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Catalyst-Free Chemoselective Synthesis of 3,4-Dihydroquinazoline-2-thiones and 2-Imino[1,3]benzothiazines

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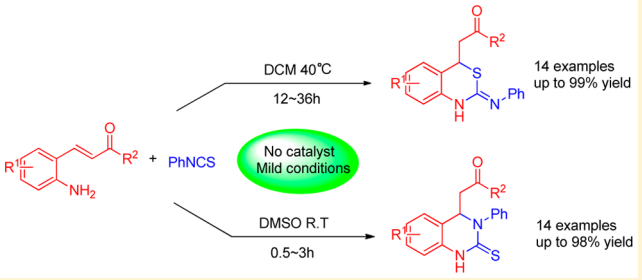
Supporting Information

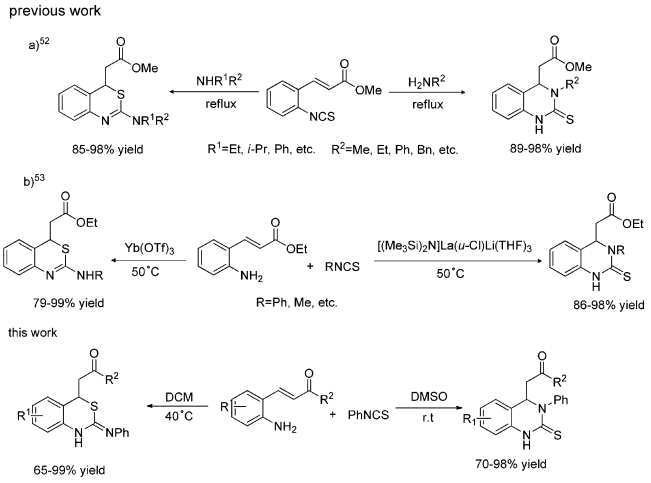
ABSTRACT: A solvent-controlled catalyst-free chemoselective reaction was developed. Both 3,4-dihydroquinazoline-2-thiones and 2-imino[1,3]benzothiazines could be efficiently constructed by the reaction of 2-amino chalcones with isothiocyanates via two different chemoselective reactions depending on the solvents. The reaction was modulated by the solvents to proceed via either aza-Michael addition or thia-Michael addition as the major reaction with excellent yields.



Chemoselective reactions are an enduring topic in organic synthesis. The strategy of using controls such as solvents to direct reactions down different pathways to favor distinct products is a well-established approach and also an efficient methodology for gaining access to chemodiversity.[1−15] However, the most practical solutions for switching the chemoselective reactive sites rely on the catalysts, because finding an appropriate condition such as a solvent for efficiently and selectively obtaining a certain product has been a long-standing challenge. We were wondering whether we could develop a catalyst-free chemoselestive reaction controlled only by a solvent instead of a catalyst. To realize that goal, an unavoidable obstacle was how to reach the transition state of the reaction for the starting materials with a solvent to provide the desired product.[16−20]

3,4-Dihydroquinazoline-2-thiones[21−28] and 2-imino[1, 3]-benzothiazines[29−36] are valuable heterocyclic moieties with broad biological and pharmaceutical activities. Numerous efficient methods[28,37−40] and novel procedures[41−48] have been developed to produce these compounds (Scheme 1). Michael addition was the most common strategy that has been utilized to construct both scaffolds; with this strategy, the initial product of the reaction was a thiourea intermediate that underwent Michael addition to selectively form one of the core structures under certain conditions.[28,37,40,49−51] Kobayashi et al. reported that the 3-(2-isothiocyanatophenyl)propanoic derivatives reacted with secondary and primary amines to selectively construct 3,4-dihydroquinazoline-2-thiones and 2-amino-3,1-benzothiazines.[52] Qi Shen et al. reported a catalyst-controlled chemoselective reaction with the corresponding skeletons delivered upon reaction of 2-aminophenyl acrylates with isothiocyanates catalyzed by different lanthanide complexes.[53] It can be seen that the strategies for selectively producing these products required either rigorous reaction conditions or costly catalysts. However, the use of heavy metal compounds should be avoided in the production of medicine because of their toxicity. Therefore, it is still highly desirable to develop a novel practical catalyst-free chemoselective reaction. So far, there have been no reports about switching between the reactive sites of the starting materials to obtain different products by changing the experimental conditions. Here, we report the development of the reaction that was modulated by the solvents to proceed

Scheme 1. Chemoselective Synthesis of 3,4-Dihydroquinazoline-2-thiones and [1,3]Benzothiazines



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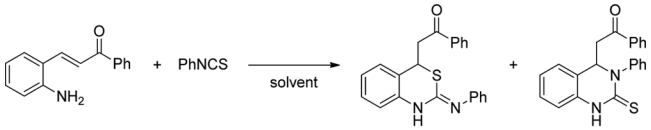
via either aza-Michael addition or thia-Michael addition as the major reaction.

Our group has been committed to the synthesis of various structures with bioactivities through organocatalytic asymmetric cascade/tandem reactions over the past several years.[54−58] We investigated the reaction by selecting 2-amino chalcone **1a** and isothiocyanate **2a** as the model substrates under the catalysis of **I** or **II** in DCM at room temperature (Table 1, entry 1 or 2,

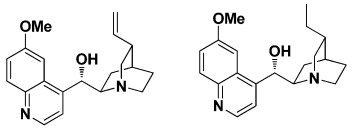
Table 1. Optimization of Experimental Conditions[a]



1a 2a 3a 4a

entry	solvent	catalyst	t (h)	T (°C)	yield of **3a** (%)[b]	yield of **4a** (%)[b]
1	DCM	I	50	rt	0	45
2	DCM	II	50	rt	0	45
3	DCM	–	24	rt	94	3
4	DCE	–	120	rt	88	0
5	THF	–	120	rt	17	0
6	toluene	–	120	rt	57	0
7	dioxane	–	120	rt	42	0
8	acetonitrile	–	120	rt	36	0
9	MeOH	–	10	rt	0	50
10	DMSO	–	0.5	rt	0	98
11	DCM	–	24	40	96	0
12	H_2O	–	120	rt	42	44
13	H_2O	–	3.5	80	0	85

[a]Unless otherwise noted, the reaction was conducted with **1a** (0.2 mmol), **2a** (0.6 mmol), and the catalyst (30 mol %) in 1 mL of the solvent. [b]Isolated yield.

