Hz, 1H), 4.17 (d, J = 2.4 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 150.1, 147.4, 146.0, 139.6, 135.5, 130.9, 130.1, 123.9, 122.1, 119.6, 116.0, 114.6, 108.2, 107.0, 100.8, 85.3, 45.5. IR (neat): 1440, 1546, 1626, 1681, 3062 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{15}N_2O_3$ (M + H)$^+$ 295.1083, found 295.1093.

3-(2-Acetylphenyl)-1,1-dimethylurea (**6a**). Prepared according to general procedure C, using dimethylamine (19 mg, 0.42 mmol) to afford 3-(2-acetylphenyl)-1,1-dimethylurea (**6a**) (43 mg, 60% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 20:80). MP = 85−88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.40 (s, 1H), 8.63 (dd, J = 8.6, 0.9 Hz, 1H), 7.84 (dd, J = 8.0, 1.5 Hz, 1H), 7.49 (ddd, J = 8.6, 7.3, 1.5 Hz, 1H), 6.98−6.94 (m, 1H), 3.07 (s, 6H), 2.63 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 203.0, 155.8, 143.4, 135.2, 131.7, 120.9, 120.3, 119.7, 36.4, 28.5. IR (neat): 1524, 1738, 2921, 3616 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{11}H_{15}N_2O_2$ (M + H)$^+$ 207.1134, found 207.1141.

3-(2-Acetylphenyl)-1,1-diisopropylurea (**6b**). Prepared according to general procedure C, using diisopropylamine (25 mg, 0.42 mmol) to afford 3-(2-acetylphenyl)-1,1-diisopropylurea (**6b**) (71 mg, 77% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 20:80). MP = 199−102 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.15 (s, 1H), 8.48 (dd, J = 8.6, 1.0 Hz, 1H), 7.83 (dd, J = 8.1, 1.6 Hz, 1H), 7.47 (ddd, J = 8.7, 7.2, 1.6 Hz, 1H), 6.96−6.92 (m, 1H), 3.98−3.88 (m, 2H), 2.64 (s, 3H), 1.38 (s, 6H), 1.37 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 202.9, 154.5, 143.7, 135.0, 131.7, 121.2, 120.5, 120.0, 46.5, 28.5, 21.2. IR (neat): 1309, 1521, 1645, 1734, 3264 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{15}H_{23}N_2O_2$ (M + H)$^+$ 263.1759, found 263.1759.

3-(2-Acetylphenyl)-1,1-diisobutylurea (**6c**). Prepared according to general procedure C, using diisobutylamine (54 mg, 0.42 mmol) to afford 3-(2-acetylphenyl)-1,1-diisobutylurea (**6c**) (78 mg, 76% yield) as a red liquid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 20:80). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.39 (s, 1H), 8.68 (dd, J = 8.6, 0.8 Hz, 1H), 7.82 (dd, J = 8.0, 1.4 Hz, 1H), 7.48−7.44 (m, 1H), 6.95−6.91 (m, 1H), 3.23 (s, 2H), 3.21 (s, 2H), 2.62 (s, 3H), 2.13−2.02 (m, 2H), 0.94 (s, 6H), 0.93 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 202.7, 155.5, 143.4, 135.1, 131.6, 120.8, 120.1, 119.7, 55.9, 28.4, 27.7, 20.2. IR (neat): 1240, 1449, 1527, 1647, 1735 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{27}N_2O_2$ (M + H)$^+$ 291.2072, found 291.2072.

N-(2-Acetylphenyl)pyrrolidine-1-carboxamide (**6d**). Prepared according to general procedure C, using pyrrolidine (30 mg, 0.42 mmol) to afford *N*-(2-acetylphenyl)pyrrolidine-1-carboxamide (**6d**) (65 mg, 80% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 20:80). MP = 96−98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.24 (s, 1H), 8.68 (dd, J = 8.6, 1.0 Hz, 1H), 7.82 (dd, J = 8.1, 1.5 Hz, 1H), 7.48 (ddd, J = 8.7, 7.3, 1.5 Hz, 1H), 6.94 (ddd, J = 8.3, 7.2, 1.2 Hz, 1H), 3.53−3.50 (m, 4H), 2.62 (s, 3H), 1.95 (s, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 202.9, 154.1, 143.4, 135.2, 131.7, 120.6, 120.1, 119.6, 45.8, 28.5. IR (neat): 1525, 1648, 1735, 2930, 3615 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{13}H_{17}N_2O_2$ (M + H)$^+$ 233.1290, found 233.1297.

