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Transition Metal-Free Visible Light-Driven Photoredox Oxidative Annulation of Arylamidines

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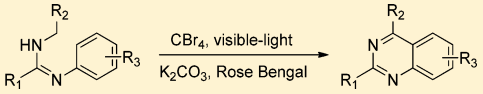
Supporting Information

ABSTRACT: A fast catalytic synthesis of multisubstituted quinazolines from readily available amidines via visible light-mediated oxidative C(sp^3)-C(sp^2) bond formation has been established. This reaction is a metal-free oxidative coupling catalyzed by a photoredox organocatalyst. The protocol features low catalyst loading (1 mol %).



The development of a novel C−C bond-forming reaction is one of the most important topics in the field of organic chemistry. Many organic reactions conducted in the presence of visible light have drawn the attention of synthetic organic chemists because of their sustainability, cost efficiency, and attractive environmental performance.[1] Recent studies in photochemistry have reported the formation of C−C and C−heteroatom bonds using visible-light and either ruthenium or iridium complexes or organic dyes as photoredox catalysts.[2] However, the high cost and potential toxicity of the ruthenium and iridium salts as well as their limited availability in the future are disadvantages of these metal-based methods. The organic dyes, for example, commercially readily available Rose Bengal, display similar photocatalytic activity in some reactions.[3] These dye photosensitizers therefore attracted our particular attention.

Quinazolines are classes of fused heterocycles that are of considerable interest because of the diverse range of their biological properties,[4] for example, antilung cancer[5] and α-adrenergic blocker.[6] Because of the wide demand for substituted quinazolines, many synthetic strategies have been developed. Recent methods toward quinazolines starting from a variety of substrates, such as 2-aminobenzylamines, 2-aminobenzoketones, *N*-arylamidines, which have been reported[7,8] (Scheme 1). Nonetheless, these methods all require the use of either strongly acidic or basic conditions and/or the preparation of activated intermediates. Recently, we developed a C−H oxidative functionalization and *N*-acyliminium cyclization for the synthesis of β-halo-pyrrolidinones[9] and pyrrolones.[10] Herein. we report a method for the synthesis of quinazolines through the versatile metal-free oxidative C(sp^3)-C(sp^2) bond-forming under photoredox conditions.

N-benzyl-*N*′-phenyl benzimidamide[8] **1a** was used as substrate to build quinazoline via a visible light photocatalysis strategy. Inspired by the common photoredox catalysts, the model reaction was performed with Eosin Y (10 mol %) as photocatalyst,[11] CBr_4 as an oxidant, and Cs_2CO_3 as the base under irradiation from a fluorescent bulb (18 W) for 4 h in DMSO.[12] Considering that the catalysts usually play important roles in photoredox catalysis, several typical photocatalysts, such as Rose Bengal, $Ir(ppy)_3$, $Ru(bpy)_3Cl_2$, Rhodamine B, and CdS were investigated to improve the reaction efficiency (Table 1, entries 2−6). A 75% GC yield of corresponding **2a** was achieved when Rose Bengal was used as the photocatalyst (Table 1, entry 2).[13] While under these conditions, a side reaction also leads to a small quantity of the brominated product **3a**, most of the simple photocatalysts were effective for this transformation under these conditions, albeit with different yields. We proposed that CBr_4 could be cracked into a CBr_3 radical and a bromide radical under the condition of visible light. The bromide radical could sequentially convert into the bromine for the bromination of **1a**, thus generating **3a**.[17] Subsequently, the examination of solvents showed that the reaction in toluene, DMF, DCE, MeCN, THF, or EtOAc did not improve the yield (Table 1, entries 7−12). In comparison with Cs_2CO_3 as the additive, K_2CO_3 led to higher yield (Table 1, entry 15).[14] To improve the conversion, we changed temperature; lower or higher temperatures resulted in lower yields with only 68% generated at 80 °C and 70% yield yield obtained at 120 °C (Table 1, entries 13 and 14). Subsequently, different equivalents of photocatalyst and oxidants were evaluated. We noticed that even lowering the amount of Rose Bengal from 10 mol % to 0.5 mol % also can restrain brominated product **3a** dramatically (Table 1, entries 16 and 17). $CBrCl_3$ has the same efficiency as CBr_4 (Table 1, entry 18).[15] Light together with CBr_4 proved essential for this transformation, and almost all of the starting material was recovered when where was no light or CBr_4 (Table 1, entries 19−21).[16] The reaction also can be conducted without photocatalysts or base (Table 1, entries 22−23). The product was generated in a lower yield mainly due to the side reaction that took place in the catalytic process.

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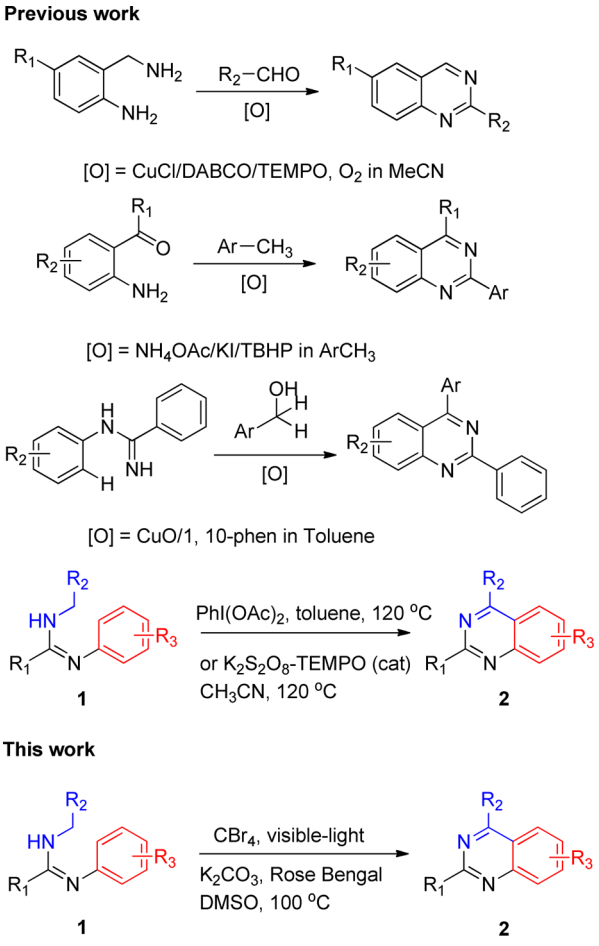
Scheme 1. Approaches To Access Quinazolines and Benzimidazoles via Oxidative sp^3C-H/sp^2C-H Cyclization of Amidines



Equipped with a set of optimized conditions, we explored the substrate scope of the visible light photocatalysis reaction delivering quinazolines, as depicted in Table 2. First, we investigated the scope of the R^1 substituent. Various aromatic groups with electron-donating and -withdrawing substituents were well-tolerated, affording the corresponding quinazolines in good to excellent yields (**2a**−**2d**). Aromatic groups with strong electron-withdrawing substituents disfavored the formation of quinazoline (**2e**, 48%). Meanwhile, the bulky naphthyl group had little influence on the reaction (**2f**, 83%). Notably, 2-tertbutyl-substituted quinazoline was generated in a comparable yield (**2g**, 62%). Next, we investigated the scope of the R^2 substituent. A range of substrates bearing electron-donating or weak electron-withdrawing group-substituted aromatic rings all underwent the oxidative cyclization smoothly and gave the desired quinazoline products in excellent yields (**2h**−**2k**). However, no desired products were obtained when R^2 was H or methyl under these conditions (**2l**, **2m**). To our delight, when the R^2 was propyl- or cycloalkyl-substituted groups, the corresponding products were generated in moderate yields (**2n**−**2p**).

Then, the effect of the substituent attached on the aniline ring (i.e., R^3) was examined (Table 3). The aniline ring with electron-rich, bromo, chloro, or fluoro group substituents were readily accommodated and provided the corresponding quinazolines in good to excellent yields, thus offering the possibility of introducing further substituents by additional coupling reactions (**5a**−**5f**). When the aniline ring was substituted at the *meta* position, there were two positions for the oxidative coupling to occur, favoring the less sterically hindered C−H bond (**5c**, 86% 5:4). However, the aniline rings with strong electron-withdrawing groups at the *para* position led to decreased yields (**5g**−**5i**).[8] Notably, the bulky naphthyl-substituted quinazoline was generated in good yield (**5j**, 82%).