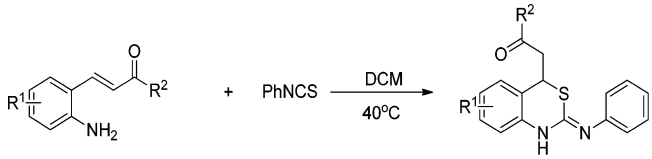


I II

respectively). The desired product **4a** was obtained in moderate yield. Surprisingly, when the reaction was performed in DCM for 24 h at room temperature in the absence of any catalysts (Table 1, entry 3), the other desired product **3a** was formed in excellent yield. Various solvents such as DCE, THF, toluene, dioxane, and acetonitrile were examined (Table 1, entries 4−8, respectively), and only product **3a** was formed, albeit with a poor yield under similar conditions. When the reaction temperature was increased to 40 °C (Table 1, entry 11), product **3a** was afforded as the only product with excellent yields (up to 96%) in DCM. It was also found that the other structure **4a** was formed as the only product in a polar solvent such as MeOH or DMSO (Table 1, entry 9 or 10, respectively), and the yield of **4a** was up to 98% within 30 min in DMSO in the absence of any catalysts. We then wondered whether the product **4a** could be obtained as the only product in pure water because water is a polar solvent. However, both compounds were formed at room temperature (Table 1, entry 12). Interestingly, when the reaction was performed in water at 80 °C for 3.5 h, product **4a** was formed in 85% yield as the only product (Table 1, entry 13).

With the reaction conditions optimized, we explored the scope of the thia-Michael addition. The results are outlined in Table 2. A range of *meta*- and *para*-substituted, electron-poor,

Table 2. Thia-Michael Addition under the Optimized Conditions[a]



1 2 3

entry	R^1	R^2	t (h)	yield of **3** (%)[b]
1	H	C_6H_5	24	96 (**3a**)
2	5-Cl	C_6H_5	28	64 (**3b**)
3	4-OMe	C_6H_5	24	91 (**3c**)
4	H	3-MeC_6H_4	24	90 (**3d**)
5	H	4-MeC_6H_4	24	99 (**3e**)
6	H	3-MeOC_6H_4	36	65 (**3f**)
7	H	4-MeOC_6H_4	36	86 (**3g**)
8	H	3-BrC_6H_4	30	92 (**3h**)
9	H	4-BrC_6H_4	36	96 (**3i**)
10	H	4-ClC_6H_4	36	98 (**3j**)
11	H	4-FC_6H_4	24	87 (**3k**)
12	H	Me	12	72 (**3l**)
13	H	α-naphthyl	30	88 (**3m**)
14	H	furyl	18	65 (**3n**)

[a]Unless otherwise noted, the reaction was conducted with **1** (0.2 mmol) and **2** (0.6 mmol) in 1 mL of DCM at 40 °C. [b]Isolated yield.

and electron-rich chalcones **1a−k** were well tolerated under the optimized conditions, giving the desired products in moderate to excellent yields. Obviously, when R^1 was an electron-withdrawing group (EWG) (Table 2, entry 2), the yield of **3** was lower than that with an electron-donating (ED) R^1 (Table 2, entry 3). It can be seen that the electronic effect of R^1 had a remarkable impact on the rate and yield of the reaction. Subsequently, the effect of R^2 on the reaction was investigated. The chalcones with various substituent groups on the phenyl ring were also well tolerated during reaction (Table 2, entries 4−11). Furthermore, the results indicated that the yields of the product with substrates bearing *para*-substituted phenyl rings were higher than those of the product with *meta*-substituted phenyl rings, regardless of whether the the substituents were EDG or EWG. However, the reactions with substrates bearing EDG proceeded faster than those with EWG. This could be attributed to substrates containing EDG having higher nucleophilic activities. The reaction with a fluoro-substituted substrate (Table 2, entry 11) took less time to complete than those with other halogen-substituted substrates (Table 2, entries 9 and 10). We hypothesized that the rate of the reaction was also influenced by the steric effect of substituents. To prove our hypothesis, two substrates were prepared; one was substituted with a small-sized methyl group (Table 2, entry 12), and the other was substituted with a large-sized α-naphthyl group (Table 2, entry 13). The reaction results proved our hypothesis to be true. The heteroaromatic group (furyl) as R^2 was also well tolerated and gave a moderate yield (Table 2, entry 14).

We then examined the scope of the aza-Michael addition, which was shown in Table 3. A variety of chalcones with

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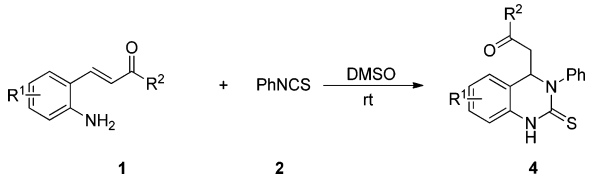
Table 3. Aza-Michael Addition under the Optimized Conditions[a]



1 2 4

entry	R^1	R^2	t (h)	yield of **4** (%)[b]
1	H	C_6H_5	0.5	98 (**4a**)
2	5-Cl	C_6H_5	2	76 (**4b**)
3	4-OMe	C_6H_5	0.5	96 (**4c**)
4	H	3-MeC_6H_4	1	95 (**4d**)
5	H	4-MeC_6H_4	1	93 (**4e**)
6	H	3-MeOC_6H_4	1	95 (**4f**)
7	H	4-MeOC_6H_4	1	97 (**4g**)
8	H	3-BrC_6H_4	2	96 (**4h**)
9	H	4-BrC_6H_4	0.5	98 (**4i**)
10	H	4-ClC_6H_4	2	95 (**4j**)
11	H	4-FC_6H_4	1	98 (**4k**)
12	H	Me	0.5	98 (**4l**)
13	H	α-naphthyl	3	94 (**4m**)
14	H	furyl	2	70 (**4n**)

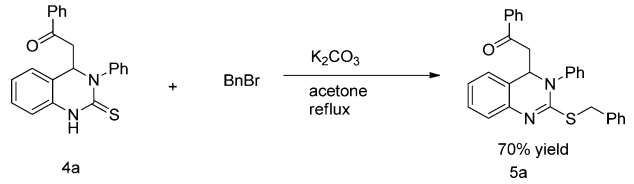
[a]Unless otherwise noted, the reaction was conducted with **1** (0.2 mmol) and **2** (0.6 mmol) in 1 mL of DMSO at rt. [b]Isolated yield.

various substituents on the phenyl ring (**1a**–**k**) were well tolerated and gave good to excellent yields under the optimized conditions. In all cases, the reactions in DMSO proceeded remarkably faster than those in DCM. The rate and yield of the reaction were influenced by the electronic effect of R^1, as shown by the different reaction results for a chloro-substituted substrate (Table 3, entry 2) and a methoxyl-substituted substrate (Table 3, entry 3). We also examined the effect of R^2 on the reaction and found that reactions with the substrates bearing EDG proceeded faster than those with substrates (Table 3, entries 4–7) bearing EWG (Table 3, entries 8 and 10). It was noticed that the reaction with the substrate bearing a fluoro-substituted phenyl group was completed within 1 h (Table 3, entry 11), which was similar to the reactions with substrates containing EDG but faster than that with a substrate bearing another halogen-substituted phenyl group (Table 3, entries 4–7). Considering all these factors, we concluded that both the electronic effect and the steric effect of substituents had a vital impact on the rate of the reaction. To further confirm the steric effect of substituents, two more experiments were performed. It was found that the reaction of the substrate with a small-sized methyl group could be completed within 30 min (Table 3, entry 12), while the reaction of the substrate with a large-sized α-naphthyl group needed 3 h to reach completion (Table 3, entry 13). The substrate containing a heteroaromatic group (furyl) as R^2 (Table 3, entry 12) could also be employed, giving the desired product in moderate yield.

