JOC The Journal of Organic Chemistry

Article

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One-Pot Copper(I)-Catalyzed Ligand/Base-Free Tandem Cyclooxidative Synthesis of Quinazolinones

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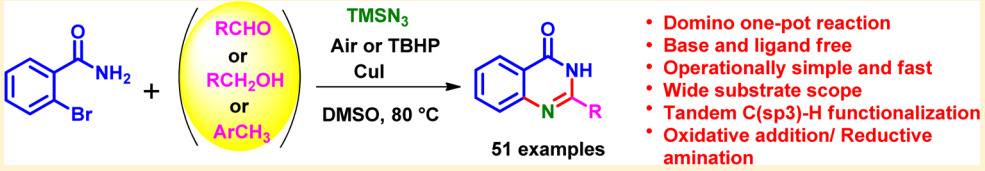
Supporting Information



ABSTRACT: A novel and efficient Cu(I)-catalyzed ligand- and base-free multipathway domino strategy has been developed for the synthesis of 2-substituted quinazolinones. The reaction utilizes 2-bromobenzamide and multiform substrates such as aldehydes, alcohols, and methyl arenes for a one-pot protocol, whereas $TMSN_3$ is used as a nitrogen source. A wide range of substrate scope, functional group tolerance, and operational simplicity are synthetically useful features.

INTRODUCTION

Quinazolin-4-(3*H*)-one represents a class of annulated six-membered nitrogen heterocycles (azaheterocycles) and a core structural component in a variety of natural products and biologically active compounds. Because of their ubiquitous nature and importance as a pharmacophore in drug candidates, they are assigned as privileged structures.[1] They are endowed with numerous pharmacological and biological activities such as anticancer,[2] antimalarial,[3] antihypertensive,[4] anti-inflammatory,[5] and antituberculosis activities.[6] In view of their remarkable significance, enormous efforts have been devoted toward efficient and convenient strategies for the construction of the quinazoline skeleton, especially 2-substituted quinazolines, as summarized in Figure 1.

Conventionally, synthesis of quinazolinone involves typical methodologies using acid/base-promoted condensation reaction of carboxylic acid derivatives with 2-aminobenzoic acid or its derivatives[7] and cascade reaction of aldehydes with *o*-aminobenzamides involving condensation, followed by oxidation of the aminal intermediate.[8] However, these protocols suffer from certain disadvantages such as multistep synthesis, use of coupling agents/bases, use of ligand or additives, harsh reaction conditions, low yields, stoichiometric or large excess amounts of toxic oxidants, and the use of highly reactive 2-aminobenzamide. Another drawback associated with these methodologies is the use of aldehyde, which is relatively unstable and synthesized from readily available alcohols via oxidation with different agents. Guo et al.[9] have reported an efficient synthesis of quinazolinone from 2-bromobenzamide and aqueous ammonia as a source of nitrogen. Moreover, while holding merit, the strategy suffers from drawbacks such as the use of the excess of ammonia as well as ligand during the reaction. Apart from these, other methodologies have also been used involving the coupling of 2-halobenzoic acid or its

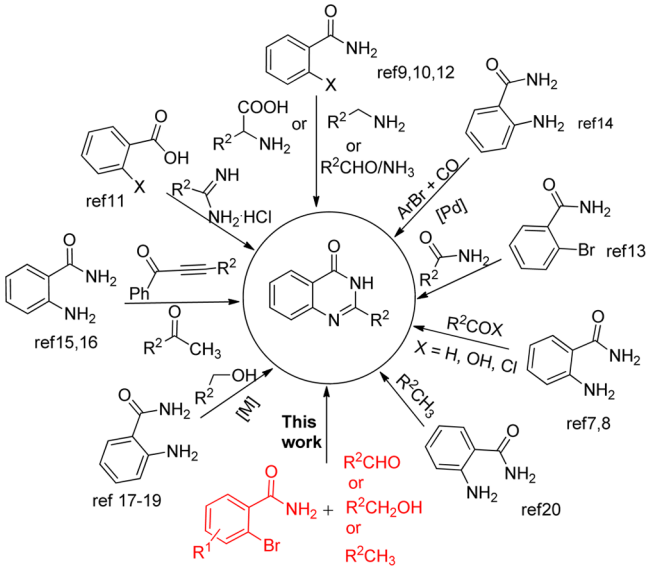


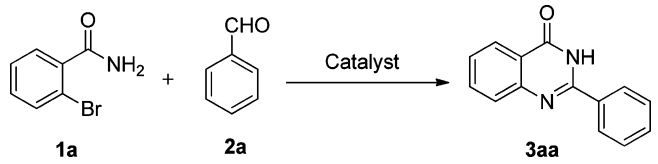
Figure 1. Methods for the synthesis of quinazolin-4-(3*H*)-one.

derivatives with ammonia sources which include benzylamines,[10] amidines,[11] amino acids,[12] and amides,[13] while all these approaches are efficient but suffered from drawbacks such as a use of the stoichiometric amounts of bases, which lead to the generation of salt wastes. Alternatively, an interesting palladium-catalyzed oxidative CO insertion reacting with 2-aminobenzamide has been reported by Wu and co-workers.[14] Recently, condensation of 2-aminobenzamide with aryl methyl ketones[15] and keto alkynes[16] was reported. During recent years,

Received: March 21, 2016
Published: May 25, 2016

DOI: 10.1021/acs.joc.6b00599
J. Org. Chem. 2016, 81, 5046−5055

Table 1. Optimizing Reaction Parameters for the Condensation of 2-Bromobenzamides with Aldehyde[a]



1a 2a 3aa

S. no.	azide equivalent	base	catalyst	solvent	T (°C)	yield[b] (%)
1	$TMSN_3$ (2 equiv)		CuCl	DMSO	80	66
2	$TMSN_3$ (2 equiv)		$Cu(OAc)_2$	DMSO	80	72
3	$TMSN_3$ (2 equiv)		Cu_2O	DMSO	80	60
4	$TMSN_3$ (2 equiv)		$Cu(OTf)_2$	DMSO	80	65
5	$TMSN_3$ (2 equiv)		CuI	DMSO	80	88
6	$TMSN_3$ (2 equiv)		CuBr	DMSO	80	76
7	$TMSN_3$ (2 equiv)		$FeCl_3$	DMSO	80	NR
8	$TMSN_3$ (1.0 equiv)		CuI	DMSO	80	60
9	$TMSN_3$ (3 equiv)		CuI	DMSO	80	87
10	NaN_3 (2.0 equiv)		CuI	DMSO	80	20
11	$TMSN_3$ (2 equiv)	K_2CO_3	CuI	DMSO	80	42
12	$TMSN_3$ (2 equiv)	Cs_2CO_3	CuI	DMSO	80	48
13	$TMSN_3$ (2.0 equiv)		CuI	DMF	80	75
14	$TMSN_3$ (2.0 equiv)		CuI	PhCl	80	64
15	$TMSN_3$ (2.0 equiv)		CuI	PEG-400	80	74
16	$TMSN_3$ (2.0 equiv)		CuI	dioxane	80	62
17	$TMSN_3$ (2.0 equiv)		CuI	^{i}PrOH	80	68
18	$TMSN_3$ (2.0 equiv)		CuI	DMSO	100	77
19	$TMSN_3$ (2.0 equiv)		CuI	DMSO	70	71
20[c]	$TMSN_3$ (2.0 equiv)		CuI	DMSO	80	85
21[d]	$TMSN_3$ (2.0 equiv)		CuI	DMSO	80	69

[a]Unless otherwise noted, the reactions were carried out with **1a** (0.5 mmol), **2a** (0.6 mmol), catalyst (0.05 mmol), and solvent (1.5 mL) at 80 °C in a sealed tube under an air atmosphere for 24 h. [b]Isolated yield of **3aa**. [c]20 mol % of catalyst used. [d]5 mol % of catalyst used.

benzyl alcohols have been used for the synthesis of quinazolinones using Ir,[17] Pt,[18] and Pd[19] as expensive and heavy metal catalysts for dehydrogenative oxidative cyclization, whereas a report on the use of methyl arenes or heteroarenes for the synthesis of quinazolinone is rare.[20] Considering all of these facts, we have next focused on the designing of a cascade reaction which uses aldehyde, alcohols, and methyl arenes to access quinazolinones. Herein, we report the use of aldehyde, alcohol, and methyl arenes/heteroarenes as coupling partners, which are cost-effective and easily available. Furthermore, the protocol is free from the use of ligand and base and uses $TMSN_3$ as nitrogen source and air/TBHP as oxidant.

RESULTS AND DISCUSSION

Taking into account the use of trimethylsilyl azide ($TMSN_3$) as ammonia equivalent in cross-coupling reactions to afford the corresponding primary amine as the sole product,[21] we initiated our investigation on a model reaction of 2-bromobenzamide (**1a**), benzaldehyde (**2a**), and $TMSN_3$ to optimize various reaction parameters as represented in Table 1.