N-(2-Acetylphenyl)morpholine-4-carboxamide (**6e**). Prepared according to general procedure C, using morpholine (37 mg, 0.42 mmol) to afford *N*-(2-acetylphenyl)morpholine-4-carboxamide (**6e**) (62 mg, 71% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 20:80). MP = 133−135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.52 (s, 1H), 8.58 (dd, J = 8.6, 0.8 Hz, 1H), 7.84 (dd, J = 8.0, 1.4 Hz, 1H), 7.50 (ddd, J = 8.7, 7.4, 1.5 Hz, 1H), 7.00−6.96 (m, 1H), 3.73 (t, J = 4.64 Hz, 4H), 3.56 (t, J = 5.12 Hz, 4H), 2.63 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 203.3, 154.9, 143.0, 135.3, 131.8, 120.9, 120.7, 119.8, 66.6, 44.0, 28.5. IR (neat): 1243, 1528, 1644, 1734, 2922 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{13}H_{17}N_2O_3$ (M + H)$^+$ 249.1239, found 249.1248.

N-(2-Acetylphenyl)-2-amino-6-oxocyclohex-1-ene-1-carboxamide (**6f**). Prepared according to general procedure C, using 3-amino-2-cyclohexen-1-one (47 mg, 0.42 mmol) to afford *N*-(2-acetylphenyl)-2-amino-6-oxocyclohex-1-ene-1-carboxamide (**6f**) (15 mg, 16% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 20:80). MP = 120−123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, J = 8.6, 0.8 Hz, 1H), 8.01 (dd, J = 8.5, 0.7 Hz, 1H), 7.77 (ddd, J = 8.3, 6.8, 1.3 Hz, 1H), 7.56 (ddd, J = 8.3, 6.8, 1.3 Hz, 1H), 3.27 (t, J = 6.04 Hz 1H), 3.05 (s, 3H), 2.80 (t, J = 6.36 Hz, 2H), 2.24−2.16 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.8, 162.2, 150.1, 148.0, 131.6, 129.3, 127.8, 126.5, 125.6, 125.5, 41.2, 34.9, 21.4, 16.2. IR (neat): 1524, 1695, 1739, 3616 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{15}H_{17}N_2O_3$ (M + H)$^+$ 273.1239, found 273.1237.

2-Methoxybenzyl (2-Acetylphenyl)carbamate (**6g**). Prepared according to general procedure D, using 2-methoxybenzyl alcohol (58 mg, 0.42 mmol) to afford 2-methoxybenzyl (2-acetylphenyl)-carbamate (**6g**) (51 mg, 53% yield) as a faint green solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 10:90). MP = 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.22 (s, 1H), 8.52 (dd, J = 8.6, 0.9 Hz, 1H), 7.86 (dd, J = 8.0, 1.5 Hz, 1H), 7.54 (ddd, J = 8.6, 7.4, 1.4 Hz, 1H), 7.41 (dd, J = 7.5, 1.6 Hz, 1H), 7.31 (td, J = 8.1, 1.7 Hz, 1H), 7.06 (ddd, J = 8.3, 7.3, 1.2 Hz, 1H), 6.96 (td, J = 7.5, 0.9 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 5.28 (s, 2H), 3.86 (s, 3H), 2.64 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 202.3, 157.5, 154.0, 141.5, 135.1, 131.7, 129.6, 129.5, 124.6, 121.6, 121.4, 120.5, 119.4, 110.5, 62.4, 55.5, 28.6. IR (neat): 1522, 1650, 1732, 3615 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{17}NO_4Na$ (M + Na)$^+$ 322.1055, found 322.1060.

3-(2-Acetylphenyl)-1-(2-hydroxyethyl)-1-methylurea (**6h**). Prepared according to general procedure C, using 2-(methylamino)-ethanol (31 mg, 0.42 mmol) to afford 3-(2-acetylphenyl)-1-(2-hydroxyethyl)-1-methylurea (**6h**) (71 mg, 86% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 112−115 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.46 (s, 1H), 8.58 (dd, J = 8.6, 1.1 Hz, 1H), 7.87−7.84 (m, 1H), 7.53−7.48 (m, 1H), 7.02−6.98 (m, 1H), 3.83 (s, 3H), 3.60−3.57 (m, 2H), 3.18−3.17 (m, 10H), 2.66−2.65 (m, 3H), 1.82 (s, 1H). ^{13}C{^{1}H} NMR

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(100 MHz, $CDCl_3$) δ 203.2, 157.1, 143.0, 135.3, 131.8, 121.2, 120.8, 120.0, 61.8, 52.1, 35.9, 28.6. IR (neat): 1203, 1452, 1644, 2923 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{16}N_2O_3Na$ $(M + Na)^+$ 259.1059, found 259.1059.