On the basis of the above studies and literature reports, a possible mechanism is proposed (Scheme 2). There is more than one reaction pathway involved.[16−19] If without Rose Bengal, CBr_4 could be cracked into a CBr_3 radical and a bromide radical under the condition of visible light.[20] The CBr_3 radical abstracts a hydrogen atom of another molecule of benzimidamide to produce the α-amino radical intermediate **A**, which once again enters the radical chain process with CBr_4 to generate iminium ion **C**. Iminium ion **C** underwent an intramolecular Friedel−Craft reaction to give intermediate **D**. Further dehydrogenation afforded hydroquinone **E**, which was finally aromatized to give the stable product quinazoline. The difference of another pathway is that the oxidative quenching of the visible light-excited Rose Bengal (RB*) by benzimidamide resulted in the formation of Rose Bengal radical anion ($RB^{\bullet-}$) and radical cation **B**. Upon transfer of an electron to CBr_4 to form the superoxide radical anion, Rose Bengal was regenerated and completed the photoredox cycle. On the other hand, radical cation **B** gave up a hydrogen atom, presumably to the radical anion to afford the CBr_3 radical, bromide anion, and radical intermediate **A**. There may be another pathway in which CBr_3 radical abstracts a hydrogen atom from radical cation **B** to generate iminium ion **C** directly following the same procedure to give the stable product quinazoline.

In summary, we have described a direct metal-free protocol for the synthesis of quinazolines from common *N*-alkyl-*N*′-arylamidine under photoredox conditions. The reaction was found to tolerate a wide range of functional groups. Our method avoids the use of potentially toxic and expensive transition metal catalysts while also providing improved reaction efficiency with lower catalyst loadings.

EXPERIMENTAL SECTION

General Remarks. All reactions were carried out at 100 °C without atmospheric precautions and stirred magnetically. ^1H and ^{13}C NMR spectra were recorded on a 600 and 400 MHz spectrometer at 25 °C. Chemical shifts values are given in parts per million and referred as the internal standard to TMS: 0.00 ppm. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; qui, quintet; m, multiplet; and dd, doublet of doublets. The coupling constants, *J*, are reported in hertz (Hz). Low-resolution mass spectra and high-resolution mass spectra were obtained using a Q-TOF microspectrometer. Melting points were determined by a laboratory device and were uncorrected or calibrated. Flash column chromatography was performed over silica gel at 100−200 m, and the eluent was a mixture of ethyl acetate and petroleum ether. Organic solutions were concentrated by rotary evaporation below 40 °C in vacuum. TLC plates were visualized by exposure to ultraviolet light.

General Experimental Procedure. *General Procedure for Synthesis of Imidamide Derivatives (Method A).*[21,22] To a cold solution of 82.5 mmol aniline in dry DCM (20 mL) was added dropwise 38.8 mmol acyl chloride in dry DCM (10 mL). The mixture was stirred at room temperature for 2 h. Water (15 mL) and concentrated HCl (1 mL at 37%) were added. The mixture was

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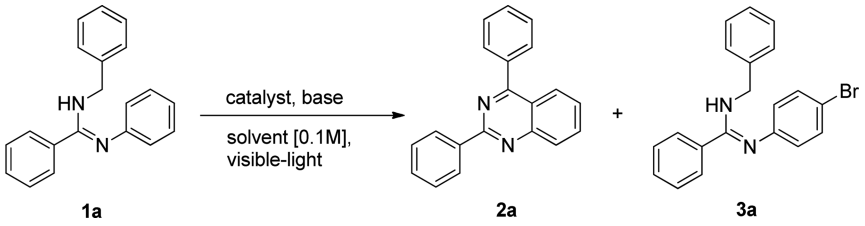
Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a

entry	catalyst (mol %)	oxidant (eq)	solvent	base (eq)	temp (°C)	1a (%)[b]	2a (%)[b]	3a (%)[b]
1	Eosin Y (0.1)	CBr_4 (1.2)	DMSO	Cs_2CO_3 (1)	100	15	65	20
2	Rose Bengal (0.1)	CBr_4 (1.2)	DMSO	Cs_2CO_3 (1)	100	10	75	11
3	$Ir(ppy)_3$ (0.1)	CBr_4 (1.2)	DMSO	Cs_2CO_3 (1)	100	4	60	31
4	$Ru(bpy)_3Cl_2$ (0.1)	CBr_4 (1.2)	DMSO	Cs_2CO_3 (1)	100	20	56	20
5	Rhodamine B (0.1)	CBr_4 (1.2)	DMSO	Cs_2CO_3 (1)	100	8	42	17
6	CdS (0.1)	CBr_4 (1.2)	DMSO	Cs_2CO_3 (1)	100	17	50	22
7	Rose Bengal (0.1)	CBr_4 (1.2)	toluene	Cs_2CO_3 (1)	100	13	62	25
8	Rose Bengal (0.1)	CBr_4 (1.2)	DMF	Cs_2CO_3 (1)	100	9	42	19
9	Rose Bengal (0.1)	CBr_4 (1.2)	DCE[e]	Cs_2CO_3 (1)	100	64	28	9
10	Rose Bengal (0.1)	CBr_4 (1.2)	MeCN[e]	Cs_2CO_3 (1)	100	54	13	17
11	Rose Bengal (0.1)	CBr_4 (1.2)	THF[e]	Cs_2CO_3 (1)	100	50	8	25
12	Rose Bengal (0.1)	CBr_4 (1.2)	EtOAc[e]	Cs_2CO_3 (1)	100	72	17	4
13	Rose Bengal (0.1)	CBr_4 (1.2)	DMSO	Cs_2CO_3 (1)	120	16	70	12
14	Rose Bengal (0.1)	CBr_4 (1.2)	DMSO	Cs_2CO_3 (1)	80	25	68	5
15	Rose Bengal (0.1)	CBr_4 (1.2)	DMSO	K_2CO_3 (1.5)	100	5	90	trace
16	Rose Bengal (0.01)	CBr_4 (1.2)	DMSO	K_2CO_3 (1.5)	100	6	91	trace
17	Rose Bengal (0.005)	CBr_4 (1.2)	DMSO	K_2CO_3 (1.5)	100	5	85	5
18	Rose Bengal (0.01)	$CBrCl_3$ (1.2)	DMSO	K_2CO_3 (1.5)	100	4	90	trace
19	Rose Bengal (0.01)	DTBP (1.2)	DMSO	K_2CO_3 (1.5)	100	87	12	
20	Rose Bengal (0.01)		DMSO	K_2CO_3 (1.5)	100	95	trace	
21[c]	Rose Bengal (0.01)	CBr_4 (1.2)	DMSO	K_2CO_3 (1.5)	100	97	3	0
22		CBr_4 (1.2)	DMSO	K_2CO_3 (1.5)	100	14	53	32
23	Rose Bengal (0.01)	CBr_4 (1.2)	DMSO		100	10	40	48
24[d]	**Rose Bengal (0.01)**	**CBr_4 (1.2)**	**DMSO**	**K_2CO_3 (1.5)**	**100**	**none**	**93**	**trace**

[a]Reaction conditions: **1a** (0.2 mmol), photocatalyst (1 mol %), solvent (4 mL), using an 18 W fluorescent lamp as the visible light source, 4 h. [b]GC yield (based on external standard calibration curve method). [c]Without light. [d][**1a**] = 0.05 M. [e]Using a sealed tube.

filtered, and the solid product was washed with water to afford the target amide. The filtrate was concentrated to provide another part of the amide. The combination of these two parts were used directly in the next step. A solution of amide (15 mmol, 1 equiv) in thionyl chloride (90 mmol, 6 equiv) was stirred at reflux (80 °C) for 6 h. After cooling to room temperature, the mixture was concentrated under reduced pressure. The residue was dissolved in toluene (15 mL × 2), and the mixture was evaporated again to generate the corresponding imidoyl chloride as a TLC pure residual oil. Amine or benzyl amine (30 mmol, 2 equiv) and Et_3N (90 mmol, 3 equiv) were mixed in dry DCM (100 mL) and stirred at 0 °C for 10 min. To this mixture was added a solution of the above-obtained imidoyl chloride in dry DCM (50 mL). The reaction mixture was stirred at 0 °C for 20 min and heated at 50 °C for another 2 h. After cooling to room temperature, the reaction mixture was extracted with ethyl acetate (100 mL × 3) and then washed with 1 M HCl (100 mL × 2). The organic layer was dried over anhydrous Na_2SO_4 followed by filtration and then condensation. The residue was purified by recrystallization to afford the corresponding product.