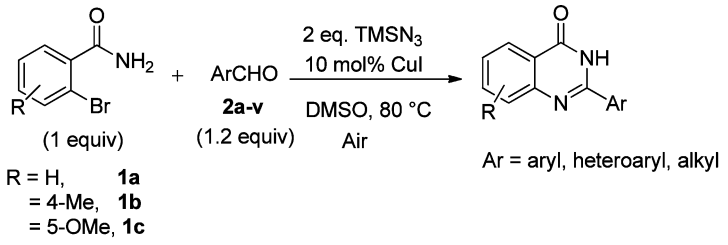
Subsequent screening of the different copper salts and $FeCl_3$ with DMSO as a solvent at 80 °C under an air atmosphere was carried out (Table 1, entries 1−7). Among all the metal salts used, CuI exhibited relatively higher catalytic activity, whereas no product was formed with $FeCl_3$. The amount of $TMSN_3$ used was also investigated. As evident from the results, the transformation was affected when the $TMSN_3$ was reduced from 2 equiv to 1 equiv, which resulted in a relatively lower yield of **3aa** (Table 1, entry 8), whereas no appreciable change was observed when loading of $TMSN_3$ was increased to 3 equiv (Table 1, entry 9). However, changing the azide from $TMSN_3$ to NaN_3 resulted in a poor yield of **3aa** (Table 1, entry 10). Addition of base proved to be detrimental to the reaction, as seen from the results, while the use of K_2CO_3 afforded only 42% of desired product, whereas Cs_2CO_3 did not result in any significant improvement in the yield of the product (Table 1, entries 11 and 12). Screening of solvents revealed that DMSO was the best solvent among the solvents (Table 1, entries 13−17). It was also observed that green solvent such as PEG-400 also afforded a good yield of the product. The effect of temperature on product yield was also monitored, and it was found out that increasing or decreasing the reaction temperature from 80 °C to 100 °C and 70 °C resulted in relatively less yield, i.e., 77% and 71%, respectively (Table 1, entries 18 and 19). No appreciable change in the yield was observed by increasing the catalyst loading from 10% to 20%. However, a decrease in the catalyst loading to 5% resulted in only 69% yield of the desired product (Table 1, entries 20 and 21).

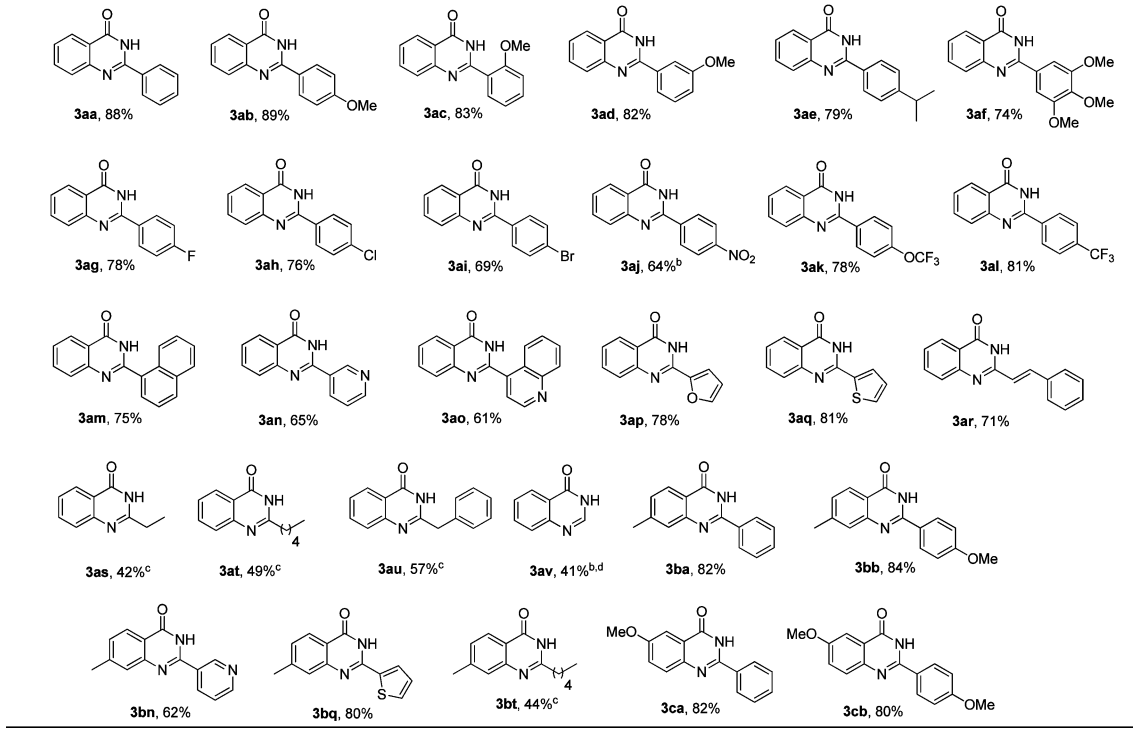
Under the optimum reaction conditions (Table 1, entry 5), the scope and generality of this CuI-catalyzed domino reaction affording 2-substituted quinazolinones were subsequently investigated (Scheme 1).

The reactions with aryl-substituted aldehydes bearing electron-donating or electron-withdrawing groups proceeded smoothly to provide the desired products **3aa−l** in 64−89% yields. It is noteworthy to mention that fused aryl (e.g., **3am**) and heteroaryl (e.g., **3an−aq**) aldehydes were also well tolerated in this reaction, producing the corresponding products in good yields. To our delight, both alkenyl- (e.g., **3ar**), benzyl- (e.g., **3au**), and alkyl-substituted aldehydes (e.g.,

DOI: 10.1021/acs.joc.6b00599
J. Org. Chem. 2016, 81, 5046−5055

Scheme 1. Scope of the Reaction for Synthesis of Various Quinazolin-4(3*H*)-ones from Aldehydes[a]



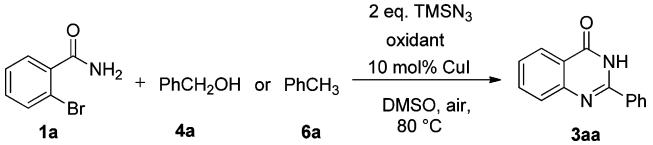


[a]Reaction conditions: **1a** (0.5 mmol), aldehyde **2a−v** (0.6 mmol), $TMSN_3$ (1.0 mmol), CuI (0.05 mmol), DMSO (1.5 mL), 80 °C, air, 24 h. The yields below the structure are isolated yields. [b]Reaction run for 48 h. [c]0.75 mmol of aldehyde used. [d]2 mL of formaldehyde used.

3as−t) were also well tolerated during this transformation to generate the corresponding products in good to moderate yields. A series of differently substituted 2-bromobenzamides such as methyl and methoxy were also successfully used in this tandem reaction to afford 2-substituted quinazolinones (**3ba−cb**) in yields ranging from 62% to 84%.

After the successful synthesis of 2-substituted quinazolinones from aldehydes, attempts to extend this methodology to alcohols and methyl arenes as substrates were then investigated. Encouraged by the previous reports of the oxidant's use in domino dual oxidative C−N coupling reactions,[20] a series of oxidants were additionally screened for the above-optimized reaction condition for the synthesis of quinazolinones as shown in Table 2. Among the various oxidants (TBHP, DTBP, DDQ, and $K_2S_2O_8$) examined, we observed that 2 equiv of TBHP proved to be the best yielding oxidant to access 2-substituted quinazolinone using alcohol instead of aldehyde in the three-component reaction (Table 2, entries 1−4). While DTBP yielded 71% of the product, the other two oxidants DDQ and $K_2S_2O_8$ proved to be inefficient. With 2 equiv of TBHP in the case of methyl arenes, the yield of the product **3aa** was only 60%, but when TBHP was increased to 3 equiv, the yield was improved to 71%. Any further increase in the amount of TBHP (4.0 equiv) reduced the yield to 63% (Table 2, entries 5−7).

Table 2. Optimization of the Reaction Conditions for the Synthesis of 2-Substituted Quinazolin-4(3*H*)-one Using Alcohols and Methyl Arenes[a]



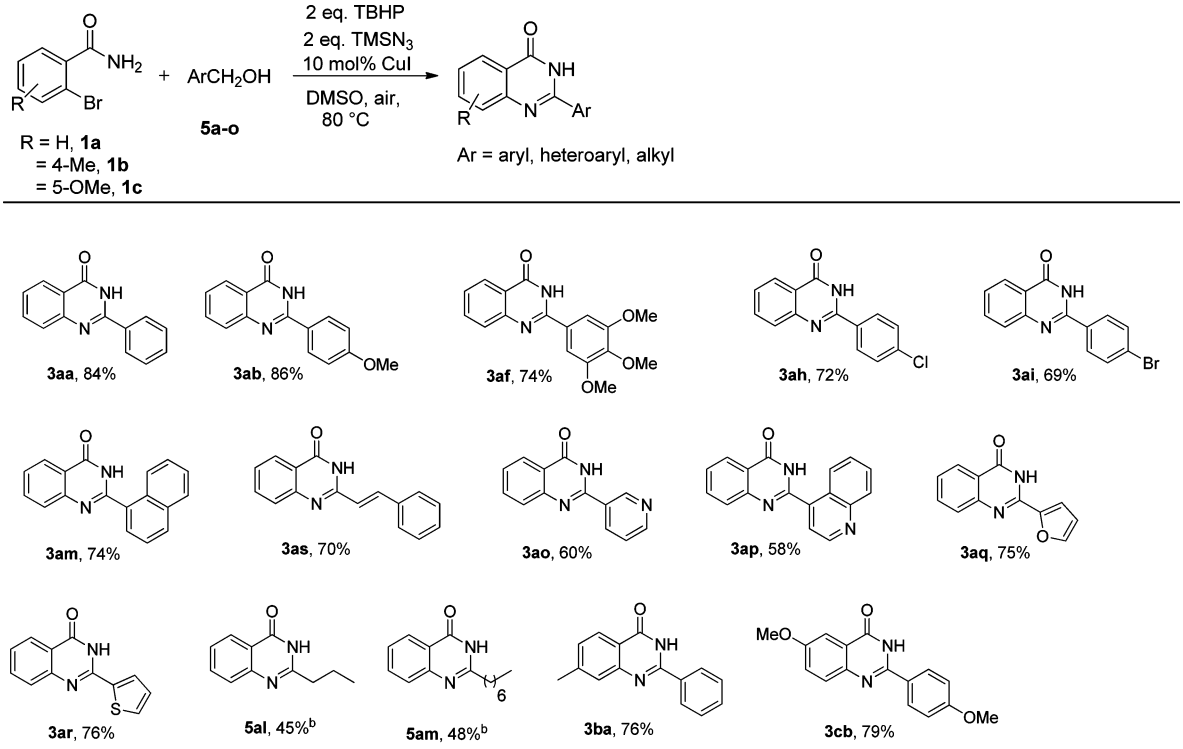
S. no.	substrate	oxidant[c]	yield[b] (%)
1	**4a**	TBHP	84
2	**4a**	DTBP	71
3	**4a**	DDQ	0
4	**4a**	$K_2S_2O_8$	trace
5	**6a**	TBHP	60
6	**6a**	TBHP (3 equiv)	71
7	**6a**	TBHP (4 equiv)	63

[a]Unless otherwise noted, the reactions were carried out with **1a** (0.5 mmol), **4a** (0.6 mmol), **6a** (2 mL) catalyst (0.05 mmol), and solvent (1.5 mL) at 80 °C in a sealed tube under an air atmosphere for 24 h. [b]Isolated yield of **3aa**. [c]0.8 mmol of oxidant was used.