The absolute structures of the thia-Michael addition product, compound **3i**, and the aza-Michael addition product, compound **4b**, were determined by X-ray crystal structure analysis. The data of X-ray crystal structures can be found in the Supporting Information.[59]

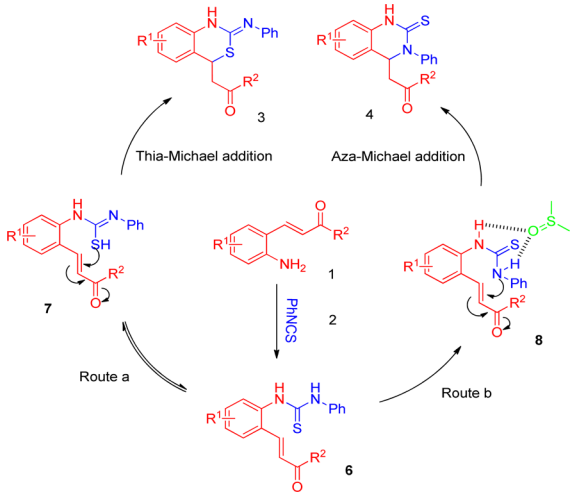
To demonstrate the potential application of this methodology, a nucleophilic substitution reaction of **4a** with benzyl bromide was performed, giving the desired product **5a** in moderate yield (Scheme 2).

Scheme 2. Potential Application of This Methodology



On the basis of the highly selective experimental results, a plausible reaction mechanism was proposed (Scheme 3). In the initial step, the 2-amino chalcone **1** reacts with isothiocyanatobenzene **2** to form a crucial active intermediate **6**. Both the S-terminus and the N-terminus of thiourea **6** have the potential to undergo an intramolecular Michael addition (route a and route b, respectively). For the thia-Michael addition, route a can be explained well on the basis of the hard–soft acid–base (HSAB) theory. Sulfur is less electronegative than nitrogen but has a larger atomic radius and therefore can be regarded as a soft base. Because the carbon cation is a typical soft acid, the S-terminus rather than the N-terminus of thiourea will serve as a nucleophile site to react with the carbon to afford the cyclizing product **3**. For the aza-Michael addition, DMSO, as broadly applied, will easily form hydrogen bonds[60−70] with the hydrogens from the amino group of thiourea to activate the N–H bond. An N-terminal nucleophile active site is then produced from the weak N–H bond of **6**, which will attack the carbon and give the cyclized product **4**. Obviously, the hydrogen bond plays a significant role in the aza-Michael addition reaction because of its function in accelerating this reaction. The data of Table 1 can now be explained well by this proposed mechanism. The desired product **4a** cannot be obtained in the low-polarity solvents because of the absence of hydrogen bonding, but **4a** can be formed in DCM with catalyst **I** or **II** with the hydrogen bonding donor.

Scheme 3. Proposed Mechanism of the Chemoselective Reaction



In summary, we have developed a novel practical catalyst-free chemoselective reaction switched by solvents. The 2-imino-[1,3]benzothiazines were afforded in moderate to excellent yield in DCM, while the 3,4-dihydroquinazoline-2-thiones were obtained in excellent yield within a very short reaction time in DMSO. The HSAB theory and hydrogen bonding activation of

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the N−H bond can be used well to explain the outstanding chemical selectivity in the reaction process.

EXPERIMENTAL SECTION

General Information. All glassware was thoroughly oven-dried. Chemicals and solvents were either purchased from commercial suppliers or purified by standard techniques. Thin-layer chromatography plates were visualized by being exposed to ultraviolet light. Flash chromatography was performed using silica gel (200−300 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer. ^{1}H NMR data are reported as follows: chemical shift (δ), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet), integration, coupling constant (hertz), and assignment. The spectra of **3** were recorded with $CDCl_3$ as the solvent at room temperature, and the spectra of **4** were recorded with *d*-DMSO as the solvent at room temperature. TMS served as an internal standard (δ 0) for ^{1}H NMR, and $CDCl_3$ was used as an internal standard (δ 77.00) for ^{13}C NMR. IR spectra were recorded on a FT-IR instrument and are reported in wavenumbers (inverse centimeters). HRMS spectra using ESI were recorded on an ESI-FTMS mass spectrometer.

General Procedure for Thia-Michael Addition under the Optimized DCM Conditions. A solution of 2-aminochalcone **1** (0.2 mmol) and isothiocyanatobenzene **2** (0.6 mmol) in DCM (1 mL) was stirred and refluxed at 40 °C. The reaction was monitored by TLC spectroscopy. After the reaction was completed, the reaction mixture was directly purified by flash column chromatograph (eluted with 5:1 EtOAc/petroleum ether) to afford the product **3**.

*1-Phenyl-2-[2-(phenylimino)-2,4-dihydro-1H-benzo[d][1,3]-thiazin-4-yl]ethanone (**3a**).* White solid: 68.8 mg, 96% yield; mp 48−49 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.30 (dd, J = 17.6, 5.1 Hz, 1H), 3.61 (dd, J = 17.6, 5.1 Hz, 1H), 4.76−4.79 (m, 1H), 7.03−7.08 (m, 2H), 7.18−7.31 (m, 5H), 7.39 (t, J = 7.92 Hz, 2H), 7.50−7.54 (m, 3H), 7.84−7.86 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.4, 44.9, 55.5, 111.6, 114.1, 119.8, 123.1, 123.7, 125.9, 128.1, 128.6, 128.8, 133.4, 136.4, 137.1, 140.2, 147,4, 156.6, 196.8; IR (KBr) ν 505.5, 577.0, 917.7, 110.6, 1149.7, 1233.7, 1314.0, 1439.4, 1479.5, 1496.9, 1579.4, 1683.0, 2925.5, 3344.5 cm^{-1}; HRMS (ESI) for $C_{22}H_{19}N_2OS$ $[M + H]^+$ calcd 359.1213, found 359.1218.

*2-[7-Chloro-2-(phenylimino)-2,4-dihydro-1H-benzo[d][1,3]-thiazin-4-yl)-1-phenylethanone (**3b**).* White solid: 49.6 mg, 64% yield; mp 59−60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.30 (dd, J = 17.6, 5.1 Hz, 1H), 3.61 (dd, J = 17.6, 5.1 Hz, 1H), 4.73−4.77 (m, 1H), 7.01−7.13 (m, 3H), 7.24−7.42 (m, 5H), 7.51−7.58 (m, 3H), 7.84 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 38.7, 45.0, 120.4, 121.4, 123.9, 124.3, 124.7, 127.7, 128.1, 128.7, 129.0, 133.6, 133.8, 136.4, 139.9 144.9, 150.3, 196.4; IR (KBr) ν 508.4, 597.5, 689.3, 753.5, 1155.0, 1221.5, 1313.3, 1440.5, 1466.3, 1570.4, 1597.5, 1683.3, 2925.3, 2955.1, 3338.7 cm^{-1}; HRMS (ESI) for $C_{22}H_{18}ClN_2OS$ $[M + H]^+$ calcd 393.0823, found 393.0826.