General Procedure for Synthesis of Imidamide Derivatives (Method B).[21,22] To a cold solution of 82.5 mmol amine or benzyl amine in dry DCM (20 mL) was added dropwise 38.8 mmol acyl chloride in dry DCM (10 mL). The mixture was stirred at room temperature for 2 h. Water (15 mL) and concentrated HCl (1 mL at 37%) were added. The mixture was filtered, and the solid product was washed with water to afford the target amide. The filtrate was concentrated to provide another part of the amide. The combination of these two parts were used directly in the next step. A solution of amide (15 mmol, 1 equiv) in thionyl chloride (90 mmol, 6 equiv) was stirred at reflux (80 °C) for 6 h. After cooling to room temperature, the mixture was concentrated under reduced pressure. The residue was dissolved in toluene (15 mL × 2) and the mixture was evaporated again to generate the corresponding imidoyl chloride as a TLC pure residual oil. Aniline (30 mmol, 2 equiv) and Et_3N (90 mmol, 3 equiv) were mixed in dry DCM (100 mL) and stirred at 0 °C for 10 min. To this mixture, was added a solution of the above-obtained imidoyl chloride in dry DCM (50 mL). The reaction mixture was stirred at 0 °C for 20 min and heated at 50 °C for another 2 h. After cooling to room temperature, the reaction mixture was extracted with ethyl acetate (100 mL × 3) and then washed with 1 M HCl (100 mL × 2). The organic layer was dried over anhydrous Na_2SO_4 followed by filtration and then condensation. The residue was purified by recrystallization to afford the corresponding product.

General Procedure for the Synthesis of Quinazolines. To a solution of imidamide **1** (0.2 mmol, 1 equiv) and K_2CO_3 (0.3 mmol, 1.5 equiv) in DMSO (4 mL) at 100 °C was added CBr_4 (0.24 mmol, 1.2 equiv). The solution was stirred at this temperature for 4 h on the condition of visible light (18 W fluorescent lamp). After cooling to room temperature, the reaction mixture was extracted with ethyl acetate (20 mL × 3) and then washed with brine (20 mL). The organic layer was dried over anhydrous Na_2SO_4 followed by filtration and then condensation. The residue was purified by silica gel column chromatography to afford corresponding product **2**.

*N-Benzyl-N′-phenylbenzimidamide (**1a**).*[8] White solid; 3.2 g; 75% yield (Method A); mp 100−101 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.45 (s, 2H), 7.37 (t, J = 6.7 Hz, 2H), 7.30 (t, J = 6.7 Hz, 1H), 7.24

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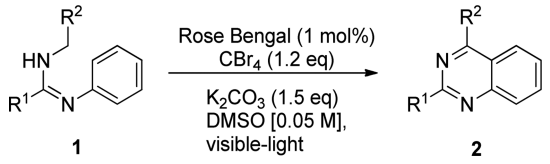
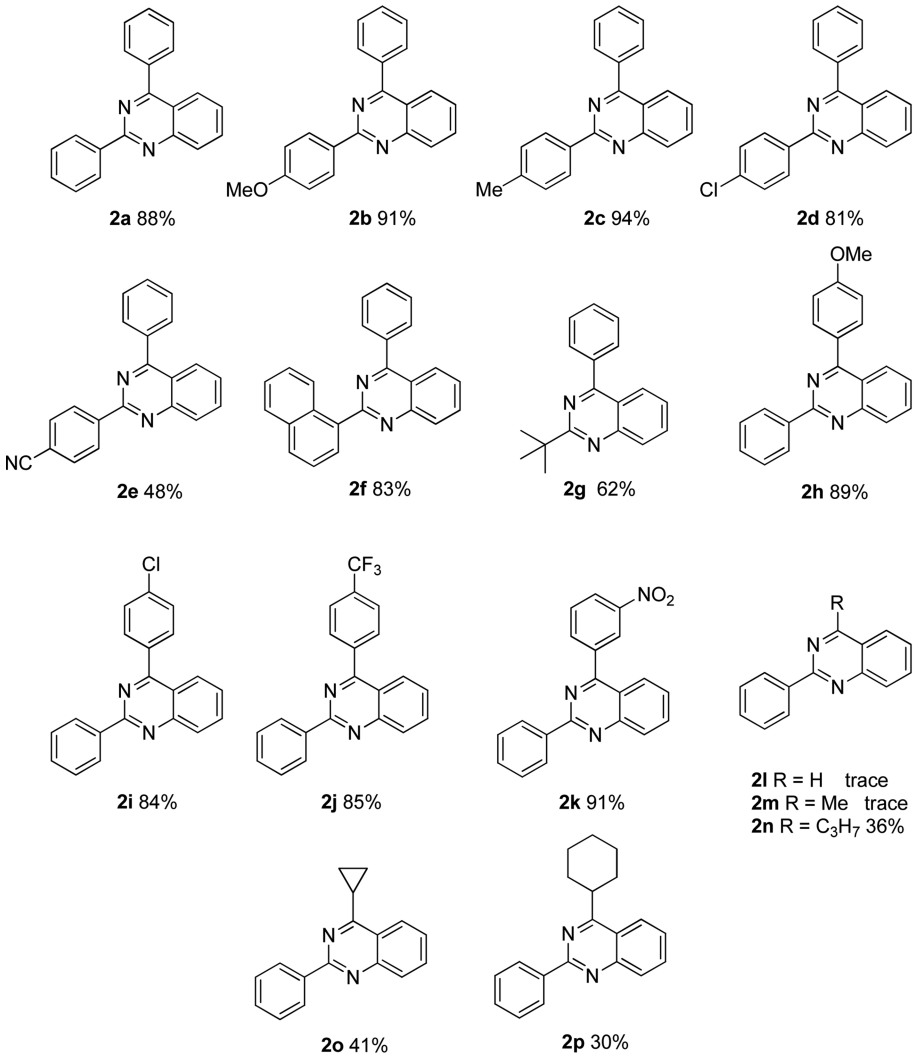
Table 2. Substrate Scope for the Photoinduced Oxidative sp^3C-H/sp^2C-H Cyclization of Amidines[a]





[a]Reaction conditions: **1a** (0.2 mmol), photocatalyst (1 mol %), solvent (4 mL), using an 18 W fluorescent lamp as the visible light source, 4 h. Isolated yield.

(m, 5H), 7.07 (t, J = 6.5 Hz, 2H), 6.82 (s, 1H), 6.68 (s, 2H), 4.77 (brs, 1H), 4.70 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.2, 150.8, 139.0, 135.1, 129.2, 128.7, 128.6, 128.4, 128.3, 128.2, 127.5, 123.1, 121.4, 46.2. Mass spectrum (ESI): m/e (% relative intensity) 287.1 (100) $(M + H)^+$.

*N-Benzyl-4-methoxy-N′-phenylbenzimidamide (**1b**).*[8] Colorless oil; 4.1 g; 87% yield (Method A). ^1H NMR (600 MHz, DMSO) δ 7.48 (s, 1H), 7.43 (d, J = 5.9 Hz, 2H), 7.35 (t, J = 7.2 Hz, 2H), 7.24 (t, J = 7.1 Hz, 1H), 7.18 (d, J = 6.9 Hz, 2H), 7.00 (t, J = 6.9 Hz, 2H), 6.82 (d, J = 7.9 Hz, 2H), 6.71 (d, J = 6.5 Hz, 1H), 6.47 (d, J = 6.9 Hz, 2H), 4.58 (s, 2H), 3.71 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 159.4, 156.5, 151.7, 140.3, 130.2, 128.2, 128.1, 127.1, 126.9, 126.4, 122.5, 120.1, 113.3, 55.1, 44.0. Mass spectrum (ESI): m/e (% relative intensity) 312.1 (100) $(M + H)^+$.

*N-Benzyl-4-methyl-N′-phenylbenzimidamide (**1c**).* White solid; 3.8 g; 86% yield (Method A); mp 69−71 °C. ^1H NMR (600 MHz, DMSO) δ 7.45 (s, 1H), 7.41 (s, 2H), 7.34 (t, J = 7.3 Hz, 2H), 7.23 (t, J = 7.1 Hz, 1H), 7.12 (s, 2H), 7.07 (d, J = 7.5 Hz, 2H), 6.98 (t, J = 6.9 Hz, 2H), 6.68 (t, J = 6.5 Hz, 1H), 6.45 (d, J = 5.6 Hz, 2H), 4.57 (s, 2H), 2.23 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 156.8, 151.6, 140.3, 138.3, 132.0, 128.6, 128.5, 128.1, 127.1, 126.4, 122.6, 122.5, 120.2, 44.0, 20.8. Mass spectrum (ESI): m/e (% relative intensity) 301.1 (100) $(M + H)^+$; HRMS (ESI): m/e calcd for $C_{21}H_{19}N_2$ $(M - H)^-$ 299.1528, found 299.1532.