With the optimized reaction conditions for best yield, we explored the scope of the oxidative tandem reaction to access a

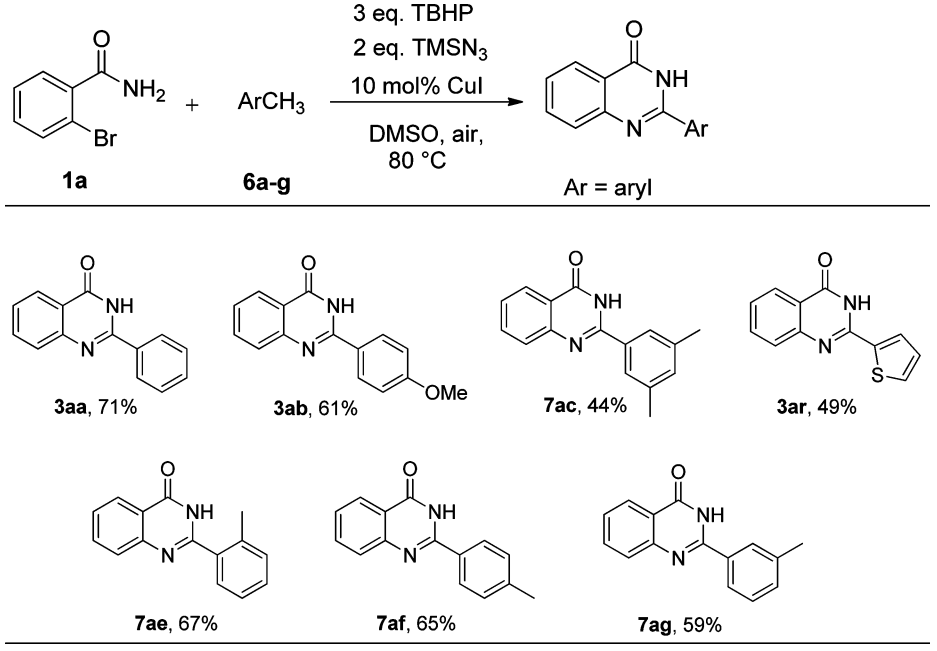
DOI: 10.1021/acs.joc.6b00599
J. Org. Chem. 2016, 81, 5046−5055

Scheme 2. Scope of the Reaction for Synthesis of Various Quinazolin-4(3*H*)-ones from Alcohols[a]



[a]Reaction conditions: **1a** (0.5 mmol), alcohol **5a–o** (0.6 mmol), $TMSN_3$ (1.0 mmol), TBHP (1.0 mmol, 70% aqueous solution), CuI (0.05 mmol), DMSO (1.5 mL), 80 °C, air, 24 h. The yields below the structure are isolated yields. [b]0.75 mmol of alcohol used.

Scheme 3. Scope of the Reaction for Synthesis of Various Quinazolin-4(3*H*)-ones from Methyl Arenes[a]



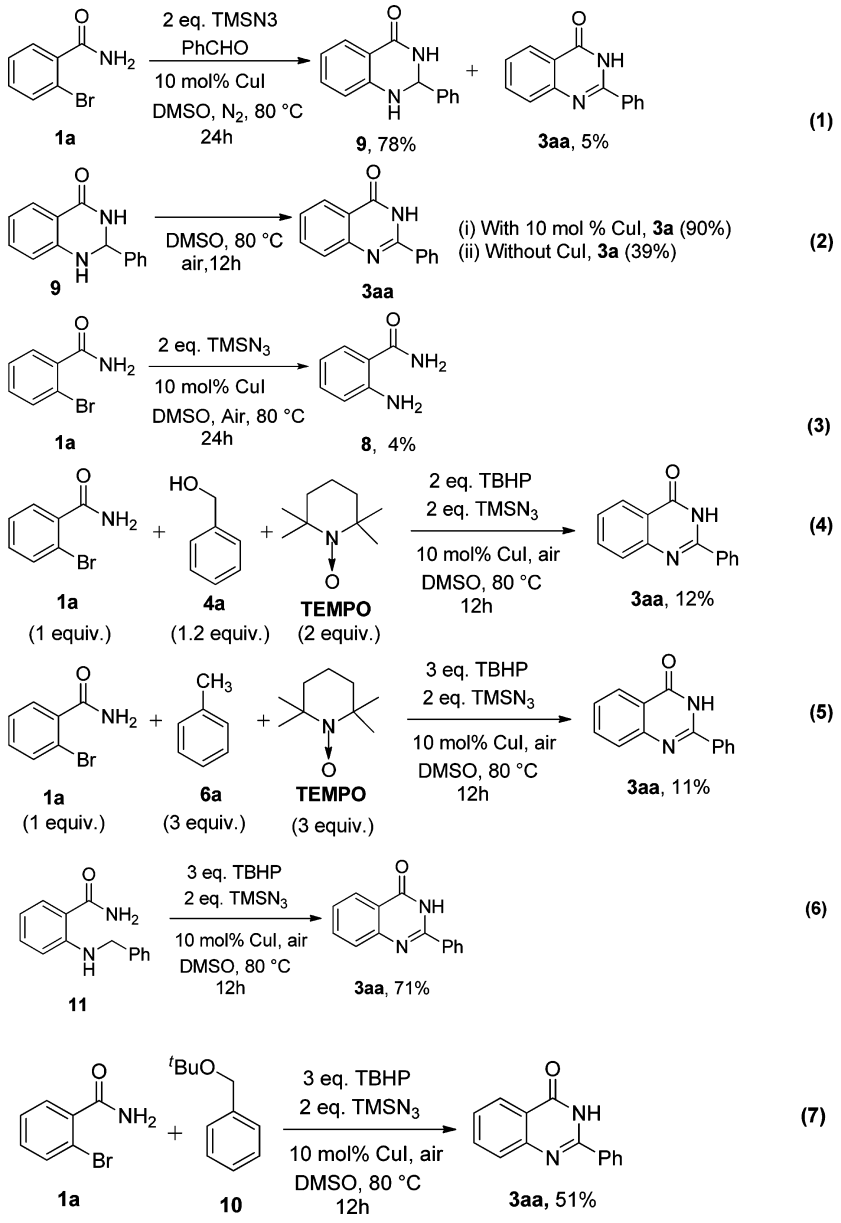
[a]Reaction conditions: **1a** (0.5 mmol), methyl arenes **6a–g** (2 mL), $TMSN_3$ (1.0 mmol), TBHP (1.5 mmol, 70% aqueous solution), CuI (0.05 mmol), DMSO (1.5 mL), 80 °C, air, 24 h.

series of 2-substituted quinazolinones derived from alcohol or methyl arenes, as depicted in Schemes 2 and 3.

Benzyl alcohols bearing electron-donating and electron-withdrawing groups readily reacted, affording 2-substituted quinazolinones in good to excellent yields (Scheme 2). It is worthy to note that chloro and bromo substituents survived during the reaction (**3ah–i**). Naphthyl alcohol, cinnamyl alcohol, and heteroaryl alcohols furnished the desired products in good to excellent yields. Interestingly, alkyl alcohols reacted well under the standard conditions to provide 2-substituted

DOI: 10.1021/acs.joc.6b00599
J. Org. Chem. 2016, 81, 5046–5055

Scheme 4. Control Experiments and Effect of Radical Inhibitor



quinazolinones in satisfactory yields (**5al**–**m**). Differently substituted 2-bromobenzamides also afforded the good yield of the respective products.