*2-[6-Methoxy-2-(phenylimino)-2,4-dihydro-1H-benzo[d][1,3]-thiazin-4-yl]-1-phenylethanone (**3c**).* White solid: 70.6 mg, 91% yield; mp 39−40 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.28 (dd, J = 17.6, 5.2 Hz, 1H), 3.62 (dd, J = 17.6, 8.7 Hz, 1H), 3.78 (s, 1H), 4.70−4.74 (m, 1H), 6.74 (d, J = 2.8 Hz, 1H), 6.384 (dd, J = 8.68, 2.8 Hz, 1H), 7.03 (t, J = 7.4 Hz, 1H), 7.20 (d, J = 8.6 Hz, 1H), 7.29 (t, J = 8.28 Hz, 2H), 7.4 (t, J = 7.6 Hz, 2H), 7.53 (t, J = 7.44 Hz, 1H), 7.58 (d, J = 7.84 Hz, 2H), 7.86 (d, J = 7.28 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.4, 44.9, 55.5, 111.6, 114.1, 119.8, 123.1, 123.7, 125.9, 128.1, 128.6, 128.8, 133.4, 136.4, 137.1, 140.2, 147,4, 156.6, 196.8; IR (KBr) ν 503.5, 690.3, 756.4, 1042.2, 1122.1, 1150.5, 1235.8, 1311.0, 1376.3, 1461.7, 1492.2, 1584.6, 1685.3, 1736.4, 2370.8, 2851.8, 2924.7, 2955.5, 3337.4 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}N_2O_2S$ $[M + H]^+$ calcd 389.1318, found 389.1320.

*2-[2-(Phenylimino)-2,4-dihydro-1H-benzo[d][1,3]thiazin-4-yl]-1-(m-tolyl)ethanone (**3d**).* White solid: 66.9 mg, 90% yield; mp 62−63 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.28 (dd, J = 17.2, 5.2 Hz, 1H), 3.61 (dd, J = 17.6, 8.8 Hz, 1H), 4.75−4.78 (m, 1H), 7.02−7.08 (m, 2H), 7.18−7.34 (m, 7H), 7.54 (d, J = 6.0 Hz, 2H), 7.65 (d, J = 9.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 39.3, 45.1, 120.3, 123.0, 123.4, 124.4, 125.4, 126.6, 128.54, 128.58, 128.7, 128.9, 134.3, 136.6, 138.5, 140.9, 143.3, 149.4, 196.9; IR (KBr) ν 505.0, 576.7, 689.6, 737.3, 758.2, 1154.9, 1313.6, 1439.2, 1496.8, 1524.7, 1579.6, 1614.1, 1679.4, 2924.7, 2955.3, 3057.8, 3343.3 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}N_2OS$ $[M + H]^+$ calcd 373.1369, found 373.1364.

*2-[2-(Phenylimino)-2,4-dihydro-1H-benzo[d][1,3]thiazin-4-yl]-1-(p-tolyl)ethanone (**3e**).* White solid: 73.7 mg, 99% yield; mp 53−55 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 3.27 (dd, J = 17.2, 5.6 Hz, 1H), 3.60 (dd, J = 17.2, 8.8 Hz, 1H), 4.75−4.78 (m, 1H), 7.06 (m, 2H), 7.18−7.32 (m, 7H), 7.53 (d, J = 7.88 Hz, 2H), 7.75 (d, J = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 39.3, 44.9, 120.4, 123.0, 123.5, 124.3, 124.4, 126.6, 128.3, 128.5, 128.9, 129.3, 134.1, 140.8, 143.2, 144.5, 149.86, 196.9; IR (KBr) ν 505.3, 572.9, 692.0, 757.2, 814.0, 1181.0, 1233.4, 1313.7, 1439.4, 1496.7, 1578.8, 1610.9, 1677.2, 2924.8, 2954.7, 3337.1 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}N_2OS$ $[M + H]^+$ calcd 373.1369, found 373.1373.

*1-(3-Methoxyphenyl)-2-[2-(phenylimino)-2,4-dihydro-1H-benzo-[d][1,3]thiazin-4-yl]ethanone (**3f**).* White solid: 50.4 mg, 65% yield; mp 70−71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.32 (dd, J = 17.6, 5.4 Hz, 1H), 3.61 (dd, J = 17.6, 8.6 Hz, 1H), 3.80 (s, 3H), 4.75−4.79 (m, 1H), 7.06 (m, 2H), 7.04−7.10 (m, 3H), 7.19−7.32 (m, 6H), 7.40−7.42 (m, 2H), 7.53 (d, J = 7.92 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.2, 45.1, 55.3, 112.0, 120.1, 120.4, 120.7, 122.8, 123.4, 124.1, 124.3, 126.5, 128.4, 128.8, 129.5, 137.7, 140.8, 142.9, 149.8, 159.7, 196.4; IR (KBr) ν 503.3, 618.2, 695.6, 757.6, 1038.2, 1158.1, 1194.4, 1255.1, 1286.2, 1437.7, 1493.3, 1526.0, 1579.7, 1597.3 1679.3, 2369.0, 2925.3, 3335.1 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}N_2O_2S$ $[M + H]^+$ calcd 389.1318, found 389.1323.

*1-(4-Methoxyphenyl)-2-[2-(phenylimino)-2,4-dihydro-1H-benzo-[d][1,3]thiazin-4-yl]ethanone (**3g**).* White solid: 67.0 mg, 86% yield; mp 71−72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.34 (dd, J = 17.2, 5.6 Hz, 1H), 3.57 (dd, J = 17.6, 8.8 Hz, 1H), 3.82 (s, 3H), 4.74−4.79 (m, 1H), 6.86 (d, J = 7.6 Hz, 2H), 7.04−7.09 (m, 2H), 7.18 (d, J = 7.3 Hz, 1H), 7.24−7.32 (m, 4H), 7.53 (d, J = 7.48 Hz, 2H), 7.83 (d, J = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.4, 44.5, 55.4, 113.7, 120.4, 123.0, 123.5, 124.2, 124.4, 126.6, 128.5, 128.9, 129.6, 130.4, 140.6, 143.0, 149.9, 163.7, 195.0; IR (KBr) ν 501.8, 617.8, 757.6, 1028.0, 1114.7, 1200.9, 1261.3, 1313.7, 1439.6, 1479.1, 1577.8, 1599.3, 1671, 2925.2, 2955.0, 3332.1 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}N_2O_2S$ $[M + H]^+$ calcd 389.1318, found 389.1324.