*1-(2-Acetylphenyl)-3-(3-hydroxypropyl)urea (**6i**).* Prepared according to general procedure E, using 3-aminopropan-1-ol (32 mg, 0.42 mmol) to afford 1-(2-acetylphenyl)-3-(3-hydroxypropyl)urea (**6i**) (25 mg, 31% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 111−113 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 10.34 (s, 1H), 8.12 (dd, J = 8.0, 1.3 Hz, 1H), 7.61 (m, 1H), 7.25−7.21 (m, 1H), 7.12 (d, J = 8.1 Hz, 1H), 4.19 (m, 4H), 2.06 (m, 2H), 2.02 (s, 3H), 1.82 (bs, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.6, 171.3, 162.5, 152.1, 138.7, 135.2, 128.5, 123.5, 115.1, 114.6, 62.5, 38.3, 27.2, 21.0. IR (neat): 1243, 1660, 1715, 1733, 2921 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{17}N_2O_3$ $(M + H)^+$ 237.1239, found 237.1240.

*1-(2-Acetylphenyl)-3-(tert-butyl)urea (**6j**).* Prepared according to general procedure C, using *tert*-butylamine (31 mg, 0.42 mmol) to afford 1-(2-acetylphenyl)-3-(*tert*-butyl)urea (**6j**) (53 mg, 65% yield) as a yellow liquid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). ^1H NMR (400 MHz, $CDCl_3$) δ 10.95 (s, 1H), 8.52 (d, J = 8.7 Hz, 1H), 7.82 (d, J = 8.1 Hz, 1H), 7.47 (t, J = 7.9 Hz, 1H), 6.95 (t, J = 7.6 Hz, 1H), 2.63 (s, 3H), 1.39 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 203.0, 154.2, 143.4, 135.1, 131.7, 120.7, 120.2, 120.1, 119.9, 51.1, 29.3. IR (neat): 1014, 1539, 1649, 1715, 3350 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{13}H_{18}N_2O_2Na$ $(M + Na)^+$ 257.1265, found 257.1247.

*4-Hydroxyquinolin-2(1H)-one (**7a**).*[7a,20] Prepared according to general procedure F, using 3-(*tert*-butylperoxy)-3-methylindolin-2-one (82 mg, 0.35 mmol) to afford 4-hydroxyquinolin-2(1*H*)-one (**7a**) (45 mg, 80% yield) as a white solid after purification using silica gel column chromatography (DCM:MeOH = 90:10). The data for this compound and for the reported compound are in agreement.

*10b-Methyl-2,3,6,10b-tetrahydro-5H-oxazolo[3,2-c]quinazolin-5-one (**9a**).* Prepared according to general procedure G, using ethanolamine (26 mg, 0.42 mmol) to afford 10b-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-*c*]quinazolin-5-one (**9a**) (58 mg, 81% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 161−163 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.25−7.22 (m, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.86−6.84 (m, 1H), 4.18−4.10 (m, 2H), 3.94 (dd, J = 14.3, 7.1 Hz, 1H), 3.66 (dt, J = 10.4, 7.0 Hz, 1H), 1.54 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.6, 134.5, 129.3, 124.5, 123.1, 122.7, 114.2, 91.9, 63.5, 43.4, 27.6. IR (neat): 1517, 1673, 3061, 3616 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{11}H_{13}N_2O_2$ $(M + H)^+$ 205.0977, found 205.0978.