*N-Benzyl-4-chloro-N′-phenylbenzimidamide (**1d**).*[8] White solid; 4.1 g; 85% yield (Method A); mp 84−85 °C. ^1H NMR (400 MHz, DMSO) δ 7.59 (s, 1H), 7.43 (d, J = 6.9 Hz, 2H), 7.34 (t, J = 8.3 Hz, 4H), 7.24 (d, J = 7.5 Hz, 3H), 7.00 (t, J = 7.3 Hz, 2H), 6.71 (t, J = 7.1 Hz, 1H), 6.48 (d, J = 7.4 Hz, 2H), 4.59 (s, 2H). ^{13}C NMR (100 MHz, DMSO) δ 156.3, 151.7, 140.5, 134.2, 134.0, 131.1, 128.8, 128.7, 128.5, 127.7, 127.0, 123.1, 121.0, 44.6. Mass spectrum (ESI): m/e (% relative intensity) 321.1 (100) $(M + H)^+$.

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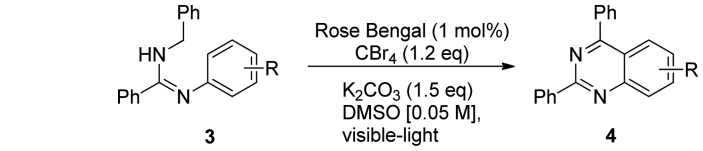
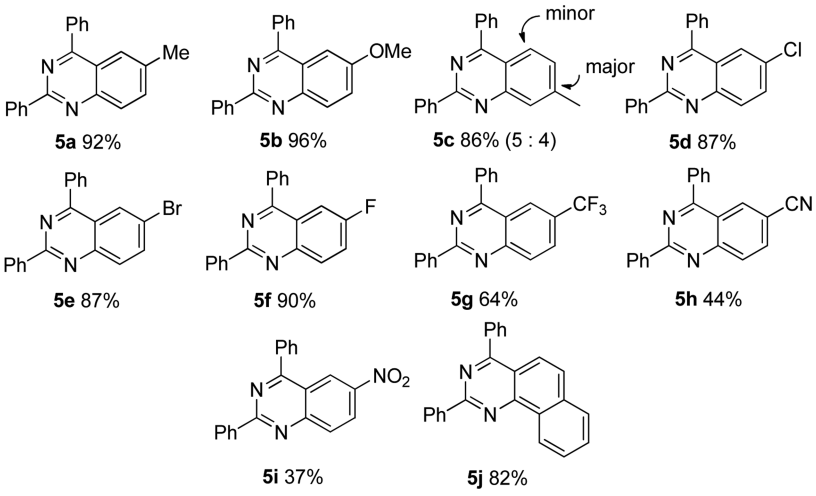
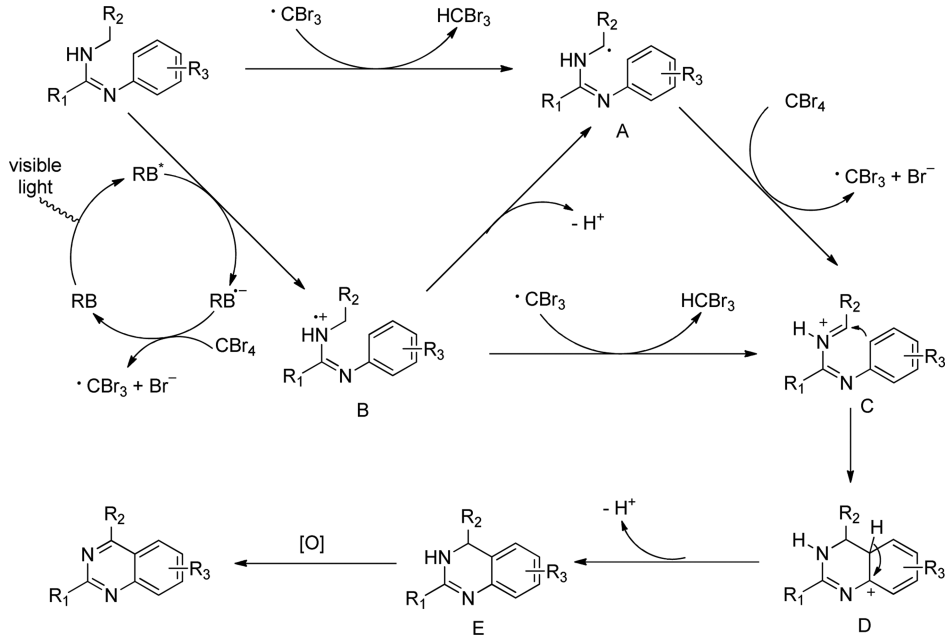
Table 3. Substrate Scope for the Photoinduced Oxidative sp^3C-H/sp^2C-H Cyclization of Amidines[a]





[a]Reaction conditions: **1a** (0.2 mmol), photocatalyst (1 mol %), solvent (4 mL), using an 18 W fluorescent lamp as the visible light source, 4 h. Isolated yield.

Scheme 2. Plausible Reaction Mechanism



*N-Benzyl-4-cyano-N′-phenylbenzimidamide (**1e**).* White solid; 3.3 g; 71% yield (Method A); mp 158–162 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 (s, 2H), 7.42 (s, 2H), 7.37 (s, 2H), 7.33 (d, J = 7.5 Hz, 3H), 7.07 (s, 2H), 6.84 (s, 1H), 6.61 (d, J = 4.9 Hz, 2H), 4.83 (brs, 1H), 4.68 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.2, 149.8, 139.4, 138.4, 132.1, 129.3, 128.8, 128.6, 128.1, 127.6, 122.8, 122.0, 118.1, 113.0, 46.2. Mass spectrum (ESI): m/e (% relative intensity) 312.1 (100) $(M + H)^+$; HRMS (ESI): m/e calcd for $C_{21}H_{18}N_3$ $(M + H)^-$ 312.1495, found 312.1504.

*N-Benzyl-N′-phenyl-1-naphthimidamide (**1f**).*[8] White solid; 3.3 g; 65% yield (Method A); mp 88–90 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (d, J = 8.1 Hz, 1H), 7.79–7.67 (m, 2H), 7.42–7.47 (m, 4H), 7.40–7.26 (m, 5H), 6.89 (s, 2H), 6.67 (s, 3H), 4.83 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.6, 150.5, 138.9, 133.2, 130.3, 129.2, 128.7, 128.3, 128.2, 128.1, 127.4, 126.8, 126.7, 126.2, 125.6, 124.8, 122.4, 121.6, 46.1. Mass spectrum (ESI): m/e (% relative intensity) 337.1 (100) $(M + H)^+$.

*N-Benzyl-N′-phenylpivalimidamide (**1g**).*[8] White solid; 2.2 g; 55% yield (Method A); mp 59–60 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (t, J = 7.1 Hz, 2H), 7.24 (t, J = 6.9 Hz, 1H), 7.16 (t, J = 7.0 Hz, 4H), 6.85 (t, J = 7.1 Hz, 1H), 6.79 (d, J = 7.6 Hz, 2H), 4.59 (s, 1H), 3.98 (s, 2H), 1.25 (s, 9H). ^{13}C NMR (150 MHz,

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$CDCl_3$) δ 160.2, 151.3, 139.3, 129.0, 128.7, 128.6, 128.4, 127.7, 127.4, 121.2, 120.7, 48.4, 38.8, 29.3. Mass spectrum (ESI): *m/e* (% relative intensity) 267.1 (100) $(M + H)^+$.

N-(4-Methoxybenzyl)-N′-phenylbenzimidamide (**1h**).[8] White solid; 3.8 g; 81% yield (Method A); mp 82−84 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (s, 2H), 7.22 (m, 5H), 7.05 (s, 2H), 6.89 (d, *J* = 7.2 Hz, 2H), 6.80 (s, 1H), 6.67 (s, 2H), 4.70 (s, 1H), 4.61 (s, 2H), 3.79 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.0, 157.2, 150.9, 135.2, 131.1, 129.5, 129.2, 128.6, 128.4, 128.3, 123.1, 121.3, 114.1, 55.3, 45.7. Mass spectrum (ESI): *m/e* (% relative intensity) 317.1 (100) $(M + H)^+$.