*1-(3-Bromophenyl)-2-[2-(phenylimino)-2,4-dihydro-1H-benzo[d]-[1,3]thiazin-4-yl]ethanone (**3h**).* White solid: 80.2 mg, 92% yield; mp 74−75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.28 (dd, J = 17.6, 5.4 Hz, 1H), 3.57 (dd, J = 17.6, 8.5 Hz, 1H), 4.73−4.77 (m, 1H), 7.04−7.09 (m, 2H), 7.17−7.32 (m, 6H), 7.54 (d, J = 7.88 Hz, 2H), 7.64 (d, J = 7.92 Hz, 1H), 7.74 (d, J = 7.84 Hz, 1H), 7.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.1, 45.2, 120.3, 122.6, 123.0, 123.5, 124.3, 124.4, 126.6, 128.6, 128.6, 130.2, 131.1, 163.3, 138.1, 140.6, 143.1, 149.3, 195.3; IR (KBr) ν 505.1, 577.5, 759.6, 1194.9, 1230.2, 1313.5, 14398.1, 1479.2, 1496.7, 1579.2, 1614.3, 1687.2, 2925.7, 2955.3, 3061.0, 3356.3 cm^{-1}; HRMS (ESI) for $C_{22}H_{18}BrN_2OS$ $[M + H]^+$ calcd 437.0318, found 437.0324.

*1-(4-Bromophenyl)-2-[2-(phenylimino)-2,4-dihydro-1H-benzo[d]-[1,3]thiazin-4-yl]ethanone (**3i**).* White solid: 83.7 mg, 96% yield; mp 75−76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.28 (dd, J = 17.6, 5.4 Hz, 1H), 3.57 (dd, J = 17.6, 8.5 Hz, 1H), 4.73−4.76 (m, 1H), 7.04−7.09 (m, 2H), 7.17−7.32 (m, 6H), 7.54 (d, J = 7.88 Hz, 2H), 7.64 (d, J = 7.92 Hz, 1H), 7.74 (d, J = 7.84 Hz, 1H), 7.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.2, 44.9, 120.2, 122.6, 123.5, 124.5, 126.5, m128.6, 128.7, 1287.9, 129.5, 131.9, 135.2, 140.5, 143.2, 149.1, 195.7; IR (KBr) ν 508.6, 757.4, 1071.0, 1231.2, 1313.0, 1349.7, 1439.2, 1581.2, 1614.2, 1685.2, 2852.5, 2924.9, 2955.2, 3348.1 cm^{-1}; HRMS (ESI) for $C_{22}H_{18}BrN_2OS$ $[M + H]^+$ calcd 437.0318, found 437.0313.

*1-(4-Chlorophenyl)-2-[2-(phenylimino)-2,4-dihydro-1H-benzo[d]-[1,3]thiazin-4-yl]ethanone (**3j**).* White solid: 76.8 mg, 98% yield; mp 70−71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.28 (dd, J = 17.6, 5.5 Hz, 1H), 3.57 (dd, J = 17.6, 8.4 Hz, 1H), 4.73−4.77 (m, 1H), 7.06 (t, J = 7.36 Hz, 2H), 7.17−7.33 (m, 5H), 7.35−7.37 (m, 2H), 7.52 (d, J = 7.84 Hz, 2H), 7.76−7.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.2, 45.0, 120.4, 122.6, 123.6, 124.3, 124.4, 126.5, 128.6, 128.95,

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128.96, 129.5, 134.7, 140.0, 140.5, 143.0, 149.6, 149.5, 195.4; IR (KBr) ν 503.5, 617.4, 693.0, 758.2, 827.1, 981.7, 1092.9, 1149.0, 1232.4, 1313.8, 1400.6, 1439.4, 1496.3, 1532.1, 1579.6, 1684.6, 2925.8, 3058.7, 3346.8 cm^{-1}; HRMS (ESI) for $C_{22}H_{18}ClN_2OS$ $[M + H]^+$ calcd 393.0823, found 393.0826.

*1-(4-Fluorophenyl)-2-[2-(phenylimino)-2,4-dihydro-1H-benzo[d]-[1,3]thiazin-4-yl]ethanone (**3k**).* White solid: 65.5 mg, 87% yield; mp 154−155 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.28 (dd, J = 17.5, 5.5 Hz, 1H), 3.57 (dd, J = 17.6, 8.4 Hz, 1H), 4.73−4.76 (m, 1H), 7.02−7.07 (m, 4H), 7.16−7.32 (m, 5H), 7.53 (d, J = 7.88 Hz, 2H), 7.84−7.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.3, 45.0, 115.7, 115.9, 120.4, 122.8, 123.6, 124.3, 124.6, 126.6, 128.6, 129.0, 130.8, 130.9, 132.9, 133.0, 140.8, 143.1, 149.6, 166.0 (d, $^1J_{C-F}$ = 254.3 Hz), 195.1; IR (KBr) ν 502.8, 571.5, 696.2, 757.8, 838.1, 983.0, 1155.9, 1233.0, 1313.5, 1439.2, 1479.5, 1523.5, 1579.3, 1614.0, 1681.8, 2925.9, 2955.6, 3061.1, 3347.2 cm^{-1}; HRMS (ESI) for $C_{22}H_{18}FN_2OS$ $[M + H]^+$ calcd 377.1118, found 377.1114.

*1-[2-(Phenylimino)-2,4-dihydro-1H-benzo[d][1,3]thiazin-4-yl]-propan-2-one (**3l**).* White solid: 37.5 mg, 72% yield; mp 140−142 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 2.05 (s, 3H), 2.86 (dd, J = 17.7, 6.0 Hz, 1H), 3.03 (dd, J = 17.7, 8.0 Hz, 1H), 4.52−4.56 (m, 1H), 7.05−7.10 (m, 2H), 7.13−7.19 (m, 2H), 7.24−7.28 (m, H), 7.33 (d, J = 7.6 Hz, 2H), 7.55 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 38.7, 49.8, 120.4, 122.7, 123.6, 124.4, 126.6, 128.5, 129.0, 140.8, 142.9, 149.3, 205.2; IR (KBr) ν 500.7, 692.7, 757.4, 1112.9, 1149.5, 1228.9, 1314.5, 1439.9, 1479.2, 1534.8, 1579.9, 1615.0, 1710.1, 2924.8, 2956.0, 3334.2 cm^{-1}; HRMS (ESI) for $C_{17}H_{17}N_2OS$ $[M + H]^+$ calcd 297.1056, found 297.1060.

*1-(Naphthalen-1-yl)-2-[2-(phenylimino)-2,4-dihydro-1H-benzo-[d][1,3]thiazin-4-yl]ethanone (**3m**).* White solid: 71.8 mg, 88% yield; mp 76−77 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.41 (dd, J = 16.8, 5.6 Hz, 1H), 3.57 (dd, J = 17.2, 8.4 Hz, 1H), 4.81−4.85 (m, 1H), 7.01−7.06 (m, 2H), 7.15−7.27 (m, 5H), 7.35 (t, J = 8.0 Hz, 1H), 7.44 (d, J = 8.0 Hz, 2H), 7.48−7.57 (m, 2H), 7.64 (d, J = 7.2 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 8.59 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.6, 47.9, 120.8, 122.7, 123.3, 123.5, 124.0, 124.1, 125.5, 126.4, 126.5, 128.0, 128.3, 128.4, 128.7, 129.4, 129.8, 133.0, 133.7, 134.9, 141.5, 142.3, 150.2, 200.3; IR (KBr) ν 491.9, 695.7, 735.4, 759.4, 775.0, 908.8, 1096.4, 1147.8, 1234.0, 1313.8, 1438.8, 1479.2, 1496.7, 1578.9, 1614.7, 1676.6, 2925.8, 2955.3, 3055.8, 3347.7 cm^{-1}; HRMS (ESI) for $C_{26}H_{21}N_2OS$ $[M + H]^+$ calcd 409.1369, found 409.1372.