*10b-Phenyl-2,3,6,10b-tetrahydro-5H-oxazolo[3,2-c]quinazolin-5-one (**9b**).* Prepared according to general procedure G, using ethanolamine (26 mg, 0.42 mmol) to afford 10b-phenyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-*c*]quinazolin-5-one (**9b**) (75 mg, 78% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 170−173 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.51 (m, 2H), 7.38−7.30 (m, 3H), 7.30−7.27 (m, 1H), 7.19 (m, 1H), 6.97 (td, J = 7.7, 1.1 Hz, 1H), 6.82 (dd, J = 8.0, 0.7 Hz, 1H), 4.26 (ddd, J = 10.7, 8.2, 5.9 Hz, 1H), 4.08 (td, J = 8.2, 5.9 Hz, 1H), 3.95 (td, J = 8.3, 5.9 Hz, 1H) 3.36 (ddd, J = 10.7, 8.4, 5.9 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.7, 143.0, 134.0, 129.5, 128.8, 128.4, 126.6, 125.1, 122.9, 121.4, 114.4, 94.2, 62.8, 43.4. IR (neat): 1434, 1602, 1670, 2920, 3212 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{16}H_{15}N_2O_2$ $(M + H)^+$ 267.1134, found 267.1131.

*10b-Benzyl-2,3,6,10b-tetrahydro-5H-oxazolo[3,2-c]quinazolin-5-one (**9c**).* Prepared according to general procedure G, using ethanolamine (26 mg, 0.42 mmol) to afford 10b-benzyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-*c*]quinazolin-5-one **9c** (71 mg, 72% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 154−156 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.28 (d, J = 7.6 Hz, 1H), 7.23 (dd, J = 7.5, 1.4 Hz, 1H), 7.20−7.16 (m, 3H), 7.05−6.98 (m, 3H), 6.75−6.73 (m, 1H), 4.11−4.06 (m, 1H), 4.00 (m, 1H), 3.84 (q, J = 7.7 Hz, 1H), 3.16 (m, 1H), 3.01 3.05 (d, J = 13.5 Hz, 1H), 2.97 (d, J = 13.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.7, 135.1, 134.9, 130.7, 129.3, 128.1, 126.9, 124.8, 122.5, 122.1, 113.9, 94.1, 64.3, 47.0, 44.1. IR (neat): 1438, 1671, 2912, 3212 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{17}N_2O_2$ $(M + H)^+$ 281.1290, found 281.1289.

*11b-Methyl-3,4,7,11b-tetrahydro-2H,6H-[1,3]oxazino[3,2-c]-quinazolin-6-one (**9d**).* Prepared according to general procedure G, using 3-aminopropan-1-ol (32 mg, 0.42 mmol) to afford 11b-methyl-3,4,7,11b-tetrahydro-2*H*,6*H*-[1,3]oxazino[3,2-*c*]quinazolin-6-one (**9d**) (58 mg, 76% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 140−142 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.37 (dd, J = 7.8, 1.4 Hz, 1H), 7.24−7.20 (m, 1H), 7.02 (td, J = 7.6, 1.1 Hz, 1H), 6.72 (dd, J = 8.0, 0.8 Hz, 1H), 4.48−4.43 (m, 1H), 4.09 (td, J = 11.4, 3.6 Hz, 1H), 3.98−3.94 (m, 1H), 3.29 (td, J = 13.2, 4.0 Hz, 1H), 2.10−1.88 (m, 2H), 1.72 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.0, 134.0, 129.3, 124.9, 124.2, 122.6, 113.6, 86.3, 60.6, 35.8, 25.1, 23.0. IR (neat): 1520, 1657, 1716, 3615 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{15}N_2O_2$ $(M + H)^+$ 219.1133, found 219.1136.

*11b-Phenyl-3,4,7,11b-tetrahydro-2H,6H-[1,3]oxazino[3,2-c]-quinazolin-6-one (**9e**).* Prepared according to general procedure G, using 3-aminopropan-1-ol (32 mg, 0.42 mmol) to afford 11*b*-phenyl-3,4,7,11*b*-tetrahydro-2*H*,6*H*-[1,3]oxazino[3,2-*c*]quinazolin-6-one (**9e**) (75 mg, 76% yield) as a faint yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 189−192 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 7.48 (d, J = 7.5 Hz, 2H), 7.41−7.36 (m, 3H), 7.28 (t, J = 7.3 Hz, 1H), 7.13 (td, J = 7.9, 1.3 Hz, 1H), 6.94−6.89 (m, 1H), 6.77 (d, J = 7.9 Hz, 1H), 4.61 (dd, J = 13.4, 3.2 Hz, 1H), 4.09−4.01 (m, 2H), 3.04 (td, J = 13.2, 3.1 Hz, 1H), 2.17−2.03 (m, 1H), 1.50 (d, J = 13.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.0, 140.9, 133.5, 129.3, 129.2, 128.2, 126.2, 123.1, 122.5, 114.1, 89.9, 62.6, 37.8, 25.3. IR (neat): 1425, 1605, 1666, 2922, 3204 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{17}N_2O_2$ $(M + H)^+$ 281.1290, found 281.1297