N-(4-Chlorobenzyl)-N′-phenylbenzimidamide (**1i**). White solid; 4.0 g; 83% yield (Method A); mp 120−122 °C. ^{1}H NMR (600 MHz, DMSO) δ 7.59 (s, 1H), 7.45 (s, 2H), 7.40 (d, *J* = 7.5 Hz, 2H), 7.31−7.18 (m, 5H), 6.97 (s, 2H), 6.69 (s, 1H), 6.46 (d, *J* = 6.6 Hz, 2H), 4.57 (s, 2H). ^{13}C NMR (150 MHz, DMSO) δ 156.7, 151.3, 139.3, 134.8, 130.9, 129.1, 128.8, 128.6, 128.1, 128.1, 128.0, 122.5, 120.4, 43.4. Mass spectrum (ESI): *m/e* (% relative intensity) 321.1 (100) $(M + H)^+$; HRMS (ESI): *m/e* calcd for $C_{20}H_{16}ClN_2$ $(M - H)^-$ 319.0997, found 319.0998.

N′-Phenyl-N-(4-(trifluoromethyl)benzyl)benzimidamide (**1j**). White solid; 4.2 g; 80% yield (Method A); mp 140−141 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (s, 2H), 7.56 (s, 2H), 7.24 (m, 5H), 7.06 (s, 2H), 6.82 (s, 1H), 6.65 (s, 2H), 4.89 (s, 1H), 4.76 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.9, 150.4, 143.3, 134.8, 129.7, 129.4, 128.5, 128.4, 128.1, 125.6, 125.6, 125.1, 123.3, 122.9, 121.6, 45.3. Mass spectrum (ESI): *m/e* (% relative intensity) 355.1 (100) $(M + H)^+$; HRMS (ESI): *m/e* calcd for $C_{21}H_{16}F_3N_2$ $(M - H)^-$ 353.1260, found 353.1274.

N-(3-Nitrobenzyl)-N′-phenylbenzimidamide (**1k**). White solid; 3.2 g; 65% yield (Method A); mp 222−225 °C. ^{1}H NMR (400 MHz, DMSO) δ 8.53 (s, 1H), 8.23 (d, *J* = 7.8 Hz, 1H), 8.14 (s, 1H), 7.75 (t, *J* = 7.9 Hz, 1H), 7.60 (s, 1H), 7.53 (d, *J* = 6.4 Hz, 3H), 7.43 (t, *J* = 7.2 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 2H), 7.20−7.14 (m, 1H), 7.09 (d, *J* = 7.5 Hz, 2H), 5.31 (s, 2H). ^{13}C NMR (100 MHz, DMSO) δ 163.1, 148.3, 138.3, 137.2, 135.5, 132.8, 130.6, 130.2, 129.3, 129.1, 128.9, 127.3, 126.5, 123.7, 123.3, 46.6. Mass spectrum (ESI): *m/e* (% relative intensity) 332.1 (100) $(M + H)^+$; HRMS (ESI): *m/e* calcd for $C_{20}H_{16}N_3O_2$ $(M - H)^-$ 330.1237, found 330.1259.

N-Methyl-N′-phenylbenzimidamide (**1l**).[7b] White solid; 1.7 g; 53% yield (Method A); mp 132−133 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (m, 5H), 7.04 (s, 2H), 6.79 (s, 1H), 6.64 (s, 2H), 4.63 (brs, 1H), 3.05 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.3, 151.0, 135.3, 129.1, 128.6, 128.3, 128.2, 123.2, 121.2, 28.9. Mass spectrum (ESI): *m/e* (% relative intensity) 211.0 (100) $(M + H)^+$.

N-Ethyl-N′-phenylbenzimidamide (**1m**). White solid; 1.8 g; 55% yield (Method A); mp 71−72 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (m, 5H), 7.04 (s, 2H), 6.79 (s, 1H), 6.63 (d, *J* = 4.8 Hz, 2H), 4.49 (brs, 1H), 3.53 (s, 2H), 1.29 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.5, 151.1, 135.5, 129.0, 128.5, 128.3, 128.2, 123.1, 121.2, 36.6, 14.6. Mass spectrum (ESI): *m/e* (% relative intensity) 225.1 (100) $(M + H)^+$.

N-Butyl-N′-phenylbenzimidamide (**1n**).[24] White solid; 2.5 g; 65% yield (Method A); mp 100−101 °C. ^{1}H NMR (600 MHz, DMSO) δ 7.24 (d, *J* = 6.4 Hz, 3H), 7.16 (s, 2H), 6.96 (t, *J* = 6.7 Hz, 3H), 6.67 (t, *J* = 6.6 Hz, 1H), 6.46 (d, *J* = 4.4 Hz, 2H), 3.33 (s, 2H), 1.59 (s, 2H), 1.39 (d, *J* = 6.7 Hz, 2H), 0.93 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (150 MHz, DMSO) δ 157.0, 151.7, 135.2, 128.6, 128.1, 127.9, 122.7, 122.6, 120.0, 40.7, 30.6, 19.9, 13.9. Mass spectrum (ESI): *m/e* (% relative intensity) 253.1 (100) $(M + H)^+$.

N-(Cyclopropylmethyl)-N′-phenylbenzimidamide (**1o**).[8] White solid; 2.4 g; 63% yield (Method A); mp 90−91 °C. ^{1}H NMR (400 MHz, DMSO) δ 7.25 (d, *J* = 4.4 Hz, 3H), 7.18 (s, 2H), 7.05 (s, 1H), 6.97 (s, 2H), 6.68 (d, *J* = 4.4 Hz, 1H), 6.46 (d, *J* = 3.6 Hz, 2H), 3.22 (s, 2H), 1.16 (s, 1H), 0.45 (d, *J* = 4.8 Hz, 2H), 0.2529 (s, 2H). ^{13}C NMR (150 MHz, DMSO) δ 157.0, 151.7, 135.1, 128.7, 128.1, 127.9, 123.6, 122.6, 120.1, 45.3, 10.5, 3.3. Mass spectrum (ESI): *m/e* (% relative intensity) 251.1 (100) $(M + H)^+$.

N-(Cyclohexylmethyl)-N′-phenylbenzimidamide (**1p**). White solid; 3.1 g; 71% yield (Method A); mp 94−95 °C. ^{1}H NMR (600 MHz, DMSO) δ 7.24 (s, 2H), 7.16 (s, 2H), 6.96 (s, 3H), 6.66 (s, 1H), 6.44 (s, 2H), 3.35 (s, 1H), 3.19 (s, 2H), 1.81 (s, 2H), 1.70 (s, 3H), 1.64 (s, 1H), 1.20 (d, *J* = 10.7 Hz, 3H), 0.98 (s, 2H). ^{13}C NMR (150 MHz, DMSO) δ 157.1, 151.8, 135.3, 128.7, 128.6, 128.1, 127.8, 122.6, 119.9, 47.2, 36.8, 30.8, 26.2, 25.6. Mass spectrum (ESI): *m/e* (% relative intensity) 293.2 (100) $(M + H)^+$; HRMS (ESI): *m/e* calcd for $C_{20}H_{23}N_2$ $(M - H)^-$ 291.1856, found 291.1867.

N-Benzyl-N′-p-tolylbenzimidamide (**4a**).[8] White solid; 3.6 g; 80% yield (Method B); mp 126−127 °C. ^{1}H NMR (600 MHz, DMSO) δ 7.46 (brs, 1H), 7.42 (s, 2H), 7.34 (t, *J* = 7.1 Hz, 2H), 7.27 (s, 3H), 7.25−7.17 (m, 3H), 6.77 (d, *J* = 6.7 Hz, 2H), 6.34 (d, *J* = 6.4 Hz, 2H), 4.57 (s, 2H), 2.10 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 156.8, 148.7, 140.3, 135.1, 128.7, 128.7, 128.6, 128.1, 128.0, 127.1, 126.4, 122.4, 122.4, 43.9, 20.2. Mass spectrum (ESI): *m/e* (% relative intensity) 301.1 (100) $(M + H)^+$.

N-Benzyl-N′-(4-methoxyphenyl)benzimidamide (**4b**).[8] White solid; 4.2 g; 88% yield (Method B); mp 115−117 °C. ^{1}H NMR (600 MHz, DMSO) δ 7.42 (m, 3H), 7.34 (t, *J* = 7.0 Hz, 2H), 7.27 (s, 3H), 7.23 (d, *J* = 13.4 Hz, 3H), 6.56 (d, *J* = 7.5 Hz, 2H), 6.37 (d, *J* = 6.7 Hz, 2H), 4.58 (s, 2H), 3.58 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 156.9, 153.3, 144.5, 140.3, 135.2, 128.6, 128.1, 128.0, 127.2, 126.4, 123.2 (d, *J* = 8.3 Hz), 113.51, 113.46, 54.9 (d, *J* = 7.1 Hz), 43.9. Mass spectrum (ESI): *m/e* (% relative intensity) 317.1 (100) $(M + H)^+$.