*1-(Furan-2-yl)-2-[2-(phenylimino)-2,4-dihydro-1H-benzo[d][1,3]-thiazin-4-yl]ethanone (**3n**).* White solid: 45.3 mg, 65% yield; mp 59−60 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.17 (dd, J = 16.8, 5.9 Hz, 1H), 44.7 (dd, J = 16.8, 8.4 Hz, 1H), 4.70−4.74 (m, 1H), 6.46−6.47 (m, 1H), 7.05−7.11 (m, 3H), 7.15−7.17 (m, 1H), 7.20−7.25 (m, 2H), 7.27−7.33 (m, 2H), 7.52−7.55 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.1, 44.7, 112.3, 117.9, 120.3, 122.6, 123.4, 124.2, 124.3, 126.5, 128.5, 128.9, 140.8, 143.0, 146.8, 149.2, 152.3, 185.4; IR (KBr) ν 509.3, 509.3, 694.3, 758.7, 903.7, 1021.8, 1149.9, 1226.6, 1314.2, 1394.4, 1439.8, 1465.3, 1534.7, 1568.5, 1613.6, 1668.4, 2853.2, 2925.3, 3320.3 cm^{-1}; HRMS (ESI) for $C_{20}H_{17}N_2O_2S$ $[M + H]^+$ calcd 349.1005, found 349.1009.

General Procedure for the Aza-Michael Addition under the Optimized DMSO Conditions. A solution of 2-aminochalcone **1** (0.2 mmol), isothiocyanatobenzene **2** (0.6 mmol) in DMSO (1 mL) was stirred at room temperature. The reaction was monitored by TLC spectroscopy. After the reaction was completed, the reaction mixture was directly purified by flash column chromatography (eluted with 5:1 EtOAc/petroleum ether) to afford the product **4**.

*1-Phenyl-2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)ethanone (**4a**).* White solid: 70.2 mg, 98% yield; mp 231−232 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 3.51−3.65 (m, 2H), 5.42 (s, 1H), 6.93 (s, 1H), 7.12−7.20 (m, 3H), 7.31−7.42 (m, 7H), 7.53−7.55 (m, 1H), 7.77 (d, J = 6.68 Hz, 2H), 11.0 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 44.0, 51.5, 60.5, 114.9, 122.6, 123.7, 126.7, 128.3, 128.8, 129.4, 129.5, 129.8, 124.3, 135.7, 137.2, 145.1, 173.3, 197.7; IR (KBr) ν 535.9, 628.2, 693.7, 743.9, 760.7, 1118.6, 1205.5, 1251.4, 1283.8, 1305.3, 1436.0, 1467.0, 1493.0, 1523.8, 1595.3, 1675.0, 2924.1, 2954.3, 3113.0, 3333.5 cm^{-1}; HRMS (ESI) for $C_{22}H_{19}N_2OS$ $[M + H]^+$ calcd 359.1213, found 359.1218.

*2-(7-Chloro-3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)-1-phenylethanone (**4b**).* White solid: 59.6 mg, 76% yield; mp 205−206 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 3.54 (dd, J = 17.2, 8.04 Hz, 1H), 3.65 (dd, J = 17.2, 3.64 Hz, 1H), 5.42 (dd, J = 7.88, 3.48 Hz, 1H), 7.01 (dd, J = 8.20, 2.08 Hz, 1H), 7.11 (d, J = 2.08 Hz, 1H), 7.19 (d, J = 8.24 Hz, 1H), 7.31−7.36 (m, 1H), 7.41−7.45 (m, 6H), 7.57−7.61 (m, 1H), 7.79−7.81 (m, 2H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 43.8, 59.9, 114.3, 121.5, 123.3, 128.5, 128.6, 128.9, 129.5, 129.7, 129.9, 133.6, 134.4, 137.0, 137.1, 144.8, 177.3, 197.7; IR (KBr) ν 530.2, 596.9, 696.0, 736.8, 1085.5, 1125.5, 1209.1, 1231.8, 1281.6, 1395.1, 1457.8, 1492.5, 1597.3, 1682.3, 2925.1, 2956.0, 3178.7 cm^{-1}; HRMS (ESI) for $C_{22}H_{18}ClN_2OS$ $[M + H]^+$ calcd 393.0823, found 393.0829.

*2-(6-Methoxy-3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)-1-phenylethanone (**4c**).* White solid: 74.5 mg, 96% yield; mp 240−241 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 3.50 (dd, J = 16.8, 8.12 Hz, 1H), 3.62−3.67 (m, 4H), 5.37 (dd, J = 7.06, 3.56 Hz, 1H), 6.70 (d, J = 2.56 Hz, 1H), 6.80 (dd, J = 8.72, 2.68 Hz, 1H), 7.02 (d, J = 8.72 Hz, 1H), 7.29−7.32 (m, 1H), 7.38−7.44 (m, 6H), 7.58 (t, J = 7.36 Hz, 1H), 7.58 (t, J = 7.36 Hz, 1H), 7.78 (d, J = 7.32 Hz, 2H), 10.92 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 44.0, 56.2, 60.6, 111.8, 115.7, 116.0, 123.7, 128.2, 128.9, 129.5, 129.8, 129.9, 130.7, 134.3, 137.2, 145.1, 155.9, 176.6, 197.8; IR (KBr) ν 518.8, 762.7, 1002.7, 1026.6, 1118.4, 1169.0, 1257.4, 1284.5, 1448.9, 1463.1, 1504.4, 1676.6, 2370.8, 2852.2, 2923.4, 3420.6 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}N_2O_2S$ $[M + H]^+$ calcd 389.1318, found 389.1324.

*2-(3-Phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)-1-(m-tolyl)ethanone (**4d**).* White solid: 70.6 mg, 95% yield; mp 224−225 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 2.29 (s, 3H), 3.50 (dd, J = 16.8, 8.4 Hz, 1H), 3.61 (dd, J = 16.8, 3.6 Hz, 1H), 5.40 (dd, J = 8.28, 3.56 Hz, 1H), 6.92−6.96 (m, 1H), 7.10 (t, 1H), 7.19−7.23 (m, 1H), 7.28−7.42 (m, 7H), 7.56−7.58 (m, 2H), 10.99 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 21.6, 44.1, 60.6, 114.9, 122.7, 123.8, 126.0, 126.8, 128.4, 129.4, 129.8, 129.9, 134.9, 135.7, 137.2, 138.9, 145.1, 177.4, 197.8; IR (KBr) 622.9, 763.2, 824.9, 1005.9, 1026.0, 1051.4, 1656.2, 2126.9, 2253.7, 3424.4 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}N_2OS$ $[M + H]^+$ calcd 373.1369, found 373.1374.