*11b-Benzyl-3,4,7,11b-tetrahydro-2H,6H-[1,3]oxazino[3,2-c]-quinazolin-6-one (**9f**).* Prepared according to general procedure G, using 3-aminopropan-1-ol (32 mg, 0.42 mmol) to afford 11b-benzyl-3,4,7,11b-tetrahydro-2*H*,6*H*-[1,3]oxazino[3,2-*c*]quinazolin-6-one (**9f**) (73 mg, 71% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 156−158 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.23 (d, J = 6.7 Hz, 1H), 7.18−7.14 (m, 1H), 7.12 (d, J = 7.3 Hz, 1H), 7.07 (t, J = 7.2 Hz, 2H), 6.96 (t, J = 7.6 Hz, 1H), 6.76−6.69 (m, 2H), 6.52−6.46 (m, 1H), 4.53 (dd, J = 13.6, 5.9 Hz, 1H), 4.27−4.20 (m, 1H), 4.01−3.96 (m, 1H), 3.66 (d, J = 13.3 Hz, 1H), 3.38 (td, J = 13.0, 4.4 Hz, 1H), 3.00 (d, J = 13.3 Hz, 1H), 2.06−1.94 (m, 1H), 1.86−1.81 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.1, 135.1, 134.6, 130.4, 129.4, 127.9, 126.8, 125.6, 122.0, 121.5, 113.2, 89.2, 60.4, 41.8, 35.7, 24.9. IR (neat): 1437, 1664, 2920 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{18}H_{19}N_2O_2$ $(M + H)^+$ 295.1446, found 295.1452

*12b-Benzyl-2,3,4,5,8,12b-hexahydro-7H-[1,3]oxazepino[3,2-c]-quinazolin-7-one (**9g**).* Prepared according to general procedure G, using 4-amino-1-butanol (37 mg, 0.42 mmol) to afford 12b-benzyl-2,3,4,5,8,12b-hexahydro-7*H*-[1,3]oxazepino[3,2-*c*]quinazolin-7-one (**9g**) (67 mg, 62% yield) as a yellow solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 195−198 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.29 (dd, J = 7.7, 1.3 Hz, 1H), 7.20−7.15 (m, 1H), 7.09−6.97 (m, 4H), 6.71−6.68 (m, 2H), 6.54 (dd, J = 8.0, 0.8 Hz, 1H), 4.39 (d, J = 13.3 Hz, 1H), 3.78 (d, J = 13.8 Hz, 1H), 3.60 (td, J = 12.2, 1.3 Hz, 1H), 3.30 (t, J = 12.5 Hz, 1H), 3.18 (d, J = 13.2 Hz, 1H), 2.98 (d, J = 13.2 Hz, 1H), 1.84−1.71 (m, 2H), 1.65−1.44 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.8, 136.5, 134.7, 130.4, 129.4, 127.7, 126.7, 125.7, 121.8, 120.6, 113.2, 92.8, 64.6, 47.3, 40.3, 29.2, 27.3. IR (neat): 1448, 1495, 1603, 1658, 2923, 3202 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{18}H_{19}N_2O_2$ $(M + H)^+$ 309.1603, found 309.1596

*(3S,10bR)-3-Ethyl-10b-methyl-2,3,6,10b-tetrahydro-5H-oxazolo-[3,2-c]quinazolin-5-one (**9h**) and (3S,10bS)-3-Ethyl-10b-methyl-2,3,6,10b-tetrahydro-5H-oxazolo[3,2-c]quinazolin-5-one (**9h′**).* Prepared according to general procedure G, using (*S*)-(+)-2-amino-1-