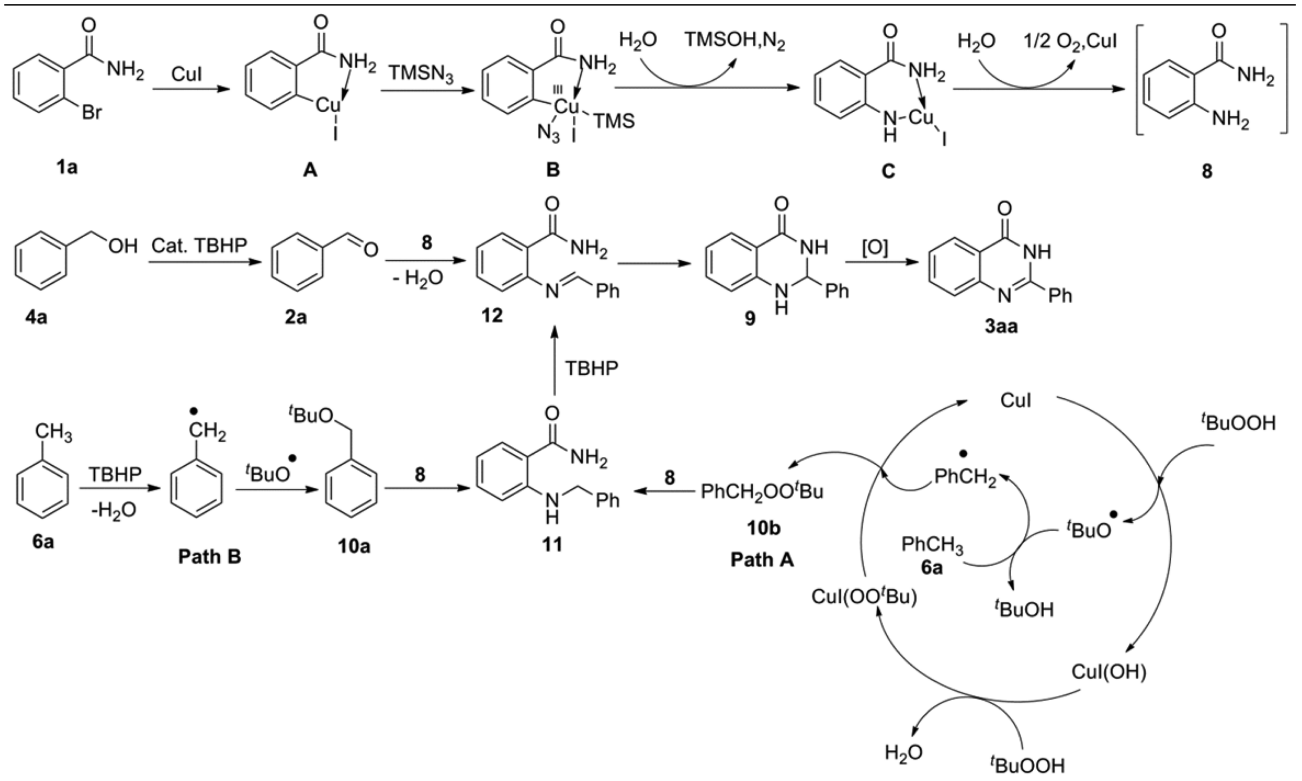
Under the optimized reaction conditions, when toluene reacted with 2-bromobenzamide, it afforded a good yield of the desired product **3aa** (Scheme 3). With electron-donating substituents such as 4-methylanisole, a drop in yield was observed (**3ab**). Reaction with substrate having more than one benzylic carbon, i.e., mesitylene, proceeded sluggishly, providing a moderate yield of quinazolinone (**7ac**). 2-Methyl thiophene also proved to be a good substrate for this transformation (**3ar**) in a moderate yield. The reaction of *ortho*-, *para*-, and *meta*-xylenes with 2-bromobenzamide afforded good to moderate yields of the respective quinazolinones without affecting their other methyl group (**7ae**–**7ag**).

To gain an insight into the cyclooxidative mechanism of quinazolinone formation from *ortho*-halobenzamides during this study, a series of control experiments were carried out. Under a N_2 atmosphere, the reaction of 2-bromobenzamide with benzaldehyde using $TMSN_3$ and CuI as catalyst at 80 °C yielded mainly the dihydroquinazolinone intermediate **9** (78%) along with the desired **3aa** (5%) (Scheme 4, eq 1). The aerial oxidation of **9** with or without CuI resulted in 90% and 39% yield of the desired product **3aa**, respectively (Scheme 4, eq 2). This indicates that the CuI and the air are essential for the transformation. However, reaction of 2-bromobenzamide with $TMSN_3$ using CuI as a catalyst at 80 °C under an air atmosphere afforded 2-aminobenzamide (**8**) in 4% yield only (Scheme 4, eq 3). This trace amount of reductive product could be explained due to the lack of proton source in this reductive cleavage.[22a]

Inhibition of reaction was observed when TEMPO (2,2,6,6-tetramethylpipridine-*N*-oxyl), a radical inhibitor, was added to the reaction system, indicating the radical process nature (Scheme 4, eq 4). This result shows that the oxidation of benzyl alcohol to benzaldehyde, which is needed in order for the reaction to proceed, is a radical process during the reaction.

DOI: 10.1021/acs.joc.6b00599
J. Org. Chem. 2016, 81, 5046–5055

Scheme 5. Possible Mechanism for the CuI-Catalyzed Domino Synthesis of 2-Aryl Quinazolinone



The same negative effect was also observed when methyl arene was used as a substrate for the synthesis of quinazolinone (Scheme 4, eq 5). In addition, it was found that the amino group played a crucial role in intermolecular C−N bond formation (Scheme 4, eq 6). According to a literature report, a *tert*-butoxy intermediate was involved in C−N bond formation.[22b] Considering this fact, we speculated that, during the reaction, *tert*-butyl benzyl ether was generated, which underwent intermolecular amination of **1a** to give **11**. According to our expection, 51% of the desired product was obtained when **1a** was reacted with **10a** under standard reaction conditions (Scheme 4, eq 7).

In accordance with the above results and the literature precedents, a possible mechanism is proposed as shown in Scheme 5. Initially, CuI undergoes oxidative addition with substrate **1a** to give complex **A**, which undergoes subsequent treatment with $TMSN_3$ to give complex **B**, followed by copper-catalyzed denitrogenative reaction in the presence of a trace amount of H_2O present in DMSO to provide complex **C**. The latter readily gets reduced into 2-aminobenzamide (**8**) with the aid of moisture present in DMSO during the reaction to complete the catalytic cycle. On the other hand, benzyl alcohol is oxidized to benzaldehyde via a radical pathway with TBHP. The reaction of benzaldehyde and 2-aminobenzamide afforded an imine (**12**). CuI-assisted decomposition of TBHP leads to formation of *tert*-butoxyl and *tert*-butylperoxy radicals. *tert*-Butoxyl radical abstracts a H· radical from toluene to give a benzyl radical. Subsequent coupling of the kinetically stable *tert*-butylperoxy radical[22c−f] and benzyl radical ($PhCH_2$· and ^{t}OOBu·) generated intermediate **10b** (Path B). This intermediate undergoes intermolecular amination by reacting with **8**, which gets oxidized to imine (**12**). Moreover, intermediate **11** formation can be explained by intermolecular C−N bond formation by *tert*-butylbenzyl ether (**10a**), which is generated by the coupling of benzyl radical and *tert*-butoxy radical (Path A). Subsequently, the imine generated underwent intramolecular cyclization, followed by oxidation, to furnish the desired product **3aa**.

CONCLUSION

In summary, we have designed and developed a convenient, highly efficient, operationally simple, ligand- and base-free one-pot protocol for the synthesis of 2-substituted quinazolinones from 2-bromobenzamide. It provides a diverse synthetic approach, utilizing inexpensive and readily available multiform substrates, aldehydes, alcohols, and methyl arenes, and uses $TMSN_3$ as nitrogen source via a multipathway coupled self-sequenced domino reaction involving oxidative addition, reductive amination, an intermolecular oxidative nitrogenation of a benzylic C(sp^3)−H bond, intramolecular cyclization, and oxidative dehydrogenation assembled in a single reactor to afford the desired product. Particularly noteworthy is that the broad substrate scope, high yield, and functional group compatibility are significant practical advantages. Even though our strategy augurs an interesting synthetic methodology, further exploring the novel synthetic approach toward the synthesis of other N-containing heterocycles and understanding a detailed mechanism is underway in our laboratory.

EXPERIMENTAL SECTION

General Information. Commercially available reagent grade chemicals were used as received. All reactions were monitored by TLC on an E. Merck Kieselgel 60 F254, with detection by UV light, spraying Dragendorff's solution. Column chromatography was performed on silica gel (60-120 and 230-400 mesh size). IR spectra were recorded as thin films or in KBr solution using an FTIR (4000−450 cm^{-1}) spectrophotometer. ^{1}H and ^{13}C NMR spectra were

DOI: 10.1021/acs.joc.6b00599
J. Org. Chem. 2016, 81, 5046−5055

recorded on 400, 300, 100, and 75 MHz spectrophotometers, respectively, in $CDCl_3$ and DMSO-d_6. Chemical shift values are reported in ppm relative to TMS (tetramethylsilane) as the internal reference, unless otherwise stated; s (singlet), d (doublet), t (triplet), dd (doublet of doublets), m (multiplet); J in hertz. The LC-ESI-MS were recorded on a triple-quadrupole (TQD) mass spectrometer, and HRMS spectra were performed using a mass spectrometer Q-TOF. The 10 μL samples (dissolved in solvent such as methanol/acetonitrile/water) were introduced into the ESI source through an autosampler. The mobile phase 90:10 MeOH/CH_3CN:H_2O flowed at the rate of 250 μL/min by an MS pump. Ion spray voltage was set at 5.3 kV and the capillary voltage at 34 V. The MS scan was run up to 2.5 min, and the spectra's printouts are averages of over 10 scans at peak top in TIC.

General Procedure for Preparation of 2-Substituted Quinazolin-4(*3H*)-ones Using Aldehydes. To a mixture of 2-bromobenzamide **1a** (0.10 g, 0.5 mmol), aldehyde **2a−v** (0.6 mmol), and CuI (0.01 g, 0.05 mmol) in DMSO (1.5 mL) was added $TMSN_3$ (0.13 mL, 1.0 mmol) in a tube under an air atmosphere. After that, the tube was sealed, and the reaction mixture was heated at 80 °C for 24 h. After completion of the reaction, water (20 mL) was added to it. A saturated aq. $Na_2S_2O_3$ solution was added until the disappearance of brown color, and the reaction mixture was extracted with ethyl acetate. The combined organic layer was dried on anhydrous sodium sulfate. The solvent was evaporated under reduced pressure, and the crude product was purified by column (SiO_2, 60-120) chromatography using 15−20% EtOAc:hexane as eluent to get pure quinazolinone products. Most of the compounds were purified without any column chromatography, where ethyl acetate was added to the crude product and the resulting suspension was filtered. It was washed with ethyl acetate 2−3 times to get a pure compound. Again, the filtrate was concentrated, and this process was repeated 2−3 times to get a good yield of the products.

General Procedure for the Synthesis of 2-Substituted Quinazolin-4(*3H*)-ones Using Alcohol. To a mixture of 2-bromobenzamide **1a** (0.10 g, 0.5 mmol), alcohol **4a−o** (0.6 mmol), and CuI (0.01 g, 0.05 mmol) in DMSO (1.5 mL) were added $TMSN_3$ (0.13 mL, 1.0 mmol) and TBHP (0.1 mL, 1.0 mmol, 70% aqueous solution) in a tube under an air atmosphere. After that, the tube was sealed, and the reaction mixture was heated at 80 °C for 24 h. After completion of the reaction, the same procedure was followed as reported above.