N-Benzyl-N′-m-tolylbenzimidamide (**4c**).[8] White solid; 3.2 g; 72% yield (Method B); mp 106−107 °C. ^{1}H NMR (600 MHz, DMSO) δ 7.54 (brs, 1H), 7.41 (s, 2H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.31−7.18 (m, 6H), 6.83 (s, 1H), 6.51 (d, *J* = 5.1 Hz, 1H), 6.36 (d, *J* = 14.6 Hz, 1H), 6.21 (s, 1H), 4.58 (s, 2H), 2.08 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 156.7, 151.1, 148.5, 140.2, 137.1, 134.9, 128.8, 128.6, 128.1, 127.9, 127.1, 126.4, 123.3, 121.2, 119.6, 44.0, 21.0. Mass spectrum (ESI): *m/e* (% relative intensity) 301.1 (100) $(M + H)^+$.

N-Benzyl-N′-(4-chlorophenyl)benzimidamide (**4d**).[8] White solid; 4.0 g; 83% yield (Method B); mp 101−102 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (s, 2H), 7.37 (t, *J* = 6.7 Hz, 2H), 7.30 (t, *J* = 7.1 Hz, 2H), 7.27−7.18 (m, 4H), 7.01 (d, *J* = 7.1 Hz, 2H), 6.59 (d, *J* = 5.6 Hz, 2H), 4.83 (brs, 1H), 4.68 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.6, 149.5, 138.7, 134.7, 129.4, 129.1, 128.9, 128.7, 128.5, 128.4, 128.1, 127.5, 127.0, 126.4, 124.3, 46.2. Mass spectrum (ESI): *m/e* (% relative intensity) 321.1 (100) $(M + H)^+$.

N-Benzyl-N′-(4-bromophenyl)benzimidamide (**3a**).[8] White solid; 4.1 g; 75% yield (Method B); mp 105−106 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (s, 2H), 7.37 (t, *J* = 6.4 Hz, 2H), 7.33−7.28 (m, 2H), 7.25 (s, 2H), 7.22 (s, 2H), 7.15 (d, *J* = 6.6 Hz, 2H), 6.54 (s, 2H), 4.83 (brs, 1H), 4.68 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.5, 150.0, 138.7, 134.6, 132.1, 131.3, 129.5, 128.7, 128.5, 128.1, 127.5, 124.8, 114.1, 46.1. Mass spectrum (ESI): *m/e* (% relative intensity) 365.1 (100) $(M + H)^+$.

N-Benzyl-N′-(4-fluorophenyl)benzimidamide (**4f**).[8] White solid; 3.2 g; 70% yield (Method B); mp 108−109 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (s, 2H), 7.37 (t, *J* = 6.7 Hz, 2H), 7.32−7.22 (m, 6H), 6.75 (t, *J* = 7.7 Hz, 2H), 6.59 (s, 2H), 4.78 (brs, 1H), 4.68 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.1, 157.6, 146.9, 138.8, 134.9, 129.3, 128.7, 128.5, 128.4, 128.1, 127.5, 124.0, 123.9, 115.0, 114.9, 46.1. Mass spectrum (ESI): *m/e* (% relative intensity) 305.1 (100) $(M + H)^+$.

N-Benzyl-N′-(4-(trifluoromethyl)phenyl)benzimidamide (**4g**).[8] White solid; 3.8 g; 71% yield (Method B); mp 88−89 °C. ^{1}H NMR (600 MHz, DMSO) δ 7.92 (s, 1H), 7.43 (s, 2H), 7.38−7.34 (m, 2H), 7.32 (m, 5H), 7.27 (s, 3H), 6.62 (s, 2H), 4.61 (s, 2H). ^{13}C NMR (150 MHz, DMSO) δ 157.8, 155.3, 139.8, 134.1, 129.3, 128.7, 128.2, 127.2, 126.5, 125.7, 125.3, 124.0, 122.9, 120.5 (d, *J* = 32.6 Hz), 44.2. Mass spectrum (ESI): *m/e* (% relative intensity) 355.1 (100) $(M + H)^+$.

N-Benzyl-N′-(4-cyanophenyl)benzimidamide (**4h**). White solid; 2.8 g; 61% yield (Method B); mp 117−119 °C. ^{1}H NMR (600 MHz, DMSO) δ 8.05 (s, 1H), 7.41 (t, *J* = 8.1 Hz, 4H), 7.34 (dt, *J* = 19.6, 7.2 Hz, 5H), 7.25 (d, *J* = 6.6 Hz, 3H), 6.57 (d, *J* = 8.3 Hz, 2H), 4.60 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (150 MHz, DMSO) δ

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158.0, 156.4, 139.6, 133.9, 132.5 (d, J = 4.3 Hz), 129.5, 128.7, 128.2 (d, J = 4.4 Hz), 127.2, 126.6, 123.5, 123.4, 119.7, 101.7, 44.2. Mass spectrum (ESI): m/e (% relative intensity) 312.1 (100) $(M + H)^+$; HRMS (ESI): m/e calcd for $C_{21}H_{16}N_3$ $(M - H)^-$ 310.1339, found 310.1337.

*N-Benzyl-N′-(4-nitrophenyl)benzimidamide Hydrochloride (**4i**).* Yellow solid; 3.5 g; 71% yield (Method B); mp 194−195 °C. ^{1}H NMR (600 MHz, DMSO) δ 12.75 (brs, 1H), 11.06 (brs, 1H), 8.10 (d, J = 6.9 Hz, 2H), 7.59 (s, 3H), 7.53 (s, 2H), 7.50−7.40 (m, 4H), 7.37 (s, 1H), 7.27 (s, 2H), 5.09 (s, 2H). ^{13}C NMR (150 MHz, DMSO) δ 162.4, 144.6, 135.4, 132.7, 130.0, 128.9, 128.6, 128.2, 127.9, 125.8, 124.7, 124.3, 119.9, 47.6. Mass spectrum (ESI): m/e (% relative intensity) 332.1 (100) $(M + H)^+$; HRMS (ESI): m/e calcd for $C_{20}H_{16}N_3O_2$ $(M - H)^-$ 330.1237, found 330.1234.

*N-Benzyl-N′-(naphthalen-1-yl)benzimidamide (**4j**).* White solid; 3.2 g; 63% yield (Method B); mp 101−102 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.75 (s, 1H), 7.51 (s, 2H), 7.43 (s, 4H), 7.33 (s, 2H), 7.22−7.01 (m, 6H), 6.39 (s, 1H), 5.00 (s, 1H), 4.85 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.0, 147.4, 139.1, 134.2, 129.3, 128.8, 128.0, 127.9, 127.7, 127.4, 125.9, 125.7, 124.9, 124.3, 121.4, 117.0, 46.2. Mass spectrum (ESI): m/e (% relative intensity) 337.1 (100) $(M + H)^+$; HRMS (ESI): m/e calcd for $C_{24}H_{19}N_2$ $(M - H)^-$ 335.1543, found 335.1536.

*2,4-Diphenylquinazoline (**2a**).*[7d] White solid; 49.6 mg; 88% yield; mp 112−113 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.70 (d, J = 7.1 Hz, 2H), 8.19 (d, J = 6.8 Hz, 1H), 8.14 (d, J = 8.2 Hz, 1H), 7.90 (s, 3H), 7.60 (s, 3H), 7.54 (dt, J = 19.1, 9.7 Hz, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.5, 160.2, 151.8, 138.0, 137.6, 133.7, 130.6, 130.2, 130.0, 128.7, 128.6, 127.1, 127.1, 121.7. Mass spectrum (ESI): m/e (% relative intensity) 283.1 (100) $(M + H)^+$.

*2-(4-Methoxyphenyl)-4-phenylquinazoline (**2b**).*[7d] White solid; 56.8 mg; 91% yield; mp 162−163 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.65 (d, J = 8.3 Hz, 2H), 8.09 (dd, J = 15.9, 8.3 Hz, 2H), 7.91−7.81 (m, 3H), 7.57 (s, 3H), 7.48 (t, J = 7.2 Hz, 1H), 7.03 (d, J = 8.3 Hz, 2H), 3.88 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.2, 161.7, 160.0, 152.0, 137.7, 133.5, 130.8, 130.3, 130.1, 129.8, 128.9, 128.5, 126.9, 126.5, 121.3, 113.8, 55.4. Mass spectrum (ESI): m/e (% relative intensity) 313.1 (100) $(M + H)^+$.