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propanol (37 mg, 0.42 mmol) to afford (3*S*,10b*R*)-3-ethyl-10b-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-*c*]quinazolin-5-one **9h** (45 mg, 55% yield) as a faint pink solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70) with MP = 185−187 °C and (3*S*,10b*S*)-3-ethyl-10b-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo-[3,2-*c*]quinazolin-5-one **9h′** (13 mg, 16% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 70:30) with MP = 184−186 °C. Diastereomers **9h** and **9h′** are present in a ratio of 3.4:1. HPLC for **9h** (CHIRALPAK IA column, *n*-heptane/isopropanol = 80/20, flow rate = 0.7 mL/min, l = 254 nm): tR = 9.62 min (major), tR= 7.23 min (minor), 97% *de*. HPLC for **9h′** (CHIRALPAK IA column, *n*-heptane/isopropanol = 80/20, flow rate = 0.7 mL/min, l = 254 nm): tR= 9.88 min (major), tR = 9.61 min (minor), 90% *de*. (3*S*,10b*R*)-3-Ethyl-10b-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-c]quinazolin-5-one (**9h**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.22 (td, J = 8.1, 1.3 Hz, 1H), 7.03 (t, J = 7.5 Hz, 1H), 6.79 (t, J = 7.1 Hz, 1H), 4.10 (td, J = 10.5, 5.5 Hz, 1H), 4.01 (dd, J = 8.4, 6.6 Hz, 1H), 3.91 (dd, J = 8.5, 4.6 Hz, 1H), 2.23−2.12 (m, 1H), 1.74−1.63 (m, 1H), 1.56 (s, 3H), 1.03 (t, J = 7.5 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.4, 134.8, 129.1, 124.0, 122.7, 114.0, 113.9, 92.4, 69.1, 59.1, 29.5, 28.0, 10.7. IR (neat): 1524, 1690, 1739, 3616 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{13}H_{17}N_2O_2$ (M + H)$^+$ 233.1290, found 233.1295. The crystals of compound **9h** were grown using dichloromethane and petroleum ether (2:1) as a solvent by slow evaporation. A needle-shaped single crystal was mounted on a loop by applying a small amount of paraffin oil. Crystal data for compound **9h**: $C_{13}H_{15}N_2O_2$, M = 231.27, orthorhombic, space group P 21 21 21 with a = 7.5792(3) Å, b = 7.7672(3) Å, c = 19.9951(7) Å, α = 90°, β = 90°, γ = 90°, V = 1177.09(8) Å^3, T = 296(2) K, R1 = 0.0306, wR2 = 0.0814 for observed data, z = 4, D_{calcd} = 1.305 g cm^{-3}, F(000) = 492, absorption coefficient = 0.725 mm^{-1}, λ = 1.54178 Å, 1999 reflections collected on a Bruker APEX-II CCD single-crystal diffractometer, and 1964 observed reflections ($I \geq 2\sigma(I)$). The largest difference peak and hole are 0.510 and −0.142 eÅ^{-3}, respectively

*(3S,10bS)-3-Ethyl-10b-methyl-2,3,6,10b-tetrahydro-5H-oxazolo-[3,2-c]quinazolin-5-one (**9h′**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.32 (dd, J = 7.6, 1.1 Hz, 1H), 7.22 (td, J = 7.8, 1.4 Hz, 1H), 7.04 (td, J = 7.5, 0.9 Hz, 1H), 6.80 (d, J = 7.9 Hz, 1H), 4.37 (dd, J = 8.8, 7.0 Hz, 1H), 4.14−4.08 (m, 1H), 3.99 (dd, J = 8.9, 2.7 Hz, 1H), 2.07−1.96 (m, 1H), 1.67−1.60 (m, 1H), 1.45 (s, 3H), 0.80 (t, J = 7.5 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.2, 134.8, 128.8, 125.5, 123.0, 122.8, 114.0, 92.4, 69.0, 56.4, 25.5, 24.1, 9.3. IR (neat): 1520, 1674, 3615 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{13}H_{17}N_2O_2$ (M + H)$^+$ 233.1290, found 233.1295.