General Procedure for the Synthesis of 2-Substituted Quinazolin-4(*3H*)-ones Using Methyl Arenes. To a mixture of 2-bromobenzamide **1a** (0.10 g, 0.5 mmol), methyl arenes **6a−g** (2 mL), and CuI (0.01 g, 0.05 mmol) in DMSO (1.5 mL) were added $TMSN_3$ (0.13 mL, 1.0 mmol) and TBHP (0.14 mL, 1.0 mmol, 70% aqueous solution) in a tube under an air atmosphere. After that, the tube was sealed, and the reaction mixture was heated at 80 °C for 24 h. After completion of the reaction, the same procedure was followed as reported above, and the crude product was purified by column (SiO_2, 230-400) chromatography using 15−20% EtOAc:hexane as eluent to get pure quinazolinone products.

2-Phenylquinazolin-4(3H)-one (***3aa***).[10] White solid; Yield: 88% (97 mg); mp 230−232 °C (lit. 232−235 °C); IR (KBr) cm^{-1}: 3403, 3019, 1670, 1403, 1069; ^1H NMR (400 MHz, DMSO-d_6): δ 12.54 (s, 1H), 8.20−8.15 (m, 3H), 7.86−7.82 (m, 1H), 7.76 (d, J = 8.00 Hz, 1H), 7.62−7.51 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6 + $CDCl_3$): δ 162.7, 152.6, 149.2, 134.8, 133.1, 131.6, 128.9, 128.1, 127.9, 126.8, 121.4. HRMS calcd for $C_{14}H_{10}N_2O$ [M + H^+] 223.0866, found 223.0862.

2-(4-Methoxyphenyl)quinazolin-4(3H)-one (***3ab***).[20] White solid; Yield: 89% (112 mg); mp 242−247 °C (lit. 247−249 °C); IR (KBr) cm^{-1}: 3400, 3019, 1676, 1403, 1385, 1069, 758 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 12.41 (br.s, 1H), 8.21−8.18 (dd, J_1 = 6.99 Hz, J_2 = 2.01 Hz, 2H), 8.14−8.12 (dd, J_1 = 7.94 Hz, J_2 = 1.15 Hz, 1H), 7.84−7.79 (m, 1H), 7.71 (d, J = 7.66 Hz, 1H), 7.50−7.46 (m, 1H), 7.10 (d, J = 9.00 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.7, 162.3, 152.3, 149.4, 135.0, 129.9, 127.7, 126.5, 126.2, 125.2, 121.1, 114.4, 55.9. HRMS calcd for $C_{15}H_{12}N_2O_2$ [M + H^+] 253.0972, found 253.0965.

2-(2-Methoxyphenyl)quinazolin-4(3H)-one (***3ac***).[23] White solid; Yield: 83% (105 mg); mp 200−202 °C (lit. 198−202 °C); IR (KBr) cm^{-1}: 3406, 1676, 1603, 1402, 1217, 1070; ^1H NMR (400 MHz, DMSO-d_6): δ 12.11 (br.s, 1H), 8.16−8.14 (dd, J_1 = 7.89 Hz, J_2 = 1.20 Hz, 1H), 7.85−7.81 (m, 1H), 7.72−7.70 (dd, J_1 = 7.56 Hz, J_2 = 1.82 Hz, 1H), 7.56−7.51 (m, 2H), 7.20 (d, J = 8.23 Hz, 1H), 7.11−7.07 (m, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.6, 157.6, 152.8, 149.5, 134.8, 132.6, 130.9, 127.8, 127.0, 126.2, 123.0, 121.4, 120.9, 112.3, 56.2. HRMS calcd for $C_{15}H_{12}N_2O_2$ [M + H^+] 253.0972, found 253.0972.

2-(3-Methoxyphenyl)quinazolin-4(3H)-one (***3ad***).[17] White solid; Yield 82% (103 mg); mp 180−182 °C (lit. 181−183 °C); IR (KBr) cm^{-1}: 3019, 1672, 1607, 1403, 1070; ^1H NMR (400 MHz, DMSO-d_6): δ 12.53 (s, 1H), 8.17 (d, J = 7.25 Hz, 1H), 7.87−7.82 (m, 1H), 7.80 (d, J = 7.79 Hz, 1H), 7.76−7.74 (m, 2H), 7.55−7.51 (t, J = 7.16 Hz, 1H), 7.48−7.44 (t, J = 7.97 Hz, 1H), 7.17−7.14 (dd, J_1 = 8.16 Hz, J_2 = 1.99 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.8, 159.8, 152.6, 148.9, 135.2, 134.4, 130.3, 127.8, 127.2, 126.3, 121.3, 120.5, 118.0, 113.0, 55.8. HRMS calcd for $C_{15}H_{12}N_2O_2$ [M + H^+] 253.0972, found 253.0964.

2-(4-(Isopropyl)phenyl)quinazolin-4(3H)-one (***3ae***).[24] White solid; Yield 79% (104 mg); mp 271−273 °C (lit. 270−273 °C); IR (KBr) cm^{-1}: 3019, 1672, 1403, 1215, 1069; ^1H NMR (400 MHz, DMSO-d_6): δ 12.48 (br.s, 1H), 8.16−8.12 (m, 3H), 7.85−7.81 (m, 1H), 7.74 (d, J = 7.66 Hz, 1H), 7.53−7.49 (m, 1H), 7.43 (d, J = 8.23 Hz, 2H), 3.02−2.95 (m, 1H), 1.25 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.7, 152.7, 152.5, 149.3, 135.0, 130.7, 128.2, 127.9, 127.0, 126.8, 126.3, 121.3, 33.8, 24.0 (2C). HRMS calcd for $C_{17}H_{16}N_2O$ [M + H^+] 265.1335, found 265.1334.

2-(3,4,5-Trimethoxyphenyl)quinazolin-4(3H)-one (***3af***).[25] White solid; Yield 74% (115 mg); mp 257−260 °C (lit. 258−260 °C); IR (KBr) cm^{-1}: 3401, 3019, 1654, 1403, 1156; ^1H NMR (400 MHz, DMSO-d_6): δ 12.51 (s, 1H), 8.16 (d, J = 7.64 Hz, 1H), 7.85−7.82 (t, J = 7.25 Hz, 1H), 7.76 (d, J = 8.03 Hz, 1H), 7.57 (s, 2H), 7.53−7.50 (t, J = 7.44 Hz, 1H), 3.91 (s, 6H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.5, 158.0, 156.9, 153.8, 145.4, 139.8, 132.8, 132.6, 131.7, 131.0, 126.0, 110.4, 65.3, 61.3. HRMS calcd for $C_{17}H_{16}N_2O_4$ [M + H^+] 313.1183, found 313.1175

2-(4-Fluorophenyl)quinazolin-4(3H)-one (***3ag***).[20] White solid; Yield: 78% (93 mg); mp 284−286 °C (lit. 284−287 °C); IR (KBr) cm^{-1}: 3402, 3019, 2400, 1659, 1403, 1215, 1069; ^1H NMR (400 MHz, DMSO-d_6): δ 12.57 (br.s, 1H), 8.27−8.24 (m, 2H), 8.17−8.14 (dd, J_1 = 7.89 Hz, J_2 = 1.10 Hz, 1H), 7.86−7.82 (m, 1H), 7.75 (d, J = 7.94 Hz, 1H), 7.55−7.51 (m, 1H), 7.42−7.37 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.7 (d, $J_{C\text{-}F}$ = 251.34 Hz), 162.7, 151.9, 149.0, 135.1, 130.8 (d, $J_{C\text{-}F}$ = 9.38 Hz), 129.6, 127.9, 127.1, 126.3, 121.2, 116.2 (d, $J_{C\text{-}F}$= 21.96 Hz). HRMS calcd for $C_{14}H_9FN_2O$ [M + H^+] 241.0772, found 241.0780

2-(4-Chlorophenyl)quinazolin-4(3H)-one (***3ah***).[20] White solid; Yield: 76% (97 mg); mp > 300 °C (lit. 298−300 °C); IR (KBr) cm^{-1}: 3408, 3308, 3021, 2401, 1672, 1606, 1480, 1409, 1154, 1093; ^1H NMR (400 MHz, DMSO-d_6): δ 12.59 (br.s, 1H), 8.21 (d, J = 8.30 Hz, 2H), 8.17 (d, J = 7.72 Hz, 1H), 7.86−7.83 (t, J = 7.34 Hz, 1H), 7.75 (d, J = 8.11 Hz, 1H), 7.64 (d, J = 8.40 Hz, 2H), 7.55−7.52 (t, J = 7.34 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6, 151.8, 149.0, 136.7, 135.1, 132.0, 130.0 (2C), 129.1 (2C), 127.9, 127.2, 126.3, 121.4; HRMS calcd for $C_{14}H_9ClN_2O$ [M + H^+] 257.0476, found 257.0478.

2-(4-Bromophenyl)quinazolin-4(3H)-one (***3ai***).[8d] White solid; Yield: 69% (103 mg); mp 292−294 °C (lit. 292−295 °C); IR (KBr) cm^{-1}: 3412, 3019, 1650, 1403, 1110, 1065; ^1H NMR (400 MHz, DMSO-d_6): δ 12.60 (br.s, 1H), 8.17−8.11 (m, 3H), 7.87−7.83 (m, 1H), 7.78−7.74 (m, 3H), 7.56−7.52 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6, 151.9, 149.0, 135.1, 132.3, 132.1, 130.2, 127.9, 127.3, 126.3, 125.7, 121.4. HRMS calcd for $C_{14}H_9BrN_2O$ [M + H^+] 300.9971, found 300.9971.