*4-Phenyl-2-(p-tolyl)quinazoline (**2c**).*[7d] White solid; 55.6 mg; 94% yield; mp 160−161 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (d, J = 7.7 Hz, 2H), 8.15 (d, J = 8.3 Hz, 1H), 8.11 (d, J = 8.3 Hz, 1H), 7.88 (t, J = 7.6 Hz, 3H), 7.59 (s, 3H), 7.53 (t, J = 7.5 Hz, 1H), 7.33 (d, J = 7.7 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.3, 160.3, 151.9, 140.8, 137.7, 135.4, 133.5, 130.2, 129.9, 129.3, 129.0, 128.6, 128.5, 127.0, 126.8, 121.6, 21.6. Mass spectrum (ESI): m/e (% relative intensity) 297.1.1 (100) $(M + H)^+$.

*2-(4-Chlorophenyl)-4-phenylquinazoline (**2d**).*[7d] White solid; 51.2 mg; 81% yield; mp 179−181 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 (d, J = 8.0 Hz, 2H), 8.18 (d, J = 7.7 Hz, 1H), 8.14 (d, J = 8.2 Hz, 1H), 7.88−7.92 (m, 3H), 7.61 (s, 3H), 7.58 (t, J = 7.5 Hz, 1H), 7.50 (d, J = 8.0 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.5, 159.2, 151.8, 137.5, 136.8, 136.6, 133.8, 130.2, 130.1, 129.0, 128.7, 128.6, 127.3, 127.1, 121.7. Mass spectrum (ESI): m/e (% relative intensity) 317.1 (100) $(M + H)^+$.

*4-(4-Phenylquinazolin-2-yl)benzonitrile (**2e**).* White solid; 29.5 mg; 48% yield; mp 198−200 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.84 (d, J = 7.2 Hz, 2H), 8.23 (d, J = 7.0 Hz, 1H), 8.18 (d, J = 8.1 Hz, 1H), 7.96 (s, 1H), 7.89 (s, 2H), 7.82 (d, J = 7.0 Hz, 2H), 7.63 (s, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.8, 158.2, 151.7, 142.2, 137.2, 134.1, 132.4, 130.3, 130.2, 129.3, 129.2, 128.7, 128.0, 127.2, 122.0, 119.0, 113.7. Mass spectrum (ESI): m/e (% relative intensity) 308.1 (100) $(M + H)^+$; HRMS (ESI): m/e calcd for $C_{21}H_{12}N_3$ $(M - H)^-$ 306.1037, found 306.1055.

*2-(Naphthalen-1-yl)-4-phenylquinazoline (**2f**).*[7d] Colorless oil; 55.1 mg; 83% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (d, J = 8.3 Hz, 1H), 8.25 (t, J = 6.8 Hz, 2H), 8.21 (d, J = 8.3 Hz, 1H), 8.02−7.91 (m, 3H), 7.90 (d, J = 5.7 Hz, 2H), 7.67−7.48 (m, 7H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.6, 162.8, 151.6, 137.4, 136.5, 134.2, 133.9, 131.4, 130.4, 130.2, 130.1, 129.8, 129.1, 128.7, 128.5, 127.6, 127.1, 126.8, 126.1, 125.9, 125.4, 121.3. Mass spectrum (ESI): m/e (% relative intensity) 333.1 (100) $(M + H)^+$.

*2-tert-Butyl-4-phenylquinazoline (**2g**).*[8] White solid; 48.9 mg; 62% yield; mp 115−117 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (d, J = 8.1 Hz, 2H), 7.83 (t, J = 9.9 Hz, 3H), 7.56 (s, 3H), 7.51 (t, J = 7.5 Hz, 1H), 1.55 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.8, 167.5, 151.3, 137.9, 133.0, 130.3, 129.7, 128.8, 128.5, 126.7, 126.6, 120.9, 39.7, 29.7. Mass spectrum (ESI): m/e (% relative intensity) 363.1 (100) $(M + H)^+$.

*4-(4-Methoxyphenyl)-2-phenylquinazoline (**2h**).*[7d] White solid; 55.5 mg; 89% yield; mp 115−116 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.69 (d, J = 7.1 Hz, 2H), 8.16 (t, J = 6.8 Hz, 2H), 7.94−7.82 (m, 3H), 7.51 (dd, J = 14.1, 7.0 Hz, 4H), 7.11 (d, J = 8.0 Hz, 2H), 3.92 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.8, 161.3, 160.1, 151.9, 138.2, 133.5, 131.9, 130.5, 130.1, 129.0, 128.7, 128.6, 127.1, 126.9, 121.6, 114.1, 55.5. Mass spectrum (ESI): m/e (% relative intensity) 313.1 (100) $(M + H)^+$.

*4-(4-Chlorophenyl)-2-phenylquinazoline (**2i**).*[7d] White solid; 53.1 mg; 84% yield; mp 142−143 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (d, J = 6.9 Hz, 2H), 8.16 (d, J = 8.3 Hz, 1H), 8.07 (d, J = 8.3 Hz, 1H), 7.89 (t, J = 7.4 Hz, 1H), 7.84 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8.2 Hz, 2H), 7.56−7.48 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.1, 160.2, 152.0, 138.0, 136.3, 136.1, 133.8, 131.6, 130.7, 129.3, 128.9, 128.7, 128.6, 127.3, 126.6, 121.5. Mass spectrum (ESI): m/e (% relative intensity) 317.1 (100) $(M + H)^+$.

*2-Phenyl-4-(4-(trifluoromethyl)phenyl)quinazoline (**2j**).* White solid; 59.5 mg; 85% yield; mp 114−115 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (d, J = 6.6 Hz, 2H), 8.17 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 8.3 Hz, 1H), 7.98 (d, J = 7.6 Hz, 2H), 7.90 (t, J = 7.6 Hz, 1H), 7.86 (d, J = 7.7 Hz, 2H), 7.58−7.47 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.9, 160.2, 152.0, 141.1, 137.8, 133.9, 131.8 (d, J = 32.5 Hz), 130.8, 130.5, 129.3, 128.6 (d, J = 4.5 Hz), 127.4, 126.4, 125.5 (d, J = 4.5 Hz), 121.4. Mass spectrum (ESI): m/e (% relative intensity) 351.1 (100) $(M + H)^+$; HRMS (ESI): m/e calcd for $C_{21}H_{12}F_3N_2$ $(M - H)^-$ 349.0947, found 349.0936.

*4-(3-Nitrophenyl)-2-phenylquinazoline (**2k**).*[7c] White solid; 59.5 mg; 91% yield; mp 180−182 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.68 (d, J = 6.9 Hz, 2H), 8.46 (d, J = 7.8 Hz, 1H), 8.26−8.15 (m, 2H), 8.03 (d, J = 8.3 Hz, 1H), 7.95 (t, J = 7.5 Hz, 1H), 7.80 (t, J = 7.8 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.54 (d, J = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.7, 160.3, 152.1, 148.4, 139.3, 137.6, 136.1, 134.2, 130.9, 129.8, 129.5, 128.7, 128.7, 127.8, 125.9, 125.1, 124.7, 121.2. Mass spectrum (ESI): m/e (% relative intensity) 328.1 (100) $(M + H)^+$.

*2-Phenyl-4-propylquinazoline (**2n**).*[7d] White solid; 17.9 mg; 36% yield; mp 60−62 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.64 (d, J = 7.2 Hz, 2H), 8.11 (dd, J = 15.8, 8.2 Hz, 2H), 7.85 (t, J = 7.3 Hz, 1H), 7.54 (ddd, J = 22.3, 14.9, 6.9 Hz, 4H), 3.32 (t, J = 7.4 Hz, 2H), 2.03 (dd, J = 14.5, 7.2 Hz, 2H), 1.12 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.4, 159.0, 149.5, 137.3, 132.4, 129.4, 128.3, 127.6, 127.5, 125.7, 123.6, 121.6, 35.5, 20.9, 13.3. Mass spectrum (ESI): m/e (% relative intensity) 249.1 (100) $(M + H)^+$.

*4-Cyclopropyl-2-phenylquinazoline (**2o**).*[23] White solid; 20.1 mg; 41% yield; mp 75−77 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (d, J = 7.3 Hz, 2H), 8.32 (d, J = 8.3 Hz, 1H), 8.15 (s, 1H), 7.87 (t, J = 7.6 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.57−7.45 (m, 3H), 2.89−2.78 (m, 1H), 1.57 (s, 2H), 1.29 (d, J = 4.8 Hz, 2H). Mass spectrum (ESI): m/e (% relative intensity) 247.1 (100) $(M + H)^+$.