*(3S,10bR)-3-Isopropyl-10b-methyl-2,3,6,10b-tetrahydro-5H-oxazolo[3,2-c]quinazolin-5-one (**9i**) and (3S,10bS)-3-Isopropyl-10b-methyl-2,3,6,10b-tetrahydro-5H-oxazolo[3,2-c]quinazolin-5-one (**9i′**).* Prepared according to general procedure G, using (*S*)-(+)-2-amino-3-methyl-1-butanol (43 mg, 0.42 mmol) to afford (3*S*,10b*R*)-3-isopropyl-10b-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-*c*]-quinazolin-5-one (**9i**) (41 mg, 48% yield) as a gray solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70) with MP = 205−208 °C and (3*S*,10b*S*)-3-isopropyl-10b-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-*c*]quinazolin-5-one **9i′** (17 mg, 20% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 70:30) with MP = 204−207 °C. Diastereomers **9i** and **9i′** are present in a ratio of 2.4:1. HPLC for **9i** (CHIRALPAK IA column, *n*-heptane/isopropanol = 80/20, flow rate = 0.7 mL/min, l = 254 nm): tR= 8.03 min (major), tR = 6.82 min (minor), 94% *de*. HPLC for **9i′** (CHIRALPAK IA column, *n*-heptane/isopropanol = 80/20, flow rate = 0.7 mL/min, l = 254 nm): tR = 13.63 min (major), tR = 8.12 min (minor), 95% *de*. (3*S*,10b*R*)-3-isopropyl-10b-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-c]quinazolin-5-one (**9i**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.38−7.34 (m, 1H), 7.22 (td, J = 7.7, 1.5 Hz, 1H), 7.03 (td, J = 7.5, 1.1 Hz, 1H), 6.77 (dd, J = 8.0, 0.7 Hz, 1H), 3.98 (dd, J = 8.4, 2.9 Hz, 1H), 3.93−3.88 (m, 1H), 3.76 (dd, J = 8.4, 5.9 Hz, 1H), 2.17−2.04 (m, 1H), 1.56 (s, 3H), 1.15 (d, J = 6.9 Hz, 3H), 1.03 (d, J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.2, 135.0, 129.1, 124.3, 124.0, 122.6, 113.8, 92.5, 67.7, 64.2, 31.8, 30.0, 19.9, 19.6. IR (neat): 1524, 1693, 1739, 3616 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{14}H_{19}N_2O_2$ (M + H)$^+$ 247.1446, found 247.1444.

*(3S,10bS)-3-Isopropyl-10b-methyl-2,3,6,10b-tetrahydro-5H-oxazolo[3,2-c]quinazolin-5-one (**9i′**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 7.0 Hz, 1H), 7.23 (td, J = 7.8, 1.4 Hz, 1H), 7.05 (td, J = 7.5, 0.9 Hz, 1H), 6.98 (s, 1H), 6.76 (d, J = 8.0 Hz, 1H), 4.26−4.21 (m, 1H), 4.13−4.09 (m, 2H), 2.69−2.59 (m, 1H), 1.45 (s, 3H), 0.89 (d, J = 7.1 Hz, 3H), 0.58 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.7, 128.7, 125.6, 125.5, 123.1, 122.9, 113.7, 92.4, 64.8, 60.0, 26.2, 25.2, 19.5, 14.7.IR (neat): 1511, 1605, 1670, 3062, 3613 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{14}H_{19}N_2O_2$ (M + H)$^+$ 247.1446, found 247.1451.

*(3S,10bR)-3-Benzyl-10b-methyl-2,3,6,10b-tetrahydro-5H-oxazolo[3,2-c]quinazolin-5-one (**9j**) and (3S,10bS)-3-Benzyl-10b-methyl-2,3,6,10b-tetrahydro-5H-oxazolo[3,2-c]quinazolin-5-one (**9j′**).* Prepared according to general procedure G, using (*S*)-2-amino-3-phenylpropan-1-ol (64 mg, 0.42 mmol) to afford (3*S*,10b*R*)-3-benzyl-10b-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-*c*]quinazolin-5-one (**9j**) (47 mg, 45% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70) with MP = 122−125 °C and (3*S*,10b*S*)-3-benzyl-10b-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-*c*]quinazolin-5-one (**9j′**) (36 mg, 35% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 70:30) with MP = 92−95 °C. Diastereomers **9j** and **9j′** are present in a ratio of 1.3:1. HPLC for **9j** (CHIRALPAK IA column, *n*-heptane/isopropanol = 80/20, flow rate = 0.7 mL/min, l = 254 nm): tR = 11.84 min (major), tR = 4.72 min (minor), 94% *de*. HPLC for **9j′** (CHIRALPAK IA column, *n*-heptane/isopropanol = 80/20, flow rate = 0.7 mL/min, l = 254 nm): tR = 13.47 min (major), tR = 11.81 min (minor), 84% *de*. (3*S*,10b*R*)-3-Benzyl-10b-methyl-2,3,6,10b-tetrahydro-5*H*-oxazolo[3,2-c]quinazolin-5-one (**9j**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 7.38−7.33 (m, 5H), 7.30−7.22 (m, 2H), 7.04 (t, J = 7.5 Hz, 1H), 6.90−6.89 (m, 1H), 4.47−4.43 (m, 1H), 4.00 (dd, J = 8.8, 5.4 Hz, 1H), 3.90 (t, J = 7.8 Hz, 1H), 3.54 (d, J = 13.2 Hz, 1H), 3.06−2.99 (m, 1H), 1.48 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.9, 137.6, 134.9, 129.7, 129.1, 128.7, 126.8, 124.0, 123.9, 122.6, 114.2, 92.7, 68.2, 58.7, 40.4, 29.2. IR (neat): 1524, 1685, 3617 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{18}H_{19}N_2O_2$ (M + H)$^+$ 295.1446, found 295.1444.