2-(4-Nitrophenyl)quinazolin-4(3H)-one (***3aj***).[26] Yellow solid; Yield: 64% (85 mg); mp > 300 °C (lit. > 300 °C); IR (KBr) cm^{-1}:

DOI: 10.1021/acs.joc.6b00599
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3402, 3019, 2399, 1643, 1522, 1403, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.82 (br.s, 1H), 8.44−8.37 (m, 4H), 8.20−8.17 (dd, J_1 = 7.85 Hz, J_2 = 1.15 Hz, 1H), 7.90−7.86 (m, 1H), 7.81−7.79 (d, J = 8.04 Hz, 1H), 7.60−7.56 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6, 151.3, 149.4, 148.7, 139.0, 135.3, 129.7 (2C), 128.1, 127.9, 126.4, 124.1 (2C), 121.6. HRMS calcd for $C_{14}H_9N_3O_3$ [M + H$^+$] 268.0717, found 268.0709.

2-(4-(Trifluoromethoxy)phenyl)quinazolin-4(3H)-one (**3ak**).[29] White solid; Yield: 78% (119 mg); mp 267−271 °C (lit. 268−271 °C); IR (KBr) cm^{-1}: 3401, 2922, 1654, 1403, 1218, 1156, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.62 (br.s, 1H), 8.32 (d, J = 7.76 Hz, 1H), 7.86−7.83 (t, J = 7.26 Hz, 1H), 7.76 (d, J = 7.97 Hz, 1H), 7.55−7.54 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6, 151.6, 150.8 (d, $J_{C\text{-}F}$ = 1.22 Hz), 149.0, 135.1, 132.3, 130.5 (2C), 128.0, 127.2, 126.3, 124.3, 121.7, 121.4, 121.3 (2C), 119.1 (q, $J_{C\text{-}F}$ = 256.6 Hz), 116.6; HRMS calcd for $C_{15}H_9F_3N_2O_2$ [M + H$^+$] 307.0689, found 307.0678.

2-(4-(Trifluoromethyl)phenyl)quinazolin-4(3H)-one (**3al**).[29] White solid; Yield: 81% (117 mg); mp > 300 °C (lit. 308−310 °C); IR (KBr) cm^{-1}: 3400, 3019, 1653, 1403, 1216, 1155, 1067, 669; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.72 (s, 1H), 8.40 (d, J = 8.03 Hz, 2H), 8.18 (d, J = 7.79 Hz, 1H), 7.91 (d, J = 8.23 Hz, 2H), 7.87−7.83 (t, J = 8.03 Hz, 1H), 7.78 (d, J = 7.93 Hz, 1H), 7.56−7.53 (t, J = 7.50 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.6, 151.6, 148.8, 137.1, 135.1 (2C), 131.5 (q, $J_{C\text{-}F}$ = 31.33 Hz), 129.1, 128.4, 128.0, 127.4, 126.3, 125.9 (d, $J_{C\text{-}F}$ = 3.43 Hz), 125.7, 123.0 (q, $J_{C\text{-}F}$ = 272.7), 121.6; HRMS calcd for $C_{15}H_{10}F_3N_2O$ [M + H$^+$] 291.0740, found 291.0742.

2-(Naphthalen-1-yl)quinazolin-4(3H)-one (**3am**).[10] White solid; Yield: 75% (102 mg); mp 297−299 °C (lit. 298−300 °C); IR (KBr) cm^{-1}: 3019, 2400, 1675, 1403, 1385, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.66 (br.s, 1H), 8.23 (d, J = 7.84 Hz, 1H), 8.19 (d, J = 7.64 Hz, 1H), 8.13 (d, J = 8.23 Hz, 1H), 8.06 (d, J = 7.25 Hz, 1H), 7.88−7.85 (t, J = 7.05 Hz, 1H), 7.81 (d, J = 6.86 Hz, 1H), 7.74 (d, J = 7.84 Hz, 1H), 7.67−7.56 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.5, 154.2, 149.1, 134.9, 133.6, 132.2, 130.8, 130.7, 128.8, 128.1, 127.8, 127.5, 127.2, 126.8, 126.3, 125.6, 125.5, 121.6. HRMS calcd for $C_{18}H_{12}N_2O$ [M + H$^+$] 273.1022, found 273.1025.

2-(Pyridin-3-yl)quinazolin-4(3H)-one (**3an**).[10] White solid; Yield: 65% (72 mg); mp 280−282 °C (lit. 278−281 °C); IR (KBr) cm^{-1}: 3400, 3019, 2926, 1677, 1402, 1215, 1108; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.72 (s, 1H), 9.30 (s, 1H), 8.76 (d, J = 4.08 Hz, 1H), 8.51−8.48 (m, 1H), 8.18−8.16 (dd, J_1 = 7.93 Hz, J_2 = 1.08 Hz, 1H), 7.88−7.84 (m, 1H), 7.78−7.76 (dd, J_1 = 8.14 Hz, J_2 = 0.57 Hz, 1H), 7.60−7.53 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6, 152.2, 151.2, 149.2, 148.9, 135.8, 135.1, 129.2, 127.9, 127.4, 126.3, 124.0, 121.5. HRMS calcd for $C_{13}H_9N_3O$ [M + H$^+$] 224.0818, found 224.0811.

2-(Quinolin-4-yl)quinazolin-4(3H)-one (**3ao**). White solid; Yield: 61% (83 mg); mp > 300 °C; IR (KBr) cm^{-1}: 3019, 1644, 1403, 1215, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.83 (br.s, 1H), 9.09 (d, J = 3.73 Hz, 1H), 8.25−8.22 (m, 2H), 8.17 (d, J = 8.59 Hz, 1H), 7.92−7.84 (m, 2H), 7.81 (d, J = 4.29 Hz, 1H), 7.78 (d, J = 8.03 Hz, 1H), 7.70−7.66 (t, J = 7.65 Hz, 1H), 7.64−7.61 (t, J = 7.47 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.1, 152.1, 150.5, 148.8, 148.4, 139.6, 135.1 (2C), 133.1, 130.3, 129.9, 128.0 (2C), 127.7, 126.3, 126.0, 122.0. HRMS calcd for $C_{17}H_{11}N_3O$ [M + H$^+$] 274.0975, found 274.0975.

2-(Furan-2-yl)quinazolin-4(3H)-one (**3ap**).[10] White solid.; Yield: 78% (82 mg); mp 275−276 °C (lit. 274−276 °C); IR (KBr) cm^{-1}: 3407, 1660, 1401, 1218, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.49 (s, 1H), 8.13 (d, J = 7.51 Hz, 1H), 7.99 (s, 1H), 7.82−7.78 (t, J = 7.28 Hz, 1H), 7.69 (d, J = 8.01 Hz, 1H), 7.63 (d, J = 3.37 Hz, 1H), 7.50−7.46 (t, J = 7.64 Hz, 1H), 6.75−6.74 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.1, 149.0, 147.0, 146.5, 144.5, 135.0, 127.6, 126.9, 121.5, 114.9, 112.9. HRMS calcd for $C_{12}H_8N_2O_2$ [M + H$^+$] 213.0659, found 213.0656.

2-(Thiophene-2-yl)quinazolin-4(3H)-one (**3aq**).[10] White solid; Yield: 81% (92 mg); mp 221−222 °C (lit. 220−221 °C); IR (KBr) cm^{-1}: 3403, 3019, 1664, 1403, 1215, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.65 (br.s 1H), 8.24−8.23 (dd, J_1 = 3.77, J_2 = 0.87 Hz, 1H), 8.14−8.12 (dd, J_1 = 7.91 Hz, J_2 = 1.17 Hz, 1H), 7.88−7.86 (dd, J_1 = 5.02 Hz, J_2 = 0.91 Hz, 1H), 7.83−7.79 (m, 1H), 7.67 (d, J = 7.96 Hz, 1H), 7.51−7.47 (m, 1H), 7.25−7.23 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6 + $CDCl_3$): δ 162.2, 149.1, 148.3, 137.8, 135.1, 132.6, 129.8, 128.9, 127.4, 126.7, 126.4, 121.3. HRMS calcd for $C_{12}H_8N_2OS$ [M + H$^+$] 229.0430, found 229.0441.

(E)-2-Styrylquinazolin-4(3H)-one (**3ar**).[9] Light yellow solid; Yield: 71% (88 mg); mp 226−228 °C (lit. 226−228 °C); IR (KBr) cm^{-1}: 3019, 2399, 1669, 1403, 1385, 1215, 1109; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.34 (br.s, 1H), 8.12 (d, J = 7.24 Hz, 1H), 7.97 (d, J = 16.25 Hz, 1H), 7.82−7.78 (m, 1H), 7.69−7.66 (m, 3H), 7.49−7.39 (m, 4H), 7.05 (d, J = 16.25 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.5, 152.2, 149.5, 138.5, 135.5, 134.8, 130.1, 129.5 (2C), 128.0 (2C), 127.4, 126.5, 126.3, 121.8, 121.5. HRMS calcd for $C_{16}H_{12}N_2O$ [M + H$^+$] 249.1022, found 249.1034.

2-Ethylquinazolin-4(3H)-one (**3as**).[12] White solid; Yield: 42% (36 mg); mp 228−230 °C (lit. 229−231 °C); IR (KBr) cm^{-1}: 3399, 3019, 2400, 1672, 1618, 1469, 1403, 1385, 1070; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.14 (s, 1H), 8.08 (d, J = 7.63 Hz, 1H), 7.77−7.73 (t, J = 7.32 Hz, 1H), 7.60 (d, J = 8.02 Hz, 1H), 7.46−7.42 (t, J = 7.32 Hz, 1H), 2.64−2.59 (quart, J = 7.40 Hz, 2H), 1.26−1.22 (t, J = 7.40 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.2, 158.7, 149.4, 134.6, 127.2, 126.3, 126.1, 121.2, 28.2, 11.7. HRMS calcd for $C_{10}H_{10}N_2O$ [M + H$^+$] 175.0866, found 175.0858.