*2-(3-Phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)-1-(p-tolyl)ethanone (**4e**).* White solid: 70.6 mg, 93% yield; mp 168−169 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 2.35 (s, 3H), 3.47 (dd, J = 16.8, 3.2 Hz, 1H), 3.71 (dd, J = 16.8, 9.6 Hz, 1H), 5.56 (dd, J = 9.20, 3.20 Hz, 1H), 6.94−7.01 (m, 2H), 7.01−7.18 (m, 3H), 7.23 (d, J = 8.01 Hz, 1H), 7.36−7.47 (m, 5H), 7.65 (d, J = 8.40 Hz, 2H), 9.94 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 22.0, 43.8, 60.6, 144.9, 122.7, 123.7, 126.7, 128.3, 129.0, 129.4, 129.6, 129.8, 130.0, 130.7, 134.8, 135.7, 144.8, 145.1, 171.2, 177.4, 197.1; IR (KBr) ν 618.8, 697.0, 734.1, 761.3, 822.8, 1005.5, 1025.8, 1050.3, 1121.5, 1284.5, 1429.8, 1492.9, 1675.1, 2923.6, 3424.8 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}N_2OS$ $[M + H]^+$ calcd 373.1369, found 373.1378.

*1-(3-Methoxyphenyl)-2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)ethanone (**4f**).* White solid: 73.7 mg, 95% yield; mp 179−180 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 3.49−3.66 (m, 2H), 3.73 (s, 3H), 5.41−5.42 (m, 1H), 6.94 (t, J = 7.28 Hz, 1H), 7.11−7.14 (m, 3H), 7.18−7.22 (m, 1H), 7.26−7.42 (m, 8H), 11.0 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 44.2, 56.1, 60.5, 113.2, 114.9, 120.6, 121.4, 122.6, 123.7, 1265.7, 128.3, 129.4, 129.8, 129.9, 130.6, 135.7, 138.6, 145.0, 160.2, 177.3, 197.5; IR (KBr) ν 618.2, 735.8, 1005.7, 1026.6, 1195.1, 1259.7, 1286.1, 1430.9, 1464.9, 1492.7, 1617.8, 1676.3, 2853.2, 2924.9, 2955.6, 3191.0, 3398.3 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}N_2O_2S$ $[M + H]^+$ calcd 389.1318, found 389.1319.

*1-(4-Methoxyphenyl)-2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)ethanone (**4g**).* White solid: 75.3 mg, 97% yield; mp 186−187 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 2.29 (s, 3H), 3.50 (dd, J = 16.8, 8.4 Hz, 1H), 3.61 (dd, J = 16.8, 3.6 Hz, 1H), 5.40 (dd, J = 8.28, 3.56 Hz, 1H), 6.92−6.96 (m, 1H), 7.10 (t, 1H), 7.19−7.23 (m, 1H), 7.28−7.42 (m, 7H), 7.56−7.58 (m, 2H), 10.99 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 42.9, 43.4, 59.5, 113.9, 121.5, 122.0, 122.8, 125.8, 126.9, 127.4, 128.1, 128.6, 128.9, 129.0, 129.1, 130.6,

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134.8, 138.2, 144.1, 176.4, 196.5; IR (KBr) ν 621.5, 763.6, 825.3, 1004.7, 1026.1, 1050.4, 1655.9, 2923.2, 2956.1, 3423.3 cm^{-1}; HRMS (ESI) for $C_{23}H_{21}N_2O_2S$ $[M + H]^+$ calcd 389.1318, found 389.1323.

*1-(3-Bromophenyl)-2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)ethanone (**4h**).* White solid: 83.7 mg, 96% yield; mp 227−228 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 3.53 (dd, J = 16.9, 8.0 Hz, 1H), 3.67 (dd, J = 17.0, 3.2 Hz, 1H), 5.39−5.41 (m, 1H), 6.96 (t, J = 7.36 Hz, 1H), 7.08 (t, J = 7.80 Hz, 1H), 7.15−7.23 (m, 2H), 7.33−7.42 (m, 6H), 7.76 (d, J = 7.84 Hz, 2H), 7.91 (s, 1H), 11.0 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 43.9, 55.3, 59.6, 114.4, 122.0, 122.5, 123.3, 126.3, 127.4, 127.9, 129.0, 129.4, 131.1, 131.2, 135.3, 136.4, 138.6, 144.6, 176.8, 196.4; IR (KBr) ν 757.5, 825.9, 1001.4, 1025.3, 1050.6, 1196.5, 1303.0, 1436.2, 1464.0, 1492.2, 1677.6, 2922.0, 3406.8 cm^{-1}; HRMS (ESI) for $C_{22}H_{18}BrN_2OS$ $[M + H]^+$ calcd 437.0318, found 437.0325.

*1-(4-Bromophenyl)-2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinolin-4-yl)ethanone (**4i**).* White solid: 83.7 mg, 96% yield; mp 236−237 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 3.51 (dd, J = 17.0, 8.12 Hz, 1H), 3.63 (dd, J = 17.0, 3.3 Hz, 1H), 5.39−5.42 (m, 1H), 6.94 (t, J = 7.36 Hz, 1H), 7.07−7.22 (m, 3H), 7.31−7.41 (m, 5H), 7.59−7.71 (m, 4H), 11.03 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 44.1, 60.4, 114.9, 122.5, 123.7, 126.7, 128.3, 128.5, 129.4, 129.7, 129.8, 130.8, 130.9, 132.5, 135.7, 136.1, 145.0, 177.3, 197.0; IR (KBr) ν 694.9, 727.6, 758.5, 817.5, 1025.2, 1121.1, 1204.9, 1224.7, 1285.7, 1378.2, 1423.1, 1460.0, 1489.7, 1583.4, 2852.4, 2922.6, 2956.4, 3316.8, 3406.0 cm^{-1}; HRMS (ESI) for $C_{22}H_{18}BrN_2OS$ $[M + H]^+$ calcd 437.0318, found 437.0323.

*1-(4-Chlorophenyl)-2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinolin-4-yl)ethanone (**4j**).* White solid: 74.5 mg, 95% yield; mp 210−211 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 3.52 (dd, J = 16.8, 8.0 Hz, 1H), 3.64 (dd, J = 17.2, 4.0 Hz, 1H), 5.43 (dd, J = 7.60, 3.61 Hz, 1H), 6.93−6.97 (m, 1H), 7.08−7.10 (m, 1H), 7.14−7.16 (m, 1H), 7.21−7.23 (m, 1H), 7.31−7.34 (m, 2H), 7.38−7.42 (m, 4H), 7.48 (d, J = 8.60 Hz, 2H), 7.79 (d, J = 8.56 Hz, 2H), 11.03 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 44.1, 60.5, 114.9, 122.5, 123.7, 124.5, 125.3, 126.8, 128.3, 129.3, 129.4, 129.5, 129.8, 130.8, 130.8, 135.7, 135.8, 139.3, 140.4, 145.0, 177.7, 196.8; IR (KBr) ν 540.2, 693.1, 759.4, 1025.7, 1119.2, 1206.7, 1287.3, 1461.3, 1491.3, 1612.6, 1671.7, 1370.3, 2924.8, 3321.5 cm^{-1}; HRMS (ESI) for $C_{22}H_{18}ClN_2OS$ $[M + H]^+$ calcd 393.0823, found 393.0829.