*(3S,10bS)-3-Benzyl-10b-methyl-2,3,6,10b-tetrahydro-5H-oxazolo[3,2-c]quinazolin-5-one (**9j′**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 7.34−7.17 (m, 8H), 7.02 (td, J = 7.5, 1.0 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 4.41−4.36 (m, 1H), 4.18 (dd, J = 8.9, 6.9 Hz, 1H), 4.03 (dd, J = 9.3, 2.4 Hz, 1H), 3.66 (dd, J = 13.2, 2.7 Hz, 1H), 2.51 (dd, J = 13.2, 10.3 Hz, 1H), 1.46 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.9, 138.0, 135.0, 129.4, 128.8, 128.7, 126.6, 125.5, 122.8, 122.7, 114.2, 92.6, 68.5, 56.8, 37.7, 25.6. IR (neat): 1523, 1685, 3615 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{18}H_{19}N_2O_2$ (M + H)$^+$ 295.1446, found 295.1443.

*3-Benzylquinazoline-2,4(1H,3H)-dione (**10a**).* Prepared according to general procedure H, using 3-benzyl-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one **3a** (63 mg, 0.25 mmol) to afford 3-benzylquinazoline-2,4(1*H*,3*H*)-dione **10a** (49 mg, 78% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 203−205 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 8.13 (d, J = 7.9 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.54−7.52 (m, 2H), 7.33−7.29 (m, 2H), 7.25−7.20 (m, 2H), 7.04 (d, J = 8.1 Hz, 1H), 5.27 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.4, 152.0, 138.6, 137.0, 135.2, 129.0, 128.7, 128.6, 127.8, 123.5, 115.0, 114.7, 44.3. IR (neat): 1459, 1645, 1735, 2922, 3282 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{15}H_{13}N_2O_2$ (M + H)$^+$ 253.0977, found 253.0968.

*3-Ethylquinazoline-2,4(1H,3H)-dione (**10b**).* Prepared according to general procedure H, using 3-ethyl-4-methylene-3,4-dihydroquinazolin-2(1*H*)-one **3p** (47 mg, 0.25 mmol) to afford 3-ethylquinazoline-2,4(1*H*,3*H*)-dione **10b** (33 mg, 69% yield) as a white solid after purification using silica gel column chromatography (EtOAc:*n*-hexane = 30:70). MP = 190−192 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s, 1H), 8.14 (d, J = 7.9 Hz, 1H), 7.61 (ddd, J = 8.2, 7.3, 1.5 Hz,

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1H), 7.25−7.21 (m, 1H), 7.14 (d, J = 8.1 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 1.32 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.3, 52.1, 138.7, 135.0, 128.4, 123.4, 115.1, 114.8, 36.3, 13.3. IR (neat): 1455, 1659, 1715, 2919, 3058 cm^{-1}. HRMS (ESI-TOF) m/z calculated for $C_{10}H_{11}N_2O_2$ $(M + H)^+$ 191.0820, found 191.0824.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00889.

Copies of ^1H and ^{13}C NMR spectra and crystallographic data (PDF).

FAIR data, including the primary NMR FID files, for compounds **3a−z**, **6a−j**, **7a**, **9a−h**, **9h′**, **9i**, **9i′**, **9j**, **9j′**, **10a**, and **10b** (ZIP)

Accession Codes

CCDC 2053446−2053447 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Boopathy Gnanaprakasam − *Department of Chemistry, Indian Institute of Science Education and Research, Pune 411008, India;* orcid.org/0000-0002-3047-9636; Email: gnanaprakasam@iiserpune.ac.in

Authors

Akash S. Ubale − *Department of Chemistry, Indian Institute of Science Education and Research, Pune 411008, India;* orcid.org/0000-0001-6893-1192

Moseen A. Shaikh − *Department of Chemistry, Indian Institute of Science Education and Research, Pune 411008, India*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c00889

Notes

The authors declare no competing financial interest.

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