2-Pentylquinazolin-4(3H)-one (**3at**).[27] White solid; Yield: 49% (52 mg); mp 152−154 °C (lit. 153−154 °C); IR (KBr) cm^{-1}: 3019, 1674, 1468, 1215, 929; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.15 (s, 1H), 8.08 (d, J = 7.20 Hz, 1H), 7.78−7.74 (t, J = 8.03 Hz, 1H), 7.60 (d, J = 8.13 Hz, 1H), 7.46−7.42 (t, J = 7.54 Hz, 1H), 2.60−2.56 (t, J = 7.44 Hz, 2H), 1.73−1.70 (m, 2H), 1.32−1.28 (m, 4H), 0.88−0.84 (t, J = 6.46 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.2, 157.9, 149.4, 134.7, 127.2, 126.3, 126.1, 121.2, 34.9, 31.2, 26.9, 22.2, 14.2. HRMS calcd for $C_{13}H_{16}N_2O$ [M + H$^+$] 217.1335, found 217.1327.

2-Benzylquinazolin-4(3H)-one (**3au**).[17] White solid; Yield: 57% (67 mg); mp 248−250 °C (lit. 245−247 °C); IR (KBr) cm^{-1}: 3401, 3019, 1619, 1403, 1215, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.37 (br.s, 1H), 8.09−8.07 (d, J = 7.66 Hz, 1H), 7.79−7.75 (t, J = 7.46 Hz, 1H), 7.62 (d, J = 8.04 Hz, 1H), 7.48−7.45 (t, J = 7.46 Hz, 1H), 7.40 (d, J = 7.18 Hz, 2H), 7.34−7.30 (t, J = 7.27 Hz, 2H), 7.26−7.22 (t, J = 7.08 Hz, 1H), 3.94 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.4, 156.5, 149.3, 137.0, 134.8, 129.3 (2C), 128.9 (2C), 127.2 (2C), 126.6, 126.1, 121.1, 41.2; HRMS calcd for $C_{15}H_{12}N_2O$ [M + H$^+$] 237.1022, found 237.1001.

Quinazolin-4(3H)-one (**3av**).[25] White solid; Yield: 41% (30 mg); mp 211−214 °C (lit. 212−214 °C); IR (KBr) cm^{-1}: 3401, 3019, 1667, 1403, 1067; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.22 (s, 1H), 8.13−8.10 (dd, J_1 = 7.93 Hz, J_2 = 1.22 Hz, 1H), 8.08 (s, 1H), 7.82−7.78 (m, 1H), 7.62 (d, J = 7.84 Hz, 1H), 7.53−7.49 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.2, 149.1, 145.8, 134.7, 127.6, 127.1, 126.2, 123.1. HRMS calcd for $C_8H_6N_2O$ [M + H$^+$] 147.0553, found 147.0543.

7-Methyl-2-phenylquinazolin-4(3H)-one (**3ba**).[10] White solid; Yield: 82% (96 mg); mp 238−240 °C (lit. 240−241 °C); IR (KBr) cm^{-1}: 3019, 1666, 1605, 1402, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.44 (s, 1H), 8.18 (d, J = 6.85 Hz, 2H), 8.05 (d, J = 8.05 Hz, 1H), 7.61−7.53 (m, 4H), 7.36 (d, J = 8.23 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.2, 152.7, 149.3, 145.5, 133.2, 131.7, 129.0 (2C), 128.4, 128.1 (2C), 127.6, 126.1, 119.0, 21.8. HRMS calcd for $C_{15}H_{12}N_2O$ [M + H$^+$] 237.1022, found 237.1012.

7-Methyl-2-(4-Methoxyphenyl)quinazolin-4(3H)-one (**3bb**).[10] Light yellow solid; Yield: 84% (111 mg); mp 248−250 °C (lit. 246−248 °C); IR (KBr) cm^{-1}: 3403, 3019, 1663, 1403, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.32 (br.s, 1H), 8.19 (d, J = 8.69 Hz, 2H), 8.03 (d, J = 8.11 Hz, 1H), 7.52 (s, 1H), 7.32 (d, J = 8.11 Hz, 1H), 7.10 (d, J = 8.69 Hz, 2H), 3.85 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6, 162.3, 152.3, 149.5, 149.4, 129.8 (2C), 128.0, 127.4, 126.1, 125.3, 118.7, 114.4 (2C), 55.9, 21.8. HRMS calcd for $C_{16}H_{14}N_2O_2$ [M + H$^+$] 267.1128, found 267.1125.

7-Methyl-2-(pyridin-3-yl)quinazolin-4(3H)-one (**3bn**). White solid; Yield: 62% (73 mg); mp 256−260 °C; IR (KBr) cm^{-1}: 3681, 3400,

DOI: 10.1021/acs.joc.6b00599
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3019, 2399, 1669, 1605, 1522, 1474, 1419, 1024, 669, 626; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.95 (br.s, 1H), 9.29 (s, 1H), 8.75 (s, 1H), 8.49 (d, J = 7.72 Hz, 1H), 8.06 (d, J = 8.05 Hz, 1H), 7.59−7.57 (m, 2H), 7.37 (d, J = 7.89 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.5, 152.2, 151.2, 149.1, 145.6, 135.7 (2C), 128.8, 127.6, 126.2, 124.0, 119.1, 21.8. HRMS calcd for $C_{14}H_{11}N_3O$ [M + H$^+$] 238.0975, found 238.0970.

*7-Methyl-2-(thiophen-2-yl)quinazolin-4(3H)-one (**3bq**).*[10] White solid; Yield: 80% (96 mg); mp 290−293 °C (lit. 291−292 °C); IR (KBr) cm^{-1}: 3401, 3018, 1660, 1403, 1215, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.55 (s, 1H), 8.22 (d, J = 3.33 Hz, 1H), 8.01 (d, J = 8.05 Hz, 1H), 7.86 (d. J = 4.90 Hz, 1H), 7.48 (s, 1H), 7.32 (d, J = 8.00 Hz, 1H), 7.24−7.22 (t, J = 4.24 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.1, 149.2, 148.3, 145.6, 137.9, 132.5, 129.7, 128.9, 128.2, 127.1, 126.2, 118.9, 21.7. HRMS calcd for $C_{13}H_{10}N_2OS$ [M + H$^+$] 243.0587, found 243.0581.

*7-Methyl-2-pentylquinazolin-4(3H)-one (**3bt**).* White solid; Yield: 44% (50 mg); mp. 180−182 °C; IR (KBr) cm^{-1}: 3394, 2925, 1675, 1616, 1403, 1217, 1068, 670; ^{1}H NMR (400 MHz, CDCl$_3$): δ 10.92 (s, 1H), 8.16 (d, J = 8.05 Hz, 1H), 7.49 (s, 1H), 7.29 (d, J = 8.37 Hz, 2H), 2.76−2.72 (t, J = 7.72 Hz, 2H), 2.50 (s, 3H), 1.89−1.82 (m, 2H), 1.46−1.35 (m, 4H), 0.93−0.90 (t, J = 6.91 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 163.5, 156.6, 149.4, 145.8, 127.9, 126.9, 126.0, 118.1, 35.9, 31.3, 27.1, 22.3, 21.9, 13.9. HRMS calcd for $C_{14}H_{18}N_2O$ [M + H$^+$] 231.1492, found 231.1495.

*6-Methoxy-2-phenylquinazolin-4(3H)-one (**3ca**).*[10] Light yellow solid; Yield: 82% (103 mg); mp 246−247 °C (lit. 249−251 °C); IR (KBr) cm^{-1}: 3400, 3019, 1664, 1403, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.49 (s, 1H), 8.17 (d, J = 6.66 Hz, 2H), 7.71 (d, J = 8.76 Hz, 1H), 7.55−7.53 (m, 4H), 7.46−7.43 (dd, J_1 = 8.81 Hz, J_2 = 2.71 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.5, 158.2, 150.5, 143.6, 133.2, 131.4, 129.6, 129.0 (2C), 127.9 (2C), 124.5, 122.2, 106.3, 56.1. HRMS calcd for $C_{15}H_{12}N_2O_2$ [M + H$^+$] 253.0972, found 253.0975.

*6-Methoxy-2-(4-methoxy)phenyl)quinazolin-4(3H)-one (**3cb**).*[28] Light yellow solid; Yield: 80% (112 mg); mp 256−258 °C (lit. 258−259 °C); IR (KBr) cm^{-1}: 3397, 1629, 1401, 1068, 770; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.37 (s, 1H), 8.17 (d, J = 8.28 Hz, 2H), 7.67 (d, J = 8.76 Hz, 1H), 7.53 (s, 1H), 7.43 (d, J = 7.05 Hz, 1H), 7.09 (d, J = 8.24 Hz, 2H), 3.89 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.1, 161.5, 157.4, 149.7, 143.4, 129.1 (2C), 129.0, 124.9, 124.0, 121.4, 113.9 (2C), 105.8, 55.6, 55.4. HRMS calcd for $C_{16}H_{14}N_2O_3$ [M + H$^+$] requires 283.1077, found 283.1078.

*2-Propylquinazolin-4(3H)-one (**5al**).*[12] White solid; Yield: 45% (42 mg); mp 198−200 °C (lit. 200−202 °C); IR (KBr) cm^{-1}: 3400, 3019, 2400, 1671, 1612, 1466, 1403, 1385, 1069; ^{1}H NMR (400 MHz, CDCl$_3$): δ 11.47 (br.s, 1H), 8.30−8.27 (dd, J_1 = 7.97 Hz, J_2 = 1.08 Hz, 1H), 7.79−7.75 (m, 1H), 2.79−2.75 (t, J = 7.66 Hz, 2H), 1.97−1.87 (sxt, J = 7.46 Hz, 2H), 1.10−1.06 (t, J = 7.37 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 164.1, 156.7, 149.6, 135.0, 130.3, 128.6, 127.4, 126.6, 126.4, 120.7, 37.9, 21.1, 13.9. HRMS calcd for $C_{11}H_{12}N_2O$ [M + H$^+$] 189.1022, found 189.1024.