*4-Cyclohexyl-2-phenylquinazoline (**2p**).*[7d] White solid; 17.3 mg; 30% yield; mp 94−95 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (d, J = 7.3 Hz, 2H), 8.16 (d, J = 8.2 Hz, 1H), 8.12 (d, J = 7.7 Hz, 1H), 7.84 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.55−7.47 (m, 3H), 3.58 (t, J = 11.1 Hz, 1H), 2.07−1.91 (m, 6H), 1.85 (d, J = 12.2 Hz, 1H), 1.62−1.51 (m, 2H), 1.48−1.38 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.0, 159.9, 150.7, 138.4, 133.2, 130.4, 129.4, 128.6, 128.5, 126.6, 124.1, 121.7, 41.5, 32.1, 26.5, 26.1. Mass spectrum (ESI): m/e (% relative intensity) 289.2 (100) $(M + H)^+$.

*6-Methyl-2,4-diphenylquinazoline (**5a**).*[8] White solid; 54.5 mg; 92% yield; mp 167−170 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (d, J = 7.5 Hz, 2H), 8.05 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 8.0 Hz, 3H),

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7.70 (d, J = 8.5 Hz, 1H), 7.59 (d, J = 5.5 Hz, 3H), 7.55−7.44 (m, 3H), 2.49 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.5, 159.5, 150.4, 138.2, 137.8, 137.2, 135.8, 130.3, 130.1, 129.8, 128.8, 128.5, 125.6, 121.6, 21.9. Mass spectrum (ESI): m/e (% relative intensity) 297.1 (100) $(M + H)^+$.

*6-Methoxy-2,4-diphenylquinazoline (**5b**)*.[8] White solid; 59.9 mg; 96% yield; mp 142−144 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.65 (d, J = 7.3 Hz, 2H), 8.08 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 6.7 Hz, 2H), 7.60 (d, J = 7.1 Hz, 3H), 7.58−7.43 (m, 4H), 7.39 (s, 1H), 3.85 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 158.6, 158.1, 148.1, 138.3, 138.0, 130.6, 130.2, 129.9, 129.8, 128.7, 128.5, 128.3, 126.3, 122.5, 104.3, 55.7. Mass spectrum (ESI): m/e (% relative intensity) 313.1 (100) $(M + H)^+$.

*7-Methyl-2,4-diphenylquinazoline (**5c**)*.[8] White solid; 50.9 mg; 86% yield ; mp 135−140 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (d, J = 7.5 Hz, 2H), 7.99 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 6.5 Hz, 2H), 7.50 (q, J = 8.6, 7.1 Hz, 8H), 2.58 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.8, 160.3, 153.1, 152.2, 144.6, 138.3, 137.8, 137.8, 136.2, 133.2, 130.5, 130.23, 130.19, 129.9, 129.3, 129.1, 129.0, 128.7, 128.5, 128.3, 128.0, 127.5, 126.7, 119.9, 23.9, 22.2. Mass spectrum (ESI): m/e (% relative intensity) 297.1 (100) $(M + H)^+$.

*6-Chloro-2,4-diphenylquinazoline (**5d**)*.[8] White solid; 55.0 mg; 87% yield; mp 194−195 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (d, J = 6.6 Hz, 2H), 8.11 (d, J = 13.6 Hz, 2H), 7.87 (d, J = 3.4 Hz, 2H), 7.82 (d, J = 8.7 Hz, 1H), 7.62 (s, 3H), 7.53 (d, J = 6.9 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.6, 160.4, 150.4, 137.6, 137.0, 134.6, 132.6, 130.81, 130.79, 130.3, 130.1, 128.8, 128.7, 128.6, 125.8, 122.2. Mass spectrum (ESI): m/e (% relative intensity) 317.1 (100) $(M + H)^+$.

*6-Bromo-2,4-diphenylquinazoline (**5e**)*.[8] White solid; 62.6 mg; 87% yield; mp 203−205 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (d, J = 7.0 Hz, 2H), 8.26 (s, 1H), 8.03 (d, J = 9.0 Hz, 1H)), 7.94 (d, J = 8.4 Hz, 1H)), 7.86 (d, J = 3.6 Hz, 2H), 7.62 (s, 3H), 7.52 (d, J = 6.5 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.5, 160.5, 150.7, 137.1, 137.8, 137.1, 131.0, 130.9, 130.3, 130.1, 129.1, 128.8, 128.7, 128.6, 122.7, 120.7. Mass spectrum (ESI): m/e (% relative intensity) 361.1 (100) $(M + H)^+$.

*6-Fluoro-2,4-diphenylquinazoline (**5f**)*.[8] White solid; 54.0 mg; 90% yield; mp 173−174 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (d, J = 7.2 Hz, 2H), 8.20−8.12 (m, 1H), 7.87 (d, J = 3.3 Hz, 2H), 7.74 (d, J = 8.9 Hz, 1H), 7.65 (t, J = 8.4 Hz, 1H), 7.60 (s, 3H), 7.51 (t, J = 8.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.8 (d, J = 5.5 Hz), 161.2, 159.9 (d, J = 2.5 Hz), 159.5, 149.1, 137.8, 137.2, 131.8 (d, J = 8.6 Hz), 130.6, 130.2, 129.9, 128.7, 128.6 (d, J = 5.8 Hz), 124.0, 123.8, 122.1 (d, J = 9.0 Hz), 110.5, 110.3. Mass spectrum (ESI): m/e (% relative intensity) 301.1 (100) $(M + H)^+$.

*2,4-Diphenyl-6-(trifluoromethyl)quinazoline (**5g**)*.[8] White solid; 44.8 mg; 64% yield; mp 145−147 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.72 (d, J = 3.1 Hz, 2H), 8.43 (s, 1H), 8.27 (d, J = 8.8 Hz, 1H), 8.05 (d, J = 8.3 Hz, 1H), 7.89 (s, 2H), 7.65 (s, 3H), 7.54 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.4, 161.9, 153.2, 137.4, 136.8, 131.7, 131.3, 131.0, 130.6, 130.5, 130.2, 129.3 (d, J = 2.9 Hz), 129.0, 128.9, 128.7, 125.1 (d, J = 4.4 Hz), 124.6, 122.8, 120.7. Mass spectrum (ESI): m/e (% relative intensity) 351.1 (100) $(M + H)^+$.

*2,4-Diphenylquinazoline-6-carbonitrile (**5h**)*. White solid; 26.8 mg; 44% yield; mp 224−225 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (s, 2H), 8.52 (s, 1H), 8.29 (d, J = 6.2 Hz, 1H), 8.03 (d, J = 5.0 Hz, 1H), 7.88 (d, J = 3.9 Hz, 2H), 7.67 (s, 3H), 7.57 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.1, 162.4, 153.2, 137.1, 136.4, 134.1, 133.7, 131.6, 130.9, 130.8, 130.2, 129.2, 129.0, 128.8, 121.2, 118.3, 110.4. Mass spectrum (ESI): m/e (% relative intensity) 330.1 (100) $(M+Na)^+$; HRMS (ESI): m/e calcd for $C_{21}H_{12}N_3$ $(M - H)^-$ 306.1037, found 306.1046.

*6-Nitro-2,4-diphenylquinazoline (**5i**)*.[7d] Yellow solid; 24.2 mg; 37% yield; mp 245−247 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.07 (s, 1H), 8.75 (d, J = 4.5 Hz, 2H), 8.66 (d, J = 9.0 Hz, 1H), 8.31 (d, J = 9.1 Hz, 1H), 7.94−7.89 (m, 2H), 7.68 (d, J = 5.0 Hz, 3H), 7.57 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.6, 162.8, 154.3, 145.5, 137.0, 136.4, 131.8, 131.1, 130.9, 130.3, 129.3, 129.1, 128.8, 127.1, 124.3, 120.5. Mass spectrum (ESI): m/e (% relative intensity) 328.1 (100) $(M + H)^+$.

*2,4-Diphenylbenzo[h]quinazoline (**5j**)*.[7d] White solid; 54.4 mg; 82% yield; mp 152−153 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.53 (d, J = 7.1 Hz, 1H), 8.84 (d, J = 7.6 Hz, 2H), 7.95 (d, J = 9.0 Hz, 1H), 7.91 (d, J = 6.6 Hz, 3H), 7.81−7.79 (m, 2H), 7.76 (d, J = 9.1 Hz, 1H), 7.52−7.61 (m, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 160.1, 151.9, 138.4, 138.0, 135.1, 130.7, 130.5, 130.3, 130.1, 129.7, 128.7, 128.5, 127.8, 127.8, 127.3, 125.3, 122.8, 119.2. Mass spectrum (ESI): m/e (% relative intensity) 333.1 (100) $(M + H)^+$.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02366.

NMR spectra of the compounds (PDF)

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Notes

The authors declare no competing financial interest.

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