*1-(4-Fluorophenyl)-2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)ethanone (**4k**).* White solid: 73.7 mg, 98% yield; mp 212−213 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 3.52 (dd, J = 16.9, 8.0 Hz, 1H), 3.63 (dd, J = 16.9, 3.8 Hz, 1H), 5.39−5.42 (m, 1H), 6.93−6.97 (m, 1H), 6.92−6.96 (m, 1H), 7.07−7.15 (m, 1H), 7.18−7.26 (m, 3H), 7.31−7.34 (m, 1H), 7.40−7.41 (m, 4H), 7.85−7.89 (m, 2H), 10.98 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 44.0, 60.4, 114.9, 116.3, 116.6, 122.6, 123.7, 126.7, 128.3, 129.4, 129.8, 131.9, 132.0, 133.9, 134.0, 135.7 145.0, 166.0 (d, $^1J_{C-F}$ = 250.8 Hz), 177.3, 196.4; IR (KBr) ν 537.3, 580.7, 753.1, 834.3, 986.3, 1052.6, 1119.7, 1155.0, 1203.7, 1286.8, 1437.9, 1493.9, 1518.5, 1614.3, 1702.3, 2922.3 cm^{-1}; HRMS (ESI) for $C_{22}H_{18}FN_2OS$ $[M + H]^+$ calcd 377.1118, found 377.1121.

*1-(3-Phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)propan-2-one (**4l**).* White solid: 58.0 mg, 98% yield; mp 152−153 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.97 (s, 3H), 3.03 (dd, J = 16.8, 3.5 Hz, 1H), 3.14 (dd, J = 16.8, 9.3 Hz, 1H), 5.32 (dd, J = 9.3, 3.5 Hz, 1H), 6.93 (d, J = 7.88 Hz, 1H), 7.02−7.05 (m, 1H), 7.18 (d, J = 7.36 Hz, 1H), 7.22−7.26 (m, 1H), 7.37−7.39 (m, 3H), 7.44−7.48 (m, 2H), 9.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 47.6, 59.7, 113.9, 121.6, 123.9, 126.3, 128.2, 128.4, 129.0, 129.4, 134.3, 143.8, 177.3, 204.9; IR (KBr) ν 695.4, 757.0, 1158.0, 1193.7, 1463.2, 1596.1, 1710.2, 2370.2, 2852.0, 2923.6, 2955.1, 3184.1 cm^{-1}; HRMS (ESI) for $C_{17}H_{17}N_2OS$ $[M + H]^+$ calcd 297.1056, found 297.1062.

*1-(Naphthalen-1-yl)-2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)ethanone (**4m**).* White solid: 76.7 mg, 94% yield; mp 230−231 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 3.58 (dd, J = 16.5, 8.4 Hz, 1H), 3.78 (dd, J = 16.5, 3.8 Hz, 1H), 5.49 (dd, J = 8.3 Hz, 1H), 6.95 (t, J = 7.44 Hz, 1H), 7.09−7.11 (m, 1H), 7.18−7.23 (m, 2H), 7.33−7.37 (m, 1H), 7.41−7.48 (m, 5H), 7.54−7.56 (m, 2H), 7.80 (d, J = 7.04 Hz, 2H), 7.94−7.96 (m, 1H), 8.07 (d, J = 8.20 Hz, 1H), 8.28−8.31 (m, 1H), 11.04 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 46.4, 60.5, 114.4, 121.9, 123.4, 125.0, 125.5, 126.3, 126.9, 128.0, 128.4, 128.9, 129.0, 129.3, 129.4, 129.5, 129.6, 133.5, 133.8, 135.1, 135.3, 144.7, 176.9, 200.8; IR (KBr) ν 620.8, 762.4, 825.3, 1002.9, 1025.5, 1049.0, 1226.6, 1266.9, 1430.2, 1462.2, 1491.8, 1656.4, 2921.6, 2955.6, 3419.2 cm^{-1}; HRMS (ESI) for $C_{26}H_{21}N_2OS$ $[M + H]^+$ calcd 409.1369, found 409.1376.

*1-(Furan-2-yl)-2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)ethanone (**4n**).* White solid: 48.7 mg, 70% yield; mp 221−222 °C; ^1H NMR (400 MHz, *d*-DMSO) δ 3.36 (dd, J = 15.9, 3.8 Hz, 1H), 3.57 (dd, J = 15.9, 9.6 Hz, 1H), 5.48 (dd, J = 9.6, 3.8 Hz, 1H), 6.64−6.65 (m, 1H), 6.91 (d, J = 7.9 Hz, 1H), 6.98 (d, J = 7.48 Hz, 1H), 7.03 (d, J = 3.6 Hz, 1H), 7.16−7.22 (m, 2H), 7.36−7.49 (m, 6H), 9.18 (s, 1H); ^{13}C NMR (100 MHz, *d*-DMSO) δ 43.2, 60.2, 113.0, 114.4, 119.8, 121.7, 123.3, 126.2, 127.9, 129.1, 129.3, 129.4, 135.2, 144.5, 148.7, 152.1, 176.8, 185.0; IR (KBr) ν 537.0, 757.4, 1025.5, 1120.3, 1157.8, 1229.3, 1291.1, 1464.3, 1492.5, 1668.1, 2371.2, 2923.2, 3397.1 cm^{-1}; HRMS (ESI) for $C_{20}H_{17}N_2O_2S$ $[M + H]^+$ calcd 349.1005, found 349.1011.

*2-[2-(Benzylthio)-3-phenyl-3,4-dihydroquinazolin-4-yl]-1-phenylethanone (**5a**).* Yellow solid: 70.6 mg, 70% yield; mp 64−65 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.32 (dd, J = 16.2, 4.5 Hz, 1H), 3.53 (dd, J = 16.2, 8.4 Hz, 1H), 4.27 (d, J = 13.3 Hz, 1H), 4.45 (d, J = 13.3 Hz, 1H), 5.41−5.45 (m, 1H), 6.95−6.99 (m, 1H), 7.03−7.05 (m, 1H), 7.19−7.30 (m, 10H), 7.34−7.39 (m, 4H), 7.47−7.51 (m, 1H), 7.74−7.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.1, 52.8, 58.9, 115.6, 124.1, 125.4, 126.5, 127.2, 127.3, 127.6, 127.8, 127.9, 128.5, 128.6, 128.7, 129.3, 133.5, 136.1, 136.3, 136.9, 146.0, 180.8, 192.2; IR (KBr) ν 695.4, 738.2, 754.5, 981.6, 1073.4, 1212.5, 1358.1, 1425.1, 1494.0, 1532.7, 1683.4, 2925.6, 3344.7 cm^{-1}; HRMS (ESI) for $C_{29}H_{25}N_2OS$ $[M + H]^+$ calcd 449.1682, found 449.1683.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01232.

3i-X-ray crystal data (CIF)
4b-X-ray crystal data (CIF)
^1H and ^{13}C spectra (PDF)

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Notes

The authors declare no competing financial interest.

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