*2-Heptylquinazolin-4(3H)-one (**5am**).*[27] White solid; Yield: 48% (58 mg); mp 123−126 °C (lit. 124−127 °C); IR (KBr) cm^{-1}: 2924, 1673, 1612, 1468, 1149; ^{1}H NMR (400 MHz, CDCl$_3$): δ 11.30 (s, 1H), 8.29−8.27 (dd, J_1 = 8.01 Hz, J_2 = 1.07 Hz, 1H), 7.79−7.75 (m, 1H), 7.71−7.69 (dd, J_1 = 8.15 Hz, J_2 = 0.58 Hz, 1H), 7.48−7.44 (m, 1H), 2.79−2.75 (t, J = 7.80 Hz, 2H), 1.91−1.83 (m, 2H), 1.49−1.42 (m, 2H), 1.41−1.34 (m, 2H), 1.30−1.25 (m, 4H), 0.89−0.85 (t, J = 6.86 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 63.8, 156.7, 149.4, 134.7, 127.2, 126.3, 126.2, 120.5, 36.0, 31.6, 29.1, 28.9, 27.5, 22.5, 14.0. HRMS calcd for $C_{15}H_{20}N_2O$ [M + H$^+$] 245.1648, found 245.1644.

*2-(3,5-Dimethylphenyl)quinazolin-4(3H)-one (**7ac**).*[24] White solid; Yield: 44% (55 mg); mp 271−273 °C (lit. 273 °C); IR (KBr) cm^{-1}: 3402, 3021, 2401, 1665, 1523, 1417, 1027, 928, 670; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.38 (s, 1H), 8.15−8.14 (d, J = 7.54 Hz, 1H), 7.85−7.81 (m, 3H), 7.75−7.73 (d, J = 8.17 Hz, 1H), 7.53−7.49 (t, J = 7.34 Hz, 1H), 7.22 (s, 1H), 2.37 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6, 152.9, 149.2, 138.2, 135.0, 133.2, 133.0, 127.9, 126.9, 126.3, 125.9, 121.4, 21.3 (2C). HRMS calcd for $C_{16}H_{14}N_2O$ [M + H$^+$] 251.1179, found 251.1178.

*2-(o-Tolyl)quinazolin-4(3H)-one (**7ae**).*[20] White solid; Yield: 67% (79 mg); mp 215−218 °C (lit. 216−218 °C); IR (KBr) cm^{-1}: 3391, 3019, 2400, 1612, 1403, 1068, 669; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.43 (s, 1H), 8.18 (d, J = 7.42 Hz, 1H), 7.85−7.82 (t, J = 6.98 Hz, 1H), 7.70 (d, J = 8.05 Hz, 1H), 7.56−7.50 (m, 2H), 7.45−7.42 (t, J = 6.98 Hz, 1H), 7.36−7.31 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.2, 154.8, 149.2, 136.5, 134.9, 134.7, 130.9, 130.3, 129.5, 127.8, 127.0, 126.2, 126.1, 121.4, 20.0. HRMS calcd for $C_{15}H_{12}N_2O$ [M + H$^+$] 237.1022, found 237.1018.

*2-(p-Tolyl)quinazolin-4(3H)-one (**7af**).*[20] White solid; Yield: 65% (76 mg); mp 241−243 °C (lit. 239−242 °C); IR (KBr) cm^{-1}:3401, 3019, 2400, 1663, 1403, 1156, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.44 (s, 1H), 8.15 (d, J = 7.44 Hz, 1H), 8.10 (d, J = 8.13 Hz, 2H), 7.83−7.79 (t, 1H, J = 7.05 Hz), 7.72 (d, J = 7.84 Hz, 1H), 7.51−7.47 (t, J = 7.44 Hz, 1H), 7.35 (d, J = 7.93 Hz. 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.7, 152.6, 149.2, 141.8, 134.9, 130.3, 129.6, 128.1, 127.8, 126.8, 126.2, 21.4. HRMS calcd for $C_{15}H_{12}N_2O$ [M + H$^+$] 237.1022, found 237.1016.

*2-(m-Tolyl)quinazolin-4(3H)-one (**7ag**).*[20] White solid; Yield: 59% (69 mg); mp 220−222 °C (lit. 221−223 °C); IR (KBr) cm^{-1}: 3407, 3019, 1674, 1403, 1216, 1069; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.46 (br.s, 1H), 8.17−8.15 (m, 1H), 8.03 (s, 1H), 7.98 (d, J = 7.24 Hz, 1H), 7.86−7.82 (m, 1H), 7.76 (d, J = 7.89 Hz, 1H), 7.54−7.50 (m, 1H), 7.46−7.39 (m, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz; DMSO-d_6): δ 162.6, 152.8, 149.2, 138.3, 135.0, 133.1, 132.4, 128.9, 128.7, 127.9, 126.9, 126.3, 125.3, 121.4, 21.4. HRMS calcd for $C_{15}H_{12}N_2O$ [M + H$^+$] 237.1022, found 237.1009.

*2-Aminobenzamide (**8**).*[9] To a mixture of 2-bromobenzamide **1a** (0.30 g, 1.5 mmol) and CuI (0.03 g, 0.15 mmol) in DMSO (3.0 mL) was added $TMSN_3$ (0.39 mL, 3.0 mmol) in a tube under an air atmosphere. After that, the tube was sealed, and the reaction mixture was heated at 80 °C for 24 h. After completion of the reaction, water (20 mL) was added to it. A saturated aq. $Na_2S_2O_3$ solution was added until the disappearance of brown color, and the reaction mixture was extracted with ethyl acetate. The combined organic layer was dried on anhydrous sodium sulfate. The solvent was evaporated under reduced pressure, and the crude product was purified by column (SiO_2, 60-120) chromatography using 20−25% EtOAc:hexane as eluent to get pure 2-aminobenzamide products. White solid; Yield: 4% (8 mg); mp 110−112 °C (lit. 110 °C); IR (KBr) cm^{-1}: 3409, 3020, 2401, 1659, 1590, 1399, 1316, 1075; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.71 (br.s, 1H), 7.54 (d, J = 7.84 Hz, 1H), 7.15−7.11 (t, J = 8.00 Hz, 1H), 7.04 (br.s, 1H), 6.69 (d, J = 8.17 Hz, 1H), 6.55 (br.s, 1H), 6.50−6.46 (t, J = 7.15 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.7, 150.6, 132.3, 129.2, 116.8, 114.8, 114.1. HRMS calcd for $C_7H_8N_2O$ [M + H$^+$] 137.0709, found 137.0713

*2-Phenyl-2,3-dihydroquinazolin-4(1H)-one (**9**).*[9] To a stirred mixture of 2-bromobenzamide **1a** (0.10 g, 0.5 mmol), benzaldehyde (0.06 mL, 0.6 mmol), and CuI (0.01 g, 0.05 mmol) in DMSO (1.5 mL) was added $TMSN_3$ (0.13 mL, 1.0 mmol) in a tube under a nitrogen atmosphere. After that, the tube was sealed, and the reaction mixture was heated at 80 °C for 24 h. After completion of the reaction, water (20 mL) was added to it. A saturated aq. $Na_2S_2O_3$ solution was added until the disappearance of brown color, and the reaction mixture was extracted with ethyl acetate. The combined organic layer was dried on anhydrous sodium sulfate. The combined organic layer was dried on anhydrous sodium sulfate. The solvent was evaporated under reduced pressure, and the crude product was purified by column (SiO_2, 60-120) chromatography using 15−20% EtOAc:hexane as eluent to get the pure dihydroquinazolinone product. White solid; Yield: 87% (0.19 g); mp 221−222 °C (lit. 220−223 °C); IR (KBr) cm^{-1}: 3297, 3019, 1659; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.27 (br.s, 1H), 7.62−7.60 (m, 1H), 7.51−7.49 (m, 2H), 7.41−7.33 (m, 3H), 7.26−7.22 (m, 1H), 7.10 (br.s, 1H), 6.76 (d, J = 8.01 Hz, 1H), 6.69−6.66 (t, J = 7.44 Hz, 1H), 5.75 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.0, 8.3, 142.1, 133.7, 128.9, 128.7 (2C), 127.8, 127.3 (2C), 117.5, 115.4, 114.8, 67.0. HRMS calcd for $C_{14}H_{12}N_2O$ [M + H$^+$] 225.1022, found 225.1013.

DOI: 10.1021/acs.joc.6b00599
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*2-(Benzylamino)benzamide (**11**).*[10] To a stirred mixture of 2-aminobenzamide (**8**; 1.0 g, 7.4 mmol), K_2CO_3 (1.0 g, 7.4 mmol), and NaI (1.1 g, 7.4 mmol) in DMF (10 mL) was added benzyl chloride (1.2 mL, 10 mmol), and the mixture was stirred at rt for 1 day. The reaction mixture was cooled and poured into water. It was extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexanes/EtOAc) to give desired product **11** (1.5 g, 90%) as a pale yellow solid: mp 170−172 °C (lit. 176−177 °C); IR (KBr) (cm−1) 3423, 3205, 1634, 1578, 1512, 1393, 1292, 1066, 747; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.60−8.57 (t, J = 5.39 Hz, 1H), 7.85 (br.s, 1H), 7.63−7.61 (m, 1H), 7.34−7.33 (m, 4H), 7.26−7.18 (m, 3H), 6.63 (d, J = 8.49 Hz, 1H), 6.55−6.51 (t, J = 7.67 Hz, 1H), 4.39 (d, J = 5.71 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.0, 150.0, 140.1, 132.9, 129.5, 128.9 (2C), 127.5 (2C), 127.2, 114.6, 111.9, 46.4. HRMS calcd for $C_{14}H_{14}N_2O$ [M + H$^+$] 227.1179, found 227.1166.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00599.

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

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

K.U. and R.K.T. would like to thank UGC, New Delhi, for providing a fellowship. We thank SAIF division, CSIR-CDRI, for the analytical facilities. Financial support of Indo French collaborative CEFIPRA project 5303-2 is greatly acknowledged. It is a CDRI communication no. 9239.

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DOI: 10.1021/acs.joc.6b00599
J. Org. Chem. 2016, 81, 5046−5055